The Economic Consequences of Delay in Radiotherapy: An Example in Early Breast Cancer

by
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Abstract

Waiting times for cancer radiotherapy have been a concern in Ontario for the past 20 years. A recent review of the clinical trials literature shows that waiting is associated with an increased risk of recurrence. Recurrence and the downstream effects thereof (metastatic disease, death) are expensive to treat. If waiting times can be reduced, the health care system could experience a reduced level of expenditure on recurrence. The magnitude and nature of such reduced expenditures is not known in the scientific literature.

This study proposed and described a methodology for estimating the net benefit of reduced waiting for radiotherapy. A cost-benefit analysis was chosen, in which costs were measured as the value of resources required to increase the capacity of a cancer centre, and benefits were measured as the value of averted recurrence, metastatic disease and death due to waiting. The association between increased capacity and reduced waiting was explored in a computer simulation model. Benefits were calculated using a Markov chain model (a mathematical model that simulates patient movement between different health states based on underlying probabilities). Costs and benefits for various lengths of waiting were combined into a summary measure: the Incremental Net Present Value of increasing capacity in a cancer centre.

A simplified population of postmenopausal (55 years and older) early breast cancer patients who receive adjuvant radiotherapy after breast-conserving surgery was used to illustrate this methodology. Accordingly, a hypothetical example in which a cancer centre treating these breast cancer patients only was presented to illustrate the methodology developed here. Markov modeling was used to compute averted treatment costs due to a
decrease in waiting for this population. The costs of operating a cancer centre were calculated based on actual operations data from the Cancer Centre of Southeastern Ontario.

This work provides a useful framework upon which subsequent investigations of this type can be built. The costs of operating a cancer centre were updated to reflect contemporary practice. Furthermore, this study modernizes the scientific literature regarding the medical care costs of local recurrence. It is our hope that the method proposed herein will be used in subsequent explorations of the issue of the economics of waiting.
Co-Authorship Statement

Ian Cromwell was responsible for the formation of the research question and methodology. He conducted all data analysis and developed the simulation model used in the capacity and waiting sections, as well as the Markov chain model. He was primarily responsible for the production (writing, analysis, etc.) of this thesis. He wrote the original draft of the manuscript incorporating all editions from the other authors.

Dr. Ana Johnson from the Division of Cancer Care and Epidemiology, Centre for Health Services and Policy Research, ICES-Queen’s Health Services Research Facility, and the Department of Community Health and Epidemiology at Queen’s University provided crucial guidance and direction in the formation of the research question and methodology, the conduct of data analysis, and editing the manuscript.

Alastair Lamb from the Department of Oncology at the Cancer Centre of Southeastern Ontario provided data from the cancer centre, and provided guidance and input for the costing section, as well as input on editing of the manuscript.

Dr. Hugh Walker from the Division of Cancer Care Epidemiology, and the Department of Community Health and Epidemiology at Queen’s University provided guidance on the development of the simulation model and input on the research methodology, as well as editing the manuscript.

Dr. William Mackillop from the Division of Cancer Care Epidemiology and the Department of Community Health and Epidemiology at Queen’s University provided crucial guidance on the research question, as well as guidance on the methodology and editing the manuscript.
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List of Abbreviations

BCR – Benefit-to-Cost Ratio
CBA – Cost-Benefit Analysis
CCO – Cancer Care Ontario
CCSEO – Cancer Centre of Southeastern Ontario
CT – Computed Tomography
FIFO – First-in-First-out
INPV – Incremental Net Present Value
Gy – Gray (unit of radiation)
KGH – Kingston General Hospital
LR – Local Recurrence
Mets – Metastatic Disease
MRI – Magnetic Resonance Imaging
NED – No Evidence of Disease
NPV – Net Present Value
PV – Present Value
WTA – Waiting Times Alliance
Chapter 1 – Introduction

The goal of this study is to propose and describe a methodology for estimating the economic consequences of reducing delay in post-operative radiotherapy. Specifically, the study addresses the following question: How could one determine the additional cost of increasing capacity of a cancer centre to reduce waiting for radiotherapy? This question is explored through a cost-benefit analysis, in which the cost of increasing the capacity of a cancer centre is compared to the benefit of averting costs associated with treatment of cancer recurrence as a result of a decrease in waiting time. As an illustrative example of the methodology, a population of early breast-cancer patients is examined to show the economic consequences of changes in a hypothetical “breast cancer only” centre’s capacity. The hypothetical cancer centre is created based on data from the Cancer Care of Southeastern Ontario, in Ontario, Canada. The cancer site and cancer centre are chosen because of the availability of data (i.e., risk of recurrence) and the relative homogeneity of treating this population (compared to other cancer sites).

Chapter 1.1 – Objectives

The goal of this study is to present a methodology for estimating the economic consequences of reducing delay in radiotherapy. The methodology presented is a cost-benefit analysis, in which the costs – increasing the capacity of a cancer centre – is compared to benefits – averted treatment costs associated with a decrease in waiting time. In order to conduct this type of economic analysis, a number of objectives are met.

1. To estimate the amount of capacity increase required to control waiting times at relevant lengths.

2. To estimate the cost of increasing the capacity of a centre to appropriate levels.
3. To estimate the economic benefit measured by averted treatment costs as a result of reduced waiting for radiotherapy.

4. To calculate the Net Present Value, a measure which compares the costs and benefits presented above.

**Chapter 1.2 – Thesis Outline**

This thesis addresses the above objectives. The next chapter presents findings from relevant scientific literature, as they pertain to the research question. Chapter 3 describes the study design and methods used to address each objective. Chapter 4 provides an in-depth description of the results of the analysis, including sensitivity analyses. In Chapter 5, a manuscript detailing the cost-benefit analysis, prepared for the International Journal of Radiation Oncology, Biology and Physics is included. Finally, Chapters 6 and 7 present discussion (including ethical considerations, strengths and limitations of the design) and conclusion, respectively.
Chapter 2 – Literature Review

Chapter 2.1 – Cost-Benefit Analysis

In this study, a cost-benefit methodology is presented. Cost-benefit analysis is a full economic evaluation that allows for the comparison of the costs of adopting a program or policy approach with the benefits experienced due to the adoption (1). Both costs and benefits are expressed as monetary amounts. This approach stands out as a method for economic evaluation because it allows for direct comparisons of two or more policy strategies that are likely to have positive (beneficial) and negative (costly) outcomes (2), for example, increasing the capacity of a cancer centre. It is an appropriate methodology when there is concern about economic efficiency. Results from this type of analysis can provide policy makers with a clear summary measure of the economic consequence of a policy change (i.e., returns on investing in federal/provincial resources).

Cost-benefit Analysis has its theoretical roots in the discipline of economics, termed welfare economics (2). Welfare economics is the study of changes in the well-being, or welfare, of individuals and society. Changes in welfare occur due to shifts in decisions regarding the allocation of resources to produce, distribute, and consume goods and services. With the evolution of welfare economics, the method has the potential to identify who gains and who pays, as well as the amount of the gain or loss (1). Cost-benefit analysis dates back to the seventeenth century when there were efforts to quantify health benefits and the value of life in monetary terms (2). It was first proposed as a technique to assist public policy decision makers in 1844 (2). More recently, 1966 marked the first use of this approach specifically in health research (2).
Cost-benefit analysis is particularly useful when evaluating health programs with a preventive focus. Examples of such programs include health counseling services, such as Brent’s investigation of the efficiency of counseling for couples at risk of HIV in Tanzania (3), or Le Goff-Pronost’s evaluation of the use of telemedicine networks in Montreal, QC (4). Both studies identified costs as the value of resources required to implement a program, and benefits as the value of avoided downstream use of health care services.

Recently, cost-benefit approaches have been used to examine vaccination programs for influenza (5), pertussis (6), chicken pox (7), and hepatitis B (8). These studies investigated the amount of nursing/staff time required, the cost of vaccines, facility costs, and other relevant economic inputs, and compared them to the avoided risk of developing the diseases in question, to determine if the initial investment would see a beneficial return in health care dollars.

In addition to interventions with a direct disease-prevention application, cost-benefit is particularly useful in evaluating economic issues for interventions with a wide range of potential health outcomes, such as midwifery education and training (9) and smoking reduction programs (10). In these studies, the costs of administrating and implementing the programs of interest were measured and compared to the value of avoided perinatal and neonatal complications, and smoking-related diseases (lung cancer, heart disease, other respiratory disease). Because the populations under study were large, cost-benefit was expressed in subgroups as well as for society as a whole.

This approach has also been used in programs designed to prevent the progression of disease, such as infection prevention in hemodialysis patients (11), methadone treatment...
(12), and the safe injection facility in Vancouver, BC (13). These studies used mathematical modeling and population-level drug or treatment usage rates to determine the benefit of avoided life lost and drug-related morbidity, and compared those to the costs of implementing and operating those programs.

This type of analysis differs from other commonly used economic analysis techniques – such as cost-effectiveness, in which the incremental cost of a health program is compared to the incremental units of a relevant health outcome (e.g., life-years gained), or cost-utility, where the incremental cost is compared to changes in quality-adjusted measures (e.g., quality-adjusted life years). Cost-benefit analysis is distinct in that it allows the combination of several different kinds of benefits into one summary measure, rather than expressing a cost per health-outcome (1). This summary measure is usually presented as the Net Present Value, which identifies the incremental value of expenditure and benefit (i.e., benefits minus costs). It can also be presented as a Benefit-to-Cost ratio, in which the value of benefits is divided by the value of costs.

Chapter 2.2 - Waiting Lists

Regional cancer centres are operated by hospitals, with standards and guidelines provided by Cancer Care Ontario. Radiotherapy clinics in Ontario plan their capacity to meet the average expected number of new cancer patients in the year, based on population risk factors (age, need for radiotherapy, treatment modality) and available resources. The system therefore does not make allowances for periods of time when the number of new patients is greater than average. While the expected mean number of patients can be estimated, the actual number of individuals coming into centres fluctuates from week to week. During certain weeks, the average number of incoming patients is
greater than the number of spaces available at cancer centres. Those patients for whom no slots are free are moved to queues and must wait for a space to become available. In a system like Ontario’s, which is set up to treat the average annual capacity, waiting times are an inevitable outcome as the average demand fluctuates (14). Waiting lists lengthen during time periods when demand exceeds capacity, which occurs randomly as patients are diagnosed and referred for radiotherapy (14,15). Currently, 54.6% of breast cancer patients in Ontario receive radiation therapy within the target length of time (16).

Building additional (above average) capacity into a cancer centre’s operation would allow the center to reduce waiting by absorbing some of the excess workload during periods of higher-than-average demand.

Simulation modeling, using computer software to approximate real-world phenomena, has been used in the literature to describe the relationship between system capacity and waiting time, though not explicitly for cancer. Such models have been used recently to simulate joint replacement therapy clinics (17), general surgery departments (18), and mammography clinics (19). One example of simulation modeling software is iThink™, published by iSee™ Systems (iSee Systems, Hanover, NH, USA). This software, designed to explore system dynamics, has been used to simulate patients receiving care for end-stage renal disease (20), from diagnosis through treatment to death.

Munro and colleagues used a different kind of mathematical modeling to show that waiting queues for cancer radiotherapy were a product of system design, and not an unavoidable random phenomenon (15). Based on the findings of this study, Thomas and colleagues constructed a Poisson-distributed statistical model of patients waiting to receive cancer radiotherapy based on a Monte Carlo simulation technique (14). The
model was limited in that it considered only a single type of waiting (failing to distinguish between waiting for an oncologist and waiting for treatment, two different phenomena), and provided no empirical evidence for its choice of the Poisson distribution. In this model, the authors showed that incorporating excess capacity within a system could control the length of waiting lists. If a cancer centre operates at above-average capacity, waiting lists for care can be controlled at a fixed length.

**Chapter 2.3 – Costs of Operating a Cancer Centre**

Increasing the capacity of a cancer centre is one potential method to reduce waiting lists, but this increased capacity comes with a monetary cost. Cancer centres are staffed by radiation oncologists, nurses, physicists, radiation therapists, and various support and maintenance staff (21,22). Radiotherapy for most cancers is typically delivered on an outpatient basis, meaning that patients arrive at the cancer centre for treatment, but do not spend nights there (23). The treatment of cancer requires the utilization of the resources (staffing, equipment), as well as overhead costs associated with the operation of the facility (i.e., utilities, administrative staff, overhead costs).

In 1999, Earle and colleagues published a paper in which they identified the cost of operating a cancer centre, using the budget for the cancer centre at the Ottawa General Hospital. The study collected budgetary data from the hospital on staffing, equipment, supplies and other departmental costs (overhead, maintenance, services, administration, etc.). A step-down method was used to allocate hospital expenditures to the radiotherapy program specifically. When the total costs were divided by the number of fractions delivered over the period of the analysis, the resulting per-fraction cost was

* All costs adjusted to 2008 Canadian dollars according to Consumer Price Index (http://www.bankofcanada.ca/en/rates/inflation_calc.html)
approximately $170 (24). It is worth noting that staffing costs represented nearly 70% of overall costs, suggesting that changes in staffing levels are likely to have noticeable effects on the costs of treatment. The authors used a “top-down” costing approach, meaning they used centre-level data and broke it down mathematically to a per-patient level, rather than a “bottom-up” approach in which individual-level resource usage (e.g., time spent per patient by health care professionals, machine time for a single patient, supplies used in a single case, etc.) is used to estimate costs at the system level. Each of these approaches has its limitations – bottom-up costing fails to account for time not spent explicitly on patient care, while top-down costing necessarily assumes that all patients require an equal level of resources, which may not be true for some cases.

Around the same time, a research team led by Dunscombe analyzed the effect that centre size had on per-patient operation costs. Using data from the Northeastern Ontario Regional Cancer Centre and a spreadsheet-based economic model, the group determined that per-patient radiotherapy costs were greater in a facility treating fewer than 1600 patients per year than in a facility treating more than that amount, but did not appreciably increase above this threshold (25). This finding suggests that past a certain point, the majority of radiotherapy costs consists primarily of the addition of new labour rather new capital.

Leighl and colleagues estimated the cost of palliative radiotherapy for non-small-cell lung cancer alongside a clinical trial. Based on reviewing the medical records of patients in the trial who had received radiotherapy, the per-fraction cost of treatment was determined to be approximately CAN $132 (26). These patients were treated with palliative, not curative, intent.
Since the above studies were conducted, linear accelerators have replaced cobalt machines as standard practice, and computed tomography has replaced X-ray and fluoroscopy as a simulation methodology (21). A recent review of the literature has attempted to unify the disparate findings on the cost of radiotherapy across the world (27). Resources were classified as process (staff and materials), clinical infrastructure (equipment costs) and supporting infrastructure (all non-treatment and non-equipment costs, i.e., building and land expenditures, administration costs). In this analysis, process resources represented the majority (54%) of expenditure for radiotherapy. The study combined resource allocations and costs from several different countries, with several different health care systems. Comparisons of this type are difficult, since different countries value health care resources differently.

Other studies have been conducted on the cost of administering radiotherapy. Goddard and Hutton calculated the resources and costs associated with administering radiotherapy, including personnel and instrumentation costs, based on data from Britain’s National Health Service (28). In a follow-up to this study, Morris, Goddard, Coyle and Drummond described the methods by which costs for radiotherapy can be calculated, based on the Continuous Hyperfractionated Accelerated RadioTherapy (CHART) Trial (29). The authors concluded that clinical trials alone cannot provide adequate information for economic evaluations (29). Suh and colleagues used a similar method to calculate the costs of different schedules of radiotherapy. A total dose of radiotherapy treatment is divided up into a number of smaller amounts, called “fractions”. A number of different schedules of treatment – higher dose, fewer fractions, lower dose, more fractions – were analyzed in a cost-minimization study. Treatment costs varied among the various
schedules, giving a clear example of how changes in practice can have considerable impact on the cost of providing health care (30).

**Chapter 2.4 – Benefits: Averted Treatment Costs Due to Waiting**

In order to estimate cancer treatment costs, in the absence of historical records, a Markov chain model can be used to estimate benefits. Markov modeling is a statistical procedure in which hypothetical cohorts of patients move between a number of mutually exclusive states (in this case, health states) according to a randomly-generated probability centered around the likelihood of occurrence, or the *transition probability*. The transitions occur over a number of time periods (cycles). Markov models, named after their inventor Andrei Markov, are limited in their applicability by the “Markov Assumption”: the model does not “remember” where patients would have been previously in the model, and treats all members of a state equally in each cycle. As such, the models assume that patient history is not relevant to a given transition. Recent advances in computing strength and sophistication have enabled scientists to create Markov models that are able to account for and bypass this assumption (1).

In addition to modeling a cohort of patients moving through treatment scenarios, Markov chains can simulate the experience of a single patient at a time, in a process called *microsimulation*. Microsimulation is used almost exclusively in contemporary analyses, due to the increased processing ability of computers compared to those machines available when this type of modeling first reached prominence. Markov modeling can be, for all intents and purposes, considered synonymous with microsimulation.
Markov modeling was first used in health care decision-making as early as 1976, when Liotta and colleagues proposed a stochastic (patient-level) model for the formation of metastatic disease from a solid tumour (31). In 1977, a cost-effectiveness (although termed ‘cost-benefit’) analysis using a Markov model was conducted by Cretin to evaluate screening for prevention of myocardial infarction (32).

Because the model simulates patient movement over a period of time, it is useful for accounting for survival and disease progression over a period of years. For example, both Kodell and Myers used Markov models to examine the association over time between disease characteristics and death from cancer (33,34). Kay used this methodology to assess the association between number of intermediate disease markers and death from cancer using survival data (35). Cowen described the natural history of prostate cancer through a Markov chain model (36), while Esik modeled survival in thyroid cancer (37).

Recently, Markov chains have been commonly used in cost-effectiveness analyses because of their ability to model both costs and life-years gained over a period of time when observational data are lacking for the entire period of interest. Van den Brink, Konski, and Krzyzanowska examined the cost-effectiveness (and/or cost-utility) of radiotherapy treatment for rectal cancer (38), prostate cancer (39) and pancreatic cancer (40), respectively. Each of these studies used Markov models to simulate patient movement between health states over time.

Chapter 2.5 – Illustrative Example: Breast Cancer and Radiotherapy

Breast cancer is the most common cancer among Canadian women, with an age-adjusted incidence rate of 103 new cases per 100,000 population per year. It is estimated to kill 5300 Canadians in 2008, and is the most common cause of cancer death in women
under 50 (41). It is the second-most common cause of all-cancer mortality in Canadian women, behind lung cancer (41). In Ontario, 5900 new breast cancer cases were diagnosed in 2008, and an estimated 2000 women died (42). Ontario also had the highest age-adjusted breast cancer incidence rate in Canada, equal to 111 per 100 000 population per year (41). Due to the high incidence of this disease, it is important to have a treatment approach that is both contemporary and comprehensive.

Patients diagnosed with breast cancer in Ontario have the option of receiving either a mastectomy (removal of the entire affected breast), or breast-conserving therapy (removal of the tumour followed by radiation therapy). Radiation is applied to the boundaries of the tumour area to destroy any residual cancer cells that would not have been removed during surgery (43). Patients with a primary tumour smaller than 5 cm, who are not pregnant, and have not received radiation previously are eligible to receive post-operative radiation, but may elect to receive mastectomy (43).

The Early Breast Clinical Trialists’ Collaborative Group conducts regular systematic reviews of the clinical trials literature. The most recently published review found breast-conserving therapy to be as effective as mastectomy in the treatment of early breast cancer (stage I/II with no evidence of lymph node involvement, or T1N0M0/T2N0M0) (44). Radiotherapy did not significantly reduce the risk of all-cause mortality, but cancer-specific mortality was lower in patients receiving radiation than in those receiving surgery alone (44). The authors hypothesized that radiation of cardiac tissue was causing non-cancer deaths, which accounted for this phenomenon (44). While radiotherapy was not found to reduce mortality, the review noted that it was highly effective in reducing ten-year rates of local recurrence – the re-emergence of cancer in the same location after
medical intervention (8.8% recurrence rate compared to 27.2% in patients not receiving radiotherapy) (44). The review also found a reduction in overall recurrence, including distal (cancer appearing in other tissues, also known as metastatic) and contralateral (cancer appearing in the opposite breast from the first incidence of disease) recurrence (44). These effects were seen across different age, stage, dose and tumour site groups (44). Because these studies included patients from cohorts that were treated many years ago, this review likely overestimates the risk of a person treated with today’s technology and methods. As is the case with any meta-analysis of clinical trials, the population observed in these trials cannot necessarily be generalized to all breast cancer patients, as the rigid exclusion criteria removes a number of patients with comorbid illness. It is likely that current practice and outcomes are different than those described in the study.

Radiotherapy is a commonly-practiced therapy regimen following first-line surgery (45). Tumour cells are more sensitive to radiation than healthy cells, so exposing these cells to low doses of radiation (expressed in Grays [Gy]) results in their destruction (28). Radiation is commonly delivered externally (as two intersecting tangential fields from a linear accelerator) as a total dose of 42.5 Gy in 16 fractions (45). Treatment commonly lasts three weeks. In some systems (in the United States, for example), the regimen of treatment is 50 Gy in 25 fractions (45). Whelan and colleagues investigated a cohort of women who had received either the 16 fraction or the 25 fraction dose (46). Ten-year results showed that both regimens deliver equal tumour control, with identical adverse effects (46).

A review of clinical trials conducted by Cancer Care Ontario concluded that radiation should be administered as soon after surgery as wound healing permits (45). This time
window is usually between 3 and 6 weeks (43) following surgery, with a maximum of 12 weeks recommended in the review. However, patients do not always receive treatment as soon as they are ready, and are placed on waiting lists.

Chapter 2.5A - Waiting Lists for Breast Cancer

Waiting can occur at various points in the health care system. Once a patient suspects she has breast cancer, she may visit her general practitioner. Following the time required to image and diagnose a case of breast cancer, the patient may wait for a surgical appointment to remove the tumour. Following surgery, she must wait three to six weeks for the surgical wounds to heal before she can be referred for radiotherapy (45).

In addition to the above types of waiting, there is waiting that occurs that is specific to a cancer centre and radiotherapy clinic. First, a patient may have to wait to be assessed for radiotherapy following her referral after surgery. Second, after being assessed and having a treatment plan created, the patient may have to wait for a space to become available on a radiation treatment machine. Cancer Care Ontario sets an acceptable benchmark of four weeks to wait from referral to treatment (47). Currently, 54.6% of breast cancer patients in Ontario receive radiation therapy within the target length of time (16).

Chapter 2.5B – Economic Evaluations of Breast Cancer Radiotherapy*

This section summarizes the literature of costs of breast cancer radiotherapy and Markov modeling (breast cancer). Several studies have examined the cost-outcome implications of radiotherapy delivered after mastectomy. Marks and colleagues used a Markov modeling approach to determine the cost-effectiveness of post-mastectomy

* All costs adjusted to 2008 Canadian dollars according to Consumer Price Index (http://www.bankofcanada.ca/en/rates/inflation_calc.html)
radiotherapy in 1999, using literature-published outcome data and charges at the Duke University medical centre. Based on an estimated treatment cost of approximately CAN $25,000 (converted from US dollars), the cost-utility of radiotherapy was $328,549 per quality-adjusted life year (QALY). QALYs are an outcome measure used primarily in cost-utility studies, in which the expected life years gained are weighted according to the quality of life of patients in each group under comparison. Marks suggested that the large cost-to-outcome ratio was due to the negligible effect that radiation had on overall survival in postmastectomy patients; when survival was increased to 6%, there was a corresponding 10-fold reduction in the cost/QALY (48). Around the same time in Canada, Dunscombe (49) and Samant (50) conducted analyses of patients treated with post-mastectomy radiotherapy using a model of a treatment centre serving 1600 patients per year, staffed according to Blue Book recommendations and based on budgetary information from the Northeastern Ontario Regional Cancer Centre. A mathematical model similar to a Markov chain was used to determine life-years gained. These studies estimated the cost of post-mastectomy radiotherapy for breast cancer at around $8000, and the corresponding cost-effectiveness and cost-utility at $22,400 per life year gained and $24,900 per quality-adjusted life year gained, respectively.

While the above studies have focused on external-beam whole-breast electron radiotherapy, there have been studies conducted on other types of radiation treatment. A Belgian study investigated the cost-benefit of supraclavicular lymph node radiotherapy (51). When compared to programs that did not include radiotherapy, the treatment dominated (cost less and saved more years of life). Another study evaluated proton radiotherapy in a hypothetical cohort of women with left-sided breast cancer (52). The
authors determined that the cost-utility ratio was $103,307/QALY (converted from 2002 EUR), determined using a Markov model. This value would be smaller in a cohort with a low risk of heart disease.

More recently, Sher and colleagues developed a Markov model comparing whole-breast to partial-breast radiation in early stage breast cancer patients (53,54). The study considered two populations of breast cancer patients – those who received radiation to the entire affected breast, and those who received treatment targeted to the tumour bed only. The study found that external partial-breast radiation was more cost-effective than whole-breast radiation or MammoSite partial-breast radiation, over a variety of assumptions and values of society’s willingness to pay for treatment.

Table 2.4.1 summarizes the findings of these studies, including the patient populations compared in the analysis, as well as the outcome measures.
Table 2.4.1 – Summary of Cost/Outcome Studies

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Treatment Group</th>
<th>Comparative Group</th>
<th>Cost per Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barton (1995)</td>
<td>Radiotherapy for various cancers</td>
<td>No radiotherapy</td>
<td>$9248.30/LYG</td>
</tr>
<tr>
<td>Liljegren (1997)</td>
<td>Post-operative radiotherapy</td>
<td>No radiotherapy</td>
<td>$71,509.35/recurrence avoided</td>
</tr>
<tr>
<td>Lee (2002)</td>
<td>High-risk pre-menopausal patients + radiotherapy</td>
<td>No radiotherapy</td>
<td>$32,876/LYG; $29,879/QALY</td>
</tr>
<tr>
<td>Marks (1999)</td>
<td>Post-mastectomy radiotherapy</td>
<td>No radiotherapy</td>
<td>$328,548/QALY</td>
</tr>
<tr>
<td>Dunscombe (2000)</td>
<td>Post-mastectomy radiotherapy</td>
<td>No radiotherapy</td>
<td>$22,400/LYG; $24,900/QALY</td>
</tr>
<tr>
<td>Lievens (2005)</td>
<td>Supraclavicular lymph node radiotherapy</td>
<td>No radiotherapy</td>
<td>Dominant</td>
</tr>
<tr>
<td>Lundkvist (2005)</td>
<td>Proton radiotherapy, left-sided breast cancer</td>
<td>No radiotherapy</td>
<td>$103,307/QALY</td>
</tr>
<tr>
<td>Sher (2009)</td>
<td>Partial-breast external beam radiotherapy</td>
<td>Whole-breast radiotherapy; MammoSite partial-breast radiotherapy</td>
<td>$802,368/QALY; Dominant</td>
</tr>
</tbody>
</table>

LYG = Life Year Gained

These studies have shown that radiotherapy is both medically and economically preferable to receiving no radiotherapy after surgery for breast cancer patients. Administering radiotherapy reduces the rate of recurrence, increases survival and improves quality of life.

*Chapter 2.5C – Benefits: Treatment Costs of Breast Cancer Recurrence*

After receiving breast-conserving surgery and radiotherapy, patients enter a period of follow-up surveillance care by their oncologist (55). Clinical diagnosis of recurrence is most often detected through screening (i.e., mammography, X-ray, other radiological procedures) (22), but symptomatic presentation of recurrence is characterized by

* Costs are presented in 2008 Canadian Dollars. Values from other countries were converted using the exchange rate into Canadian dollars for that year, then adjusted for inflation using the Consumer Price Index.
bleeding, ulceration, pain, edema, and brachial plexopathy (23). Once recurrence has been detected, patients receive surgical intervention (mastectomy) and systemic therapy (chemotherapy, hormonal therapy) (56). Medical oncologists oversee patient care during systemic therapy, which can last for several years (57).

Patients who develop recurrence are at increased risk of death (58). Elder and colleagues analyzed a cohort of breast cancer patients who had experienced a local recurrence of their disease. Survival analysis was conducted on 2509 recurrent breast cancer patients, which found a five-year survival rate of 41% (58). This rate was significantly lower than 91.1% survival among patients with no recurrence (44). Survival in the Elder study was lowest among patients with distant recurrence (58).

Many patients who develop local recurrence go on to develop metastatic disease, even though they receive systemic treatment (59). Lê and colleagues analyzed a cohort of patients presenting with local recurrence of early-stage breast cancer. The ten-year control rate for local recurrence was 56%, meaning that 44% of patients moved on to develop metastatic disease, while 91% of patients with metastatic disease died of their cancer (60).

Treating breast cancer recurrence is more expensive than treating initial presentation. Lamerato and colleagues analyzed a cohort of breast cancer patients based on administrative data from the United States (61). The investigators found that the cost of treating breast cancer recurrence was higher than the cost of first-line treatment, even though the up-front cost of treatment was greater in patients with no recurrence than patients with recurrence. Marks and colleagues used Relative Value Units (a measure of the resources utilized in a schedule of treatment) to estimate the cost of treating a
locoregional recurrence at $34,847 (converted from 2000 US dollars) (48). Will and others calculated an average cost of $8276 to treat a local recurrence (62). The disparity in these two cost results was due in part to different payment systems, costing inputs and methodologies – for example the use of relative value units as opposed to population-based modeling to determine cost.

Drug and drug administration costs can vary greatly depending on the type of chemotherapeutic agent used (63). Certain regimens of chemotherapy such as Tamoxifen, Letrozole and Anastrozole cost the health care system around $1600 (64), whereas other types of drugs such as monoclonal antibody drugs (MAb) can cost upwards of $40,000 (65). Wai and colleagues used patient records to investigate the health care system costs associated with metastatic breast cancer treatment in British Columbia in the mid-1990s. The average cost of care was $46,000 in a cohort of 75 patients; however, pharmaceutical costs represented only $1600 of this total (64). In contrast, Drucker and colleagues estimated the drug and resource utilization costs for the delivery of therapy with trastuzumab and bevacizumab, two commonly-used MAbs, and found an average cost of $53,000 for trastuzumab and $51,500 for bevacizumab, which is greater than the total treatment cost in the Wai study (65). Vu and colleagues found that Docetaxel and Paclitaxel, two taxane chemotherapy drugs, had an administration cost of $30,800 and $25,000 respectively in the treatment of metastatic breast cancer (66).

Rao and colleagues analyzed a matched case-control cohort of patients in the United States being treated for metastatic breast cancer. Mean Medicare charges among patients were found to be $64,800 (converted from U.S. dollars) (67). Although U.S. dollars have
been converted here, it is important to note, however the U.S. and Canadian health care systems operate differently, and as such place different dollar values on resources. End-of-life treatment is associated with its own specific resource utilization, and accompanying cost. Payne and colleagues analyzed a cohort of British Columbian patients over the age of 65 years between 1991 and 2002. They examined physician, hospital and pharmacy costs according to provincial billing rates and Resource Intensity Weights (RIWs), a method of assigning costs to patients based on case mix. Among patients who died during the observation period, health care costs engendered during the last year of life were greater than $30,000 (68). This cohort included all causes of death, not just cancer.
Chapter 3 – Study Design and Methods

This study proposes the use of a cost-benefit analysis to address the issue of waiting for radiotherapy: costs are measured as the value of resources required to increase the capacity of a cancer centre, and benefits are calculated as the value of averted treatment costs due to reduced waiting (as a result of an increase in cancer centre capacity). The study is intended to demonstrate a methodology by which the cost-benefit of reducing radiotherapy waiting times can be calculated, using early breast cancer as a simplified illustrative example. The methodological steps are listed as follows.

1. The amount of excess capacity required in a cancer centre to control waiting times at a given length of interest is estimated using a simulation model.
2. The costs of creating new patient spaces in order to increase capacity are determined based on budgetary and staffing information from a regional cancer centre.
3. The economic benefits of reducing waiting from \( i \) weeks to \( j \) weeks are calculated using a Markov chain model relying on values from the scientific and economic literature.
4. The present-day value of the incremental costs and benefits is compared for various levels of capacity over time, and the cost-benefit is calculated.

The following section describes the approaches used in this project.

Chapter 3.1 – Capacity and Waiting

In this chapter, details are presented on how a simulation model is created to determine how an increase in the capacity of a cancer centre would affect a patient’s waiting time for radiotherapy. In order to estimate this effect, a computer simulation
model is created in iThink (High Performance Systems, Hanover, NH, U.S.A). “Waiting” in this project is defined as the amount of time between patients being referred to a radiotherapy clinic and the date of their first radiation treatment. It is measured as the number of weeks that the last patient on the waiting list can expect to wait.

The simulation model differentiates between two distinct types of waiting that can occur after surgery once a patient is referred to a cancer centre: “Assessment” waiting and “Treatment” waiting. First, a patient may have to wait to see a radiation oncologist for assessment and treatment planning if the specialist does not have any clinic time to see a new patient (“Assessment” waiting, also known as “Referral – Consult”). Second, following being seen by a radiation oncologist, a patient may have to wait to be treated on a linear accelerator if the machine is running at full capacity and cannot accommodate another new patient (“Treatment” waiting, also known as “Ready-to-Treat – Treatment”) (47).

The simulation model created here operates as follows. Patients enter the cancer centre randomly according to a statistical distribution, and are assessed by a radiation oncologist. If there are no available radiation oncologists, patients must wait for a space to become available. Once patients are assessed, they are treated on a linear accelerator. Again, if there is no space for new patients available at the linear accelerator, they will wait. Once patients begin treatment, they are treated with 16 fractions over three weeks, after which time their treatment is complete. Treated patients move out of the cancer centre, and their treatment spaces are filled by patients on the waiting list in a “First-in-First-out” (FIFO) way – in which the first patient to enter the list (in) is the first one to be
seen (out). The model is run at weekly intervals over a time period of ten years (520 weeks). The process is illustrated in Figure 3.1.1.

Figure 3.1.1 – Cancer Centre Patient Flow

NewPatients: Patients referred into the cancer centre for radiotherapy
Assessment: Waiting to be assessed by a radiation oncologist (assessment waiting)
ToRadOnc: Transition to radiation oncologist assessment
RadOnc: Patient being assessed by radiation oncologist
Assessed: Transition to treatment phase
Treatment: Waiting to be treated on linear accelerator (treatment waiting)
ToTx: Transition to treatment on linear accelerator
RT: Patient being treated at a linear accelerator
TreatTime: Transition out of cancer centre
Treated: Patient has been assessed and treated and moves out of cancer centre

Patient referral patterns are approximated to a statistical distribution. The number of weekly assessment and treatment spaces is calculated by dividing the number of patients assessed and treated in the period of a year by the number of weeks in a year. The baseline assumption of the model is that the radiotherapy clinic is staffed to treat the average number of patients each week. The simulation considers that a number of patients may be waiting for assessment and treatment at the outset of the model run.

To calculate the association between cancer centre capacity and waiting times, the following analytic steps are taken.
1. The simulation program is run for 1000 iterations. The assessment, treatment, and total waiting times are reported at six-month intervals over the ten-year timeline (necessary for subsequent steps in this methodology). A 95% confidence interval is calculated for total waiting time at each interval. Waiting length is determined according to a ‘maximum waiting time’ approach, which identifies the amount of time the last person on the waiting list can expect to wait. This length of time is a function of the number of people on the list and the number of spaces available per week, according to the following specification: \( \text{wait length (weeks)} = \frac{\text{number of patients waiting}}{\text{number of spaces available}}. \)

2. Since the number of new patients in a given week is the product of a random function, the capacity increase must reduce waiting times to desired levels in a majority (defined here as the 95% confidence limit) of model runs. Accordingly, the waiting length for each interval is determined as the upper confidence value of the confidence interval.

3. The overall waiting time for the model (denoted as \( i \) weeks of waiting) is calculated as the average of the upper confidence values in each 6-month period.

4. The capacity at the assessment and/or treatment phase is increased by one space per week. The smallest capacity increase required to reduce waiting is made.

In this way, values of \( i \) (number of weeks waiting) are calculated for different levels of assessment and treatment capacity. Since different combinations of capacity levels may result in the same value for \( i \), the level that requires the smallest capacity increase – the fewest additional spaces – is chosen.
It is important to note that waiting can occur at two points in the simulation model – waiting to be assessed by a radiation oncologist, and waiting for treatment at the machine site. It is conceivable that patients may wait further upstream (waiting for surgery, waiting to be referred to a radiation oncologist), but these types of waiting (that occur outside the cancer centre) are beyond the scope of this project and are not considered here. Simulation model inputs are described in Table 3.1.1.

Table 3.1.1 – Inputs for Simulation Model of Capacity and Waiting

<table>
<thead>
<tr>
<th>Model input</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average demand</td>
<td>Number of new patients per year / 52</td>
</tr>
<tr>
<td>Distribution of referrals</td>
<td>Number of referrals per week</td>
</tr>
<tr>
<td>Capacity of Cancer Centre</td>
<td>Number of patient spaces per week</td>
</tr>
<tr>
<td>Prevailing Waiting Times</td>
<td>Number of patients waiting at representative centre</td>
</tr>
</tbody>
</table>

Chapter 3.2 – Estimation of Costs

Costs of delivering radiotherapy in a cancer centre are estimated according to three principal categories: personnel, equipment and overhead (69). Table 3.2.1 lists inputs for costs.
Table 3.2.1: Project Cost Inputs

<table>
<thead>
<tr>
<th>Resource Item</th>
<th>Personnel</th>
<th>Equipment</th>
<th>Overhead</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nurses</td>
<td>Mammography</td>
<td>Administration</td>
</tr>
<tr>
<td></td>
<td>Physicians</td>
<td>CT Scanner</td>
<td>Secretarial</td>
</tr>
<tr>
<td></td>
<td>Physicists</td>
<td>MRI Scanner</td>
<td>Utilities</td>
</tr>
<tr>
<td></td>
<td>Radiation Therapists</td>
<td>Linear Accelerator</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Planning</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Computed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tomography (CT)s</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>X-Ray Machine</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Concrete Bunker</td>
<td></td>
</tr>
</tbody>
</table>

Personnel costs are calculated as the average salary and benefits for staff associated with radiation treatment. The total cost of equipment is determined according to manufacturer’s costs, adjusted for depreciation (70) using a straight-line method (69) over a relevant life of ten years (71,72). Overhead costs (e.g., maintenance, utilities) are calculated using a “hotel cost” (1,73) approximation method (measuring costs that are relatively invariant across patients, for example, facility costs, overhead, medical supplies, and dividing those costs by the number of patients affected). All yearly resource use and cost categories presented in Table 3.2.1 are summed to obtain a total operating cost per year.

Two distinct scenarios for increasing the capacity of a cancer centre are considered as follows: a) increasing assessment capacity by hiring new radiation oncologists plus increasing treatment capacity by buying new treatment machines and hiring additional
staff; and (b) increasing assessment capacity (as in a) plus increasing treatment capacity by hiring additional staff to use existing treatment infrastructure.

Chapter 3.3 – Estimation of Benefits

In this project, the benefits of increasing the average capacity of a cancer centre are measured as the averted costs of treating recurrences, metastatic disease, and death due to decreasing waiting time for radiotherapy. To estimate the avoided cost, a Markov chain microsimulation model is constructed. In Markov modeling, one is able to create a trajectory with hypothetical cohorts of individuals waiting for radiotherapy moving through the different health states at fixed time periods (74). The Markov model created here calculates the value of resources spent on patients who wait for \( i \) weeks before receiving radiotherapy. The model is run in six-month intervals (cycles) over a period of ten years.

Patients (modeled one at a time) start in the Markov model in the “well” state, having received post-operative radiotherapy. From this state, the patient transitions to other disease states: local recurrence, no evidence of disease after mastectomy; and distant metastasis. A patient then can transition into death from cancer and death from other causes (the two feasible terminal states). A 10-year time horizon (20 cycles of 6 months each) is used in the model, created in iThink (iSee Systems, Hanover, NH, U.S.A). A schematic of the model, based on a similar model by Sher (53) is provided in Figure 3.3.1.

Transition between health states (Well, Local Recurrence, Metastatic Disease, Death from Cancer and Death from other causes) occurs according to the risk of the event happening, or transition probability. In the Markov model, one patient moves through the
system in each model run, with transition between health states governed by a “Monte Carlo” function through a random number generator - if the random number (between 1 and 100) is equal to or greater than the transition probability, the patient moves to the next state; otherwise, the patient remains in the same health state for another cycle.

Figure 3.3.1 – Markov Model

NED = No Evidence of Disease

For the cost-benefit methodology, the following inputs are used from the literature to inform the Markov model: (i) the likelihood (or probability) of transition from one health state to another; and (ii) the cost of treatment associated with the health state.

3.4 – Cost-Benefit Analysis

The cost-benefit analysis in this study consists of a structural plan followed by analytic steps. The structural plan includes specifying the perspective of the analysis, the time horizon for evaluating costs and benefits, and the discount rate. The perspective of a study relates to who pays for and who benefits from a program. This analysis adopts a health care system perspective, meaning that costs and benefits experienced by the health
care system are included. This perspective is chosen because the intended audience of the analysis is policy-makers and cancer centre administrators.

A time horizon of 10 years is chosen, since patients who have not experienced a recurrence within 10 years following diagnosis have a low probability of recurrence after this time period (21,57), and 10 years is a reasonable useful life for medical equipment such as linear accelerators (23). Costs and benefits that are experienced in the future are discounted at a rate of 3%, as recommended by the Panel on Cost-Effectiveness in Health and Medicine (75). Discounting is a technique used in economics to convert future costs and consequences to their present value. Independent from inflation, the underlying assumption is that economic resources are more highly valued in the present than in the future. This concept should not be confused with “willingness to pay” which is a measure of the amount of money a patient would give out of their own pocket to receive a treatment.

Costs and benefits for the cost-benefit analysis are calculated as outlined in Chapters 3.2 and 3.3. Once costs and benefits are calculated, the Net Present Value can be determined. All costs and benefits are measured in dollars and combined into a summary measure, the Net Present Value:

\[
NPV = \sum_{t=0}^{N} \left\{ \frac{(Benefits_i - Benefits_j) - (Costs_i - Costs_j)}{(1+r)^t} \right\}_{t=0}^{N}
\]

where
- \( t = \) year (from 0, 1, 2, ... \( N \)),
- \( N = \) number of years being valued (here, \( N = 10 \)),
- \( r = \) discount rate (\( r = 3\% \)),
- \( i = 2, 3, 4 \ldots \) weeks of waiting
- \( j = 1, 2, 3 \ldots \) weeks of waiting
The incremental costs of increasing the capacity of a cancer centre to reduce waiting (from \(i\) weeks to \(j\) weeks) are subtracted from the incremental benefit (averted recurrence treatment costs) due to decreased waiting (\(i\) to \(j\) weeks) for each year of analysis (\(t\)). A discount rate of 3% is used. Finally, all annual incremental values are added to yield the Net Present Value for each scenario of capacity increase. A Net Present Value larger than 0 indicates that the incremental benefit of increasing capacity measured in terms of averted recurrence treatment costs at cancer centres outweighs the incremental cost of increasing capacity.

The Net Present Value is useful in a decision-making context, but may not present all relevant information that a policy-maker needs in order to make a decision. Using Net Present Value to allocate resources can pose problems because the final result (the absolute difference between discounted benefits and costs) provides no direct information about resource requirements of a project. For example, if a policy maker were told only that the Net Present Value of increasing cancer centre capacity were $2,000,000 and that it was the largest capacity increase, he or she would have no idea that $20,000,000 worth or resources would be needed to implement the capacity increase. What if the decision maker did not have any access to such resources? Thus, it is sometimes useful, when presenting a Net Present Value, to also present the discounted benefits and costs. This additional information gives the audience some idea of the scale of investment that is being analyzed.

A Benefit-to-Cost ratio (BCR) is also calculated, wherein the total benefit is divided by the total cost according to Equation 2:

\[
\frac{PV_{\text{Benefits}}}{PV_{\text{Costs}}} \tag{2}
\]
where

\[ PV_{\text{Benefit}} = \text{Present Value of Benefits} \]
\[ PV_{\text{Cost}} = \text{Present Value of Costs} \]

For example, a cost-benefit analysis may yield a Benefit-to-Cost ratio equal to 1.2:1. This would mean that for every dollar invested in increasing capacity at the cancer centres (cost), society would gain (averted costs in preventing cancer recurrence = benefit) $1.20. When a Benefit-to-Cost ratio is greater than 1, decision-makers may consider the possibility of increasing capacity. However, Benefit-to-Cost ratio must be viewed with caution. While a ratio is helpful for determining the relative size of the return on investment, it may obscure its actual size. For example, a ratio of 2:1 applies to both a $10:$5 and a $1,000,000:$500,000 return. However, if a decision-maker does not have $500,000 to invest, the benefit is not within financial reach despite the favourable ratio.

Analysis in this study is based on a number of key assumptions. It is assumed that a cancer centre is staffed and operates to serve average demand, without excess treatment capacity built into the system. Patients are referred immediately after healing from surgery, and are treated with radiotherapy only. Staffing levels remain fixed over the time horizon of ten years. It is also assumed that the additional risk of local recurrence and associated downstream effects are the sole cost drivers associated with waiting.

Chapter 3.5 – Sensitivity Analysis

Sensitivity analysis is conducted in economic evaluations to determine the degree to which the output of the evaluation varies with uncertainty in the inputs, and to identify the factors to which the outcome measure is most sensitive, meaning the extent to which change in that factor affects the cost-benefit calculation (1) in this instance. One-way sensitivity analyses are conducted. The values for costs (cost of equipment, salary, overhead) and benefits (risk of recurrence, transition probabilities, costs of medical
treatment) are adjusted one at a time above and below the baseline value, to show how variation in any single factor changes the outcome. “Best case” and “worst case” sensitivity analyses are also calculated, in which parameters are adjusted to their maximum and minimum values simultaneously to determine the possible range of Net Present Value. Probabilistic sensitivity analysis, in which the inputs of a model are allowed to vary according to statistical distributions around the mean values, was also performed for the patients entering into the cancer centre and in the Markov model, to determine how fluctuation in the costs of treatment and the transition probabilities affect the Net Present Value.
Chapter 4 – Results

In the following section, a hypothetical cancer centre treating a population of patients who have received adjuvant radiotherapy following breast-conserving surgery for early breast cancer (stage I/IIA with no lymph node involvement, or T1N0M0/T2N0M0) was created. This population was chosen because of evidence from the literature regarding the risk of recurrence, and treatment for this population tends to be more homogenous than for other cancer populations.

Capacity levels for this hypothetical ‘breast-only’ centre were determined according to levels of current operation at the Cancer Centre of Southeastern Ontario (CCSEO). The association between increased capacity and reduction in waiting times was estimated through a capacity/waiting simulation model. The costs associated with increased capacity levels for the hypothetical centre were based on budgetary information from the CCSEO, including salary, equipment and overhead. Benefits (averted recurrence as a result of reduced waiting time) were calculated using a Markov model with input values from the literature. Finally, the relative costs and benefits of increasing capacity were calculated. Sensitivity analysis was performed on model inputs to investigate the extent to which changes affected the outcome.

Chapter 4.1 – Capacity and Waiting

Chapter 4.1A - Capacity at the Cancer Centre of Southeastern Ontario (CCSEO)

The CCSEO, formerly the Kingston Regional Cancer Centre (KRCC), is a provincial cancer centre located within the Kingston General Hospital in Kingston, Ontario, Canada. The radiotherapy clinic within the centre has four linear accelerators and one Computed Tomography (CT) simulation machine, in addition to various diagnostic and radiology
machines. All values are for the fiscal year 2007/2008. A summary of clinic activity is presented in Table 4.1.1. (Note that all values are rounded up to the nearest integer to reflect the fact that patients are indivisible units.)

Table 4.1.1 – Patient Volume at CCSEO in 2007/2008 Fiscal Year

<table>
<thead>
<tr>
<th>Item</th>
<th>All-Sites</th>
<th>Breast Cancer Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy fractions delivered</td>
<td>24,829</td>
<td>7,177</td>
</tr>
<tr>
<td>Total clinic visits</td>
<td>6,532</td>
<td>993</td>
</tr>
<tr>
<td>New patient clinic visits</td>
<td>1,712</td>
<td>323</td>
</tr>
<tr>
<td>Total radiation cases treated</td>
<td>1,360</td>
<td>323</td>
</tr>
</tbody>
</table>

Average Demand for services at the CCSEO

Eight radiation oncologists assessed 1,712 new patients at the CCSEO during fiscal year 2007/2008. This works out to a figure of \([1,712/8=]\) 214 new patients per radiation oncologist per year, or \([214/52 = 4.12\) or] 5 patients per week. Four linear accelerators delivered 24,829 fractions of radiotherapy. Each machine, therefore, delivered \([24,829/4=6207.25\) or] 6,208 fractions. As of March 2009, the 90\(^{th}\) percentile waiting time for breast cancer treatment at the CCSEO was 5 weeks for assessment, and 4 weeks for treatment. Patients are treated with 16 fractions of radiotherapy over three weeks.

Chapter 4.1B – Capacity of a Hypothetical ‘Breast-Only’ Centre

The capacity of the hypothetical ‘breast-only’ centre was calculated based on the actual number of breast cancer patients treated at the CCSEO. For assessment capacity, given that one radiation oncologist can assess 214 patients (see above), for the hypothetical centre, two radiation oncologists were needed to assess at least the 323 hypothetical cohort of breast cancer patients. Since 4.12 patients are seen weekly by one radiation oncologist (based on CCSEO from above), the hypothetical centre with two
A radiation oncologist can assess [4.12 patients per oncologist x 2 oncologists = 8.24 patients per week or] 9 patients per week. For treatment capacity, given that the hypothetical centre treats 323 breast cancer patients per year (Table 4.1.1), its treatment capacity is equal to [323/52=6.21 or] 7 patients per week.

Likewise, prevailing waiting times at the hypothetical centre were estimated based on historical data from the CCSEO. Therefore, the number of patients waiting was calculated to be [5x9 =] 45 and [4x7 =] 28, respectively. These numbers were included at the beginning of the simulation run.

A summary of inputs into the iThink simulation model is provided in Table 4.1.2.

Table 4.1.2 – Inputs into the Capacity and Waiting Simulation Model

<table>
<thead>
<tr>
<th>Model Input</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Demand</td>
<td>7 patients/wk</td>
</tr>
<tr>
<td>Distribution of Referrals</td>
<td>Normal, μ = 7, s = 4.17</td>
</tr>
<tr>
<td>Rate of Outflow</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Number of Assessment Spaces/Week</td>
<td>9</td>
</tr>
<tr>
<td>Number of Treatment Spaces/Week</td>
<td>7</td>
</tr>
<tr>
<td>Waiting for Assessment</td>
<td>45 patients</td>
</tr>
<tr>
<td>Waiting for Treatment</td>
<td>28 patients</td>
</tr>
</tbody>
</table>

Chapter 4.1C – Simulation Modeling Results for Hypothetical Centre

Increasing capacity in the assessment phase moves patients through to the treatment phase more quickly than if capacity is not increased. If treatment capacity is not increased concurrently, patients simply wait for treatment, shifting the burden from the assessment phase to the treatment phase. On the other hand, increasing treatment capacity but not increasing assessment capacity does not reduce waiting times significantly. Increasing treatment capacity does not shorten waiting for patients in the assessment phase (waiting to see a radiation oncologist). No amount of treatment phase increase will reduce
assessment phase waiting, since the two phenomena are separate. In sum, in order to reduce waiting times it is necessary to increase both assessment and treatment capacity simultaneously. Assessment phase waiting must be reduced to an acceptable level, and then treatment capacity increased to accommodate the increased throughput.

The capacity and waiting simulation model was run in the way described above (in Chapter 3.1). Increasing the number of weekly spaces in the assessment and treatment phases reduced waiting times to as little as one week. Table 4.1.3 summarizes the effect of adding additional assessment and treatment spaces. Overall waiting length \( i \) is the length of waiting in weeks experienced by patients, as calculated above. It was determined as the average of the upper 95\% confidence intervals across the six-month periods. This table also lists the number of weekly assessment and treatment spaces required to achieve the various values of \( i \) (number of weeks waiting), and the number of spaces above baseline (excess) that this increase represents.

Table 4.1.3 – Additional Capacity and Waiting Times

<table>
<thead>
<tr>
<th>Overall Waiting Length in Weeks ( (i) )</th>
<th>Assessment Spaces (# above average)</th>
<th>Treatment Spaces (# above average)</th>
<th>Total Spaces Created</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>13 (4)</td>
<td>10 (3)</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>13 (4)</td>
<td>11 (4)</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>12 (3)</td>
<td>13 (6)</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>14 (5)</td>
<td>11 (4)</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>14 (5)</td>
<td>12 (5)</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>15 (6)</td>
<td>12 (5)</td>
<td>11</td>
</tr>
</tbody>
</table>

Chapter 4.2 – Estimation of Costs

Operating costs, including salary/benefits for staff, the cost of equipment, and overhead costs for the hypothetical centre were based on the CCSEO for the 2007/2008 fiscal year. All values are presented in 2008 Canadian dollars.
Chapter 4.2A – Costs at the Cancer Centre of Southeastern Ontario

The costs of operating a cancer centre were divided into three categories: salary and benefits for staff, the cost of equipment, and the overhead costs of facility operation. Values for these categories were determined by conducting face-to-face interviews with administrative and clinical staff at the CCSEO and through e-mail contact with finance administrators at the Kingston General Hospital (KGH), in which the CCSEO is housed.

Salary/Benefit Costs at the CCSEO

Staffing levels, average salary amounts (including benefits), and the total annual cost associated with salary/benefits at the CCSEO are presented in Table 4.2.1. Note that the role of nurses at the CCSEO is primarily focused on systemic therapy.
Table 4.2.1 – Salary and Benefit Costs at the CCSEO

<table>
<thead>
<tr>
<th>Category</th>
<th># of Personnel</th>
<th>Salary</th>
<th>Benefits</th>
<th>Annual Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing</td>
<td>7.5</td>
<td>$73,729</td>
<td>$14,745.80</td>
<td>$663,561</td>
</tr>
<tr>
<td>Radiation Oncology</td>
<td>8</td>
<td>$400,000</td>
<td>N/A</td>
<td>$3,200,000</td>
</tr>
<tr>
<td>Radiation Therapy</td>
<td>23</td>
<td>$75,445</td>
<td>$15,089.00</td>
<td>$2,082,282</td>
</tr>
<tr>
<td>Physics</td>
<td>5</td>
<td>$128,583</td>
<td>$25,716.60</td>
<td>$771,498</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>$6,717,341</strong></td>
</tr>
</tbody>
</table>

Equipment Costs at the CCSEO

The cost of medical equipment was depreciated over a useful life of 10 years (72) according to a “straight-line depreciation” method (1) at an annual rate of 17.5% (70).

The annual cost of equipment was determined according to the following method:

\[ C_{Dn} = P_{n-1} \times D \]  

where

- \(C_{Dn}\) = depreciated value of the equipment for a given year;
- \(n\) = year of interest;
- \(P_{n-1}\) = value of the equipment in the previous year; and
- \(D\) = annual depreciation percentage.

For example, an X-ray machine has a purchase cost of $500,000. Over the course of the first year, its depreciated value is:

\[
\begin{align*}
&\$500,000 \times 0.175 \\
&= \$87,500.
\end{align*}
\]

In the second year, the depreciated value is:

\[
\begin{align*}
&(\$500,000 - \$87,500) \times 0.175 \\
&= \$72,187.50.
\end{align*}
\]

The purchase price and average annual depreciated value of equipment, as calculated above, is listed in Table 4.2.2. The value of a concrete bunker, used to house each linear accelerator, is determined from a study by Wodinsky, depreciated over a relevant life of 40 years, and adjusted to 2008 Canadian dollars using the Consumer Price Index (76).
Table 4.2.2 – Equipment Costs at the CCSEO

<table>
<thead>
<tr>
<th>Category</th>
<th># of Items at CCSEO</th>
<th>Cost per Item</th>
<th>Average Annual Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear Accelerator</td>
<td>4</td>
<td>$2,700,000</td>
<td>$922,252</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging Machine</td>
<td>1</td>
<td>$2,750,000</td>
<td>$234,833</td>
</tr>
<tr>
<td>X-Ray Machine</td>
<td>2</td>
<td>$500,000</td>
<td>$85,394</td>
</tr>
<tr>
<td>Computed Tomography Simulator</td>
<td>1</td>
<td>$1,740,000</td>
<td>$148,585</td>
</tr>
<tr>
<td>Mammography Machine</td>
<td>3</td>
<td>$800,000</td>
<td>$204,945</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>4</td>
<td>$220,000</td>
<td>$75,146</td>
</tr>
<tr>
<td>Concrete Bunker</td>
<td>4</td>
<td>$235,559</td>
<td>$94,224</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>$1,765,379</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Overhead Costs at the CCSEO**

Overhead costs, the costs not directly associated with the treatment of patients, are comprised of the amount charged to the CCSEO by the KGH over the span of a single year. Utilities refer to amount paid for items such as electricity, water, and maintenance. Administration/secretarial includes the salaries paid to administration staff and reception. Other facility costs include finance, human resources, purchasing, rent, telecommunications, public relations, and information systems. A summary of these values is provided in Table 4.2.3.
Table 4.2.3 – Overhead Costs at the CCSEO

<table>
<thead>
<tr>
<th>Input</th>
<th>Cost of item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utilities</td>
<td>$630,996</td>
</tr>
<tr>
<td>Administration/secretarial</td>
<td>$680,000</td>
</tr>
<tr>
<td>Other facility costs</td>
<td>$3,857,958</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$5,168,954</strong></td>
</tr>
</tbody>
</table>

**Operating Costs at the CCSEO**

The total annual cost of operation of the CCSEO is therefore \[6,717,341 + 1,765,379 + 5,168,954 = 13,651,674\]. Given that a total of 24,829 radiation fractions are given per year at the CCSEO, the per-fraction cost (i.e., the cost of giving one fraction) is \[13,651,674/24,829 = 550\]. Since breast cancer is treated with 16 fractions at the CCSEO, the per-patient radiotherapy treatment cost is approximately \[550*16 = 8,800\]. Therefore, at the CCSEO, it costs $8,800 to treat an early breast cancer patient with radiation.

**Chapter 4.2B – Costs at the Hypothetical ‘Breast-Only’ Centre**

Staffing levels, equipment, and overhead costs at the hypothetical ‘breast cancer only’ centre were based on costs and breast cancer patient volume seen at the CCSEO during the 2007/2008 fiscal year.

**Salary/Benefit Costs at the Hypothetical Centre**

The costs and staffing levels for the hypothetical ‘breast cancer only’ centre were based on the costs and number of patients treated at the CCSEO. For example, at the CCSEO, eight radiation oncologists oversaw 1,712 new patient clinic visits, which works out to \[1712/8 = 214\] new patients per radiation oncologist, per year. Since 323 new breast patient clinic visits occurred in 2007/2008, two radiation oncologists would be needed to assess patients. Other hypothetical staffing levels were calculated in this way,
and are presented in Table 4.2.4. Given the importance of nurses in the health care system, it is likely that the hypothetical centre created here would have at least one full-time-equivalent nurse on staff for auxiliary patient care. One full-time-equivalent is included in the overall cost of the hypothetical centre. Similarly, one medical physicist is included in the overall cost of the hypothetical centre, though his/her role is largely centered around the testing of novel approaches and simulation of complex patients – rarely participating in the treatment of an individual patient, particularly early breast cancer.

Table 4.2.4 – Salary and Benefit Costs at the Hypothetical Centre

<table>
<thead>
<tr>
<th>Category</th>
<th># of personnel</th>
<th>Salary</th>
<th>Benefits</th>
<th>Total Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing</td>
<td>1</td>
<td>$73,729</td>
<td>$14,746</td>
<td>$88,475</td>
</tr>
<tr>
<td>Radiation Oncology</td>
<td>2</td>
<td>$400,000</td>
<td>N/A</td>
<td>$800,000</td>
</tr>
<tr>
<td>Radiation Therapy</td>
<td>8</td>
<td>$75,445</td>
<td>$15,089</td>
<td>$724,272</td>
</tr>
<tr>
<td>Physics</td>
<td>1</td>
<td>$128,583</td>
<td>$25,717</td>
<td>$154,300</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>$1,767,047</strong></td>
</tr>
</tbody>
</table>

Equipment Costs at the Hypothetical Centre

Equipment costs for the hypothetical centre were determined in a similar method to staffing levels and costs. For the CCESO, four linear accelerators delivered 24,829 fractions of radiotherapy in one year of which 7,177 were for breast cancer. Given that a linear accelerator delivered approximately \([24,829/4=6207.25]\) or 6208 fractions per year, it was inferred that two machines would be needed for the hypothetical centre (to account for the 7,177 fractions for breast cancer). The equipment required for the operation of the hypothetical centre was determined in the same way, and the cost of each calculated according to Equation 4. A summary of equipment costs is presented in Table 4.2.5.
Table 4.2.5 – Equipment Costs at the Hypothetical Centre

<table>
<thead>
<tr>
<th>Category</th>
<th># of items</th>
<th>Cost per item</th>
<th>Average Annual Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear Accelerator</td>
<td>2</td>
<td>$2,700,000</td>
<td>$461,126</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging Machine</td>
<td>1</td>
<td>$2,750,000</td>
<td>$234,833</td>
</tr>
<tr>
<td>X-Ray Machine</td>
<td>1</td>
<td>$500,000</td>
<td>$42,697</td>
</tr>
<tr>
<td>Computed Tomography Simulator</td>
<td>1</td>
<td>$1,740,000</td>
<td>$148,585</td>
</tr>
<tr>
<td>Mammography Machine</td>
<td>1</td>
<td>$800,000</td>
<td>$68,315</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>2</td>
<td>$220,000</td>
<td>$37,573</td>
</tr>
<tr>
<td>Concrete Bunker</td>
<td>2</td>
<td>$235,559</td>
<td>$47,112</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>**</td>
<td><strong>$1,040,241</strong></td>
<td></td>
</tr>
</tbody>
</table>

Overhead Costs at the Hypothetical Centre

Overhead costs were calculated by multiplying the associated expenditure by the proportion of fractions delivered, since these costs cannot be separated into individual resource inputs in the same way that staffing and equipment can. Breast fractions represented \( \frac{7,177}{24,829} = 29\% \) of total cancer centre radiotherapeutic output, so the overhead costs for the hypothetical centre are calculated as \( \$5,168,954 \times 29\% = \$1,498,997 \). Utilities are \( \$630,996 \times 29\% = \$182,989 \) of this cost.

Operating Costs at the Hypothetical Centre

Thus, the hypothetical centre had an average annual expenditure of \( \$1,767,047 + \$1,040,241 + \$1,498,997 = \$4,306,285 \). The breakdown in costs for the hypothetical centre was the following: salary costs (“process inputs” according to Ploquin (27)) represented 41%, equipment (“clinical infrastructure”) represented 23% and overhead (“supporting infrastructure”) represented 36% of total costs.
Chapter 4.3 – Estimation of Benefits

The estimation of benefits was illustrated by a hypothetical example of a cohort of breast cancer patients. As stated above, a Markov model was used to calculate averted treatment of cancer recurrence costs, and in this instance, it was based on the model for early breast cancer developed by Sher and colleagues (70;71). The likelihood of a patient experiencing a health event (transition probability) was taken from the clinical literature, and the cost associated with treating each event was determined from the health economics literature. The values were entered into the Markov model, which was run 10,000 times to calculate expenditure in treating this patient population.

Transition Probabilities

Transition probabilities were taken from the literature (1;2;14;32) over the time horizon of 10 years. The additional risk of waiting was factored into the risk of developing local recurrence from the “Well” state, by calculating the incremental weekly risk based on a monthly relative risk of 1.10 (77). For example, the weekly relative risk of waiting is \[1.00 + \{(1.10-1.00)/4 \text{ weeks per month}\} = 1.025 \text{ per week}.\] The absolute risk of recurrence is 0.067 (54), corresponding to a \[(1.025 - 1) \times 0.067 = 0.00168 \text{ incremental risk of recurrence per week}.\] A patient who waits for two weeks therefore has a \[(2 \times 0.00168) + 0.067 = 0.070 \text{ probability of recurrence}.\]

A patient’s transition probability from the “Well” state to the “Local Recurrence” state was the product of the absolute risk of recurrence and the relative risk due to waiting, with waiting length being informed by the output of the simulation model. A summary of these probabilities is provided in Table 4.3.1.
Table 4.3.1 – Inputs into Markov Model

<table>
<thead>
<tr>
<th>Event</th>
<th>Probability</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Ratio per week of waiting</td>
<td>1.025</td>
<td>(78)</td>
</tr>
<tr>
<td>“Well” to “Local Recurrence”</td>
<td>6.7% (1-5y)</td>
<td>(79)</td>
</tr>
<tr>
<td></td>
<td>3.3% (6-10y)</td>
<td>(79)</td>
</tr>
<tr>
<td>“Well” to “Metastatic Disease”</td>
<td>11% (10y)</td>
<td>(80)</td>
</tr>
<tr>
<td>“Local Recurrence” to “Metastatic Disease”</td>
<td>20% (10y)</td>
<td>(81)</td>
</tr>
<tr>
<td>“Metastatic Disease” to “Cancer Death”</td>
<td>32.8% (1y)</td>
<td>(82)</td>
</tr>
<tr>
<td>Any state to “Death from Other Cause”</td>
<td>0.5% (1y)</td>
<td>(77)</td>
</tr>
</tbody>
</table>

Cost of Treating Health Events

The cost of treating each health event was determined from the economics literature. A MEDLINE search was conducted using combinations of the search keywords “breast cancer”, “cost”, “economic”, “systemic therapy”, “chemotherapy”, “recurrence”, “metastatic”, “death” and “Canada”. Only Canadian costing data were considered, as different countries have differing payment systems and structures, making transferability of results difficult. Studies based on a patient cohort were favoured over those that used economic modeling (e.g., Markov chain, Monte Carlo simulation) to determine treatment costs.

Cost of Treatment for Local Recurrence

The per-patient costs of local recurrence treatment were divided into assessment, treatment, and follow-up:

- assessment costs are the costs of initial detection of recurring disease, including clinic and nursing hours, hospital admission costs, diagnostic imaging and other procedures,
- treatment costs were defined as the costs of surgery (radical mastectomy), systemic therapy (chemotherapy) drug and administration costs and hospitalization costs, and
- follow-up costs are the costs associated with regular oncologist visits after initial diagnosis.
Table 4.3.2 presents cost of treatment for local recurrence from various sources from the literature, adding up to $11,882.57. Will et al. used a population-based statistical model to estimate the cost of treating local recurrence at $11,812.64 (62). For the Markov model a value of $12,000 was used.
Table 4.3.2 – Recurrence Treatment Cost Inputs

<table>
<thead>
<tr>
<th>Phase</th>
<th>Item</th>
<th>Cost(^1)</th>
<th>Range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment</td>
<td>Clinic visit</td>
<td>$164.05</td>
<td></td>
<td>(83)</td>
</tr>
<tr>
<td></td>
<td>Oncology consultation</td>
<td>$124.45</td>
<td></td>
<td>(83)</td>
</tr>
<tr>
<td></td>
<td>Clinic nursing cost</td>
<td>$63.22</td>
<td></td>
<td>(84)</td>
</tr>
<tr>
<td></td>
<td>Hospital Admission</td>
<td>$132.10</td>
<td></td>
<td>(84)</td>
</tr>
<tr>
<td></td>
<td>Chest imaging</td>
<td>$22.45</td>
<td>$20.27 – $35.81</td>
<td>(84,85,86)</td>
</tr>
<tr>
<td></td>
<td>Bone scan</td>
<td>$241.67</td>
<td>$241.67 - $263.40</td>
<td>(84,86)</td>
</tr>
<tr>
<td></td>
<td>Tumour biopsy</td>
<td>$156.31</td>
<td></td>
<td>(84)</td>
</tr>
<tr>
<td></td>
<td>Breast ultrasound</td>
<td>$177.12</td>
<td></td>
<td>(86)</td>
</tr>
<tr>
<td></td>
<td>Biochemistry</td>
<td>$45.99</td>
<td></td>
<td>(86)</td>
</tr>
<tr>
<td></td>
<td>CT Scan with contrast</td>
<td>$509.85</td>
<td>$509.85 - $1265.54 (with PET scan)</td>
<td>(87,84)</td>
</tr>
<tr>
<td></td>
<td>MRI Scan with enhancement</td>
<td>$396.33</td>
<td>$396.33 - $421.27</td>
<td>(84,87)</td>
</tr>
<tr>
<td></td>
<td><strong>Total Assessment Cost</strong></td>
<td><strong>$2033.54</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Treatment     | Radical mastectomy        | $930.23    | $930.23 - $1162.63     | (88,86) |
|               | Hospitalization           | $6197.52   | $2358.86 - $6197.52    | (86,88) |
|               | Average chemotherapy drug cost | $2290.10 |               | (66,84,89) |
|               | Chemotherapy nursing cost | $92.43     |                        | (84)   |
|               | Chemotherapy physician cost | $61.55 |                        | (84)   |
|               | Clinic cost               | $277.19    |                        | (83,86) |
|               | **Total Treatment Cost**  | **$9,849.02** |                        |        |

**Total Cost** | **$11,882.56**

\(^1\) All costs are expressed in 2008 Canadian dollars
**Cost of Metastatic Disease Treatment**

Will et al. used the same population-based statistical model (mentioned above) to estimate the cost of treatment of metastatic disease at $36,078 (62). Since the publication of Will’s study, new chemotherapy regimens, with different acquisition and administration costs, have come on the market. Skedgel used a literature-based Markov model to estimate the cost of monthly treatment with herceptin, weighted for the population proportion of HER-2-neu patients, at $23,962.36 per month (90). Vu and colleagues reviewed data for a cohort of metastatic breast cancer patients and found a total per-patient cost of $10,681.55 for docetaxel and $3330.84 for paclitaxel in metastatic breast cancer patients (66). Drucker used drug acquisition and medical resource utilization data to estimate the lifetime costs for adjuvant treatment of metastatic breast cancer with trastuzumab, a Monoclonal Antibody drug, at $45,083 (65). For the Markov model, $40,000 per case is used (halfway between the Will and Drucker estimates since these studies used population-based estimates).

**Cost of End-of-Life Treatment**

Wai and colleagues used a linked cohort of several health databases in British Columbia to determine the costs incurred by breast cancer patients from diagnosis of metastatic disease to death, determined to be $47,620 (64). A subsequent chart review of patients who died of cancer between 1993 and 2000, conducted by Fassbender and colleagues, found the cost of care during the last year of life to be $34,330 for cancer patients. This sample was comprised of a majority of digestive and respiratory cancer patients (91). The authors further noted that long-term-care costs made up the majority of end-of-life expenditure (91).
colleagues identified the cost of metastatic treatment of breast cancer with trastuzumab at $30,051 (65). Romanus and colleagues calculated a lifetime cost of $74,307 in an incidence-based chart review of metastatic breast cancer patients treated with prophylactic oral clodronate, of which $6,159 related to drug costs, and $17,955 were attributed to the cost of terminal care (83). For the Markov model, the Romanus’ estimate of the cost of terminal care (~$18,000) was used since this value was based on the observed cost of a large cohort of patients receiving treatment for metastatic breast cancer.

Cost of Follow-up

Skedgel and colleagues (90) identified an annual cost of $1,192.12 for follow-up in the first 2 years, and $367.61 for years 3 and beyond. These values were included in the model as the cost of remaining in the “Well” state or the “No Evidence of Disease” state.

Cost Inputs to the Markov Model

A summary of these values is presented in Table 4.4.3.

Table 4.3.3 – Input Costs for Markov Model

<table>
<thead>
<tr>
<th>Event</th>
<th>Value</th>
<th>Range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well – Local Recurrence</td>
<td>$12,000</td>
<td>$8,300 - $13,100</td>
<td>Table 4.3.2, (62)</td>
</tr>
<tr>
<td>Local Recurrence – Metastatic Disease</td>
<td>$40,000</td>
<td>$36,000 - $45,000</td>
<td>(22;85)</td>
</tr>
<tr>
<td>Death</td>
<td>$18,000</td>
<td>$12,600 - $34,000</td>
<td>(83)</td>
</tr>
<tr>
<td>Follow-up: Years 1-2</td>
<td>$1192.12/yr</td>
<td>$700 - $1700</td>
<td>(90)</td>
</tr>
<tr>
<td>Years 3+</td>
<td>$367.62/yr</td>
<td>$200 - $550</td>
<td></td>
</tr>
</tbody>
</table>

Chapter 4.4 – Cost-Benefit Analysis

Once costs and benefits were calculated for the hypothetical breast cancer centre and cohort, the cost-benefit of increasing capacity in such a centre was calculated as follows:
\[
\text{NPV} = \sum_{t=0}^{N} \frac{\left(\text{Benefits}_i - \text{Benefits}_j\right) - \left(\text{Costs}_i - \text{Costs}_j\right)}{(1+r)^t}
\]

where
\[
\begin{align*}
  t & = \text{year (from 0,1,2, ... N),} \\
  N & = \text{number of years being valued (here, N=10),} \\
  r & = \text{discount rate (r=3%),} \\
  i & = 1, 2, 3, 4 \text{ weeks of waiting} \\
  j & = 0, 1, 2, 3 \text{ weeks of waiting}
\end{align*}
\]

The values of costs and benefits were calculated as described in the previous sections.

In order to perform a cost-benefit analysis, these values were expressed as the annual value of resources spent at a cancer centre that treats 323 patients per year, over a timeline of ten years. Two scenarios (described below) were compared. Each scenario was associated with different levels of operating capacity levels at the hypothetical cancer centre, which in turn, corresponded to waiting time for radiotherapy measured in weeks. The incremental costs were subtracted from the incremental benefits for each year \((t)\), and discounted at 3%. The values at each year were summed to generate the Net Present Value.

**Chapter 4.4A – Cost of Increasing Capacity**

In what follows is a presentation of the different scenarios used for increasing the capacity of the hypothetical cancer centre. As mentioned above, both assessment and treatment capacity need to be increased in order to see a rise in the number of patient spaces per week. Two scenarios were considered: increasing assessment capacity (by hiring an additional radiation oncologist) plus increasing treatment capacity in the form of purchasing new equipment; and b) increasing assessment capacity (by hiring an additional radiation oncologist as in a) plus increasing treatment capacity in form of hiring additional staff only.
Scenario A: Increase Assessment Capacity (Hiring a new Radiation Oncologist) Plus Increase Treatment Capacity (New Equipment)

Given that each radiation oncologist managed treatment for \(\frac{1,712}{8} = 214\) patients each (see Chapter 4.1), hiring a new radiation oncologist would create an additional 214 spaces per year. Assuming that the number of treatment machines (as opposed to diagnostic machines) limits the ability of the cancer centre to treat additional patients, purchasing a new linear accelerator creates additional treatment spaces. In the same method as performed by Earle, the value of depreciation was calculated in each year over the ten-year timeline. Four additional radiation therapists would be hired as well in order to maximize the use of the machine. The cost of hiring a new radiation therapist is $90,534 per year (including salary and benefits), so the cost of hiring four radiation therapists is \([90,534 \times 4 =] 362,136\). Linear accelerators represent \([\frac{461,126}{1,040,241} =] 44\%\) of equipment costs at the hypothetical centre. Accordingly, increasing the number of linear accelerators from two to three increases the cost of utilities to \([\frac{3}{2} \times 44\% \times 182,989 =] 120,773\), or an incremental increase of $40,258. A new bunker would be built to house the machine. According to Wodinsky (92), an additional $23,556 (adjusted for inflation to 2008 Canadian dollars) in construction costs would be incurred in each year. See Table 4.4.1 for a summary of all costs added due to increase in new equipment. Please note that the equipment cost presented in this table is the average depreciated amount.
Table 4.4.1 – Annual Cost of Adding a Linear Accelerator

<table>
<thead>
<tr>
<th>Resource input</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Linear Accelerator</td>
<td>$230,563</td>
</tr>
<tr>
<td>4 New radiation therapists</td>
<td>$362,136</td>
</tr>
<tr>
<td>Utilities</td>
<td>$40,258</td>
</tr>
<tr>
<td>Construction</td>
<td>$23,556</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$656,513</strong></td>
</tr>
</tbody>
</table>

Four linear accelerators at the CCSEO treated 1360 new patients. Therefore, a new machine would be able to treat \([1360/4=\] 340 new patients per year.

**Scenario B: Increase Assessment Capacity (Hiring a new Radiation Oncologist) Plus Increase Treatment Capacity (Additional Staff only)**

*Assessment capacity is increased as stated above.* If staffing were to limit a cancer centre’s ability to treat patients (i.e., adequate equipment available but not enough people to run it), new staff can be hired to expand capacity. Assuming that hiring new radiation oncologists does not decrease treatment waiting, that nurses do not participate much in the treatment of radiation patients, and that physicists are not involved in individual patient planning except in extreme cases, staffing increases largely concern radiation therapists. Since 23 radiation therapists (see Table 4.2.1) treated 1360 new patients per year (see Table 4.1.1) at the CCSEO hiring a new radiation therapist would create \([1360/23 = 59.13 \text{ or } 60\] new annual patient spaces.

The cost to create one space per week was multiplied by the number of additional weekly spaces required to reduce waiting to \(i\) weeks, as calculated by the capacity and waiting simulation model. These values were converted to the capacity increase and resulting cost per year. The cost of reducing waiting was the product of this multiplication. Table 4.4.2 summarizes the number of additional yearly spaces and the
yearly costs (in thousands of dollars) of increasing capacity to reduce waiting to various levels of $i$.

Table 4.4.2 – Capacity Increase (Assessment and Treatment Number of Spaces) and Costs (in thousands of dollars) to Reduce Waiting

| Increase Assessment Capacity and Buy New Linear Accelerator |
|---|---|---|---|---|---|---|---|---|---|---|
| $i$ | Assess | Treat | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 | Year 7 | Year 8 | Year 9 | Year 10 |
| 6 | 208 | 156 | $867 | $829 | $797 | $771 | $750 | $733 | $718 | $706 | $696 | $688 |
| 5 | 208 | 208 | $1,026 | $975 | $933 | $899 | $871 | $847 | $828 | $812 | $799 | $788 |
| 4 | 156 | 312 | $1,247 | $1,171 | $1,109 | $1,057 | $1,014 | $979 | $950 | $926 | $907 | $890 |
| 3 | 260 | 208 | $1,123 | $1,072 | $1,031 | $996 | $968 | $944 | $925 | $909 | $896 | $885 |
| 2 | 260 | 260 | $1,282 | $1,219 | $1,167 | $1,124 | $1,088 | $1,059 | $1,035 | $1,015 | $998 | $985 |
| 1 | 312 | 260 | $1,379 | $1,316 | $1,264 | $1,221 | $1,186 | $1,156 | $1,132 | $1,112 | $1,096 | $1,082 |

| Increase Assessment Capacity and Hire Additional Staff |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $i$ | Assess | Treat | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 | Year 7 | Year 8 | Year 9 | Year 10 |
| 6 | 208 | 156 | $624 | $624 | $624 | $624 | $624 | $624 | $624 | $624 | $624 | $624 |
| 5 | 208 | 208 | $703 | $703 | $703 | $703 | $703 | $703 | $703 | $703 | $703 | $703 |
| 4 | 156 | 312 | $762 | $762 | $762 | $762 | $762 | $762 | $762 | $762 | $762 | $762 |
| 3 | 260 | 208 | $800 | $800 | $800 | $800 | $800 | $800 | $800 | $800 | $800 | $800 |
| 2 | 260 | 260 | $878 | $878 | $878 | $878 | $878 | $878 | $878 | $878 | $878 | $878 |
| 1 | 312 | 260 | $975 | $975 | $975 | $975 | $975 | $975 | $975 | $975 | $975 | $975 |

“$i$” = Weeks of waiting  
“Assess” = Additional assessment spaces created per year  
“Treat” = Additional treatment spaces created per year

Chapter 4.4B – Benefits of Reduced Waiting

The Markov model was run 10,000 times to estimate averted treatment costs.

Expenditure was expected to be directly related to the lengths of waiting time (e.g., treatment for patients whose waiting time was reduced to 6 weeks were expected to cost more than patients whose waiting time was reduced to 2 weeks). The amount of money spent on patients treated at the hypothetical centre at different levels of waiting (in weeks) is presented in Table 4.4.3. In the hypothetical centre, 323 patients are treated each year, over ten years. Patients treated at the centre in Year 1 contribute ten years of follow-up expenditure; patients treated in Year 2 contribute nine years, and so on. The
The sum of annual expenditures at the level of the cancer centre, discounted to present day value, is presented in Table 4.4.3. Lengths of wait from 6 weeks to 1 week are presented, based on the output of the capacity and waiting model.

**Table 4.4.3 – Average Expenditure by Year and Length of Wait**

<table>
<thead>
<tr>
<th>$i$ (weeks)</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
<th>Year 7</th>
<th>Year 8</th>
<th>Year 9</th>
<th>Year 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>$476</td>
<td>$1,132</td>
<td>$1,671</td>
<td>$2,287</td>
<td>$3,019</td>
<td>$3,811</td>
<td>$4,656</td>
<td>$5,557</td>
<td>$6,482</td>
<td>$7,361</td>
</tr>
<tr>
<td>5</td>
<td>$464</td>
<td>$1,120</td>
<td>$1,637</td>
<td>$2,247</td>
<td>$2,933</td>
<td>$3,669</td>
<td>$4,474</td>
<td>$5,289</td>
<td>$6,120</td>
<td>$6,963</td>
</tr>
<tr>
<td>4</td>
<td>$459</td>
<td>$1,094</td>
<td>$1,614</td>
<td>$2,265</td>
<td>$3,013</td>
<td>$3,798</td>
<td>$4,636</td>
<td>$5,475</td>
<td>$6,325</td>
<td>$7,185</td>
</tr>
<tr>
<td>3</td>
<td>$459</td>
<td>$1,086</td>
<td>$1,601</td>
<td>$2,226</td>
<td>$2,958</td>
<td>$3,741</td>
<td>$4,582</td>
<td>$5,411</td>
<td>$6,256</td>
<td>$7,132</td>
</tr>
<tr>
<td>2</td>
<td>$455</td>
<td>$1,098</td>
<td>$1,619</td>
<td>$2,240</td>
<td>$2,971</td>
<td>$3,766</td>
<td>$4,604</td>
<td>$5,416</td>
<td>$6,235</td>
<td>$7,102</td>
</tr>
<tr>
<td>1</td>
<td>$453</td>
<td>$1,078</td>
<td>$1,584</td>
<td>$2,223</td>
<td>$2,966</td>
<td>$3,750</td>
<td>$4,587</td>
<td>$5,428</td>
<td>$6,278</td>
<td>$7,113</td>
</tr>
</tbody>
</table>

**Table 4.4.4 – Present Value of Expenditure for Selected Lengths of Wait**

<table>
<thead>
<tr>
<th>$i$ (weeks)</th>
<th>Lower 95% CI</th>
<th>Present Value</th>
<th>Upper 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>$29,750,000</td>
<td>$30,400,000</td>
<td>$31,150,000</td>
</tr>
<tr>
<td>5</td>
<td>$28,600,000</td>
<td>$29,150,000</td>
<td>$30,020,000</td>
</tr>
<tr>
<td>4</td>
<td>$29,100,000</td>
<td>$29,900,000</td>
<td>$30,750,000</td>
</tr>
<tr>
<td>3</td>
<td>$28,750,000</td>
<td>$29,600,000</td>
<td>$30,500,000</td>
</tr>
<tr>
<td>2</td>
<td>$28,700,000</td>
<td>$29,600,000</td>
<td>$30,300,000</td>
</tr>
<tr>
<td>1</td>
<td>$28,105,000</td>
<td>$28,970,000</td>
<td>$29,515,000</td>
</tr>
</tbody>
</table>

**Chapter 4.4C – Calculating Cost-Benefit**

The present value of incremental costs and the present value of incremental benefits (comparing weeks of waiting) were calculated. Because of the stochastic nature of the Markov modeling and the capacity and waiting model in which a normal distribution is approximated to reflect patient entry into the hypothetical cancer centre, as well as factors such as the low risk of recurrence in this population and the small relative risk increase due to waiting, the range for both incremental benefits and costs encompassed negative numbers. Table 4.4.5 shows the present value of costs and benefits when $i = 6$ and $j = 5$.
as representative weeks of waiting. The range of values for other comparisons is provided in the same table.

Table 4.4.5 – Present Value of Incremental Costs and Benefits

<table>
<thead>
<tr>
<th>Weeks of Waiting</th>
<th>PV Incremental Benefit</th>
<th>PV Incremental Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>New Equipment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Additional Staff</td>
</tr>
<tr>
<td>( i )</td>
<td>( j )</td>
<td>$1,250,000</td>
</tr>
</tbody>
</table>

A reduction in waiting from six to five weeks \((i = 6, j = 5)\) yields a Net Present Value of $162,000 under the “New Equipment” scenario, and $256,000 under the “New Staff” scenario. By increasing the capacity level of the hypothetical cancer centre such that the costs of such an investment yield a reduction in waiting for radiotherapy from 6 to 5 weeks, results in a net gain ranging between $162,000 and $256,000 (depending on the type of capacity increase) when considering the averted treatment costs of breast cancer recurrence.

The Benefit-to-Cost ratios (BCRs) yielded 1.04 (new equipment) and 1.62 (additional staff): every $1 spent in increasing the capacity of the cancer centre through purchasing new equipment (and staff to run the equipment) yielded $1.04 in benefits (or averted treatment costs due to a decrease in recurrence); and every $1 expended in increasing capacity through hiring additional staff yielded $1.62 in benefits (averted treatment costs).

Chapter 4.5 – Sensitivity Analysis

The estimates of values used to calculate costs (equipment, salary, overhead, depreciation rate) and benefits (transition probabilities, costs of treatment, relative risk of recurrence) were adjusted above and below their baseline values to determine the extent
to which variation in any one value at a time affected the cost-benefit calculation in a one-way sensitivity analysis, best/worst case sensitivity analysis (values were altered simultaneously in turn to a best case and then to a worst case scenario), and probabilistic sensitivity analyses (values were allowed to vary according to an underlying statistical distribution (1)) (see Table 4.5.1). Transition probabilities varied according to a Gaussian (normal) distribution ($s = 0.01$), treatment costs according to a Poisson distribution ($\lambda =$ point estimate for cost), and the relative risk of recurrence due to waiting according to a log-normal distribution ($\sigma = 0.01$) (93). A population of pre-menopausal patients was also modeled by doubling the risk of local recurrence (54).
### Table 4.5.1 – Sensitivity Analysis of Costs and Benefits

<table>
<thead>
<tr>
<th>Input</th>
<th>Baseline</th>
<th>Range</th>
<th>Source</th>
<th>NPV EQ</th>
<th>NPV Stf</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capacity and Waiting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Capacity</td>
<td>9/7 (Assessment /Treatment)</td>
<td>6/4 12/10</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Statistical Distribution of Referral</td>
<td>Normal (Gaussian)</td>
<td>Poisson (14)</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Standard Deviation of Referrals</td>
<td>4.17</td>
<td>3.17 – 5.17</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td><strong>Costs and Benefits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiation Oncologist Salary</td>
<td>$400,000</td>
<td>$200,000 - $600,000</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Radiation therapist salary</td>
<td>$75,445</td>
<td>$65,000 - $85,000</td>
<td></td>
<td>$230,000</td>
<td>$646,000</td>
</tr>
<tr>
<td>Purchase price of linear accelerator</td>
<td>$2,700,000</td>
<td>$2,400,000 - $3,000,000</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Depreciation rate</td>
<td>17.5%</td>
<td>15% - 20%</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Overhead cost</td>
<td>$40,258</td>
<td>$30,000 - $50,000</td>
<td></td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Cost of recurrence treatment</td>
<td>$12,000</td>
<td>$8,300 - $13,100</td>
<td>Table 4.4.1</td>
<td>$134,000</td>
<td>$521,000</td>
</tr>
<tr>
<td>Cost of metastatic treatment</td>
<td>$40,000</td>
<td>$36,000 - $45,000</td>
<td>(24,65)</td>
<td>$61,000</td>
<td>$448,000</td>
</tr>
<tr>
<td>Cost of end-of-life treatment</td>
<td>$18,000</td>
<td>$12,600 - $34,300</td>
<td>(68;82)</td>
<td>$114,000</td>
<td>$501,000</td>
</tr>
<tr>
<td><strong>Probability of “Well” to “Local Recurrence”</strong></td>
<td>0.067</td>
<td>0.02 - 0.20</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Probability of “Well” to “Metastatic Disease”</td>
<td>0.11</td>
<td>0.05 - 0.2</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Probability of “Local Recurrence” to “Metastatic Disease”</td>
<td>0.2</td>
<td>0.1 - 0.4</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Probability of “Metastatic Disease – “Death””</td>
<td>0.328</td>
<td>0.164 - 0.492</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Relative Risk of Recurrence per week</td>
<td>1.025</td>
<td>1.01 - 1.0375</td>
<td>(77)</td>
<td>- $220,000</td>
<td>$167,000</td>
</tr>
<tr>
<td><strong>Probabilistic Sensitivity Analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transition Probabilities</td>
<td></td>
<td>Normal distrib. (s = 0.1)</td>
<td>(93)</td>
<td>$171,000</td>
<td>$558,000</td>
</tr>
<tr>
<td>Costs of treatment</td>
<td></td>
<td>Poisson distrib.</td>
<td>(93)</td>
<td>$171,000</td>
<td>$558,000</td>
</tr>
<tr>
<td>Relative Risk of Recurrence due to Waiting</td>
<td></td>
<td>Log-normal distrib. (σ = 0.1)</td>
<td>(93)</td>
<td>$171,000</td>
<td>$558,000</td>
</tr>
<tr>
<td><strong>Menopausal Status of Patients</strong></td>
<td></td>
<td>Post-menopausal</td>
<td>(54)</td>
<td>$1,057,000</td>
<td>$1,444,000</td>
</tr>
<tr>
<td><strong>Discount Rate</strong></td>
<td></td>
<td>Pre-menopausal</td>
<td>(54)</td>
<td>$1,057,000</td>
<td>$1,444,000</td>
</tr>
</tbody>
</table>

NPV EQ – Increase assessment capacity and buy new equipment  
NPV Stf – Increase assessment capacity and hire new staff  
N/A – Adjustment yielded negative result for benefits
Chapter 5 – Manuscript

This manuscript is written according to specifications for submission to the peer-reviewed journal *Journal of Radiation Oncology, Biology, Physics*.

**Title:**

Cost-benefit analysis of reducing waiting times for post-surgical radiotherapy: An example for early breast cancer

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INTRODUCTION

Waiting times for radiotherapy have been a concern in the health care system since the late 1980s (94). Waiting lists accumulate due to fluctuations in demand for a resource provided to meet the average needs of the population (15). When demand at a given point exceeds the capacity of the system (i.e., there are more patients needing treatment than there are spaces to treat them), patients must wait to be assessed and treated (15). Increasing the capacity of a cancer centre is one potential method to reduce waiting lists, but this increased capacity comes with a monetary cost. Cancer centres are staffed by radiation oncologists, nurses, physicists, radiation therapists, and various support and maintenance staff (21).

Patients are commonly diagnosed using X-ray imagery, Magnetic Resonance Imaging (MRI) and/or Computer Tomography (CT) scanning, and are treated with X-ray radiation delivered from linear accelerators (21,22). The treatment of cancer requires the utilization of the resources identified above (staffing, equipment), as well as costs associated with the operation of the facility (i.e., utilities, administrative staff, overhead costs) (27;35;39;61). However expensive it may be to increase the capacity of a cancer centre, there are also costs associated with allowing patients to wait for radiotherapy. Patients for whom radiotherapy is delayed have a greater likelihood of their disease returning when compared to patients who do not wait (12;36;56). If care is delivered to treat above-average demand, then waiting lists can be controlled (14). Increasing the capacity of a cancer centre requires increased expenditure by the health care system; however, there is likely to be a corresponding decrease in downstream health care expenditure as a result of a possible decrease in recurrence rates.
This study presents a methodology for investigating the additional cost, if any, of increasing the capacity of a cancer centre to reduce radiotherapy waiting times. A cost-benefit analysis is used. In such an analysis, both costs and benefits are described in monetary terms. As an illustration, a simplified hypothetical cancer centre (that treats early breast cancer cases following breast-conserving therapy for post-menopausal women) is created based on data from the Cancer Centre of Southeastern Ontario (CCSEO), in Kingston, Ontario, Canada. This population was chosen due to its relative homogeneity compared to other cancer sites, as well as evidence of association between waiting and recurrence for breast cancer in the clinical trials literature.

A review of early breast cancer clinical trials found that radiotherapy reduced rates of local recurrence (re-growth of cancerous cells after surgical intervention), when compared to regimens that did not include radiotherapy, by 66% (44). Chen and colleagues reviewed 22 clinical trials and conducted a meta-analysis on the relationship between waiting and recurrence (77). The review found a relative risk of local recurrence of 1.10 per month of waiting for breast cancer radiotherapy (77). Lamerato and colleagues analyzed a cohort of cancer patients based on administrative data from the United States (61). The investigators found that the cost of treating breast cancer recurrence was higher than the cost of first-line treatment, even though the up-front cost of treatment was higher in non-recurring patients (61).

**STUDY DESIGN AND METHODS**

In this study, a cost-benefit methodology of reducing waiting times to avert treatment as a result of waiting is presented. Cost-benefit analysis is a full economic evaluation that allows for the comparison of the net cost of implementation of a program or policy.
approach with the net benefit experienced due to the implementation (1). Both costs and benefits are expressed in monetary terms. This approach stands out as a method for economic evaluation because it allows for direct comparisons of two or more policy strategies that are likely to have monetarily positive (beneficial) and negative (costly) outcomes (2). Results from this type of analysis can provide policy makers with a clear summary measure of the economic consequence of a policy change (i.e., returns on investing in federal/provincial resources).

This type of analysis differs significantly from other commonly used economic analysis techniques – such as cost-effectiveness, in which the incremental cost of a health program is compared to the incremental change in a relevant health outcome (e.g., life-years gained), or cost-utility, where the incremental cost is compared to changes in quality-adjusted measures (e.g., quality-adjusted life years). Cost-benefit is distinct in that it allows the combination of several different kinds of benefits into one summary measure, rather than expressing a cost-per-health-outcome (1).

The cost-benefit analysis proposed here requires several analytic steps: (i) estimating the number of new patient spaces required in the system to reduce waiting times to policy-relevant lengths (capacity and waiting); (ii) determining the cost of increasing capacity (estimation of costs); (iii) calculating the economic benefits of reducing waiting to policy-relevant lengths (estimation of benefits); (iv) calculating the net present value (NPV); and (v) conducting sensitivity analysis to assess the robustness of the results given uncertainty surrounding various parameters.

All monetary values in this analysis are measured in 2008 Canadian dollars, adjusted for inflation according to the Consumer Price Index. A time horizon of ten years is
chosen to reflect the relevant life for medical equipment (71,72) and the time window for local recurrence (55). Future costs and benefits are discounted at a rate of 3% (75).

**Capacity and Waiting** - Waiting in this study is defined as the amount of time between a patient being referred to a radiotherapy clinic and the date of the first radiation treatment, and is measured as the number of weeks that the last patient on the waiting list can expect to wait. In order to determine the size of the capacity increase required to reduce waiting, a simulation model is constructed. The simulation model differentiates between two distinct types of waiting that can occur in a cancer centre: waiting in the assessment phase (Referral to Consult), and in the treatment phase (Ready-to-Treat to Treatment) (47). This methodology makes the assumption that patients are referred to a cancer centre for radiotherapy immediately after they are deemed ready to be treated.

The simulation operates as follows. Patients enter the cancer centre and are assessed by a radiation oncologist. If there are no available radiation oncologists, patients must wait for a space to become available. Once they are assessed, they are treated on a linear accelerator. If there is no space for new patients available at the linear accelerator, they wait. Patients are treated for three weeks then move out of the cancer centre, and their treatment spaces are filled by patients on the waiting list. The period of the simulation is ten years (520 weeks). The process is illustrated in Figure 1.
Figure 1 – Cancer Centre Patient Flow

NewPatients: Patients referred into the cancer centre for radiotherapy
Assessment: Waiting to be assessed by a radiation oncologist (assessment waiting)
ToRadOnc: Transition to radiation oncologist assessment
RadOnc: Patient being assessed by radiation oncologist
Assessed: Transition to treatment phase
Treatment: Waiting to be treated on linear accelerator (treatment waiting)
ToTx: Transition to treatment on linear accelerator
RT: Patient being treated by radiation oncologist
TreatTime: Transition out of cancer centre
Treated: Patient has been assessed and treated and moves out of cancer centre

To calculate the association between cancer centre capacity and waiting times, the simulation program is run for 1000 iterations, and the total waiting time (assessment plus treatment) is reported at six-month intervals over the ten-year timeline. The average of upper 95% confidence value of total waiting times ($i$ weeks of waiting) is calculated at each six-month interval for different levels of assessment and treatment capacity. Since different combinations of capacity levels may result in the same waiting time, the level that requires the smallest capacity increase – the fewest additional spaces – is chosen.

**Estimation of Costs** – Costs are grouped into sub-categories: personnel (nurses, physicians, physicists, radiation therapists), equipment (Computed Tomography scanner, Magnetic Resonance Imaging scanner, linear accelerator, planning Computed
Tomography, X-ray machines, concrete bunker), and overhead (administration, secretarial, utilities).

Two distinct scenarios for increasing the capacity of a cancer centre are considered as follows: a) increasing assessment capacity by hiring new radiation oncologists plus increasing treatment capacity by buying new treatment machines and hiring additional staff; and (b) increasing assessment capacity (as in a) plus increasing treatment capacity by hiring additional staff to use existing treatment infrastructure.

**Estimation of Benefits** - Benefits are calculated by estimating averted costs of treating cancer recurrence, as well as any downstream health consequences (i.e., metastatic disease, terminal illness). A Markov model (a statistical technique that simulates the transition of patients among health states) is used to estimate the benefits of avoided recurrence (53). Patients waiting for radiotherapy start in the model in the “Well” state, (see Figure 2). From this state, a patient transitions to other disease states: local recurrence; no evidence of disease (NED) after operation; and distant metastasis. A patient then can transition into death from breast cancer and death from other causes (the two feasible terminal states). The model assumes that a patient’s history is not relevant to his/her transition into different cycles, otherwise known as the “Markov memoryless assumption.”
**Cost-Benefit Analysis** – In the cost-benefit analysis, two hypothetical cohorts of patients are examined at a time: a group that waits $i$ weeks following surgery for radiotherapy, and one that waits $j$ weeks (waiting lengths informed by the Capacity and Waiting Simulation model). Thus, the incremental cost-benefit of increasing capacity is calculated using Equation 1

$$NPV = \sum_{t=0}^{N} \frac{(Benefits_i - Benefits_j) - (Costs_i - Costs_j)}{(1+r)^t}$$

where
- $t = \text{year (from 0, 1, 2, ... N)}$,
- $N = \text{number of years being valued}$,
- $r = \text{discount rate}$,
- $i = 2, 3, 4,...n \text{ weeks of waiting}$
- $j = 1, 2, 3,...m \text{ weeks of waiting}$

The incremental costs of increasing the capacity of a cancer centre to reduce waiting (from $i$ weeks to $j$ weeks) are subtracted from the incremental benefit (averted recurrence treatment costs) due to decreased waiting ($i$ to $j$ weeks) for each year of analysis ($t$). A discount rate of 3% is used. Finally, all annual incremental values are added to yield the Net Present Value for each scenario of capacity increase. A Net Present Value larger than 0 indicates that the incremental benefit of increasing capacity measured in terms of
averted recurrence treatment costs at cancer centres outweighs the incremental cost of increasing capacity.

The Net Present Value is useful in a decision-making context, but may not present all relevant information that a policy-maker needs in order to make a decision. Using Net Present Value to allocate resources can pose problems because the final result (the absolute difference between discounted benefits and costs) provides no direct information about resource requirements of a project. For example, if a policy maker were told only that the Net Present Value of increasing cancer centre capacity were $2,000,000 and that it was the largest capacity increase, he or she would have no idea that $20,000,000 worth of resources would be needed to implement the capacity increase. What if the decision maker did not have any access to such resources? Thus, it is sometimes useful, when presenting a Net Present Value, to also present the discounted benefits and costs. This additional information gives the audience some idea of the scale of investment that is being analyzed.

A Benefit-to-Cost ratio (BCR) is also calculated, wherein the total benefit is divided by the total cost according to Equation 2:

$$ BCR = \frac{PV_{Benefits}}{PV_{Costs}} $$

where

$PV_{Benefit} = \text{Present Value of Benefits}$

$PV_{Cost} = \text{Present Value of Costs}$

**Sensitivity Analysis** – One-way sensitivity analysis, “best/worst case” sensitivity analysis, and probabilistic sensitivity analysis are computed for cost and benefit inputs: costs (cost of equipment, salary, overhead) and benefits (risk of recurrence, transition probabilities, costs of medical treatment).
RESULTS

In order to illustrate the methodology presented here, a simplified hypothetical cancer centre (that treats only early breast cancer cases following breast-conserving surgery) was created based on data from the literature and from the Cancer Centre of Southeastern Ontario (CCSEO) in Ontario, Canada for the fiscal year 2007/2008. Resources utilized and budgetary information regarding the operation of the CCSEO were obtained by conducting face-to-face interviews with radiotherapy practitioners and administrative staff at the CCSEO. The patient population chosen for the illustrative example consists of postmenopausal women, aged 55 years or older, having undergone breast-conserving surgery for the treatment of early breast cancer (stage I/IIa with no evidence of lymph node involvement, or T1N0M0/T2N0M0) was created. This population was chosen because of evidence from the literature regarding the risk of recurrence, and treatment for this population tends to be more homogenous than for other cancer populations.

The Cancer Centre of Southeastern Ontario (CCSEO)

The CCSEO, formerly the Kingston Regional Cancer Centre, is a provincial cancer centre contained within the Kingston General Hospital in Kingston, Ontario, Canada. The radiotherapy clinic within the centre has four linear accelerators and one Computed Tomography (CT) simulation machine, in addition to various diagnostic and radiology machines. During the 2007/2008 fiscal year, the radiotherapy clinic at CCSEO served 1360 new cancer patients, 323 of which were breast cancer cases. A total of 24,829 fractions of radiation were administered, 7177 of which were for breast cancer.

Capacity and Waiting
Capacity for the assessment and treatment phases in the hypothetical ‘breast-only’ centre was determined based on the number of clinic visits (assessment phase) and new radiation cases (treatment phase) at the CCSEO during the 2007/2008 fiscal year. Note that since it is not possible to assess a fraction of a patient, values were rounded up. Eight radiation oncologists assessed 1,712 new patients, or \( \lceil \frac{1,712}{8} \rceil = 214 \) each per year, at the CCSEO. Given that the hypothetical ‘breast-only’ centre in this analysis is set up to treat 323 patients per year, two radiation oncologists were required \((214 \text{ patients per year} \times 2 \text{ radiation oncologists} = 428 \text{ patients per year})\) to assess at least the 323 hypothetical cohort of breast cancer patients. This yields a theoretical assessment capacity of \( \lceil \frac{428}{52 \text{ weeks per year}} \rceil = 8.23 \text{ patients per week, rounded up to 9.} \) If treatment capacity is equal to average demand, the weekly treatment capacity is \( \lceil \frac{323 \text{ patients}}{52 \text{ weeks per year}} \rceil = 7 \text{ spaces per week.} \) The length of treatment time was based on practice guidelines and assumed to be 3 weeks (45).

New patient entry into the hypothetical cancer centre was approximated to a Normal (Gaussian) distribution (\( s = 4.17, p = 0.177, \text{ Anderson-Darling test} = 0.5320 \)). The 90th percentile wait for breast cancer patients is currently (historical records from the CCSEO for March, 2009) 5 and 4 weeks for the assessment and treatment phases, respectively. To determine the number of patients waiting, the length of wait (in weeks) was multiplied by the number of new assessment and treatment patients per week. Therefore, the number of patients waiting at the beginning of the model run was \( 9 \times 5 = 45 \) and \( 7 \times 4 = 28 \) during the assessment and treatment phases, respectively.

The capacity of the hypothetical ‘breast-only’ centre was calculated based on the number of breast cancer patients seen and the average demand for services at the
CCSEO. Eight radiation oncologists assessed 1,712 new patients at the CCSEO during fiscal year 2007/2008. This works out to a figure of \( \frac{1,712}{8} = 214 \) new patients per radiation oncologist per year, or \( \frac{214}{52} = 4.12 \) or 5 patients per week. Four linear accelerators delivered 24,829 fractions of radiotherapy. Each machine, therefore, delivered \( \frac{23,829}{4} = 6207.25 \) or 6,208 fractions in the 2007/2008 year. As of March 2009, the 90th percentile waiting time for breast cancer treatment at the CCSEO was 5 weeks for assessment, and 4 weeks for treatment.

Thus, the hypothetical centre was set up to treat 323 new patients per year based on the number of breast cancer patients that were actually treated at CCSEO. Given that one radiation oncologist would assess 214 patients (see above), for the hypothetical centre, two radiation oncologists were needed to assess at least the 323 hypothetical cohort of breast cancer patients. Since 4.12 patients are seen weekly by one radiation oncologist (based on CCSEO from above), the hypothetical centre with two radiation oncologists can assess \( 4.12 \times 2 = 8.24 \) patients per week. The average demand at the cancer centre equals to the number of patients that the centre can expect to treat in a given week. Since the hypothetical centre (and the CCSEO) treats 323 breast cancer patients per year, the average number of patients per week treated is \( \frac{323}{52} = 6.21 \) or 7.

Likewise, prevailing waiting times at the hypothetical centre were estimated based on historical data from the CCSEO. Based on the 90th percentile waiting time for breast cancer treatment at the CCSEO and given that the assessment capacity of the hypothetical ‘breast-cancer only’ centre is nine patients per week, and treatment capacity is seven patients per week, the number of patients waiting was calculated to be \( 5 \times 9 = 45 \) and
[4x7 =] 28, respectively. These numbers were included at the beginning of the simulation run.

**Estimation of Costs**

Costs for the hypothetical centre were based on operating costs for the CCSEO (Table 1). The staffing level for the hypothetical ‘breast-cancer only’ centre was determined by dividing the number of staff by the number of patients assessed/treated at the CCSEO. The yearly cost of medical equipment was depreciated over a useful life of ten years (72,71) according to a “straight-line depreciation” method (69). At the CCSEO, four linear accelerators delivered 24,829 fractions of radiotherapy in the 2007/2008 fiscal year, of which 7,177 were for breast cancer. A linear accelerator delivered approximately 6200 fractions per year at the CCSEO, new patient spaces, meaning that two machines are needed for the hypothetical centre. Since breast cancer fractions represented [7,177/24,829 =] 29% of total cancer centre radiotherapeutic output, the overhead costs for the hypothetical centre were calculated to be equal to [5,168,954 x 29% =] $1,498,997. Other facility costs include finance, human resources, purchasing, rent, telecommunications, public relations, and information systems.

**Table 1– Operating Costs for Cancer Centre**

<table>
<thead>
<tr>
<th>Input Category</th>
<th># of Input at CCSEO</th>
<th># of Input at Hypothetical Centre</th>
<th>Cost Per Item</th>
<th>Annual Cost at Hypothetical Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing</td>
<td>7.5</td>
<td>1</td>
<td>$88,475</td>
<td>$88,475</td>
</tr>
<tr>
<td>Radiation Therapist</td>
<td>23</td>
<td>8</td>
<td>$90,534</td>
<td>$724,272</td>
</tr>
<tr>
<td>Radiation Oncologist</td>
<td>8</td>
<td>2</td>
<td>$400,000</td>
<td>$800,000</td>
</tr>
<tr>
<td>Physicist</td>
<td>5</td>
<td>1</td>
<td>$154,300</td>
<td>$154,300</td>
</tr>
<tr>
<td></td>
<td><strong>Salary Subtotal</strong></td>
<td></td>
<td><strong>$1,767,047</strong></td>
<td></td>
</tr>
<tr>
<td>Linear Accelerator</td>
<td>4</td>
<td>2</td>
<td>$2,700,000</td>
<td>$461,126</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging Machine</td>
<td>1</td>
<td>1</td>
<td>$2,750,000</td>
<td>$2,750,000</td>
</tr>
<tr>
<td></td>
<td>Qty</td>
<td>Qty</td>
<td>Cost</td>
<td>Cost</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----</td>
<td>-----</td>
<td>-----------</td>
<td>-------</td>
</tr>
<tr>
<td>X-Ray Machine</td>
<td>2</td>
<td>1</td>
<td>$500,000</td>
<td>$500,000</td>
</tr>
<tr>
<td>Computed Tomography Simulator</td>
<td>1</td>
<td>1</td>
<td>$1,740,000</td>
<td>$1,740,000</td>
</tr>
<tr>
<td>Mammography Machine</td>
<td>3</td>
<td>1</td>
<td>$800,000</td>
<td>$800,000</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>4</td>
<td>2</td>
<td>$220,000</td>
<td>$440,000</td>
</tr>
<tr>
<td>Concrete Bunker</td>
<td>4</td>
<td>2</td>
<td>$235,559 (92)</td>
<td>$471,118</td>
</tr>
<tr>
<td><strong>Equipment Subtotal</strong></td>
<td></td>
<td></td>
<td><strong>$1,040,241</strong></td>
<td></td>
</tr>
<tr>
<td>Utilities</td>
<td></td>
<td></td>
<td>$182,989</td>
<td></td>
</tr>
<tr>
<td>Administration/Secretarial</td>
<td></td>
<td></td>
<td>$197,200</td>
<td></td>
</tr>
<tr>
<td>Other Facility Costs</td>
<td></td>
<td></td>
<td>$1,118,808</td>
<td></td>
</tr>
<tr>
<td><strong>Overhead Subtotal</strong></td>
<td></td>
<td></td>
<td><strong>$1,498,997</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Total Annual Operation Cost</strong></td>
<td></td>
<td></td>
<td><strong>$4,306,285</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Estimation of Benefits**

Benefits were measured as averted costs of treatment due to recurrence. Averted costs of recurrence were calculated using a Markov model over ten years, in 20 cycles lasting 6 months each and values from the literature to populate the model (Table 2). Follow-up was comprised of the cost to the health care system of regular post-treatment screening for a breast cancer patient. Local recurrence treatment was made up of the diagnosis (clinical screening, radiology, biopsy) and treatment (radical mastectomy with systemic therapy) of locally recurrent disease. The cost of treating metastatic breast cancer and of end-of-life care (including hospitalization, palliative care, systemic therapy) for cancer patients estimated based on studies in the literature. The model was run for 10,000 iterations.
Table 2. Inputs in Markov Model

<table>
<thead>
<tr>
<th>Input</th>
<th>Value</th>
<th>Range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transition Probabilities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Well” to “Local Recurrence”</td>
<td>6.7% (1-5 yr)</td>
<td>2–20%</td>
<td>(78)</td>
</tr>
<tr>
<td>“Well” to “Metastatic Disease”</td>
<td>3.3% (6-10 yr)</td>
<td>2–5%</td>
<td>(78)</td>
</tr>
<tr>
<td>“Local Recurrence” to “Metastatic Disease”</td>
<td>11% (10 yr)</td>
<td>5–20%</td>
<td>(79)</td>
</tr>
<tr>
<td>“Metastatic Disease” to “Death from Cancer”</td>
<td>20% (10 yr)</td>
<td>10–40%</td>
<td>(80)</td>
</tr>
<tr>
<td>Any State to “Death from Other Cause”</td>
<td>38% (1 yr)</td>
<td>16.4–49.2%</td>
<td>(81)</td>
</tr>
<tr>
<td>Relative Risk of Local Recurrence due to Waiting (per week)</td>
<td>1.025 (1 wk)</td>
<td>1.01–1.0375</td>
<td>(77)</td>
</tr>
<tr>
<td><strong>Costs of Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up (Years 1-2)</td>
<td>$1192.12</td>
<td>–</td>
<td>(90)</td>
</tr>
<tr>
<td>(Years 3+)</td>
<td>$367.62</td>
<td>(19;21;47;62;63)</td>
<td></td>
</tr>
<tr>
<td>Local Recurrence</td>
<td>$12,000</td>
<td>$8,300 - $13,100</td>
<td>(19;21;47;62;63)</td>
</tr>
<tr>
<td>Metastatic Disease</td>
<td>$40,000</td>
<td>$36,000 - $45,000</td>
<td>(22;85)</td>
</tr>
<tr>
<td>Death</td>
<td>$18,000</td>
<td>$12,600 - $34,300</td>
<td>(83)</td>
</tr>
</tbody>
</table>

**Cost-Benefit Calculation**

The costs and benefits experienced by two cohorts, one that has waited $i$ weeks and one that has waited $j$ weeks to receive radiotherapy were compared over a timeline of ten years. The values for costs and benefits were determined as described above. Values for $i$ and $j$ were determined based on the output of the simulation model. Two different scenarios for increasing the capacity of the centre were considered.

**Scenario A: Increase Assessment Capacity (Hiring a new Radiation Oncologist) Plus Increase Treatment Capacity (New Equipment)**

The annual salary for a radiation oncologist is $400,000. Given that 8 radiation oncologists assessed 1,712 new patients at the CCSEO during the 2007/2008 fiscal year,
it can be calculated that each physician assesses \(\frac{1712}{8} = 214\) patients. If a new radiation oncologist is hired, this corresponds to a cost of \(\frac{400,000}{214} = \$1900\) per space. To add a linear accelerator, the following annual costs are incurred

\begin{itemize}
  \item[a)] linear accelerator at an average depreciated cost = \$230,563 \text{(Table 1)};
  \item[b)] four additional radiation therapists = \(\frac{90,534 \times 4}{1} = \$362,136\) \text{(Table 1)};
  \item[c)] a new bunker = \$23,556 \text{(92)}
  \item[d)] utilities = \$40,258 \text{ (utilities costs increased by 44\%, increasing the number of linear accelerators from 2 to 3)}
\end{itemize}

for a total cost = \(\$230,563 + \$326,136 + \$23,556 + \$91,494 = \$707,749\). Adding a linear accelerator creates \(\frac{1360 \text{ new spaces}}{4 \text{ linear accelerators at CCSEO}} = \) 340 spaces per year.

**Scenario B: Increase Assessment Capacity (Hiring a new Radiation Oncologist) Plus Increase Treatment Capacity (Additional Staff only)**

Assessment capacity is increased as stated above. In this scenario, treatment capacity was increase to expand capacity. Assuming that hiring new radiation oncologists does not decrease treatment waiting, that nurses do not participate much in the treatment of radiation patients, and that physicists are not involved in individual patient planning except in extreme cases, staffing increases largely concern radiation therapists. The cost of hiring one new radiation therapist is \$90,534. Given that 23 radiation therapists treat 1360 new patients per year (at the CCSEO), hiring a new radiation therapist would create \(\frac{1360}{23} = 59.12 \text{ or} \) 60 new annual patient spaces.

For the cost-benefit analysis, the present value of incremental costs and the present value of incremental benefits (comparing weeks of waiting) were calculated. Because of
the stochastic nature of the Markov modeling and the capacity and waiting model in which a normal distribution is approximated to reflect patient entry into the hypothetical cancer centre, as well as factors such as the low risk of recurrence in this population and the small relative risk increase due to waiting, the range for both incremental benefits and costs encompassed negative numbers. Table 4.4.5 shows the present value of costs and benefits when \( i = 6 \) and \( j = 5 \). The range of values for other comparisons is provided in the same table.

Table 3 – Present Value of Incremental Costs and Benefits

<table>
<thead>
<tr>
<th>Weeks of Waiting</th>
<th>PV Incremental Benefit</th>
<th>PV Incremental Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>( i ) ( j )</td>
<td>( i ) ( j )</td>
<td>( i ) ( j )</td>
</tr>
<tr>
<td>6 5</td>
<td>$1,250,000</td>
<td>$1,208,000</td>
</tr>
<tr>
<td>6 to 1 6 to 1</td>
<td>(-$768, $1,417,000)</td>
<td>(-$497,000, $4,334,000)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>($369,000, $3,466,000)</td>
</tr>
</tbody>
</table>

A reduction in waiting from six to five weeks \( i = 6, j = 5 \) yields a Net Present Value of $42,000 under the “New Equipment” scenario, and $476,000 under the “New Staff” scenario. By increasing the capacity level of the hypothetical cancer centre such that the costs of such an investment yield a reduction in waiting for radiotherapy from 6 to 5 weeks, results in a net gain ranging between $42,000 and $476,000 (depending on the type of capacity increase) when considering the averted treatment costs of breast cancer recurrence. The Benefit-to-Cost ratios (BCRs) yield 1.04 (new equipment) and 1.62 (additional staff), or there will be $1.04 in benefits for every $1 in costs (new equipment), and there will be $1.62 in benefits for every $1 in costs (additional staff).
**Sensitivity Analysis**

The estimates of values used to calculate costs (equipment, salary, overhead, depreciation rate) and benefits (transition probabilities, costs of treatment, relative risk of recurrence) were adjusted above and below their baseline values to determine the extent to which variation in any one value at a time affected the cost-benefit calculation in a one-way sensitivity analysis, best/worst case sensitivity analysis (values are altered simultaneously in turn to a best case and then to a worst case scenario), and probabilistic sensitivity analyses (values are allowed to vary according to an underlying statistical distribution (1)) (see Table 4). Transition probabilities varied according to a Gaussian (normal) distribution ($s = 0.01$), treatment costs according to a Poisson distribution ($\lambda = \text{point estimate for cost}$), and the relative risk of recurrence due to waiting according to a log-normal distribution ($\sigma = 0.01$) (93). A population of pre-menopausal patients was also modeled by doubling the risk of local recurrence (45).
Table 4 – Sensitivity Analysis of Costs and Benefits

<table>
<thead>
<tr>
<th>Input</th>
<th>Baseline</th>
<th>Range</th>
<th>Source</th>
<th>NPV EQ</th>
<th>NPV Stf</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capacity and Waiting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Capacity</td>
<td>9/7 (Assessment /Treatment)</td>
<td>6/4 12/10 ±3</td>
<td>$162,000</td>
<td>$549,000</td>
<td></td>
</tr>
<tr>
<td>Statistical Distribution of Referral</td>
<td>Normal (Gaussian)</td>
<td>Poisson (14)</td>
<td>$162,000</td>
<td>$549,000</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation of Referrals</td>
<td>4.17</td>
<td>3.17 – 5.17 ±1.00</td>
<td>$162,000</td>
<td>$549,000</td>
<td></td>
</tr>
<tr>
<td><strong>Costs and Benefits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiation Oncologist Salary</td>
<td>$400,000</td>
<td>$200,000 - $600,000</td>
<td>±50%</td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Radiation therapist salary</td>
<td>$75,445</td>
<td>$65,000 - $85,000</td>
<td>±$10,000</td>
<td>$230,000</td>
<td>$646,000</td>
</tr>
<tr>
<td>Purchase price of linear accelerator</td>
<td>$2,700,000</td>
<td>$2,400,000 - $3,000,000</td>
<td>±$300,000</td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Depreciation rate</td>
<td>17.5%</td>
<td>15% - 20% ±2.5%</td>
<td>$162,000</td>
<td>$549,000</td>
<td></td>
</tr>
<tr>
<td>Overhead cost</td>
<td>$40,258</td>
<td>$30,000 - $50,000</td>
<td>±$10,000</td>
<td>$162,000</td>
<td>$549,000</td>
</tr>
<tr>
<td>Cost of recurrence treatment</td>
<td>$12,000</td>
<td>$8,300 - $13,100</td>
<td>Table 4.4.1</td>
<td>$134,000</td>
<td>$521,000</td>
</tr>
<tr>
<td>Cost of metastatic treatment</td>
<td>$40,000</td>
<td>$36,000 - $45,000</td>
<td>(24,65)</td>
<td>$61,000</td>
<td>$448,000</td>
</tr>
<tr>
<td>Cost of end-of-life treatment</td>
<td>$18,000</td>
<td>$12,600 - $34,300</td>
<td>(68;82)</td>
<td>$114,000</td>
<td>$501,000</td>
</tr>
<tr>
<td>Probability of “Well” to “Local Recurrence”</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5 years</td>
<td>0.067</td>
<td>0.02 - 0.20</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>6-10 years</td>
<td>0.033</td>
<td>0.02 - 0.05</td>
<td>(78)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Probability of “Well” to “Metastatic Disease”</td>
<td>0.11</td>
<td>0.05 - 0.20</td>
<td>$679,000</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Probability of “Local Recurrence” to “Metastatic Disease”</td>
<td>0.2</td>
<td>0.1 - 0.4</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Probability of “Metastatic Disease – “Death”</td>
<td>0.328</td>
<td>0.164 - 0.492</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Relative Risk of Recurrence per week</td>
<td>1.025</td>
<td>1.01 - 1.0375</td>
<td>(77)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>“Best Case” Scenario</td>
<td></td>
<td></td>
<td></td>
<td>$2,770,000</td>
<td>$3,050,000</td>
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<tr>
<td>“Worst Case” Scenario</td>
<td></td>
<td></td>
<td></td>
<td>-$883,849-$604,008</td>
<td></td>
</tr>
<tr>
<td><strong>Probabilistic Sensitivity Analysis</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Transition Probabilities</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Costs of treatment</td>
<td>Normal distrib. (s = 0.1)</td>
<td>Poisson distrib. (95)</td>
<td>$171,000</td>
<td>$558,000</td>
<td></td>
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<td>Relative Risk of Recurrence due to Waiting</td>
<td>Log-normal distrib. (σ = 0.1)</td>
<td>(93)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Menopausal Status of Patients</td>
<td>Post-menopausal</td>
<td>Pre-menopausal</td>
<td>$1,057,000</td>
<td>$1,444,000</td>
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**DISCUSSION**

We have illustrated a novel method for calculating the cost-benefit of reducing wait-times for radiotherapy. The methodology entailed the following steps: (i) to determine the size of investment required to reduce waiting, in this case increasing the capacity of a
cancer centre using a simulation model; (ii) to determine the cost of implementing such an increase; (iii) to calculate benefits expressed as averted treatment of recurrence costs through a Markov model, using data from the scientific and economic literature; (iv) to compare costs and benefits to determine the net value of reducing waiting for radiotherapy at a cancer centre. Our procedure blended several different scientific methodologies to address a research question that has, before now, not been explored scientifically.

This methodology was illustrated with a hypothetical cancer centre treating a population of patients who have received adjuvant radiotherapy following breast-conserving surgery for early breast cancer (stage I/IIA with no lymph node involvement, or T1N0M0/T2N0M0). This population was chosen because of evidence from the literature regarding the risk of recurrence, and treatment for this population tends to be more homogenous than for other cancer populations. Paradoxically, it is likely that information about waiting for breast cancer was available precisely because patients are allowed to wait, since the risk of recurrence and death is low. Capacity levels for this hypothetical ‘breast-cancer only’ centre were determined according to levels of current operation at the Cancer Centre of Southeastern Ontario (CCSEO).

Patients can wait for radiotherapy during various treatment junctures: waiting to be diagnosed, to receive surgery, to be referred, to consult with a radiation oncologist, and to receive radiotherapy. Only the latter two types of waiting were considered here. Furthermore, although all cancer patients referred to the hypothetical centre were assumed to be referred to receive radiotherapy, in reality, not all patients referred to a cancer centre receive radiotherapy – radiation is not appropriate for all tumours.
Additionally, patients may be triaged ahead of others whose cancer is more severe. However, the model could be adjusted to allow for all types of waiting as well as percentage of patients referred to radiotherapy.

As part of the estimation of costs, a cost analysis was conducted at a regional cancer centre. With an annual operating cost of $13,651,674, the CCSEO delivered 24,829 fractions at a cost of $550 per fraction. The cost per fraction is higher than the 2008 CDN $173 per fraction value found by Earle (69) and $225 per fraction found by Wodinsky (92). This change may reflect the increased cost of equipment and salary/benefits for staff. Also likely is the reality of different staffing levels at the CCSEO (more radiation oncologists, physicists than in the comparator centres), and an increase in the cost of radiotherapy as linear accelerators have replaced cobalt machines, and collimators have replaced lead moulds as preferred treatment practices since these earlier studies were published. For the CCSEO, process inputs (salary/benefits), clinical infrastructure (equipment) and support infrastructure (overhead, land costs) represented 49%, 13% and 38% of total costs, respectively, compared to 54%, 29% and 17% found in Ploquin’s review (27), likely for the same reasons as outlined above.

The cost-benefit analysis proposed here is from the perspective of the health care system. As a result indirect benefits and costs of radiotherapy, such as productivity loss and out-of-pocket expenses are not included. This study represents the first attempt in the scientific community to calculate the cost-benefit of reduced waiting for radiotherapy. This methodology can be replicated for other cancer sites and for other diseases in which waiting is associated with negative downstream outcomes.
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Chapter 6 – Discussion

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Chapter 6.1 – General Discussion of Findings

Capacity and Waiting
The referral pattern calculated here was based on data from the CCSEO and approximated a Normal distribution. These referral numbers were based on all referrals to the cancer centre, including patients who were being re-referred for treatment. Not all patients were new, and not all were being referred for radiotherapy. This overestimates the number of new patient referrals with radiotherapy-indicated disease. There is no reason to suspect that there is any bias with respect to the proportion of referred patients that are eligible for radiotherapy (i.e., the same percentage of patients per week receive radiotherapy), but smaller numbers may change the shape of the distribution. Radiation-specific numbers for new patients were not available. This is in contrast with the findings of Thomas who found that patient referral was Poisson distributed (1). Thomas used referral rates to a radiation oncologist rather than a cancer centre to generate a statistical distribution, and did not consider treatment waiting as a separate phenomenon.

It may cost less for a larger centre to reduce waiting by increasing average capacity than it would for a smaller centre. This is a function of the Central Limit Theorem, that suggests that the larger a sample becomes, the smaller its variance becomes, and the less frequent large deviations from the mean become.

The small numbers used in the simulation model (relatively small number of patients moving through the centre per year) and the approximation method used in the project (using a proportion of patients from a full-service cancer centre) likely create some mathematical artifacts that are not representative of reality. For example, the number of spaces, the pattern of referrals, and the staffing levels may be different in an actual centre that treats only one cancer site. In the hypothetical example, one cancer site was used for illustrative purposes. While there are no such centres being operated in Ontario, there are
such centres in the United States (for example). Furthermore, the illustrative example shown here can be representative of a cancer center in Ontario or Canada that treats a relatively homogenous group of patients.

**Costs of Operating a Cancer Centre**

The per-fraction cost calculated in this analysis ($550 per fraction) is higher than the values found in Earle ($173) (2) and Wodisnky ($225) (3). This is potentially due to a number of factors. First, different methodologies of cost calculation were used. The relevant life of equipment in the Earle study was 12 and 15 years, whereas it was only 10 years in this analysis. It was not possible to determine from the Earle study what the annual discounting rate used was, what the initial price of equipment was, or what relevant life was considered for each piece of equipment. Similarly, staffing levels and individual salary were not included in Earle, and are likely different at the CCSEO.

Salaries have also changed in the past 10 years (apart from inflation), and since salary costs make up the largest component of the cost of radiotherapy, even a modest change can result in a noticeable difference in the per-fraction cost. Even when adjusted for inflation and the relative catchment area of the cancer centre, overhead and administrative costs at the CCSEO are higher than those found in the Earle study. Finally, there have been technological advances in the past 10 years since the Earle article was published, which represents the last time that the cost of radiotherapy was calculated in the Canadian scientific literature. It is conceivable that the real costs of radiotherapy have increased since then. Based on a systematic review of costing studies for radiotherapy, Ploquin suggests that costs of radiotherapy have increased only 5.5% over the past 15 years, but this is based on a methodology that mixes costs from a variety of different
health care systems, and is based on literature that is still relatively dated (4). For the CCSEO, process inputs (salary/benefits), clinical infrastructure (equipment) and support infrastructure (overhead, land costs) represented 49%, 13% and 38% of total costs, respectively, compared to 54%, 29% and 17% found in Ploquin’s review (27), likely for the same reasons as outlined above.

Without knowing precisely what the proportional increase in utility consumption would be if a new linear accelerator were installed, our estimate for this cost input may not be completely accurate. A true micro-costing of the value of utilities would give us a better estimate, but would require a great deal of time and effort to obtain a relatively small piece of the overall estimate of cost-benefit.

For the cost-benefit analysis, two different scenarios were used to calculate the cost of creating additional treatment capacity in a cancer centre. The preferred method of treatment capacity increase will depend on the characteristics of a given centre. For example a centre that runs its machines for the maximum amount of time possible cannot increase capacity without adding a new machine and associated staff. Conversely, a centre with reserve machine capacity but no reserve staffing hours might increase treatment spaces by hiring new staff. Having existing staff work overtime is another option that was not explored in this analysis; however, the very idea of using overtime to increase capacity assumes that staff are willing to work overtime, which they may not be. Any changes in practice should consider the availability of resources and the willingness of staff to make changes.

Radiation therapy takes place over a work day schedule (i.e., 9 AM to 5 PM, 5 days a week). One of the scenarios explored here (scenario B), increasing staff numbers, would
not necessarily increase the number of treatment spaces available, since any additional staff would be using the same treatment machines unless the cancer centre has sufficient unused machine time to justify hiring new staff. If a centre had reserve machine time that were used only in times of great need, staffing guidelines would require an additional four radiation therapists be hired to operate it. The most practical method of increasing the capacity of a centre is to lengthen the work day. This approach would have its own difficulties, since it is not reasonable to hire staff to work for the one or two additional hours required to create enough spaces to reduce waiting to policy-relevant lengths.

**Estimation of Benefits**

The Markov model used in the proposed cost-benefit analysis is limited by what is known as the “Markov memoryless assumption”. The model necessarily assumes that each state is “memoryless” – that is, that the transition probability is equal for each cycle, regardless of how long patients have remained in the state. For example, a patient who has been in the “Metastatic Disease” state for six cycles has the same probability of transition to death as one who has been in that state for one. However, in reality, a patient is highly unlikely to live three years with metastatic disease, and if such a patient did exist, he/she would be much more likely to die within six months than a newly-diagnosed person. As such, the model may overestimate the benefit of avoided recurrence due to downstream events. However, by the same token, patients are more likely to remain in the “Well” state than would be expected in reality, which would underestimate the benefit. In the interest of adhering as closely as possible to the published, validated scientific literature, no steps were taken in this project to bypass the Markov assumption. Future explorations of this subject ought to explore a discrete-event model, in which an
individual patient moves through the simulation and “remembers” the clinical trajectory the patient has experienced.

For the hypothetical example, the output of the Markov model showed that weekly reductions in waiting did not have a dramatic effect on average health care expenditures for the population of breast cancer patients. In fact, for many comparisons the reduction in waiting seemed to decrease the benefit. This effect was likely due to the low rate of recurrence and association between waiting and breast cancer, since the incremental difference in benefits was driven by the risk of recurrence. Incremental benefit values were not significantly different from each other so that confidence values overlapped for expenditure, and incremental benefit values were close to zero.

Breast-conserving therapy does not reduce the risk of mortality significantly when compared to treatment regimens that do not include radiotherapy. The economic benefit of reducing waiting is likely to be larger in cancer sites with a stronger link between radiotherapy and mortality (e.g., head and neck cancer, lung cancer) than in breast cancer. Breast cancer was chosen for the hypothetical example because of the relative wealth of scientific data (compared to other cancer sites) available linking delay of radiotherapy treatment to recurrence. This availability is likely due to the fact that many physicians prioritize breast cancer radiation below radiation treatment for other aggressive tumours. Because breast patients are allowed to wait longer than patients with other, more aggressive cancers, there is more information available on the associated risks of delay in breast radiotherapy. Future studies ought to focus on cancer sites for which waiting is not common.
The value of resources used for the calculation of benefits is based on findings from the literature. It is likely for a number of reasons that the cost of treatment (i.e., benefit) is an underestimate of the true cost of waiting. First, these costs were based on old chemotherapy regimens – newer drugs are more expensive than their older counterparts, and chemotherapy represents a large component of the cost of adjuvant treatment nowadays. Second, the clinic costs represented an underestimate of the “true” cost of detecting and treating a recurrence. Recurrent disease can be detected during routine follow-up screening, but can also manifest itself according to symptoms. In the case of symptomatic detection, a larger amount of resources are required for treatment (e.g., pain medication, pre-surgical hospitalization) than for detection by screening.

Cost-Benefit Analysis

The analysis is conducted from the health care system’s perspective. Costs experienced by the society at large (in terms of economic loss due to time taken off work) and by patients (out-of-pocket expenses for items such as drugs, transportation, and parking) are not reflected in this analysis. Previous economic studies of radiotherapy have shown that these costs are not a major contributors to the overall cost of treatment (49;50;52;53). Future investigations into the issue of the costs of waiting ought to include these considerations.

Sensitivity Analysis

Net Present Values remained unchanged for sensitivity adjustment in many variables. As stated above, because the change from \( i = 6 \) to \( j = 5 \) requires the addition of one treatment space per week without a corresponding increase in assessment space, radiation oncology salary has no effect on the Net Present Value. Furthermore, because the cost
inputs increase in both scenarios by the same amount, the incremental cost for this comparison is zero. However, it is worthwhile to note that while the incremental cost of increase doesn’t change, the absolute cost does. Any sensitivity adjustment that reduces costs should increase the Benefit-to-Cost ratio.

Changes in the costs of treatment, particularly for the end-of-life and metastatic states, yielded large variation in the Net Present Value. These health events appear to be the major cost-drivers of the benefit calculation. From the literature, hospitalization and therapeutic drugs were the largest components of the cost of treatment for these states – suggesting that as drug prices increase, so too will the benefit of reduced waiting.

Negative values for benefits were seen when the transition from “Well – “Local Recurrence” was increased. This seems counter-intuitive, since a higher risk of recurrence should yield more recurrent events as waiting times increase. The effect is possibly an artifact caused by the low underlying relative risk of recurrence due to waiting, and the time horizon of analysis, as the major difference in benefits is seen in years 5+.

Decreasing the risk of spontaneous metastasis (“Well” – “Metastatic Disease”) increased the Net Present Value. When local recurrence is the only state through which metastatic disease and death are likely, reducing the risk of local recurrence makes a large difference. Conversely, when metastatic disease is likely from any point, and reducing waiting has no effect on metastatic development, the benefits approach zero.

The issue of error in the Markov model – expenditure values being statistically identical – may explain some of the counterintuitive results found in sensitivity analysis.

Other considerations
Increasing capacity is not the only method of reducing waiting. Changes can be made in referral and treatment practices that will have a substantial effect on waiting. An example of such a change is the adoption of a hypofractionated (16 fractions) schedule for breast cancer. While a 25-fraction schedule was, and is still in many places in the literature, considered standard practice, a 16-fraction schedule reduces treatment time and therefore increases the speed at which patients are treated. New technologies such as brachytherapy (implanting radioactive material directly into cancer tissue) allow for even larger doses of radiation to be delivered in each fraction, further shortening treatment time (due to higher patient turnover). Increasing capacity should be seen as one element of an overall strategy to shorten waiting, rather than a single-pronged solution.

Patients can wait for radiotherapy during various treatment junctures: waiting to be diagnosed, to receive surgery, to be referred, to consult with a radiation oncologist, and to receive radiotherapy. Only the latter two types of waiting were considered here. Furthermore, although all cancer patients referred to the hypothetical centre were assumed to be referred to receive radiotherapy, in reality, not all patients referred to a cancer centre receive radiotherapy – radiation is not appropriate for all tumours. Additionally, patients may be triaged ahead of others whose cancer is more severe. However, the model could be adjusted to allow for all types of waiting as well as percentage of patients referred to radiotherapy.

Furthermore, from the patient’s perspective, waiting occurs as soon as a lump is detected. He/she waits to see his/her family physician, waits for diagnostic tests, waits for a surgical appointment, and then waits to be referred to radiotherapy assessment. These types of waiting are not included in this analysis, though their effect on the risk of
recurrence may be as great or greater than the post-surgical delays included above. As previously stated, waiting is a complex issue made up of several variables, both systemic and patient-driven. The health care system should focus on removing barriers to prompt care that are created by the system itself, to provide the best quality of care possible.

The scope of this investigation assumes that costs, particularly salaries and treatment costs, exist in a state of partial equilibrium (do not change as market forces fluctuate over time). If this methodology modeled a state in general equilibrium (allowing costs and benefits to change over time), it is likely that salaries and treatment costs would increase. Since salary costs fall on the costs side of the cost-benefit equation, with treatment costs falling on the benefits side, it is likely that a general equilibrium-based model would see change in the Net Present Value. Since increasing capacity is likely to have a number of effects aside from simply reducing waiting times (e.g., change in physical referral patterns, increased utilization of radiotherapy, lower overall recurrence rate as treatment and screening improve), it is not possible to predict what direction these secondary general-equilibrated effects might have on the cost-benefit.

**Chapter 6.2 – Ethics, Strengths, Limitations**

**Ethical Considerations**

Because this project did not use individual patient data, many ethical concerns typical to epidemiological research did not apply. For example, there was no risk of a breach in confidentiality, since no individual information was collected or analyzed. For this same reason, threats to anonymity did not apply to this study design. All records from interviews were anonymized (names were removed) and were stored in an electronic form on a password-secured computer. This information will be kept for seven years,
after which time, it will be destroyed. This project obtained expedited ethics review from the Queen’s University Research Ethics Board (EPID-284-09).

**Strengths of the Project**

There are a number of strengths of our approach: the development of a new cost-benefit analysis methodology, developing a capacity and waiting model, obtaining operation costs of a cancer centre, building a Markov model with waiting to estimate treatment costs of recurrence, and the overall applicability of the model.

While not as widely used as other forms of economic analysis, such as cost-effectiveness and cost-utility, cost-benefit is a well-recognized methodology for addressing policy alternatives. Our cost-benefit analysis did not, however, consider the value of life-years gained or quality of life. It is both procedurally and ethically difficult to put a dollar value on a year of a patient’s life, or the quality of that life. Because we used a Markov model that can identify when patients die, it is possible to calculate life-years gained and to weight it with an appropriate quality-of-life measure, but that is beyond the scope of this design.

The association between capacity and waiting and the cost of operating a radiotherapy clinic were both based closely on approaches developed in the literature (6,1). The advantage of using these methods is that the study design is guided by a conceptual framework, rather than requiring a new methodological approach for every project. A full cost analysis of the operation of a cancer centre was performed, using actual costing and capacity data from the Cancer Centre of Southeastern Ontario. This approach is preferable to one that uses theoretical models (e.g., approximating to a statistical distribution, using scientific literature only), as it is based on real expense and patient
information. A second advantage of using this information is that it is more contemporary than data available from scientific papers, which often have a lag time of upwards of a year from the date of data collection to publication. The Markov model created here is based on the literature but includes waiting.

Finally, this approach can be applied widely to a number of diseases for which waiting is a long-term determinant of subsequent health outcomes. For example, if the scientific literature was explicit that waiting for surgical procedures such as hip replacement therapy leads to downstream health complications (above and beyond the exacerbation of problems while patients are waiting for surgery), this method could be used to calculate the cost-benefit of reducing surgical times.

**Limitations of the Project**

There are some limitations to our approach: the lack of primary information for treatment costs of recurrence, the limits of simulation modeling, our assumptions about the cost of waiting, a specific patient population for the hypothetical example, and the applicability of the overall approach.

The analysis components are based on theoretical (and in some cases, historical) data, rather than a real-time cohort. Ideally, this project would be based on the actual experiences of patients as they moved through the health care system. The project would observe what resources patients utilized, and how they interacted with different sites of care (i.e., physicians, nurses, other staff, hospitals, machines). As previously mentioned, the scope of this project precludes such an investigation. Observing and tracking such a cohort would take several years and a large research staff. As it is, those resources are not available to us, and so a theoretical approach was chosen instead.
The simulation modeling approach is another limitation within the project. In the ideal case, the analysis would be based on patients who are waiting for treatment, and actual changes in operations policy would be used to determine the association between capacity and waiting (observational study). Similarly to the previous point, the resources required to accomplish this type of observation exceed the scope of the project. Furthermore, it would be difficult both ethically and procedurally to change capacity levels at a cancer centre for the purpose of experimentation. It is, perhaps, also important to note that waiting and treatment are much more complex processes than illustrated in the simulation model. Patients can be assessed and then not treated (due to disease characteristics), and can be moved up waiting lists if their need is immediate. The model in this analysis does not account for these relatively-common treatment realities. While it is possible to create a more accurate model of capacity and waiting, it is likely that any changes in the association would be quite small.

The simulation model has limited applicability to the issue of waiting. The software allows for a First-In-First-Out (FIFO) type of waiting. In theory, if patients came in with uniform disease characteristics (i.e., disease severity) then waiting would be a FIFO system. In reality, some patients are triaged ahead of others, meaning that the order in which patients are treated is not based solely on the order in which they arrive. Since some patients move up the list (wait less than average) and others are bumped back (wait more than average), a FIFO system may approximate reality, albeit roughly.

The assumption that the risk of recurrence is the sole cost driver for waiting may not reflect reality. It is conceivable that there are other economic consequences of delay in receiving radiotherapy. For example, waiting may be associated with anxiety and other
psychological phenomena. However, in the brief period (4+ weeks) that patients must wait, it is unlikely that other physiological phenomena will occur. This project is delimitied to the cost of recurrence as it is a well-established consequence of waiting.

For the hypothetical cohort, the project is based on a specific patient population: early breast patients receiving radiotherapy following breast-conserving surgery. While this is a common clinical presentation for several patients, it certainly does not represent all breast cancer patients, and especially not cancer patients in general. Future research would be able to identify the costs and benefits of reduction in waiting times for radiotherapy in all cancer sites.

Much of this methodology is pinned on the assumption that a cancer centre operates at average capacity rather than above-average. It is possible that some centres already build reserve capacity into their operation. What this analysis shows is that operating at average capacity can produce waiting times that can be controlled with a small capacity increase over mean demand.

This methodology can be replicated in the “real world”. This study would use observational data to identify resources consumed in the treatment of recurrence, and then would apply values to these resources according to reimbursement schedules, with operating costs coming from top-down hospital costing methods. However, each of these methods is greatly labour-intensive and beyond the scope of a master’s thesis. While the approximation method is not as rigorous as the methodology described above, it is a practical way of approximating all of the required components. Future analyses of this issue can and should build on the conceptual framework outlined in this manuscript.
**Theoretical and Practical Significance**

We hope that the publication of this method will spark renewed interest, debate, and further scientific inquiry into the issue of the economics of waiting times, particularly for radiotherapy. The Canadian Medical Association estimates that the economic cost of waiting is equal to as much as 40% of Ontario’s health care budget (7).

This approach is a “first-pass” attempt at developing a methodology for this type of inquiry. While we have proposed an entirely novel approach to economic analysis of radiotherapy, we recognize that elements of our procedure can be improved. We hope that this method will be replicated in other cancer sites, and that the methods’ constituent elements (cost of reducing waiting, expenditure in recurring patients, benefits of waiting reduction) will be examined by the scientific community and improved to account for some of the limitations outlined above.

**Chapter 6.3 – Policy and Practice Implications**

Reducing waiting times is a complicated and complex issue. Increasing the capacity of a cancer centre can be considered as one method in a large systemic effort to control waiting. However, when compared to the cost of the outlay of capital for new centres, hiring more physicians, and funding several research projects, the cost required to increase the treatment capacity of 14 provincial cancer centres by a handful of spaces may be an acceptable and economically viable method of controlling waiting, which could likely have an immediate effect. Each cancer centre must consider the method of increasing capacity (e.g., new equipment versus new staff).
Chapter 6.4 – Knowledge Translation Plan

This project has had significant input from administrators at the Cancer Centre of Southeastern Ontario, particularly from the Director of the Department of Oncology (Alastair Lamb), who is an author on this thesis. The manuscript portion of this thesis (Chapter 5) will be submitted for publication in the literature. As waiting times is a contentious topic, we expect that the publication will spark debate and discussion among economists and health care policy researchers. The authors of this thesis will monitor and participate in these discussions.

A portion of this work (poster and oral presentation entitled “The Cost of Waiting: Economic Benefit of Reduction in Waiting for Early Breast Cancer Radiotherapy”) has been presented at the Canadian Association of Health Services and Policy Researchers (CAHSPR) annual conference in Calgary, AB (May, 2009) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) annual conference in Orlando, FLA (May, 2009). The findings were presented and discussed among scientists and economists with the primary author.
Chapter 7 – Conclusion

A method for estimating the cost-benefit of reducing waiting times for radiotherapy was presented in the above analysis. In this method, the cost of creating space was compared to the benefit of reducing waiting. These two concepts are linked by a model that examines the effect that increasing the assessment and treatment capacity of a cancer centre has on patient waiting times. An example was presented using a hypothetical population of post-menopausal patients treated for early breast cancer with breast-conserving surgery and lumpectomy.

The policy implications of the findings of this study are limited. While the utmost effort was undertaken to make the analysis externally valid, measures had to be taken to maintain internal validity, such as the mathematical creation of a hypothetical centre and the use of simulation and Markov modeling instead of an in vivo cohort. Despite the limitations of the findings, the methodology can be applied to other cancer sites, provided there are sufficient data regarding the association between waiting and recurrence in the scientific literature, or in a different form such as patient records.

This study has updated the scientific literature in terms of the cost of radiotherapy, and the effect of increasing cancer centre capacity. Additionally, a novel method has been developed to estimate the economic effects of reducing waiting times for radiotherapy, or indeed any therapy that has a significant impact on rates of recurrence or metastases. Furthermore, this study is the first of its kind to examine waiting as an economic phenomenon, for which a specific policy change could have an impact.
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