Appendix 2 (as supplied by the authors): Evidence to Decision Framework

Question

Should **screening for breast cancer by mammography** vs. **usual care** be used for **women aged 40 – 74 years not at increased risk of breast cancer**?

POPULATION:	Women not at increased risk for breast cancer aged 40 to 74 years.
INTERVENTION:	Screening for breast cancer.
COMPARISON:	Usual care
MAIN OUTCOMES:	Breast Cancer Mortality; All-Cause Mortality, Overdiagnosis, False positive rates,
SETTING:	Primary care
PERSPECTIVE:	Task Force

Background

The purpose of this update is to determine whether new evidence on outcomes of breast cancer screening as well as women's values and preferences around screening, would require modification of earlier task force recommendations (1) on breast cancer screening for women aged 40 to 74 years not at increased risk of breast cancer.

The systematic review that informed task force recommendations in 2011 reported a reduction in breast cancer mortality with mammography screening for women aged 40 to 74 years. However, net benefit for women less than 50 years of age was equivocal given their lower absolute risk as well as their higher probability of being over-diagnosed and having false positive screens compared to women aged 50 to 74 years (2).

For this update of the 2011 task force guideline, an overview of reviews was undertaken by the Ottawa Hospital Research Institute's Evidence Review and Synthesis Centre on patient-important outcomes (breast cancer mortality, all-cause mortality, overdiagnosis and false positive rates with ensuing biopsies) from breast cancer screening (3) as well as a systematic review by the University of Alberta's Evidence Review and Synthesis Centre of values and preferences about outcomes of breast cancer screening, and how they use these valuations in decision-making(4).

Assessment

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
PROBLEM	**Is the problem a priority?** ○ No ○ Probably no ○ Probably yes x Yes ○ Varies ○ Don't know	While breast cancer mortality rates among Canadian women have been in decline for decades from 41.7 per 100,000 women in 1988 to a projected rate of 23.2 per 100,000 women in 2017, age-standardized incidence has remained at 130 per 100,000 since 2004 (5). Declining mortality with stable incidence could reflect improvements in breast cancer treatment, timely detection of symptomatic cancer, screening programs, or all of these (5).	

Appendix to: Klarenbach S, Sims-Jones N, Lewin G, et al.; for the Canadian Task Force on Preventive Health Care. Recommendations on screening for breast cancer in women aged 40–74 years who are not at increased risk for breast cancer. *CMAJ* 2018. doi: 10.1503/cmaj.180463

<table>
<tr><th></th><th>JUDGEMENT</th><th>RESEARCH EVIDENCE</th><th>ADDITIONAL CONSIDERATIONS</th></tr>
<tr><td>DESIRABLE EFFECTS (BENEFTIS)</td><td>How substantial are the desirable anticipated effects (benefits)?

○Trivial
X Small
○ Moderate
○ Large

○ Varies
○ Don't know</td><td rowspan="2"><u>Anticipated benefits:</u>

All-Cause Mortality
Low certainty of evidence from 8 trials, indicated no difference in all-cause mortality from breast cancer screening using mammography, with 0.69 fewer deaths per 1,000 women (95% CI: 0.00 to 1.38 fewer) of all ages with women in control groups at moderate baseline risk of breast cancer (3).

Breast Cancer Mortality
Very low to low certainty of evidence from 8 trials using short case accrual with moderate baseline risk in the control group for women of all ages and 50 to 59 years of age (3):
<table><tr><th>Age</th><th>Absolute effect per 1,000 (95% CI)</th><th>Certainty of Evidence</th></tr><tr><td>All ages</td><td>0.58 fewer (.27 fewer to .85 fewer)</td><td>⊕⊕OO LOW[A]</td></tr><tr><td>40-49</td><td>0.58 fewer (0.27 fewer to 0.85 fewer)</td><td>⊕⊕OO LOW[A]</td></tr><tr><td>50-59</td><td>0.75 fewer (from 0.35 fewer to 1.10 fewer</td><td>⊕OOO VERY LOW[B]</td></tr><tr><td>60-69</td><td>0.92 fewer (from 0.43 fewer to 1.35 fewer)</td><td>⊕⊕OO LOW[A]</td></tr><tr><td>70-74</td><td>1.55 fewer (from 0.72 fewer to 2.27 fewer)</td><td>⊕OOO VERY LOW[C]</td></tr></table>A: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies.
B: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies and serious concerns about inconsistency as heterogeneity may be moderate (I2=26%); (p-value=0.24) and serious concerns about imprecision because although the number of events and total population are large (>300 threshold for events) the 95% CIs include the null and do cross appreciable benefit (RR 0.75).
C: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies and serious concerns about imprecision because although the total population is large (>2,000) the 95% CIs include the null and do cross appreciable benefit (RR 0.75).</td><td rowspan="2"></td></tr>
<tr><td>UNDESIRABLE EFFECTS (HARMS)</td><td>How substantial are the undesirable anticipated effects (harms)?

○ Large
X Moderate
X Small
○ Trivial

○ Varies
○ Don't know</td></tr>
</table>

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	Number needed to screen to prevent one breast cancer death (95% CI) in three cycles of screening (3): For women aged 40 to 49 years 1,724 (1,176 to 3,704) women needed to be screened to prevent a single breast cancer death. For women aged 50 to 59 years 1,333 (909 to 2,857) women needed to be screened to prevent a single breast cancer death. For women aged 60 to 69 1,087 (741 to 2,326) women needed to be screened to prevent a single breast cancer death. For women aged 70 to 74 years 645 (441 to 1,389) women needed to be screened to prevent a single breast cancer death. **Anticipated harms:** **Overdiagnosis:** Overdiagnosis and treatment of cancer that would not have become apparent in a woman's lifetime or caused harm if left untreated is a critical undesirable anticipated effect of breast cancer screening. **Overdiagnosis estimates from CDN RCT (6) at moderate risk of bias (3):**	

		Percentage of Breast Cancers Estimated as Over-Diagnosed	
Age of Women at Initial Screen	Years Post Screen	Invasive and In Situ Cancers	Invasive Cancers
40 to 49	5	41%	32%
	20	55%	48%
50 to 59	5	25%	16%
	20	16%	5%

False Positive Results and Ensuing Biopsies observational data:
Consequences of false positive screening results can be both psychological and physical and include follow-up tests such as invasive biopsies.

Results are from an analysis of data from the Canadian Partnership Against Cancer report (2016)(7). The data are presented as a weighted average and are used to approximate a cohort of women entering the screening program for four cycles over a median of 11 years assuming women are screened every 2 to 3 years (3).

False Positive Results per one breast cancer death prevented (7):

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		Among women aged 40 to 49 years, 508 experienced a false positive result to prevent one breast cancer death. Among women aged 50 to 59 years 392 experienced a false positive result to prevent one breast cancer death. Among women aged 60 to 69 years 278 experienced a false positive result to prevent one breast cancer death. Among women aged 70 to 74 years 141 experienced a false positive result to prevent one breast cancer death. **Unnecessary Biopsies from False Positives per one breast cancer death prevented (7):** Among women aged 40 to 49 years 74 experienced a biopsy on a false positive result per one breast cancer death prevented. Among women 50 to 59 years 50 experienced a biopsy on a false positive result per one breast cancer death prevented. Among women aged 60 to 69 years 38 experienced a biopsy on a false positive result per one breast cancer death prevented. Among women aged 70 to 74 years 19 experienced a biopsy on a false positive result per one breast cancer death prevented.	
CERTAINTY OF EVIDENCE	**What is the overall certainty of the evidence of effects?** X Very low x Low ○ Moderate ○ High ○ No included studies	A: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies. B: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies and serious concerns about inconsistency as heterogeneity may be moderate (I2=26%); (p-value=0.24) and serious concerns about imprecision because although the number of events and total population are large (>300 threshold for events) the 95% CIs include the null and do cross appreciable benefit (RR 0.75). C: very serious concerns about risk of bias because randomization and allocation concealment either not reported or had serious deficiencies and serious concerns about imprecision because although the total population is large (>2,000) the 95% CIs include the null and do cross appreciable benefit (RR 0.75).	Eight trials (RCT), some of which were randomized and others quasi-randomized, provided information on the impact of mammography screening on breast cancer and all-cause mortality. Sample sizes in the trials at randomization ranged from 18,000 to 160,000 with mean follow-up from less than 18 to 30 years and screening intervals between 12 and 33 months (3). These trials have been criticized for having been conducted prior to important changes in cancer detection and treatment, being poorly reported and the fact that for some of them it is not possible to obtain information to accurately assess risk of bias (3).

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		Note: The systematic review conducted for this guideline presents screening outcomes using both short- and long-case accrual methods (3). In short-case accrual (initial + seven subsequent screens; 23 years of follow-up) only those cases diagnosed during the screening period are included (median 7 years; range 3 to 12 years), whereas long-case accrual (initial + four subsequent screens; 14 years of follow-up) includes all cases diagnosed to the end of the follow-up period. Short-case accrual reduces bias due to contamination because women in the control group would not have been screened until the trial is over, while long-case accrual may underestimate the benefits of screening as women in the control group are more likely being screened after the trial (3).	
VALUES	**Is there important uncertainty about or variability in how much people value the main outcomes?** ○ Important uncertainty or variability X Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	While the reductions in breast cancer mortality from breast cancer screening are modest, they are valued by Canadian women for whom a reduced risk of breast cancer mortality is valued as a benefit regardless of how harms were presented (4). This meant that women were often willing to accept harms of screening including the potential for over-diagnosis with subsequent treatment for reduced risk of breast cancer mortality. **Women 40 to 49:** • A substantial proportion appear to reduce or reverse their initial perceptions of a high benefit-to-harm ratio for breast cancer screening when provided with accurate estimates on the absolute benefits and harms for their age group **Women 50 to 69 years** • Reduction in breast cancer mortality outweighed concerns around harms of screening. • Studies that provided more extensive descriptions of overdiagnosis found it may outweigh the benefit of reduced breast-cancer mortality for a small but important proportion of women during their 50s and 60s • Previous screening experience likely competes with outcome valuations during decision-making **Women 70 +** • Acceptance of continuing to screen may be quite high for women in their 70s, particularly if relatively healthy.	Relative valuation of outcomes was hindered by accuracy of how these outcomes were portrayed to women in the 24 studies included in the systematic review commissioned for the updated guideline on women's values and preferences The valuations were largely obtained from studies that provided information on breast cancer mortality with moderate-to-high benefits and low-to-moderate harms (even for younger women); in the few studies where information on all-cause mortality was provided the willingness to accept harms of screening decreased.

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
BALANCE OF DESIRABEL AND UNDESIRABLE EFFECTS	**Does the balance between desirable and undesirable effects favor the intervention or the comparison?** ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	The balance between desirable and undesirable effects differs by age. For women aged 40 to 49: **Probably favors the comparison**. There is low-certainty evidence that women aged 40 to 49 years experience a modest absolute reduction in breast cancer mortality from screening. Compared to women aged 50 years and older, they have higher rates of overdiagnosis with resulting harms from treatment for a cancer which would not have caused harm in their lifetime, and they are more likely to experience consequences from false positive screens, including biopsies (3). Evidence on women's preferences suggests that a substantial proportion of women would not choose to be screened if they knew their age group's absolute risk reduction for breast cancer mortality and increased potential for harm from screening (4). After balancing the overall benefits and harms of screening, and considering values and preferences of these women, in the judgement of the task force the undesirable effects of overdiagnosis and consequences of false positive results outweigh potential benefits; therefore, the recommendation is against screening women of this age. This recommendation is conditional as some women in this age group may wish to be screened based on their values and preferences; in this circumstance, care providers should engage in shared decision-making with women who express an interest in being screened. For women aged 50 to 69: **Probably favors the intervention**. There is very low-certainty evidence that women aged 50 to 69 years experience modest absolute reduction in breast cancer mortality from screening (3). Rates of overdiagnosis and consequences of false positive screening results, while lower than for younger women, remain a concern. Women in this age group generally weigh even modest reductions in breast cancer mortality as more important than harms in their decision to be screened (4). In balancing the overall benefits and harms of screening for women aged 50 to 69 years, and considering their values and preferences, the task force places greater weight on women's preferences for screening to reduce breast cancer mortality by a modest amount than on harms and therefore recommends in favour of screening using mammography every 2 to 3 years. Care providers should engage women of this age in shared decision-making as those who place a higher value on avoiding harms, as compared to a modest absolute reduction in breast cancer mortality, may choose to not undergo screening. For women aged 70 to 74: **Probably favors the intervention.** There is very low-certainty	

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		evidence of a modest absolute reduction in breast cancer mortality for women aged 70 to 74 years, and the consequences of false positive screening results remains a concern. There was no evidence identified on the risk of overdiagnosis for these women (3). Healthy women of this age generally accept screening, perhaps due to familiarity (4). In balancing the overall benefits and harms, the task force places relatively more weight on women's acceptance of screening programs in the context of a modest absolute reduction in breast cancer mortality and lower weight on the risk of harms and thus recommends in favour of screening these women using mammography every two to three years. Care providers should engage in shared decision-making with women of this age as those who place a higher value on avoiding harms as compared to a modest absolute reduction in breast cancer mortality may choose to not undergo screening.	
RESOURCES REQUIRED	**How large are the resource requirements (costs)?** ○ Large costs x Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	A systematic review on cost-effectiveness of breast cancer screening was not conducted for this guideline.	Estimates from Statistics Canada (2015) on resources used by breast cancer screening programs indicate that costs for screening alone vary by screening interval and age of women at initiation of screening (8).
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**What is the certainty of the evidence of resource requirements (costs)?** ○ Very low ○ Low ○ Moderate ○ High x No included studies	Not conducted.	

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
COST EFFECTIVENESS	**Does the cost-effectiveness of the intervention favor the intervention or the comparison?** ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies x No included studies	No information was available from the systematic reviews.	
EQUITY	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced x Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No information was available from the systematic reviews.	Breast cancer screening for women aged 50 to 69 years has been part of routine care across Canada since the early 1990s (5). In the judgement of the task force, present recommendations are both feasible and acceptable to women and clinicians. They are not expected to have an increased negative impact on health equity than earlier recommendations, and are likely to pose no additional costs to the health care system.
ACCEPTABILITY	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ○ Probably yes x Yes		As above – screening programs in place across Canada since 1990's.

	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	○ Varies ○ Don't know		
FEASIBILITY	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes x Yes ○ Varies ○ Don't know		As above.

Summary of judgements

	JUDGEMENT							IMPLICATIONS
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know	Breast cancer remains a health issue for women in Canada.
DESIRABLE EFFECTS (BENEFITS)	Trivial	Small	Moderate	Large		Varies	Don't know	Benefits are greater for women ≥50 years of age.
UNDESIRABLE EFFECTS (HARMS)	Large (overdiagnosis)	Moderate	Small (false positives)	Trivial		Varies	Don't know	Harms are greater for women ≤ 50 years of age.
CERTAINTY OF EVIDENCE WOMEN AGE 40 TO 49	Very low	Low	Moderate	High			No included studies	Low certainty of evidence gives consideration of patient values and preferences more weight.

	JUDGEMENT							IMPLICATIONS
CERTAINTY OF EVIDENCE WOMEN AGE 50 TO 69	Very low	Low	Moderate	High			No included studies	Very low certainty of evidence gives consideration of patient values and preferences more weight.
CERTAINTY OF EVIDENCE WOMEN AGE 70 TO 74	Very low	Low	Moderate	High			No included studies	Very low certainty of evidence gives consideration of patient values and preferences more weight.
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				Indicates importance of shared decision - making.
BALANCE OF EFFECTS – WOMEN AGE 40 TO 49	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the comparison	Favors the intervention	Varies	Don't know	No new evidence to change current recommendation although certainty of evidence downgraded on reappraisal.
BALANCE OF EFFECTS – WOMEN AGE 50 TO 69	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know	No new evidence to change current recommendation although certainty of evidence downgraded on reappraisal.
BALANCE OF EFFECTS – WOMEN AGE 70 TO 74	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know	No new evidence to change current recommendation although certainty of evidence downgraded on reappraisal.
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	

	JUDGEMENT							IMPLICATIONS
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies	
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	Provinces have screening programs in place.
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know	54% of Canadian women 50 to 69 years are screened each year in screening programs.
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know	Provinces have screening programs in place.

Conclusions:

Based on two evidence reviews, the task force has determined that recommendations for screening women for breast cancer should remain similar to those in the 2011 task force guideline. Although breast cancer screening has the potential to reduce breast cancer mortality, it increases risk of harms particularly due to the risk of overdiagnosis leading to unnecessary treatment and consequent adverse sequelae. Women should be supported to make an informed decision on screening that fits with their values and preferences. Future challenges include reducing uncertainty in estimates of benefits and harms from screening and gaining a greater understanding of Canadian women's values and preferences about breast cancer screening.

(1) Should screening for breast cancer by mammography vs. usual care be used for women not at increased risk aged 40 to 49 years?

TYPE OF RECOMMENDATION	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention

	o	X	o	o	o
RECOMMENDATION	For women aged 40 to 49 years, we recommend not screening with mammography; the decision to undergo screening is conditional on the relative value a woman places on possible benefits and harms from screening. (Conditional recommendation; low-certainty evidence)				
JUSTIFICATION	There is low-certainty evidence that women aged 40 to 49 years experience a modest absolute reduction in breast cancer mortality from screening. Compared to women aged 50 years and older, they have higher rates of overdiagnosis with resulting harms from treatment for a cancer which would not have caused harm in their lifetime, and they are more likely to experience consequences from false positive screens, including biopsies (3). Evidence on women's preferences suggests that a substantial proportion of women would not choose to be screened if they knew their age group's absolute risk reduction for breast cancer mortality and increased potential for harm from screening (4). After balancing the overall benefits and harms of screening, and considering values and preferences of these women, in the judgement of the task force the undesirable effects of overdiagnosis and consequences of false positive results outweigh potential benefits; therefore, the recommendation is against screening women of this age. This recommendation is conditional as some women in this age group may wish to be screened based on their values and preferences; in this circumstance, care providers should engage in shared decision-making with women who express an interest in being screened.				
SUBGROUP CONSIDERATIONS	None.				
IMPLEMENTATION CONSIDERATIONS	The recommendations apply to women aged 40 to 74 years not at increased risk for breast cancer. Women at increased risk include women with a personal or family history of breast cancer; women who are carriers of gene mutations such as BRCA1 or BRCA2 or have a first-degree relative with these gene mutations; and women who had chest radiation therapy before 30 years of age or within the last eight years. The current task force recommendation is to screen women for breast cancer with mammography because of the absence of evidence on clinical outcomes of screening by MRI, ultrasound, digital breast tomosynthesis or clinical breast examination and evidence that performing breast self-examination has no impact on all-cause or breast cancer mortality. The recommendation is also to screen women every two to three years because screening intervals in the trials ranged from 12 to 33 months with a pooled analysis indicating similar benefits across intervals.				
MONITORING AND EVALUATION	The task force suggests that quality assurance indicators for breast cancer screening programs continue to be monitored through the Canadian Partnership Against Cancer, including false positive rates and resulting biopsies as well as stage of cancer at diagnosis. The recommendations on screening for breast cancer are conditional on women's values and preferences and as such not all women age 50 to 74 should be screened. Quality improvement programs should focus on ensuring that the shared decision-making process occurs in women age 50 to 74 as the ideal proportion of women to be screened is unknown. Strategies that promote increasing the proportion of women screened (such as through financial inducements) instead of the shared decision-making process are not aligned with the recommendations.				
RESEARCH PRIORITIES	More and better-quality evidence is needed on the impact of breast cancer screening for women of all ages and particularly for women younger than 50 years and older than 70 years of age. These populations are currently the focus of the AgeX cluster randomized trial underway in the United Kingdom with results expected in 2026 (9). The task force did not review evidence on supplemental screening for women with dense breast tissue as it was beyond the scope of this guideline. However, a recent review for the USPSTF identified that studies are needed to clarify approaches to classification and called for rigorous comparative studies to determine patient important outcomes of supplemental screening for these women (10). Hanley et al (2013) proposed alternative approaches to interpreting screening outcomes because of diminishing returns from screening after its cessation. They recommend calculating breast cancer mortality rates by year of screening rather than estimating cumulative mortality (11). Greater understanding of the risk of overdiagnosis from screening requires a common definition and agreed-upon denominator as well as more rigorous study, particularly for women aged 60 to 74				

	years (12). Additional studies on Canadian women's values and preferences for screening that are conducted using accurate estimates of both benefits and harms would assist in guiding future recommendations. Finally, better estimates of the costs of screening programs would also support future recommendations.

(2) Should screening for breast cancer by mammography vs. usual care be used for women not at increased risk aged 50 to 69 years?

TYPE OF RECOMMENDATION	Strong recommendation against the intervention o	Conditional recommendation against the intervention o	Conditional recommendation for either the intervention or the comparison o	Conditional recommendation for the intervention X	Strong recommendation for the intervention o
RECOMMENDATION	For women aged 50 to 69 years, we recommend screening with mammography every two to three years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening. (Conditional recommendation; very low-certainty of evidence)				
JUSTIFICATION	There is very low-certainty evidence that women aged 50 to 69 years experience modest absolute reduction in breast cancer mortality from screening (3). Rates of overdiagnosis and consequences of false positive screening results, while lower than for younger women, remain a concern. Women in this age group generally weigh even modest reductions in breast cancer mortality as more important than harms in their decision to be screened (4). In balancing the overall benefits and harms of screening for women aged 50 to 69 years, and considering their values and preferences, the task force places greater weight on women's preferences for screening to reduce breast cancer mortality by a modest amount than on harms and therefore recommends in favour of screening using mammography every 2 to 3 years. Care providers should engage women of this age in shared decision-making as those who place a higher value on avoiding harms, as compared to a modest absolute reduction in breast cancer mortality, may choose to not undergo screening.				
SUBGROUP CONSIDERATIONS	None				
IMPLEMENTATION CONSIDERATIONS	The recommendations apply to women aged 40 to 74 years not at increased risk for breast cancer. Women at increased risk include women with a personal or family history of breast cancer; women who are carriers of gene mutations such as BRCA1 or BRCA2 or have a first-degree relative with these gene mutations; and women who had chest radiation therapy before 30 years of age or within the last eight years. The current task force recommendation is to screen women for breast cancer with mammography because of the absence of evidence on clinical outcomes of screening by MRI, ultrasound, digital breast tomosynthesis or clinical breast examination and evidence that performing breast self-examination has no impact on all-cause or breast cancer mortality. The recommendation is also to screen women every two to three years because screening intervals in the trials ranged from 12 to 33 months with a pooled analysis indicating similar benefits across intervals.				
MONITORING AND EVALUATION	The task force suggests that quality assurance indicators for breast cancer screening programs continue to be monitored through the Canadian Partnership Against Cancer, including false positive rates and resulting biopsies as well as stage of cancer at diagnosis. The recommendations on screening for breast cancer are conditional on women's values and preferences and as such not all women age 50 to 74 should be screened. Quality improvement programs should focus on ensuring that the shared decision-making process occurs in women age 50 to 74 as the ideal proportion of women to be screened is unknown. Strategies that				

	promote increasing the proportion of women screened (such as through financial inducements) instead of the shared decision-making process are not aligned with the recommendations.
RESEARCH PRIORITIES	More and better-quality evidence is needed on the impact of breast cancer screening for women of all ages and particularly for women younger than 50 years and older than 70 years of age. These populations are currently the focus of the AgeX cluster randomized trial underway in the United Kingdom with results expected in 2026 (9). The task force did not review evidence on supplemental screening for women with dense breast tissue as it was beyond the scope of this guideline. However, a recent review for the USPSTF identified that studies are needed to clarify approaches to classification and called for rigorous comparative studies to determine patient important outcomes of supplemental screening for these women (10). Hanley et al (2013) proposed alternative approaches to interpreting screening outcomes because of diminishing returns from screening after its cessation. They recommend calculating breast cancer mortality rates by year of screening rather than estimating cumulative mortality (11). Greater understanding of the risk of overdiagnosis from screening requires a common definition and agreed-upon denominator as well as more rigorous study, particularly for women aged 60 to 74 years (12). Additional studies on Canadian women's values and preferences for screening that are conducted using accurate estimates of both benefits and harms would assist in guiding future recommendations. Finally, better estimates of the costs of screening programs would also support future recommendations.

(3) Should screening for breast cancer by mammography vs. usual care be used for women not at high risk aged 70 to 74 years?

TYPE OF RECOMMENDATION	Strong recommendation against the intervention o	Conditional recommendation against the intervention o	Conditional recommendation for either the intervention or the comparison o	Conditional recommendation for the intervention X	Strong recommendation for the intervention o
RECOMMENDATION	For women aged 70 to 74 years, we recommend screening with mammography every two to three years; the decision to undergo screening is conditional on the relative value that a woman places on possible benefits and harms from screening. (Conditional recommendation; very low-certainty of evidence)				
JUSTIFICATION	There is very low-certainty evidence of a modest absolute reduction in breast cancer mortality for women aged 70 to 74 years, and the consequences of false positive screening results remains a concern. There was no evidence identified on the risk of overdiagnosis for these women (3). Healthy women of this age generally accept screening, perhaps due to familiarity (4). In balancing the overall benefits and harms, the task force places relatively more weight on women's acceptance of screening programs in the context of a modest absolute reduction in breast cancer mortality and lower weight on the risk of harms and thus recommends in favour of screening these women using mammography every two to three years. Care providers should engage in shared decision-making with women of this age as those who place a higher value on avoiding harms as compared to a modest absolute reduction in breast cancer mortality may choose to not undergo screening.				
SUBGROUP CONSIDERATIONS	None				
IMPLEMENTATION CONSIDERATIONS	The recommendations apply to women aged 40 to 74 years not at increased risk for breast cancer. Women at increased risk include women with a personal or family history of breast cancer; women who are carriers of gene mutations such as BRCA1 or BRCA2 or have a first-degree relative with these gene mutations; and women who had chest radiation therapy before 30 years of age or within the last eight years. The current task force recommendation is to screen women for breast cancer with mammography because of the absence of evidence on clinical outcomes of screening by MRI, ultrasound, digital breast tomosynthesis or clinical breast examination and evidence that				

	performing breast self-examination has no impact on all-cause or breast cancer mortality. The recommendation is also to screen women every two to three years because screening intervals in the trials ranged from 12 to 33 months with a pooled analysis indicating similar benefits across intervals.
MONITORING AND EVALUATION	The task force suggests that quality assurance indicators for breast cancer screening programs continue to be monitored through the Canadian Partnership Against Cancer, including false positive rates and resulting biopsies as well as stage of cancer at diagnosis. The recommendations on screening for breast cancer are conditional on women's values and preferences and as such not all women age 50 to 74 should be screened. Quality improvement programs should focus on ensuring that the shared decision-making process occurs in women age 50 to 74 as the ideal proportion of women to be screened is unknown. Strategies that promote increasing the proportion of women screened (such as through financial inducements) instead of the shared decision-making process are not aligned with the recommendations.
RESEARCH PRIORITIES	More and better-quality evidence is needed on the impact of breast cancer screening for women of all ages and particularly for women younger than 50 years and older than 70 years of age. These populations are currently the focus of the AgeX cluster randomized trial underway in the United Kingdom with results expected in 2026 (9). The task force did not review evidence on supplemental screening for women with dense breast tissue as it was beyond the scope of this guideline. However, a recent review for the USPSTF identified that studies are needed to clarify approaches to classification and called for rigorous comparative studies to determine patient important outcomes of supplemental screening for these women (10). Hanley et al (2013) proposed alternative approaches to interpreting screening outcomes because of diminishing returns from screening after its cessation. They recommend calculating breast cancer mortality rates by year of screening rather than estimating cumulative mortality (11). Greater understanding of the risk of overdiagnosis from screening requires a common definition and agreed-upon denominator as well as more rigorous study, particularly for women aged 60 to 74 years (12). Additional studies on Canadian women's values and preferences for screening that are conducted using accurate estimates of both benefits and harms would assist in guiding future recommendations. Finally, better estimates of the costs of screening programs would also support future recommendations.

Appendix II: Reference List

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