Evidence Gaps Research Taxonomy Table
Topic: Research Gaps for Screening for Breast Cancer

To fulfill its mission to improve health by making evidence-based recommendations for preventive services, the USPSTF routinely highlights the most critical evidence gaps for creating actionable preventive services recommendations. The USPSTF often needs additional evidence to create the strongest recommendations for everyone, especially those with the greatest burden of disease. In some cases, clinical preventive services have been well studied, but there are important evidence gaps that prevent the USPSTF from making recommendations for specific populations.

In this table, the USPSTF summarizes the gaps in the evidence for screening for breast cancer and emphasizes health equity gaps that need to be addressed to advance the health of the nation. Although the health equity gaps focus on Black women because they have the poorest health outcomes from breast cancer, it is important to note that all studies should actively recruit enough women of all racial and ethnic groups, including Black, Hispanic, Asian, Native American/Alaska Native, and Native Hawaiian/Pacific Islander participants, to investigate whether the effectiveness of screening, diagnosis, and treatment vary by group.

The research taxonomy is intended to provide general guidance to investigators. Investigators are encouraged to develop research designs that are responsive to the research taxonomy outlined in the table, in collaboration with their research teams and areas of expertise and experience. The research developed will be reviewed according to standard USPSTF criteria for inclusion in its evidence report; inclusion criteria are summarized in the final Research Plan (https://www.uspreventiveservicestaskforce.org/uspstf/document/final-research-plan/breast-cancer-screening-adults) and Procedure Manual (https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual).

For some research areas, such as risk-based breast cancer screening, the USPSTF has deferred calling for specific research, as studies are currently in process (e.g., the WISDOM trial) that may help to inform future research approaches. For the research gap related to the natural history of ductal carcinoma in situ, clinically oriented studies would subsequently be needed to help inform an evidence-based clinical approach. Such studies would likely be informed by the results of the currently specified research gap.

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
Research is needed to determine the benefits and harms of screening for breast cancer in women age 75 years or older.	KQ1 KQ2 KQ3	Direct and indirect	Grade assignment; health equity by age	Randomized, controlled trials; controlled clinical trials. Prospective cohort studies with contemporaneous comparison groups who are well-matched on baseline clinical and demographic characteristics.‡	Adult females age 75 years or older; racial and ethnic groups representative of U.S. population; studies should be adequately powered to detect differences in outcomes in Black women and other racial and ethnic groups at higher risk of breast cancer mortality.	Compare screening mammography with no screening. Among women screened, compare different screening intervals (or strategies) (e.g., biennial vs. triennial).	KQ1: Breast cancer morbidity (e.g., adverse effects of treatment and no treatment, physical/functional impairment). Quality of life or subjective well-being. Breast cancer mortality. All-cause mortality. KQ2: Detection of advanced cancers (e.g., stage IIA/IIB) and stage distribution of any invasive breast cancer at the time of screening and across multiple rounds of	Settings applicable to U.S. primary care.

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
							followup, including interval cancers. KQ3 (Harms, including): False-positive and false-negative findings at screening and biopsy. Recall rate (need for further evaluation). Overdiagnosis and overtreatment. Psychological harms (e.g., anxiety, depression). Quality of life and subjective well-being. Radiation exposure.	
Research is needed to help clinicians and patients understand the best strategy for breast cancer screening in women found to have dense breasts on a screening mammogram, which occurs for more than 40% of women screened.	---	---	---	---	---	---	---	---
Research is needed to determine the benefits and harms of supplemental screening (e.g., ultrasonography, MRI, and contrast-enhanced mammography) compared with usual care (DBT or DM alone) for women with dense breasts. Studies are needed that report health outcomes such as quality of life and breast cancer–associated morbidity and mortality.	KQ1 KQ3	Direct	Grade assignment; health equity	Randomized, controlled trials; controlled clinical trials. Prospective cohort studies with contemporaneous comparison groups who are well-matched on baseline clinical and	Adult females; racial and ethnic groups representative of U.S. population.	In persons with dense breasts and an otherwise normal screening mammogram, compare screening mammography plus supplemental screening (e.g., ultrasound, MRI, and contrast-enhanced mammography) or	KQ1: Breast cancer morbidity (e.g., adverse effects of treatment, physical/functional impairment). Quality of life or subjective well-being. Breast cancer mortality. All-cause mortality.	Settings applicable to U.S. primary care.

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
				demographic characteristics.‡		compare different supplemental screening strategies with screening mammography alone; stratify and statistically compare results by breast density category—(C) heterogeneously dense and (D) extremely dense.	KQ3 (Harms, including): False-positive and false-negative findings at screening and biopsy. Interval cancers (false negative and incident cancers presenting clinically between screening visits). Recall rate (need for further evaluation). Overdiagnosis and overtreatment. Psychological harms (e.g., anxiety, depression). Quality of life and subjective well-being. Radiation exposure.	
Research is needed to determine the benefits and harms of supplemental screening (e.g., ultrasonography, MRI, and contrast-enhanced mammography) compared with usual care (DBT or DM alone) for women with dense breasts. Studies are needed that report outcomes such as the rates of advanced breast cancers diagnosed across consecutive screening rounds (evidence of stage shift), in addition to the rates of diagnosis of breast cancer.	KQ2 KQ3	Indirect	Grade assignment; health equity	Randomized, controlled trials; controlled clinical trials. Prospective cohort studies with contemporaneous comparison groups who are well-matched on baseline clinical and demographic characteristics.‡	Adult females; racial and ethnic groups representative of U.S. population.	In persons with dense breasts and an otherwise normal screening mammogram, compare screening mammography plus supplemental screening (e.g., ultrasound, MRI, and contrast-enhanced mammography) or compare different supplemental screening strategies with screening	KQ2: Detection of advanced cancers (e.g., stage IIA/IIB) and stage distribution of any invasive breast cancer at the time of screening and across multiple rounds of followup, including interval cancers. KQ3 (Harms, including): False-positive and false-negative findings at screening and biopsy. Recall rate (need for further evaluation).	Settings applicable to U.S. primary care.

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
						mammography alone; stratify and statistically compare results by breast density category—(C) heterogeneously dense and (D) extremely dense.	Overdiagnosis§ and overtreatment. Psychological harms (e.g., anxiety, depression). Quality of life and subjective well-being. Radiation exposure.	
Research is needed to understand and address the higher breast cancer mortality among Black women.	---	---	---	---	---	---	---	---
Research is needed to understand why Black women are more likely to be diagnosed with breast cancers that have biomarker patterns that confer greater risk for poor health outcomes.	Foundational		Health equity; grade assignment	Basic research that identifies high-risk biomarker patterns, epigenetic phenomena, or physiologic and environmental risk factors (e.g., chronically high inflammatory markers).	Preclinical studies; adult females; racial and ethnic groups representative of the U.S. population.			Settings applicable to the U.S.
Research is needed to understand how variations in care (including diagnosis and treatment) leads to increased risk of breast cancer morbidity and mortality in Black women, across the spectrum of stages and biomarker patterns, and on effective strategies to reduce this disparity.	Implementation, KQ1		Health equity; grade assignment	Observational studies that investigate variations in care delivery across the spectrum of breast cancer care (by race and ethnicity, SES, or social determinants) and strategies (e.g., pragmatic trials) to mitigate variations.	Adult females; racial and ethnic groups representative of the U.S. population.		Breast cancer morbidity (e.g., adverse effects of treatment, physical/functional impairment). Quality of life or subjective well-being. Breast cancer mortality. All-cause mortality.	Settings applicable to the U.S.
Research is needed to determine whether the benefits differ for annual vs. biennial breast cancer screening among women overall, and whether there is a different balance of benefits	KQ1 KQ2 KQ3	Direct and indirect	Grade assignment; health equity	Randomized, controlled trials; controlled clinical trials.	Adult females; racial and ethnic groups representative of U.S. population;	Compare annual screening mammography with biennial screening (in all women and	KQ1: Breast cancer morbidity (e.g., adverse effects of treatment, physical/functional impairment).	Settings applicable to U.S. primary care.

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
and harms among Black women compared with all women.				Prospective cohort studies with contemporaneous comparison groups who are well-matched on baseline clinical and demographic characteristics.‡	studies should be adequately powered to detect differences in outcomes in Black women and other racial and ethnic groups at higher risk of breast cancer mortality.	stratified and statistically compared by race and ethnicity). Prioritize studies in Black women, who are at higher risk of breast cancer mortality.	Quality of life or subjective well-being. Breast cancer mortality. All-cause mortality. KQ2: Detection of advanced cancers (e.g., stage IIA/IIB) and stage distribution of any invasive breast cancer at the time of screening and across multiple rounds of followup, including interval cancers. KQ3 (Harms, including): False-positive and false-negative findings at screening and biopsy. Recall rate (need for further evaluation). Overdiagnosis and overtreatment. Psychological harms (e.g., anxiety, depression). Quality of life and subjective well-being. Radiation exposure.	
Research is needed to identify approaches to reduce the risk of overtreatment of breast lesions identified through screening that may not be destined to cause morbidity and mortality.	---	---	---	---	---	---	---	---

Research Gap	Key Questions* or Contextual Questions	Direct/ Indirect Pathway†	Type of Gap	Study Characteristics	Population	Intervention/ Comparison	Outcomes/Timing	Setting
Research is needed on the natural history of DCIS and to identify prognostic indicators to distinguish DCIS that is unlikely to progress to invasive breast cancer.	Foundational, KQ3			Large, nationally representative observational cohorts. Large, nationally representative cohorts for prognostic indicator (e.g., biomarkers, demographic factors, or multivariate risk models) creation. Prospective large, nationally representative cohorts for prognostic indicator validation (cohorts should be adequately powered to detect differences in performance in Black women and other racial and ethnic groups at higher risk of breast cancer mortality).	Adult females; racial and ethnic groups representative of U.S. population; studies should be adequately powered to detect differences in prognostic indicator performance in Black women and other racial and ethnic groups at higher risk of breast cancer mortality.		Breast cancer incidence and subtype.	Settings applicable to U.S. primary care.

* Key questions are an integral part of the approach to conducting systematic reviews that the USPSTF uses in its recommendation process. Along with the analytic framework, these questions specify the logic and scope of the topic and are critical to guiding the literature searches, data abstraction, and analysis processes (https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual).

† The direct pathway is typically derived from RCTs of the targeted screening or preventive intervention that adequately measure the desired health outcomes in the population(s) of interest. If certainty for net benefit cannot be derived from the direct pathway, then the USPSTF determines if the evidence is sufficient across the key questions and linkages in the indirect pathway to determine overall certainty.

‡ For example, age, race, SES, and family history.

§ Overdiagnosis is defined as detection of breast cancer that would not have become symptomatic during a woman's lifetime if no screening had taken place.

Abbreviations: DBT=digital breast tomosynthesis; DM=digital mammography; KQ=key question; MRI=magnetic resonance imaging; RCT=randomized, controlled trial; SES=socioeconomic status; USPSTF=U.S. Preventive Services Task Force.