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Proposal: Personalized Breast Cancer Screening by Combining Screening and Diagnostic Decisions

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Abstract. Mammography screening has been shown to be the most effective method for reducing breast cancer mortality. However, it still faces significant inefficiencies, primarily due to three factors: a high false-positive rate, an excessive number of unnecessary follow-up examinations, and a lack of individualized screening guidelines. In this research, we aim to address these inefficiencies by combining screening and post-mammography diagnostic decisions into a unified framework to derive personalized policies for managing patients throughout the breast cancer screening pathway. We formulate this problem as a partially observable Markov decision process (POMDP), where our decision variables are twofold: screening decisions, which determine the optimal timing for mammography, and diagnostic decisions, which involve selecting the appropriate follow-up method to verify suspicious imaging results. We hypothesize that screening and diagnostic decisions are inherently interconnected, and that addressing them separately could result in suboptimal and less personalized screening pathways for patients.

Key words: partially observable Markov decision processes, dynamic programming, decision analysis, medical decision making, breast cancer, mammography screening, personalized screening

1. Introduction

Breast cancer is the first and most prevalent cancer diagnosed among women in Canada, with approximately 29,400 cases reported in 2023 (Canadian Cancer Society (CCS 2023)). Breast cancer is also the second leading cause of cancer death among women in Canada, accounting for approximately 5,400 deaths in 2023 (CCS 2023). It is estimated that 29,800 new cases of breast cancer will be diagnosed, with 5,700 related deaths in 2024 (CCS 2023). This means that about 1 in 8 women will be diagnosed with breast cancer, and 1 in 33 women will die because of it.

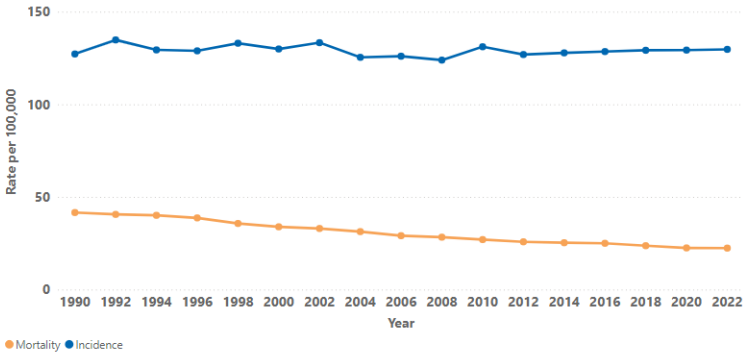
Early diagnosis of breast cancer is critically important, as it significantly improves survival rates by allowing interventions at stages when the cancer is more localized (Eby et al. 2022, Helvie et al. 2014, Pocobelli and Weiss 2015). This impact is evident in the dramatic increase in the 5-year survival rate, which rises from 23% at stage 4 to 92% at stage 2 (Ellison and Saint-Jacques 2023).

Breast cancer is characterized by the formation of malignant cells within the breast tissues. It progresses through various pathological types and is classified using the American Joint Committee on Cancer (AJCC) staging system (Keung and Gershenwald 2018). This system assesses the disease based on tumor size, lymph node involvement, and the extent of spread to other parts of the body. Breast cancer is staged from 0 to IV, with early stages indicating smaller tumors and localized disease, which generally correlates with a better prognosis and higher treatment success rates (Ellison and Saint-Jacques 2023). Beyond staging, breast cancer can be categorized as in situ, such as ductal carcinoma in situ (DCIS), confined to the ducts or lobules without invading surrounding tissue, or invasive, where cancer cells have spread beyond their original site. Stage 0 is reserved for in situ cancers, while invasive cancers are staged from I to IV, depending on their progression and extent of spread. In addition to staging, grading evaluates the aggressiveness of the cancer cells, with higher grades indicating more rapid growth and spread.

Mammography screening remains the most effective method for early breast cancer detection and reducing its mortality rate at the population level, which can detect abnormalities in breast tissue 1.5 to 2.3 years before symptoms appear or are noticeable by patients (Løberg et al. 2015, Tabár 2018, Duffy 2020). In Canada, the age-standardized mortality rate dropped from 41.6 per 100,000 women in 1990 to 22.4 in 2022, largely attributed to increased screening and improved treatments (CCS 2023). This trend, along with the age-standardized incidence rate, is illustrated in Figure 1. Although the breast cancer incidence rate rose in the 1980s-90s due to increased mammography use and hormonal factors, it has since been stabilized. While several randomized control trials (RCTs) have demonstrated the benefit of mammography screening programs in reducing breast cancer mortality, accounting for approximately 20% reduction in mortality rate (Marmot et al. 2013), several meta-analyses and studies show that these programs still face significant inefficiencies, primarily due to three sources: high rate of false-positive, high rate of unnecessary follow-up examinations (Løberg et al. 2015), and lack of individualization in screening guidelines (Ayer et al. 2012). We aim to build our work focusing on these three sources of inefficiency.

The trade-off between the benefits and risks of mammography screening is a nuanced issue. The primary benefit of mammography screening is the reduction in breast cancer mortality rate, while

Figure 1 Age-standardized rate for incidence and mortality for breast cancer (female), Canada, 1990 to 2022.



Note. Data from Statistics Canada (2021).

the risks involve a high rate of false positives and unnecessary follow-up procedures. While more frequent screening increases early detection, it also raises the risk of false positives, leading to unnecessary follow-ups that cause anxiety, health risks, and higher costs. Public guidelines typically recommend the starting and ending age for mammography screening, as well as the screening frequency (Annual, Biennial, Triennial). However, since the 1980s, significant and ongoing controversy has persisted among various public healthcare organizations regarding the optimal age to begin and end screening, as well as the appropriate frequency. For instance, while some organizations advocate for screening starting at age 40, others advise against it. This issue has received extensive media coverage (NYTimes 2024, CBC 2024). We will further elaborate on both sides of this controversy after a detailed discussion of current public screening programs.

A false-positive mammogram, as the first and most important source of inefficiency in screening programs, may appear with a likelihood ranging from 2.5% to 14% based on different factors such as age, breast density, cancer type, screening guidelines, radiologist's expertise, and their risk behavior (Løberg et al. 2015, Tosteson et al. 2014). According to CCS (2023), 2.8 million mammograms were performed in Canada in 2018, of which approximately 392,000 yielded false-positive results. A false-positive mammogram occurs when a suspicious finding on a mammogram is incorrectly labeled as cancerous, even though no cancer is present. In such cases, the abnormal finding is followed by additional diagnostic imaging, which ultimately confirms that there is no cancer. Several factors can contribute to false-positive mammograms. Dense breast tissue can obscure images, making it challenging to distinguish between benign and malignant cells. Younger women generally have denser breast tissue, increasing the likelihood of false positives compared to older women (Corsetti et al. 2008). Benign breast conditions, such as cysts, fibroadenomas, or

calcifications, may also appear abnormal on a mammogram. Additionally, radiologists' expertise plays a significant role, as variability in interpretations can sometimes result in false positives, especially in borderline or unclear cases (Alberdi et al. 2011).

False-positive mammograms have several adverse consequences: they cause significant anxiety for patients and their families (Brewer et al. 2007), lead to unnecessary follow-up examinations and overtreatment, and contribute to over-screening at the population level. Specifically, relatives of patients with false-positive diagnoses may be misclassified as having intermediate risk, resulting in unnecessarily aggressive screening protocols, such as annual rather than biennial mammography. This issue is particularly concerning at the population level, given that 1 in 8 Canadian women are diagnosed with breast cancer during their lifetime.

An unnecessary follow-up examination, as the second source of inefficiency in screening programs, may occur after a suspicious mammogram finding. Following mammography, patients typically follow one of two paths: if no abnormalities are detected, they continue with their regular screening schedule. However, if suspicious findings are present, radiologists may recommend one or a combination of follow-up diagnostic examinations, which could include additional diagnostic mammograms, biopsies, ultrasounds, or MRIs. These tests are usually scheduled immediately or at intervals of 3, 6, or 12 months.

The BI-RADS reporting system, introduced by the American College of Radiology, is widely used for the assessment of mammography results and the management of follow-up diagnostic examinations (Magny et al. 2023). This system also classifies breast density, which can affect the visibility of abnormalities on mammograms. This system facilitates consistent communication of predicted risk levels among healthcare providers and patients through its standardized format. It categorizes the likelihood of malignancy on a scale from 1 to 6, with corresponding follow-up recommendations for each category as shown in Table 1. However, the BI-RADS system's subjectivity, influenced by radiologists' expertise and risk tolerance, often leads to overestimation of the cancer risk in many cases, leading to lots of false-positive assessments (Alberdi et al. 2011). Another shortcoming is its broad and generalized follow-up recommendations, especially for category 4, where biopsy is recommended for a very broad group of patients with cancer risk between 2% and 98%, regardless of other personal factors. The majority of BI-RADS 4 findings (70–80%), which suggest a suspicious abnormality requiring a biopsy, are later determined to be benign after performing the biopsy and removing the abnormal lesion (Liu et al. 2024). This underscores the significant issue of unnecessary biopsies and the need for more personalized

follow-up strategies. The problem extends beyond biopsies: a framework for action published by the Canadian Partnership Against Cancer (CPAC) shows that from 2004 to 2017, abnormal call rates (ACR) rose from 6.1% to 7.8%, while cancer detection rates remained stable, reducing the positive predictive value (PPV). Lowering the ACR to 6% by 2029 could prevent 310,000 mammograms, 250,000 ultrasounds, and 46,000 biopsies, saving $110 million (CPAC 2023).

Assessment	**Likelihood of Cancer**	**Diagnostic Recommendation**
Category 0: Incomplete	N/A	Recall
Category 1: Negative	Essentially 0%	Routine screening
Category 2: Benign	Essentially 0%	Routine screening
Category 3: Probably Benign	$\geq 0\%$ but $\leq 2\%$	Short-interval (6-month) follow-up
Category 4: Suspicious	$> 2\%$ but $< 95\%$	Biopsy
Category 5: Highly Suggestive of Malignancy	$\geq 95\%$	Biopsy
Category 6: Known Biopsy-Proven Malignancy	N/A	Surgical extraction

Table 1 BI-RADS Categories, Likelihood of Cancer, and Diagnostic Recommendations

Considering the lack of personalization in current mammography screening guidelines, several studies highlight the need for tailoring mammography screening guidelines based on factors beyond age, such as demographics, breast density, previous mammograms, and genetics (Gail and Rimer 1998, Ayer et al. 2012). Current public guidelines typically suggest the start and end ages for screening and the frequency (annual, biennial, triennial). As shown in Table 2, there are key differences between several Canadian and U.S. guidelines, especially regarding the starting age for screening. Unlike most U.S. programs, including the U.S. Preventive Services Task Force, the Canadian Task Force on Preventive Health Care recommends against starting screening at age 40. They reason that for every 1,000 women screened, 294 will receive false positives, 43 will undergo unnecessary biopsies, and 7 will be diagnosed with breast cancer. Of those, 3 will be treated for cancer that wouldn't have posed a threat, and fewer than 1 death will be prevented. Indeed, to prevent a single death in this age group, 1,724 women would need to be screened (CTFPHC 2024).

The main controversy around public mammography screening programs concerns the starting age for screening. Since the inception of public screening programs in the 1980s, some organizations have adjusted their guidelines in response to expert opinions. For instance, the U.S. Preventive

Program	Age Group	Guideline
Alberta Breast Cancer Screening Program (ABCSP) October 2023	40-44	Referral needed
	45-74	Every 2 years
	75+	Referral needed
Canadian Task Force on Preventive Health Care (CTFPHC) May 2024	40-49	Not recommended
	50-74	Every 2 or 3 years
	75+	Referral needed
British Columbia Cancer Breast Screening Program (BCCSP) May 2024	40-74	Every 2 years
	75+	Can continue every 2 years if they are healthy
American Cancer Society December 2023	40-44	Have option for every year
	45-54	Every year
	55+	Every 2 years as long as healthy
United States Preventive Services Task Force (USPSTF) April 2024	40-74	Every 2 years
	75+	Insufficient evidence to assess benefits to harms
American College of Physicians (ACP) 2019	40-49	Referral needed
	50-74	Every 2 years
	75+	Discontinue

Table 2 Breast Cancer Screening Guidelines

Services Task Force (USPSTF) lowered the recommended starting age from 50 to 40 in 2023 (USPSTF 2024). In this controversy, proponents argue early screening is crucial as breast cancer tends to be more aggressive and fatal in younger women (Jayasinghe et al. 2005). As evidenced in the literature, the median tumor doubling time is 80 days for women under 50, compared to 157 days for those aged 50-70 and 188 days for those over 70, showing higher tumor aggression in younger patients (Peer et al. 1993, Michaelson et al. 1999). Conversely, critics highlight

the higher false-positive rate of mammography in younger women, necessitating more cautious guidelines (Kerlikowske et al. 2000). Additionally, the rapid cancer progression in younger women may also lead to a considerable number of missed diagnoses between screening intervals, making screening less effective for younger women.

Beyond the statistics, ethical debates surrounding this issue have also been covered in the media (Prevention 2016). The dilemma involves balancing the well-being of many individuals against the goal of saving a single life. On the one hand, we face the potential to prevent a single death; on the other, we risk the well-being of many, subjecting them to unnecessary stress, anxiety, and medical procedures.

Balancing the trade-off between the risks and benefits of mammography screening is inherently controversial and largely depends on how policymakers prioritize these factors at the population level. Considering the patient's perspective, this balance is subjective and varies based on how individuals perceive the benefits and risks. This trade-off also influences mathematical models used to optimize screening guidelines, particularly in how their objective functions are defined. For example, if the goal of a mathematical model is to maximize life years gained, it may tend to prioritize more frequent screening for younger individuals. Conversely, if the objective is to maximize cancer detection, the model may focus on screening older individuals more frequently, as breast cancer incidence rates are higher in this group.

An emerging approach to address these controversies is the personalization of screening and diagnostic policies. Numerous studies indicate that multiple factors beyond age, such as family history, breast density, gene mutations, and previous test results are critical in determining breast cancer risk. Given the variability in breast cancer risk among women of the same age group, personalized screening and diagnostic policies could enhance life-saving outcomes for high-risk women while reducing unnecessary screening and diagnostic examinations for low-risk women.

In this research, we aim to combine screening decisions and post-mammography diagnostic decisions into a unified framework for designing personalized policies to manage patients throughout the breast cancer screening pathway. We formulate this problem as a partially observable Markov decision process (POMDP), with two decision variables: (1) determining the optimal timing for mammography(screening decisions) and (2) selecting the appropriate follow-up examination method (diagnostic decisions).

We hypothesize that screening and diagnostic decisions are inherently interconnected and affecting each other, and that considering these two problems in isolation could lead to a suboptimal and less individualized screening pathway for patients.

Notes

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