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Research

Cost-effectiveness of mammography from a publicly funded health care system perspective

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Abstract

Background: The implementation of population-wide breast cancer screening programs has important budget implications. We evaluated the cost-effectiveness of various breast cancer screening scenarios in Canada from a publicly funded health care system perspective using an established breast cancer simulation model.

Methods: Breast cancer incidence, outcomes and total health care system costs (screening, investigation, diagnosis and treatment) for the Canadian health care environment were modelled. The model predicted costs (in 2012 dollars), life-years gained and quality-adjusted life-years (QALYs) gained for 11 active screening scenarios that varied by age range for starting and stopping screening (40–74 yr) and frequency of screening (annual, biennial or triennial) relative to no screening. All outcomes were discounted. Marginal and incremental cost-effectiveness analyses were conducted. One-way sensitivity analyses of key parameters assessed robustness.

Results: The lifetime overall costs (undiscounted) to the health care system for annual screening per 1000 women ranged from $7.4 million (for women aged 50–69 yr) to $10.7 million (40–74 yr). For biennial and triennial screening per 1000 women (aged 50–74 yr), costs were less, at about $6.1 million and $5.3 million, respectively. The incremental cost–utility ratio varied from $36 981/QALY for triennial screening in women aged 50–69 versus no screening to $38 142/QALY for biennial screening in those aged 50–69 and $83 845/QALY for annual screening in those aged 40–74.

Interpretation: Our economic analysis showed that both benefits of mortality reduction and costs rose together linearly with the number of lifetime screens per women. The decision on how to screen is related mainly to willingness to pay and additional considerations such as the number of women recalled after a positive screening result.

The implementation of a population-wide breast cancer screening program has important budget implications for publicly funded health care systems because of the use of substantial resources. Mammography screening recommendations are periodically updated by different countries.[1–4] The age range and frequency for population mammography screening programs as well as their effectiveness and cost-effectiveness have been topics of debate over many years.[5–10] Given the fact that screening parameters (e.g., age range, frequency) vary among the various organized publicly funded screening programs across Canada, it is important to understand the trade-offs between improved health outcomes, potential harm and monetary costs of the decisions regarding whether to screen, whom to screen, and the age range and interval for screening. We recently published an economic analysis of the impact of various screening scenarios on costs and outcomes from an overall societal perspective.[11] In that analysis, we found that screening every 3 years and screening every 2 years in women aged 50–69 years were the most cost-effective strategies, at $94 762 and $97 006 per quality-adjusted life-year (QALY), respectively, compared with no screening. Screening annually had a much higher ratio ($226 278 per QALY). However, we did not assess the value of screening programs from a publicly funded health care system perspective.

Given the fact that policy decision-makers are interested in understanding the specific impact of new interventions/strategies on their health care systems, the objective of this work was to evaluate the costs, outcomes and cost-effectiveness of

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mammography for various screening policies in the general population of Canadian women from the perspective of a single-payer publicly funded health care system. To do so, we used a previously validated computer model for the natural history, detection and treatment of breast cancer and conducted lifetime analyses for several relevant screening strategies.

Methods

Model design

We modified the University of Wisconsin Breast Cancer Epidemiology Simulation Model[12] to reflect the Canadian context and conduct our analysis. The model was developed under the Cancer Intervention and Surveillance Modeling Network program, funded by the US National Cancer Institute.[13,14] It is a discrete-event, stochastic simulation modelling approach to replicate incidence and mortality in breast cancer based on the US population. Complex interacting processes, including natural history, detection of breast cancer, treatment for breast cancer and competing mortality, are modelled over time, simulating the lives of women at 6-month intervals. Model outputs include age-specific incidence rates by stage and age-specific mortality rates. This microsimulation model is applied to a birth cohort of 2 000 000 women. Based on empirical probabilities for events, breast cancers are stochastically initiated at various time points in a fraction of these women. All tumours, including ductal carcinoma in situ, grow following a Gompertz function,[15] with a distribution of randomly assigned growth rates. In the model, tumours are followed over time as the cohort ages. Tumours are assumed to initially be in situ, and all tumours grow until they reach a maximum size.[16,17] Size is used as a surrogate for stage, and cancers are classified into 4 groups: in situ, localized, regional metastasis or distant metastasis. Thresholds for detection are defined for clinical discovery of the cancers or for detection by screening. The sensitivity of detection by screening is calibrated by adjusting model parameters so that the model outputs match empirical cancer detection data. The model also contains a specificity function to create false-positive detections. Screening sensitivity and specificity parameters are specific for the age and breast density of the women as well as for the examination's being an initial one or a recurring annual or biennial screen.[18] Women are also randomly assigned hormonal and HER2 status of breast cancers via a weighted distribution reflecting population data. Treatments are given according to current guidelines based on in situ or invasive disease, age, hormonal status and HER2 status. Published clinical response data are used to predict outcome. The model tracks outcome (alive, breast cancer death, other cause of death) at 6-month intervals. The use of a discrete-event system simulation modelling approach allowed us to not make Markovian assumption for tumour growth, as tumour growth is most likely not memoryless. State-transition modelling would have forced us to represent tumour growth as a first-order or second-order Markovian process. The model conducts individual and separate simulation modelling based on all women born in 1960 (1960 birth cohort). It has been validated against US data[12,16] and, in its modified form, against Canadian data.[19]

Screening scenarios

Our screening scenarios involved various frequencies (annual, biennial, triennial and hybrids of these) across various age bands. We modelled the costs and outcomes for 11 screening scenarios as well as no screening from the perspective of the publicly funded health care system (in this case, Ontario). The scenarios included screening regimens that are currently being used in Canada[19] and the United States as well as those that have been recommended by bodies such as the US Preventive Services Task Force,[3] the Canadian Task Force on Preventive Health Care,[1] Choosing Wisely Canada[20] and the American Cancer Society.[4] Health care system resources (mammography, diagnostics, medical personnel, cancer management) were included. Treatment for breast cancer included surgery (mastectomy, lumpectomy), hormonal therapy, chemotherapy as appropriate (by stage of disease) and radiation (number of fractions), depending on stage at diagnosis. We modelled that women with newly diagnosed invasive breast cancer would receive some form of adjuvant systemic treatment (chemotherapy and/or hormonal therapy). Finally, we assumed that all women with invasive HER2+ cancer would receive trastuzumab, whereas women with ductal carcinoma in situ would not.

Data sources

Evidence for resource use and costs included guidelines, reports, peer-reviewed literature and expert opinion as found in formal and informal searches of the peer-reviewed and grey literature (Supplementary Table 1, Appendix 1, available at www.cmajopen.ca/content/6/1/E77/suppl/DC1). We assumed that 100% of eligible women would be screened, that all positive screening results and all clinical diagnoses incurred a noninvasive investigation cost, and that a subset of positive screening results and clinical diagnoses incurred costs of further invasive investigation. Model assumptions and input data related to benefit have been fully described elsewhere.[11,21,22]

Outcomes

We used life-years and QALYs as benefit measures. The model provided survival information, and we applied health preference values to determine QALYs. We used age-specific population health preference values derived from studies based on US populations (2001 Medical Expenditures Panel Survey, based on 22 523 subjects, and 2001 National Health Interview Survey, based on 32 472 subjects) and applied the EuroQol EQ-5D instrument using US scoring.[23,24]

For women with newly diagnosed ductal carcinoma in situ or nonmetastatic invasive breast cancer, we applied decrements for stage lasting for 2 years after diagnosis based on values assigned to disease and treatment phases by experts in breast cancer and public health (Appendix 1), after which each woman would return to her appropriate age-specific health preference value. For those with regional disease, we applied decrements for 2 years after diagnosis of regional disease. For women with a diagnosis of metastatic breast cancer, the decrement was applied to their remaining lifetime. We also assumed small, short-term decrements in quality of life for screening and diagnostic investigation in

cases with positive screening results (0.006 for 1 wk and 0.105 for 5 wk, respectively).[23]

Resources and costs

The model estimated costs of screening and treatment for each scenario for the lifetime of the cohort from the health care system perspective. We applied Canadian unit costs (in 2012 Canadian dollars) to each of the resources used and modelled (Can$1 = US$1.01 based on Dec. 31, 2012[25]). Costs from years other than 2012 were converted to 2012 values with the use of the Consumer Price Index (www.bankofcanada.ca). Cost sources included formularies, statistics and the published literature. Capital or institutional costs of equipment were not included in this analysis. For medications, we identified the average costs of first-line, second-line and third-line medications through expert opinion and guidelines. We determined costs for eligible therapies used and an average value for all medications.

Statistical analysis

We calculated both marginal (relative to no screening) and incremental cost-effectiveness ratios (ICERs) to evaluate the screening scenarios, as both types provide information that is useful for different purposes. A public health screening program is generally launched in an effort to make the maximum impact in reducing mortality and/or morbidity for a target population. When implementing such a program, one needs to examine the number of deaths averted or QALYs gained and the average cost per death averted compared to no screening; hence, the marginal cost-effectiveness ratio or cost–utility ratio would be of interest. In cases of competing priorities for limited resources, where there is consideration of trading some degree of benefit for a reduction of cost, it is the cost of the last death averted or QALY gained that is of interest and where incremental analysis is more useful. We determined ICERs (cost/life-year gained) and incremental cost–utility ratios (ICURs) (cost/QALY) comparing screening scenarios. All costs and health outcomes were discounted at a rate of 1.5%, recently proposed by the Canadian Agency for Drugs and Technologies in Health.[26] To understand the impact of resource costs on overall costs and the value of each screening scenario, we varied the input cost for key resources in one-way sensitivity analyses (Supplementary Table 2, Appendix 1). We also briefly explored the effect of the reduction of the annual discount rate on incremental values by comparing ICURs estimated at 5%, 3% and 1.5%.[27]

Results

The overall cost (undiscounted) to the health care system associated with the no-screening scenario was $3.0 million per 1000 women over a lifetime time horizon. The overall health care system cost for annual screening per 1000 women ranged from $7.4 million (for those aged 50–69 yr) to $10.7 million (for those aged 40–74 yr). For biennial and triennial screening per 1000 women (50–74 yr), costs were less, at about $6.1 million and $5.3 million, respectively (Table 1).

In the marginal analysis, all screening scenarios improved life-years and QALYs but did so at an added cost compared to no screening (Table 2, Figure 1) (full data given in Supplementary Table 3, Appendix 1). The marginal cost-effectiveness ratios for each screening scenario compared to no screening were generally under $50 000/life-years gained

Table 1: Disaggregated undiscounted and total costs per 1000 women for various breast cancer screening scenarios from the perspective of a single-payer publicly funded health care system

Scenario	Cost, $					Screening as proportion of total cost
	Screening	Clinical investigation	Procedure*	Treatment†	Total	
No screening	0	83 936	1 220 608	1 713 473	3 018 018	0.00
Annual age 40–49 yr, biennial age 50–69 yr	4 551 101	49 334	1 479 841	1 788 107	7 868 384	0.58
Annual age 40–49 yr, biennial age 50–74 yr	5 027 968	39 529	1 567 832	1 832 766	8 468 095	0.59
Annual age 40–69 yr	6 540 531	40 605	1 530 563	1 694 982	9 806 681	0.67
Annual age 40–74 yr	7 314 735	30 529	1 618 139	1 707 003	10 670 406	0.69
Annual age 50–69 yr	4 127 472	47 245	1 487 568	1 713 469	7 375 754	0.56
Annual age 50–74 yr	4 908 452	37 013	1 575 399	1 724 528	8 245 393	
Biennial age 40–74 yr	3 931 877	41 542	1 557 638	1 855 982	7 387 038	0.53
Biennial age 50–69 yr	2 175 956	55 863	1 437 689	1 807 948	5 477 456	0.40
Biennial age 50–74 yr	2 672 157	46 018	1 524 021	1 849 832	6 092 028	0.44
Triennial age 50–69 yr	1 573 325	61 405	1 406 127	1 821 409	4 862 266	0.32
Triennial age 50–74 yr	1 911 210	53 721	1 477 251	1 864 335	5 306 517	0.36

*Includes surgery and radiation costs.
†Includes systemic treatment with medications including trastuzumab.

Table 2: Marginal cost-effectiveness and cost–utility ratios of various screening scenarios (discount = 1.5%) per 1000 women compared to no screening

Scenario	Modelled overall health care system cost, $	Modelled life-years	Modelled QALYs	Marginal cost-effectiveness ratio, $/life-year gained	Marginal cost–utility ratio, $/QALY
No screening	1 965 899	30 602	24 998	–	–
Triennial age 50–69 yr	3 368 225	30 648	25 036	30 536	36 981
Triennial age 50–74 yr	3 642 494	30 653	25 039	33 026	40 193
Biennial age 50–69 yr	3 835 726	30 662	25 048	30 879	37 265
Biennial age 50–74 yr	4 217 275	30 669	25 053	33 715	40 851
Annual age 50–69 yr	5 250 458	30 688	25 069	38 366	45 855
Annual age 40–49 yr	4 310 198	30 639	25 030	63 167	73 414
Annual age 50–74 yr	5 789 126	30 694	25 075	41 313	49 587
Annual age 40–49 yr, biennial age 50–69 yr	6 072 758	30 697	25 078	43 419	51 442
Annual age 40–49 yr, biennial age 50–74 yr	6 444 999	30 703	25 083	44 221	52 603
Annual age 40–69 yr	7 516 630	30 721	25 098	46 705	55 386
Annual age 40–74 yr	8 051 766	30 727	25 103	48 718	57 938

Note: QALY = quality-adjusted life-year.

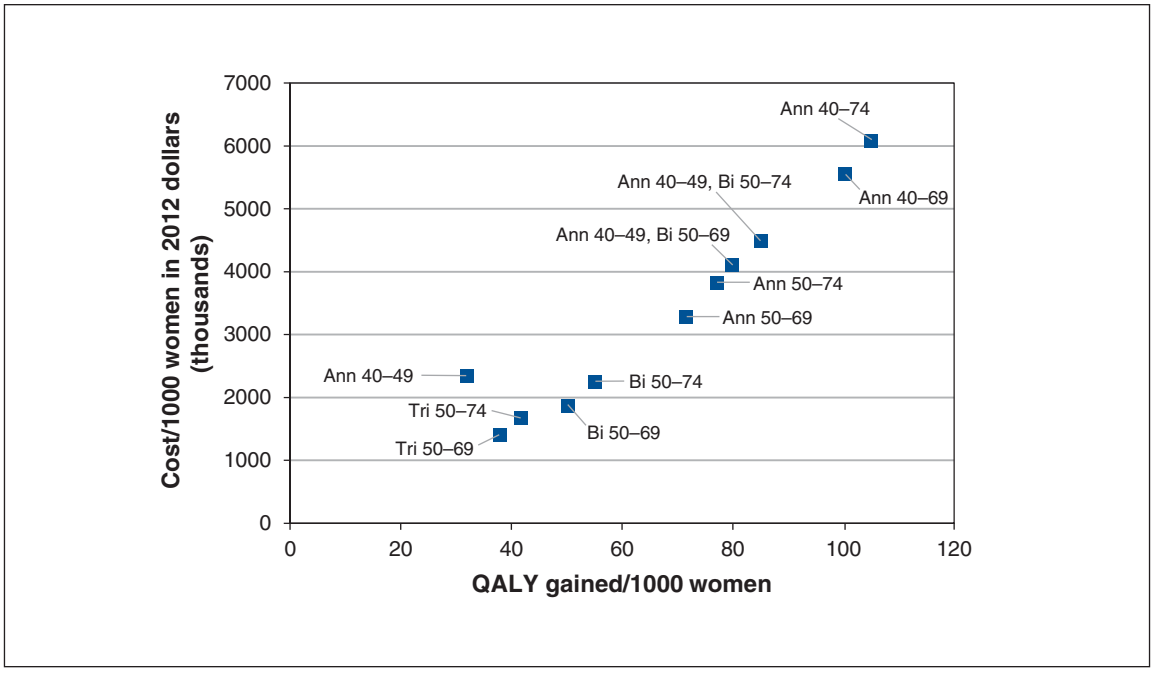

Figure 1: Marginal cost–utility plane for various screening scenarios compared to no screening from health care system perspective. Note: Ann = annual, Bi = biennial, QALY = quality-adjusted life-year, Tri = triennial.

and $60 000/QALY. The lowest ratio modelled was for the least frequent screening with the smallest age band (triennial screening for women aged 50–69), at $30 536/life-year gained and $36 981/QALY. The most aggressive scenario compared to no screening, namely, annual screening for women aged 40–74 years, was associated with the highest marginal ratio, at $48 718/life-year gained and $57 938/QALY.

In the univariate sensitivity analysis, in most cases, the marginal ratios did not change dramatically. The notable exception was omission of systemic treatments, which increased the mar-

ginal cost-effectiveness ratio to more than $150 000/life-year gained (Table 3) (full data given in Supplementary Table 4, Appendix 1), but this is not a viable clinical option. The model was also sensitive to modifications in health preference values, with more favourable marginal cost–utility ratios when the health preference values were increased by 25%, thereby showing greater benefits between the screening and no-screening scenarios. Participation, mammography sensitivity and use of trastuzumab did not affect model results markedly. The insensitivity of marginal cost-effectiveness ratios and cost–utility ratios to the decreased screening compliance rate is understandable because screening costs account for one-third to one-half of the total health cost in the scenarios. A decline in screening results in decreased screening costs, but this is paralleled by a corresponding decrease in the number of invasive cancers detected, affecting life-years gained and QALYs. This results in the ratios' being fairly stable. The sensitivity of mammography is already fairly high for most women; therefore, the impact of an increase is limited. Finally, a relatively small fraction of the cohort would receive and benefit from trastuzumab treatment.

Results of the incremental analysis are presented in Table 4 and Figure 2 (complete data given in Supplementary Table 5, Appendix 1). Several of the scenarios are weakly dominated. For those that are not dominated, ICURs range from $36 981/QALY for triennial screening for women aged 50–69 to $110 994/QALY for annual screening for women aged 40–74, with a difference of 67 QALYs per 1000 women between these extremes.

With triennial screening in women aged 50–74 as the reference, the ICURs for decreasing the screening interval to biennial or annual were $42 900 and $71 481, respectively (Table 5) (full data presented in Supplementary Table 6, Appendix 1). The ICUR for extending the age range to 40–74 years for annual screening was $80 986.

We also used biennial screening in women aged 50–74 years, which is the standard of several programs in Canada, as a reference for an incremental analysis (Table 6) (full data given in Supplementary Table 7, Appendix 1). Screening annually in women aged 50–74 years was weakly dominated, but the ICUR for annual screening in those aged 50–69 was $62 549/QALY, for those aged 40–69 years, $79 266/QALY, and for those aged 40–74 years, $110 994/QALY. Less-intensive screening reduced both QALYs and costs. For example, eliminating biennial screening for women aged 70–74 years resulted in a decrease of 5 QALYs, with a cost reduction of $77 308 per QALY lost.

Decreasing the discounting rate from 5% to 3% to 1.5% (with no screening as the reference) resulted in a reduction in the ICUR from $65 743/QALY to $52 672/QALY to $38 142/QALY, respectively, for biennial screening in women aged 50–69 years and from $156 743/QALY to $121 160/QALY to $83 845/QALY, respectively, for annual screening in those aged 40–74 (data not shown).

Interpretation

We compared the cost-effectiveness of various policy-driven mammography screening programs conducted from the perspective of a Canadian publicly funded health care system using a validated breast cancer risk model. From a pure cost

Table 3: Univariate sensitivity analysis, marginal: active screening scenarios compared to no screening where the outcome is cost per quality-adjusted life-year (discount = 1.5%)

	Marginal cost-effectiveness ratio, $						
Scenario	Base case	No treatment	50% missed screens	100% sensitivity	No trastuzumab	Utilities +25%*	Utilities –25%*
No screening							
Triennial age 50–69 yr	36 981	165 119	33 327	27 487	33 035	29 585	46 227
Triennial age 50–74 yr	40 193	179 359	36 920	30 283	36 243	32 154	50 241
Biennial age 50–69 yr	37 265	207 737	32 768	26 606	33 498	29 812	46 581
Biennial age 50–74 yr	40 851	205 444	36 442	29 581	36 848	32 681	51 064
Annual age 50–69 yr	45 855	247 211	36 556	34 224	42 836	36 684	57 318
Annual age 40–49 yr	73 414	1 248 787	58 199	75 173	64 669	58 731	91 767
Annual age 50–74 yr	49 587	276 755	40 447	24 491	46 545	39 669	61 983
Annual age 40–49 yr, biennial age 50–69 yr	51 442	373 350	42 949	36 529	46 656	41 153	64 302
Annual age 40–49 yr, biennial age 50–74 yr	52 603	371 187	44 603	37 739	47 731	42 082	65 753
Annual age 40–69 yr	55 386	370 904	43 883	40 491	51 114	44 309	69 232
Annual age 40–74 yr	57 938	415 165	46 069	42 313	53 467	46 351	72 423

*More favourable marginal cost–utility ratio when the health preference values were increased by 25%, thereby showing greater benefits between the screening and no-screening scenarios.

Table 4: Incremental cost–utility ratios of various screening scenarios (discount = 1.5%) per 1000 women compared to no screening*

Scenario	Modelled overall health care system cost, $	Modelled life-years	Modelled QALYs	Health care system incremental cost, $	Incremental QALYs	Incremental cost–utility ratio, $/QALY
No screening	1 965 899	30 602	24 998			
Triennial 50–69 yr	3 368 225	30 648	25 036	1 402 326	38	36 981
Triennial 50–74 yr	3 642 494	30 653	25 039	274 269		Weakly dominated
Biennial 50–69 yr	3 835 726	30 662	25 048	467 501	12	38 142
Biennial 50–74 yr	4 217 275	30 669	25 053	381 549		Dominated
Annual 50–69 yr	5 250 458	30 688	25 069	1 414 732	21	65 944
Annual 50–74 yr	5 789 126	30 694	25 075	538 668		Weakly dominated
Annual 40–49 yr, biennial 50–69 yr	6 072 758	30 697	25 078	283 631		Weakly dominated
Annual 40–49 yr, biennial 50–74 yr	6 444 999	30 703	25 083	372 241		Weakly dominated
Annual 40–69 yr	7 516 630	30 721	25 098	2 266 172	29	79 266
Annual 40–74 yr	8 051 766	30 727	25 103	535 136	5	110 994

Note: QALY = quality-adjusted life-year.

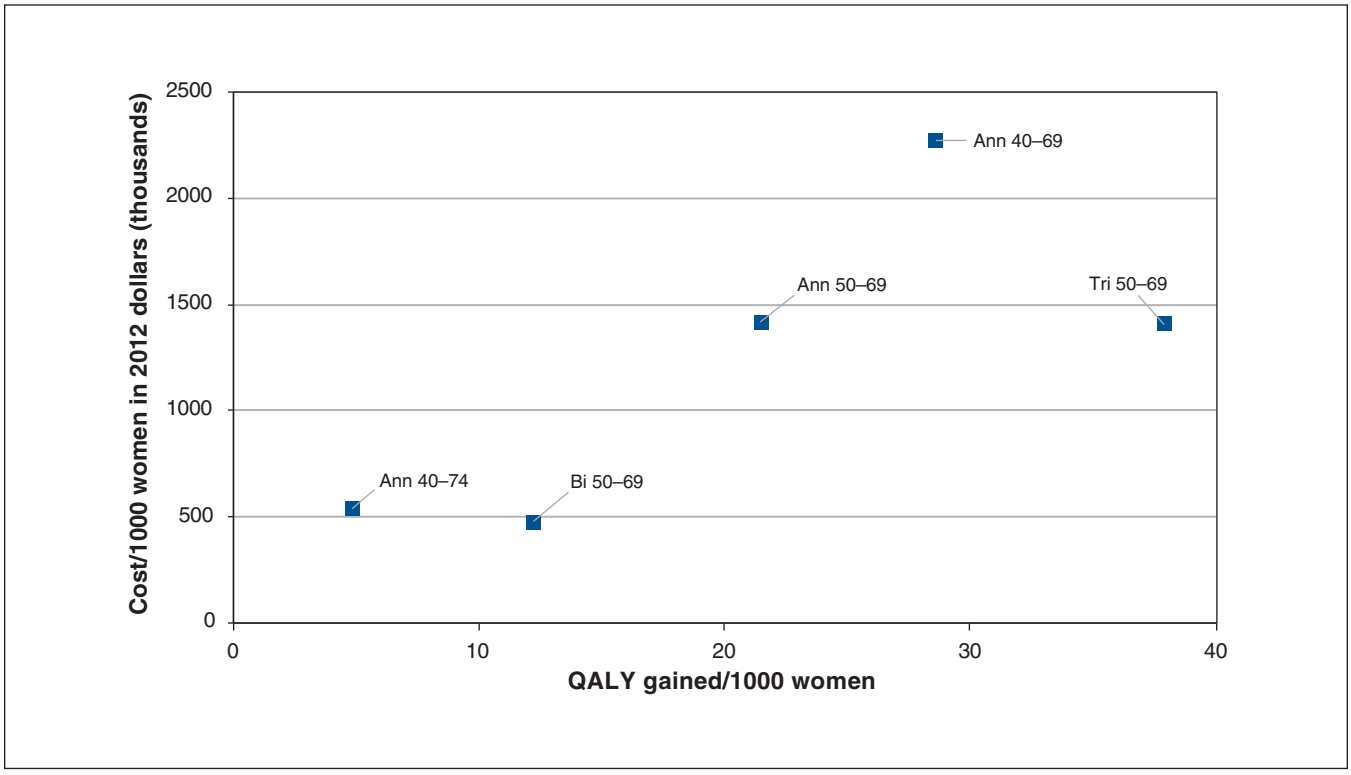

Figure 2: Incremental cost–utility plane for various screening scenarios compared to no screening from health care system perspective. Only nondominated scenarios are shown. Note: Ann = annual, Bi = biennial, QALY = quality-adjusted life-year, Tri = triennial.

perspective, and not considering clinical outcomes, all active screening scenarios modelled (undiscounted) were cost drivers and represented one-third to two-thirds of the total cost of breast cancer management (screening, investigation and treatment) to the health care system. The ratio of the cost of screening to overall cost was directly proportional to the

Table 5: Incremental cost–utility ratio for changes in screening frequency and age at which to start screening

Scenario	Modelled overall health care system cost, $	Modelled life-years	Modelled QALYs	Health care system incremental cost, $	Incremental QALYs	Incremental cost–utility ratio, $/QALY
Triennial 50–74 yr	3 642 494	30 653	25 039			
Biennial 50–74 yr	4 217 275	30 669	25 053	574 781	13	42 900
Annual 50–74 yr	5 789 126	30 694	25 075	1 571 851	22	71 481
Annual 50–74 yr	5 789 126	30 694	25 075			
Annual 40–74 yr	8 051 766	30 727	25 103	2 262 640	28	80 986
Annual 50–69 yr	5 250 458	30 688	25 069			
Annual 40–69 yr	7 516 630	30 721	25 098	2 266 172	29	79 266
Biennial 50–74 yr	4 217 275	30 669	25 053			
Annual 40–49 yr, biennial 50–74 yr	6 444 999	30 703	25 083	2 227 723	30	74 164

Note: QALY = quality-adjusted life-year.

Table 6: Effect of changing the screening scenario from the baseline of biennial screening in women aged 50–74 years

Scenario*	Modelled overall health care system cost, $	Modelled life-years	Modelled QALYs	Health care system incremental cost, $	Incremental cost-effectiveness ratio, $/life-year	Incremental cost–utility ratio, $/QALY
Increasing						
Biennial 50–74 yr	4 217 275	30 669	25 053			
Annual 50–69 yr	5 250 458	30 688	25 069	1 033 183	54 862	62 549
Annual 50–74 yr	5 789 126	30 694	25 075		Weakly dominated	
Annual 40–49 yr, biennial 50–69 yr	6 072 758	30 697	25 078		Weakly dominated	
Annual 40–49 yr; biennial 50–74 yr	6 444 999	30 703	25 083		Weakly dominated	
Annual 40–69 yr	7 516 630	30 721	25 098	2 266 172	68 184	79 266
Annual 40–74 yr	8 051 766	30 727	25 103	535 136	88 088	110 994
Decreasing						
Biennial 50–74 yr	4 217 275	30 669	25 053			
Biennial 50–69 yr	3 835 726	30 662	25 048	381 549	61 296	77 307.62
Triennial 50–74 yr	3 642 494	30 653	25 039		Weakly dominated	Weakly dominated
Triennial 50–69 yr	3 368 225	30 648	25 036	467 501	31 958	38 142
No screening	1 965 899	30 602	24 998	1 402 326	30 536	36 981

Note: QALY = quality-adjusted life-year.
*Increasing = scenarios in which screening is increased from baseline; decreasing = scenarios in which screening is decreased from baseline. Incremental cost-effectiveness ratios and cost–utility ratios express dollars saved per life-year or QALY lost.

aggressiveness of the screening strategy. Treatment costs were slightly higher for screening than for no screening. Lowering the age at which screening starts to 40 years from 50 years added roughly $1.3 million–$2.4 million per 1000 women ($1300–$2400 per woman over her lifetime) to the overall cost. Increasing the upper limit of 69 years by 5 years added about $0.5 million–$0.9 million per 1000 women ($500–$900 per woman) to the overall cost. Interestingly, the scenario commonly used in Canada, biennial screening for women aged 50–74, was weakly dominated by annual screening for

those aged 50–69. Presumably, the impact of reducing interval cancers in younger women outweighs that of detecting cancer in women aged 70–74.

Several models of breast cancer natural history have been developed to project the impact of different mammography screening scenarios in women.[13,28–32] We selected the modified Wisconsin Cancer Intervention and Surveillance Modelling Network model for our analysis because it allowed simulation of the growth of a distribution of breast cancers within a cohort of women and separate consideration of the individual effects of various detection strategies and treatment regimens on mortality or other outcomes. In addition, the Canadianized version used empirical data on the sensitivity and specificity of modern screening mammography specific to the Canadian perspective. The model performed quite well in predicting breast cancer incidence in the absence of screening in the Canadian context.[21] Despite the fact that annual-screening scenarios had higher incremental ratios than less-frequent scenarios, they were associated with greater life-years gained and QALY benefits. The more aggressive the screening strategy, the more cancers are detected and the more breast cancer deaths are averted and life-years gained.

A comparison of the ratios for all the active screening scenarios compared to the no-screening scenario showed a relatively tight range of marginal ratios, within roughly $20 000 of one another. Extending the upper age limit for screening from 69 to 74 years marginally increased the ratios owing to additional screening costs, but this was balanced by improved outcomes. Lowering the age at which screening started to 40 years resulted in increased ratios, mostly due to the increased screening costs, but also yielded more life-years gained and QALYs. Since both life-years gained and QALYs and costs rise together almost linearly with the number of lifetime screens per woman, the decision on how to screen is related mainly to willingness to pay by the system and avoiding recalling too many women for further examinations after positive screening results. Certainly, if examined by age band (50–69 yr and 50–74 yr), the modelled ratios for annual, biennial and triennial screening scenarios compared to no screening were very similar. Interestingly, the current standard in some provinces and the regimen recommended by the US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care, biennial screening for women aged 50–74, was a weakly dominated scenario, as were the 2 hybrids of annual screening for those aged 40–49 followed by biennial examinations. When choosing a screening scenario based on the value assessments, one should also consider the improvement in life-years gained and QALYs associated with more frequent screening.

It is useful to consider the effect of the discounting rate on cost-effectiveness and cost–utility estimates. Discounting assigns progressively reducing values to costs and improvements in health outcome that occur in the future. It is traditional to use the same annual discounting rate for both.[33] With higher discount rates, this essentially has the effect of making both costs and benefits that occur many years after the beginning of a program virtually negligible. When, as in a screening program, many of the costs are borne toward the beginning of the program, whereas the benefits (absence of breast cancer death or years or QALYs gained) occur many years later, the effect is to reduce estimated benefits much more than costs, increasing ICURs. It has been argued that this puts a disproportionate emphasis on the "here and now."[34] In 2012, it was common to use a discounting rate of 5%. Recommended reductions since that time to 3% and now to 1.5% have reduced ICURS by about 20% and 45%, respectively, making them more attractive to payers.[26]

Our discounted model predicted that all screening scenarios were more effective than no screening. All ratios comparing active scenarios to no screening fell below commonly accepted and proposed thresholds.[35–38] Several studies have evaluated the cost-effectiveness of screening strategies, but most have been conducted from the perspective of the US health care system and/or have considered different risk factors such as early and late age and genetic profile.[4,13,39–41] Gocgun and colleagues[42] constructed a model to estimate the Canadian cost per life saved using data from the Canadian National Breast Cancer Screening Study.[43,44] That model was not validated and was based on study results from the 1980s, when film mammography (now obsolete) was used. Unlike several other studies,[45] the Canadian National Breast Cancer Screening Study did not show a mortality benefit of mammographic screening, which would make any screening strategy not effective or cost-effective. The study showed that there was a decrease in mortality when the frequency of screening was increased. However, when considering cost-effectiveness, the strategy that Gocqun and colleagues[42] found to be the most cost-effective included avoiding screening in women aged 40–49 and screening those aged 50–69 every 5 years, at a cost of $537 000 per life saved. Screening women aged 50–69 every 3 years or every other year yielded results close to the optimal strategy ($626 973 and $654 940, respectively) while continuing to avoid screening in women aged 40–49. Other differences between our model and that of Gocgun and colleagues[42] include variability in costs, variability in discount factor (3.1% v. 1.5%), differential sources of the treatment distribution data, older survival data and no examination of QALYs, only of life-years.

Pataky and colleagues[46] also used a Markov model to predict the cost-effectiveness of screening mammography in the British Columbia Screening Program. They focused exclusively on the question of using annual versus biennial screening for women with high breast density and did not consider the various scenarios. Furthermore, those authors did not describe the independent validation of the model, whereas the Cancer Intervention and Surveillance Modelling Network model has been extensively validated.

Limitations

Limitations of the model that we used were outlined in previous work.[11,21,22] Essentially, our baseline assumption was that 100% of eligible women would be screened, whereas, in reality, compliance is lower with an organized screening program.[47] We did not include the cost of premature death in the economic

evaluation to avoid the possibility of double counting. However, given the significance of premature death to society, we expect that more frequent screening would substantially decrease the costs associated with premature death due to breast cancer. Work examining the cost of premature death in this model is planned.

Conclusion

The current work will be helpful in informing the question regarding the most appropriate mammography screening scenario for a population. We have shown that the greatest single cost contributor in a screening program is screening itself. The more screens that a women receives in her life, the greater the financial cost to the health care system, but the greater the gain in life-years and QALYs. The decision on how to screen is related mainly to willingness to pay and a determination as to what is an acceptable rate for recalling women for further examinations after positive screening results.

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