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Cost-effectiveness of breast cancer screening policies using simulation

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ABSTRACT

In this paper, we study breast cancer screening policies using computer simulation. We developed a multi-state Markov model for breast cancer progression, considering both the screening and treatment stages of breast cancer. The parameters of our model were estimated through data from the Canadian National Breast Cancer Screening Study as well as data in the relevant literature. Using computer simulation, we evaluated various screening policies to study the impact of mammography screening for age-based subpopulations in Canada. We also performed sensitivity analysis to examine the impact of certain parameters on number of deaths and total costs. The analysis comparing screening policies reveals that a policy in which women belonging to the 40–49 age group are not screened, whereas those belonging to the 50–59 and 60–69 age groups are screened once every 5 years, outperforms others with respect to cost per life saved. Our analysis also indicates that increasing the screening frequencies for the 50–59 and 60–69 age groups decrease mortality, and that the average number of deaths generally decreases with an increase in screening frequency. We found that screening annually for all age groups is associated with the highest costs per life saved. Our analysis thus reveals that cost per life saved increases with an increase in screening frequency.

Introduction

Breast cancer is the most common cancer among women. It is estimated that in 2014, 24,400 Canadian women will develop breast cancer, and nearly 5000 of them will die from breast cancer [1]. There are certain risk factors affecting the development of breast cancer; examples include age, family history, breast density, and race. Breast cancer can be detected at early stages through mammography screening periodically applied to women through a screening program. Women diagnosed with cancer then receive treatment to cure the disease. Since mammography screening enables the detection of cancer at early stages, the resulting treatment may be more effective as compared to cancers presenting clinically, usually at later, more advanced stages.

Mammography screening is believed to lead to a reduction in breast cancer mortality by bringing forward the time of the diagnosis of cancer. It has been estimated that breast cancer mortality is reduced by 15% when mammography is applied [2]. Yet, there is controversy as to whether it should be applied to women belonging to certain age groups. This is mainly due to the fact that in some studies no effect of mammography screening was found, while mammography causes *overdiagnosis*, which is the diagnosis of cancers that would not otherwise present, leading to patient anxiety and unnecessary diagnostic procedures and treatment. Additionally, mammography leads to false-positive results, when the screening test suggests that an abnormality is present while cancer is actually absent.

Further, there is also controversy regarding the optimal screening policy that would specify the start age and end age of screening along with screening frequency. For example, the Canadian Task Force on Preventive Health Care recommends not routinely screening the 40–49 age group with mammography and recommends routinely screening the 50–69 age group every two to three years [3]. On the other hand, the American Cancer Society recommends annual mammography for women beginning at age 40 [4].

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In this paper, we study the impact of mammography screening for age-based subpopulations in Canada. In particular, we address the question of which screening policy is the most cost-effective for the Canadian population. The study perspective of our work is the health system. Using a multi-state Markov model, we develop a breast cancer progression model, which includes both screening and treatment stages. We use computer simulation to evaluate various screening policies to determine optimal screening policy. We also perform sensitivity analysis on certain model parameters to identify which parameters have high impact on the output measures.

Literature review

There have been numerous studies on breast cancer screening [5–11]. While some studies have used computer simulation to measure the effect of screening policies, a large body of this research has focused on the U.S. population [12–16], with fewer conducted for the Canadian population [17–20]. We review the related literature below.

Humphrey et al. studied the effect of mammography screening on breast cancer in randomized, controlled trials [21]. They found that mammography led to a reduction in breast cancer mortality among women 40–74 years of age. Schousbe et al. studied the health benefits and cost-effectiveness of mammography [22]. Using a Markov microsimulation model, they evaluated various screening policies considering risk factors such as age, breast density, and family history of breast cancer. The result of their work indicates that mammography should be personalized on the basis of risk factors such as age and breast density. Hunter et al. developed a simulation model for breast cancer screening to evaluate the impact of including the 40–49 age group into the ongoing screening program in Ontario [17]. They estimated the total cost of screening and initial treatment for the case where age eligibility requirements change.

Okonkwo et al. studied the cost-effectiveness of breast cancer screening policies for India. They used a microsimulation model to estimate the cost of breast cancer screening, its effects on mortality, and its cost-effectiveness [23]. Their analysis focused on two modalities: physical breast examination and mammography screening. Ahern and Shen studied the cost-effectiveness of mammography and physical breast examination [24]. Using a microsimulation model, they compared screening policies recommended by a few major organizations against alternative policies. The results of their work indicate that alternative screening policies are more efficient.

Mandelblatt et al. studied the effects of mammography screening under different screening schedules [25]. They developed models of breast cancer incidence and mortality in the United States. The results of their work indicated that screening every other year maintained an average of 81% of the benefit of annual screening. In addition, they found that screening every other year from ages 50–69 years resulted in a median 16.5% reduction in breast cancer deaths as compared to no screening. Mandelblatt et al. modeled the impact of population screening on breast cancer mortality in the United States [26]. They used six simulation models to evaluate screening outcomes under varying strategies. The results of their study indicate that screening every other year from ages 50–74 years reduces the probability of breast cancer death. They also found that screening annually from ages 40–84 years lowers mortality, yet it yields more false-positives and over-diagnosed cases as compared to screening every other year. Hendrick and Helvie evaluated the recommendations of United States Preventive Services Task Force regarding mammography screening [27]. Using six Cancer Intervention and Surveillance Modeling Network models, they examined various screening policies. The results of their work suggest that annual screening of women 40–84 years old results in around 40% mortality reduction as compared to no screening.

In a recent study, Taghipour et al. evaluated breast cancer screening policies using simulation [18]. They developed a multi-state Markov model for cancer progression to evaluate the effect of mammography on women aged 40–59. Differing from our model, their model does not include cancer stages nor does it consider cancer progression after treatment.

Model description

Breast cancer progresses through stages and may be detectable in the preclinical stage through mammography screening. Women are screened periodically during a fixed period to detect breast cancer at an early stage. Screening detects cancers with a certain probability, which is called *sensitivity* of the screening test. If screening results are positive, then a woman will be referred to undergo diagnostic procedures. Further, a woman diagnosed with breast cancer will be referred to undergo treatment, which can be applied until the cancer is deemed to be in remission and then only reapplied if necessary (i.e., if the cancer recurs). The types of treatment used depend on various characteristics (eg, size, stage, and histology) of the cancer at initial diagnosis.

We model breast cancer progression using a multi-state Markov model. We chose this type of model because it was successfully used for modeling breast cancer progression [18,28–30] and it allows us to incorporate the effect of different states on output metrics. Our model consists of the following states:

H: *Healthy state*
0–3: Preclinical states
4: *Clinical state*
5: O*ther-cause death*
6: Death due to breast cancer

States 0–3 are preclinical (i.e., screen-detectable) states, which are primarily determined on the basis of tumor size. State 0 represents 'in-situ' cancer, with the other preclinical states being 'invasive' cancer states. State 4 indicates a breast cancer that presents clinically. We assume that cancer progresses sequentially through states 0–4 [17,23]. Further, state transition in our model occurs as follows. A woman in Healthy state can transition to any of the following states: State 0, Other-cause death, or continue to remain in the Healthy state. Transition from Healthy state to Other-cause death occurs when a woman dies of a cause other than breast cancer. A woman in any of States 0–2 can transition to the next preclinical state (e.g., from state 1–2), Other-cause death, or continue to remain in her current state. On the other hand, a woman in State 3 can transition to State 4 (clinically-evident cancer state), Other-cause death, or continue to remain in State 3. A woman in State 4 can transition to Death due to Breast Cancer, Other-cause death, or continue to remain in State 4. (see Fig. 1 for the schematic view of the progression model). Further, due to the Markovian property, the time each woman stays in a given state is assumed to follow an exponential distribution.

Note that the multi-state model depicted in Fig. 1 represents a natural progression of breast cancer, and therefore does not display how progression is affected when treatment is applied. More specifically, it does not describe how cancer progresses when it is detected through screening. We therefore provide the impact of detection of cancer through screening on cancer progression in Fig. 2, which shows that the diagnosis of a cancer can occur either