Submission

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Breast Cancer Screening Guidelines Study

Expert Recommendations for Breast Cancer Screening in Canada

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Overview

The draft breast cancer screening guidelines released by the Canadian Task Force on Preventive Health Care (Task Force) on May 30, 2024, fail to adequately prioritize early detection of breast cancer and the health of Canadians. This brief discusses the scientific flaws in the guidelines, as well as issues with the guideline creation process.

Why is early detection important?

In 2024, it is estimated that 30,500 Canadian women will be diagnosed with breast cancer and 5,500 will die from it. [1] Early detection helps to decrease the likelihood of death from this disease. Multiple studies show strong, consistent mortality benefits on the order of 53%. [2] Living in a province that includes screening for women in their 40s is associated with a 1.9% increase in 10-year net survival and 3.3% in 45-49, [3] and a lower stage of breast cancer at diagnosis in women in their 40s and 50s. [4] In addition to decreasing deaths, early-stage diagnosis means less need for harsh treatments, such as mastectomy and chemotherapy, and less disfiguring lymphedema. [5] There is also less need for costly drugs used for treating advanced cancer. Early detection means better quality of life for women with breast cancer.

What are the 2024 draft breast cancer screening recommendations from the Task Force?

The 2024 draft guidelines [6] recommend against screening women aged 40-49, but allow for personal choice. The guidelines recommend screening women 50-74 years every 2-3 years. They recommend against supplemental screening for women with dense breasts and against screening women aged 75 and above.

What are the recommendations from breast cancer screening experts?

The Canadian Association of Radiologists, [7] the Canadian Society of Breast Imaging, as well as expert North American academic societies [8] recommend:

1. Screening annually, starting at age 40 [9] as 13.5% of breast cancers are [10] diagnosed in women aged 40-49, and 25% of years of life lost [11] to breast cancer are to women diagnosed in their 40s. Screening these women would reduce deaths by 3 to 4 per thousand, which equates to 400 to 600 avoidable deaths each year in Canada. [12] There would be even more lives saved by screening women over age 74, and by offering supplemental screening to women with dense breasts.
2. Women with dense breast tissue should have annual mammograms [13] and be offered additional MRI or ultrasound screening [14]. Dense tissue increases the risk of developing cancer, as well as the risk that cancer can be hidden on a mammogram. Women with the densest tissue are 13[15]-18[16] times more likely to be diagnosed with an interval cancer (cancer diagnosed in the interval between planned mammograms) than women with fatty breasts. Supplemental screening with ultrasound [17] or MRI [18] has been shown to decrease interval cancers. A reduced interval cancer rate is considered a surrogate measure of mortality reduction. [19]

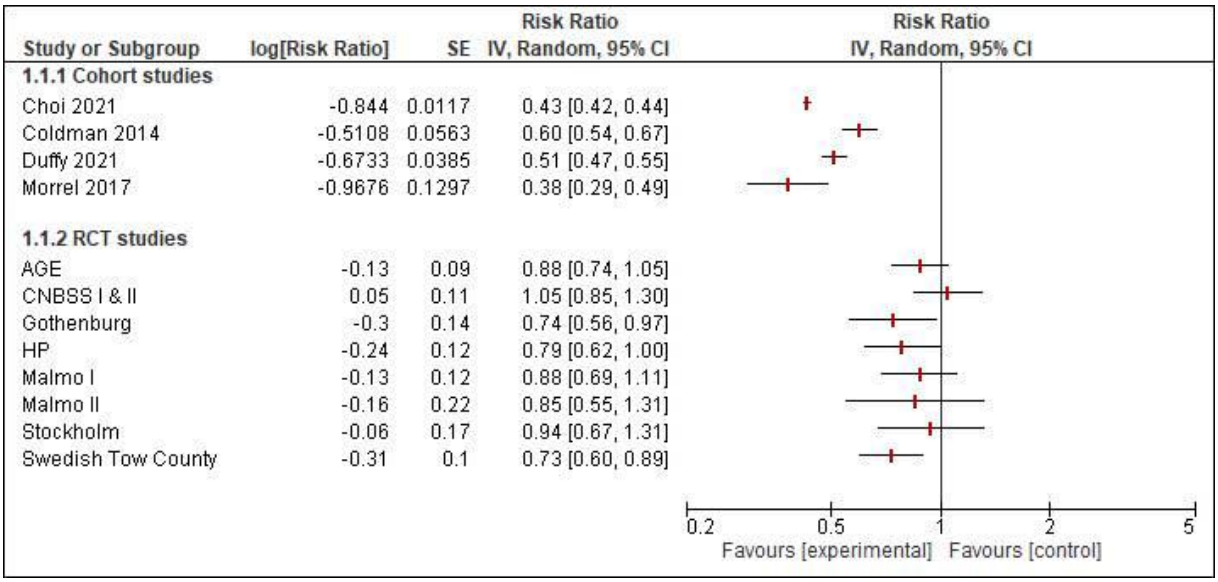
Why are there differences in the recommendations from breast cancer screening experts and the Task Force?

1. Subject matter experts do not vote: While Task Force members are experts in their own fields, they are not specialists in breast cancer. The current panel includes nurse practitioners and family doctors, as well as a gastroenterologist, nephrologist, and emergency room doctor. The lack of fulsome expert clinical involvement resulted in errors in the choice of and interpretation of evidence. Subject matter experts and patients were excluded from voting on the recommendations.

2. Outdated data: Contrary to recommendations from clinical and scientific experts, the 2024 guidelines are anchored in Randomized Control Trials (RCTs) performed in the 1960s to 1990s. This is in part due to a rigid attitude of Task Force leadership that the only high-quality evidence comes from a RCT. The RCTs do not reflect the reality of diagnostic and treatment advances and current practice. The inclusion of 40–60-year-old data overlooks the many advances in screening technology and breast cancer treatment. In addition, only trials which included "screened" and "unscreened" arms were allowed to be included, limiting the ability to use modern data (race, ethnicity, density). [20]

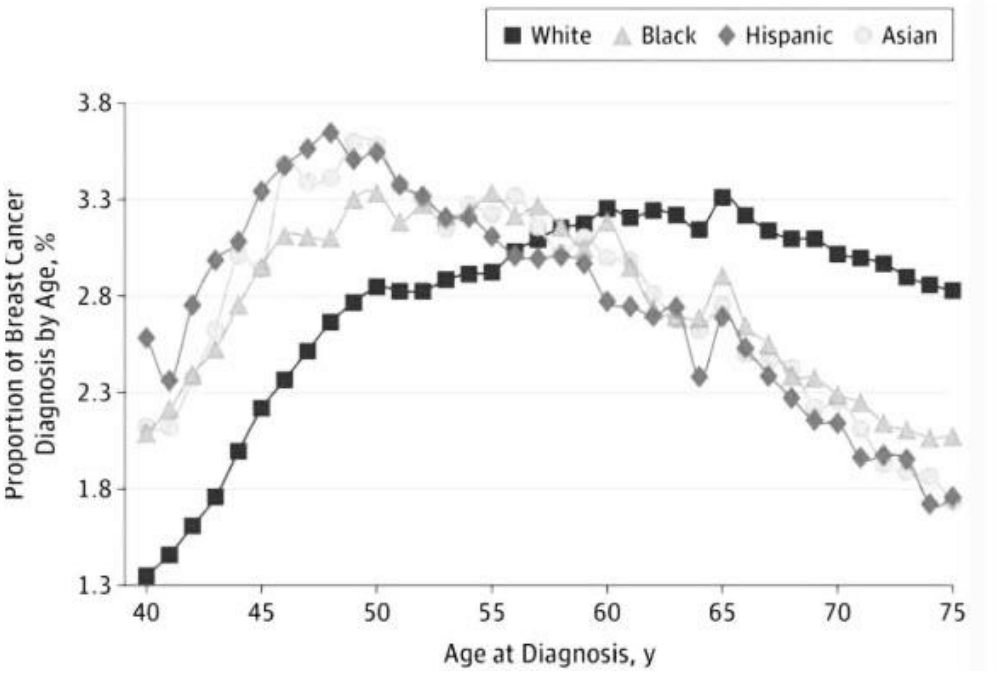
3. Downgrading of Observational Studies: The Task Force downgraded recent observational studies involving millions of women comparing screening to no screening with updated diagnosis and treatment. In 2024, the Ottawa Evidence Review Team assessed the mortality reduction benefit from the old RCTs at 15%, and benefit from observational data at 53%. [21] Even though the observational trials were generally performed in the 1990's and later, and results showed consistent substantial benefit, their data was automatically downgraded using GRADE to below RCT data. A comparison of old RCTs versus more recent observational studies is given in the Forest plots (Figure 1). Downgraded studies include the Pan Canadian study involving 2.8 million women screened over 20 years, which demonstrated a 44% reduction in breast cancer mortality in women in their 40s. [22] Similar studies in Sweden show 50 to 60% mortality reduction for women aged 40-74 years detected via screening compared to those diagnosed symptomatically. [23]

Figure 1.



4. Systematic Discrimination: The RCTs were performed in Europe and North America, mainly with white subjects. The CNBSS was based on 98% white participants. [24] The peak incidence for Black, Asian, and Hispanic women is in the mid-forties. (Figure) [25] Recent Canadian analysis shows that White women are the only group whose peak incidence is beyond age 50. [26] The Task Force acknowledged data showing higher mortality in Black women in the 40s but did not lower the screening age. Data on Black mortality, in part led to the US Task Force lowering the screening age. [27] Preliminary data from Statistics Canada suggests similar findings to the US. See Figure below.

Figure : Distribution of Age at Diagnosis for Women with Breast Cancer



5. Increasing incidence: Recently published data shows the rate of breast cancer in women under the age of 50 in Canada has increased significantly in the past 34 years. [28] Increasing incidence in younger women is seen across the globe. [29] The US Task Force cited this as another reason for lowering the screening age to 40. [30]

6. Harms vs Benefits: The Task Force concluded that the balance between benefit and harm was less favourable for younger women, than for older women. Given that the benefits include 53% fewer breast cancer deaths, [31] and better quality of life, one might wonder what the "harms" are. The first "harm" is described as the anxiety that women may experience if recalled for additional imaging. Mammography is not perfect; some examinations will prompt a recall to increase the confidence that no cancer is present. The Task Force no longer refers to callbacks as "false positives," but overemphasizes the harm of transient anxiety. After the additional tests, 95% of recalled women are told that they do not have cancer. [32] The Task Force uses a false equivalency: in the benefits to harms weighting, they equate transient anxiety to avoidable death. The Task Force does not include the benefit of earlier stage diagnosis in their 1000 person tool, which is used to facilitate shared-decision making.

The Task Force also disproportionately focuses on "overdiagnosis" (the diagnosis of a cancer which would never have caused problems for an individual). Overdiagnosis is only a harm if overtreatment occurs. We currently do not know which, if any, cancers do not require treatment, so all are treated. Whereas overdiagnosis was estimated to be 48% in the 2018 guideline, [33] it is now estimated to be 11% when including the discredited CNBSS and 6% when the CNBSS is excluded. [34]

7. Shared decision making: The Task Force couches its recommendations in "shared-decision making", between patient and primary care providers. When family physicians receive inaccurate information about harms and benefits, with a recommendation NOT to screen, it undermines decision-making.

8. The Task Force does not monitor the outcomes of its recommendations: After the Task Force changed its recommendation in 2011 to not routinely screen women in their 40s, women aged 40-59 in provinces without access to screening until age 50 were more likely to be diagnosed with more advanced cancers and had poorer survival. [35] There was a 10% increase in stage IV breast cancer in women in their 40s and 50s between 2011 and 2020. [36]

9. A failure to act on the risks of dense breasts The Task Force acknowledged that women with dense breasts were twice as likely to develop breast cancer as women with non-dense breasts, but ignored the reduced sensitivity of mammography in women with dense breasts. The Task Force arbitrarily extrapolated data from "average risk women" instead of reviewing the many trials that look at breast density. [37]

The Task Force ignored high quality RCTs that showed that screening with ultrasound or MRI in addition to mammography reduced the interval cancers (those cancers found by symptoms after a normal mammogram) by 80% and by 50%.[38] Interval cancers are larger and more often spread, and lead to poorer outcomes, so reducing interval cancers is a goal of screening. Reduction of interval cancers has been shown to be an acceptable surrogate for reduction of breast cancer mortality, which takes 10 years or more to demonstrate.[39]

What are the guidelines internationally?

On April 30, 2024, the US Preventive Services Task Force lowered the screening age from 50 to 40. Seven other countries start screening at age 40: Iceland, Sweden, USA, Brazil, Japan, Korea, and Turkey. Austria, Cyprus, Hungary, Israel, Columbia, and Portugal start at 45, but women in Austria and Hungary may opt to start at 40.

Supplemental screening for women with dense breasts is recommended in 11 European countries.[40] In Europe, women aged 50-70 with the highest density are recommended to have MRI every 2 to 3 years. This chart shows that although the incidence of breast cancer in Canada is lower than Norway, Austria, Sweden and the USA, our mortality is higher. [41]

Country	Age standardized Incidence/100,000	Age standardized Mortality/100,000
Norway	83.1	10.7
Australia	96	11.7
Sweden	83.9	12.0
United States	90.3	12.4
Canada	82.1	**13.3**
UK	87.7	14.0
France	99.1	15.6
World	47.8	13.6

Canadian Cancer Society: In May 2024, the Canadian Cancer Society changed their recommendation to recommend breast cancer screening begin at age 40.

Why do the Task Force guidelines matter?

Even though 10 out of 12 Canadian jurisdictions have already lowered the screening age to the 40s or have committed to do so, Task Force recommendations influence provincial clinical practice guidelines and physician's and women's access to screening. The variability in provincial screening

policies has led to inequity. This has resulted in differences in stage at diagnosis [42] for women, based on where they live, which may affect their survival.

Currently, the following provinces offer self-referral at 40: BC, PEI, YT, NS, NL, NB

Starting soon: ON (Fall) SK (Jan 2025)

Under review: QC, MB

Self-referral at 45 or after first screen 40-44: AB, NWT

What are the financial costs of poor screening practices?

The guidelines also lead to higher long-term costs. Researchers have shown the exponential costs of treating cancers with increasing stages.[43] (Table 1). Stage IV breast cancer is up to 11x more costly to treat than stage I breast cancer. Mean cost is $39,263 for stage I and $370,398 for stage IV. [44] A recent Canadian study found that screening women annually with mammography from age 40-74 not only pays for itself, it could save 350M dollars annually in Canada.[45]

Table 1. Cost per treatment of case of breast cancer by subtype and stage. All costs in 2023C$.

Subtype	Stage				
	DCIS	I	II	III	IV
HR+	14,505	28,201	60,289	117,269	256,693
HR+/HER2+		C$ 56,401	76,547	86,653	516,415
HER2+		47,201	67,136	75,954	514,992
TN		25,247	101,811	C110,798	193,490
Mean	14,505	39,263	76,446	97,668	370,398

Recommendations: Breast Cancer Screening Practices

1. Risk assessment beginning at age 25-30 and revisited every few years.
2. Screening average-risk women 40-49 annually by self-referral.
3. Screening women 50 and older every 1 to 2 years for as long as they are in good general health, with a life expectancy of 10 years.
4. Supplemental screening if an individual has category C or D density.

Recommendations: Task Force Reform [46]

1. Restructure the Task Force with a robust governance and accountability structure.
2. Monitor outcomes and any deteriorating outcomes should be quickly addressed.
3. Involve ethicists in both the restructuring of the Task Force as well as the choice of topics.
4. Involve patients at every level. Provide adequate training and support for patients.
5. Require full disclosure of the credentials of panel members in all documentation, including the final published guidelines.
6. Modernize methodology using updated concepts, such as EBM+.

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