Response to Stakeholder & Peer Review Comments

Notes:
Peer Review comments in blue text
Boulanger & Yang both separately gave comments in the research plan document; responses to these comments are in a separate table below.

Question 1: The Task Force is committed to creating guidelines that enhance equity.

Are there additional specific populations that should be considered for this topic, and do you have any concerns or suggestions regarding how specific populations of interest within the background and PICO table have been described?

Individual(s)	Answer	Comment	Response
Boulanger	**Yes**	The population considered seems adequate for the evaluation questions. The question of the choice of the comparative population for the evaluation of dense breasts seems important to me for decision-making. The comparison of the two extremes (Bi-RADS) show differences in screening efficiency. The comparison with a Bi-RADS 2 reduces this difference.	Thank you for the comments. It has been clarified that the main comparisons of interest for breast density are Bi-RADS A-B vs. C-D and A-C vs. D (or similar with different grading methods), and if other comparisons are included, we interpret in light of this.
Carol	**No response**	N/A	N/A
Chiarelli, Fienberg, McCurdy, Salleh, Truscott, Walker:	**Yes**	• Breast density definition can be variable for high breast density. For KQ1, regarding breast density, consider separating out those with BI-RADS D as well as BI-RADS C, instead of just BI-RADS D vs. BI-RADS A/B/C. • Harms of screening- consider including BIRADS 3, which is short term follow up of benign lesions, as a harm of screening. This may or may not include biopsy, and is probably more significant than negative biopsy. • In KQ2, the age groups were not specified as in KQ1. Suggest doing the same as in KQ2. • Using the female-sex specific breast tissue criterion may not capture all relevant populations (e.g., Two-Spirit, transfeminine or nonbinary people that have taken feminizing hormone therapy), suggest expanding criterion to include this population as well. • Consider describing included populations using more inclusive language.	Thank you for the comments. It has been clarified that the main comparisons of interest for breast density are Bi-RADS A-B vs. C-D and A-C vs. D. The task force did not add category BIRADS 3 as a harm outcome; they will consider other several harm outcomes. For KQ2, it has been clarified that age sub-categories are of interest, though they were not prespecified by the USPSTF which is the review being used for this KQ. We have revised the population criteria to use more inclusive language, “cisgender women and other

			adults assigned female at birth (including transgender men and nonbinary persons)". The task force is not targeting people who were not assigned female at birth, e.g. that have taken feminizing hormone therapy. The Task Force recognizes that trans women and non-binary individuals taking feminizing HRT have increased risk of breast cancer over cis men but our recommendations do not apply to them due to fundamental differences in their risk and the non-generalizability of existing evidence to their risk or reality.
Earle	**No**	If data are available, it is particularly important to ensure that Indigenous populations are considered in race/ethnicity.	Thank you. These populations are definitely of interest.
Holmes & Said	**Yes**	It is really important for the language in the key questions to be clear and for individuals to be able to see themselves in it. Based on the language in the 2017 protocol being mirrored in the 2018 guideline release and recommendation language, we are concerned that "Adults aged 40 years and older with female sex-specific breast tissue and at average or above average risk*" will be the language used in the final recommendations. It is a very technical definition that guides the research, but has the potential if carried through into the final publication to limit comprehension, inclusion and equity. We suggest exploring gender additive language for a plain language research question that will guide future recommendation language and keeping the technical population definition within the inclusion/exclusion criteria of the study protocol. We're really pleased to see the inclusion of average and above average (sometimes called elevated) risk. We recommend the addition of high-risk category as well to be inclusive of everyone who is eligible for breast screening and have one set of guidelines with breast screening recommendations that both individuals and healthcare providers can refer to for all of the information that they need.	Thank you. We have revised the language about the population to be more inclusive and the task force will consider your suggestions further when describing the population for their recommendations. The task force will be engaging with patients and other members of the public to help develop their messaging. The task force is not targeting those at high-risk due to the expectation these individuals should be receiving consultation with a specialist.
Ibezi	**Yes**	Bearing in mind the "Healthy Immigrant Effect" and that immigrant health declines sharply over time since migration to reach the Canadian-born population's health levels or lower, Could the immigrant population be considered as specific population for this topic?	Thank you. Immigrant status (and time since immigration) was not added explicitly to the list of specific populations but will be considered particularly when interpreting data where this factor intersects

			with others such as race/ethnicity and socioeconomic status.
Kumar	**Yes**	The concern I have is related to the fact that some jurisdictions do not collect information on race and ethnicity. There are no unique identifiers for Indigenous population either.	We agree that data on race/ethnicity could be more comprehensive in Canada and certainty within research studies generally. It will likely be difficult to find data to help determine any possible disparities in outcomes from screening. The task force will also be using other available information (not reported in the eligible studies of the reviews) to inform these considerations.
Payne	**Yes**	I appreciate the effort to consider determinants of health in the review. My concerns are: 1. Population (risk): it will be important to capture the definition of risk as there is not a clear standard on the definition of 'high' risk (e.g., 20%, 25%). 2. the intersection between race/ethnicity and socioeconomic status – although race/ethnicity may imply some different genetic risk, often the differences are actually those attributed to socioeconomic status (e.g., access) – I would worry that releasing results that focus on race/ethnicity (social constructs) may contribute to harm given the difficulty in communicating these results. 3. geography: urban/rural are context-specific unless using some Canadian standard; that said, their meaning is still different (e.g., rural PEI is very different than rural AB). 4. Breast density: the definition of 'extreme' and 'high' are not standard, so important to collect the details (BI-RADS v5 D is relatively recent). 5. family history: important to gather the details when possible – 1st degree? Maternal vs paternal? (PICO table not included in materials provided although I presume content appears in tables provided)	Thank you for the comments; 1. We appreciate this matter. There are exclusion criteria set forth describing high-risk for the purpose of the reviews, but it will be noted to describe this in detail in the recommendations. 2. We agree very much and will be careful when interpreting data/information about these populations. 3. Thanks. We revised this to be specific to its intent, "Availability of mammography screening" 4. Thank you we will consider this. **5.** Data will be extracted as reported.
Ryan	**Yes**	Importantly, age, ethnicity, race, socioeconomic status, and urban/rural status are included in the PICO table. However, given the changes to populations over time, consideration should be given to the applicability of older research (including clinical trails) needs to be considered.	We agree that considering the age of the data is important. This will be addressed when rating the certainty of the evidence (within the "directness" domain). This was also used to provide rationale for

		Particularly, the specific sample populations included in clinical research. Also, what is the justification for choosing the lower age bracket of 40 years?	only including more recent observational data – we want to include observational studies that are more applicable to current practice than the existing trials so they are not rated down during ratings of certainty any more than usual due to their study design**.** The task force is considering those 40 and older because there is an increasing interest for starting to screen at 40, and many programs offer self-referral at 40.
Tracer	**No**	No comment	N/A
ThundeByass	**Yes**	The immigrant population, geographical location from sub-Saharan African countries, Ethnicity and race- Black population. Within the population- how do we truly define socioeconomic status. If this is defined by income alone, could some groups be missed; although they are within the income bracket but lack other social support that further disadvantage them.	Thank you. We will extract anything possible relevant from the studies, if reported, and consider the complexities as you mention.
Yang	**Yes**	It's obvious that the Task Force is committed to creating equity. But creating equity is about to reduce the factors are unfair and unjust, I'm not sure how the clinical guidelines will address this as guideline is based on weighing the benefits and potential harms of screening strategies through evidence synthesis. Breast cancer survivors (breast cancer was cured). They have higher risk for developing another primary breast cancer.	Thank you. The task force will also consider other information (e.g., equity, feasibility, patient partner feedback, acceptability), apart from these reviews, when developing their recommendations. This guideline is not targeting those at high risk which includes those with previous breast cancer.
YongHing	**Yes**	No comment	N/A
Sheffield	**No**	No comment	N/A
Wittmer	**No**	No comment	N/A
Question 2: Do you have any comments or suggestions related to the eligibility criteria (interventions, comparisons, outcomes) for the research questions? (see relevant tables *[Tables 2-4]*)			

Boulanger	**Yes**	Considering the importance of tomosynthesis in breast cancer screening, it would be interesting to evaluate the effectiveness of this modality (3D +/- 2D / 2Ds). Recent literature makes it possible to assess this. INESSS is currently working on this issue.	Thank you. Tomosynthesis is an eligible intervention for KQ1 and, in comparison with 2D, for KQ2.
Carol	**Yes**	There are two things that need investigation. One is the benefit of the additional intervention, but also what criteria should be applied for each intervention. Without clear criteria for whether or not to supplement mammography with another intervention, there is a risk that patients will undergo additional interventions unnecessarily.	Thank you. We agree and appreciate your comments. The specific populations (e.g., age, risk factors including dense breasts) will be considered when looking at supplemental screening.

Chiarelli, Fienberg, McCurdy, Salleh, Truscott, Walker	**Yes**	• Consider separating out questions related to primary and supplemental screening for people with high breast density, from primary screening for people without dense breasts.
		  ○ If looking at supplemental screening, the comparative group should be people who have had mammography alone and not those who have not screened.
		  ○ Studies on people with high breast density may use other modalities for primary screening (i.e, MRI), without mammography; these studies should be included.
		  ○ Question: will ABUS be considered as a supplemental screening modality?
		• Consider including sensitivity/specificity and DCIS in outcomes.
		• In outcomes, for false positives, consider imaging only as well as requiring biopsy or biopsy and imaging.
		• For KQ3- would consider identifying which outcomes are critical, vs important as in other questions.
		• For KQ3-Additionally, consider separately looking at outcomes for people with high breast density vs not, as well as increased vs. average risk people.
			Thank you.
			
			Dense breasts (and which category) is an important sub-population of interest for all comparisons. You are correct that the comparison group for supplemental screening (MRI, ultrasound) is mammography and this is in KQ2. The interest for MRI and ultrasound is only as supplemental screening rather than replacing mammography, but this will be put forth for consideration in the future. Currently, primary screening with MRI is only available for high risk populations (outside our guideline). ABUS will be eligible for a type of supplemental screening.
			
			We will capture DCIS when looking to see what is assessed related to overdiagnosis. The reviews will assess false positive rates rather than overall accuracy (sensitivity/specificity), because this outcome is considered more patient-centered. Relying on accuracy information is usually only used when no data on other outcomes including mortality and other patient-important outcomes are not available.
			
			For false positives we are capturing any FPs (regardless of method to resolve) and FP resolved by biopsy; the amount resolved by imaging alone can be easily seen when comparing these two.

			Our methods rate outcomes related to intervention effects (KQ1 and 2) as critical versus important for decision-making, whereas KQ3 is not looking at intervention effects but the preferences around those critical outcomes. For this reason, the outcomes as per KQ1 will determine which *exposures* we look at in KQ3. We have specified outcomes as preference-based (i.e. health state utilities and direct trade offs/rating scales) versus not preference-based (e.g. attitudes, intentions, where we need to infer the relative importance of the benefits vs harms) and will place more weight on the preference-based outcomes. We will extract population details related to breast density and other risk factors; we have added ethnicity/race and risk for breast cancer as specific sub-populations and will try to tease out any differences in findings.
Earle	**Yes**	I want to make sure the settings, described as being generalizable to primary care, would include studies of organized population-based screening programs, correct? I note that the information being accepted on the portal is broader than what will be considered as evidence. It may be helpful for stakeholders submitting documents to know how things like Government reports or reports from other organizations will be considered.	Thank you. Yes, organized population-based screening programs are of interest; this has been clarified. We agree this information will be helpful to share. The submissions were much appreciated to screen for relevant research studies to include but will also be considered for additional information for use by the task force.
Holmes & Said	**Yes**	Tables 2 and 3: In the outcomes section, it's important that all the harms (overdiagnosis, false-positive rate and interval cancers) be weighed equally. We haven't seen any data that show that overdiagnosis or false-positive results have different levels of harms (anxiety) on the individual. Note: Table 3 references outcomes "as per Table 1" but the outcomes are in Table 2	Thank you for the input. KQ3 also tries to assess the relative importance of these outcomes to patients. Thank you for pointing out this error which has been fixed.

Ibezi	**Yes**	I suggest specific populations - race/ethnicity, socioeconomic status to be considered for KQ2 population.	Thank you. We will definitely consider specific populations when assessing evidence for KQ2, and have added this to the table.
Kumar	**No**	No comment	N/A
Payne	**Yes**	Table 2 Intervention - For clarity, wording of intervention #1 and #2 should be consistent with wording of other items: e.g., 2D mammography alone; 2D digital mammography supplemented with 3D digital mammography (tomosynthesis) – there should also be additional capture of the type of digital mammography (full field vs CR as they differ in performance and I believe that CR is still in use in parts of Canada) – I would also like to see included studies that focus on CEM alone and 3D alone (ie not as a supplement to 2D) – it's not clear to me if item #1 implies 2D mammo (that's how I interpreted it) – for clarity, different forms of mammo alone should be evaluated separately (ie 2D (FFDM/CR), 3D, CEM); Table 2 Outcome – it is not clear to me why there is a focus on treatment – treatment choices are to some extent a direct result of the cancer pathology – treatment choices are not a result of method of detection (screen vs not) – screening aims to improve cancer diagnostic pathology (mortality being a crude downstream measure of this) – so if there were more data to be collected, it should be to expand on cancer pathology beyond stage – ditto comment for breast cancer morbidity; Missing from the mortality measures is the possibility of relative survival (ie survival corrected for age – competing risk); It is not clear to me why 'prospective' is indicated in the 'critical harms' section – is this meant to refer to person-specific follow-up data? Also, is there any consideration to distinguishing between overdiagnosis and overtreatment? The harms are inherently different (DCIS is harmful given the diagnosis, but is it also being overtreated? Ie additional harm); Table 2 Study Designs – why limit the false positive data to CPAC data? There are other organized screening programs internationally with comparable approaches and therefore data (UK, AUS, NZ for eg);	Thank you for your thorough review. Table 2 Intervention We have revised the wording of the interventions. As intended but not clearly reported, we will include studies of CEM or 3D alone and treat these separately from 2D. Table 2 Outcome The outcomes related to treatment are meant as surrogate markers of treatment-morbidity and stage at diagnosis. The possibility to avoid chemotherapy was thought potentially highly patient-important. Some, such as more surgeries may help inform the impact of overdiagnosis. We are very interested in mortality among different ages to start screening, and therefore less interested in survival corrected for age. We will look at life years saved though. For the critical harm outcome (overdiagnosis) the task force is relying on prospective studies and the excess incidence approach for their assessment, recognizing that harms may come from treatment or a label of a diagnoses. Data will be presented by whether or not DCIS is included. Input from clinical experts has suggested that DCIS is treated in almost all cases. Table 2 Study Designs Assuming we can get data from CPAC we do not feel that we need to use data from other countries and would prefer to keep this data as applicable as possible. We are hoping to use quite recent data. Table 3. We had essentially replicated the USPSTF criteria because we were not planning to change any of their data. We will interpret their findings in light of

		Table 3 – cannot comment as I don't really understand the research question; one comment on settings – it's the intent to refer to Canadian primary care settings (not US); Table 4 – I'm a bit uncomfortable with including age 35-39 as the assessments by this group are more hypothetical as they have not been faced with the choices (ie different than asking someone in their 40s who has already chosen (or not) to be screened; Table 4 Outcomes – I'm concerned at the narrow focus on quantitative outcomes although I understand the logistical reasoning behind this – I'm concerned that harms/benefits are context-specific (cultural norms in different populations) and that qualitative data could add substantial richness	considerations relevant to Canada though e.g. the higher FP rates in US studies, age of study data. Table 4. Thank you for your thoughts. We think leaving this age a bit open to 5 years is reasonable for those making choices about screening. Several studies recruit ages slightly lower than their target population in part to lower the number who have already screened and may have different attitudes (e.g. belief perseverance). Studies with many people below 35 will be considered carefully and rated as high risk of bias. Table 4 Outcomes. We appreciate the expression that qualitative data can be very informative for some research questions. For this research question we are looking for clear trade-off type data, as possible, or attitudes and intentions. The beliefs and factors (e.g. social, environmental) underlying these data are interesting and relevant but beyond the scope of what this question is doing.
Ryan	**Yes**	Seeking clarification on why different inclusion dates are proposed for RCTs versus observational studies.	Thank you. We have clarified that the interest in newer observational studies is so that we are only focusing on those studies most applicable to current practice, mainly with respect to many changes to cancer treatments. When we rate the certainty of the evidence, observational studies start at low certainty (vs RCTs starting at high) and we want to try to capture studies that will not need to be rated down further for indirectness/inapplicability. The task force would not want to rely on older observational studies when they have data from RCTs for the same time period.
Tracer	**Yes**	For KQ3, the research plan notes "For age and other variables of interest (e.g. chemotherapy use) we will allow for <20% of the sample to be ineligible (i.e., those at high risk of breast cancer). I would suggest doing a sensitivity analysis excluding studies that include ineligible	Thanks. We have added risk factors as a key variable of interest for the analysis.

		populations, or stratifying results by eligible vs ineligible populations (average risk vs higher risk), if possible. It is plausible that persons who know they're at high risk would value the benefits and/ or harms of breast cancer screening differently than those at average risk.	
ThundeByass	**Yes**	Benefits- reduction in late stage diagnosis especially in the population that is not considered by the task force i.e new immigrant population.	Thank you. The task force will consider the intersection of immigrant status (and time since immigration) when considering race/ethnicity and other specific populations. While we need to identify major specific populations of interest for the analysis this does not supersede looking at information on other factors that may impact outcomes from screening. The addition of access to screening data from other sources than this review will hopefully capture some of the issues faced by new immigrants.
Yang	**Yes**	I provided comments in the research plan document.	Thank you we appreciate this. The next table has responses to the comments not added to this table.
YongHing	**No**	I would change where it says "Digital mammography (2 or 3D)" to "Digital mammography (2 or digital breast tomosynthesis (DBT))"	Thank you we have revised the description of the interventions.
Sheffield	**No**	No comment	N/A
Wittmer	**No**	No comment	N/A
Question 3: Do the research questions address the clinically important issues?			
Boulanger	**Yes**	Evaluation questions are relevant. Would an evaluation of efficiency help to better support decision-making?	Thanks for the suggestion/question. The task force is not explicitly asking a research question on efficiency but may look at this during their considerations.
Carol	**No response**	N/A	N/A
Chiarelli, Fienberg, McCurdy, Salleh,	**Yes**	• The questions do address this clinically important questions. • For consistency KQ3 should be consistent with others and include age examined; sex and risk level in description.	Thank you. We have revised the wording about the populations to be consistent.

Truscott, Walker			
Earle	**Yes**	No comment	N/A
Holmes & Said	**No**	Add a fourth question or follow-up to key question 3 to build on the idea of relative importance an individual place on potential benefits and harms and to better understand how they receive and process information about benefits and harms to make a decision about whether breast screening is right for them. This will help address improving equity depending on the changes made to the guideline recommendations and how they are communicated/utilized. It's important for women to see themselves represented in the guidelines and to improve access to and understanding of the guidelines.	Thank you. We appreciate this suggestion and will consider this in the future. For this update, the task force is partnering with patients for interpreting the reviews and also to help with developing the messages used in the recommendations, in hopes that this will help women see themselves as represented in, and able to better use, the guideline.
Ibezi	**Yes**	No comment	N/A
Kumar	**Yes**	No comment	N/A
Payne	**Yes**	Res Qu #2: I think I'm having difficulty understanding this – exactly what is being compared? (Res Qu#1 clearly states that the comparison group is 'no screening) – could the language be clarified? Benefits compared to harms? I'm trying to understand the study design that would address this question; Res Qu #3: 'relative importance' according to whom? Presumably patients/women – should be clear, ie it's not provider-driven.	Thanks for this. In KQ2 all studies must have at least one arm with use of only film or digital mammography (DM). The study may compare different ages to start or stop, different screening intervals, use of personalized screening criteria, use of tomosynthesis vs DM, or the addition of MRI, tomosynthesis or ultrasound to DM.
Ryan	**Yes**	Yes, they reflect clinically important issues. They also help to illustrate differences across sub-populations. As per question 1, what is the justification for choosing the lower age bracket of 40 years?	The task force is considering those 40 and older because there is an increasing interest for starting to screen at 40, and many programs offer self-referral at 40.
Tracer	**Yes**	No comment	N/A
ThundeByass	**Yes**	No comment	N/A

Yang	**Yes**	Some terminology needs to be defined. For example, the term supplemental- a second test when the first test is normal or diagnostic test after a BIRAD 0 or 3?	Thank you. We have replaced “supplemental” with ”with” to avoid implying it has to be only for those with a normal mammography (i.e., in everyone); it may be used concurrently in all people. We want to focus on screening versus diagnostic testing.
YongHing	**Yes**	No comment	N/A
Shaffield	**Yes**	No comment	N/A
Whittmer	**Yes**	No comment	N/A
Question 4: Are there any important sources of studies (i.e databases or organizational websites) that we did not include that should be considered in our review? If yes, please provide additional sources?			
Boulanger	**Yes**	INESSS has worked on a document concerning the imaging to be used for screening people with dense breasts if it is ever useful for you. We are currently updating it. https://www.inesss.qc.ca/publications/repertoire-des-publications/publication/densite-mammographique-et-depistage-du-cancer-du-sein.html INSPQ is the organization that evaluates the breast cancer screening program in Quebec. They publish an annual dashboard on program performance. There may be useful information for you. https://www.inspq.qc.ca/equipe-d-evaluation-du-programme-quebecois-de-depistage-du-cancer-du-sein	Thank you very much.
Carol	**No response**	N/A	N/A
Chiarelli, Fienberg, McCurdy, Salleh, Truscott, Walker	**No**	No comment	N/A

Earle	**Yes**	Given that emphasis of false-positive harms is a bit of a lightning rod for criticism of the guidelines, is it enough to only rely on the Canadian studies for this? How did the USTFPH handle this?	Thank you. We would like to make data as applicable to Canada as possible for this and other outcomes. The USPSTF only evaluated research evidence on the differences in FPs between different screening strategies, and this will be reported in KQ2. They did not review any more evidence on screening versus no screening. Their modelling likely provided information to help inform differences in harm by age and other variables. Additionally we will examine false positive results from our modeling data
Holmes & Said	**Yes**	CPAC Report: - Breast Cancer Screening in Canada (monitoring and evaluation of quality indicators)	Thank you.
Ibezi	**No**	No comment	N/A
Kumar	**Yes**	No comment	N/A
Payne	**Yes**	It's not clear to me how this grey literature (observational data but not published in peer-reviewed literature) will be used relative to the systematic reviews. Is the intent to gather information that can deal with the outcomes listed in the systematic review? That said, it should be noted that CPAC data (false positives) is somewhat outdated at this point. Comprehensive data (quality indicators) for Canadian screening programs was last published for 2011-12 data, although individual screening programs would likely have those data compiled and potentially availably public (i.e., more current false positive data that reflects current practise re technical and provider skills & experience)).	Data on false positives (total and resolved through biopsy) will rely on Canadian studies and data, and we are expecting to have relatively recent data from CPAC (2019) and will consider provincial/territorial reports or data. Apart from this outcome, other data from research studies meeting our eligibility criteria will be included regardless of whether it has been published in a peer-reviewed journal. Additionally we will examine false positive results from our modeling data
Ryan	**Yes**	How is the search strategy being created to ensure that all important sources are identified? Who is responsible for ensuring the development of an effective search strategy?	The review teams have experienced information specialists designing highly comprehensive searches in multiple databases. Apologies if you would have liked this information in the research plan which was designed to be fairly concise to focus on the eligibility criteria for the broad and large stakeholder review.

			The search strategy will be available with the final systematic review
Tracer	**No**	No comment	N/A
ThundeByass	**Yes**	The study design is robust. However local experts that treat under represented groups might have additional resources. Dr. Aisha Lofters from Women's College, Toronto.	Thank you.
Yang	**Yes**	Studies on the performance of tomosynthesis at population level are important evidence.	This review plan to focus on evidence on the outcomes considered of most important to patients, and would only include accuracy studies if nothing else existed. KQ2 will be used to examine comparisons in FP rates and interval cancers between DM and tomosynthesis.
YongHing	**Yes**	Canadian Society of Breast Imaging to submit list of resources.	Thank you.
Sheffield	**No**	No comment	N/A
Whittmer	**No**	No comment	N/A
Question 5: Are there specific reports or publications of research studies, or ongoing studies that might fit the inclusion criteria, that the Task Force should consider?			
Boulanger	**No**	No comment	N/A
Carol	**No response**	N/A	N/A
Chiarelli, Fienberg, McCurdy, Salleh, Truscott, Walker	**Yes**	The following health technology assessment from Ontario Health on supplemental breast cancer screening in people with dense breasts should be included in the review: https://www.hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/supplemental-screening-as-an-adjunct-to-mammography-for-breast-cancer-screening-in-people-with-dense-breasts	Thank you for the suggestion. We are not planning to include reviews as a primary data source (except for reliance on the USPSTF review for KQ2 due to its breadth of coverage) but can compare results with this report and check to see if there are any studies missed that meet our (or KQ2's) eligibility criteria.
Earle	**No**	Not that I'm aware of that wouldn't be picked up by the protocol.	N/A

Ibezi	**No**	No comment	N/A
Kumar	**No**	No comment	N/A
Payne	**No**	No comment	N/A
Ryan	**Yes**	Would these not be determined based on the search strategy as well as the inclusion criteria?	Yes, we would screen any studies to see if they meet the criteria. We develop very comprehensive searches but there is always the possibility of missing a study or there being a report of research that has not been published.
Tracer	**No**	No comment	N/A
ThundeByass	**No**	Not that I am aware of, however local experts might be useful.	Thank you.
Yang	**Yes**	Quality determinants of breast cancer screening and monitoring reports from CPAC. Evidence from a population-based program should weighed differently vs evidence from a medical model.	Thank you. We will seek out data from CPAC related to the outcomes of interest.
YongHing	**Yes**	Canadian Society of Breast Imaging to submit list of resources.	Thank you.
Sheffield	**No**	No comment	N/A
Whittmer	**No**	No comment	N/A
Question 6: Do you have any major concerns about the protocol that we should address?			
Boulanger	**No**	The evaluation questions are relevant and will make it possible to take a position on breast cancer screening.	Thank you.
Carol	**No response**	N/A	N/A
Chiarelli, Fienberg, McCurdy, Salleh,	**Yes**	• The protocol could be strengthened by providing the rationale for and potential risks of using streamlined review methods alongside the description of the deviations described in Table 1. • For title and abstract/full text screening, consider verifying at least some percentage of unreviewed records filtered out and screened by the DistillerSR AI tool.	Thank you. We have made it clear that our methods still meet criteria for systematic reviews. We will definitely add a quality assurance for the use of DistillerAI. Thank you for the input about ecologic study designs – we appreciate the limitations from this

Truscott, Walker		• There is concern that for KQ1 ecological design studies would be examined for outcomes. • The scope of the research plan seems wide, and includes both primary and supplemental screening modalities for people in average and increased risk groups. While recommendations in all these areas are important to the breast screening field, consider prioritizing recommendations for people ages 40-49 given the recent US recommendations and implementation of population-level screening for this group in different Canadian provinces, as well as the Fall release timelines.	type of data and plan to rely on it when there is an absence/scarcity of other evidence. We appreciate your concern for our timelines. We will work hard to make sure there is enough time to carefully examine the evidence.
Earle	**Yes**	There is a discrepancy in the representation of the support that CPAC (my organization) can provide. I suggest the first sentence of the Modelling section be changed to: The Task Force is engaging with the Canadian Partnership Against Cancer to identify experts in the modelling community who are able to carry out modelling using the OncoSim model to supplement the above KQs and inform their recommendations on breast cancer screening.	Thank you very much for this clarification. Many apologies that this was in error; we revised as suggested**.**
Holmes & Said	**Yes**	This protocol or a complementary review should include an assessment of shared decision making, its overall effectiveness and what the enablers and barriers are when it comes to accessing breast screening. Shared decision making requires access to a healthcare provider and it's important to consider how the guidelines are received in the absence of a health care provider.	Thank you for this suggestion and the input. We do not believe there will be time for a wholesome review of this nature within our timelines, but can consider to add this for future work to inform many guidelines. We will consider this input for the current guidance.
Ibezi	**Yes**	To ensure study population accurately reflects the diverse population of Canada, by targeting and inviting groups that are often under-represented and disadvantaged in research.	Thank you. We appreciate the concern you have. We will look for data on outcomes for a diverse range of populations, and will also look to other sources of information (e.g. epidemiological) to help inform the recommendations in the absence of research studies within the scope of these reviews.
Kumar	**No**	As always, I am hoping that you will base your recommendations on evidence and not succumb to advocacy not based on evidence.	Thank you very much.
Payne	**Yes**	It will need to be transparent as to why the TF chose to single out Res Qu#2 in terms of approach (ie adopt/modify' the USPSTF approach) –	Thank you. KQs 1 and 3 are answered using de novo reviews and task force methods as the USPSTF did not undertake reviews in these areas in their latest analysis. However, to avoid duplicating efforts (and

		presumably the USPSTF took similar approaches to what is proposed for both Res Qu #1 & #3	avoid research waste) and because the USPSTF had very similar eligibility criteria to which the task force would use for KQ2, this review was chosen to be used as is, with slight modification to its assessments to allow for considerations about the applicability of the evidence to Canada and current practices. We will make sure this is clear when reporting on this data.
Ryan	**No**	No major concern	N/A
Tracer	**No**	I don't have major concerns. However, I think it would be important to consider the applicability of evidence for KQ2 (comparative effectiveness of different screening strategies) from US sources (e.g., the BCSC) to specific Canadian populations of interest.	Thank you we will take this into account.
ThundeByass	**No**	No comment	N/A
Yang	**No**	No comment	N/A
YongHing	**No**	No comment	N/A
Sheffield	**No**	No comment	N/A
Whittmer	**No**	No comment	N/A
General comment			
Email by Dr Warner	**N/A**	The approach looks very comprehensive. My only comment is that where possible I think we need to make a distinction between women who are at average risk and women at moderately increased risk (up to 20-25% lifetime risk). Not all studies make this distinction but some do. It doesn't make sense to me that screening guidelines should be the same for these 2 groups	Thank you; the task force plans to consider data (including different assumed absolute risks in the absence of clear data by risk level) for these two risk groups separately.

Additional comments added to Research Plan document

Section & excerpt	Comment	ERSC/ST/WG Chairs Response
Overall	**Huiming Yang:** We have a national breast cancer screening network with many experts who are not only up to date in the literature, but also understand the context and limitations of many published studies as well as current challenges and issues in breast cancer screening in Canada. I'm surprised that none of them on any of these lists. Frankly, many people would have questions about this approach. Currently, there are significant discrepancies in CTFPHC and provincial breast cancer screening guidelines which have resulted confusion among the providers and the public. In reality, each province uses its own guidelines instead. I think this is a good opportunity to help harmonize the guidelines. Exclusion of national breast cancer screening network experts and CPAC from the lists would not be helpful for guideline harmonization.	Thank you. The Canadian Breast Cancer Screening Network was contacted as a stakeholder for review of the research. Additionally, CPAC has been included as a stakeholder for this guideline update and has been consulted for feedback on this research plan. We are also communication with the breast screening network within CPAC
Key questions: KQ2b) Do the comparative benefits and harms differ by population characteristics (e.g., age, breast density, race and ethnicity, socioeconomic status, geographical area, family history)?	**Huiming Yang:** People with breast implants? **Huiming Yang:** With screening and better treatment, there are a large proportion of population who have survived their first breast cancer (cured), but are at higher risk for another primary breast cancer, how to screen / surveillance this group?	Thank you. We recognize there are populations that are not captured as being the main specific populations of interest. This guideline is not targeting those at high risk including women with previous breast cancer.
Key questions: The review will not include studies focusing on those with high risk (e.g., at higher than 20% lifetime risk).	**Jim Boulanger:** Would it be good to give examples for high risks? As you did for the moderate risk...	Thank you, we have added examples to the table, please refer to table 2.
Table 2, KQ1 – Eligibility criteria, population Specific populations (using within and between-study data where able):	**Huiming Yang:** Suggest comparing with breast cancer epidemiology in Canadian populations	We will look at this data in addition to the reviews highlighted in this research plan.
Table 2, KQ1 - Eligibility criteria, population Breast density (e.g., extremely [e.g., BI-RADS category D] vs not extremely dense breasts; other comparisons))	**Jim Boulanger:** Which Bi-RADS category were you thinking of comparing with? Studies often compare the two extremes (Bi-RADS D with Bi-RADS A), although these groups are poorly represented in the population. An adequate comparison should be made with Bi-RADS B for which it is recommended to continue annual screening.	Thank you. We have clarified the main comparisons of interest are A to C vs D, and A and B vs C and D.

Section & excerpt	Comment	ERSC/ST/WG Chairs Response
Table 2, KQ1 - Eligibility criteria, intervention Any mammography screening modality (i.e., film or digital mammography [2D mammography], digital breast tomosynthesis [3D mammography]) with or without clinical breast examination (CBE)/breast self-examination (BSE):	**Huiming Yang:** Not sure film mammography is still relevant to current practice. It can still be used as background info.	We will include studies using film mammography and interpret the evidence in light of these considerations. The type of screening device is one of several (e.g. treatment changes over time) considerations to consider.
Table 2, KQ1 - Eligibility criteria, intervention Any mammography screening modality (i.e., film or digital mammography [2D mammography], digital breast tomosynthesis [3D mammography]) with or without clinical breast examination (CBE)/breast self-examination (BSE):	**Jim Boulanger:** Is the 2D generated by a tomo device considered (2D or 2Ds)? **Jim Boulanger:** Will the different modalities of tomosynthesis be considered? (3D only, 3D + 2D synthetic)	Thank you. We have added that 2Ds is an intervention of interest and have revised our description of these. We will also consider the different modalities of tomosynthesis if available
Table 2, KQ1 - Eligibility criteria, intervention Any mammography screening modality (i.e., film or digital mammography [2D mammography], digital breast tomosynthesis [3D mammography]) with or without clinical breast examination (CBE)/breast self-examination (BSE):	**Huiming Yang:** Supplemented could mean using it as diagnostic exam if any doubt on the screening mammogram or could mean doing both sequentially	We have modified the term to "with" and will include MRI or ultrasound if used concurrently (i.e., in everyone) or after a negative mammography. We want to focus on screening versus diagnostic testing.
Table 2, KQ1 – Outcomes	**Huiming Yang:** Currently, the benefits are measured almost entirely by mortality reduction only which is important but also biased. Early detection may improve survival time, quality of life due to lesser aggressive treatment. In addition potential years of life loss may be a better measurement as saving a 70 year old may be different from saving a 45 year old patient.	Thank you. We agree that other outcomes are important to consider and have included life years lost/gained as well as

Section & excerpt	Comment	ERSC/ST/WG Chairs Response
		treatment morbidity and stage shifts (i.e fewer advanced stage) as outcomes of interest.
Table 1 – eligibility criteria The review will not include studies focusing on those with high risk. Strong family history of breast cancer will be defined as per the CDC..[9]	**Jim Boulanger:** I would have indicated what the CDC considers a strong family history.	We have left this as a link in the research plan but can add specifics in the recommendation as appropriate and/or applicable.