The Cost-Effectiveness of Mammography-Based Breast Cancer Screening in Canada: A Systematic Review

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Abstract

Background: The current literature on female breast cancer screening is largely focused on the health outcomes that result from screening. There is comparatively little data on the cost-effectiveness of the screening.

Methods: This systematic review sought to identify all studies published within the last 10 years that analyzed the cost-effectiveness of mammography-based female breast cancer screening policies in Canada.

Results: Seven studies were included, and four were applicable to the average-risk Canadian women. Triennial screening for average-risk women aged 50–69 years was the most cost-effective in terms of cost per QALY. The use of MRI with mammography for women with the BRCA1/2 mutation was cost-effective, while annual mammography-based screening for women with dense breasts was cost-ineffective.

Conclusion: Analyses of the cost-effectiveness of mammography-based screening within Canadian populations are few in numbers and have heterogeneous methodologies. The existing data suggest that Canada’s current screening policy to screen average-risk women aged 50–74 years, biennially or triennially is cost-effective.

Résumé

Contexte : La documentation actuelle sur le dépistage du cancer du sein chez la femme est principalement axée sur les résultats cliniques qui découlent du dépistage. Il existe relativement peu de données sur le rapport coût/efficacité du dépistage.

Méthodologie : Cette revue systématique a tenté de repérer toutes les études publiées au cours des dix dernières années qui ont analysé la rentabilité des politiques de dépistage du cancer du sein par mammographie chez la femme au Canada.

Résultats : Sept études ont été retenues, et quatre d’entre elles s’appliquent aux femmes canadiennes à risque moyen. Le dépistage triennal chez les femmes à risque moyen âgées de 50 à 69 ans est le plus rentable en ce qui concerne le coût par AVAQ. L’utilisation de l’IRM couplée à la mammographie chez les femmes présentant la mutation BRCA1/2 est rentable, tandis que le dépistage annuel par mammographie chez les femmes aux seins denses ne l’est pas.

Conclusion : Les analyses du rapport coût/efficacité du dépistage par mammographie au sein des populations canadiennes sont peu nombreuses et leurs méthodologies sont hétérogènes. D’après les données existantes, la
The cost-effectiveness of mammography

Background

Mammography-based female breast cancer screening is a modern staple of preventive healthcare.\(^1\) It is administered in primary care facilities across Canada and the cost of the intervention is covered under Canada's public healthcare system.\(^1\) While there is no direct policy associated with screening for breast cancer, the Government of Canada makes recommendations to primary care physicians and the general public about screening protocols.\(^1\) It is currently recommended that women between the ages of 50–74 years who are at an average-risk of developing breast cancer are screened via mammography biennially or triennially.\(^1\) There are established benefits to breast cancer screening, particularly because of its high prevalence and variable mortality rates across different stages.\(^2,3\) In Canada, breast cancer represents 25% of all cancer diagnoses among women and 13% of all cancer diagnoses overall.\(^2\) However, as a result of the implementation of screening practices and improved therapeutic interventions, the mortality rate for female breast cancer has decreased by 48% since its peak in 1986.\(^2\) Since 2010, more than 80% of all female breast cancer diagnoses have occurred at stage I and II, with only 5% being diagnosed at stage IV.\(^2\) However, the statistics on mortality rates and disease incidence only tell the story of breast cancer from an epidemiological perspective. To truly understand how to create an effective policy for organized breast cancer screening across Canada, it is necessary to investigate the cost-effectiveness of the current screening protocols.

Breast cancer screening recommendations are officially developed by the Canadian Task Force on Preventive Health Care (CTFPHC).\(^1\) The most recent breast cancer screening guidelines were released by the CTFPHC in 2018.\(^1\) While these guidelines and embedded recommendations incorporate a variety of factors, the emphasis is generally placed on patient costs and benefits. There is comparatively little exposure given to the financial costs of screening and false-positive scenarios. There is no analysis of cost-effectiveness within the current 2018 Canadian breast cancer screening guidelines and there is only a cursory discussion of the economic implications of screening within the older 2011 guidelines. Moreover, the two articles that were cited for cost-effectiveness in the 2011 CTFPHC guidelines were studies conducted in South Korea and the United States.\(^4\)

To make informed policy decisions about breast cancer screening, it is imperative to analyze Canadian data on cost-effectiveness.\(^1,4\) Cost-effectiveness studies from other countries have been excluded due to differences in breast cancer incidence and costs of healthcare. The prevalence of breast cancer varies in different populations and is influenced by both lifestyle and genetic factors.\(^5,6\) For example, the 5-year prevalence of breast cancer in Canada is 622.87/100,000, compared to 640.31/100,000 in the United States.\(^7\) The cost of breast cancer screening and treatment can also be influenced by geographic region and is often affected by the fact as to whether a country has a single payer or multi-payer healthcare system.\(^8\) Lastly, there are differences in breast cancer survival across different countries. In fact, breast cancer survival seems to be significantly impacted by socioeconomic status and access to healthcare.\(^9–11\) Therefore, to limit the interference of regional variances in breast cancer prevalence, cost, and survival rates, this systematic review will focus on studies analyzing the cost-effectiveness of mammography-based breast cancer screening strategies within the Canadian female population.

Methods

A systematic literature review for all original studies that addressed breast cancer screening and/or those that attempted to evaluate cost-effectiveness was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines for reporting.\(^12,13\) No protocol exists for this review. Criteria for literature searches and inclusion criteria were determined \textit{a priori} and followed for all methods (TT, MMWa, RT, and MMWb).

Search strategy

Systematic searches were performed within the PubMed, MEDLINE, Embase, Canadian Agency for Drugs and
Technologies in Health (CADTH), EconLit, Web of Science, and National Health Service Economic Evaluation Database (NHSEED) electronic databases for articles published in peer-reviewed journals, with a full text available in English. Only papers published within the last 10 years were included to ensure that the review was relevant to current breast cancer screening practices and treatment methods within Canada. In collaboration with a Master of Library and Information Science librarian, we developed a search strategy tailored to each database using search terms such as “cost effectiveness,” “cost–benefit analysis,” “cost evaluation,” “Canada,” “screening,” “mammography,” “cancer,” “neoplasm,” “sarcoma,” and “breast” to identify studies investigating the cost-effectiveness of mammogram screening in Canadian female populations. Refer to Supplementary file 1 for the full search strategy.

Eligibility criteria
Title and abstract screening was conducted independently by RT and MMWb to identify studies for a full-text review. The search was limited to studies that featured data on the cost-effectiveness of mammography-based female breast cancer screening policies in a Canadian population. Only English full-text, original research articles published within the past 10 years were eligible for inclusion. Any discrepancies raised during the screening process were resolved through consensus. Full-text articles of selected publications were retrieved and assessed for eligibility in duplicate by TT and MMWα. Following the full-text review, papers that contained original research content related to breast cancer screening policies in Canada were included. Reference lists of included papers were also assessed to collect additional records and ensure that all relevant studies were captured. Agreement among the two investigators at this stage was calculated using the κ statistic.

Data extraction and analysis
Should the publication have met all eligibility criteria, data such as the study characteristics, parameters of the model used, discounting rate, time horizon, screening intervention, primary outcome, incremental cost-effectiveness ratios, average total cost of screening, incremental cost per death averted, and number of women screened to avert one death was extracted by TT and MMWα. If eligible studies did not report data necessary for inclusion in the systematic review, efforts were made to contact the corresponding authors directly.

Quality assessment
Study quality was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist. Refer to Supplementary file 2 for the completed checklist. This 24-item evaluation tool includes guidelines for critically appraising the quality of reporting economic model characteristics, analytic methods, study parameters, incremental costs and outcomes, amongst others. For each item, evidence of its description within each study was reported. The CHEERS Checklist was completed independently by TT and MMWα. Final quality assessment evaluations were determined through consensus and review of source documents. It was not possible to assess the risk of bias as the included studies all utilized simulation models.

Results
This search identified a total of 1087 citations. Following duplicate removal, 673 papers underwent title and abstract screening; after which, 35 articles were selected to undergo a full-text review. This initial round of screening did not apply the recency requirement of 10 years mentioned previously. Upon applying this recency requirement during the examination of full-text articles, seven papers were accepted and included in this systematic review (κ = 1.000) (Figure 1).
The cost-effectiveness of mammography

The cost-effectiveness of mammography but addressed the topic from different perspectives. The Mittmann et al. paper considered cost-effectiveness from a single payer public healthcare system perspective, whereas the 2015 paper by the same lead author considered cost-effectiveness from a societal perspective. Both studies also used digital mammography as the screening intervention, expressed their costs in 2012 Canadian dollars using Ontario-based costs (Ontario Health Insurance Plan (OHIP)) for screening and treatment, and employed a lifetime horizon for cost calculation. The homogenous methodologies applied across these two papers thus made their respective estimates easy to compare. In comparison, the Pataky et al. paper attempted to calculate the cost-effectiveness of population-based mammography screening strategies for the province of British Columbia using a different microsimulation model. In addition to using a different model, Pataky et al. expressed their costs in 2010 Canadian dollars and used the BC Medical Services Fee Commission Schedule instead of OHIP. However, similar to the two Mittmann et al. papers, Pataky et al. employed a lifetime horizon.

Both the Mittmann et al. papers and the Pataky et al. study concluded that the benefits of mortality reduction rose approximately linearly with costs, while costs were linearly dependent on the number of lifetime screens per woman. Then, the decision to screen is largely based on willingness to pay. To compare cost-effectiveness, an analysis of the incremental cost-effectiveness ratios (ICERs) of the three studies was performed (Table 3).

The Mittmann et al. study had far higher ICERs due to its inclusion of costs to society, particularly loss in productivity. Only three screening scenarios are examined in Table 2, characteristics of included articles are presented in Table 1. The CHEERS Checklist was applied to these seven studies. Upon evaluation, every article fulfilled most of the criteria on the checklist and thus were deemed to be of good quality. All studies clearly presented well-defined research questions, characterized the study population, and provided justifications for the specific type of analytical model used. A notable difference between the articles was the presence of confidence intervals. The 2015 and 2018 papers by Mittmann et al. did not contain confidence intervals or any other metric expressing uncertainty about their point estimates. However, the fact that the papers incorporated a variety of cost, sensitivity, and incidence data to generate their models may explain the omission of confidence intervals within these studies.

This review takes a qualitative approach at evaluating the included studies. A meta-analysis could not be conducted due to the significant heterogeneity between the studies. In addition, the use of different models with varying input parameters, discounting rates, time horizons, and costs made it infeasible to statistically combine the studies.

The included studies varied in the populations studied, which were subdivided into two categories: those presenting a cost-effectiveness analysis for screening women at an average-risk for breast cancer and those assessing cost-effectiveness for high-risk women. Four articles calculated the cost-effectiveness for screening average-risk women: Mittmann et al., Gocgun et al., Pataky et al., and Mittmann et al. (Table 2).

Both papers by Mittmann et al. used the same University of Wisconsin Breast Cancer Epidemiology Simulation model, Table 1. Characteristics and findings of included studies

<table>
<thead>
<tr>
<th>Study authors</th>
<th>Year</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pataky et al.</td>
<td>2013</td>
<td>Annual mammography in conjunction with MRI screening of BRCA1/2 mutation carriers resulted in an ICER of $50,900/QALY.</td>
</tr>
<tr>
<td>Pataky et al.</td>
<td>2014a</td>
<td>Screening average risk women aged 50–69 years and 40–69 years biennially were the most cost-effective strategies yielding ICERs of $28,921/QALY and $86,029/QALY, respectively.</td>
</tr>
<tr>
<td>Pataky et al.</td>
<td>2014b</td>
<td>Annual screening of women with high breast density resulted in an ICER of $565,912/QALY.</td>
</tr>
<tr>
<td>Gocgun et al.</td>
<td>2015</td>
<td>Screening average-risk women aged 50–69 years once every 5 years is the most optimal strategy with regard to cost per life saved. Annual mammogram screening is not cost-effective.</td>
</tr>
<tr>
<td>Mittmann et al.</td>
<td>2015</td>
<td>Screening average-risk women aged 50–69 once every 3 years is the most cost-effective at $83,070 per life year gained and $94,762 per QALY.</td>
</tr>
<tr>
<td>Mittmann et al.</td>
<td>2018</td>
<td>Screening average risk women aged 50–69 years biennially yielded an ICER of $381,42/QALY while triennial screening within the same age group resulted in an ICER of $36,981/QALY.</td>
</tr>
<tr>
<td>Furzer et al.</td>
<td>2020</td>
<td>Annual mammography-based screening starting from age 25 in adolescent women treated for Hodgkin lymphoma was the most cost-effective screening strategy and resulted in an ICER of $43,000/QALY.</td>
</tr>
</tbody>
</table>
Table 2. Characteristics of studies assessing the cost-effectiveness of screening average-risk and high-risk women

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary outcome</th>
<th>Screening intervention</th>
<th>Time horizon</th>
<th>Costs</th>
<th>Discounting rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average-risk women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pataky et al. (2014a)(^{18})</td>
<td>Incremental cost per quality-adjusted life year (QALY)</td>
<td>Film-based mammography</td>
<td>Lifetime</td>
<td>2010 Canadian dollars using BC-based costs for screening and treatment</td>
<td>3.5%</td>
</tr>
<tr>
<td>Gocgun et al. (2015)(^{17})</td>
<td>Incremental cost per death averted</td>
<td>Film-based mammography</td>
<td>20 years</td>
<td>2015 Canadian dollars using Ontario-based costs for screening and treatment</td>
<td>3.1%</td>
</tr>
<tr>
<td>Mittmann et al. (2015)(^{15})</td>
<td>Incremental cost per QALY</td>
<td>Digital mammography</td>
<td>Lifetime</td>
<td>2012 Canadian dollars using Ontario-based costs for screening and treatment</td>
<td>5%</td>
</tr>
<tr>
<td>Mittmann et al. (2018)(^{16})</td>
<td>Incremental cost per QALY</td>
<td>Digital mammography</td>
<td>Lifetime</td>
<td>2012 Canadian dollars using Ontario-based costs for screening and treatment</td>
<td>1.5%</td>
</tr>
<tr>
<td><strong>High-risk women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pataky et al. (2013)(^{19})</td>
<td>Incremental cost per quality-adjusted life year (QALY)</td>
<td>Magnetic resonance imaging in conjunction with digital mammography</td>
<td>Lifetime</td>
<td>2008 Canadian dollars using British Columbia–based costs for screening and treatment</td>
<td>3.5%</td>
</tr>
<tr>
<td>Pataky et al. (2014b)(^{20})</td>
<td>Incremental cost per QALY</td>
<td>Film-based mammography</td>
<td>Lifetime</td>
<td>2007 Canadian dollars using British Columbia–based costs for screening and treatment</td>
<td>3%</td>
</tr>
<tr>
<td>Furzer et al. (2020)(^{21})</td>
<td>Incremental cost per QALY</td>
<td>Magnetic resonance imaging and digital mammography</td>
<td>Lifetime</td>
<td>2015 Canadian dollars using Ontario-based costs for screening and treatment</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

The third study that examined cost-effectiveness for average-risk women was conducted by Gocgun et al.\(^{17}\) This study cannot be directly compared against the Mittmann et al. and Pataky et al. studies because it did not calculate incremental cost per quality adjusted life year (QALY), instead Gocgun et al. opted to calculate incremental cost per death averted.\(^{17}\) Moreover, unlike the previous three studies, it did not use a lifetime horizon. Instead, costs were evaluated over a horizon of 20 years.\(^{17}\) Gocgun et al. used data from the Canadian National Breast Cancer Screening Study to create and validate their model.\(^{17}\) It should be noted that the data used to create this model was generated using film-based mammography, a screening technique that has since been replaced with digital mammography.\(^{17}\) The increased sensitivity of digital mammography may result in lower incremental cost per death averted. Ontario (OHIP) data expressed in

as the 50–69 years age group closely approximates the current Canadian recommendation to screen average-risk women between 50 and 74 years of age. In both Mittmann et al. studies, the simulations with the 50–74 years age group were weakly dominated by the 50–69 years age group, as the 50–69 years age group was clinically superior and cost-effective.\(^{15,16}\) Similarly, Pataky et al. found that screening women aged 50–74 years was dominated by screening women aged 40–69 years for both biennial and triennial screening.\(^{18}\) However, biennial screening of women aged 50–69 years was the most cost-effective in a constrained budget. These studies provide support to the argument that average-risk women aged 70–74 years should not be screened using digital mammography. Furthermore, the Pataky et al. study suggests that if the budget allows, higher priority should be given to screen women aged 40–49 years in comparison to women aged 70–74 years.\(^{18}\)
The 2015 Canadian dollars was used to input costs of screening and treatment scenarios.17

Gocgun et al. concluded that more aggressive screening scenarios generate greater health benefits, but at an increased cost (Table 4).17 Screening average-risk women aged 50–69 years every 5 years was found to have the lowest incremental costs, but the highest number of women were screened to avert one death. Biennial screening for average-risk women between 50 and 69 years had the most favorable combination of incremental cost per death averted and the number of women screened to avert one death. Similar to Mittmann et al. and Gocgun et al. found a sharp increase in cost per utility, or in this case, cost per death averted when comparing biennial or triennial screening to annual screening.17

The remaining 2013 and 2014b studies by Pataky et al. as well as the 2020 study by Furzer et al. focused on populations at a high-risk for breast cancer (Table 2).19–21 Both Pataky et al. studies constructed their Markov models based on breast cancer incidence, treatment, and screening costs in British Columbia using a lifetime horizon for the calculation of costs.19,20 Meanwhile, the Furzer et al. study used costs specific to OHIP, but still used a lifetime horizon.21

The Pataky et al. study examined cost-effectiveness of using Magnetic Resonance Imaging (MRI) in conjunction with mammography for women carrying the BRCA1/2 mutation, expressing costs in 2008 Canadian dollars.19 Women with the BRCA1/2 mutation are at a higher risk of developing breast cancer; therefore, they may benefit from the higher sensitivity of the MRI.22 Pataky et al. found an ICER of $50,911/QALY for using MRI in conjunction with mammography instead of using mammography alone.19 At a willingness to pay of $100,000/QALY, the use of MRI screening is cost-effective 85.6% of the time. However, Pataky et al. found the model to be highly dependent on the cost of an MRI scan, which may change the applicability of the result in locations where an MRI scan is more expensive.19

The 2014b study by Pataky et al. investigated the cost-effectiveness of annual versus biennial mammography screening for women with dense breasts, expressing costs in 2007 Canadian dollars.20 The sensitivity of mammography screening was significantly lower in women with dense breasts, consequently making them more likely to be diagnosed with interval cancers.23 The study found that screening breast cancer in women with dense breasts annually instead of biennially has an ICER of $565,912/QALY.20 The extremely high ICER coupled with the fact that only 43.4% of the simulations showed annual screening to reduce QALYs relative to biennial screening indicate the cost-ineffectiveness of this strategy.20 Moreover, the sensitivity data used in this study were for film-based mammography instead of digital mammography, making it difficult to judge cost-effectiveness in a healthcare environment dominated by digital mammography. Based on this study, annual breast cancer screening for women with dense breasts can effectively be considered cost-ineffective until further research proves otherwise.20

The Furzer et al. study evaluated the cost-effectiveness of early breast cancer surveillance in survivors of thoracic radiation-treated adolescent Hodgkin lymphoma. While this population was highly specific, it still fell within the scope of this review.21 Furzer et al. found that annual mammography-based breast cancer screening beginning at age 25 was associated with an ICER of $43,000/QALY, while a switch to annual MRI starting at age 50 had an ICER of $148,000/QALY.21 Lastly, screening using annual MRI starting from age 25 had an ICER of $227,222/QALY.21 However, despite large differences in ICERs, the life expectancy between the various surveillance methods had very little variation, as it ranged from 45.73 years (for annual mammography starting at age 30 years) to 45.90 years (for annual mammography and MRI starting at age 25 years).21 These findings suggest that the strategy of screening via mammography annually starting at age 25 years may be the most practical and cost-effective in survivors of thoracic radiation-treated adolescent Hodgkin lymphoma.

**Discussion**

To the best of our knowledge, this is the first systematic review that assesses the cost-effectiveness of mammography-based breast cancer screening within Canadian female populations. The results of the seven studies included in this
review ultimately suggest that aggressive screening strategies incur higher costs, but they also provide more health benefits. The optimal strategy for any given situation is decided largely by the willingness to pay. However, a public health-care system like that in Canada must make concrete decisions on which screening practices to implement based on clinical parameters and cost-effectiveness. To make such a decision, it is necessary to understand the thresholds for cost-effectiveness within the field of oncology.

According to a 2010 paper that evaluated the attitudes of US and Canadian physicians on cost-effectiveness, the majority of oncologists in both Canada and the United States see $100,000/life-year as the threshold for cost-effective oncology treatments. Traditionally, when examining healthcare interventions, the threshold of $50,000/QALY (USD) has been cited. However, in recent literature, the trend has been to use a threshold of $100,000/QALY with the World Health Organization, with many economists arguing that thresholds of anywhere from $110,000 to $160,000 per QALY should be used in a population like that in the United States, given the median household income and other factors. If one were to extrapolate these results to Canada, it seems that at the very minimum a value of $100,000/QALY should be used when evaluating the cost-effectiveness of breast cancer screening procedures.

Having made this assumption, we find that the estimates given by both the 2015 and 2018 Mittmann et al. studies as well as the Pataky et al. study for biennial and triennial screening of average-risk women between the ages of 50 and 69 years fall below the threshold of $100,000/QALY. It seems that even with the inclusion of societal costs such as loss in productivity, biennial and triennial screening of women aged 50–69 years is cost-effective. The results of the study by Gocgun et al. cannot be analyzed by the metric of cost-effectiveness we have used above, as the study did not integrate QALYs in its incremental cost-effectiveness ratios. Moreover, more than any other study in this review, Gocgun et al’s study suffered from a poorly constructed model that was forced to make multiple simplifying assumptions due to data scarcity. For example, due to data scarcity, Gocgun et al. assumed the stage distribution of clinically presenting cancer for the 60–69 years age group to be the same as that for the 50–59 years age group. As a result, our analysis of the cost-effectiveness of Canada’s current breast cancer screening policies do not take into account the results of Gocgun et al.

There were also some interesting findings about cost-effectiveness in papers that examined populations at a high risk of developing breast cancer. The study by Pataky et al. on the cost-effectiveness of annual versus biennial mammography-based breast cancer screening for women with dense breasts found an ICER of $565,912/QALY. This ICER far exceeds our established cost-effectiveness threshold of $100,000/QALY, which indicates that it is very cost-ineffective to employ annual mammography-based breast cancer screening in women with dense breasts. The Pataky et al. study looking at using MRI screening in conjunction with mammography on women carrying the BRCA1/2 mutation found an ICER of $50,911/QALY as compared to mammography screening alone. This is well below our cost-effectiveness threshold of $100,000/QALY and suggests that using MRI in conjunction with mammography is indeed cost-effective for that specific population of women. Lastly, the Furzer et al. study examining the cost-effectiveness of breast cancer screening in survivors of thoracic radiation-treated adolescent Hodgkin lymphoma found that annual mammography-based breast cancer screening beginning at age 25 was most cost-effective. At an ICER of $43,000/QALY, that screening recommendation falls well below the threshold of $100,000/QALY and therefore should be considered cost-effective.

This systematic review demonstrates that the current breast cancer screening policies of Canada, to screen average-risk women aged 50–74 years biennially or triennially, are cost-effective. However, the results of the above studies suggest that it is cost-ineffective to screen women with dense breasts annually, and that it is cost-effective for women with the BRCA1/2 mutation to be given the option of using MRI in conjunction with digital mammography. It is also cost-effective to employ annual mammography-based screening for survivors of radiation-treated adolescent Hodgkin’s lymphoma beginning at age 25.

The results of the review must be tempered by the heterogeneity and limitations of the constitutive studies. The papers included in this review used different models that were validated with different reference data, utilized different time horizons, and conducted different numbers of simulations. Moreover, the cost-effectiveness of breast cancer screening programs tends to be highly sensitive to the discounting rate, as many of the costs are accrued near the beginning of the program, while the benefits are reaped near the end. Every study used a different discounting rate, with 1.5% as the lowest and 5% as the highest. The methodological differences between studies means that the results of this review must be interpreted with caution, and that it is difficult to make firm statements about the cost-effectiveness of breast cancer screening in Canada.
Conclusions

Despite the heavy focus on optimizing breast cancer screening protocols, there is a scarcity of literature available on the cost-effectiveness of breast cancer screening within the Canadian population. Further studies are required to be able to make stronger recommendations regarding cost-effectiveness, which will prove critical in making decisions regarding resource allocation. The concerns presented in this review could serve as a basis for consideration by health policy makers, who must consider cost as a major factor when evaluating mammogram screening programs.

Availability of Data

All data generated or analyzed during this study are included in this article and its supplementary information files.

Patient and Public Involvement

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

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Author Contributions

TT and MWWa were involved with study conception and design; RT and MMWb were responsible for title and abstract screening, and TT and MMWa for a full-text screening; TT and MMWa were concerned with data extraction and analysis, and drafting and preparation of the manuscript; TT, MMWa, RT, and MMWb were responsible for critical review of the manuscript, and TT, MMWa, RT, and MMWb for the approval of the manuscript.

Competing Interests

None declared.

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References

12. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies
Supplementary File 1. Search Strategies.

**Medline search strategy**

1. cost effectiveness.mp.
2. cost-effectiveness.mp.
3. Cost-Benefit Analysis/
4. cost-benefit analysis.mp.
5. cost benefit analysis.mp.
6. “Costs and Cost Analysis”/
7. evaluation.mp.
8. cost benefit.mp.
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10. Canada/
11. screen*.mp.
12. Mammography/
13. cancer*.mp.
14. neoplasm*.mp.
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16. Neoplasms/
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24. mammogra*.mp.
25. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 22
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27. 11 or 12 or 24
28. 13 or 14 or 15 or 16 or 17 or 20 or 21
29. 18 or 19
30. 25 and 26 and 27 and 28 and 29

**EMBASE search strategy**

1. cost effectiveness.mp.
2. cost-effectiveness.mp.
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30. 25 and 26 and 27 and 28 and 29

**PubMed search strategy**

(((cost effectiveness) OR cost-effectiveness) OR cost-benefit analysis) OR cost benefit analysis) OR evaluation) OR cost benefit)) OR cost-benefit) OR cost*) AND (screen*) OR mammogra*) AND (((cancer*) OR neoplasm*) OR sarcoma*) OR carcinoma*) AND (breast*)

**EconLit search strategy**

(AB cost effectiveness OR AB cost-effectiveness OR AB cost-benefit analysis OR AB cost benefit analysis OR AB evaluation OR AB cost benefit OR AB cost-benefit OR AB cost*) AND (AB Canad*) AND (AB screen* OR AB mammogra*) AND (AB cancer* OR AB neoplasm* OR AB sarcoma* OR AB carcinoma*) AND (breast*)

**Canadian Agency for Drugs and Technologies in Health (CADTH) search strategy**

breast cancer (with the filter “reports” under result type; and the filter “cancer” under disease and conditions)

**Web of science search strategy**

AB = ((cost effectiveness OR cost-effectiveness OR cost-benefit analysis OR cost benefit analysis OR evaluation OR cost benefit OR cost-benefit OR cost*) AND (Canad*) AND (screen* OR mammogra*) AND (cancer* OR neoplasm* OR sarcoma* OR carcinoma*) AND (breast*)

**National Health Service Economic Evaluation Database (NHSEED) search strategy**

(Canada AND breast AND cancer).ti.
<table>
<thead>
<tr>
<th>Item No.</th>
<th>Section/item</th>
<th>Supplementary File 2. CHEERS Checklist for Included Articles.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abstract</td>
<td>1. Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis,” and describe the interventions compared.</td>
</tr>
<tr>
<td>2</td>
<td>Background and objectives</td>
<td>2. Provide a structured summary of the objectives, perspectives, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.</td>
</tr>
<tr>
<td>3</td>
<td>Target population and subgroups</td>
<td>3. Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.</td>
</tr>
<tr>
<td>4</td>
<td>Setting and location</td>
<td>4. Describe characteristics of the base case population and subgroups analyzed, including why they were chosen.</td>
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<tr>
<td>5</td>
<td>Study perspective</td>
<td>5. State relevant aspects of the system(s) in which the decisions need to be made.</td>
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<tr>
<td>6</td>
<td>Comparators</td>
<td>6. Describe the perspective of the study and relate this to the costs being evaluated.</td>
</tr>
<tr>
<td>7</td>
<td>Time horizon</td>
<td>7. State the time horizon(s) over which costs and consequences are being evaluated and why they are appropriate.</td>
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<tr>
<td>8</td>
<td>Discount rate</td>
<td>8. Report the choice of discount rate(s) used for costs and outcomes and why they are appropriate.</td>
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<tr>
<td>9</td>
<td>Choice of health outcomes</td>
<td>9. Report the choice of benefits measured in the analysis and why they are appropriate.</td>
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<tbody>
<tr>
<td>Measurement of effectiveness</td>
<td>11a</td>
<td>Single study–based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Measurement and valuation of preference-based outcomes. Estimating resources and costs.</td>
<td>12</td>
<td>If applicable, describe the population and methods used to elicit preferences for outcomes.</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>13a Single study–based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td>N/A</td>
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<tr>
<td>13b Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td>Page 4 (Table 1)</td>
<td>Page 2, 3 (Table 2)</td>
<td>Page 4 (Table 1)</td>
<td>Page 3 (Tables 1, 2, 3)</td>
<td>Page 6 (Table 5)</td>
<td>Page 2, 3</td>
<td>Page 2–4</td>
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<tr>
<td>Currency, price date, and conversion</td>
<td>14</td>
<td>Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.</td>
<td>Page 4</td>
<td>Page 2, 3</td>
<td>Page 5</td>
<td>Page 3</td>
<td>Page 6 (Table 5)</td>
<td>Page 3</td>
<td>Page 2</td>
</tr>
<tr>
<td>Choice of model</td>
<td>15</td>
<td>Describe and give reasons for the specific type of decision analytical model used. Providing a figure to show model structure is strongly recommended.</td>
<td>Page 2, 3</td>
<td>Page 2</td>
<td>Page 2</td>
<td>Page 2, 3</td>
<td>Page 2, 3</td>
<td>Page 2</td>
<td>Page 2, 3</td>
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<tr>
<td>Item</td>
<td>No.</td>
<td>Recommendation</td>
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<tr>
<td>Assumptions</td>
<td>16</td>
<td>Describe all structural or other assumptions underpinning the decision-analytical model.</td>
<td>Page 2, 3, Page 2, 4</td>
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<tr>
<td>Analytical methods</td>
<td>17</td>
<td>Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half-cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.</td>
<td>Page 4, 5, Page 2–4</td>
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<tr>
<td>Study parameters</td>
<td>18</td>
<td>Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.</td>
<td>Page 6 (Table 4), Page 3, Page 4 (Table 1), Page 5 (Table 3), Page 4</td>
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<tr>
<td>Incremental costs and outcomes</td>
<td>19</td>
<td>For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.</td>
<td>Page 6 (Table 5), Page 4 (Tables 2, 3), Page 5 (Table 3), Page 4 (Table 4), Page 7, N/A</td>
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<tr>
<td>Characterizing uncertainty</td>
<td>20a</td>
<td>Single study–based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).</td>
<td>Page 8, Page 5, Page 7, Page 7, Page 8, Page 5, Page 6</td>
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<tr>
<td>20b</td>
<td>Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.</td>
<td>Page 8, Page 5, Page 7, Page 7, Page 8, Page 8, 9, Page 6</td>
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<tr>
<td>Characterizing heterogeneity</td>
<td>21</td>
<td>If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.</td>
<td>N/A, N/A, N/A, N/A, N/A, N/A, N/A, N/A</td>
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<tbody>
<tr>
<td>Study findings, limitations, generalizability, and current knowledge</td>
<td>22</td>
<td>Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.</td>
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<td>Page 7, 8</td>
<td>Page 7, 8</td>
<td>Page 8, 9</td>
<td>Page 8, 9</td>
<td>Page 6, 7</td>
</tr>
<tr>
<td>Source of funding</td>
<td>23</td>
<td>Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other nonmonetary sources of support.</td>
<td>Page 8</td>
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<td>Conflicts of interest</td>
<td>24</td>
<td>Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.</td>
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