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Multilevel Factors in Cancer Screening

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Multilevel Factors in Cancer Screening

by

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DISSERTATION

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Committee in Charge

Dedication

I am thankful for the opportunity UCSF offered me by accepting me into the PhD in Epidemiology and Translational Science. The faculty and students with whom I interacted made me a stronger epidemiologist and I appreciate the chances I had to learn from and with all of you.

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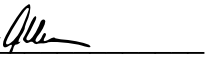
Acknowledgement of Previously Published Materials

A version of Chapter 1 in this dissertation was published in *Clinical Interventions in Aging* in 2018.[1] The Dissertation Committee members supervised this research that forms the basis of this dissertation chapter, the published material is substantially the product of Joshua Demb's period of study at UCSF and was primarily conducted and written by him. The work he completed for this published manuscript is comparable to a standard dissertation chapter.

Approved:  Isabel Allen, PhD, Dissertation Chair

[1] Demb J et al. Screening mammography use in older women according to health status: a systematic review and meta-analysis. Clin Interv Aging. 2018; Volume 13:1987-1997. doi:10.2147/CIA.S171739.

MULTILEVEL FACTORS IN CANCER SCREENING

Joshua B. Demb

ABSTRACT

Cancer is the second leading cause of death in the United States, with cancer of the breast and cancer of the lung and bronchus together accounting for approximately 29% of all cancer cases and 32% of all cancer deaths. Cancer screening tests are a means to reduce mortality of these two cancer types. While the current guidelines aim to maximize the potential benefits from screening while minimizing harms, there is still significant effort needed to achieve optimal breast and lung cancer screening uptake. This dissertation builds upon recent research leveraging multilevel frameworks to examine factors affecting cancer screening use and their importance in clinical practice and in screening guidelines.

The first chapter comprehensively examines the current evidence regarding how various life expectancy factors are associated with screening mammography uptake among women ages 65 and older. The primary objective was to understand the important role life expectancy could play in patient-provider communication regarding whether to continue screening at an advanced age. The second chapter focuses on the variation in performance of lung cancer screening scans, which use low-dose computed tomography. This project sought to identify the potential institutional-level predictors that could lead to radiation doses outside the current guidelines for these scans, potentially impacting the expected margin of benefit from screening. The third and final chapter is a multilevel assessment of the effect of employment status on screening mammography utilization during the Great Recession, to better understand how societal changes can influence individual-level cancer screening behaviors.

Together these projects highlight the interdependence of factors at multiple levels in the cancer screening environment. Examination of these multilevel factors can improve integration of new interventions to optimize cancer screening uptake and ensure that early detection practices are successful, thus improving treatment outcomes and maximizing survival.

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1. INTRODUCTION

Cancer is the second leading cause of death in the United States.[1] In 2018, it is estimated that there will be over 1.7 million new cases of cancer diagnosed in the United States, and over half a million people will die from cancer.[2,3] The two leading anatomic sites of cancer incidence and death are cancers of the lung and bronchus and cancers of the breast, which together account for approximately 29% of all new cancer cases and 32% of all cancer deaths in the United States.[3] Further, it is estimated that the yearly national expenditures for cancer care in the United States will exceed $170 billion over the next two years.[4] The ongoing burden of these cancers and their relative contribution to mortality in the United States highlights the need to prioritize early detection of cancer to improve the likelihood of successful cancer treatment and lower risk of mortality.

Cancer screening is an important secondary prevention method with an overarching goal to reduce the burden of cancer morbidity and mortality by detecting a tumor before the onset of symptoms.[5] To achieve this goal, the ideal cancer screening regimen must maximize potential benefits—such as earlier detection of cancer and longer survival among eventual cancer cases—against possible harms, such as detection of indolent or slow-growing cancers with low risk of becoming malignant (overdiagnosis) or the risk of false-positive screening results, both of which lead to unnecessary and potentially invasive diagnostic workup.[5,6] As more evidence is found regarding the efficacy of different types of cancer screening, the recommendations and guidelines evolve to maximize the margin of benefit.[7]

Screening mammography has been an endorsed breast cancer screening tool for more than 50 years, with several recent quality improvements occurring within the last 20 years, including the development of the Mammography Quality Standards Act in 1992.[8–11] Screening for lung cancer—a low-dose computed tomography (LDCT) scan—on the other hand, was found to have a potential benefit within the last 15 years.[12–14] Table 1.1 shows the criteria for

which the U.S. Preventive Services Task Force (USPSTF) currently supports both of these screening tests, which influences whether screenings are included as essential health benefits as part of healthcare coverage.[15] In addition to the USPSTF guidelines, the US Department of Health and Human Services has sought to improve uptake of cancer screening as part of the Healthy People 2020 initiative, specifically targeting a 10% improvement in breast cancer screening uptake among eligible women.[16] Furthermore, recent findings indicate that implementing current lung cancer screening guidelines in community health facilities is very challenging, and current guidelines are not being properly implemented.[17–19]

Table 1.1: USPSTF screening guidelines for breast and lung cancer screening

Screening Modality	**Mammography[20] (Breast Cancer)**	**Low-dose CT[21] (Lung Cancer)**
Screening Frequency	Biennial	Annual
Age of Initiation	Age 50	Age 55
Age of Cessation	Age 74	Age 80
Other Eligibility Factors	None	30 pack-year smoking history Former Smokers: Quit ≤15 years prior to screening

Note: These guidelines have A or B rating based on most recent USPSTF recommendations

Despite these efforts, there is still more work to be done to achieve optimal breast and lung cancer screening implementation and uptake. Achieving optimal cancer screening uptake requires that the guidelines adapt to current trends in cancer incidence and mortality, that a clear margin of benefit is maintained, and any harms are minimized. At the same time, successful implementation of cancer screening in practice requires buy-in from providers and institutions and an understanding of the population needing to be screened. Understanding these factors influences the development of policies that affect access to cancer screening services. Accomplishing all of this requires a holistic assessment and more complex conceptualization of the system in which cancer screening tests exist.

1.1 THE CANCER SCREENING SYSTEM

In recent years, various researchers have developed different conceptualizations of the system in which cancer care exists. One model, known as the Cancer Care Continuum, aimed

to identify different areas across the full spectrum of the natural history of cancer where health care quality could be improved in response to the Institute of Medicine report, *Ensuring Quality Cancer Care*.[22,23] Even with this longitudinal approach to cancer care, a more complex system exists with multiple levels of influence that could affect provider delivery and patient utilization of cancer care services.[22,24,25] Zapka et al. used this knowledge to develop a Quality in the Continuum of Cancer Care framework to evaluate the quality of secondary prevention in breast cancer and cervical cancer, highlighting the factors contributing to failures in care processes, as well as the potential strategies that could reduce failures.[22]

In practice, a common approach for improving quality of care has been to focus on one of the individual steps within the cancer care continuum. The problem, however, as Taplin et al. have argued, is that a lack of coordination or lack of patient-centered approach across the continuum leads to poor implementation of these improvments.[26] Instead, they argue that care should be considered as "a process in a dynamic system", leveraging the theory of complex adaptive systems to think about the entire system.[26–29] This theory notes that individuals and layers within a system are constantly adapting to their surroundings.[26]

McLeroy et al. explain a multilevel, interactive approach to epidemiology that focuses efforts on modifying organizational behavior and helps develop and advocate for policies that support public health behaviors.[30,31] The model focuses on five levels of factors. Intrapersonal factors emphasize characteristics of the individual, such as knowledge and behavior. Interpersonal processes and primary groups focus on the individual's social network and support systems. Institutional factors include social institutions with organizational characteristics. Community factors focus on the relationships among organizations and institutions. Finally, public policy encapsulates the local, state and national laws that govern the preceding levels of influence.[30] Warnecke et al. developed a similar conceptual model, influenced by the efforts of Taylor et al.[32], Berkman et al.[33], and Glass and McAtee[34] to model socio-ecological factors involved in population health.[35] While this model is a more general

framework to understand population health, it clarifies the interplay of factors that can lead to disparate health outcomes, particularly within the cancer screening environment.

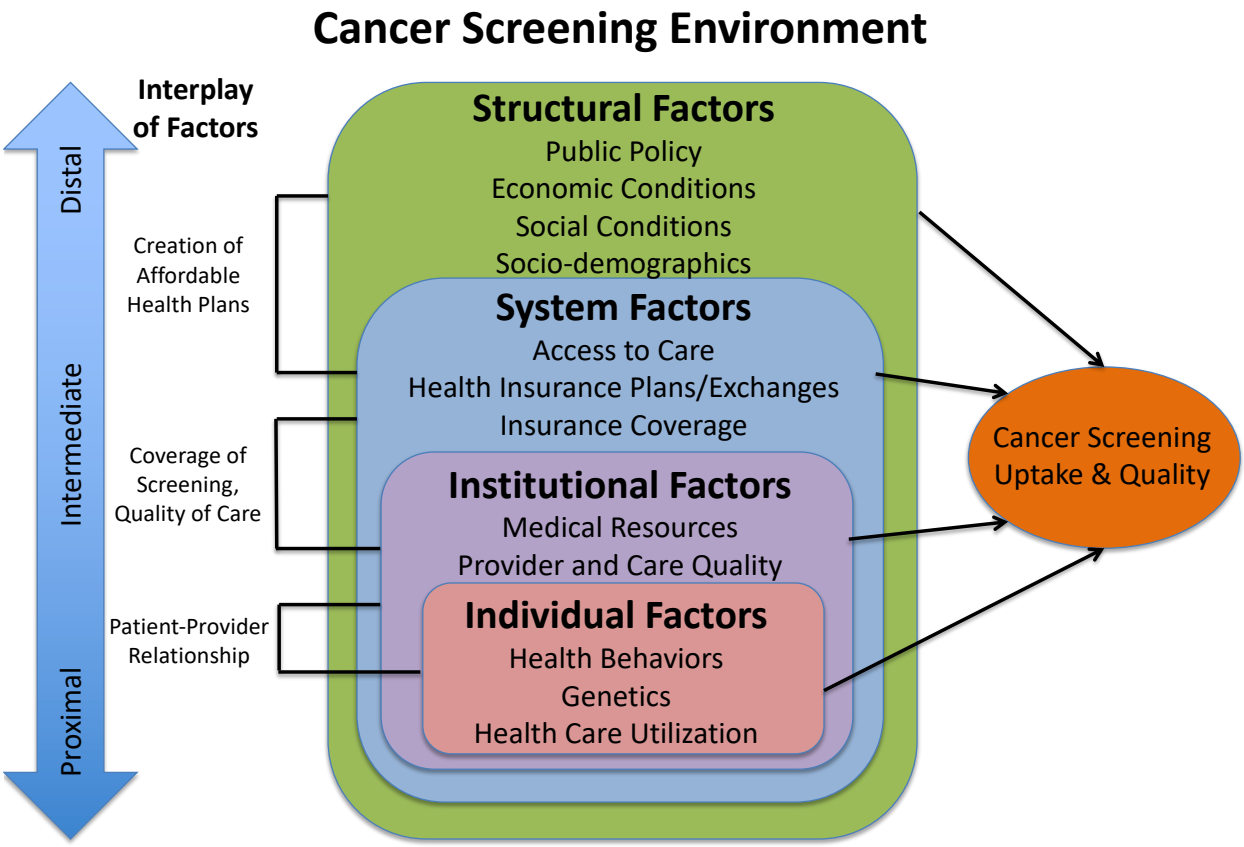
Rimer and Glanz also apply an ecological framework to cancer screening epidemiology, highlighting two key themes: 1) behavior both affects and is affected by multiple levels of influence, and 2) individual behavior both shapes and is shaped by the social environment (reciprocal causation).[31,36] Rimer and Glanz apply this framework to a case study of a woman deciding whether or not get a mammogram.[31]

> "A woman may weigh the pros and cons of getting a mammogram and hesitate to screen because of concerns about detecting cancer. At the interpersonal level, this decision may never come up between her and her primary care provider, due to either minimization by the woman, or neglect to discuss on the part of the provider. At the organizational level, the woman might change her mind and decide to get a mammogram, only to find out that scheduling an appointment is more difficult than she anticipated. Further, the woman might realize that her health insurance does not fully cover the costs of a mammogram (institutional level). The ultimate result to not screen is thus shaped by a host of factors at multiple levels."[31]

The outcome of this case study is particularly concerning in low income women and African American women, who are up to three times more likely to present with advanced stage cancer compared with other groups.[37,38] Further, it stresses the importance about understanding the intersection of population risk and individual risk as it relates to cancer screening.

To better understand how to improve current cancer screening practices, it is clear that research must adopt a complex systems approach. Adapting conceptual frameworks from Zapka et al., Taplin et al., McLeroy et al., Rimer and Glanz and Warnecke et al., Figure 1.1 emphasizes the cancer screening environment as whole, illustrating the multilevel factors and their interdependencies, and their impact on cancer screening utilization and the quality of cancer screening services. Within this system, there are four major levels of factors: 1) structural factors, encompassing population-level effects; 2) system factors, focusing on aspects of healthcare such as insurance and access; 3) institutional factors, which include aspects of medical care within specific health institutions and provider-level effects; and 4) individual factors, focused on the patient and their interactions with the health care system.

Figure 1.1: Socio-ecological Framework of Multilevel Factors Involved in Cancer Screening.



1.2 OBJECTIVES OF DISSERTATION

The overall goal of this dissertation is to examine various factors involved in the multilevel cancer screening environment, and their importance in both clinical practice and in screening policy and guidelines. This will be considered in three different chapters: 1) systematic assessment of screening mammography utilization among older women by life expectancy factors; 2) identification of institutional factors that contribute to variation in radiation dose from low-dose lung cancer screening scans; and 3) examination of how a national event, the Great Recession, contributed to the effect of employment status on screening mammography utilization in the United States.

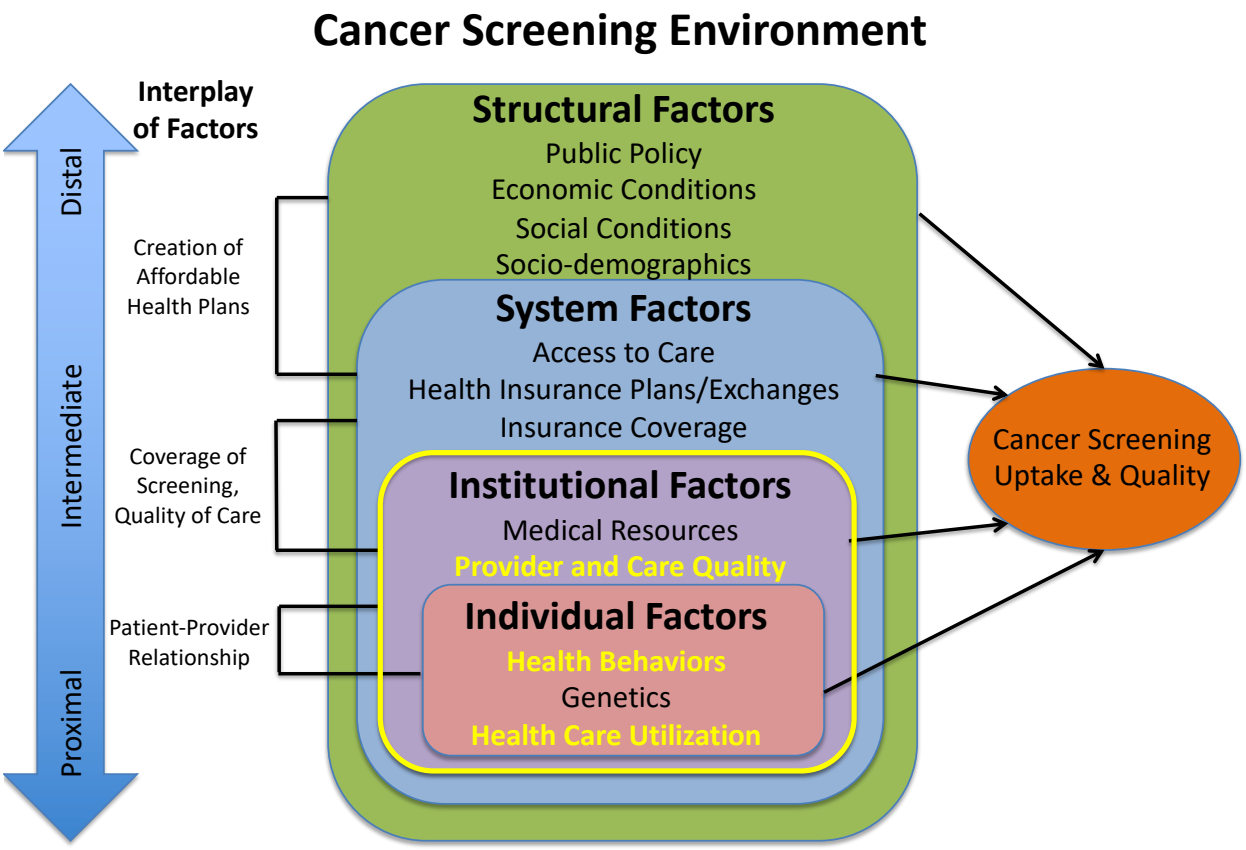
Chapter 1 is a systematic review and meta-analysis of the current literature of US-based studies examining the effect of life expectancy factors—comorbidity, functional status and prognostic factors—on screening mammography utilization in older women (women ages ≥65). This chapter focuses on the patient-provider interaction and contextualizing how life expectancy factors affect screening uptake, and how these factors should be considered when older women consider undergoing screening mammography. Chapter 2 examines institutional and system factors in current computed tomography practices in lung cancer screening across several US institutions. It uses US data from an international radiation dose registry to understand the factors that influence variation in radiation doses for the scans, which can affect the potential margin of benefit conferred from undergoing screening. Finally, Chapter 3 addresses the interaction of structural and societal factors by leveraging data from the Health and Retirement Study to evaluate the effect of employment status on screening mammography utilization before, during and after the Great Recession (2007-2009). In this final chapter, the goal was to understand whether temporal trends existed in this association, notably whether being less than full-time employed during the Great Recession led to lower screening mammography utilization.

On their own, each chapter evaluates an important question that exists within different ecological levels of the cancer screening environment. Examined together, these projects contextualize the individual-, institutional- and structural-level factors that influence cancer screening in practice and in policy, and further exemplify the importance of understanding cancer screening from a systematic perspective.

2. CHAPTER 1: Screening mammography use in older women according to health status: a systematic review and meta-analysis

Joshua Demb MPH, Tomi Akinyemiju PhD, Isabel Allen PhD, Tracy Onega PhD, Robert A. Hiatt MD PhD, Dejana Braithwaite PhD

Figure 2.1: Conceptual Framework for Multilevel Factors Involved in Cancer Screening, Multilevel Factors for Chapter 1 Highlighted



2.1 ABSTRACT

Background: The extent to which screening mammography (SM) recommendations in older women incorporate life expectancy factors is not well established.

Objective: Evaluate evidence on SM utilization in older women by life expectancy factors.

Data Sources: MEDLINE, EMBASE and Web of Science from January 1991 to March 2016.

Study Selection: We included studies examining SM utilization in women ages ≥65 years that measured life expectancy using comorbidity, functional limitations or health or prognostic status.

Data Extraction and Synthesis: Odds ratios and 95% confidence intervals (CIs) were extracted and grouped by life expectancy category. Findings were aggregated into pooled odds ratios and 95% CIs and meta-analyzed by life expectancy category.

Main Outcomes and Measures: The primary outcome was SM utilization within the last five years. Life expectancy factors included number of comorbidities, Charlson Comorbidity Index (CCI), activities of daily living, instrumental activities of daily living, self-reported health status and 5-year prognostic indices.

Results: Of 2606 potential titles, we identified 25 meeting the inclusion criteria (Comorbidity: 8 studies; Functional Status: 11 studies; Health/Prognostic Status: 13 studies). Women with higher CCI scores had decreased SM utilization (Pooled OR: 0.75 95% CI: 0.67-0.85) but increased absolute number of comorbidities were weakly associated with increased SM utilization (Pooled OR: 1.17 95% CI: 1.00-1.36). Women with more functional limitations had lower SM use odds than women with no limitations (Pooled OR: 0.72 95% CI: 0.62-0.83). Screening utilization odds were lower among women with poor versus excellent health (Pooled OR: 0.85 95% CI: 0.74-0.96).

Conclusion: Greater CCI score, functional limitations and lower perceived health were associated with decreased SM use, whereas higher absolute number of comorbidities was associated with increased SM use. SM guidelines should consider these factors to improve assessments of potential benefits and harms in older women.

2.2 INTRODUCTION

More than 50% of new invasive breast cancer cases diagnosed each year in the United States (U.S.) occur among older women—women ages 65 years and older.[39] The increasing life expectancy of women in the US and attendant rise in the absolute number of breast cancer cases in older women will likely lead to an increasing absolute number of mammograms performed in the ≥65 age group.[40] In 2010, the United States Centers for Disease Control and Prevention estimated that older women reported the highest prevalence of mammography use within the past two years.[41] However, the U.S. Preventive Services Task Force currently does not recommend screening mammography in women ages 75 and older due to insufficient evidence.[20] Although older women have a higher risk of breast cancer and lower risk of false-positive mammography results than younger women, their shorter life expectancy decreases the potential benefits of screening.[20,42,43]

A recent review concluded that screening for breast cancer is most appropriate for women with a life expectancy of at least 10 years.[44] Because the full benefit of screening is only realized with reduction in mortality, numerous studies have accounted for life expectancy factors to better identify the margin of benefit a woman might expect from undergoing screening.[41,44–47] To date, comorbidity burden, functional status, and self-reported heath are the strongest predictors of life expectancy.[48–51] However, the current guidelines for screening mammography do not account for life expectancy factors other than chronological age.[20,52]

In light of the current demographic, epidemiologic, and policy environment, it is important to understand the extent to which the current practice of screening mammography is targeted to healthy older women and avoided in older women with limited life expectancy. In this study, we report the results of a systematic review and meta-analysis of the literature of studies assessing mammography screening utilization rates of older women in relation to age, functional limitations, and health status, including but not limited to comorbidity. The main objective of this study is to outline the current practices that exist for screening mammography utilization in older

women and the association between screening and life expectancy factors in order to help guide future screening mammography guidelines.

2.3 METHODS

This systematic review and meta-analysis has a published protocol,[53] and is registered with PROSPERO with the registration number, CRD42016032661. A PRISMA checklist is included in **Appendix Table S1**. The study is covered under an IRB with exempt status submitted and approved by the University of California, San Francisco IRB.

Search strategy and selection criteria

We performed a systematic search of the literature using MEDLINE (using PubMed interface), EMBASE, and Web of Science (January 1, 1991-March 1, 2016) to identify relevant studies. “Breast neoplasms” was combined with the permutations, variations, and abbreviations of the relevant Medical Subject Headings (MeSH) keywords and non-MeSH key terms for mammography, age, health status and comorbidity, including (e.g., cardiovascular diseases, comorbidity, cognition disorders, diabetes mellitus, functional limitation, health status, myocardial infarction, stroke, etc.). Complete search strategies are provided in the **Appendix Sections 2.7.1 and 2.7.2**.

The broad criteria for this review allowed for the evaluation of multiple study designs published in English. The inclusion criteria were as follows: i) women aged 65 years and older in the United States, ii) assessment of women’s comorbidity (either as a specific condition or a summary score) and/or functional impairments and/or health status, and iii) an outcome measure that addresses recent screening mammography utilization. Additional studies were obtained through citations of review articles or contacting breast cancer screening experts regarding any unpublished articles that may be suitable for inclusion in the systematic review. Case reports were excluded. Data were extracted from the full text article.

Most, if not all, of the target population is Medicare beneficiaries, with screening mammography covered based on policy changes implemented in 1991.[54] At that time, Medicare Part B medical insurance, for which most women become eligible when they turn 65 years, covered the full cost of annual mammography for all women age 40 and over.[20,40] To account for this Medicare policy change, we excluded studies evaluating screening utilization prior to 1991.[54] Women eligible for Medicare ages 65-74 are near the upper limit of the USPSTF primary screening mammography guidelines (age 74 years) and USPSTF guidelines note that data are currently inconclusive to provide screening recommendations for women ages 75 and older.[55]

Quality assessment and data extraction

To evaluate the quality of included studies, we used the Newcastle-Ottawa Scale (NOS) and Cochrane Collaboration Risk of Bias (CCRB) tool[56,57] to evaluate observational studies and clinical trials, respectively. The NOS measures the methodological quality of observational studies, giving predefined criteria, some of which have to be further specified based on topic. We specified these criteria in a consensus meeting with the authors (**Appendix Tables S2A and S2B**) before assessing the studies.

Studies were assessed for quality of selection (representativeness, selection of controls, ascertainment of exposure); comparability (adjustment for confounding); and outcome or exposure (assessment of outcome/exposure, length and adequacy of follow-up) independently by two authors (JD and TA). Measures of age, socio-economic status (such as race, education, income), health insurance, and number of physician visits were identified as important confounders. Cohort and case-control studies could earn a maximum of 9 points, and cross-sectional and randomized clinical trials could earn a maximum of 10 points. Studies with scores of 6 to 8 points were considered to be of moderate-to-good study quality, and scores of 9 or higher were deemed excellent. All studies were summarized irrespective of quality score.

A data extraction form was used to collect study characteristics, including type of study,

number of participants, length of follow-up, exposure(s), outcome(s), and quality assessment. Exposures logged in this form were life expectancy factors, including comorbidity scales or specific diseases considered, functional limitation scales used, and measures of health status. The primary outcome was screening mammography utilization, defined as screening mammography occurring within the last 1-5 years. We extracted odds ratios and corresponding 95% confidence intervals (CIs) from most studies, with some studies providing risk ratios or proportions of utilization. Quantitative results were extracted from text and tables, choosing preferably those adjusted for important confounders. Two authors (JD and TA) independently performed study quality assessment and data extraction. Discrepancies were discussed and resolved by the review team.

Qualitative Synthesis and Meta-Analysis

We conducted a qualitative synthesis to describe the findings of included studies, explore associations of interest and examine the quality of the studies and robustness of the systematic review. Study findings were separated into the four exposure categories: comorbidity (measured using an absolute count, Charlson Comorbidity Index (CCI) and individual disease conditions), functional limitations (activities of daily living, instrumental activities of daily living), health status and prognostic status. For each exposure, we aggregated study findings to perform meta-analyses assessing the overall magnitude of the association with recent screening mammography utilization. Pooled ORs and corresponding 95% CIs were reported. Given the variation in measurement of exposures, we stratified our findings to address study heterogeneity. Heterogeneity was measured using I^2 values and Cochran's Q statistic. Pooled results were analyzed using random effects models to control for heterogeneity.

We also performed sensitivity analyses to examine potential publication bias including jackknife analyses[58] and reported these findings in addition to the primary study findings and subgroup analyses.[59] We also performed meta-regression to understand how study traits contributed to heterogeneity of pooled effect estimates.[60,61] The meta-analysis results are

graphically displayed using forest plots.[59] All analyses were performed using STATA 13 (Stata, College Station, TX, USA).

2.4 RESULTS

Study characteristics, including number of subjects, age range, years of data accrual, study design, assessment of outcome and assessment of exposure are summarized in **Table 2.1**. We tabulated the full Newcastle Ottawa findings of individual studies for descriptive purposes (see **Appendix Tables S2A and S2B**). Full descriptive results by exposure type are found in **Appendix Tables S3-S5.**

Literature search

We identified 2,606 potentially relevant titles through PubMed, EMBASE, and Web of Science (see PRISMA flowchart in **Figure 2.2**). After excluding titles that: did not report (a) screening mammography utilization, (b) comorbidity, health status and/or functional status, (c) original research, did not include (d) populations from the United States, (e) screening mammography utilization prior to 1991 and (f) results for women <65 years old, we identified 142 studies published between January 1,1991 and March 31, 2016. After review of abstracts, we excluded 95 articles that did not meet the inclusion criteria. After reviewing 47 full text articles,[54, 62, 71–80, 63, 81–90, 64, 91–100, 65, 101–107,66–70] 25 studies were included in the review, published between 1996 and 2016: there were 10 cohort studies[66, 68,69, 76,77, 79, 93, 100,101,105] and 15 cross-sectional studies.[54, 64, 97–99, 102, 106, 70, 73,74, 81, 83, 88,89,96] No case-control studies were found, which is likely due to the highly common outcome of screening utilization. Characteristics of included studies are shown in **Table 2.1.** Since 3 studies did not include odds ratios, only 22 of the 25 studies were included in the meta-analysis.

Quality Assessment

All of the studies used a combination of surveys, Medicare insurance claims data, and/or medical records to examine associations between the predictor(s)—comorbidity, functional

status or health status—and the outcome, mammography utilization. Based on the quality assessment using the Newcastle-Ottawa Scale (no clinical trials were included),[56] all studies were found to be of moderate to excellent quality, despite several studies using self-reported outcome assessment.

Estimates of the effect of the comorbidity on utilization of screening mammography

A full list of comorbidities measured in each study can be found in **Appendix Tables S3A, S3B and S3C**. Eight studies measured the association of comorbidity with screening mammography utilization, with four studies using an unweighted number of comorbid conditions measure[69, 74, 96,108] and four studies using the Charlson Comorbidity Index (CCI) (**Figure 2.3**).[81, 88, 101,106] The pooled result showed no significant association between comorbidity and screening mammography utilization (OR: 0.94 95% CI: 0.80-1.10). However, when stratified by comorbidity measurement, increased comorbidity measured using CCI was associated with decreased screening mammography utilization (OR: 0.75 95% CI: 0.67-0.85), while increased absolute number of comorbidities was weakly associated with increased screening mammography utilization (OR: 1.17 95% CI: 1.00-1.36). Meta-regression results indicated studies measuring comorbidity using CCI showed significantly lower screening mammography utilization (Pooled OR: 0.64 95% CI: 0.50-0.82). Jack-knife analyses showed that removal of McBean et al. study and the 2004 Schonberg et al. study, the two studies with the most extreme results, from CCI and absolute number of comorbidities groups, respectively, led to insignificant decreases in study heterogeneity and no marked change in the summary estimates.

In addition, nine studies measured individual comorbid conditions and their association with screening mammography utilization (**Appendix Table S3C**).[66, 69, 75, 79, 81, 89, 93, 97,102] Physical conditions measured included hypertension, diabetes, lung disease, cancer, arthritis, myocardial infarction, stroke, heart disease and hip fracture. Mental conditions measured included cognitive impairment, Alzheimer's disease, depression and psychological distress. In pooled analyses, individual comorbid conditions were not significantly associated with screening

mammography utilization (OR: 0.97 95% CI: 0.89-1.06) (**Appendix Figure S1**). When stratified by type of condition, neither physical conditions (OR: 1.03 95% CI: 0.93-1.14) nor mental conditions (OR: 0.85 95% CI: 0.72-1.01) were significantly associated with screening mammography utilization.

Estimates of the effect of functional status on utilization of screening mammography

Ten studies measured the effect of functional limitations on screening mammography utilization (**Figure 2.4),** with three studies measuring functional limitations in multiple ways. Five studies measured activities of daily living (ADLs),[66, 70, 79,99,100] five studies measured instrumental activities of daily living (IADLs),[69, 74, 79, 93,96] and three studies used a scale incorporating both IADLs and ADLs.[69, 96,106] Overall, functional limitations were associated with decreased screening mammography utilization (Pooled OR: 0.72 95% CI: 0.62-0.83). Of the five studies measuring ADLs, three calculated odds ratios, showing a significant pooled effect of higher number of ADLs on decreased screening mammography utilization (Pooled OR: 0.55 95% CI: 0.35-0.85) in **Figure 2.4**. Two studies reported chi-square results comparing screening mammography utilization by ADL status (yes/no), with both studies showing a significant difference in screening utilization among women experiencing ADL limitations compared to women with no ADL limitations [70,100].

Among the four studies measuring IADLs, the pooled result showed that higher numbers of IADLs were associated with decreased screening mammography utilization (Pooled OR: 0.79 95% CI: 0.64-0.98). Three studies measuring IADL limitations in conjunction with ADL limitations found inverse associations.[69, 96,106] Pooled results indicated that ADL limitations or IADL dependency led to decreased screening mammography utilization (Pooled OR: 0.72 95% CI: 0.57-0.91).

In jack-knife analyses, removal of Schootman et al. Long-term ADL and Long-term IADL, and Caban et al. findings led to study heterogeneity in ADL (p=0.674), IADL (p=0.106) and ADL/IADL (p=0.683) groups being no longer statistically significant, respectively. However, the

pooled estimate still had significant study heterogeneity and did not change appreciably despite removal of these studies (p=0.003). Meta-regression analyses found no significant predictors of study heterogeneity.

Estimates of the effect of health status, life expectancy or prognosis on utilization of screening mammography

Nine studies measured the association of health status on screening utilization, with eight studies measuring perceived general health[66, 69, 76, 83, 97,98,106] and two measuring health status using the Short Form-12 (SF-12) survey (**Appendix Table S5**).[54,64] The pooled result shown in **Figure 2.5** demonstrated that lower perceived health was associated with lower screening mammography utilization (Pooled OR: 0.80 95% CI: 0.69-0.93). Jack-knife analyses showed no significant decrease in study heterogeneity and meta-regression analyses did not find significant predictors of study heterogeneity.

Five studies measured prognostic index or life expectancy measures against utilization of screening mammography (**Appendix Table S5**).[68, 83, 97, 100,105] The pooled effect of the three studies shown in **Figure 2.5** measuring life expectancy using regression showed a nonsignificant inverse association between life expectancy index score and screening mammography utilization (Pooled OR: 0.73 95% CI: 0.53-1.00).

2.5 DISCUSSION

Meta-analysis of the studies addressing life expectancy factors and screening mammography utilization revealed that older American women with higher numbers of functional limitations, higher Charlson Comorbidity Index score and lower perceived health are less likely to undergo routine screening mammography. Prognostic indices, absolute number of comorbidities and specific disease conditions were not significantly associated with screening mammography utilization. These observational studies provide a means to understanding how different measures of life expectancy affect screening mammography utilization.

While increased CCI score was associated with a decrease in screening mammography, the absolute number of comorbidities showed a conflicting, weak positive association with screening mammography utilization. It is possible that having more comorbid conditions increased women's contact with their healthcare provider leading to a greater likelihood of using preventive care.[69,74] Conversely, one study measuring CCI showed no indication that physicians had advocated for cancer screening in the population of individuals with diabetes.[88] Other studies noted that there is little time in the primary care clinic to estimate each individual's candidacy for screening, especially older patients with multiple medical problems, which might lead physicians to screen everyone to avoid confusion with recommendations or medico-legal consequences.[54, 74,96] The conflicting results show that more studies need to be conducted to determine who should receive screening mammography, and how comorbidity burden should factor into a provider's assessment of who is eligible for screening mammography.

Studies consistently indicated that greater numbers of functional limitations decreased screening mammography utilization. Studies using scales incorporating ADL limitations (i.e., needing help with activities such as showering, dressing, getting in and out of bed/chairs, etc.) showed particularly pronounced effects, which might indicate that access factors, such as fewer resources and social supports to facilitate travel to and care navigation at mammography facilities, may lead to lower utilization rates.[66] It is therefore possible that women with ADL limitations may need more support to receive mammography utilization. Another study indicated that the strong association found between ADL and IADL (i.e., needing help with everyday household chores, shopping, and overall getting around) dependence and mammography screening might be indicative of providers considering life expectancy when referring women to screening mammography.[106] However, the fact that the finding did not occur across other measured preventive screenings makes this theory questionable and requires further investigation.

Poorer self-rated health was also found to be associated with decreased screening

utilization, despite some conflicting findings. In one study, pain and discomfort, a potential indicator of poorer health, was a common reason why women might decide not to screen.[69] Conversely, a study done by Walter et al. showed that older women with poorer health status, measured with the Medical Outcomes Study 12-item Short Form Physical Summary Scale (SF-12), did not avoid screening. Although Walter et al. did not have mortality follow-up information on the sample, there is strong evidence that life expectancy is limited in women with worst health status measured by the SF-12.[54]

Pooled analysis of prognostic index scores found no significant association with screening mammography utilization, even though some individual studies had significant findings. Koya et al. found mammography use significantly associated with four-year mortality risk and not age alone, attributing their finding to including age, comorbidity in functional status in their measurement of mortality risk.[83] They hypothesized that the association means clinicians are skilled at identifying predictors of life expectancy in older individuals.[83] However, findings from other included studies seem to contradict this theory.[97,105]

Findings from these studies show that functional limitations and comorbidities when measured using the Charlson Comorbidity Index are associated with decreased screening mammography utilization, while absolute number of comorbidities was weakly associated with increased screening utilization. When discussing screening mammography with older women, providers should ask questions or consult medical records to learn more about these life expectancy factors to better assess the potential benefit older women might receive from undergoing screening mammography. Decision aids have been developed in breast cancer screening to measure key comorbidity and functional measures, though none have been widely implemented.[109,110] While more research is necessary to further understand the importance of life expectancy in measuring harms and benefits of screening mammography, these findings indicate that providers may be weighing more than just age when discussing continuing screening mammography with an older woman. Further assessment of current clinical

recommendations and determination of eligibility for screening mammography could lead to more accurately tailored screening referrals.

Strengths and limitations of studies and analysis

Our systematic review/meta-analysis had key strengths, such as incorporating searches from three major research publication databases ensuring full capture of the literature on life expectancy factors and screening mammography utilization in older women. The use of quality assessment tools allowed us to quantitatively rate the quality of the studies included in our analyses. In addition, the use of stratification to clearly review the life expectancy factors ensured a limited degree of study heterogeneity when measuring our various exposures and screening mammography utilization. Our study also was able to leverage meta-regression in sensitivity analyses to learn more about how different study features contributed to heterogeneity found in pooled results from meta-analyses.

Our review also had several limitations. The 20-year timespan of systematic review could lead to varied results due to secular trends but examining the study results by year does not indicate that a trend exists. While this might account for some variation in the results, the lack of significant changes in screening mammography guidelines or public outreach within this older age group make any difference in effects due to secular trends minimal. Of the 25 studies included in our analysis, 17 relied on self-reported information for measurement of the exposure, while 16 relied on self-reported information to measure screening mammography utilization. This raises concerns about recall bias, particularly when citing screening utilization within the last two to five years. Furthermore, self-reported health status is not a precise measurement of an individual's health, as it uses a Likert scale to assess health at the instance of interview, which might not represent an individual's overall health outside of the clinical environment. Studies that ascertained screening utilization through insurance claims[66, 68, 73, 76,77, 79, 88,89,100,101] were unable to distinguish between mammograms undertaken for screening and diagnostic purposes. However, it is reasonable from a clinical perspective to assume that the

majority were screening procedures, since diagnostic procedures are performed only when a woman presents with symptoms of breast cancer.[66,88,89] The inability to distinguish the two types of mammography might lead to the measured population being slightly sicker than the normal screening mammography population, which would lead to an overestimate of association.

More than half of the studies included were cross-sectional by design, which restricts the ability to ensure temporality of the exposure/outcome relationship. Despite this concern, all but two studies were of moderate to excellent study quality based on our cross-sectional study-specific quality assessment using the Newcastle-Ottawa Survey.

2.6 CONCLUSION

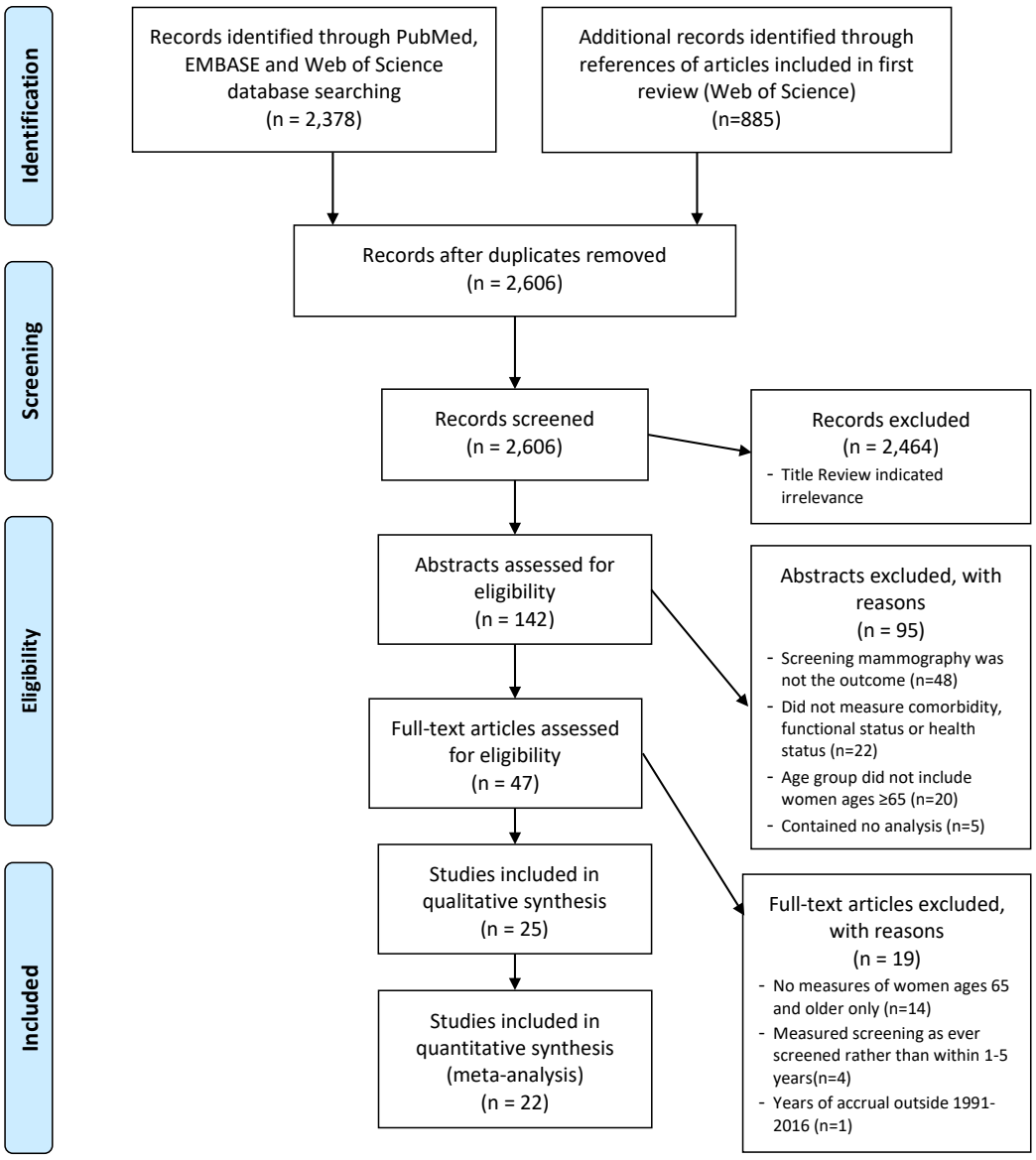
Studies have shown that the primary determinant of screening with mammography, regardless of age, is a physician's recommendation.[96,111–113] It is therefore critical that the guidelines be updated to reflect the importance of characteristics such as the presence of severe functional dependencies in activities of daily living and severe comorbidity as caused by conditions such as end-stage renal disease, severe dementia in concert with clinical judgment to estimate an individual's potential risks and benefits from screening rather than basing screening decisions on age alone. This systematic review and meta-analysis show that consideration of functional status and comorbidity might be occurring in practice, but still needs to be further weighed in screening mammography recommendations, and targeted interventions are needed to facilitate precision cancer screening.

Source	Number of Subjects	Age Range, years	Accrual Years	Study Design	Assessment of Comorbidity/ Functional Status/ Health Status	Assessment of Mammography Utilization	Outcome(s)
Ives et al., 1996[79]	2,175	65-79	1991-1992	Cohort (prospective)	Medicare Claims	Medicare Claims	≥1 screening in 2 years
Kiefe et al., 1998[81]	1,764	≥50	1995	Cross-sectional	Medical Records Review	Medical Records Review	≥1 screening within 2 years
Blustein et al., 1998[66]	2,352	≥75	1991-1992	Cohort (retrospective)	Self-reported	Medicare Claims	≥1 screening within 2 years
Wright et al., 2000[106]	526	≥70	1992-1993	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Barr et al., 2001[64]	309	≥65	2000	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Scinto et al., 2001[100]	844	≥65	1990-1995	Cohort (prospective)	Self-report; Medicare Claims	Medicare Claims	≥1 screening within 5 years
Caplan, 2001[70]	--	50-69 ≥70	1991-1992 1997-1998	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Heflin et al., 2002[74]	2,225	≥65	1992	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Van Harrison et al., 2003[73]	10,000	≥65	1993-1997	Cross-sectional	Medicare Claims	Medicare Claims	≥1 screening within 5 years
Schootman et al., 2003[99]	4,477	≥40	1996	Cross-sectional	Self-reported	Self-reported	≥1 screening within 1 year
Schonberg et al., 2004[96]	882	≥80	2000	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Walter et al., 2004[54]	3,988	≥70	2000-2001	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Bynum et al., 2005[68]	722,310	≥65	2000-2001	Cohort (retrospective)	Medicare Claims	Medicare Claims	≥1 screening within 2 years
Holt et al., 2006[76]	5,461	≥65	1998-2002	Cohort (retrospective)	Self-reported	Self-reported; Medicare Claims	≥1 screening within 1 year
Thorpe et al., 2006[102]	3,655	≥65	1999-2001	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
McBean et al., 2007[88]	99,438	≥65	1997-1998	Cross-sectional	Medicare Claims	Medicare Claims	≥1 screening within 2 years

Table 2.1: Characteristics of studies identified in literature search

Source	Number of Subjects	Age Range, years	Accrual Years	Study Design	Assessment of Comorbidity/ Functional Status/ Health Status	Assessment of Mammography Utilization	Outcome(s)
Schonberg et al., 2008[98]	4,683	≥65	2005	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Williams et al., 2008[105]	4,222	≥65	2002-2004	Cohort (retrospective)	Validated Measures	Self-reported	≥1 screening within 2 years
Mehta et al., 2010[89]	4,312	≥70	2002	Cross-sectional	Interview	Medicare Claims	≥1 screening within 2 years
Caban et al., 2011[69]	4,610	≥65	2004-2005	Cohort (retrospective)	Self-reported	Self-reported	≥1 screening within 1 year
Reyes-Ortiz et al., 2010[93]	1,272	≥75	2004-2005	Cohort (retrospective)	Self-reported	Self-reported	≥1 screening within 2 years
Koya et al., 2011[83]	4,836	≥65	2002	Cross-sectional	Self-reported	Self-reported	≥1 screening within 1 year
Tan et al., 2012[101]	716,279	≥75	2006-2007	Cohort (retrospective)	Medical Record Claims	Medicare Claims	≥1 screening within 2 years
Schonberg et al., 2013[97]	2,266	≥75	2008, 2010	Cross-sectional	Self-reported	Self-reported	≥1 screening within 2 years
Hubbard et al., 2016[77]	49,775	≤65	2005-2010	Cohort (retrospective)	Medicare Claims	Medicare Claims	≥1 screening within 2 years

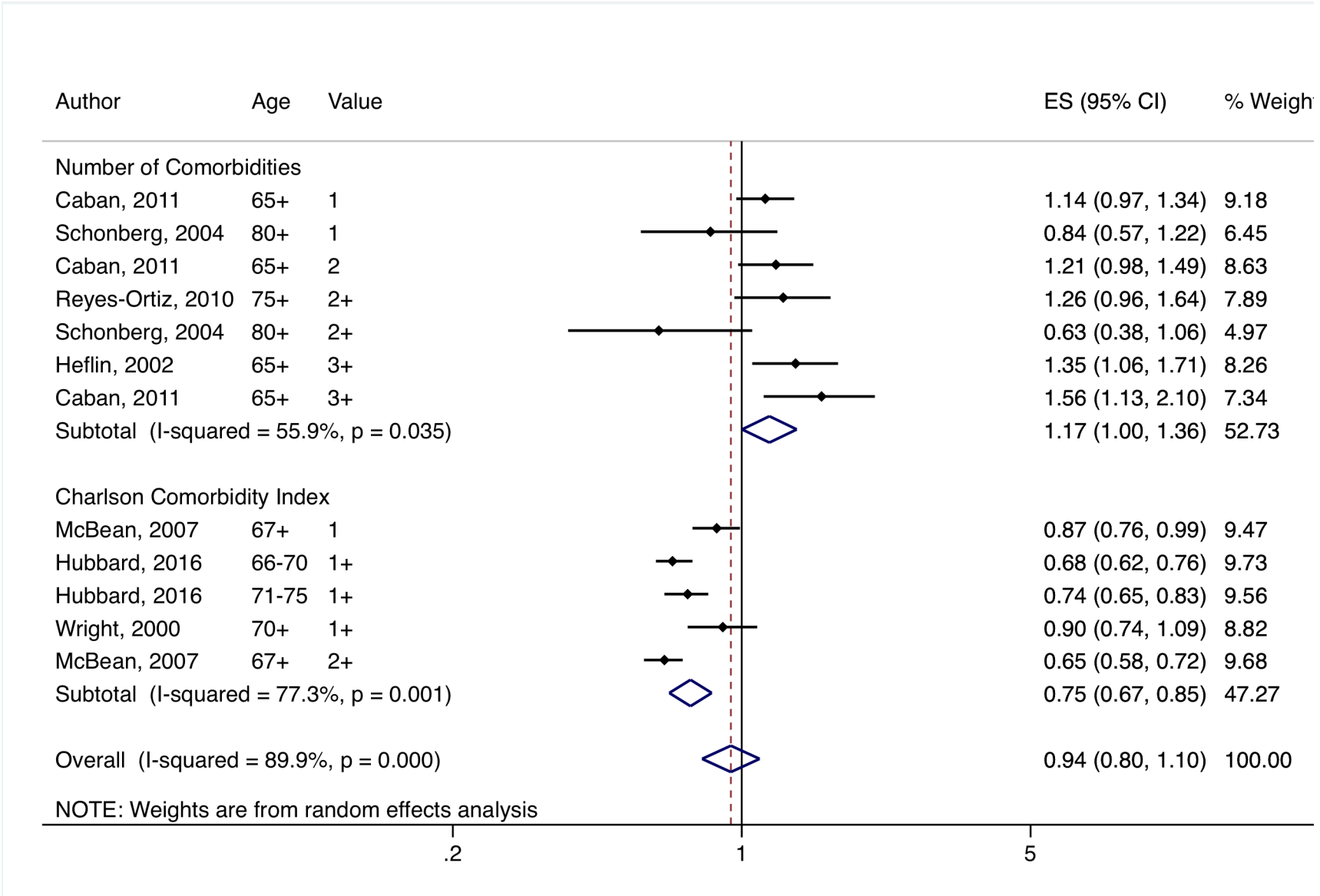
Figure 2.2: PRISMA Flowchart of Included Studies



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 2.3: Forest plot of Effect of Comorbidity on Screening Mammography Utilization by Study and Measure Type



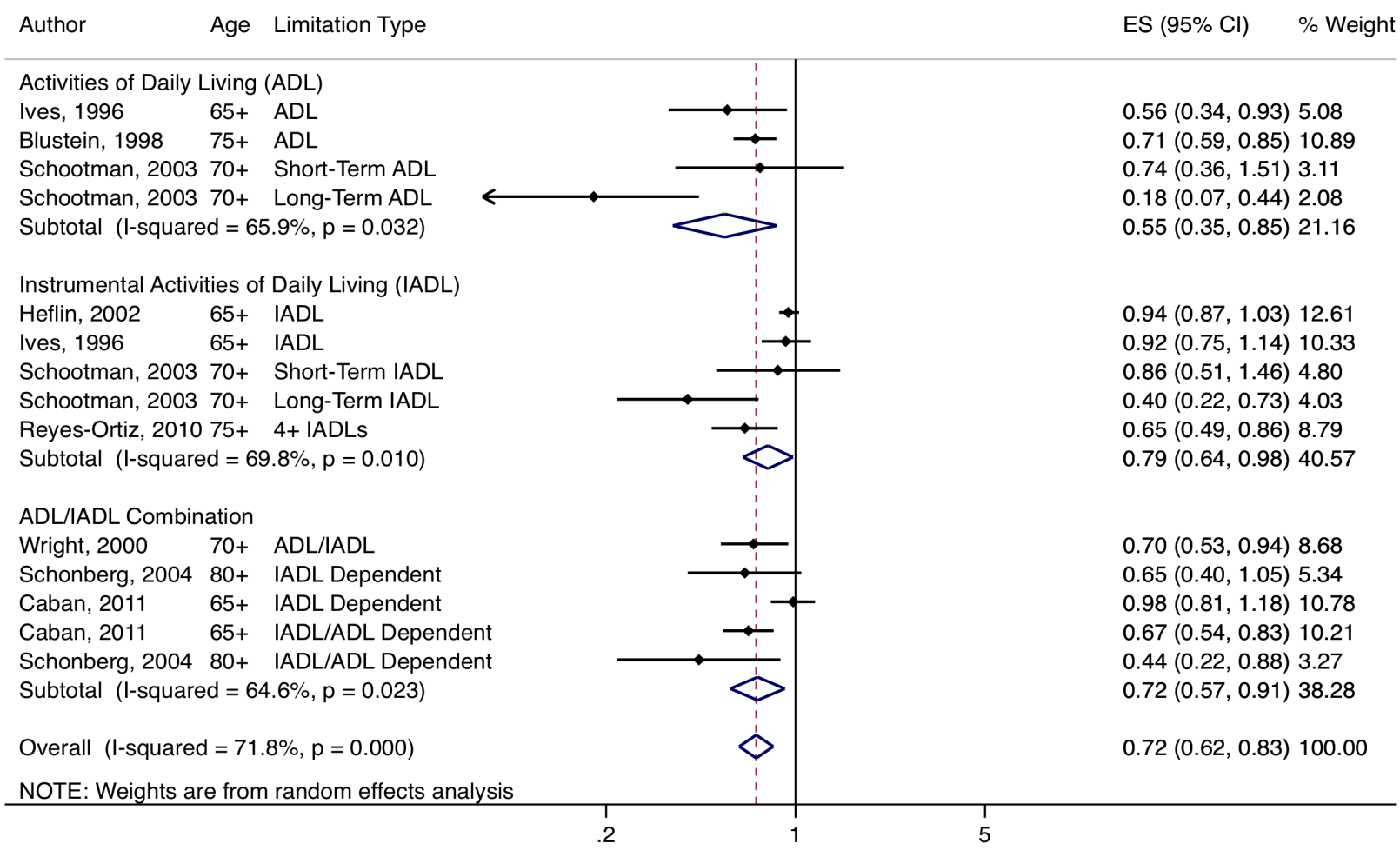
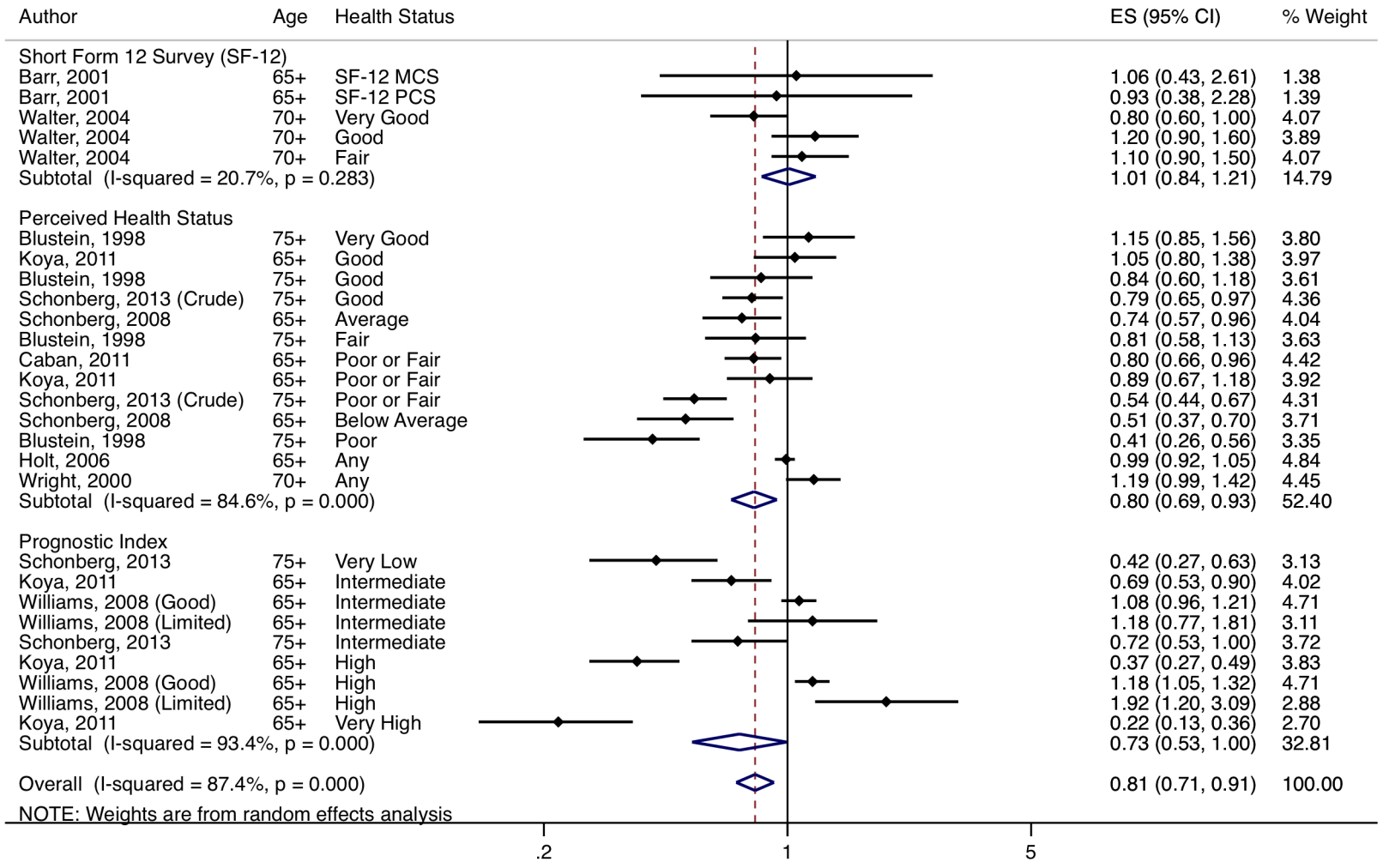


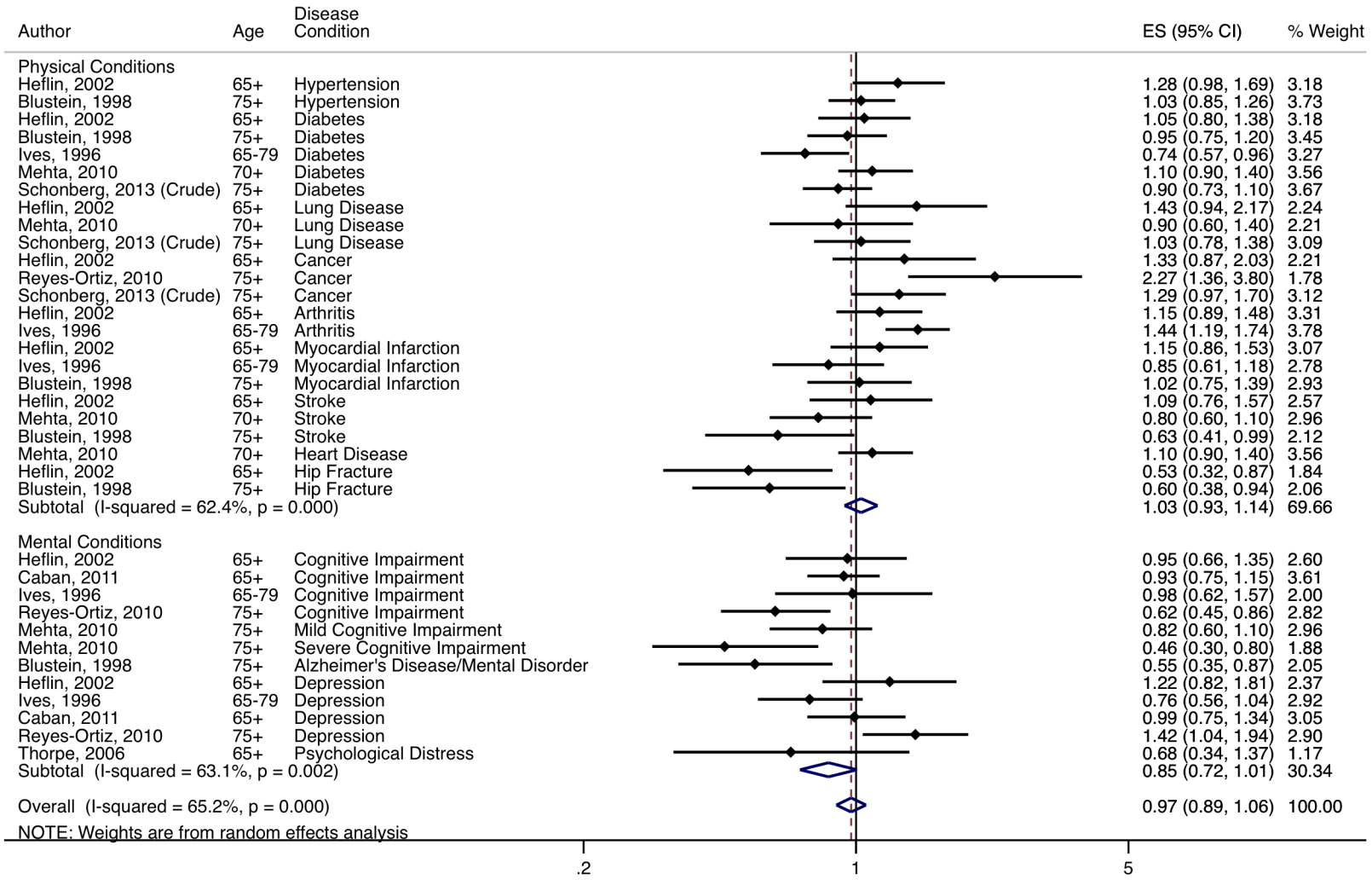
Figure 2.4: Forest plot of Effect of Functional Limitations on Screening Mammography Utilization by Study and Measure Type

Figure 2.5: Forest plot of Effect of Health Status and Prognostic Score on Screening Mammography Utilization by Study and Measure Type



2.7 APPENDIX

Figure S1: Forest plot of Effect of Specific Disease Conditions on Screening Utilization by Study and Measure Type



Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	7
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	8
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	9
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	9-10
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	10
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	10
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix (45-47)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	10
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	11-12
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	11-12

Table S1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	12
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	12
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	12-13
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	12-13
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	13, 23
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	21-22
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	14-16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	14-16
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	14-16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	14-16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16-19

Section/topic	#	Checklist item	Reported on page #
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19-20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

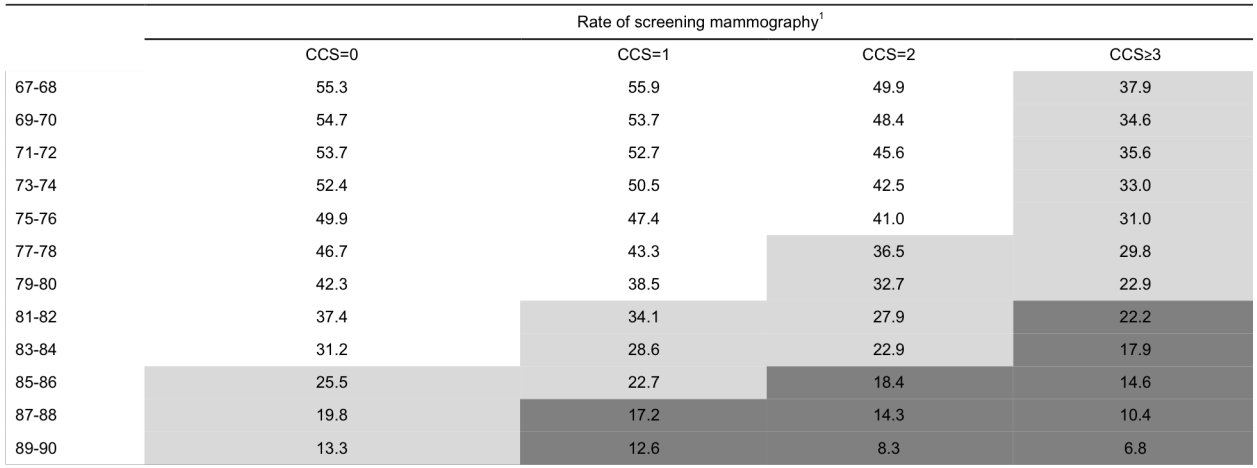
Table S2A: Critical evaluation of the quality and limitations of cohort studies evaluating benefits and harms of screening mammography according to comorbidity

Table S2A: Critical evaluation of the quality and limitations of cohort studies evaluating benefits and harms of screening mammography according to comorbidity											
		Selection				Comparability		Outcome			Evidence Quality[2]
Source	Study Design	Representativeness of Exposed	Unexposed Comparability	Exposure Ascertainment	Temporality Established	Controls for Age	Controls for SES	Assessment	Sufficient Follow-up Time (1-5 years)	Adequate Follow-up (~80%)	
Blustein et al., 1998	Cohort Study	*	*		*	*	*	*	*	*	Excellent
Bynum et al., 2005	Cohort Study	*	*	*		*		*	*	*	Moderate
Caban et al., 2010	Cohort Study	*	*	*		*	*		*	*	Moderate
Holt et al., 2006	Cohort Study	*	*		*	*	*	*	*	*	Excellent
Hubbard et al., 2016	Cohort Study	*	*	*	*	*	*	*	*	*	Excellent
Ives et al., 1996	Cohort Study		*			*	*	*	*	*	Moderate
Reyes-Ortiz et al., 2010	Cohort Study	*	*	*		*	*		*	*	Moderate
Scinto et al., 2001	Cohort Study	*	*	*	*	*	*	*	*	*	Excellent
Tan et al., 2012	Cohort Study	*	*	*	*	*		*	*	*	Excellent
Williams et al., 2008	Cohort Study	*	*	*	*	*	*		*	*	Moderate

Table S2B: Critical evaluation of the quality and limitations of cross-sectional studies evaluating benefits and harms of screening mammography according to comorbidity										
		Selection				Comparability		Outcome		Evidence Quality[2]
Source	Study Design	Sample Representativeness	Sample Size	Unexposed Comparability	Exposure Ascertainment	Controls for Age	Controls for SES	Assessment	Statistical Test	
Barr et al., 2001	Cross-sectional Study			*	**	*	*	*	*	Moderate
Caplan, 2001	Cross-sectional Study	*		*	*	*		*	*	Moderate
Harrison et al., 2002	Cross-sectional Study	*	*	*	**	*	*	**	*	Excellent
Heflin et al., 2002	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Kiefe et al., 1998	Cross-sectional Study			*	*	*	*	**	*	Moderate
Koya et al., 2011	Cross-sectional Study	*		*	**	*	*	*	*	Moderate
McBean et al., 2007	Cross-sectional Study	*		*	**	*	*	**	*	Excellent
Mehta et al., 2010	Cross-sectional Study	*		*	**	*	*	*	*	Moderate
Schonberg et al., 2004	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Schonberg et al., 2008	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Schonberg et al., 2013	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Schootman et al, 2003	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Thorpe et al., 2006	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Walter et al., 2004	Cross-sectional Study	*		*	*	*	*	*	*	Moderate
Wright et al., 2000	Cross-sectional Study	*		*	*	*		*	*	Moderate

Table S2B: Critical evaluation of the quality and limitations of cross-sectional studies evaluating benefits and harms of screening mammography according to comorbidity

Table S2A: Summary of findings from studies that evaluated the effect of summary measures of comorbidity burden on screening utilization

Comorbidity Indices				
Source	**Age**	**Measures of Comorbidity**	**Adjusted Measure of Association**	**Covariates**
Hubbard et al., 2016	≥65	Charlson Comorbidity Index Age 66-70: 0 ≥1 Charlson Comorbidity Index Age 71-75: 0 ≥1	 OR: 1.00 OR: 0.68 (0.62, 0.76) OR: 1.00 OR: 0.74 (0.65, 0.83)	Linguistic Isolation, Diversity index, Median Disposable Income, Median Household Income, Average Annual Health Expenditures, Average Public Transportation Expenditures, Education, Internet Access, Readers of Health Magazines, Newspaper Readers.
McBean et al., 2007	≥67	Charlson Comorbidity Index: 0 1 ≥2	 OR: 1.00 OR: 0.87 (0.76, 0.99) OR: 0.65 (0.58, 0.72)	Age, Race, Rural Residence, Medicaid Status, Median Household Income, Hospitalization History, Medical Specialty, Average number of Physicians Visits per Year, Number of Diabetes Services Received
Wright et al., 2000	≥70	Charlson Comorbidity Index	OR: 0.90 (0.74, 1.09)	Age, Functional Status, Health Status
Tan et al., 2010	≥65			

Number of Comorbid Conditions				
Source	**Age**	**Measures of Comorbidity**	**Adjusted Measure of Association**	**Covariates**
Caban et al., 2010	≥65	Number of Comorbidities: 0 1 2 ≥3	 OR: 1.00 OR: 1.14 (0.97, 1.34) OR: 1.21 (0.98, 1.49) OR: 1.56 (1.13, 2.10)	Age, Race, Education, Zip Code income, Marital Status, HMO Status, Self-rated Health, Number of Comorbidities, Cognitive Deficits, Depression
Heflin et al., 2002	≥65	Number of Comorbidities: <3 ≥3	 OR: 1.00 OR: 1.35 (1.06, 1.71)	Age, Race, Education, Income, Primary Care, Urban/Rural, MIADLs, Proxy Response, Imputation
Reyes-Ortiz et al., 2010	≥75	Number of Comorbidities: 0-1 ≥2	 OR: 1.00 OR: 1.26 (0.96, 1.64)	Education, Annual Household Income, Health Insurance, Financial Strain, Acculturation, Age, Marital Status, Medical Conditions, Functional Status, Cognitive Function
Schonberg et al., 2004	≥80	Number of Comorbidities: 0 1 ≥2	 OR: 1.00 OR: 0.84 (0.57, 1.22) OR: 0.63 (0.38, 1.06)	Age, Race/Ethnicity, Education, Income, Insurance Status, Region, Usual Care, Visited Doctor in Past Year, Current Use of Hormone Replacement Therapy

Table S3A: Summary of findings from studies that evaluated the effect of summary measures of comorbidity burden on screening utilization

Table S3B: Summary of findings from studies that evaluated the effect of specific disease burden on screening utilization

Specific Comorbid Conditions					
Source	**Age**	**Condition**	**Crude Measure of Association**	**Adjusted Measure of Association**	**Covariates**
Blustein et al., 1998	≥75	Hypertension	OR: 1.05 (0.86, 1.28)	OR: 1.03 (0.85, 1.26)	Age
		Diabetes	OR: 0.99 (0.79, 1.24)	OR: 0.95 (0.75, 1.20)	
		Myocardial Infarction	OR: 1.02 (0.76, 1.37)	OR: 1.02 (0.75, 1.39)	
		Stroke	OR: 0.58 (0.38, 0.88)	OR: 0.63 (0.41, 0.99)	
		Hip Fracture	OR: 0.46 (0.29, 0.72)	OR: 0.60 (0.38, 0.94)	
		Alzheimer's Disease/Mental Disorder	OR: 0.54 (0.34, 0.85)	OR: 0.55 (0.35, 0.87)	
Caban et al., 2010	≥65	Depression		OR: 0.99 (0.75, 1.34)	Age, Race, Education, Zip Code income, Marital Status, HMO Status, Self-rated Health, Number of Comorbidities, Cognitive Deficits, Depression
		Cognitive Deficits			
		No		OR: 1.00	
		Yes		OR: 0.93 (0.75, 1.15)	
Heflin et al., 2002	≥65	Myocardial Infarction		OR: 1.15 (0.86, 1.53)	Age, Race, Education, Income, Primary Care, Urban/Rural, MIADLs, Proxy Response, Imputation
		Stroke		OR: 1.09 (0.76, 1.57)	
		Hypertension		OR: 1.28 (0.98, 1.69)	
		Diabetes Mellitus		OR: 1.05 (0.80, 1.38)	
		Cancer		OR: 1.33 (0.87, 2.03)	
		Broken Hip		OR: 0.53 (0.32, 0.87)	
		Chronic Lung Disease		OR: 1.43 (0.94, 2.17)	
		Arthritis		OR: 1.15 (0.89, 1.48)	
		Depression		OR: 1.22 (0.82, 1.81)	
		Cognitive Impairment		OR: 0.95 (0.66, 1.35)	
Ives et al., 2006	65-79	Myocardial Infarction		OR: 0.85 (0.61, 1.18)	Age, Education, Insurance Status, Comorbidity, Functional Status
		Diabetes		OR: 0.74 (0.57, 0.96)	
		Arthritis		OR: 1.44 (1.19, 1.74)	
		Depression		OR: 0.76 (0.56, 1.04)	
		Dementia		OR: 0.98 (0.62, 1.57)	

Source	Age	Condition	Crude Measure of Association	Adjusted Measure of Association	Covariates
Kiefe et al., 1998	65-74	Angina	OR: 0.40	OR: 0.34	Age, Clinic, Attending Clinic within last year, Number of Visits in Prior Year, History of Breast Biopsy, Ambulatory Care
		Congestive Heart Failure	OR: 0.88	OR: 0.64	
		Myocardial Infarction	OR: 1.52	OR: 1.88	
		Hypertension	OR: 1.14	OR: 1.00	
		Diabetes			
		No end-organ damage	OR: 1.16	OR: 0.92	
		With end-organ damage	OR: 0.74	OR: 0.51	
		Mild Renal Disease	OR: 1.53	OR: 1.15	
		Asthma	OR: 0.50	OR: 0.69	
		COPD	OR: 0.87	OR: 0.70	
		Osteoarthritis	OR: 0.97	OR: 0.91	
		Rheumatoid Arthritis	OR: 1.00	OR: 1.20	
		Peptic Ulcer	OR: 0.97	OR: 0.79	
		GI Bleeding	OR: 0.24	OR: 0.17	
Kiefe et al., 1998	≥75	Angina	OR: 0.66	OR: 0.58	Age, Clinic, Attending Clinic within last year, Number of Visits in Prior Year, History of Breast Biopsy, Ambulatory Care
		Congestive Heart Failure	OR: 0.41	OR: 0.39	
		Myocardial Infarction	OR: 1.08	OR: 1.05	
		Hypertension	OR: 1.43	OR: 1.18	
		Diabetes			
		No end-organ damage	OR: 1.64	OR: 1.46	
		With end-organ damage	OR: 0.89	OR: 0.84	
		Mild Renal Disease	OR: 0.64	OR: 0.68	
		Asthma	OR: 1.45	OR: 1.59	
		COPD	OR: 0.99	OR: 0.61	
		Osteoarthritis	OR: 2.01	OR: 1.90	
		Rheumatoid Arthritis	OR: 0.25	OR: 0.36	
		Peptic Ulcer	OR: 0.58	OR: 0.56	
		GI Bleeding	OR: 1.08	OR: 0.72	
Mehta et al., 2010	≥70	Cognitive Status			Age, Race/Ethnicity, Education, Net Worth, Marital Status
		Normal	OR: 1.00	OR: 1.00	
		Mild-to-Moderate Impairment	OR: 0.60 (0.50, 0.80)	OR: 0.82 (0.60, 1.10)	
		Severe Impairment	OR: 0.28 (0.20, 0.50)	OR: 0.46 (0.30, 0.80)	
		Heart Disease	OR: 0.91 (0.70, 1.10)	OR: 1.10 (0.90, 1.40)	
		Diabetes	OR: 1.00 (0.80, 1.30)	OR: 1.10 (0.90, 1.40)	
		Stroke	OR: 0.59 (0.43, 0.80)	OR: 0.80 (0.60, 1.10)	
		Lung Disease	OR: 0.91 (0.62, 1.30)	OR: 0.90 (0.60, 1.40)	

Source	Age	Condition	Crude Measure of Association	Adjusted Measure of Association	Covariates
Reyes-Ortiz et al., 2010	≥75	Cancer Depression (CES-D) <16 ≥16 Cognitive Impairment (MMSE) >18 ≤18		OR: 2.27 (1.36, 3.80) OR: 1.00 OR: 1.42 (1.04, 1.94) OR: 1.00 OR: 0.62 (0.45, 0.86)	Education, Annual Household Income, Health Insurance, Financial Strain, Acculturation, Age, Marital Status, Medical Conditions, Functional Status, Cognitive Function
Schonberg et al., 2013	≥75	Cancer: History No History Diabetes Yes No COPD Yes No	 OR: 1.29 (0.97, 1.70) OR: 1.00 OR: 0.90 (0.73, 1.10) OR: 1.00 OR: 1.03 (0.78, 1.38) OR: 1.00		Race/Ethnicity, Education, Insurance, Geographical Region, Marital Status, Annual Family Income, usual Source of Medical Care, Number of Doctor Visits in Last Year, Receipt of Flu Vaccine in Last Year, Receipt of Pneumonia Vaccine, History of Benign Breast Biopsy, Family History of Breast Cancer, Perceived Breast Cancer Risk
Thorpe et al., 2006	≥65	Psychological Distress		OR: 0.68 (0.34, 1.37)	Age, Race/Ethnicity, Marital Status, Education, Respondent Risk-taking Attitudes, Value of Medical Care, Income Level, Employment Status, Health Insurance Coverage, Usual Source of Medical Care, Census Region, Impairment, Health Status, Charlson Comorbidity Index

Source	Age	Measure of Functional Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Blustein et al., 1998	≥75	ADL Limitations: No Yes	 OR: 1.00 OR: 0.57 (0.48, 0.68)	 OR: 1.00 OR: 0.71 (0.59, 0.85)	Age
Caban et al., 2010	≥65	Disability No Moderate Severe	 OR: 1.00 OR: 0.76 (0.64, 0.91) OR: 0.46 (0.40, 0.54)	 OR: 1.00 OR: 0.98 (0.81, 1.18) OR: 0.67 (0.54, 0.83)	Age, Race, Education, Zip Code income, Marital Status, HMO Status, Self-rated Health, Number of Comorbidities, Cognitive Deficits, Depression
Caplan, 2001	≥70 (subgroup)	Activity Limitation: Unable to Perform Major Activity No Limitation		Chi-Square 36.0% 52.7% (p<0.001)	
Heflin et al., 2002	≥65	MIADLs		OR: 0.94 (0.87, 1.03)	Age, Race, Education, Income, Primary Care, Urban/Rural, MIADLs, Proxy Response, Imputation
Holt et al., 2006	≥65	Activities of Daily Living		OR: 0.91 (0.86, 0.97)	Age, Race/Ethnicity, Education, Annual Income, Metropolitan Residence, Living Alone, Supplemental Insurance, Proxy Response

Table S3: Summary of findings from studies that evaluated the effect of functional status on screening utilization

Source	Age	Measure of Functional Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Ives et al., 2006	65-79	ADLs Independent Needs Assistance IADLs Independent Needs Assistance		OR: 1.00 OR: 0.56 (0.34, 0.93) OR: 1.00 OR: 0.92 (0.75, 1.14)	Age, Education, Insurance Status, Comorbidity, Functional Status
Reyes-Ortiz et al., 2010	≥75	IADLs 0-3 ≥4		OR: 1.00 OR: 0.65 (0.49, 0.86)	Education, Annual Household Income, Health Insurance, Financial Strain, Acculturation, Age, Marital Status, Medical Conditions, Functional Status, Cognitive Function
Schonberg et al., 2004	≥80	Functional Status: No Impairment IADL Dependent Only ≥1 ADL Dependency		OR: 1.00 OR: 0.65 (0.40, 1.05) OR: 0.44 (0.22, 0.88)	Age, Race/Ethnicity, Education, Income, Insurance Status, Region, Usual Care, Visited Doctor in Past Year, Current Use of Hormone Replacement Therapy

Source	Age	Measure of Functional Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Schonberg et al., 2013	≥75	Functional Status: IADL Dependency No IADL Dependency Difficulty Walking	OR: 0.37 (0.30, 0.45) OR: 1.00 OR: 0.50 (0.42, 0.60)		Race/Ethnicity, Education, Insurance, Geographical Region, Marital Status, Annual Family Income, usual Source of Medical Care, Number of Doctor Visits in Last Year, Receipt of Flu Vaccine in Last Year, Receipt of Pneumonia Vaccine, History of Benign Breast Biopsy, Family History of Breast Cancer, Perceived Breast Cancer Risk
Schootman et al., 2003	≥40 (Subgroup ≥70)	Activities of Daily Living: No Long-term Short-term		OR: 1.00 OR: 0.18 (0.07, 0.44) OR: 0.74 (0.36, 1.51)	Race, Marital Status, Education, Age, Poverty Level, Health Insurance, Usual Source of Care, Number of Office-based Physician Visits, Time since Last Blood Pressure Check
Scinto et al., 2001	≥65	Activities of Daily Living No Yes	 67.7% 32.3% (p<0.001)		
Wright et al., 2000	≥70	Functional Status		OR: 0.70 (0.53, 0.94)	Age, Comorbidity, Self-Rated Health

Table S4: Summary of findings from studies that evaluated the effect of health status on screening utilization

Source	Age	Measure of Health Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Barr et al., 2001	≥65	SF-12: Physical Component Score Mental Component Score	 OR: 1.05 (0.51, 2.18) OR: 1.23 (0.60, 2.54)	 OR: 0.93 (0.38, 2.28) OR: 1.06 (0.43, 2.61)	Age, Education, Health Beliefs, Health Plan
Blustein et al., 1998	≥75	General Health: Excellent Very Good Good Fair Poor	 OR: 1.00 OR: 1.14 (0.85, 1.52) OR: 0.84 (0.61, 1.15) OR: 0.82 (0.60, 1.17) OR: 0.44 (0.28, 0.68)	 OR: 1.00 OR: 1.15 (0.85, 1.56) OR: 0.84 (0.60, 1.18) OR: 0.81 (0.58, 1.13) OR: 0.41 (0.26, 0.56)	Age
Bynum et al., 2005	≥65	Propensity to Die (% Screened) Overall 1 2 3 4 5		 39% 61% 49% 33% 19% 5%	Exposure Time
Caban et al., 2010	≥65	Self-Rated Health: Excellent/Very Good/Good Fair/Poor		 OR: 1.00 OR: 0.80 (0.66, 0.96)	Age, Race, Education, Zip Code income, Marital Status, HMO Status, Self-rated Health, Number of Comorbidities, Cognitive Deficits, Depression
Holt et al., 2006	≥65	Self-assessed Health Status		OR: 0.99 (0.92, 1.05)	Age, Race/Ethnicity, Education, Annual Income, Metropolitan Residence, Living Alone, Supplemental Insurance, Proxy Response

Source	Age	Measure of Health Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Koya et al., 2011	≥65	Health Status Fair/poor Good Excellent/Very Good Prognostic Index Risk Group 1 (Low) Risk Group 2 (Intermediate) Risk Group 3 (High) Risk Group 4 (Very High)		 OR: 1.00 OR: 1.18 (0.90, 1.54) OR: 1.12 (0.85, 1.49) OR: 1.00 OR: 0.69 (0.53, 0.90) OR: 0.37 (0.27, 0.49) OR: 0.22 (0.13, 0.36)	Marital Status, Race, Education, Income, Number of Office Visits, HMO Coverage, Had Flu Vaccine in last year, Ever had Pneumonia Vaccine, Pap test in last year, Health Status
Schonberg et al., 2008	≥65	Self-Rated Health: Above Average Average Below Average		 OR: 1.00 OR: 0.74 (0.57, 0.96) OR: 0.51 (0.37, 0.70)	Race/Ethnicity, Education, Annual Family Income, Insurance Status, Geographic Region, Usual Source of Care, Number of Doctor Visits in Last Year
Schonberg et al., 2013	≥75	Life Expectancy High Medium Low Perceived Health Excellent/Very Good Good Poor/Fair	 OR: 1.00 OR: 0.79 (0.65, 0.97) OR: 0.54 (0.44, 0.67)	 OR: 2.40 (1.60, 3.70) OR: 1.40 (1.00, 1.90) OR: 1.00	Race/Ethnicity, Education, Insurance, Geographical Region, Marital Status, Annual Family Income, usual Source of Medical Care, Number of Doctor Visits in Last Year, Receipt of Flu Vaccine in Last Year, Receipt of Pneumonia Vaccine, History of Benign Breast Biopsy, Family History of Breast Cancer, Perceived Breast Cancer Risk

Source	Age	Measure of Health Status	Crude Measure of Association	Adjusted Measure of Association	Covariates
Scinto et al., 2001	≥65	Prognostic Stage: I (≤80, climbs stairs, no ADLs) II (>80 or ADL or not climb stairs) III (Two poor prognostic items) IV (>80, ADLs, not climb stairs)		47.5% 27.3% 18.2% 7.0% (p=0.001)	
Walter et al., 2004	≥70	Health Status Quartile: 1 (best) 2 3 4 (worst)		OR: 0.80 (0.60, 1.00) OR: 1.20 (0.90, 1.60) OR: 1.10 (0.90, 1.50) OR: 1.00	Age, Health Status Quartile, Race/Ethnicity, Education, Income, Marital Status
Williams et al., 2008	≥65	Prognostic Index Good Low Middle High Limited Low Middle High	 RR: 1.00 RR: 1.04 (0.94, 1.16) RR: 1.20 (1.10, 1.32) RR: 1.00 RR: 1.20 (0.82, 1.76) RR: 1.52 (1.05, 2.18)	 RR: 1.00 RR: 1.08 (0.96, 1.21) RR: 1.18 (1.05, 1.32) RR: 1.00 RR: 1.18 (0.77, 1.81) RR: 1.92 (1.20, 3.09)	Age, Race/Ethnicity, Education, Proxy Respondent, Rural Residence
Wright et al., 2000	≥70	Self-assessed Health Status		OR: 1.19 (0.99, 1.42)	Age, Functional Status, Comorbidity Score

2.7.1 PubMed Search Strategies 1991-2016, English articles

#1

((“breast cancer” [tiab] OR “breast neoplasms” [mh] OR "breast tumor" [tiab] OR "breast tumors" [tiab] OR "breast tumour" [tiab] OR "breast tumours" [tiab] OR breast diseases [mh]) AND (mass screening [mh] OR screening [tiab] OR screened [tiab] OR screen [tiab])) OR “breast cancer screening” OR mammography [tiab] OR mammogram* [tiab] OR mammography [mh]

#2

comorbidity [mh] OR comorbidities [tiab] OR comorbid [tiab] OR “co morbidity” [tiab] OR “co morbidities” [tiab] OR multimorbidity [tiab] OR multimorbidities [tiab] OR “daily life activity” [tiab] OR “activities of daily living” [mh] OR “disabled persons” [mh] OR disabled [tiab] OR disability [tiab] OR disabilities [tiab] OR “functional assessment” [tiab] OR “functional disease” [tiab] OR “functional diseases” [tiab] OR “functional impairment” [tiab] OR “functional limitation” [tiab] OR “health status” [mh] OR “health status” [tiab] OR “mobility impairment” [tiab] OR “motor dysfunction” [tiab] OR “motor impairment” [tiab] OR “motor limitation” [tiab] OR “physical disability” [tiab] OR “physical disease” [tiab] OR “physical diseases” [tiab] OR “physical impairment” [tiab] OR “physical limitation” [tiab] OR “physical functioning” [tiab] OR “walking difficulty” [tiab] OR alcoholism [mh] OR alcoholic [tiab] OR alcoholics [mh] OR “Alzheimer disease” [mh] OR Alzheimer’s [tiab] OR dementia [mh] OR dementia [tiab] OR arthritis [mh] OR arthritis [tiab] OR asthma [mh] OR asthma [tiab] OR “cardiovascular disease” [tiab] OR “cardiovascular diseases” [tiab] OR “cardiovascular diseases” [mh] OR stroke [mh] OR stroke [tiab] OR “cerebrovascular disease” [tiab] OR “chronic arthritis” [tiab] OR “chronic bronchitis” [tiab] OR “bronchitis, chronic” [mh] OR “chronic disease” [mh] OR “chronic diseases” [tiab] OR “chronic disease” [tiab] OR “chronic illness” [tiab] OR “chronically ill” [tiab] OR “terminally ill” [mh] OR “terminally ill” [tiab] OR “chronic condition” [tiab] OR “chronic conditions” [tiab] OR “chronic hepatitis” [tiab] OR “hepatitis, chronic” [mh] OR “chronic inflammation” [tiab] OR “renal insufficiency, chronic” [mh] OR “chronic kidney disease” [tiab] OR “chronic kidney diseases” [tiab] OR “kidney failure, chronic” [mh] OR “chronic kidney failure” [tiab] OR “chronic kidney failures” [tiab] OR “pulmonary disease, chronic obstructive” [mh] OR COPD [tiab] OR “chronic obstructive pulmonary disease” [tiab] OR “chronic respiratory failure” [tiab] OR “cognitive defect” [tiab] OR “cognitive defects”[tiab] OR “cognitive impairment” [tiab] OR “cognitive impairments” [tiab] OR “cognitive decline” [tiab] OR “cognitive declines” [tiab] OR “cognition disorders” [mh] OR “cognition disorders” [tiab] OR “cognition disorder” [tiab] OR depression [mh] OR depression [tiab] OR “depressive disorder” [mh] OR “depressive disorders” [tiab] OR “depressive disorder” [tiab] OR “diabetes mellitus” [mh] OR diabetes [tiab] OR diabetic [tiab] OR diabetics [tiab] OR renal dialysis [mh] OR dialysis [tiab] OR “myocardial infarction” [mh] OR “heart attacks” [tiab] OR “heart attack” OR “heart disease” [tiab] OR “heart diseases” [mh] OR hypertension [mh] OR hypertension [tiab] OR “life expectancy” [mh] OR “life expectancy” [tiab] OR “liver diseases” [mh] OR “liver diseases” [tiab] OR “liver disease” [tiab] OR “mental disorders” [mh] OR “mental disorder” [tiab] OR “mental disorders” [tiab] OR “mental diseases” [tiab] OR “mental disease” [tiab] OR “lung diseases” [mh] OR “lung diseases” [tiab] OR “pulmonary diseases” [tiab] OR “pulmonary disease” [tiab] OR “serious health events” [tiab]

#3

Aged [mh] OR aged [tiab] OR elderly [tiab] OR “aged, 80 and over” [mh] OR “frail elderly” [mh] OR age factors [mh] OR “age factors” [tiab] OR “age factor” [tiab]

#4 (430 articles)

#1 AND #2 AND #3 Filters: Publication date from 1991/01/01 to 2016/10/25; English

2.7.2 EMBASE (Elsevier) search strategies 1991-2016 English articles

#1

(('breast tumor'/de OR 'breast cancer'/de OR breast NEAR/3 cancer OR ‘breast cancer’:ab,ti) AND ('cancer screening'/de OR 'mass screening'/de OR 'screening'/de OR screen OR screened OR screening)) OR ‘breast cancer screening’:ab,ti OR 'mammography'/de OR mammogram:ab,ti OR mammograms:ab,ti OR mammography:ab,ti

#2

Comorbidity/de OR comorbidity:ab,ti OR comorbidities:ab,ti OR comorbid:ab,ti OR 'co morbidity':ab,ti OR 'co morbidities':ab,ti OR 'co morbid':ab,ti OR multimorbid* OR multi NEXT/1 morbid* OR age:ab,ti OR 'daily life activity'/de OR disabled OR 'disabled person'/de OR 'disability'/mj OR disability:ab,ti OR disabilities:ab,ti OR 'functional assessment'/mj OR 'functional disease'/de OR functional NEAR/3 (impairment* OR limitation* OR mobilit* OR status) OR mobility NEAR/3 (impairment* OR limitation*) OR 'motor dysfunction'/de OR motor NEAR/3 (impairment* OR limitation*) OR 'physical disability'/de OR 'physical disease'/mj OR physical NEAR/3 (impairment* OR limitation*) OR 'physical functioning' OR 'walking difficulty'/de OR 'alcoholism'/de OR alcoholic OR alcoholics OR 'alzheimer disease'/de OR alzheimer* OR arthritis:ab,ti OR asthma:ab,ti OR 'cardiovascular disease'/mj OR 'cardiovascular disease':ab,ti OR 'cardiovascular diseases':ab,ti OR 'cerebrovascular accident'/mj OR 'cerebrovascular disease'/mj OR 'chronic bronchitis' OR 'chronic condition' OR 'chronic conditions' OR 'chronic disease' OR 'chronic diseases' OR 'chronic hepatitis' OR 'chronic illness' OR 'chronic illnesses' OR 'chronic inflammation'/de OR 'chronic kidney disease' OR 'chronic kidney diseases' OR 'chronic kidney failure' OR 'chronic kidney failures' OR 'chronic obstructive lung disease'/de OR 'chronic obstructive lung diseases' OR 'chronic patient'/de OR 'chronic respiratory failure'/de OR 'chronically ill' OR copd:ab,ti OR 'cognitive defect' OR 'cognitive defects' OR 'cognitive impairment' OR 'cognitive impairments' OR 'cognitive decline' OR 'cognitive declines' OR 'cognition disorder' OR 'cognition disorders' OR 'cognitive disorder' OR 'cognitive disorders' OR 'cognitive status' OR 'dementia'/de OR dementia:ab,ti OR 'depression'/de OR 'diabetes mellitus'/de OR diabetes:ab,ti OR diabetic*:ab,ti OR 'dialysis'/de OR dialysis:ab,ti OR 'heart attack':ab,ti OR 'heart disease'/de OR 'heart disease':ab,ti OR 'heart diseases':ab,ti OR 'health status'/de OR ‘health status’:ab,ti OR 'hypertension'/de OR hypertension:ab,ti OR 'heart infarction'/de OR 'myocardial infarction':ab,ti OR 'kidney disease'/de OR 'kidney failure':ab,ti OR 'late life depression'/de OR ‘late life depression’:ab,ti OR 'life expectancy'/de OR ‘life expectancy’:ab,ti OR 'liver disease'/mj OR ‘liver disease’:ab,ti OR ‘liver diseases’:ab,ti OR 'lung disease'/mj OR ‘lung disease’:ab,ti OR ‘lung diseases’:ab,ti OR 'major depression'/de OR depression:ab,ti OR 'mental disease'/mj OR ‘mental disease’:ab,ti OR ‘mental diseases’:ab,ti OR obese:ab,ti OR 'obesity'/de OR obesity:ab,ti OR stroke:ab,ti OR stroke/de OR ‘frail elderly’/de OR ‘frail elderly’:ab,ti

3

Aged/exp OR aged:ab,ti OR elderly:ab,ti OR ‘very elderly’/de OR older:ab,ti OR ‘age factors’:ab,ti OR ‘age factor’:ab,ti OR age:ti

#4

#1 AND #2 AND #3 AND [article]/lim AND [english]/lim AND [1991-2016]/py

#5

mammography OR mammogram OR mammograms OR 'breast cancer screening' AND (aged OR older OR elderly)

#6

utilization:ti,ab OR utilization:ti,ab OR use:ti OR stress OR anxiety OR distress OR harm OR harms OR benefit* OR 'false positive' OR 'upper age limit' OR 'over diagnosis' OR 'stage of diagnosis' OR outcome OR outcomes OR 'decision making' OR mortality OR 'life expectancy' OR ‘quality adjusted life expectancy’ OR ‘risk assessment’ OR ‘gain one life year’ OR age:ti OR discontinuation

#7

‘co morbidity’ OR ‘co morbidities’ OR comorbid OR comorbidity OR comorbidities OR 'functional impairment'/exp OR 'functional impairment' OR 'functional impairments' OR 'disability'/exp OR disability OR 'health status'/exp OR 'health status' OR 'intellectual impairment' OR 'intellectual impairments' OR 'quality of life' OR 'chronic disease' OR 'terminally ill' OR limitation OR age:ti

#8

#5 AND #6 AND #7 AND [article]/lim AND [english]/lim AND [1991-2016]/py

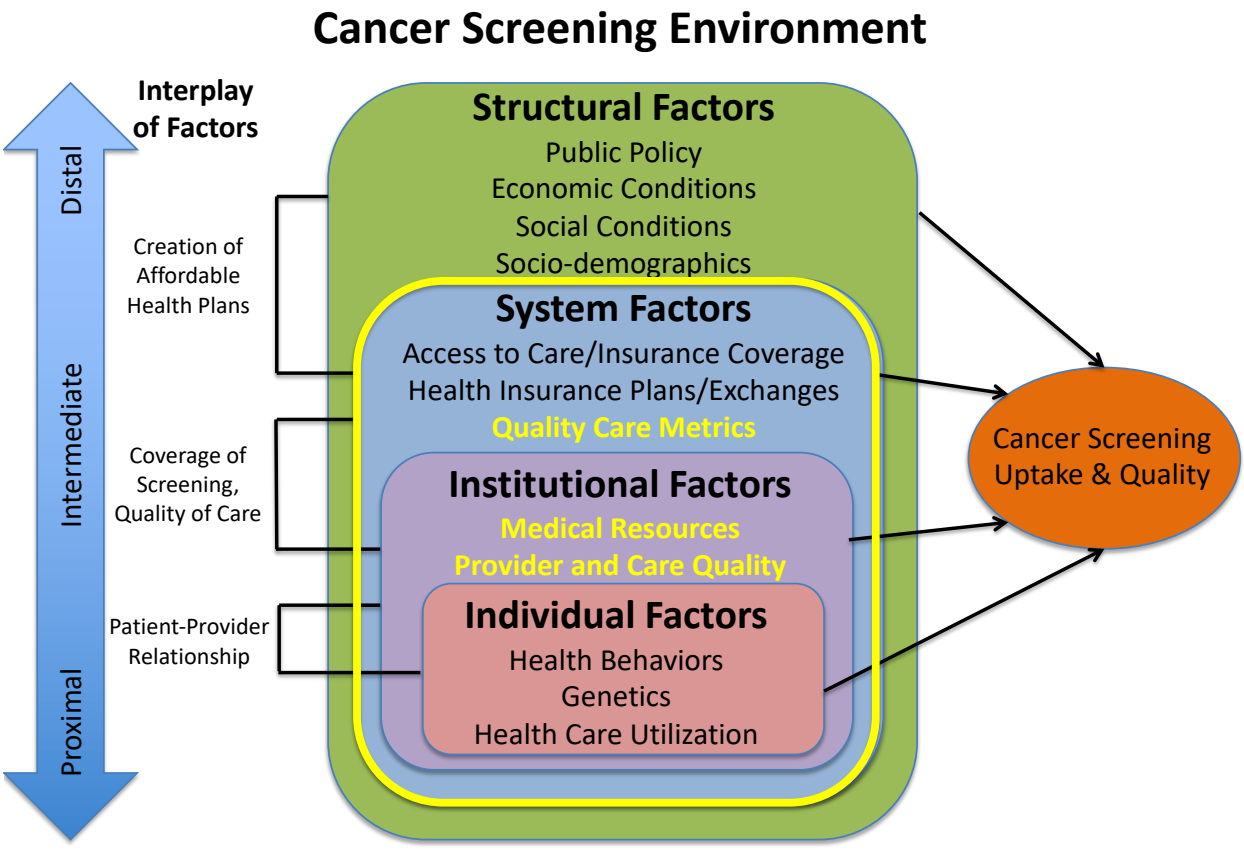
#9

#4 OR #8

3. CHAPTER 2: Factors that influence radiation doses used for lung cancer screening: Analysis of data from a large US dose registry

Joshua Demb, Philip Chu MS, Sophronia Yu, Robin Whitebird PhD, Leif Solberg PhD, Diana L. Miglioretti PhD, Rebecca Smith-Bindman MD

Figure 3.1: Conceptual Framework for Multilevel Factors Involved in Cancer Screening, Multilevel Factors for Chapter 2 Highlighted



3.1 ABSTRACT

Importance: The American College of Radiology (ACR) has targeted radiation doses for lung cancer screening (LCS) computed tomography (CT). Without standard protocols, doses could be unnecessarily high, reducing screening benefits.

Objective: Characterize LCS radiation doses and identify factors explaining variation.

Design, Setting, Participants: Prospectively collected LCS exam dose metrics, 2016-2017, from 74 US institutions in the University of California, San Francisco CT Radiation Dose Registry.

Main Outcomes and Measures: Log-transformed measures of: (1) mean volume computed tomography dose index (CTDIvol, mGy), average dose per slice and (2) mean effective dose (ED, mSv), total dose received, reflecting number of scans and estimated future cancer risk. Also measured (3) proportion of exams above ACR benchmarks (CTDIvol ≤3 mGy, ED ≤1 mSv); and (4) proportion of exams above 75th percentile of registry doses (CTDIvol ≤2.7 mGy, ED ≤1.4 mSv). Institution-level factors, as predictors, were collected through baseline survey. Mixed-effects linear and logistic regression models were estimated using forward variable selection. Results are percentage excess dose and odds ratios (ORs) with 95% confidence intervals (CIs).

Results: Of 74 institutions, 19 (26%) had median CTDIvol and 54 (73%) had median ED higher than ACR guidelines. Institutions allowing any radiologists to establish protocols had 44% higher mean CTDIvol (mean dose difference [MDD]: 44%; 95%CI: 19-69%) and 26% higher mean ED (MDD: 26%; 95%CI: 4-49%) compared to limiting who establishes protocols. These institutions had higher odds of exams exceeding ACR CTDIvol guidelines (OR: 10.8; 95%CI: 2.0-58.1), and 75th percentile of registry CTDIvol (OR 10.6; 95%CI: 1.8-63.8) or ED (OR 7.04; 95%CI: 1.5-32.2). Having only lead radiologists establish protocols resulted in lower odds of doses exceeding ACR ED guidelines (OR 0.04; 95%CI: 0.01-0.29). Having external rather than internal medical physicists was associated with increased odds of exceeding ACR CTDIvol

guidelines (OR: 4.7; 95%CI: 1.5-14.9) and 75th registry percentile (OR 8.2; 95%CI: 2.3-29.4). Institutions reporting protocol updates as needed had 22% higher mean CTDIvol (MDD: 22%; 95%CI: 3%-40%).

Conclusion and Relevance: Facilities varied in LCS CT-dose distributions. Institutions that limited protocol creation to lead radiologists and had internal medical physicists had lower doses.

3.2 INTRODUCTION

Few explicit standards exist for the radiation doses to use for computed tomography (CT) scans. Several organizations including the American College of Radiology (ACR) promote performing CT scans using the "as low as reasonably achievable" principle for radiation doses. However, the lack of specific guidelines and established standards for the numerous types of CT examinations results in doses variation within and across institutions.[114–118] Institutional decisions, such as about use of multiphase scanning, and choices about technical parameters can result in large differences in radiation doses that patients receive.[116,119] Further, little data explores institution-level factors that could influence CT doses.

One protocol receiving increased focus is low-dose CT for lung cancer screening (LCS). LCS must balance the potential for earlier cancer detection through screening with concerns about false positives, invasive work-ups and increased cancer risk from CT radiation exposure.[120–124] LCS is beneficial when low-dose techniques are used but not when higher CT doses—similar to those used for routine chest CT scans—are used, because radiation from higher doses may cause almost as many cancers as are detected early by screening.[125]

As part of Centers for Medicare and Medicaid Services (CMS) requirements for LCS reimbursement, institutions must use low-dose techniques and participate in a dose registry. The ACR recommends that LCS scans have a volume computed tomography dose index (CTDIvol) of 3 mGy and an effective dose (ED) of 1 mSv.[126–130] Although variation in LCS doses is reported,[131,132] the proportion of patients receiving appropriately low-dose exams is unknown. Further, no study identified factors associated with optimum low-dose performance.

This study identified factors associated with CT dose variation among institutions participating in a large CT radiation-dose registry. We assessed how often patients received appropriate low-dose LCS examinations according to ACR guidelines and identified institution-level factors associated with high CT radiation doses. Identifying institution-level factors will help facilities performing CT scans avoid unnecessary variation in LCS CT doses.

3.3 METHODS

CT Radiation Dose Registry

In 2015, we established an international CT radiation dose registry at the University of California, San Francisco to collect radiation doses for CT exams on consecutive patients from 150 institutions in the United States and seven other countries. All institutions participating in the registry use the same radiation dose-monitoring software (Radimetrics, Bayer, Whippany, NJ), enabling data sharing within the registry using HIPAA-compliant tools. For the Partnership for Dose trial (NIH NCI R01-CA181191), a National Institutes of Health-funded pragmatic randomized comparative effectiveness study on approaches to optimizing radiation doses for routine head, chest, abdomen, and combined chest and abdomen CT exams, we surveyed institutions prior to trial start about characteristics including how they perform and oversee CT. Data from the organizational survey and the dose registry were combined to assess relationships between institutional characteristics and radiation dose.

Inclusion/Exclusion

Only US institutions that performed a minimum 24 LCS scans during the study period (2016-2017) and returned a completed survey were included (N=74). Because LCS is recommended for patients aged ≥40 with risk factors for cancer (e.g., ≥30 pack-year smoking history and current smoking or quitting <15 years ago), analyses were limited to patients aged ≥40. We could not determine patients' smoking history, which is an eligibility requirement for insurance coverage of LCS scans. Non-US institutions were excluded because their CT LCS scans are not subject to the ACR LCS guidelines.

Organizational Survey Predictors and Scan Covariates

All institutions eligible for our study completed the organizational survey, which was required to participate in the Partnership for Dose trial. The survey asked about structural and organizational aspects of the institution's CT imaging workflow that might be associated with radiation dose, including type of facility and role of individuals who establish and modify CT

protocols, which are the instructions that technologists use to program CT scanners. Protocols vary by reasons for scans and by institution. The survey also asked: 1) the type of institution, as academic/teaching hospital, trauma center (Level 1, 2, or 3), public hospital, community hospital, private hospital, acute care facility, primary care institution, pediatric hospital, tertiary referral hospital, or outpatient imaging institution (not mutually exclusive); 2) if a medical physicist was involved in creating protocols and if so, if the physicist was employed by the organization on staff or external; 3) individual(s) who established or altered protocols for the institution (manufacturer, organizational leadership, organization-level medical physicist, site-level medical physicist, radiology site, lead radiologists, any individual radiologists, head technologist, technologists performing exams, or other individuals, not mutually exclusive); 4) frequency at which protocols were updated (as needed, less than yearly, yearly or more than yearly); and 5) if protocols were locked, meaning unchangeable after being established (yes/no). Of the 150 institutions in the registry, 116 completed the organizational survey (77% response rate).

We included patient-level factors in all analyses including age, sex, and chest diameter (to account for patient size).

Outcomes

We evaluated two measures of dose, CTDIvol and ED. CTDIvol reflects the average radiation dose output per standardized volume, typically described as dose per slice in mGy. ED is the total dose output of the scanner (dose per slice x length scanned or total number of slices) weighted by organ sensitivity in anatomic scan region to represent the future risk of cancer from this exposure in mSv. Choices made by technologists performing scans directly influence both CTDIvol and ED. While LCS should include only single CT scans, multiple CT scans may be performed, for example for diagnostic CT. Multiple scans would be reflected only in ED, not CTDIvol measures, since average dose per slice does not vary by number of scans.

ACR and CMS guidelines for LCS specify doses of ≤3.0 mGy for CTDIvol and ≤1 mSv for ED for a standard patient defined as 170 cm and 70 kg with a body mass index of 24.3. Because these doses are about 15%-50% lower than doses used for standard chest CT,[133,134] LCS scans are described as low-dose CT. Doses for LCS CT vary by patient size: patients who are larger or smaller than the standard size receive doses slightly above or below guideline thresholds. We accounted for dose variation by size by adjusting doses using average chest diameters measured on CT images. We calculated the 75th percentile of the distribution of radiation doses in the registry and defined doses above this percentile as high dose. To account for the non-normal nature of the CTDIvol and ED measures, these variables were log-transformed for incorporation into linear models.

Statistical Analysis

We assessed facility-level distributions of CTDIvol and ED for LCS scans using boxplots, adjusted for chest diameter by standardizing facility-level doses by median facility-level chest diameter. We used mixed-effects linear regression models to evaluate predictors associated with adjusted CT dose levels.[135] We included facility-level and machine-level random effects to account for correlation among exams performed on the same machine or at the same facility. Variables included in models were selected using forward selection. After models were selected, coefficients were exponentiated to calculate excess percentage of dose, with corresponding 95% confidence intervals (CIs). Mixed-effects logistic regression with forward selection was used to evaluate associations between institutional factors and having doses above ACR guidelines and the 75th percentile benchmark. Statistical analyses were performed using SAS 9.4 (SAS Corporation, Cary, NC).

3.4 RESULTS

Data were for 12,771 LCS CT scans performed at 74 institutions (**Table 3.1**). Overall, 58% of participants were male, and the median age was 65 years (interquartile range [IQR]: 60-

70). The mean ED for LCS adjusted for chest diameter was 1.9 mSv (standard deviation [SD]: 2.4 mSv) and the mean CTDIvol adjusted for patient size was 2.4 mGy (SD: 2.0 mGy). Unadjusted values were 1.3 mSv (SD 1.6 mSv) for ED and 2.3 mGy (SD: 2.0 mGy) for CTDIvol. Distributions of adjusted CTDIvol and ED are in **Figures 3.2 and 3.3**. We found 19 institutions (26%) with a median adjusted CTDIvol value higher than the ACR guideline of 3 mGy (median: 2.4, IQR: 1.5-2.7) and 54 (73%) with a median adjusted ED higher than the ACR guideline of 1 mSv (median: 1.1 mSv, IQR: 0.7-1.5). Of all CT scans, 51% had an ED higher than ACR guidelines and 20% had a CTDIvol higher than guidelines. The results did not appreciably change when we used unadjusted values to characterize the number of institutions and patients whose doses exceeded guidelines.

Institutional responses to the organizational survey are in **Table 3.2**. Most (59%) institutions reported serving as outpatient imaging facilities, with lead radiologists (86%) or a head technologist (49%) establishing scan protocols. Technologists performing exams were the most likely to alter scan protocols (32%) compared to other personnel. The most common method of reviewing protocols was reported as "as needed" (49%). Most institutions (59%) lock their protocols after they are established.

Predictors of CTDIvol

Predictors of CTDIvol levels by CT scan type are in **Table 3.3**. Doses and likelihood of exceeding benchmarks increased with patient size and doses were higher among women, although differences were not large.

CT scans performed at private hospitals were associated with greater odds of a high-dose exam (odds ratio [OR]: 49.5, 95%CI: 1.9-1280), though the sample size was inadequate for inferring an effect. When the medical physicist was external instead of being on staff at the institution, doses were higher (OR for exceeding ACR benchmarks: 4.7, 95%CI: 1.5-14.9; OR for exceeding 75th percentile: 8.2, 95%CI: 2.3-29.4). For institutions reporting that any radiologist could establish protocols, doses were also higher (44% higher mean dose; 95%CI:

19%-69%; OR for a study exceeding ACR guidelines: 10.8, 95%CI: 2.0-58.1; OR for exceeding 75th percentile benchmark: 10.6, 95%CI 1.8-63.8). Institutions reporting that only lead radiologists altered protocols had a 27% lower CTDIvol (95%CI: -53% to -1%). Institutions that updated protocols "as needed" had higher average doses (22% higher dose, 95%CI: 3%-40%).

Predictors of ED

Significant ED predictors are in **Table 3.4** and are similar to CTDIvol predictors. Age, gender and chest diameter were significant ED predictors. Having any individual radiologist establish protocols was associated with higher doses (26% excess effective dose, 95%CI: 4%-49%; OR for exceeding 75th percentile benchmark: 7.04, 95%CI: 1.54-32.2). Having only the lead radiologist (OR: 0.04, 95%CI: 0.01-0.29) or technologist performing exams (OR: 0.12, 95%CI: 0.02-0.85) responsible for establishing protocols led to lower odds of exceeding ACR effective dose guidelines. Having any type of medical physicist (OR: 0.23, 95%CI: 0.08-0.69) establish the LCS CT protocol led to decreased odds of exceeding the 75th percentile benchmark.

3.5 DISCUSSION

Overall, we found wide variation in the distribution of LCS CT doses across facilities participating in our study, despite defined ACR guidelines. We found that 73% of participating institutions had median EDs for LCS scans that exceeded ACR guidelines, with a significant number of patients receiving doses above benchmarks created to ensure low radiation-dosage exams. ED reflects doses used for imaging and can indicate future cancer risk resulting from these studies. Over half of patients received doses above ACR targets after accounting for patient size, measured using chest diameter. If LCS CT exams are not performed using low-dose techniques, potential screening benefits and margins of benefits over risks are reduced.[132] While the risk of radiation-induced cancer and resultant risk of mortality is low compared to the

benefits of LCS using low-dose techniques, the risk of radiation-induced cancer rises in parallel with doses used.

We identified several institution-level factors associated with using doses higher than needed. The magnitude of associations was as high as 44%, and the identified factors increased the odds of a high-dose exam by as much as 50-fold. The factors that were most predictive of high doses included allowing individual radiologists to establish protocols, having an external rather than an internal staff medical physicist, being a private hospital, and updating protocols as needed instead of yearly. While we cannot establish causality in this observational study, our results suggest that considering these factors (for example, allowing only lead radiologists to establish protocols) could have a meaningful impact on dose, and could be important areas to develop interventions to optimize doses of CT protocols.

The inclusion of any individual radiologists in protocol establishment led to markedly higher odds of increased radiation dose. A potential cause of this finding could be the lack of training on dose optimization and motivation to change in some radiologists.[136–140] Specifically, radiologists may not believe CT radiation risk is particularly concerning, may prefer that people not involved in reading scans alter protocols, or prefer the image quality available in higher-dose diagnostic CT scans rather than the lower quality of LCS.[140] Ways to improve dose levels in institutions where individual radiologists establish protocols may include: ensuring that radiologists are aware of the current CT scan guidelines and the potential for harmful effects related to dose, particularly for standardized protocols such as LCS; and providing feedback to radiologists on the doses they use, which is currently not standard practice.

Having an on-staff medical physicist led to an institution having significantly decreased odds of scans with high CTDIvol compared to institutions with medical physicists who are outside consultants or employed by a CT manufacturer. Similarly, odds of ED exceeding the 75th percentile benchmark were lower when any medical physicist, internal or external to the institution, was involved in establishing protocols. Given that medical physicists are trained to

focus on safe, effective application of radiation in medical imaging, having a medical physicist on staff at an institution and actively involved in CT protocol development may help radiologists better manage CT radiation doses;[141] our data supported this possibility. On-staff medical physicists may provide quality control more closely or more frequently. External medical physicists may focus more on phantom studies and less on reviewing doses for examination subtypes such as LCS. Furthermore, as medical physicists are responsible for monitoring a practice's doses against national benchmarks, having a medical physicist onsite instead of contracted for annual or less frequent visits may better ensure that institutions maintain appropriate radiation dose levels.[141]

Involving technologists who perform exams in protocol establishment process also led to lower odds of EDs higher than ACR guidelines. Interestingly, no association was seen with CTDIvol levels, meaning that in general, technologists who established protocols used shorter scan lengths or used single rather than multiple CT scans more often. Technologists may be less sensitive to image quality than radiologists, as technologists do not interpret scans.

Being able to modify protocols can lead to lowering doses at some institutions, but can also lead to higher doses.[142] Our results indicated that the type of personnel involved in establishing protocols may have a profound impact on CT radiation doses delivered. Allowing any individual radiologist to adjust protocols tended to result in higher doses, whereas having lead radiologists manage protocol adjustment may lower doses. Given the clear guidelines for low-dose LCS, having fewer individuals involved in scan protocols may avoid unnecessary variation in radiation doses. Future studies should further investigate the effects of limiting personnel involved in protocol development on CT scan radiation dose levels.

Our study has several strengths, including employing data from the largest trial of CT scan radiation doses to date, using data from a wide variety of types of institutions performing CT scans, and including random effects to account for institution-level and scanner-level

variation. Analyses also adjusted for key, individual-level scan factors such as age, gender and patient diameter, which can slightly affect resultant radiation doses.

Our study had several limitations. Since we measured only LCS scans and resultant radiation doses, we did not follow individuals longitudinally to assess the relationships among CT dose and lung cancer detection or resultant effects on reducing mortality. These data would be informative for learning how exposures affect long-term outcomes. Our survey relied on self-reporting by leaders at participating facilities. These leaders were responsible for providing responses that represented practices throughout their institution but could be biased and reflect aspirational goals rather than current practice. To ensure that responses were representative of their facility, leaders were asked to contact institutional medical physicists, technologists and radiologists. Data were collected during a trial to optimize CT doses. However, the trial was not focused on LCS and we did not see changes in LCS during the trial.

We identified LCS CT by finding scans that were indicated as LCS in their protocol name or study description. Some scans might have been misclassified as LCS scans, which could lead to misrepresentation of radiation dose distributions within an institution. However, we thoroughly reviewed our sorting methodology and performed sensitivity analyses to account for potential misclassification, and our findings were robust to these concerns. Our statistical analyses measured institution-level factors while clustering at the facility and machine levels; thus, some estimates from mixed models have wide standard errors due to small sample sizes for some institutions and machines. Lastly, we did not determine if patients were appropriate candidates for LCS based on risk factors such as smoking history.

3.6 CONCLUSION

Among institutions performing low-dose CT scans for LCS, a significant proportion of institutions and patients exceeded guideline-recommended dose levels. Institutional characteristics such as allowing any individual radiologists to establish CT scan protocols,

updating protocols as necessary rather than annually or at other fixed times, and being a private hospital were associated with likelihood of higher radiation doses than other institutions. Conversely, having on-staff medical physicists, lead radiologists, technologists performing exams, or any medical physicists responsible for establishing protocols was associated with lower radiation doses. These findings indicated that dose-optimization practices may benefit from being tailored to specific practice types, as well as different organizational structures, to have a higher likelihood of meeting dose guidelines.

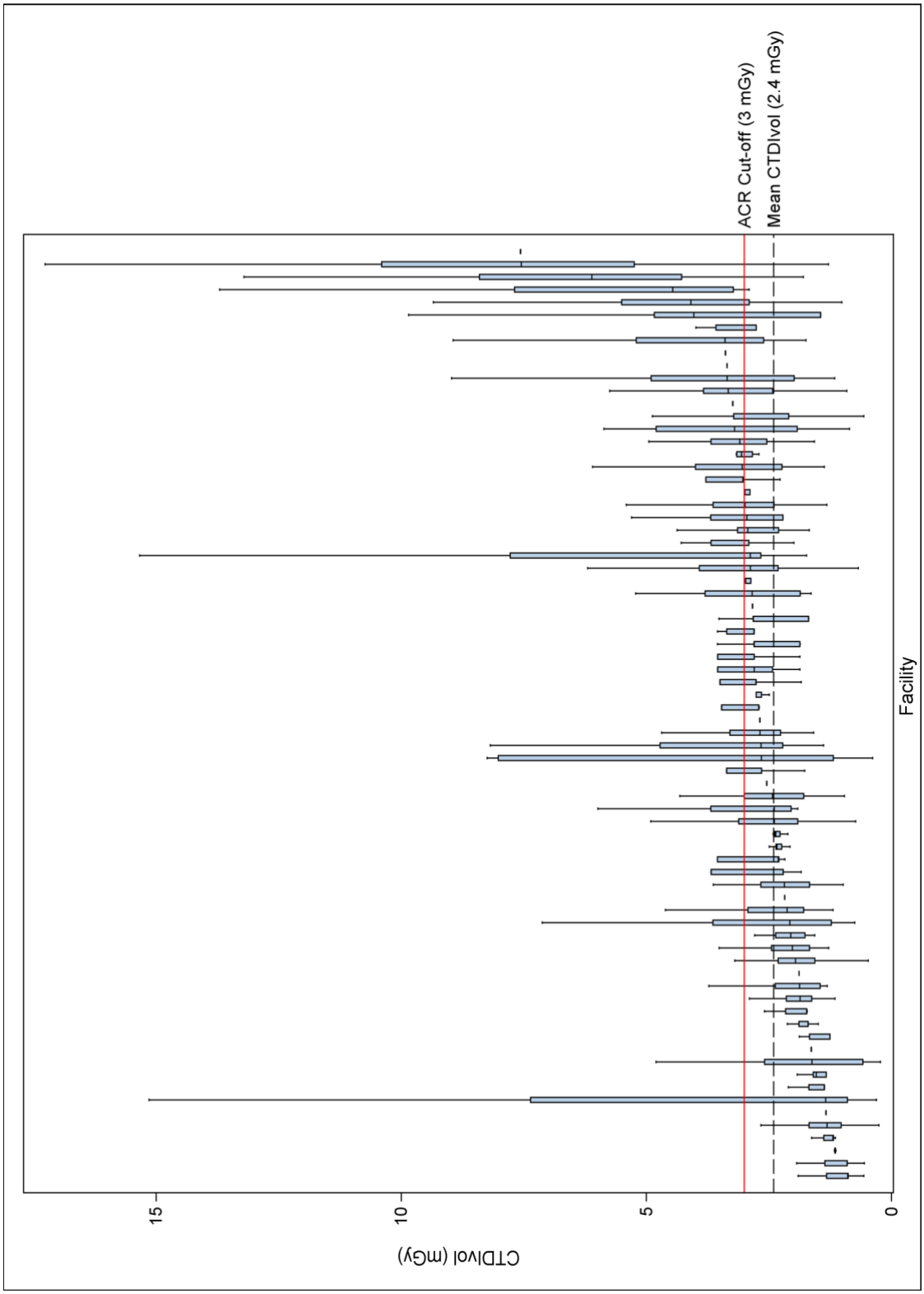


Figure 3.2: CTDIvol for Lung Cancer Screening Scans by Facility, adjusted for Chest Diameter

Figure 3.3: Effective Dose for Lung Cancer Screening Scans by Facility, adjusted for Chest Diameter

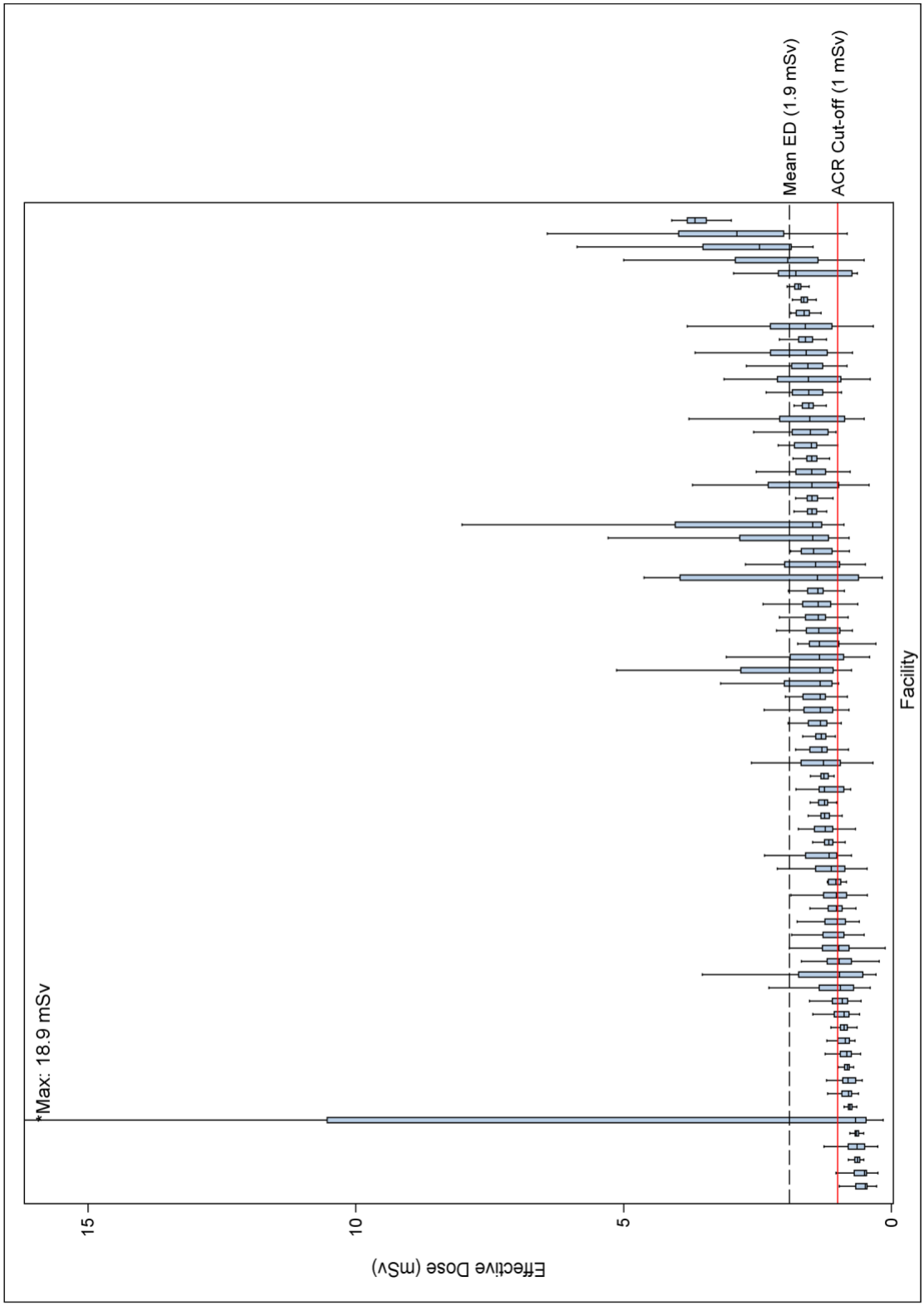


Table 3.1: Characteristics of all low-dose CT lung cancer screening scans

	Lung Cancer Screening
Number of Scans (Average/Facility)	12,771 (173)
Age, Median (IQR)	65 (60, 70)
Gender, % Male	58%
Effective Dose (mSv)	
Unadjusted for Patient Diameter	
Mean (SD)	1.3 (1.6)
Median (IQR)	1.0 (0.7, 1.4)
Adjusted for Patient Diameter	
Mean (SD)	1.9 (2.4)
Median (IQR)	1.4 (1.0, 1.9)
CTDIvol (mGy)	
Unadjusted for Patient Diameter	
Mean (SD)	2.3 (2.0)
Median (IQR)	2.0 (1.3, 2.7)
Adjusted for Patient Diameter	
Mean (SD)	2.4 (2.0)
Median (IQR)	2.1 (1.5, 2.7)

CT, computed tomography; IQR, interquartile range; SD, standard deviation, CTDIvol, volume computed tomography dose index; ACR, American College of Radiology

Table 3.2: Institutional Characteristics

	Institutions that Perform Lung Cancer Screening (N=74) N (%)
Institution Type within Organization (choose all that apply)	
Academic/Teaching Hospital	15 (20)
Trauma Center	17 (23)
Public Hospital	10 (14)
Community Hospital	19 (26)
Private Hospital	3 (4)
Acute Care Facility	18 (24)
Primary Cancer Facility	13 (18)
Pediatric Hospital	4 (5)
Tertiary Referral Hospital	7 (9)
Outpatient Imaging Facility	44 (59)
Medical Physicist Type	
External Consultant	34 (48)
Who Establishes Protocols (choose all that apply)	
Manufacturer	14 (19)
Organizational Leadership	8 (11)
Medical Physicist - One for the Organization	20 (27)
Medical Physicist - At Particular Site	0 (0)
Radiology Site	14 (19)
Lead Radiologists	64 (86)
Any Individual Radiologists	9 (12)
Head Technologist	36 (49)
Technologists Performing Exams	10 (14)
Other	4 (5)
Who Alters Protocols (choose all that apply)	
Manufacturer	2 (3)
Organizational Leadership	2 (3)
Medical Physicist - One for the Organization	3 (4)
Medical Physicist - At Particular Site	1 (1)
Radiology Site	3 (4)
Any individual Radiologists	9 (12)
Lead Radiologists	9 (12)
Head Technologist	22 (30)
Technologists Performing Exams	24 (32)
Other	1 (1)
How Frequently are Protocols Updated?	
As Needed	36 (49)
Less Than Yearly	11 (15)
Yearly	25 (34)
More Than Yearly	2 (3)
Are the Protocols Locked?	
Yes	44 (59)

	Percentage Difference from Mean Dose Mean Dose (95% CI)	High Dose Compared with ACR Guidelines Odds Ratio (95% CI)	High Dose Compared with 75th Percentile Benchmark from the Registry Odds Ratio (95% CI)
Age (by Decade)	-1% (-2%, -0.2%)	0.99 (0.98, 1.00)	0.99 (0.98, 0.99)
Sex (Female)	-5% (-6%, -3%)	0.79 (0.69, 0.91)	0.81 (0.71, 0.93)
Patient Diameter (per cm)	0.5% (0.5%, 0.6%)	1.04 (1.03, 1.04)	1.04 (1.04, 1.05)
What Type of Facility? Private			49.5 (1.9, 1280)*
Medical Physicist Type External Consultant		4.7 (1.5, 14.9)	8.2 (2.3, 29.4)
Who Establishes Protocols Any individual Radiologists	44% (19%, 69%)	10.8 (2.0, 58.1)	10.6 (1.8, 63.8)
Who Alters Protocols Lead Radiologists	-27% (-53%, -1%)		
How Frequently are Protocols Updated? As Needed	22% (3%, 40%)		

*Confidence intervals are unstable to due to small sample sizes within institutions.
Only statistically significant factors are included.
CTDIvol, volume computed tomography dose index; CI, confidence interval; ACR, American College of Radiology

Table 3.3: Patient and facility factors associated with CTDIvol.

Table 3.4: Patient and facility factors associated with effective dose.

	Mean Dose Percentage Difference from Mean Dose (95% CI)	High Dose Compared with ACR Guidelines Odds Ratio (95% CI)	High Dose Compared with 75th Percentile Benchmark from the Registry Odds Ratio (95% CI)
Age	-2% (-3% to -1%)	0.99 (0.98-0.99)	0.99 (0.99-1.00)
Sex (Female)	3% (1%-5%)		1.34 (1.19-1.52)
Patient Diameter (per cm)	0.91% (0.90%-0.93%)	1.05 (1.04-1.05)	1.03 (1.03-1.04)
Who Establishes Protocols			
Medical Physicist			0.23 (0.08-0.69)
Any individual Radiologists	26% (4%-49%)		7.04 (1.54-32.2)
Lead Radiologists		0.04 (0.01-0.29)	
Technologist Performing Exams		0.12 (0.02-0.85)	
How Frequently are Protocols Updated?			
As Needed		2.92 (0.67-12.7)	

Only statistically significant factors are included.
CI, confidence interval; ACR, American College of Radiology

Chapter 3: The impact of employment change on screening mammography utilization during the U.S. Great Recession: The Health and Retirement Study

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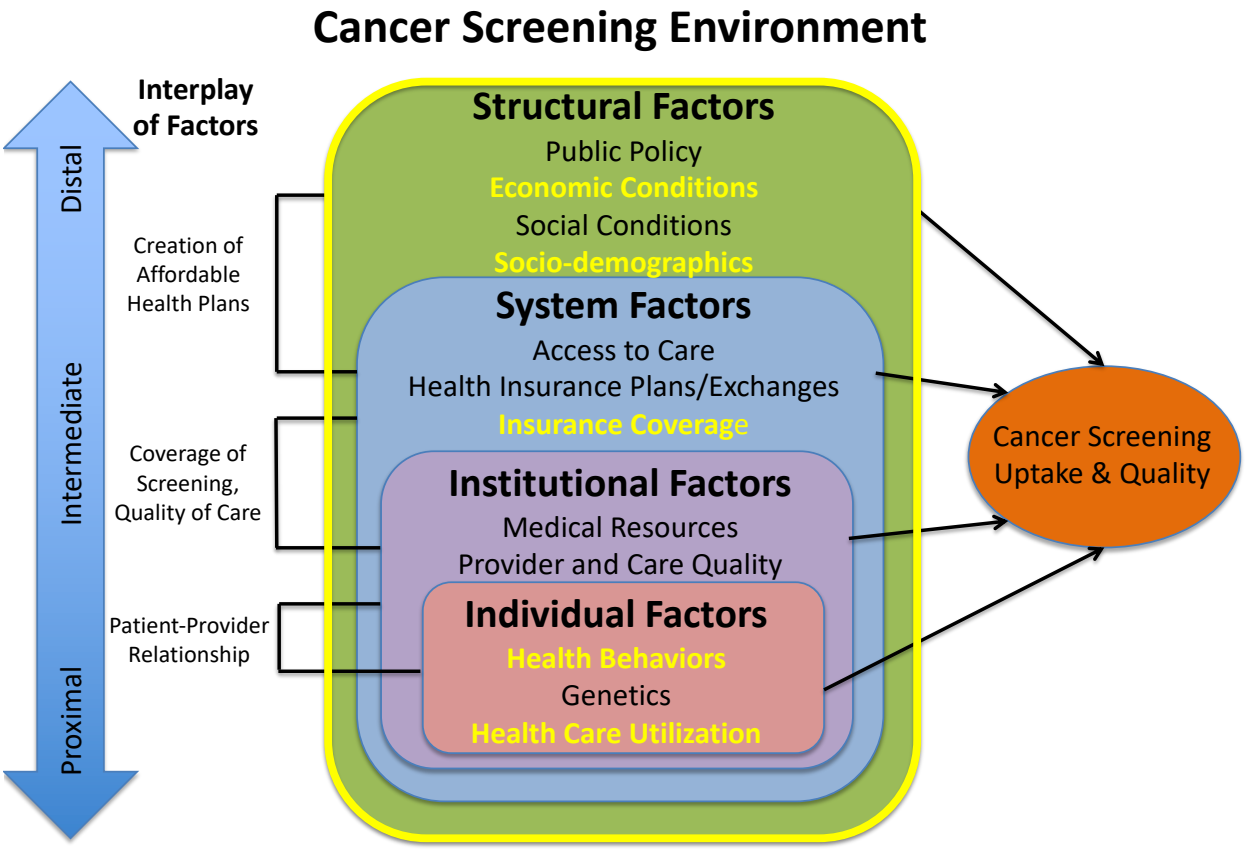
Dejana Braithwaite PhD

Figure 4.1: Conceptual Framework for Multilevel Factors Involved in Cancer Screening, Multilevel Factors for Chapter 3 Highlighted



4.1 ABSTRACT

INTRODUCTION: Despite recent efforts to improve access to cancer screening, major structural events at a societal level may radically impact screening behaviors. Between 2007 and 2009, the Great Recession in the United States led to spikes in unemployment nationwide and left many low and middle-income families uninsured due to an acute decrease in employer-sponsored health insurance. These changes in employment and employer-sponsored insurance could have exacerbated existing inequalities in cancer screening access.

METHODS: Using data from 2002-2012 in the longitudinal, population-based Health and Retirement Study (HRS), we assessed how individual-level employment status affected screening mammography utilization during the Great Recession, potential variation by insurance access or race/ethnicity, and temporal trends. Multilevel models accounted for state-level factors as random intercepts and study year as random slopes.

RESULTS: The HRS study population of 8,512 women ages 50-64 was weighted to represent the general US population. Rates of screening mammography were 77% in 2004, 76% in 2008 and 69% in 2012. At baseline, 38% of women had full-time employment and only 3% of women were unemployed. From 2002 to 2012, proportions of uninsured women increased from 20% to 27%. Part-time employment (OR: 0.80, 95%CI: 0.70-0.92), unemployment (OR: 0.76, 95%CI: 0.60-0.97) and other employment status (disability or out of work force) (OR: 0.79, 95%CI: 0.68-0.91) were associated with decreased screening mammography utilization. Our findings also showed being uninsured was significantly associated with reduced odds of screening utilization (OR: 0.46, 95% CI: 0.39-0.53). There was significant interaction between insurance status and employment status ($p<0.01$), with uninsured women having lower predicted probability of screening mammography utilization compared to insured women across all employment status groups.

CONCLUSION: Part-time employment, unemployment, and being disabled or out of the work force ("other" employment) decreased odds of screening mammography utilization. Furthermore, uninsured women had significantly lower likelihood of screening mammography utilization compared to insured women. Future research should further clarify the role of employment and insurance status in screening utilization.

4.2 INTRODUCTION

Breast cancer accounts for 30% of cancer incidence and is the second leading cause of cancer death among women in the United States (US).[3] Screening mammography, the only population-based method for early detection of breast cancer, was shown to be effective in reducing breast cancer mortality in women ages 50-74, and breast cancer survival rates drop significantly when cancer is detected in later stages.[143] In 2016, the US Preventive Services Task Force (USPSTF) recommended biennial screening among women ages 50-74.[20] Despite these potential benefits and the high level recommendation for screening, socioeconomic disparities continue to exist in screening utilization, which can have tremendous impact on the population-level benefits of these early detection practices.[37]

Unemployment could serve as a contributor to lower screening utilization and persistence of disparities in screening mammography use among women. Recent studies have shown that unemployment is associated with decreased cancer screening utilization.[144–148] The findings have indicated that job insecurity or unstable job positions can lead to greater stress and pressure that could influence an individual's time or willingness to undergo cancer screening.[149] Furthermore, unemployment or job insecurity can lead to a loss of employer-sponsored health insurance, which could affect an individual's ability to afford health insurance and access to a usual source of care, both of which are factors shown to lower screening mammography utilization.[150–154] Given these findings, it is possible that times of economic downturn, which are felt at a population level, could expand the current screening disparities.

Between 2007 and 2009, the US experienced the Great Recession, a time period of major spikes in unemployment, and lower healthcare utilization due to an acute decrease in employer-sponsored insurance.[155] While one recent study found higher rates of unemployment during the recession associated with decreased breast cancer incidence and treatment, it is unclear if the lower cancer incidence is related to decreases in screening mammography

utilization.[156] Furthermore, it is unclear if certain groups of women already facing screening disparities were further disproportionately affected by these recession effects.

The objective of this study was to examine the effect of employment status on screening mammography utilization within a nationally representative cohort of women before, during and after the Great Recession (2007-2009). We also aim to assess temporal trends and potential differences by race/ethnicity in this effect. Our primary hypothesis was that being less than full-time employed during the Great Recession would lead to decreased screening mammography utilization.

4.3 METHODS

Study Design and Sample

We used data from the Health and Retirement Study (HRS), a national, observational, longitudinal panel study started in 1992 that surveys a representative sample of noninstitutionalized Americans ages 50 and older and their spouses every two years.[157] To maintain a "steady state" sample, a new cohort of individuals ages 50-55 years were added every 6 years.[158,159] This study utilizes data measured in 2002, 2004, 2006, 2008, 2010 and 2012 HRS waves. We included women ages 50-64 years, excluding women over age 64 who have an annual mammogram covered under Medicare Part B insurance. We also excluded any women with a prior cancer diagnosis to remove any women with prior breast cancer. To avoid extreme standard errors in our analyses, we also excluded women in 15 US states or territories where the number of included women in any study wave was less than 11. Our final analytic sample included 8,512 women.

Outcome

The primary outcome was self-reported mammogram utilization since the previous wave. Questions regarding mammogram uptake were asked of the entire sample of women every four years, so mammogram utilization data was extracted from years 2004, 2008 and 2012.

Specifically, women were asked if they received a mammogram or x-ray of the breast to search for cancer since the previous interview (two-year reporting window),

Predictor and Covariates

The main predictor of interest was a woman's employment status—measured as current status in the labor force during the years 2002, 2006 and 2010. These data were purposively lagged; employment status was extracted from HRS waves prior to the 2-year outcome reporting windows to ensure temporality between the predictor and screening mammography utilization. Employment status was classified as working full-time, part-time (includes individuals reporting being partially retired), unemployed, retired, or other (includes disabled and individuals not in the labor force). This variable was created using responses from multiple HRS employment variables.[160] Full-time status was defined as working ≥35 hours per week for ≥36 weeks per year, whereas less than this was considered part-time. Women defined as unemployed were not currently working for pay, but still looking for work. Retirement status was defined as any mention of retirement in other employment questions and the woman was not looking for a job. If a woman mentioned retirement but was still working, she was considered "partially retired", and grouped with women who were working part-time. All other employment statuses, being disabled or not in the work force, were grouped into the "other" category, creating five employment categories overall. We also included insurance status as a second predictor, which was self-reported insurance at the time of interview and tested potential effect modification of this relationship by employment status. This was measured in years 2002, 2006 and 2010.

Covariates included age, race/ethnicity, education, marital status, poverty status based on household income and state-level yearly unemployment measures. Race/ethnicity was categorized first by Hispanic ethnicity, and then separated into whether individuals were White, Black or other. Aggregate state-level measures of yearly unemployment were ascertained from the US Department of Labor.[161] Poverty status and aggregate state-level measures of yearly

unemployment were treated as time-varying covariates and were ascertained from the years 2002, 2006 and 2010.

Statistical Analysis

Data were weighted to better reflect US population-level estimates using HRS-provided weights.[157,158] Individual respondent weights were standardized around a mean of 1 within each year. We measured differences in covariates over time using Cochran-Armitage trend test with a two-sided p-value of 0.05 used to determine statistical significance. We also compared covariates by employment status group using chi-square tests with a two-sided p-value of 0.05 used to determine significance.

We used mixed-effects logistic regression models to assess the effect of employment status (reference group is full-time employment) on screening mammography utilization. A second analysis was conducted to test the effect of insurance status on screening mammography utilization. We included state-level random effects to account for correlation among women based on state-level policies around preventive care, particularly cancer screening. Models were adjusted for age, race/ethnicity, education, marital status and state-level unemployment rate. Poverty status was also included as a covariate in the second analysis examining insurance status as the main predictor. We included interaction terms for the exposure and year to assess whether the effect of employment status or insurance status on screening mammography utilization varied across time. We were interested in three time periods: prior to the Recession (2002-2004), during the Recession (2006-2008) and after the Recession (2010-2012). We also tested for potential interaction by race/ethnicity.

For the second analysis, we also included interaction terms for insurance status and employment status, to assess whether the effect varied by employment status. A two-sided p-value of 0.10 was used to determine statistical significance of interaction. Regression coefficients were exponentiated to calculate odds ratios and corresponding 95% confidence intervals (CI) and converted to probabilities to calculate predicted probabilities of screening

mammography use for each employment status across time. Statistical analyses were performed using SAS 9.4 (SAS Corporation, Cary, NC).

4.4 RESULTS

Our study included 8,512 US women ages 50-64 across 35 states. **Table 4.1** presents the descriptive information for all women in the analytic sample. Most participants in our sample were ages 55 and older (77%), non-Hispanic White (76%), married (68%) and had at least some college education (55%). **Table 4.2** presents proportions of time-varying covariates by year. The percentage of uninsured women significantly increases from 2002 (20%), to 2006 (23%), to 2010 (27%) with a p-trend of <0.01. The proportions of full-time employed (2002: 38% to 2010: 45%) and unemployed women (2002: 3% to 2010: 5%) increased over time, while the proportion of women with "other" employment status decreased over time (2002: 20% to 2010: 12%), each with p-trend values of <0.01.

When stratifying covariates by employment status, all covariates were found to be significantly different by employment status group with chi-square p-values of <0.01 (**Table 4.3**). Women who had full-time employment were ages 55 and older (72%), mostly non-Hispanic White (79%), mostly had at least some college education (63%), were married or partnered (65%) and were mostly insured (89%). Unemployed women, which made up only 3% of the study population, were mostly ages 55 and older (72%), had at least some college education (52%), and only 54% were insured, the lowest rate among all employment groups. Part-time employed women had at least some college education (59%) and were mostly married (75%). Retired women were mostly ages 60 and older (58%) and mostly had a high school diploma or less (54%). Women designated as having an "other" employment status (on disability or not in the labor force) had a high school diploma or less (66%), were mostly married or partnered (74%), included 24% of women below the poverty line, and only 56% were insured.

Overall, rates of screening mammography were 77% in 2004, 76% in 2008 and 69% in 2012. Women with full-time employment had a 76% predicted probability (95% CI: 73%, 78%) of screening mammography utilization, which was comparable to retired women (Probability: 73%, 95% CI: 70%, 77%) (**Table 4.4**). Unemployed (70%, 95% CI: 64%, 75%), part-time employed (71%, 95% CI: 68%, 75%) and women with other employment (71%, 95% CI: 67%, 75%) had 5-6% lower probability of screening mammography utilization. Overall, women who had part-time employment (OR: 0.80, 95% CI: 0.70, 0.92), were unemployed (OR: 0.76, 95% CI: 0.60, 0.97), or were classified as having an "other" type of employment status (disability or not in work force) (OR: 0.79, 95% CI: 0.68, 0.91) had decreased odds of screening mammography utilization compared to women with full-time employment. In summary, part-time employed, women with "other" employment and unemployed women had the lowest rates of screening mammography.

In addition to the overall findings that less than full-time employment status was associated with increased screening mammography utilization, we found no significant interaction between employment status and study wave (p=0.50) (**Table 4.4**). Among women who had part-time employment, odds of screening increased from 2002-2004 (OR: 0.73, 95% CI: 0.55, 0.96) to 2006-2008 (OR: 0.91, 95% CI: 0.71, 1.16) then decreased in 2010-2012 (OR: 0.78, 95% CI: 0.65, 0.95). Among women with other employment, screening mammography odds decreased from 2002-2004 (OR: 0.82, 95% CI: 0.63, 1.07) to 2006-2008 (OR: 0.66, 95% CI: 0.51, 0.85) and then increased in 2010-2012 (OR: 0.88, 95% CI: 0.70, 1.10). There was also no interaction between employment status and race/ethnicity (p=0.27).

Additionally, when assessing the effect of insurance status on screening utilization, lack of insurance (OR: 0.46, 95% CI: 0.39, 0.53) was associated with significantly decreased screening mammography utilization (**Table 4.5**). There was also significant interaction between employment status and insurance status (p<0.01). Across all employment status groups, there was a significant difference in predicted probability of screening mammography use when comparing women with versus without insurance. Part-time employed women who were

uninsured (OR: 0.32, 95% CI: 0.24, 0.41) had the lowest odds of screening compared to insured women. Women with "other" employment who were uninsured (OR: 0.71, 95% CI: 0.54, 0.91) only had a 29% decreased odds of screening mammography compared to insured women who had "other" employment.

4.5 DISCUSSION

In a nationally representative study of women ages 50-64, our findings showed that employment status was significantly associated with odds of screening mammography utilization. Treating full-time employment as a reference, women who had part-time employment, were unemployed, or had "other" employment status defined by disability or not being in the labor force had decreased odds of screening mammography utilization, aligning with our hypothesis that employment status directly affects someone's likelihood to screen. However, our findings indicate that the associations between employment status and screening mammography did not vary meaningfully across the three studied time periods (2002-2004, 2006-2008, 2010-2012). Further, in a secondary analysis of the effect of insurance status on screening mammography utilization, lack of insurance significantly decreased screening mammography odds, and the effect varied by employment status.

Our findings were similar to prior studies that have evaluated how employment status affected screening utilization.[162,163] In a cross-sectional study, Calo et al. found that census tract-level unemployment was associated with decreased colorectal cancer screening adherence, potentially representing a breakdown in healthcare access within an area of high unemployment or economic instability.[162] Hamad et al. similarly found that outpatient healthcare utilization overall decreased among individuals at manufacturing plants where there were higher rates of layoffs in a cohort study.[163] Our study found significant effects among employment status groups indicating less than full-time employment, with the exception of being retired.

Prior studies measuring trends in cancer screening before, during and after the Great Recession, did not consider the independent effect of employment status on screening utilization. Wyatt et al. found that screening mammography odds decreased during the Great Recession, and then decreased again during the post-Recession, Affordable Care Act initiation period, when measuring trends over time.[164] While our findings show a downward trend in the predicted probability of screening mammography utilization across most employment status groups, the magnitude of the effect of employment status on screening mammography did not meaningfully change across time.

The results indicating similar screening mammography utilization probabilities among retired women compared to full-time employed women both overall and over the course of the Great Recession aligned with findings from previous studies.[145,164] Both Fedewa et al. and Wyatt et al. included adults ages 50 and older in their study whereas our study only included women ages 50-64, which would likely only include women who have retired early, who might be different from persons who do not retire early.[145,164] While US citizens earn the full benefits of retirement around age 65 or older, citizens may retire at age 62 and start receiving Social Security benefits with percentage reductions based on the number of months prior to the defined "full retirement age".[165] Despite this early access to Social Security, retirees do not gain earlier access to Medicare, which covers preventive screenings such as mammography.[166] Thus, it is possible that this sustained access to screening is related to potential unmeasured factors related to being retired.

Insurance status was also found to have an independent effect on screening mammography utilization, with uninsured women having markedly lower likelihood of undergoing mammography compared to their insured counterparts. This effect was stable over time and persisted across all employment groups. These findings align with prior research, which indicated that insurance access is positively associated with greater screening mammography utilization.[164,167] Rates of insurance status decreased over the course of the

Great Recession, highlighting a critical need to better understand the importance of insurance status on cancer screening uptake, particularly in times of economic downturn.

The findings of lower screening mammography utilization overall among part-time, unemployed or other employment type women could be related to less time and resources, which has previously been considered a barrier to receiving preventive care.[148] Kim et al. evaluated the effect of job status on accessibility to cancer screening among wage earners, finding that part-time workers had difficulty participating in prevention programs.[168] This aligns with research in behavioral economics around the theory of "effect budgeting", where people have limited time that requires prioritization of all tasks and activities.[169] Catalano et al. suggest that given these limited resources, we budget them in a way to reflect expected costs and benefits, particularly in times of economic downturn, when priorities and resources can change.[169] This would align with the findings of decreases in screening mammography utilization across all employment status groups after the Great Recession (2010-2012 analysis). Our study findings indicate that women with less than full-time employment have lower odds of screening utilization, but the Great Recession did not exacerbate this effect.

Our study had some limitations. Mammography use was only measured every four years, limiting more consistent measure of routine screening mammography, which is recommended biennially. Furthermore, mammography use was measured via self-report, which has previously been found to potentially lead to overestimation of the true mammography utilization.[170] We did not follow women to potential breast cancer outcomes to measure if mammography use differences by employment status affected breast cancer risk. Future studies could extend these findings to better understand if such an association exists.

Despite these limitations, our study had key strengths including leveraging a national, diverse population-based cohort of women to measure longitudinal uptake of screening mammography over a 10-year period. This differs from prior studies, which have considered cross-sectional study waves without longitudinal follow-up of individuals.[163,164] In addition, the

analyses were weighted to reflect a population-based sample, improving generalizability of the sample. The use of mixed modeling also enabled clustering of state-level Great Recession effects to better estimate local economic impacts. To ensure the robustness of our models, we tested both a lagged longitudinal model as well as three time-stratified models reflecting effects before, during and after the Great Recession, finding similar results among the different model types. We also tested a positive control effect, measuring the independent effect of employment status on insurance status. The findings confirmed that our tested covariates were appropriate, and further confirmed that while an effect of employment status on insurance status differed over time, a similar effect did not exist for our tested research question.

4.6 CONCLUSION

Overall, part-time employed women, unemployed women and women who were disabled or out of the work force ("other" employment status) were less likely to get a screening mammogram compared to full-time employed women. Furthermore, our findings indicated that the association between employment status and screening mammography did not significantly vary over the course of the Great Recession, though probability of screening mammography utilization decreased across all employment status groups over the course of the study. Similar to other studies, uninsured women had lower predicted probability of screening and lower odds of screening mammography utilization in all employment status groups compared to insured women, particularly among full-time employed and part-time employed women. These findings highlight an important need to learn about how employment status affects cancer screening utilization in women, and how insurance access factors into this relationship in light of recent health care reform and changes to health care access.

Table 4.1: Overall proportions of covariates across study population

	Overall
	Weighted %
Age (%)	
50-54	23
55-59	43
60-64	34
Race/Ethnicity (%)	
Non-Hispanic White	76
Non-Hispanic Black	12
Hispanic	9
Other	4
Education (%)	
Less than High School	12
High School Diploma or GED	33
Some College	28
College Graduate or Higher	27
Marital Status (%)	
Married or Partnered	68
Separated/Divorced/Widowed	27
Not Married	5

Table 4.2: Overall proportions of selected covariates across study waves

	Baseline (2002-2004) %	During (2006-2008) %	After (2010-2012) %	P-Value
Poverty Status (%)				
Below Poverty Line	11	9	11	0.16
Insurance Type (%)				
Insured	80	77	73	<0.01
Private	68	67	65	<0.01
Public	5	4	3	<0.01
Other	8	6	6	<0.01
Uninsured	20	23	27	<0.01
Employment Status (%)				
Full-time Employment	38	44	45	<0.01
Part-time Employment or Partial Retirement	18	18	19	0.31
Unemployed	3	2	5	<0.01
Retired	21	21	19	<0.01
Other	20	15	12	<0.01

Percentages are based on weighted sample using HRS weights
Two-sided P-values correspond to Cochran-Armitage trend tests

Table 4.3: Employment status by covariates across study period, All percentages (%)

	Full-time Employment	Part-time Employment or Partial Retirement	Unemployed	Retired	Other
Age (%)					
50-54	28	24	28	9	22
55-59	48	43	49	32	44
60-64	24	33	23	58	34
Race/Ethnicity (%)					
Non-Hispanic White	79	80	67	73	64
Non-Hispanic Black	11	9	14	15	11
Hispanic	6	8	13	8	19
Other	3	3	7	3	5
Education (%)					
Less than High School	6	9	12	17	30
High School Diploma or GED	31	32	36	37	36
Some College	30	29	31	26	20
College Graduate or Higher	33	30	21	20	14
Marital Status (%)					
Married or Partnered	65	75	60	63	74
Separated/Divorced/Widowed	28	21	32	32	21
Not Married	7	4	8	5	5
Poverty Status					
Below Poverty Line	3	6	19	19	24
Insurance Type (%)					
Insured	89	78	54	63	56
Private	84	66	42	45	43
Public	2	2	2	10	5
Other	3	10	10	8	8
Uninsured	11	22	46	37	44

Percentages are based on weighted samples using HRS weights; Percentages are column percentages (percent by covariate); Comparisons were conducted using chi-square analysis (all had $p<0.01$)

	Fully-Adjusted Model			
Overall	**Predicted Probability**	**95% CI**	**Odds Ratio**	**95% CI**
Full-time Employment	0.76	(0.73, 0.78)	1.00	--
Part-time Employment or Partial Retirement	0.71	(0.68, 0.75)	0.80	(0.70, 0.92)
Unemployed	0.70	(0.64, 0.75)	0.76	(0.60, 0.97)
Retired	0.73	(0.70, 0.77)	0.89	(0.77, 1.03)
Other	0.71	(0.67, 0.75)	0.79	(0.68, 0.91)
2002-2004				
Full-time Employment	0.78	(0.74, 0.81)	1.00	--
Part-time Employment or Partial Retirement	0.72	(0.66, 0.77)	0.73	(0.55, 0.96)
Unemployed	0.76	(0.64, 0.85)	0.88	(0.50, 1.57)
Retired	0.78	(0.73, 0.83)	1.00	(0.74, 1.36)
Other	0.74	(0.69, 0.79)	0.82	(0.63, 1.07)
2006-2008				
Full-time Employment	0.78	(0.74, 0.81)	1.00	--
Part-time Employment or Partial Retirement	0.76	(0.71, 0.80)	0.91	(0.71, 1.16)
Unemployed	0.73	(0.60, 0.83)	0.79	(0.44, 1.41)
Retired	0.74	(0.68, 0.78)	0.81	(0.62, 1.04)
Other	0.69	(0.64, 0.75)	0.66	(0.51, 0.85)
2010-2012				
Full-time Employment	0.71	(0.67, 0.74)	1.00	--
Part-time Employment or Partial Retirement	0.66	(0.61, 0.70)	0.78	(0.65, 0.95)
Unemployed	0.64	(0.56, 0.71)	0.73	(0.54, 0.98)
Retired	0.69	(0.64, 0.73)	0.90	(0.73, 1.10)
Other	0.68	(0.63, 0.73)	0.88	(0.70, 1.10)

Fully-adjusted mixed effects model includes lagged employment status exposure, year, age, race/ethnicity, education, marital status, state-level unemployment rate, and a random intercept and slope for state.
$P_{interaction}$ employment status*year = 0.50; $P_{interaction}$ employment status*race/ethnicity = 0.27
2002-2004: Effect of Employment Status for 2002 on 2004 Screening Mammography Uptake
2006-2008: Effect of Employment Status for 2006 on 2008 Screening Mammography Uptake
2010-2012: Effect of Employment Status for 2010 on 2012 Screening Mammography Uptake

Table 4.4: Mixed model results of individual-level employment and screening mammography utilization, stratified by year

Table 4.5: Mixed model results of individual-level insurance status and screening mammography utilization, and interaction results with employment status, stratified by insurance status

	Fully-Adjusted Model			
	Predicted Probability	**95% CI**	**Odds Ratio**	**95% CI**
Overall				
Uninsured	0.63	(0.59, 0.66)	0.46	(0.39, 0.53)
Insured	0.79	(0.76, 0.81)	1.00	--
Insured = 0				
Full-time Employment	0.56	(0.50, 0.62)	0.34	(0.27, 0.42)
Part-time Employment or Partial Retirement	0.55	(0.49, 0.61)	0.32	(0.24, 0.41)
Unemployed	0.64	(0.56, 0.72)	0.57	(0.35, 0.92)
Retired	0.68	(0.62, 0.72)	0.53	(0.41, 0.68)
Other	0.68	(0.63, 0.73)	0.71	(0.54, 0.91)
Insured = 1				
Full-time Employment	0.80	(0.77, 0.82)		
Part-time Employment or Partial Retirement	0.79	(0.76, 0.82)		
Unemployed	0.77	(0.70, 0.82)		
Retired	0.80	(0.77, 0.84)		
Other	0.76	(0.72, 0.80)		

Fully-adjusted model includes employment status, study wave year, age, race/ethnicity, education, marital status, state-level unemployment rate, poverty status, and interaction term insurance status*employment

$P_{interaction}$ Employment status*Insurance Status = <0.01

5. CONCLUSIONS

The three studies described within this dissertation critically assessed the effects of multilevel factors across the socioecological environment of cancer early detection for screening uptake, clinical practices and methodology, and social determinants on utilization. The first study found that greater comorbidity, functional limitations, and lower perceived health were associated with lower mammography utilization, indicating that providers should weigh these life expectancy factors when making screening mammography recommendations for their elderly patients. In the second study, wide variation in radiation dose for lung cancer screening scans was documented, and institutions limiting protocol creation to lead radiologists and hiring internal medical physicists had lower radiation doses. In the third study, the Great Recession decreased odds of screening mammography utilization across part-time employed women, unemployed women and "other" employed women (disabled women or women out of the labor force). However, the most pronounced effect was among uninsured women, who had a significantly lower likelihood of screening mammography utilization compared to insured women, independent of employment status. Overall, the findings from each socioecological level provide a lens on different but interacting contexts and solutions to key issues that exist in the cancer screening environment.

Numerous cancer screening studies in recent years have considered multilevel factors in their research questions to better understand predictors of cancer screening uptake. Shariff-Marco et al. measured the effect of individual-level and neighborhood-level predictors on colorectal cancer screening uptake, concluding that factors such as locality, primary care resources and membership in a health maintenance organization (HMO) were key determinants of colorectal cancer screening uptake, while socioeconomic status and segregation did not predict uptake.[171] A study conducted by Hubbard et al. using data from the Breast Cancer Surveillance Consortium linked with Medicare claims data assessed individual-level and

community-level predictors of long-term adherence to screening mammography among older women, finding that women with less than a high school education and a Charlson Comorbidity Index score of at least one were more likely to be non-adherent at baseline and less likely to remain adherent over time.[77] The findings were critical to identifying vulnerable populations who may not be screening or adhere to screening guidelines, which can pave the way for more targeted interventions to optimize screening uptake.

The first chapter of this dissertation contributed a comprehensive review of the current evidence around how life expectancy factors affect screening mammography utilization, making a crucial argument for more targeted guidelines for screening among older women. As described previously, a primary determinant of screening mammography uptake is a physician's recommendation.[111–113] Without properly accounting for life expectancy when a physician recommends whether a woman should under screening mammography, it is possible that a benefit be limited, potentially opening an older woman up to greater risk of experiencing deleterious effects. Schonberg et al. are testing a screening mammography decision aid to inform women ages 75 and older of the potential harms of undergoing further screening, particularly among those with limited life expectancy.[110] While the goal of this decision aid is to strengthen the autonomy of older women unsure of whether to screen, future decision aid research should also incorporate the provider in this discussion to maintain healthy patient-provider communication that could be critical to other aspects of women's health.

As evidenced from the second study, identifying key institutional-level predictors can help target areas of concern that can be optimized to improve the quality of cancer screening to maximize the margin of benefit. In another study also looking at lung cancer screening, Carter-Harris and Gould identified key patient-level, provider-level and system-level barriers to implementation of an effective lung cancer screening program, advocating that effective screening implementation should consider all of these factors to proactively address potential challenges that might arise.[172] Additionally Kim et al. measured patient-level and provider-level

factors affecting colorectal cancer screening uptake, and found that having an annual physical exam, being non-Hispanic White, and having a provider with medical doctor credentials were the strongest predictors of increased screening uptake.[173] Focusing on system-level and provider-level factors illustrates the critical role the provider plays in both encouraging appropriate screening uptake and ensuring screening tests are performed to the highest standard.

The findings from the third study indicated that employment status affects screening mammography utilization, and insurance status also affects screening mammography utilization, though neither effect was exacerbated by the Great Recession. Prior research shows that individuals are not likely to change their screening behavior unless strongly compelled to do so.[174] Thus, the persistence of disparities in cancer screening tends to be related to the factors influencing the individual's initial intent or capacity to screen.[174] Better understanding these factors can help uncover an underlying context that affects the likelihood that an individual will use screening services. Furthermore, these findings could further help clinicians develop more targeted interventions or make screening more appropriately accessible for the individuals with the greatest need.

In sum, the findings from this dissertation illustrate three different scenarios across a multilevel cancer screening framework in which research can help fill current evidence gaps. Within the cancer screening environment, many interdependent factors influence whether individuals undergo screening, how screening is implemented, and the current guidelines for insurance coverage of screening. Future studies into predictors of cancer screening uptake and performance should examine factors at multiple socioecological levels more comprehensively in order to understand how different predictors are influenced by the complex cancer screening environment. Identifying the role these factors play can improve upon current interventions to optimize cancer screening uptake and ensure that screening tests maximize potential benefits while minimizing potential harms.

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