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0^s value rounded to 0 (zero) where there is a meaningful distinction between true zero and the value that was rounded
^{p} preliminary
^{r} revised
x suppressed to meet the confidentiality requirements of the *Statistics Act*
^{E} use with caution
F too unreliable to be published
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Total cost-effectiveness of mammography screening strategies

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Abstract

Background: Breast cancer screening technology and treatment have improved over the past decade. This analysis evaluates the total cost-effectiveness of various breast cancer screening strategies in Canada.

Data and methods: Using the Wisconsin Cancer Intervention and Surveillance Monitoring Network (CISNET) breast cancer simulation model adapted to the Canadian context, costs and quality-adjusted life years (QALY) were evaluated for 11 mammography screening strategies that varied by start/stop age and screening frequency for the general population. Incremental cost-effectiveness ratios are presented, and sensitivity analyses are used to assess the robustness of model conclusions.

Results: Incremental cost-effectiveness analysis showed that triennial screening at ages 50 to 69 was the most cost-effective at $94,762 per QALY. Biennial ($97,006 per QALY) and annual ($226,278 per QALY) strategies had higher incremental ratios.

Interpretation: The benefits and costs of screening rise with the number of screens per woman. Decisions about screening strategies may be influenced by willingness to pay and the rate of recall for further examination after positive screens.

Key words: Breast screening, economic analysis, microsimulation model, preventive health

Implementation of screening programs can have significant budget implications, depending on the size of the population affected and the health care system resources involved. Recommendations for mammography screening are continually being updated and modified—the age range, frequency, effectiveness and cost-effectiveness of population-wide screening are ongoing topics of debate.[1-3] Decisions about whether to screen, who should be screened, what modalities to use, and how frequently to screen are best made when the trade-offs between improved health outcomes, potential harm, and the economic impact are understood.

Economic evaluation of mammography screening is particularly important in countries like Canada that have single-payer publicly funded health care systems. Studies have estimated the costs of breast cancer treatment from the Canadian perspective.[4-8] However, none have examined or incorporated the full cost of screening, even though breast cancer natural history models have been developed to project the impact of different mammography strategies.[9-14] The objective of this analysis was to evaluate the costs, outcomes and cost effectiveness of various mammography strategies, using a validated breast cancer simulation model.[15]

Data and methods

Model

The framework for this analysis is the Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model, developed under the U.S. National Cancer Institute-funded Cancer Intervention and Surveillance Modeling Network (CISNET) program[15-17] (www.cisnet.cancer.gov/breast/). This study describes inputs specific to resource use and analyzes the cost-effectiveness of screening.[18] A total of 11 screening strategies are examined—annual, biennial, and triennial across different age groups (starting at age 40 or 50 and ending at age 69 or 74)—compared with No Screening. The results are based on calculations for a 1960 birth cohort of women in the general population. Clinical model inputs are described in the original model[12]; details of the Canadianized modified inputs are provided elsewhere.[18]

Resources

Resources associated with screening, diagnosis, and cancer management were identified: mammography, clinic visits, physicians, diagnostic procedures, and treatment (surgery, radiation, medication). To account for the societal perspective, the costs of lost productivity related to screening, screening results and diagnosis, and the cost of premature death were included. Once identified, quantities of resources utilized were determined based on guidelines, reports, peer-reviewed literature, and expert opinion (Appendix Table A). The base case assumed that 100% of eligible women would be screened using digital mammography. All positive screens and all detection of suspicious findings outside of screening were assumed to incur *non-invasive* work-up costs; a subset of these positive screens and suspicious findings incurred *invasive* work-up costs. It was assumed that all women took time off work for the mammogram, and during the first year after a diagnosis. Productivity loss associated with premature death due to breast cancer was also counted.

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All women diagnosed with breast cancer received either a mastectomy or a lumpectomy with or without radiation. Chemotherapy was assigned by stage of disease. Hormonal treatment was assigned by estrognen receptor status (ER+/ER-). Traztuzumab was assigned by human epidermal growth factor receptor 2 (HER2) status. Women with ductal carcinoma *in situ* did not receive trastuzumab (Appendix Table A).

Costs

Canadian unit costs ($2012CAN) were applied to each resource used and modelled ($1.01US = $1CAN, based on December 31, 2012).[19] Non-2012 costs were converted to 2012 values using the Consumer Price Index.[20] The sources consulted to determine costs were provincial drug formularies, national statistics programs, costing programs, health resource management, and the literature. Capital or institutional costs of the equipment were not included. Lost productivity costs were based on the literature and the average wage per woman (Appendix Table A).

Utility values

Age-specific population health preference values[21] were derived from U.S. Medical Expenditure Panel Survey data applying the EuroQoL EQ-5D instrument using U.S. scoring.[22] For women with newly diagnosed breast cancer, decrements to quality of life based on stage lasting for one year post-diagnosis were assumed, after which the women would return to their appropriate age-specific value. For women diagnosed with Stage IV breast cancer, the decrement was applied to their remaining lifetime. For screening-related health states, disutilities of 0.006 for one week and 0.105 for five weeks were applied for a screening mammogram and a positive screening result, respectively.[23]

Analyses

To estimate lifetime costs of screening and management, the overall costs and for premature death for each strategy and for No Screening were calculated. The outcome was quality-adjusted life-years (QALY).

The costs and outcomes of each screening strategy were compared in an incremental stepwise cost-effectiveness analysis: a strategy was considered to be efficient if it was not "dominated," that is, if no alternative strategy had improved outcomes for the same or lower cost, or no combination of two other strategies had improved outcomes for the same cost. Incremental cost-utility ratios (ICURs) were computed as the difference in cost divided by the difference in outcomes only for the efficient strategies. The average cost-effectiveness of each screening strategy relative to No Screening was also determined. All costs and health outcomes for the incremental analyses were discounted at a 5% rate. Univariate sensitivity analyses were conducted in which values for key parameters such as screening rates, screening sensitivity and specificity, health preference, treatment costs, cost of medications, and discount rate were varied (Appendix Table B).

Results

The overall costs (undiscounted) for *annual* screening of 1,000 women in the general population ranged from $11.3 million (ages 50 to 69) to $16.0 million (ages 40 to 74) (Table 1). Costs for *biennial* and *triennial* screening of 1,000 women ranged from $8.4 million to $11.2 million (ages 50 to 69 and 50 to 74), and from $7.6 million to $8.3 million (ages 50 to 60 and 50 to 74), respectively. The overall cost of No Screening for 1,000 women was $4.9 million ($4,875 per woman) over a lifetime.

Active screening itself was a cost-driver, making up a substantial portion of the overall cost. The ratio of the cost of screening to the overall cost was proportional to the aggressiveness of the strategy. Treatment costs were slightly higher for active strategies, compared

Table 1
Component costs per 1,000 women over a lifetime, by screening strategy (no discount)

Screening strategy	Screening	Diagnostic and clinical work-up	Surgical and radiation	Adjuvant medication†	Indirect (based on lost productivity)	Overall cost	Additional cost of premature death
No Screening	$0	$83,936	$1,220,608	$1,713,473	$1,856,569	$4,874,587	$12,671,495
Annual ages 40 to 69	$6,540,531	$40,605	$1,530,563	$1,694,982	$4,864,284	$14,670,965	$6,180,986
Annual ages 40 to 74	$7,314,735	$30,529	$1,618,139	$1,707,003	$5,322,003	$15,992,409	$5,794,587
Annual ages 50 to 69	$4,127,472	$47,245	$1,487,568	$1,713,469	$3,904,655	$11,280,409	$7,847,010
Annual ages 50 to 74	$4,908,452	$37,013	$1,575,399	$1,724,528	$4,364,947	$12,610,339	$7,408,591
Biennial ages 50 to 69	$2,175,956	$55,863	$1,437,689	$1,807,948	$3,019,322	$8,496,778	$9,261,094
Biennial ages 50 to 74	$2,672,157	$46,018	$1,524,021	$1,849,832	$3,350,174	$9,442,203	$8,866,323
Triennial ages 50 to 69	$1,573,325	$61,405	$1,406,127	$1,821,409	$2,724,921	$7,587,187	$10,085,986
Triennial ages 50 to 74	$1,911,210	$53,721	$1,477,251	$1,864,335	$2,964,934	$8,271,452	$9,778,164
Annual ages 40 to 49/Biennial ages 50 to 69	$4,551,101	$49,334	$1,479,841	$1,788,107	$3,985,553	$11,853,937	$7,552,892
Annual ages 40 to 49/Biennial ages 50 to 74	$5,027,968	$39,529	$1,567,832	$1,832,766	$4,316,621	$12,784,716	$7,130,482
Annual ages 40 to 49	$2,484,365	$75,590	$1,276,581	$1,705,534	$2,848,195	$8,390,266	$10,795,828

†adjuvant chemotherapy, hormonal therapies (for example, tamoxifen, aromatase inhibitors) and traztusumab
Source: Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model.

Table 2
Cost-effectiveness ratios of screening strategies, varied by age and frequency from societal perspective†

Screening strategy	Total cost (per 1,000 women)	Total quality-adjusted life-years (QALYs) per 1,000 women	Incremental cost per QALY	Average cost per QALY relative to No Screening
	$		$	$
No Screening	1,387,948	14,059	. . .	Base case
Annual ages 40 to 69	6,668,051	14,094	216,828	150,938
Annual ages 40 to 74	6,943,065	14,095	262,828	154,187
Annual ages 50 to 69	3,970,099	14,082	159,858	114,778
Annual ages 50 to 74	3,970,099	14,083	226,278	120,521
Biennial ages 50 to 69	2,885,565	14,075	97,006	95,313
Biennial ages 50 to 74	3,083,486	14,076	Dominated‡	100,912
Triennial ages 50 to 69	2,511,486	14,071	94,762	94,762
Triennial ages 50 to 74	2,652,005	14,072	Dominated‡	99,670
Annual ages 40 to 49/ Biennial ages 50 to 69	5,572,348	14,088	Dominated‡	146,333
Annual ages 40 to 49/ Biennial ages 50 to 74	5,767,102	14,089	Dominated‡	146,951
Annual ages 40 to 49	4,156,667	14,073	Dominated‡	Higher cost/Worse outcome

† cost and QALYs discounted at 5%
‡ alternative strategy had improved outcomes for same or lower cost, or combination of two other screening strategies had improved outcomes for same cost
. . . not applicable
Source: Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model.

with No Screening. Screening costs for more aggressive strategies were proportionally higher when compared with treatment and procedure costs.

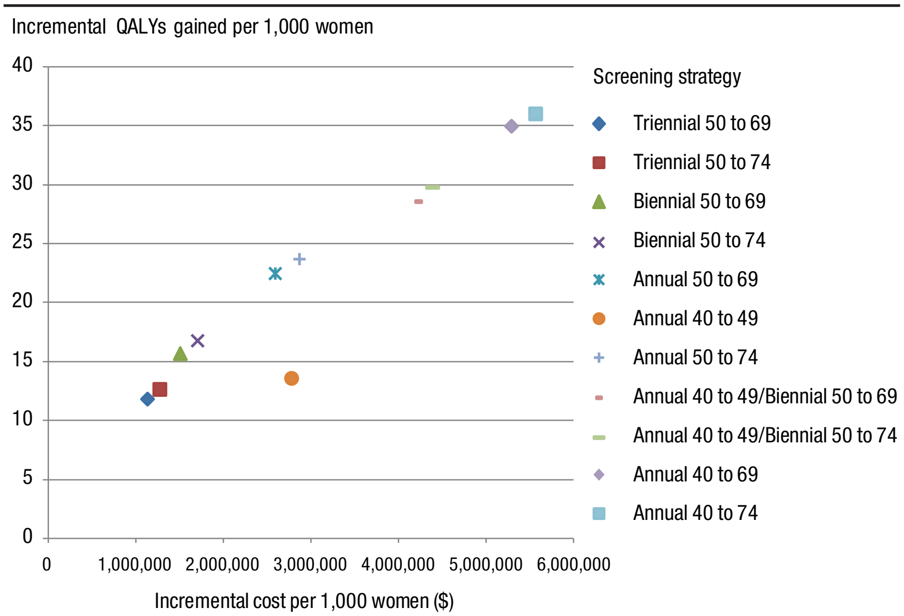
Lowering the age of eligibility for screening from 50 to 40 added $2 to $3 million to the cost for 1,000 women ($2,000 to $3,000 lifetime cost per woman). Raising the upper age limit from 69 to 74 added approximately $1 million per 1,000 women ($1,000 per woman). If the cost of premature death was included in the total cost, the overall cost increased by $7.4 to $10.8 million, depending on the strategy, with more aggressive screening being associated with fewer lives lost lives, and thus, lower costs due to premature deaths.

For the cost-effectiveness analysis, screening strategies for women aged 50 to 69 had lower incremental ratios than strategies in which screening continued to age 74 (Table 2). Annual screening at ages 40 to 69 and at ages 40 to 74 were considered the dominant strategies, compared with annual screening of narrower age ranges.

Compared with No Screening, all incremental ratios for the societal perspective were less than $155,000/QALY. The most favourable (lowest) ratios were for the least frequent screening (triennial) of the narrowest age group (50 to 69): $94,762/QALY. The most aggressive strategy (annual screening at ages 40 to 74) yielded the least favourable (highest) cost-effectiveness ratio: $154,187/QALY (Table 2, Figure 1).

A comparison of active screening strategies with No Screening revealed that the major cost drivers were no treatment (medication, surgery, or radiation) after a diagnosis and no subsequent

Figure 1
Costs and quality-adjusted life-years (QALYs) gained compared with No Screening, by screening strategy



Source: Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model.

screening (Table 3). The model was generally insensitive to changes in missed screening and no subsequent screening, but showed more favourable incremental ratios when the percentage receiving adjuvant chemotherapy was reduced, when screening costs were decreased, and when specificity and sensitivity were 100%. Not providing treatment, and thereby expediting disease progression, had the greatest impact on the ICUR. The model was sensitive to modifications in utility values, with more favourable (lower) incremental cost-utility ratios when the utility values were increased by 25%, thereby showing greater incremental benefits between the active screening strategies and No Screening. When the utility values were decreased by 25%, less favourable (higher) cost-utility ratios were modelled, owing to smaller differences in the benefit. Finally, changing the discount rate to 0% substantially reduced the ICURs.

Discussion

Early diagnosis of breast cancer through screening mammography can save lives, but costs and possible harms may be associated with screening and subsequent treatment. This is the first analysis of the lifetime cost-utility of various mammography screening strategies for Canada using an accepted population health model.

The main cost driver of the active screening strategies was the frequency of screening. A significant reduction in the cost of premature death was associated with more frequent screening, with an inverse relationship between the cost of screening and the cost of premature death.

Narrower age groups and less frequent screening were optimal when *cost-effectiveness* rather than *lifesaving* was considered. The exception was annual screening at ages 40 to 74, which was not dominated, but had high incremental cost utility ratios.

All active screening strategies were more effective than not screening. Compared with No Screening, incremental ratios for active screening strategies generally fell below $150,000 per QALY. The average incremental ratios generated from the model are in line with other ICURs used in oncology decision-making ($/QALY).[24] Moreover, the incremental ratios are well below the willingness-to-pay threshold of $300,000/QALY, which is defined as

Table 3
Univariate sensitivity analysis: Cost per quality-adjusted life-year (QALY) compared with No Screening, by screening strategy and screening variables (discount = 5%)

Screening strategy	Base case	Utility values 25%	"Utility values -25%"	Specificity 100%	Sensitivity 100%	50% missed screenings	Disutility excluded	Screening cost = $100	No treatment (drug, surgery, radiation)	No subsequent screening	75% receive adjuvant chemotherapy	Discount rate = 0%
No Screening	-	...	...	...	...	...	...	...	...	...	...	...
Annual ages 40 to 69	$150,937	$120,211	$201,250	$125,147	$128,592	$131,972	$190,762	$116,971	$4,081,165	$241,662	$137,604	$58,900
Annual ages 40 to 74	$154,187	$122,810	$205,583	$128,097	$131,177	$134,090	$195,009	$119,646	$4,726,306	$241,662	$138,757	$63,233
Annual ages 50 to 69	$114,778	$91,076	$153,037	$99,421	$101,858	$103,318	$132,970	$89,701	$1,240,537	$93,624	$103,592	$52,077
Annual ages 50 to 74	$120,522	$95,675	$160,695	$105,048	$107,224	$108,112	$140,148	$94,347	$1,410,235	$241,662	$107,059	$57,858
Biennial ages 50 to 69	$95,313	$75,461	$127,083	$80,679	$83,935	$94,904	$107,993	$76,713	$1,616,400	$93,624	$87,140	$41,984
Biennial ages 50 to 74	$100,912	$79,954	$134,549	$86,120	$89,992	$99,722	$114,702	$81,461	$1,870,599	$93,624	$90,735	$47,597
Biennial ages 40 to 74	$126,612	$100,640	$168,816	$103,579	$107,306	$120,253	$154,502	$100,680	$5,968,018	$241,662	$116,064	$51,194
Triennial ages 50 to 69	$94,762	$74,849	$126,349	$78,780	$85,837	$95,995	$107,858	$77,384	$1,963,362	$93,624	$86,364	$41,575
Triennial ages 50 to 74	$99,700	$78,812	$132,932	$83,793	$91,707	$100,339	$113,732	$81,684	$2,017,095	$93,624	$89,826	$46,703
Annual ages 40 to 49/ Biennial ages 50 to 69	$146,333	$116,540	$195,111	$121,352	$122,534	$135,003	$184,737	$114,221	$5,834,291	$241,662	$135,983	$53,166
Annual ages 40 to 49/ Biennial ages 50 to 74	$146,950	$117,061	$195,934	$123,180	$124,491	$136,750	$184,756	$114,985	$5,968,397	$241,662	$135,473	$55,855

... not applicable
Source: Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model.

"good value for money" by about half of Canadian and American oncologists, with another third using $100,000/LYG to define good value.[25] A recent editorial on incremental ratios questioned the wisdom of existing thresholds.[26]

Annual screening strategies had higher average incremental ratios than did less frequent screening, but they were associated with greater benefits. For this analysis, assumptions about total costs were based on lost productivity—having a screening mammogram (1/2 day), a positive screen (5 weeks), and a diagnosis of invasive cancer (one year). Any change in these conservative time estimates would affect the overall cost. The more aggressive the screening strategy, the more recalls for no cancer, and the more cancers detected, both of which result in more lost productivity, higher incremental costs, and higher incremental ratios (that is, less favourable cost-effectiveness). Because QALYs and costs rise with the number of screens per woman, decisions about screening strategies are mainly related to willingness to pay and avoiding the recall of too many women for further examinations after positive screens. Thus, a screening tool that provides higher specificity would be beneficial.

A comparison of the active screening strategies with No Screening showed a relatively tight range of incremental ratios: within $40,000 to $60,000 of each other. Raising the age of eligibility from 69 to 74 marginally increased the incremental ratios because of additional screening costs, but it also improved outcomes. Lowering the age of eligibility from 50 to 40 increased incremental ratios, again because of higher screening costs, but this, too, yielded more QALYs.

When examined by age group (50 to 69 and 50 to 74), the cost-effectiveness ratios for annual, biennial and triennial screening compared with No Screening showed similar values. The choice of a screening strategy based on cost-effectiveness should also consider the improvement in QALY associated with more frequent screening.

For the univariate sensitivity analysis, based on the analyses for the societal perspective (discount = 5%), where the QALYs of different screening strategies were compared with No Screening, the model was generally robust. The incremental ratio was generally insensitive to changes in missed screening, no subsequent screening, and reductions in the percentage of women receiving adjuvant chemotherapy. The model, however, was sensitive to decreased screening costs and improved specificity and sensitivity, which led to more favourable (lower) ICURs. Not providing treatment (medication, radiation, surgery), and thus expediting disease progression, had the greatest impact on the ICUR. Modifying the same parameters for the cost-utility analysis produced results similar to the cost-effectiveness analysis, but also showed that the model was sensitive to modifications in utility values—more favourable (lower) ICURs were predicted when the utility values were increased by 25%, thereby showing greater incremental benefits between active screening and No Screening. By contrast, when the utility values were decreased by 25%, less favourable (higher) ICURs were generated as a result of smaller differences in the benefit, which led to higher ratios. Most notably, incremental ratio values fell substantially when the no discount rate was applied; discounting significantly affected long-term effectiveness outcomes over the model time horizon, whereas costs were up front.

According to an analysis published in 2014 of population-based mammography screening from a Canadian health system perspective using screening diagnostic, treatment costs and utility values, the most cost-effective strategies were biennial screening of women aged 50 to 69 and 40 to 69.[27] That model used different costs per treatment, did not consider triennial screening strategies, and did not include the cost of lost productivity or consider the societal perspective.

What is already known on this subject?

- Early diagnosis of breast cancer through screening mammography can save lives, but costs and possible harms are associated with the screening and subsequent treatment.
- Implementation of screening programs have substantial budget implications, depending on the size of the population affected and the health care system resources involved.
- Studies have estimated the costs of breast cancer treatment from the Canadian perspective, but none have examined or incorporated the full cost of screening, including lost productivity.

What does this study add?

- This analysis evaluates the costs, outcomes and cost effectiveness of different mammography strategies, using a validated breast cancer simulation model.
- The main cost driver of the active screening strategies was the frequency of screening.
- Narrower age groups and less frequent screening were optimal when cost effectiveness was considered.

Strengths and limitations

The Wisconsin model allowed simulation of the growth of a distribution of breast cancers within a cohort of women and consideration of the individual effects of various detection strategies and treatment regimens on mortality and other outcomes. The strength of the Wisconsin model is that it has been validated against empirical U.S. data. Modified for use in the Canadian context, the model performed well in predicting breast cancer incidence in the absence of screening.[18] In addition, the model used empirical data on the sensitivity and specificity of screening mammography versus age and breast density to describe the screening process. Canadian data on the use of therapies and on costs were employed, and no assumptions about the mortality reduction associated with screening were applied explicitly in the model.

Most studies that have evaluated the cost-effectiveness of screening strategies have been conducted from a U.S. health system perspective and focused on different risk factors such as early and late age and genetic profile.[9,11,28,29] Unlike the present analysis, no studies have examined the impact of lost productivity from the societal perspective in a general population of women, or for Canada.

The results of this analysis should be interpreted in the context of several limitations. First, the model itself has shortcomings that have been outlined in previous work.[18]

Second, the model assumed that 100% of eligible women would be screened, whereas compliance is markedly lower. In Ontario, the 2010/2011 screening rate through an organized program was 61% for women aged 50 to 74.[30] When the screening rate was lowered to 50% in the present model, incremental ratios remained similar to those of the base case, mainly because along with a decrease in the costs of screening, the number of invasive cancers detected, which affects QALY, also decreased.

Finally, to avoid double-counting, the incremental evaluations did not include the cost of premature death. However, more frequent screening might be expected to reduce costs associated with premature deaths from breast cancer.

Conclusion

The results of this analysis may be used to help determine appropriate breast screening strategies for a population. The single greatest cost contributor in a screening program is the mammography itself, which exceeds the costs of therapy. Because lives saved and costs both rise with the number of screens per woman, decisions about screening strategies are mainly related to willingness to pay and avoiding recalling too many women for further examination with no cancer detected. Future models will consider the impact of different screening technologies and populations on both costs and outcomes. ■

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Appendix

Table A
Cost input parameters and resource utilization

Variables	Definitions and descriptions	Resource utilization (RU)	Cost (2012CAN$)
Screening and diagnosis			
Breast cancer screening program	RU: Assume all eligible women would be screened Cost: Includes mammography physician[31]	100% of women eligible for screening	$183.00 per screen
Non-invasive work-up	RU: Assume all women with a positive mammogram Cost: Includes work-up mammography, radiology, physician clinic visit[31]	100% of women with positive screening exam	$445.95 per work-up
Invasive work-up (needle biopsy)	RU: 14.7% of women who get non-invasive work-up receive invasive procedure[32] Cost: physician clinic visit, needle biopsy, pathology[31]	82.1% of women who receive invasive work-up	$745.46 per work-up
Invasive work-up (excisional)	RU: 14.7% of women who get non-invasive work-up receive invasive procedure[32] Cost: physician clinic visits, excision, pathology[31]	17.8% of women who receive invasive work-up	$1,652.44 per work-up
Treatment			
Chemotherapy	RU: Percentage of women receiving chemotherapy Cost: Mean value of first-, second- and third-generation chemotherapies[33,34]	Women receiving chemotherapy with invasive cancer (see below) Women receiving chemotherapy with DCIS = 0% (see below)	$7,376.10 per course
Trastuzumab	RU: Assume all HER2+ women receive Trastuzumab Cost: Treatment costs based on 8 cycles; includes chemotherapy costs recommended for Trastuzumab (paclitaxel), health care personnel costs and physician clinic visits associated with administration[33-35]	14% with invasive cancer 0% with DCIS	$29,709 per course
Tamoxifen	RU: Assume use of Tamoxifen for appropriate population for 10 years Cost: Annual cost (excludes markup and dispensing) + physician clinic visit 4 times per year[36]	100% for invasive cancer in eligible women 100% for DCIS in eligible women	$383.40 per annum
Aromatase inhibitors (AI)	RU: Assume use of AI for appropriate population for 10 years Cost: Annual cost of letrozole (excludes markup and dispensing) + physician clinic visits 4 times per year[36]	100% for invasive cancer in eligible women 0% for DCIS	$822.40 per annum
Treatment cost per appropriate cohort			
ER+, younger than 50, DCIS, annual cost	RU: Tamoxifen only (for 10 years) Cost: Tamoxifen only[36]	100%	$383.40
ER+, younger than 50, invasive, annual cost	RU: Tamoxifen (for 10 years) + chemotherapy Cost: Tamoxifen (for 10 years) + chemotherapy[33,34,36]	100%	$7,759.50
ER+, younger than 50, invasive, annual cost with Trastuzumab	RU: Tamoxifen (for 10 years) + chemotherapy + Trastuzumab Cost: Tamoxifen (for 10 years) + chemotherapy + Trastuzumab[33,34,36]	100%	$37,462.50
ER+, 50 or older, DCIS, annual cost	RU: Tamoxifen only (for 10 years) Cost: Tamoxifen only[36]	100% of women in this cohort received this regimen	$383.40
ER+, 50 or older, invasive, annual cost	RU: Chemotherapy + AI (for 10 years) Cost: Chemotherapy + AI (for 10 years)[33,34,36]	100% of women in this cohort received this regimen	$8,198.50
ER+, 50 or older, invasive, annual cost with Trastuzumab	RU: Chemotherapy + AI (for 10 years) + Trastuzumab Cost: Chemotherapy + AI (for 10 years) + Trastuzumab[33,34,36]	100% of women in this cohort received this regimen	$37,901.50

Table A
Cost input parameters and resource utilization (continued)

Variables	Definitions and descriptions	Resource utilization (RU)	Cost (2012CAN$)
ER-, younger than 50, DCIS, annual cost	No drug therapy, based on expert opinion	100% of women in this cohort received this regimen	$0
ER-, younger than 50, invasive, annual cost	RU: Chemotherapy Cost: Chemotherapy[32,34,36]	100% of women in this cohort received this regimen	$7,376.10
ER-, younger than 50, invasive, annual cost with Trastuzumab	RU: Chemotherapy + Trastuzumab Cost: Chemotherapy + Trastuzumab[33,34,36]	100% of women in this cohort received this regimen	$37,079.10
ER-, 50 or older, DCIS, annual cost	No drug therapy, based on expert opinion	100% of women in this cohort received this regimen	$0
ER-, 50 or older, invasive, annual cost	RU: Chemotherapy Cost: Chemotherapy[33,34]	100% of women in this cohort received this regimen	$7,376.10
ER-, 50 or older, invasive, annual cost with Trastuzumab	RU: Chemotherapy + Trastuzumab Cost: Chemotherapy + Trastuzumab[33,34,36]	100% of women in this cohort received this regimen	$37,079.10
Procedures			
Radiation for invasive cancer	RU: Percentage of women with breast cancer who received radiation therapy[8] Cost: 25 fractions * $138 (1996) or $188.39 (2012)[20,31,37]	67%	$5,014.05 per radiation
Surgery for invasive cancer	RU: Percentage of women with breast cancer receiving surgery[38]	90%	Costs stratified by lumpectomy and mastectomy
Surgery (lumpectomy for invasive cancer)	RU: Percentage of all women receiving surgery Cost: Ontario Case Costing Initiative (OCCI) 2012[39]	63% Report by Canadian Institute for Health Information and Canadian Partnership Against Cancer shows wide provincial variation in annual rates for the two treatments.	$4,937.06 per surgery
Surgery (mastectomy for invasive cancer)	RU: Percentage of all women receiving surgery Cost: OCCI 2012[39]	37% Report by Canadian Institute for Health Information and Canadian Partnership Against Cancer shows wide provincial variation in annual rates for the two treatments.	$6,956.77 per surgery
Radiation for DCIS	RU: Percentage of DCIS women receiving radiation therapy Cost: 25 fractions * $138 (1996) or $188.39 (2012)[20,31,37]	50%	$5,014.05 per radiation
Surgery (lumpectomy for DCIS)	RU: Percentage of DCIS women receiving surgery[41] Cost: OCCI 2012[39-41]	67%	$4,937.06 per surgery
Surgery (mastectomy for DCIS)	RU: Pecentage of DCIS women receiving surgery Cost: OCCI 2012[39-41]	33%	$6,956.77 per surgery
Indirect costs			
Time off for screening	RU: Assume 4 hours based on travel, appointment and waiting time Cost: $22.87/hour[42]	100%	$91.48 per time off for screening
Lost productivity in first year	RU: Assume all women working; lost 27% of annual income because of breast cancer treatment[43] Cost: $22.87/hour[42]	100%	$12,838.18 per annum
Premature death	RU: Assumption, all women who died Cost: $22.87/hour * 40 hours * 52 weeks[42]		

DCIS = ductal carcinoma *in situ*
ER+/ER- = estrogen receptor status
HER2+ = human epidermal growth factor receptor 2

Table B
Values of variables for univariate sensitivity analyses

Variable	Base case value	Sensitivity analysis value	Source and comments
Cost of mammography	$183.00 per screen	$100.00 per screen	Assumption: Reduction in cost
Percent of eligible women who missed screening	0%	50%	In Ontario, 60% of women older than 50 participate in regular screening, about 43% through the organized program. The retention rate after a previous screen is about 85%.[44]
Screening rates for population	100% first screen	No subsequent screens	Assumption: Impact of repeat screening/ retention
Sensitivity	Model calibrated as per empirical data[45;46,]	100%	Assumption: Ideal scenario
Specificity	As per empirical data	100%	Assumption: Ideal scenario
Treatment	Surgery, radiation, chemotherapy, hormonal	0% treated	Assumption: Applied to all women in model
Adjuvant chemotherapy	100% of cohort received adjuvant chemotherapy	75% of cohort received chemotherapy	Assumption: Not all patients receive chemotherapy
Utility values	Model values	+ /- 25%	Assumption: Change in utility values
Disutility	Model values	No disutility	Assumption: Change in utility values
Discount rate	Model rate (5%)	0%	Assumption: Applied to all women in model