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SCREENING AND SELECTION: THE CASE OF MAMMOGRAMS

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ABSTRACT

Debates over whether and when to recommend screening for a potential disease focus on the causal impact of screening for a typical individual covered by the recommendation, who may differ from the typical individual who responds to the recommendation. We explore this distinction in the context of recommendations that breast cancer screening start at age 40. The raw data suggest that responders to the age 40 recommendation have less cancer than do women who self-select into screening at earlier ages. Combining these patterns with a clinical oncology model allows us to infer that responders to the age 40 recommendation also have less cancer than women who never screen, suggesting that the benefits of recommending early screening are smaller than if responders were representative of covered individuals. For example, we estimate that shifting the recommendation from age 40 to age 45 results in over three times as many deaths if responders were randomly drawn from the population than under the estimated patterns of selection. These results highlight the importance of considering the characteristics of responders when making and designing recommendations.

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1 Introduction

Whether and when to recommend screening for potential diseases is a highly controversial and evolving policy area, with active academic research.[1] Much of the debate – both in public policy and in academia – centers on the causal impact of screening for a typical individual covered by the recommendation. Estimating this causal impact is challenging for several well-known reasons. First, there are the usual challenges to causal inference. Second, many of the potential costs and benefits of screening are difficult to measure and to monetize.[2] In this paper, we highlight another important – and, we believe, overlooked – challenge in analyzing and designing screening policies: the typical individual *covered* by a recommendation may be very different from the typical individual who *responds* to the recommendation. As a result, the estimated impact of the screening for a randomly selected individual may be quite different from the impact for an affected individual.

We explore this distinction in the context of the current controversy over whether to recommend annual mammograms for women starting at age 40. Results from randomized trials have consistently failed to show statistically significant mortality benefits of mammograms for women in their 40s, and in 2009 this prompted the US Preventive Services Task Force (USPTF) to change its recommendation for routine mammograms to begin at age 50 rather than at age 40. This change generated substantial public controversy (Kolata, 2009; Saad, 2009; Berry, 2013).

This debate has focused on the costs and benefits of mammograms for typical ("average-risk") 40 year old women, with little attention paid to what types of women respond to a screening recommendation and whether the costs and benefits for them may differ from the average woman. To investigate the type of women who respond, we draw on two primary data sources. The first is insurance claims data on mammogram choices and their results (negative, false positive, or true positive) for privately insured women aged 35-50 from the Health Care Cost Institute (HCCI). The second is cancer registry data, from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database, on the size and stage of detected tumors for women aged 35-50 who were diagnosed with breast cancer.

The visual evidence shows sharp and pronounced changes in behavior and outcomes at age 40. There is an over 25 percentage point jump in the annual mammogram rate at age 40, from 10 percent to 35 percent of women. Women who respond to the recommendation have a lower incidence of cancer than do women who choose screening in the absence of the recommendation: there is a roughly 30 percent decline (from 0.84% to 0.56%) in the share of screened women diagnosed with cancer (i.e. true positives) at age 40. Given the high rate of false positives (about 90 percent of initial positive mammograms turn out to be false positives), the sharp increase in the mammogram rate at age 40 translates into a substantial increase in the number of women experiencing false positives (from about 10 per thousand women to about 40). This is consistent

[1] For example, Welch, Schwartz,, and Woloshin (2011) argue that although many medical conditions – such as high blood pressure, elevated blood glucose levels, low bone density, and high cholesterol – benefit from treatment, there has been a trend over time towards widespread use of medical screening tests and increasingly low diagnostic thresholds that recommend treating patients for whom the benefits from treatments are quite small. By contrast, Maciosek et al. (2010) review these same screening efforts and conclude that they save a large number of lives at relatively low cost .

[2] The costs and benefits of screening include monetary costs, clinical outcomes, discomfort from unnecessary procedures, and psychological effects induced by the screening process, including pre-screening apprehension and anxiety due to false positives (e.g Ong and Mandl, 2015; Welch, 2015; Welch and Passow, 2014; Nelson et al., 2009; Brett et al., 2005).

with a key concern regarding false positives that motivated moving the recommended age of mammogram from 40 to 50 (Nelson et al., 2009). Moreover, among those diagnosed with cancer, the registry data show a sharp decline in the average tumor's stage and size starting at age 40. For example, the share of detected tumors that are invasive (i.e. later stage) as opposed to in situ falls by about 6 percentage points (or 7 percent) at age 40.

These descriptive results indicate that women who respond to the recommendation for a mammogram have lower risk of cancer than those who seek mammograms in the absence of the recommendation. Interestingly, we find that women who respond to the recommendation also appear to be more likely to comply with other types of recommended preventive care, such as cervical cancer screening tests and flu shots. This is consistent with Oster (2018)'s finding that when a health behavior is recommended, those who comply with the recommendation tend to exhibit other positive health behaviors.

To assess the implications of these findings and to quantify costs and health outcomes under various counterfactual selection scenarios, we specify a model of mammogram demand that is a function of a woman's age, her (undiagnosed) cancer type (no cancer, in situ, or invasive), and whether or not a mammogram is recommended at her age. We estimate the model by method of moments, using two key inputs. First, we leverage our data on the observed patterns of mammogram decisions and mammogram outcomes (specifically, cancer type) for women by age. Second, we bring in a clinical oncology model of the underlying rate of onset of breast cancer by age, as well as cancers' clinical progression in the absence of detection and treatment. In the absence of a clinical model, these objects are inherently difficult (or impossible) to observe: cancer incidence is not observed in the non-screened population, and almost all detected cancer is treated immediately upon detection. The clinical model of breast cancer incidence and progression is drawn from a large scale, coordinated project funded by the National Cancer Institute (NCI) involving seven different research groups (Clarke et al., 2006); we show robustness of our findings to a range of alternative assumptions about the onset and distribution of cancer type by age.

The estimates from our model indicate that women who would select into mammograms in the absence of the recommendation have much higher rates of both in situ and invasive cancer than the general population. We refer to this as "positive selection" into mammograms (positive with respect to cancer incidence). However, our estimates indicate that the women who select into mammograms due to the recommendation are much *less* likely to have invasive cancer – and are no more likely to have in-situ cancer – than women who do not select into mammograms. The relative degree of selection pre- and post- the age 40 recommendation is identified directly from our data; the clinical model of underlying cancer incidence is needed to assess whether the observed selection either pre- or post-age 40 is positive with respect to the underlying population, whose cancer incidence is not directly observed.

We apply our model and its estimates to illustrate how the nature of selection in response to the recommendation affects the impact of the recommendation. Specifically, we estimate that shifting the recommendation from age 40 to age 45 results in more than three times as many deaths – at similar cost savings – if we assume that those who respond to the recommendation are randomly drawn from the population rather than drawn based on the estimated selection patterns. We view this as a particularly instructive counterfactual since assuming the individuals who respond are randomly drawn from the population is conceptually simi-

lar to using estimates of the impact of mammography from randomized experiments (with full compliance). Because in practice those who respond to the recommendation have a much lower rate of invasive cancer than the underlying population, the mortality cost of moving the recommendation to age 45 is lower than under random selection. Conversely, our model also illustrates that if it were feasible to target the recommendations to those with higher rates of cancer, the mortality cost of moving the recommendation from age 40 to 45 could be substantially larger than even the random selection assumption would imply. This is consistent with recent interest in reducing over-diagnosis by developing targeting, precision screening for individuals at higher risk (Elmore, 2016; Esserman et al., 2009).

Our paper relates to several distinct literatures. Most narrowly, it speaks to the large body of work on mammograms. A sizable number of randomized trials has explored the impact of mammograms on subsequent health outcomes (Alexander et al., 1999; Bjurstam et al., 2003; Habbema et al., 1986; Miller et al., 2000, 2002; Moss et al., 2006; Nyström et al., 2002). In addition, several studies have examined so-called "over-diagnosis" – i.e. screening of a cancer that never would become clinically relevant (Jørgensen and Gøtzsche, 2009); these studies have analyzed the extent to which increased mammogram screening rates are associated with increased incidence of small or early stage tumors with no corresponding increase in large or late-stage tumors, suggesting that increased screening may be identifying tumors that would never have developed into life-threatening cancers (Bleyer and Welch, 2012; Harding et al., 2015; Jørgensen and Gøtzsche, 2009; Jørgensen et al., 2017; Welch et al., 2016; Zackrisson et al., 2006). Several studies have combined these existing estimates to quantify the costs and benefits of mammograms (e.g. Welch and Passow, 2014; Ong and Mandl, 2015). All of these studies have focused on the average effect of mammograms on the female population, and did not consider the potential selection that is our focus.

A related strand of literature investigates how mammogram rates are influenced by factors such as distance to women's health clinics (Lu and Slusky, 2016), health insurance coverage (Bitler and Carpenter, 2016; Cooper et al., 2017; Fedewa et al., 2015; Finkelstein et al., 2012; Habermann et al., 2007; Kelaher and Stellman, 2000; Mehta et al., 2015), and recommendations (Kadiyala and Strumpf, 2011, 2016; Jacobson and Kadiyala, 2017). Most of these studies break out effects by income, education, race, and other individual-level characteristics, but are not able to link these demographic characteristics to cancer outcomes. Of these, Kadiyala and Strumpf (2016) is most closely related to our work; they document a sharp increase in self-reported mammograms at age 40 and estimate that most of the "newly detected" cancers are early stage cancers.

Beyond the specific application of mammograms, there is a broader health policy debate about whether and when to recommend medical screening tests (e.g. Welch, Schwartz,, and Woloshin, 2011). A central challenge that has limited empirical research on this topic is that – in the datasets typically available to researchers – the testing decision is observed but the outcome of the test is not. An attractive feature of our setting is that the outcome of the test (i.e. cancer incidence and type of cancer) is measurable both in claims data and in registry data. In this sense our analysis is similar in spirit to Abaluck et al. (2016), who are able to measure the outcome of imaging tests for pulmonary embolism in claims data, which they use to investigate whether and when that imaging test is being "overused." Both our paper and Abaluck et al. (2016) share a common feature with the racial profiling literature on stop and frisks (e.g. Anwar and Fang

2006; Persico 2009): the object of interest is only observed conditional on an action. This raises an empirical challenge for analyzing how the action (in our case, screening) relates to the underlying object of interest (in our case, the underlying incidence of cancer and cancer types). In our setting, we overcome this empirical challenge by combining two insights. First, the recommendation at age 40 serves as an exogenous source of variation in the screening rate, allowing us to estimate the cancer type of the marginal person affected by the recommendation. Second, the clinical oncology model of cancer incidence and growth allows us to use the observed moments (namely, outcomes conditional on screening under different regimes) to model outcomes under counterfactual regimes.

More broadly, our paper speaks to the value of complementing reduced form estimates of causal effects with economic models of behavior, and particularly of selection. Reduced form methods – both quasi-experimental and randomized experiments – aim to estimate causal effects by shutting down any endogenous choices. In practice, however, most policies involve an element of choice, so that the ultimate impact of the policy depends not only on the distribution of causal treatment effects but also on which individuals select into treatment. In this sense our paper relates broadly to the literature on Roy selection, or selection on gains. In the healthcare context specifically, Einav et al. (2013) emphasize that the impact on healthcare spending of offering a high deductible health insurance plan may be very different than what would be estimated from random assignment of high deductible plans across individuals, because the types of people who choose high deductible plans can have very different health care utilization responses to cost sharing than a typical individual. Our analysis speaks to a similar issue, in the context of evaluating recommendations for disease screening.

The rest of the paper proceeds as follows. Section 2 briefly summarizes the relevant institutional details of our empirical context (breast cancer and mammography). Section 3 describes our data and presents descriptive results. Section 4 presents our model of mammogram choice and describes how we estimate it using the observed descriptive patterns together with a clinical oncology model. Section 5 presents the model estimates and discusses their implications for the impact of changing the age of recommendation for mammogram under both observed and counterfactual selection patterns. The last section concludes.

2 Empirical context

2.1 Breast cancer

The earliest stages of breast cancer typically produce no symptoms and are not detectable in the absence of screening technologies.[3] As breast cancer progresses, it can spread within the breast, to adjacent tissues, to adjacent lymph nodes, and to distant organs (known as metastases). In clinical settings, tumors are classified according to the size of the tumor, the extent to which it has spread to lymph nodes, and whether it has metastasized. Public health research typically relies on a standardized classification – namely, the SEER classification system, which includes four stages: in situ, local, regional, and distant; the last three stages are collectively referred to as "invasive" tumors.

[3] Unless otherwise noted, the discussion in this section draws from American Cancer Society (2017a).

Our analysis focuses on the distinction between in situ and invasive tumors, because this distinction has been a key focus of the policy debate around mammography recommendations. In situ refers to abnormal cells that have not invaded nearby tissues, instead remaining confined to the ducts or glands in which they originated. Some but not all in situ tumors will become invasive. Expected survival time varies greatly by stage at diagnosis: patients who are diagnosed with localized breast cancer are 99% as likely as cancer-free women to survive to 5 years after diagnosis, compared to 85% for regional breast cancer, and 27% for distant-stage breast cancer.[4] Within a stage, survival also varies with tumor size. For example, among women with regional disease, 5-year survival (again, relative to comparable cancer-free women) is 95% for tumors smaller than 2 centimeters in diameter, 85% for tumors of 2-5 centimeters, and 72% for tumors greater than 5 centimeters.[5]

2.2 Mammography

Asymptomatic breast cancer can be detected by a mammogram, which is a low-dose x-ray procedure that allows visualization of the internal structure of the breast. If an abnormality is detected on a routine screening mammogram, the woman is typically called back in for a diagnostic mammogram and – if needed – a confirmatory biopsy (Cutler, 2008; Hubbard et al., 2011). Once a diagnosis has been confirmed, the patient may undergo surgery to remove the tumor, as well as other treatments which aim to reduce the risk of recurrence, such as radiation therapy, chemotherapy, hormone therapy, and/or targeted therapy.

Mammography is based on the theory of early detection of invasive cancer, rather than detection and removal of precancerous lesions (Humphrey et al., 2002). The efficacy of mammography is the subject of considerable debate. Mechanically, mammography is most beneficial if machines can detect tumors in their earliest stages, and if tumors (on average) rapidly become more difficult to treat the longer they go undetected. The benefits from mammography will be lower if a tumor is slow to advance from stage to stage, if mortality when treatment begins at a later stage is similar to when tumors are treated earlier, or if mammogram machines are unlikely to correctly identify tumors. In practice, because most patients diagnosed with breast cancer are treated immediately upon detection, there is little information about the natural history of breast cancer tumors, making it difficult to know how an individual tumor would have progressed had it not been treated (Zahl et al., 2008). This complicates attempts to quantify the benefits of mammography.

In principle, the major potential health benefit of mammography is reduced mortality. However, in practice randomized trials of the impact of mammogram on mortality have documented mixed results. There have been nine trials in total, with the first one dating back to the 1960s (Welch and Black, 2010). Their estimates of relative risk reduction in breast cancer mortality due to invitation to mammography range from 0% to 31% (Welch and Passow, 2014), but many of these studies have lacked the statistical power to separately determine effects in different age groups (Humphrey et al., 2002). In particular, while most studies indicate that mammography reduces mortality among average-risk women over age 50, recent trials specifically designed to study mammography in younger women (aged 40-49) have estimated statistically

[4]These tabulations are drawn from US SEER cancer registry data from 2007-2013, as in American Cancer Society (2017a).
[5]These tabulations are drawn from US SEER cancer registry data from 2000-2014, as in American Cancer Society (2017a).

insignificant reductions in breast cancer mortality in this age group (Bjurstam et al., 2003; Moss et al., 2006).

The potential costs of mammography include financial, physical, and psychological costs. These costs arise from the initial screening, the finding of false positives, and the treatment of cancers that would not have become clinically relevant in a woman's lifetime (often referred to as "over-diagnosis"). Some of these costs, such as the financial cost of a screening, are easy to quantify, while others are much more difficult to estimate. Estimates of the rate of over-diagnosis of breast cancer (from both observational work and inferences from randomized control trials) range from less than 5% to more than 50% of diagnosed breast cancers (Oeffinger et al., 2015). Aggregating observational data and randomized studies, Welch and Passow (2014) estimate that for every 1,000 women aged 40-49 who undergo annual mammography for 10 years, 0.1-1.6 women will avoid dying from breast cancer, while 510-690 will have at least one false positive result and up to 11 women will be over-diagnosed and (unnecessarily) treated.

In the 1980s, following the first randomized trials of routine mammography, the National Institutes of Health (NIH), the National Cancer Institute (NCI), and eleven other health care organizations issued recommendations for routine screenings of women over age 40 (Kolata, 2009). These recommendations became the subject of controversy over time as more trials were published, and the US federal government subsequently reconsidered its position. In 1997, an NIH panel concluded that there was insufficient evidence to recommend routine screening for women in their 40s, a finding that one radiologist described as a "death sentence" for women (Taubes, 1997). After public pressure, the Senate encouraged an advisory board to reject that conclusion (Kolata, 2009). In 2009, following the publication of experimental data that failed to show statistically significant mortality benefits of mammograms for women in their 40s, the US Preventive Services Task Force (USPSTF) recommended that women begin screening at age 50. Again, this conclusion generated backlash from patient advocacy groups like the American Cancer Society, which at the time recommended annual screening for women aged 40 and above (American Cancer Society, 2018).[6] This negative reaction was exacerbated by fears that the Affordable Care Act (ACA, then being drafted) would allow insurers to refuse to cover mammograms for younger women. The USPSTF stood by its recommendation, but a poll found that 84% of women aged 35-49 did not plan to follow the new recommendations, and the ACA was modified to mandate that insurers reimburse mammograms for women aged 40 and over (Saad, 2009). Although in the last few years most patient advocacy organizations have begun to moderate their stances, the question of whether mammography should be recommended in the 40-49 age group remains controversial.

Importantly, both the academic literature and the policy debate over the costs and benefits of mammograms has focused on the average impacts of mammograms for specific ages. In contrast, our focus is on the characteristics of women whose decision to get a mammogram is influenced by the mammogram recommendation, and how their underlying cancer incidence and characteristics may differ from that of a randomly selected woman in the population.

[6]The American Cancer Society currently recommends annual screening for women between ages 45-54 and screening every 2 years for women 55 years and older (American Cancer Society, 2018).

3 Data and descriptive patterns

3.1 Data and variable construction

Our analysis of mammogram choices and outcomes focuses on women aged 35-50 and draws on two primary data sources. The first is claim-level data provided by the Health Care Cost Institute (HCCI) consisting of all claims paid by three large commercial insurers (Aetna, Humana, and UnitedHealthcare) from January 2008 through December 2012. Together, these three insurers represented about one-quarter of individuals under age 65 with commercial insurance (HCCI, 2012). The data capture the billing-related information contained in the claims that these insurers pay out to medical providers; this includes the exact date and purpose of each claim, as well as the amount paid by the insurer and the amount owed out of pocket. The data also include a (masked) person identifier as well as the individual's birth year and gender.

The claim-level information in the HCCI data allow us to construct variables measuring whether an individual had a screening mammogram,[7] whether the result was positive or negative, and whether the positive result was true positive or false positive. Our coding of screening mammograms (hereafter "mammograms") – as well as their outcomes – broadly follows the approach of Segel, Balkrishnan,, and Hirth (2017), which we cross-validated using Medicare claims data linked to cancer registry data (see Appendix A for more details).

The original HCCI data contain about 28.7 million privately insured women aged 25-64, and over 70 million woman-years. We limit the data to woman-years aged 35-50 who are covered continuously for at least three years between January 2008 and December 2012; we keep all the years of coverage except the first and last (since for every woman-year we need to observe the previous year to define screening mammograms and the subsequent year to measure outcomes). This results in about 7.4 million woman-years, and 3.7 million distinct women.

The primary drawback of the HCCI data is that we are not able to observe information on a breast cancer diagnosis beyond its detection. To overcome this limitation of the HCCI data, we therefore also analyze the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) database. This is an administrative, patient-level cancer registry of all cancer diagnoses in 13 US states, covering about one quarter of the US population (SEER, 2019). We analyze all the breast cancer diagnoses in the data between 2000 and 2014 for women aged 35-50 at the time of diagnosis; this covers about 230,000 diagnoses. All cancer diagnoses are required to be reported, with data collected directly from the cancer patients' medical records at the time of diagnosis (rather than self reports).[8] For each diagnosed cancer, the SEER data contain information about the size and stage of each tumor at diagnosis. They also contain basic demographics for the patient including age at time of diagnosis, race, and insurance coverage, as well as subsequent mortality information through December 2013.

In our HCCI sample, the average woman's age is 43 and 27% of woman-years are under 40. In the

[7] A "screening mammogram" is a routine test that is conceptually different -- and coded differently in the data -- from a "diagnostic mammogram," which would typically follow the emergence of a possible breast cancer symptom (such as a positive screening mammogram).

[8] See `https://seer.cancer.gov/manuals/2018/SPCSM_2018_maindoc.pdf` for more information. SEER registries are required to collect data on persons who are diagnosed with cancer and who, at the time of diagnosis, are residents of the geographic area covered by the SEER registry.

SEER data, because cancer risk increases with age, the average age at diagnosis is a bit higher (44.7) and only 13% of the SEER diagnoses occur in women under 40. In SEER, where we can observe race, slightly over three-quarters of the sample is white. And unlike the HCCI data where, by construction, everyone is privately insured, in the SEER data only 84% are privately insured, while 13% are on Medicaid.

Table 1 documents mammogram rates and test results in the HCCI data. About 30% of woman-years are associated with a mammogram. The vast majority (89.6%) of mammograms are negative, and another 9.7% are false positives. Only 0.7% are true positives. Among all woman-years with a mammogram, total (insurer plus out-of-pocket) health care spending in the 12 months starting from (and including) the mammogram averages $4,900; while it is slightly higher (by ~$1,500) for those with a false positive, it is dramatically higher for those with true positives, averaging about $47,000. Out-of-pocket spending in the 12 months post mammogram is about $2,800 for women with a positive mammogram, compared to $710 for women with a negative mammogram and $915 for women with a false positive.

The SEER data provide more information on tumor stage and tumor size for the 230,000 true positives (i.e. diagnoses) we observe. Just over 15% are are in situ; the rest are invasive. Of the invasive, about 57% are localized, 38% are regional, and the remaining 5% are distant.

3.2 Mammograms and outcomes, by age

Figure 1 shows the age profile of annual mammogram rates in the HCCI data. Because we observe birth year, the mammogram rate at age, say, 40 is the share of women who got a mammogram in the year they turned 40. Between ages 39 and 41, the mammogram rate jumps by over 25 percentage points, from 8.9% to 35.2%. This pronounced jump in mammogram rates at age 40 has been previously documented in self-reported mammograms in survey data (Kadiyala and Strumpf, 2011, 2016).[9] One might be concerned that the existence of a recommendation for mammograms at age 40 could bias upward survey self reports at that age. However, our analysis using claims data confirms a real change in mammogram behavior at 40. Indeed, as we show in Appendix Figure A.1, the increase in mammogram rates that we estimate at age 40 in the HCCI data is very similar to what we estimate using survey self reports (from the Behavioral Risk Factor Surveillance System Survey, or BRFSS), although – consistent with prior work (Blustein, 1995; Cronin et al., 2009) – we estimate lower mammogram rates at every age in claims data compared to self-reported data.

Figure 2 documents the outcomes of these mammograms – negative, false positive, and true positive – in the HCCI data. Figure 2a documents that the vast majority (on the order of 85-90%) of mammograms are negative, and that almost all the remainder are false positive. Figure 2b narrows in on the rates of false positives and true positives by age. Between ages 39 and 41, the share of true positives falls by one-third (from 0.84% to 0.56%). This indicates that the marginal women who choose to have a mammogram because of the screening recommendation at age 40 have lower underlying rates of cancer (i.e. true positive diagnoses). The share of mammograms that are false positives is generally declining smoothly in age, because the prob-

[9] Our data span the time period when the 2009 US Preventive Services Task Force changed its recommendation for routine mammograms to begin at age 50 rather than at age 40. Past analyses such as Block et al. (2013) have documented that this appears to have had little affect on women's mammography behavior, which is not surprising given the substantial public controversy over this recommendation change.

ability of a false positive is higher for women with denser breast tissue, and density generally decreases with age (Susan G. Komen Foundation, 2018). The exception is a small "spike" in false positives around age 40; this likely is attributable to the fact that the probability of a false positive mammogram is highest for a woman's first mammogram (American Cancer Society, 2017b). Note, however, that while the share of false positives is trending fairly smoothly in age, the *number* of women experiencing a false positive rises considerably at age 40, given the 25 percentage point increase in the share of women having mammograms. Given an approximately 12 percent false positive rate around age 40, the increase in the share of women having mammograms due to the recommendations implies that the number of women experiencing a false positive quadruples, from about 10 to 40 per thousand women.

Figure 3 documents the age profile of tumor type among all diagnoses in the SEER data. Between ages 39 and 41, the share of detected tumors that are in situ (as opposed to invasive) rises by 6 percentage points, from 11.6 percent to 17.7 percent; this is consistent with prior findings from Kadiyala and Strumpf (2016). The average size of a detected tumor falls by over 9 percent, from 27mm at age 39 to 24.4mm at age 41, although the pattern is less dramatic since detected tumor size is also falling (albeit less rapidly) at earlier ages.

Taken together, these descriptive results from both the HCCI and SEER data suggest that the women brought into screening by the recommendation at age 40 have a lower cancer disease burden than those who sought screening prior to the age 40 recommendation. This manifests itself in lower rates of cancer, detection of cancer at earlier stages, and smaller tumors conditional on cancer detection.

In Figure 4 we return to the HCCI data to examine the implications of these findings for the age profile of spending in the 12 months post mammogram. Figure 4a shows, unsurprisingly, that healthcare spending increases with age, and is higher for individuals with mammograms than without. More interestingly, it also shows that the difference in spending between those with and without mammograms exhibits a pronounced decline at age 40. Figure 4b shows that spending is much higher for true positives than false positives and negatives, and that spending for true positives is increasing with age, but there is no obvious break at age 40.

Presumably therefore, the several hundred dollar decrease at age 40 in the average spending of those who get mammograms in Figure 4a reflects selection: those who select into mammograms due to the recommendation at age 40 have lower healthcare spending than those who choose to have mammograms prior to age 40. Indeed, we show in Appendix Figure A.2a that prior year spending among those who get mammograms drops precipitously at age 40, consistent with these individuals being healthier overall (in addition to having lower underlying incidence of cancer). Similarly, Appendix Figure A.2b shows a precipitous decline in the number of emergency room visits in the prior year for women who get mammograms starting at age 40, which may indicate better health and possibly better health behaviors. Women who select into mammograms following the age 40 recommendation also appear more prone to complying with other recommended preventive care: they have higher rates of pap tests (that is, cervical cancer screening tests) and flu shots in the year before the mammogram for those who select into mammograms at age 40 rather than at earlier ages (see Appendix Figures A.3a and A.3b). These results are consistent with Oster (2018)'s finding that when a health behavior is recommended, those who take up also tend to exhibit other positive health behaviors.

Finally, Figure 5 documents 5-year mortality post-diagnosis in the SEER data by age of diagnosis,

separately for tumors initially diagnosed as in situ and invasive tumors. Mortality is almost three times higher for invasive tumors compared to in-situ tumors. For example, at age 40, the five-year mortality rate is 17.2% for invasive tumors compared to 5.6% for in-situ tumors. However, the mortality rate is roughly flat by age within tumor type.

4 Model and estimation

The empirical patterns documented in the preceding section indicate that the women who respond to the mammogram recommendation have a lower incidence of cancer than those who seek mammograms in the absence of a recommendation. To evaluate the implications of this selection for alternative, counterfactual timings of the screening recommendation (such as at age 45 instead of age 40), we write down a stylized model of mammogram decision making. We then estimate this model using the observed patterns shown in Section 3 combined with a clinical oncology model of the underlying cancer incidence in the population and tumor evolution in the absence of detection. The clinical oncology model provides the (hitherto absent) crucial information on the cancer disease burden of women who respond to the mammogram recommendation compared to women who not get mammograms; naturally we explore sensitivity to alternative clinical assumptions.

4.1 A descriptive model of mammogram choice

We model the annual decision of whether or not to have a mammogram; annual decision frequency seems natural given that mammogram screening tends not to be done more frequently than once a year. Absent any recommendation to do so, we assume the "organic" decision to have a mammogram follows a simple probit, so that

$$Pr\left(m_{it}^{o}=1\right)=Pr\left(\alpha^{o}+\gamma^{o}a_{it}+\delta_{c}^{o}I(c_{it}=c)+\varepsilon_{it}^{o}>0\right), \tag{1}$$

where m_{it}^{o} is an indicator for whether woman i had a mammogram in year t, a_{it} is woman i's age in year t, c_{it} describes woman i's undiagnosed cancer status in year t, and ε_{it}^{o} is a (standard) normally distributed error term. Following our discussion in Section 3, our baseline specification summarizes cancer status c_{it} with two indicator variables, one that indicates an in-situ tumor and another that indicates an invasive tumor; the omitted category is no cancer.

If it is recommended that woman i obtain a mammogram, we model her response to the recommendation as a second, subsequent decision that is taken within the same year. That is, if a woman has already decided to have a mammogram "organically" based on equation (1), a recommendation has no additional impact. But for women who decided not to have a mammogram organically (that is, $m_{it}^{o}=0$), a second decision point arises due to the recommendation, and we model this second decision point in a similar fashion, except that

the parameters are allowed to be different:

$$Pr\left(m_{it}^{r}=1|m_{it}^{o}=0\right)=Pr\left(\alpha^{r}+\gamma^{r}a_{it}+\delta_{c}^{r}I(c_{it}=c)+\varepsilon_{it}^{r}>0\right), \tag{2}$$

where ε_{it}^{r} is a (standard) normally distributed error term, drawn independently from ε_{it}^{o}.[10] This model assumes that the impact of the recommendation is (weakly) monotone for all women. For each woman, it only increases the probability that she has a mammogram, a feature that seems (to us) natural.

Since we do not directly observe whether a mammogram was taken for organic reasons or in response to a recommendation, the probability that woman i obtains a mammogram in year t is given by

$$Pr\left(m_{it}=1\right)=\begin{cases} Pr\left(m_{it}^{o}=1\right) & \text{if not recommended} \\ Pr\left(m_{it}^{o}=1\right)+Pr\left(m_{it}^{r}=1|m_{it}^{o}=0\right)Pr\left(m_{it}^{o}=0\right) & \text{if recommended} \end{cases}.$$

We use the model's results to quantify the degree of selection into mammograms in the presence and absence of a recommendation, and to examine how the nature of this selection affects the impact of recommendations. To do so, we use the model estimates to predict mammogram rates and mammogram outcomes under the current recommendation to begin mammograms at age 40 as well as under a counterfactual recommendation to begin at age 45. Consistent with our focus on selection, we also examine how alternative, counterfactual selection into mammograms in response to the recommendation would change the impact of changing the recommended age at which to begin mammograms from 40 to 45.

Discussion

Importantly, this is a descriptive, or statistical model of mammogram choice, rather than a behavioral one. This is most apparent from the fact that we use the cancer status c_{it} as an explanatory variable, when naturally this cancer status is unknown by undiagnosed women. Cancer status c_{it} is also unobserved by the econometrician; we describe below the clinical model of tumor evolution which we use to "fill in" these missing data, thus essentially integrating over the population distribution of this cancer status component.

We take this modeling approach for several reasons. First, many of the outcomes in this setting are difficult to assess or monetize, e.g. the stress and anxiety associated with false positive test results or the non-monetary costs associated with the breast cancer treatment (even if successful). This makes it difficult to translate the rich set of outcomes into a single metric of utility. Second, our key focus is on the impact of the recommendation policy. With a perfectly informed population of patients, recommendations should have no impact, yet the data in Section 3 show a clear increase in the mammogram rate in response to the age 40 recommendation. We could try to attribute this recommendation-induced increase in mammogram rate to improved information, but this would require us to make assumptions about what type of information is being revealed and how, or why patients did not have such information to begin with. We prefer instead to remain agnostic about the behavioral channel by which the recommendation affects screening rates. Finally,

[10] While this independence assumption may appear restrictive, note that equation (2) only applies to those women who elected not to obtain an "organic" mammogram. It is therefore effectively restricted to women with "low enough" ε_{it}^{o}'s, so that much of the potential correlation is already conditioned out.

a descriptive model of decision making does not require us to try to reconcile observed patterns of decisions with optimal behavior, or model deviations from optimality. The drawback is, of course, that we will not be able to engage in other policy changes or in the impact of changes in the recommendation policy on patient welfare directly, but rather will only evaluate changes in recommendation policies through their effect on observed outcomes.

Another key feature of our setup is that we model the mammogram decision to be a static – and perhaps naive – one. The decision is static in the sense that we assume individuals do not take into account, for example, the time elapsed since their most recent mammogram (if any).[11] The decision is naive in the sense that we assume that women, when deciding to get a mammogram or not, do not explicitly take into account their propensity to get a mammogram in future years. This assumption seems not unrealistic, and simplifies the model. This assumption is particularly important in the context of our counterfactual exercise, which holds the estimated model as given while we change the age at which it is recommended to begin mammograms. Specifically, in considering the changes that occur when the mammogram recommendation begins at age 45 instead of 40, our static model assumes this would have no impact on women aged 39 or younger; in a dynamic model with forward looking agents, however, it could increase the propensity of women below age 40 to get a mammogram. Our current model could in principle capture such dynamics implicitly by allowing serial correlation in ε_{it}^{o} and in ε_{it}^{r}. However, because we have a relatively short panel, and because we only use age to match the two main data sets, it would be hard to identify such a serial correlation structure. Consistent with this being a fairly inconsequential assumption, Figure 2 shows very low rates of pre-recommendation mammograms, and no evidence that mammograms decline in the year or two years that are right before age 40 (when forward looking women might anticipate their future mammogram).

4.2 Implementation

A clinical model of tumor appearance and evolution

To complete the empirical specification, we specify a clinical oncology model of tumor appearance and tumor evolution, which allows us to "fill in" cancer status for women who do not get diagnosed. This clinical model delivers two key elements. First, it produces the underlying incidence of cancer (and cancer type) by age; this cannot be directly observed in data since cancer incidence is only observed conditional on screening. Second, it provides (counterfactual) predictions of the rate at which tumors would progress in the absence of detection and treatment (the so-called "natural history" of the tumor); since breast cancer is usually treated once diagnosed, rather than being monitored without treatment, it is difficult (perhaps impossible) to directly estimate the natural history of tumors from existing data.

For the clinical model, we draw on an active literature creating clinical/biological models of cancer arrival and growth. Specifically, we draw on the work of the Cancer Intervention and Surveillance Modeling

[11] While restrictive, there is no strong evidence of such dynamic patterns in the data. We only have a short panel of at most three years for each woman, so it is difficult to apply any formal statistical testing. However, conditional on having two mammograms during the three years we observe (2009-2011), the frequency of getting a mammogram "every other year" (that is, getting mammograms in 2009 and 2011 but not in 2010) is not more likely than getting a mammogram in consecutive years (34%, relative to 39% for 2009 and 2010, and 27% for 2010 and 2011).

Network (CISNET) project funded by the National Cancer Institute to analyze the role of mammography in contributing to breast cancer mortality reductions over the last quarter of the 20th century. As part of this effort, seven different groups[12] developed models of breast cancer incidence and progression (Clarke et al., 2006). For convenience, we focus on one of these models, the Erasmus model (Tan et al., 2006). We also show robustness of our results below to alternative specifications designed to produce markedly different estimates for the key objects: namely, the underlying incidence of cancer and cancer types.

We briefly summarize the Erasmus model here; Appendix B describes the model in much more detail. Starting with a cancer-free population of 20-year-old women, the Erasmus model assumes that breast tumors appear at a given age-specific rate (that is increasing in age). When they appear, tumors are endowed with a given invasive potential and initial rate of growth, and then evolve accordingly over time with respect to those two characteristics. Tumors can either be invasive, leading to death of the patient if not detected early enough, or be in situ. In-situ tumors are not themselves harmful but may either transform into a harmful invasive tumor or remain benign. In some sense, a key issue in the debate over mammograms is the extent to which tumors that are detected early (e.g. in-situ tumors) would have become harmful if not detected or would have remained benign; Marmot et al. (2013) discusses how, depending on the method of analysis, a wide variety of estimates can be obtained when trying to answer this question. The Erasmus model further classifies tumors by whether or not they are detectable by screening, which in the case of invasive tumors depends on their size and in the case of in-situ tumors depends on their sub type. Finally, the model assumes that beyond a certain size, invasive tumors are fatal.

The original Erasmus model was calibrated using a combination of Swedish trial data and US (SEER) population data. To better match the cancer incidence rates from the SEER (birth cohorts 1950-1975), we introduce a proportional shifter of overall cancer incidence and calibrate this parameter on the SEER data. Appendix Figure A.4 shows the calibrated model's predictions – under the assumption of no screening – of the share of women with cancer at each age, and the share of existing cancers that are in situ (rather than invasive) by age.

Estimation and Identification

We estimate the model using method of moments. The observed moments we try to match are the mammogram screening rate at each age (Figure 1), the true positive rate at each age (Figure 2b), and the share of tumors at each age that are in situ conditional on true positive (as in Figure 3).[13] Because identification is primarily driven by the discontinuous change in screening rates at age 40, we weight more heavily moments that are closer to age 40 than moments that are associated with younger and older ages.[14]

[12] The composition of the CISNET consortium has changed over time, but the seven groups who produced models for the original publication in 2006 were affiliated with the Dana-Farber Cancer Center, Erasmus University Rotterdam, Georgetown University Medical Center, University of Texas M.D. Anderson Cancer Center, Stanford University, University of Rochester, and University of Wisconsin-Madison.

[13] Figure 3 shows the share of all diagnosed cancers (in the SEER data) that are in situ, but the model produces a different metric: the share of *screening mammogram-diagnosed cancers* that are in situ. Cancers that are clinically diagnosed are highly unlikely to be in situ, so the SEER value likely underestimates the true value of share in situ for screening mammogram-diagnosed cancers. Appendix C describes how we adjust the SEER moments to account for this.

[14] Specifically, the weight on moments associated with ages 39 and 41 is 10/11 of the weight on the age 40 moment, the weight on moments associated with ages 38 and 42 is 9/11 of the weight on the age 40 moment, and so on.

To generate the corresponding model-generated moments, we simulate a panel of women starting at age 20, and use the clinical model described above to generate cancer incidence and tumor growth for each woman. We then apply our mammogram decision model, by age and recommendation status, to each simulated woman who is alive and has yet to be diagnosed with cancer. The simulated cohort allows us to see the fraction of women with a detectable (by mammogram) tumor at each age, and thus generate the mammogram rate, and the true positive rate (by cancer type) conditional on screening. As mentioned above, for cancer type, we distinguish only between in-situ and invasive tumors.

With this simulated population of women, an assumed value of parameters associated with the mammogram decisions with and without recommendation (equations 1 and 2) and the observed policy recommendation (40 and above), the model generates an age-specific share of women who are screened, and the tumor characteristics (in-situ and invasive rates), conditional on getting screened. We then search for the parameters that minimize the (weighted) distance between these generated moments and the observed moments described above.

Although the model is static, it does have a dynamic element because we calculate the model-generated moments only for women who were not diagnosed with cancer in previous years, and for those who did not die (from breast cancer or other causes) prior to the given age. Specifically, because the mammogram decision applies to women who have yet to be diagnosed with cancer, fitting the model requires calculating the rate of cancer among the population who is eligible to be screened, which includes those who have currently undiagnosed cancer or no cancer, but does not include those who are dead or already diagnosed. Appendix C provides more detail on this and other aspects of the estimation.

For our counterfactual exercises, the estimates from the mammogram choice model – and the assumption that choices would be smooth in age through age 40 in the absence of the recommendation – allow us to predict mammogram decisions and outcomes under counterfactual scenarios. Crucially, the model estimates allow us to forecast the cancer characteristics of women who (counterfactually) do not get screened and whose cancer may therefore progress in the absence of diagnosis. The key parameters are δ^o and δ^r, which capture the nature of selection into mammogram screening. Positive selection (i.e. positive δ) implies that women with cancer (or with invasive vs. in-situ cancer) are more likely to get a mammogram than are woman without cancer. A negative δ implies the opposite. Both types of selection are plausible. Positive selection could arise, for example, if women with a greater risk of breast cancer (e.g. due to family history) are more likely to get a mammogram; negative selection could arise, for example, if women with certain underlying characteristics (e.g. risk aversion) are both more likely to get a mammogram and also more likely to avoid risk factors linked to breast cancer. Importantly, by allowing δ^o and δ^r to be different, the model allows for the nature of selection to be different for organic and recommendation-driven mammograms. Identification of these selection effects is driven by comparing the share of cancer in the population (which is "data" provided by the clinical oncology model) to the true positive mammogram rates. The extent to which this relationship changes discretely at age 40, when the recommendation kicks in, allows us to separately identify δ^o and δ^r.

5 The impact of alternative screening policies

5.1 Model fit and parameter estimates

Figure 6 presents the model fit to the key moments, which we view as quite reasonable. The parameter estimates are shown in Table 2. It may be easiest to see the implications of these parameters in the context of our counterfactual results, but one can already infer the general pattern by focusing on the four δ parameters, which indicate the extent of selection into mammogram. The two δ^o parameters are positive and relatively large, indicating strong positive selection into the "organic" decision to have a mammogram. For example, for the average woman-year in the sample (that is, using the distribution of ages in the sample), the estimated coefficients imply that the "organic" mammogram rates for women with either an in-situ or invasive tumor are much higher (0.30 and 0.57, respectively) relative to the "organic" mammogram rates for cancer-free women (0.20).

In contrast, the two δ^r parameters tell a different story. The estimates suggest that there is no differential selection into the "recommended" decision for women with in-situ tumors (relative to cancer-free women), and that essentially no woman with an invasive tumor selects into mammogram due to the recommendation. This result is driven by precisely the patterns in the data that identify these parameters, and which were presented in Figure 3. Namely, conditional on diagnosis, the share of in-situ tumors rises sharply at age 40, so that virtually all the increase in detected cancers reflects in-situ tumors. As we show below, this pattern has a critical effect on our results, because women without cancer or with in-situ tumors – who constitute the primary incremental positive mammogram results – may not face drastic health implications if those tumors would instead be discovered several years later.

We note that the large standard errors on $\delta^o_{invasive}$ and $\delta^r_{invasive}$ reflect the fact that the estimates imply that virtually all women with invasive tumors who get screened do so organically, with essentially no women with invasive tumors getting screened in response to the recommendation; as a result, the likelihood function is fairly flat for high values of $\delta^o_{invasive}$ and low values of $\delta^r_{invasive}$. But for exactly the same reason, these imprecise estimates of the parameter have little impact on the counterfactual results, as reflected by the much tighter standard errors associated with the counterfactuals of interest reported in the next section.

5.2 Implications

We apply the estimated parameters from Table 2 to analyze outcomes under various counterfactual recommendations. For concreteness, we focus on outcomes under the current recommendation to begin mammograms at age 40 as well as under a counterfactual recommendation to begin at age 45. Our model is well suited for such a counterfactual exercise: we simply assume that mammogram decisions are based on the "organic" decision until age 45, and only at age 45 is there a second, recommendation-induced decision. Given the static nature of the model, mammogram rates will remain the same until age 40, and would be the same (conditional on cancer status) from age 45 and on, but will decrease for women aged 40-44 without a recommendation. We choose a counterfactual recommendation that begins at age 45 because this is not too far out of sample, and also in the range of realistic policy alternatives; Canada, for instance, recommends routine screening beginning at age 50 (Kadiyala and Strumpf, 2011).

For both the age 40 and age 45 recommendations, we examine how alternative, counterfactual selection into mammograms in response to the recommendation would change the recommendation's impact. The main outcomes we generate under the various counterfactuals are age-specific mammogram rates, mammogram outcomes (specifically, negative, false positive, and true positive, as well as tumor type), total health care spending, and mortality. We do not attempt to quantify other potential consequences of a change in recommendation (such as the opportunity to use less invasive treatments for early-stage diagnoses, or increased anxiety from false positive results, which are more uncertain (Welch and Passow, 2014)).

Throughout the counterfactual exercises, mammogram rates are generated directly from the parameter estimates in Table 2, and mammogram outcomes are generated based on the the parameter estimates in Table 2 and the underlying incidence and natural history of breast cancer tumors from the Erasmus model. We also use the Erasmus model's parameters in order to map detection of tumors to subsequent mortality, allowing us to translate the estimated changes in detection into implied changes in mortality. Finally, we use the auxiliary data from Figure 4 on how healthcare spending varies with age and mammogram outcomes to translate the estimated change in mammogram rates and mammogram outcomes into implied spending changes. Appendix D provides more details behind these counterfactual calculations.

5.2.1 Shifting the age of recommendation from 40 to 45

Table 3 shows the implications of shifting the recommendation from age 40 to age 45, given the estimated response to recommendations from Table 2. We focus on the implications for women ages 35-50.

Panel A summarizes the implications for screening and spending; Figure 7 shows how the age profile of screening and screening outcomes change with this counterfactual. Changing the recommended age from 40 to 45 reduces the average number of mammograms a woman receives between ages 35 and 50 from 4.7 to 3.8, an almost 20 percent decline. By design, all of the "lost" mammograms occur between ages 40 and 44. Naturally, the vast majority of these "lost" mammograms would have been negative (89.5%) or false positive (10.4%). Moving the recommendation to age 45 decreases the average number of false positives a woman experiences over age 30-45 by 0.09. The fraction of true positive mammograms that are "lost" due to the later recommendation, while small in absolute number (0.0004 per woman), is not negligible, and it constitutes an approximately 6% reduction in the cancer detection rate. Of the "lost" true positives, however, all are in situ since our estimates imply that the recommendation effectively induces no additional women with invasive cancer to get screened. Thus, any changes in mortality are due to in-situ tumors that go unscreened and later become invasive.

The last row of Panel A shows that changing the recommendation age to 45 reduces total healthcare spending over ages 35-50 per woman by about $320, or about half a percent. This reduction in spending arises from a combination of a level and composition effect. The dominant factor is naturally the decline in the overall number of mammograms. We estimate that women who have a mammogram in a given year are expected to spend approximately $490 more (on average, averaging over ages 40-44) over the subsequent 12 months relative to women with no mammograms, and that moving the recommendation age to 45 results in 0.9 fewer mammograms per woman. This would mechanically result in approximately $440 lower spending. The estimated spending reduction is lower ($320) because of selection. The "lost" mammograms

are disproportionally negative or false positive, and the true positive mammogram results are associated with, by far, the highest expected subsequent spending (see Figure 4b). true positive mammograms account for a larger share of mammograms in the counterfactual scenario (0.53%, relative to 0.44% under age-40 recommendation).

Panel B documents the implications of this counterfactual for health outcomes. The lower detection rate of cancers is associated with 5 more women per 100,000 who are dead by the age of 50; all of this increase in deaths comes from increased breast cancer mortality. The results thus suggest that, relative to an age-45 recommendation, an age-40 recommendation increases spending by about $32 million per 100,000 women (during their 35-50 age span), and prevents about 5 additional deaths by age 50 per 100,000 women; the cost per life saved is thus about $6 million.

Naturally, these mortality implications are driven by the assumptions in the clinical oncology model, about which there is a range of views (Clarke et al., 2006; Welch and Passow, 2014). In addition, our analysis considers only the costs in terms of health care spending, and does not consider the disutility of stress and anxiety created by false positives or additional medical care. For both reasons, our goal here is not to emphasize a specific estimate of the cost per life saved per se, but rather to examine whether and how this type of counterfactual policy exercise can be affected by the nature of selection into mammograms in response to the recommendation, a question we turn to in the next section.

5.2.2 Consequences of selection patterns in response to mammogram

Table 4 illustrates the importance of selection in response to the recommendation. To do so, Panel A replicates the results from Table 3, while Panels B and C contrast them with what the results would be under alternative selection responses to the recommendation. Under both alternative selection models, we maintain our estimated selection associated with the "organic" mammogram decision, but vary the nature of selection into mammograms in response to the recommendation. One case (Panel B) assumes no selection, which is conceptually consistent with the idea of using estimated mammogram treatment effects from randomized experiments to inform the recommendation policy (as in, for example, Welch and Passow (2014)); in practice we do this by assuming that $\delta^r = 0$.[15] The other case (Panel C) assumes that selection in response to the recommendation is positive, and is the same as in the "organic" decision; we implement this counterfactual by assuming that δ^r is equal to our estimated δ^o.

In both counterfactual selection cases we consider, we adjust the model to maintain the same age-specific mammogram rates under a given recommendation regardless of the assumed selection, so that only the nature of selection changes; Appendix D provides more detail. By design, therefore, the mammogram rates (first row of each panel) remain almost the same across all three selection models,[16] and therefore

[15] Note that we here have in mind a *conceptual* randomized experiment with full compliance. Of course, in practice, full compliance is rare, and the complier population to the experiment is itself not random, although it may be differentially selected from the complier population to the recommendation. In a recent paper, Kowalski (2018) argues that in practice the women most likely to receive mammograms when encouraged to do so in a randomized clinical trial are healthier, and hence benefit less from mammograms.

[16] Although not seen in the table due to rounding, the mammogram rates are not exactly the same across the panels because the nature of selection leads to differential mortality (discussed below), which in turn (slightly) affects the set of women "eligible" for a screening mammogram.

the spending effect associated with each of these cases also remains almost identical (second row of each panel). In contrast, the importance of selection is shown in the third row of each panel: different patterns of selection affect the reduction in deaths from moving the recommendation to age 40 compared to age 45. For example, while our estimates that are based on observed selection imply that moving the recommendation from 45 to 40 saves 5 additional lives (by age 50) per 100,000 women, which corresponds to a cost of about $6.3 million per life saved, random selection would imply over three times as many lives saved (18 per 100,000), corresponding to a cost of about $1.9 million per life saved. At a more extreme case of selection, assuming that the strong positive selection associated with "organic" selection would also apply to the selection in response to the recommendation, would imply almost nine times as many lives saved (45 per 100,000 women), corresponding to a cost per life saved of about $0.86 million.

The qualitative results are intuitive. As selection associated with the recommendation is more negative (i.e. women who respond are less likely to have cancer), the recommendation for earlier mammograms is less effective in finding tumors that would have not been found otherwise or tumors that would otherwise be found only later. However, if the selection associated with the recommendation were very positive (i.e. women who respond are more likely to have cancer), an earlier recommendation would be more effective. Thus, out of the three selection scenarios considered, earlier recommendation is most beneficial if the selection response to the recommendation is the same as under "organic" selection, which was highly positive (Panel C). While it is not immediately clear how in practice to achieve such strong positive selection in response to the recommendation, this result suggests that better targeting of the recommended mammogram to women with higher a-priori risk of cancer could – if feasible – have dramatic effects on the mortality benefits from the recommendation.[17] The comparison between our estimated selection (panel A) and the "no selection" case (panel B) is an intermediate case. Because we estimate negative selection for invasive tumors, an earlier recommendation is more effective (i.e. more women with cancer would be screened) under random selection, and the cost per life saved is therefore be lower.

5.2.3 Sensitivity

We observe in the data (see Figures 2b and 3) that those who select into screening via the recommendation are healthier than those get screened organically prior to the recommendation. However, a key question underlying our results is how women who are screened compare to those who do not get mammograms. In particular, we need to make assumptions about how the health of these women would have developed if they were screened at a later age instead. These assumptions depend on the underlying natural history ("clinical") model of breast cancer. We therefore examine the sensitivity of our conclusions to changing key features of this model.

This sensitivity analysis serves to highlight a point we have tried to emphasize throughout: the reader should not place much (or any) weight on our particular, quantitative estimates of the cost per life saved

[17] The potential benefits of personalizing breast cancer screening recommendations have been made in the medical literature (e.g. Schousboe et al. (2011)), and current breast cancer screening recommendations often differ across average risk and high risk women (where the latter is, e.g., women with a family history of breast cancer). But to the best of our knowledge our point about selection responses to recommendations has not been made previously. Our consistent selection model is one way of illustrating the potential gains from recommendation designs that affect take-up of mammograms based on unobservables.

of having the recommended age to start screening at 40 instead of at 45; these are quite sensitive to the assumptions underlying the clinical model. By contrast, the question we focus on – how the nature of the selection response to the recommendation affects any estimate of the impact of an earlier recommendation – is less affected by the specific clinical model.

We focus on three different adjustments to the Erasmus clinical model that we use; the details can be found in Appendix E. First, as discussed in Section 4.2, in our baseline analysis we adjusted upward the original Erasmus estimates of the underlying incidence rate of cancer to match the US population, rather than the combination of Swedish and US data on which it was originally calibrated (see Appendix B); in our first sensitivity analysis, we undo this adjustment and use the original Erasmus incidence assumptions. Second, the Erasmus model implies that almost two-thirds of in-situ tumors will become invasive if not treated; a review of the literature suggests that this is on the high end of model estimates, which range from 14% to 60% (Burstein et al., 2004). We therefore examine sensitivity to adjusting the model so that only 14% or 28% of in-situ tumors will become invasive, rather than the 62.5% in our baseline model. Finally, the Erasmus model implies that about 6% of all tumors for women aged 35-50 are non-malignant, i.e. have no potential to be invasive and therefore would never result in a breast cancer mortality. In contrast, another clinical model – the Wisconsin model (Fryback et al., 2006) – implies a much higher share (42%) of non-malignant tumors, while an estimate from a randomized control trial (in which women in the control group were not invited to be screened at the end of the active trial period) suggests that 19% of tumors would not have become malignant (Marmot et al., 2013). We therefore increase the share of in-situ tumors with no malignant potential at all ages in a proportional shift so that the share of non-malignant tumors at age 40 is either 19% or 42%.

For each sensitivity analysis, we first reproduce the Erasmus model natural history with the appropriate adjustments. We then re-estimate the mammogram decision model using the same data moments (see Figure 6) and the women simulated using the revised natural history model. To construct counterfactuals, we apply the new parameter estimates to the revised natural history model. Qualitatively, we can anticipate the impact of these changes: reducing the overall incidence of cancer, reducing the share in situ that will transition to invasive, and increasing the share non-malignant all serve to make screening less effective, and therefore delaying screening becomes less consequential.

The results are summarized in Table 5. As we emphasized earlier, the details of the model are critical for the quantitative results, and indeed the mortality levels vary considerably compared to the baseline model in all specifications. In addition, the mortality cost of delaying the recommendation falls. This occurs for two reasons. First, conditional on the same mammogram decision model estimates, screening is less effective with fewer malignant tumors. Therefore, delaying screening is less costly. In addition, changing the share of tumors that are non-malignant affects the estimation of $\delta^r_{in-situ}$ as shown in Appendix Table A.10. In these sensitivity checks, $\delta^r_{in-situ}$ is lower than in the baseline estimates. This occurs because the natural history model now has more in-situ tumors. One of the moments we match is the share of in-situ tumors among diagnoses. In order to observe the same amount of in-situ diagnoses with more underlying in-situ tumors, we must be screening fewer in-situ women and more invasive women. The magnitude of this selection change depends on the magnitude of the change in the sensitivity specification; the last specification is the

most aggressive in increasing the in-situ tumor share. Since the women who chose to get screened due to the recommendation now have fewer in-situ tumors (which could potentially become invasive), screening is less effective as well.

More importantly, we also examine how these sensitivity analyses affect our selection results, and here we find that the qualitative conclusions are quite robust. In all cases except one (the incidence shift, reported in row (1) of Table 5)**,** moving from the estimated selection to no selection (or consistent selection) has a large (relative) effect on the number of women who die by age 50. The intuition is as in the baseline model. Under the estimated selection, the women who select into the recommendation are healthier and less likely to have invasive or in-situ cancer. Therefore, the cost of delaying the recommendation (in terms of lives lost) is low. If there were no selection, the women who responded to the recommendation would be more likely to have cancer than in the estimated selection specification. Thus delaying the recommendation would have a higher cost in terms of an increase in deaths. Finally, if there were consistent selection, the women who chose to get screened due the recommendation would be more likely to have cancer. In this case, the recommendation would be highly effective and delaying screening would be very costly in terms of mortality. The one exercise for which this result does not hold is the incidence shift, since in this case the re-estimated mammogram decision model has one different parameter sign. As shown in Appendix Table A.10, in this case $\delta^r_{in-situ}$ is positive, implying recommendation-induced positive selection.

6 Conclusions

The debate over whether and when to recommend screening for a particular disease involves a host of empirical and conceptual challenges with which the existing literature has grappled, including how to estimate the "health" return to early screening, how to measure non-health benefits or costs, and how to monetize all of these factors (Humphrey et al., 2002; Nelson et al., 2009; Marmot et al., 2013; Welch and Passow, 2014; Ong and Mandl, 2015). We make no pretense of "resolving" these issues. Instead, we suggest an additional important and largely overlooked factor that can – and should – be considered: the nature of selection in response to the recommendation.

We illustrate this point in the specific context of the (controversial) recommendation that women should begin regular mammogram screenings at age 40. We document that this recommendation is associated with a sharp (25 percentage point) increase in mammogram rates, and that those who respond to the recommendation have substantially lower rates of cancer incidence than those who choose to get mammograms in the absence of the recommendation (i.e. before age 40); conditional on having cancer, women who respond to the recommendation also have lower rates of the more lethal invasive cancer, relative to the less lethal in situ cancer. These data speak directly to the relative cancer risks of women who select mammograms in the absence and presence of a recommendation. To further assess how the cancer risk of those who select mammograms either pre or post recommendation compare to those who do not select mammograms, we draw on a clinical oncology model to provide the underlying cancer incidence in the non-screened population (since this is not directly observed). These results suggest that those who choose mammograms in the absence of a recommendation have substantially higher rates of both invasive and in situ cancer than women who do not

get screened; women who choose mammograms in response to the recommendation have similar rates of in situ cancer to unscreened women but much *lower* rates of invasive cancer than unscreened women.

To illustrate the potential consequences of these selection responses to recommendations, we write down a stylized model of the mammogram decision – which depends on age, cancer status, and recommendation. We estimate this model using the observed empirical patterns combined with the clinical oncology model, the latter of which provides both the underlying incidence of cancer and the (counterfactual) tumor evolution in the absence of detection. We then apply the model to assess the implications for spending and mortality of changing the recommended age for beginning mammograms from 40 to 45. The specific numbers that we estimate will be naturally sensitive to the modeling assumptions, and – moreover – our estimates do not attempt to measure the potential impacts of mammograms on outcomes such as stress.

Our focus instead is on the consequences of the selection response to the recommendation, which our estimates suggest are non-trivial. Specifically, we consider the impact of moving the recommended age of mammograms from 45 to 40, and how this varies under alternative selection responses to the recommendation; we hold the change in mammogram rates (and consequently the cost increase) from changing the recommendation constant, and show that the mortality implications from earlier recommended mammograms vary markedly with selection patterns. For example, under the observed selection pattern, the number of lives saved by moving the recommendation from age 45 to 40 is less than a third what it would be if those who responded to the recommendation were instead drawn at random from the population. This difference arises because we estimate that those who respond to the recommendation have much lower rates of invasive cancer than the general population. Conversely, our results also suggest that if it were feasible to target the recommendations to those with higher rates of cancer, shifting the recommendation from age 45 to 40 would save substantially more lives than either the observed selection patterns or random selection.

Our findings suggest that future work exploring how recommendations can be designed to affect the behavior of higher risk individuals could have important welfare implications. More broadly, our findings suggest that the ongoing debates over whether and when to recommend screening for a disease should consider not only average costs and benefits from screening, but also the nature of selection associated with those who respond to the recommendation.

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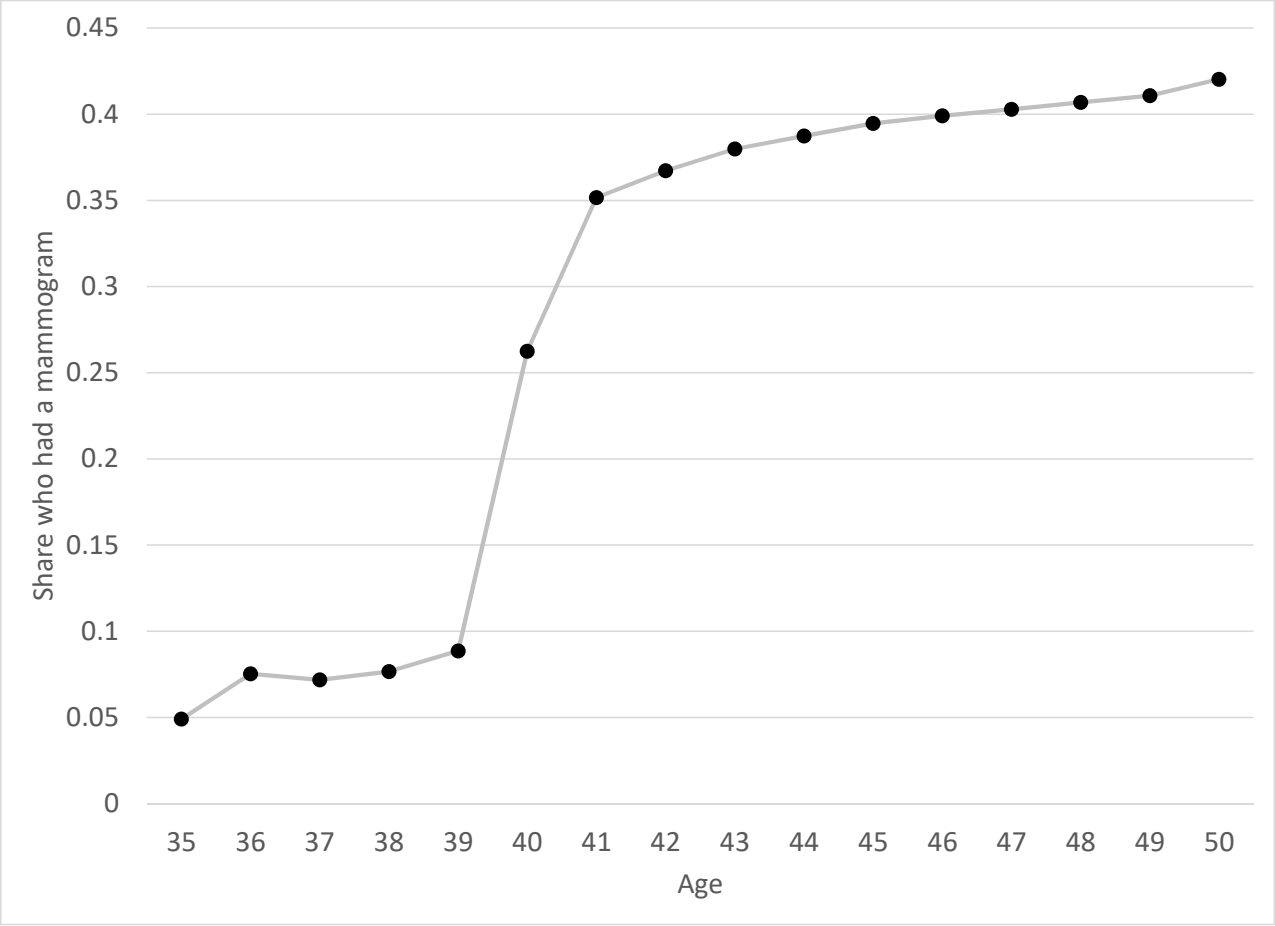
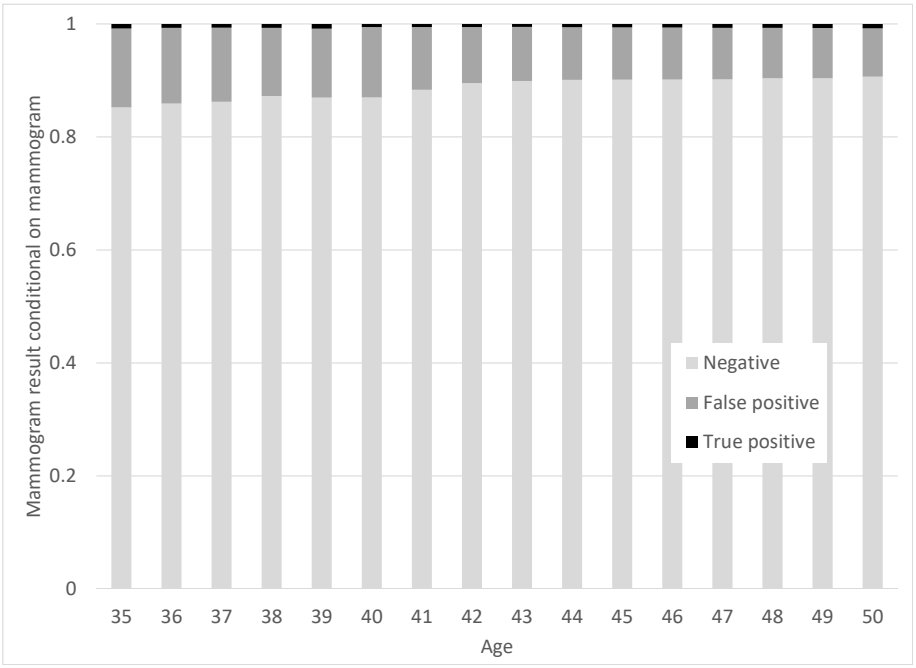
Figure 1: Mammogram rates by age

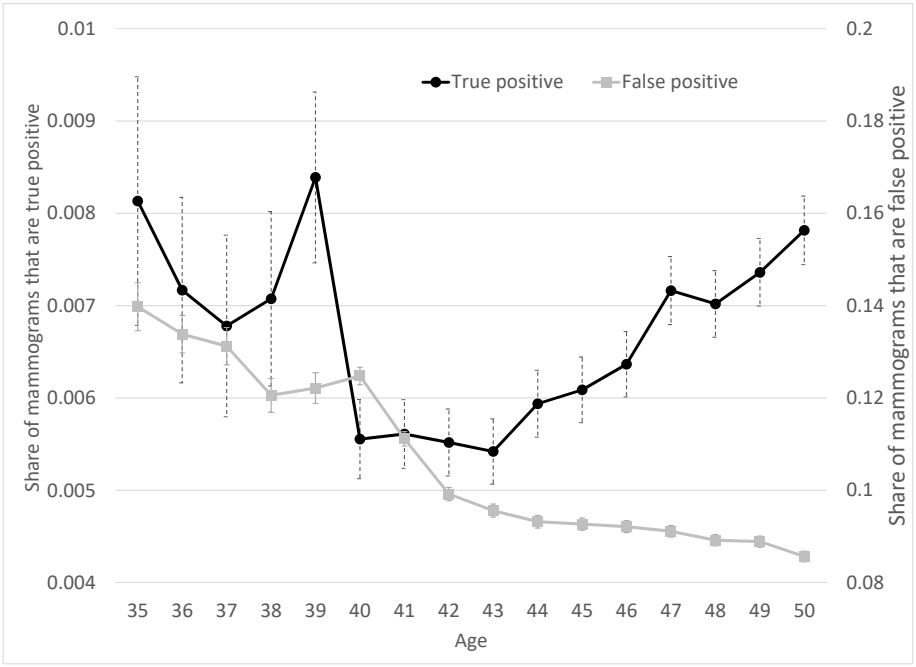


Notes: Figure shows share of women who had a mammogram by age, from insurance claims data on a set of privately insured woman-years from 2009- 2011. Because we observe birth year, age is measured as of the start of the calendar year. Thus the mammogram rate at age 40 is the share of women who got a mammogram in the year they turned 40. Error bars (small, and therefore not visible in the figure) reflect 95% confidence intervals. N = 7,373,302 woman-years.

Figure 2: Mammogram outcomes by age



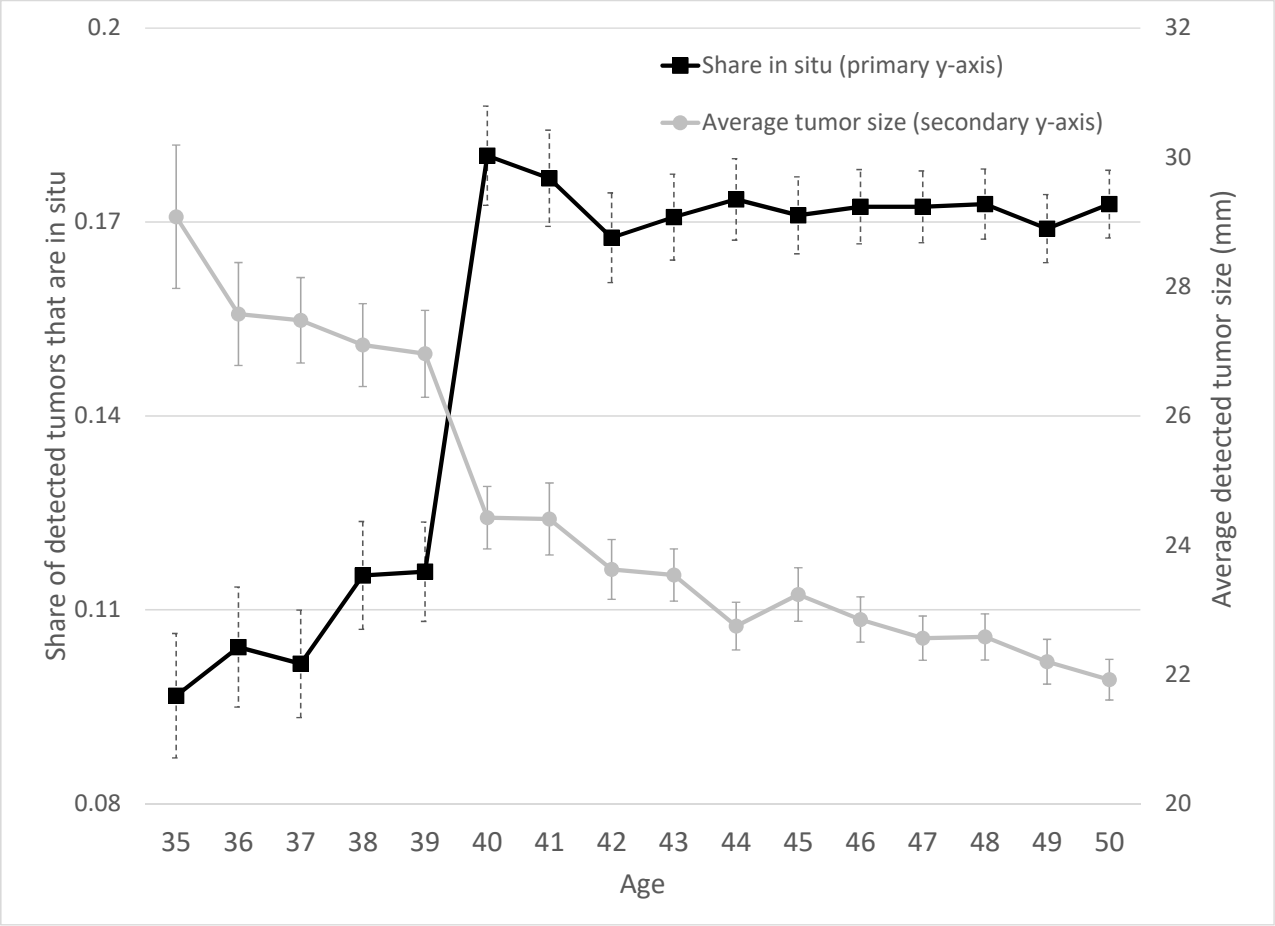
(a) Mammogram Results Conditional on Mammogram



(b) Share True Positive and False Positive

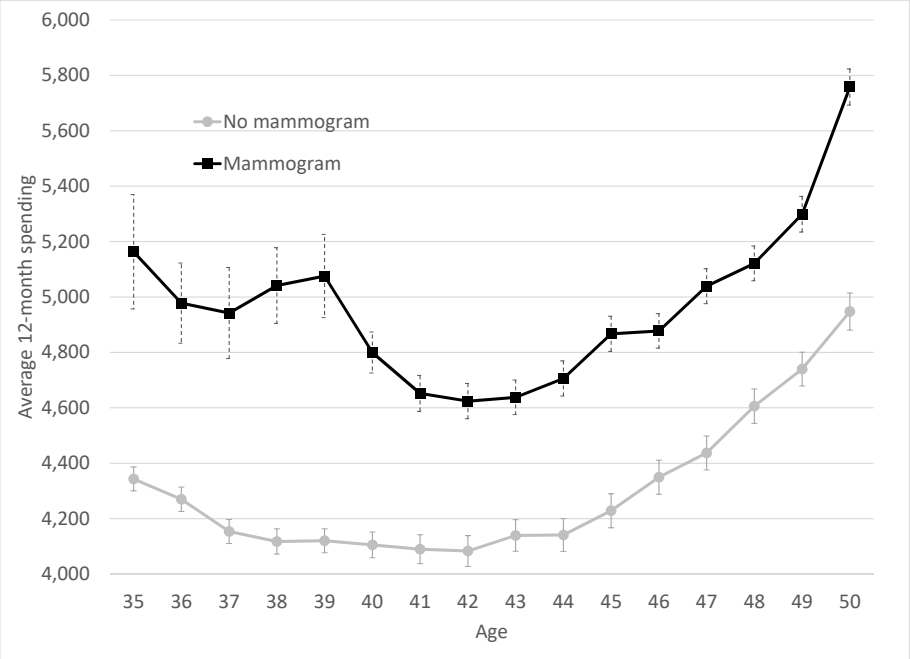
Notes: Sample is limited to the set of privately insured woman-years from the private insurance claims data who had a mammogram. N = 7,373,302 woman-years. For each age (measured by the age at the beginning of the calendar year), panel A shows the share with each mammogram outcome. Panel B presents no new information but, for expositional ease, reports on a different scale the share of mammograms at each age that are true positive (left hand axis) and false positive (right hand axis). Error bars reflect 95% confidence intervals.

Figure 3: Tumor stage and size by age

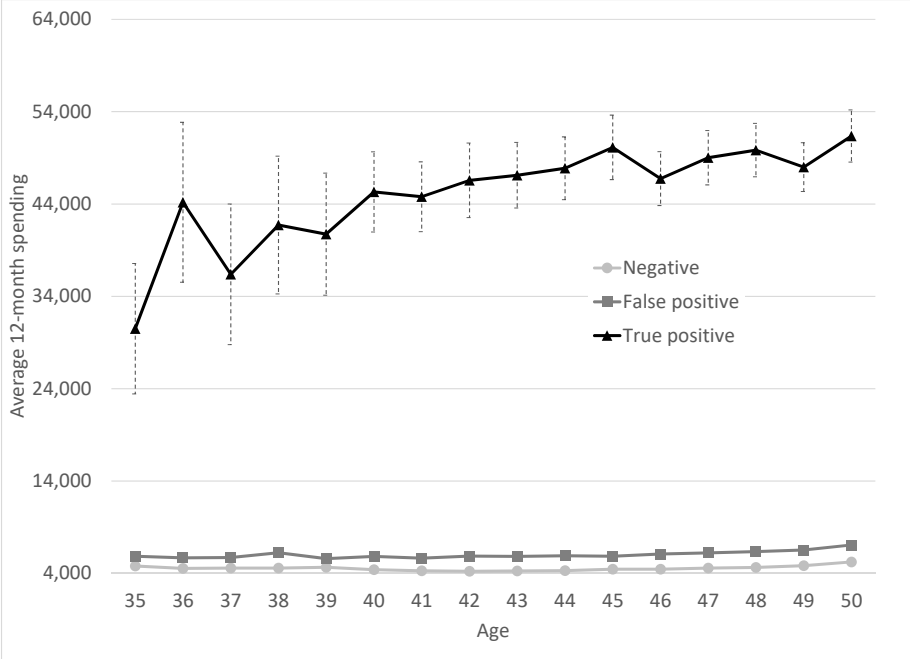


Notes: Figure shows diagnosed breast cancer tumors in the SEER (2000-2014) data by age. Primary y-axis shows share of breast cancer tumors that are in situ. Secondary y-axis shows average size of diagnosed tumors. Error bars reflect 95% confidence intervals. N =197,956 breast cancer diagnoses.

Figure 4: Spending by age



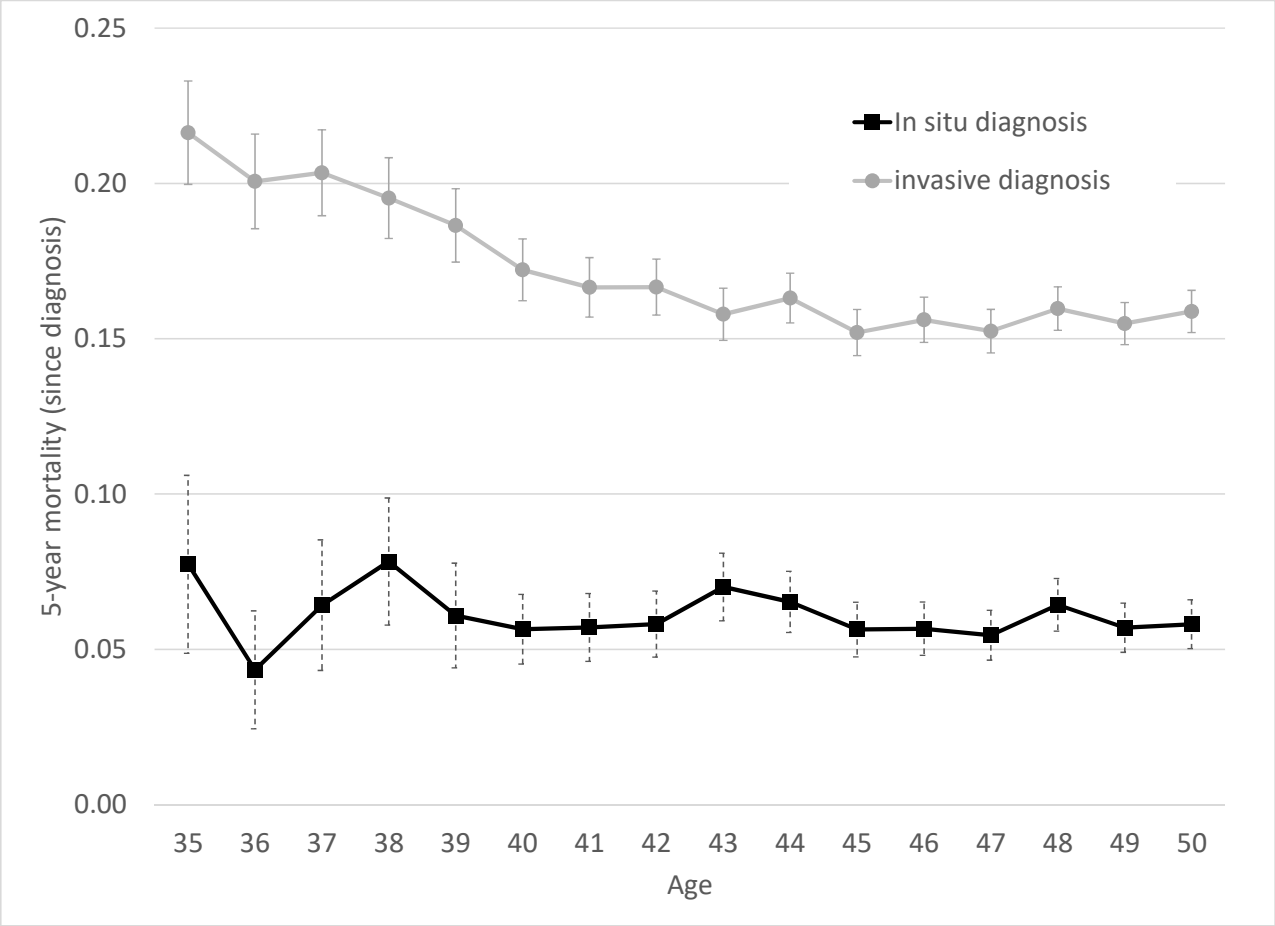
(a) Mammogram versus no mammogram



(b) By mammogram outcome

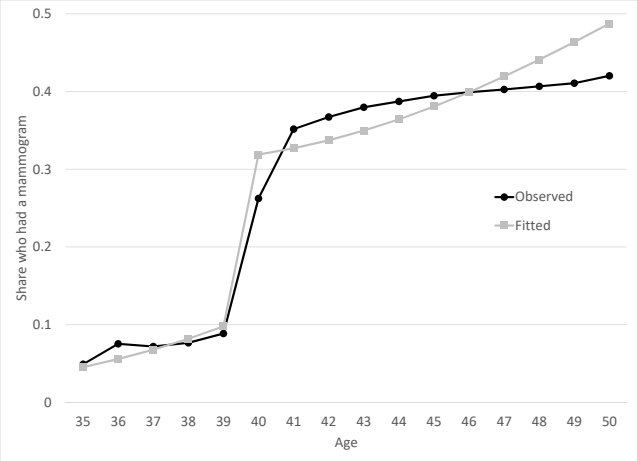
Notes: Sample is insurance claims data on a set of privately insured woman-years from 2009- 2011. In Panel A, for each age (defined based on age at the beginning of the calendar year), we report the spending in the 12 months following the mammogram. For those without a mammogram, we draw a reference date from the distribution of actual mammograms in that year. All reference dates are set to be the first of the given month. Spending is measured in the 12 months after this reference date. Panel B focuses only on the woman-years with mammograms and shows subsequent 12-month spending separately based on mammogram outcome. Error bars (not always visible) reflect 95% confidence intervals. N = 7,373,302 woman-years.

Figure 5: Mortality

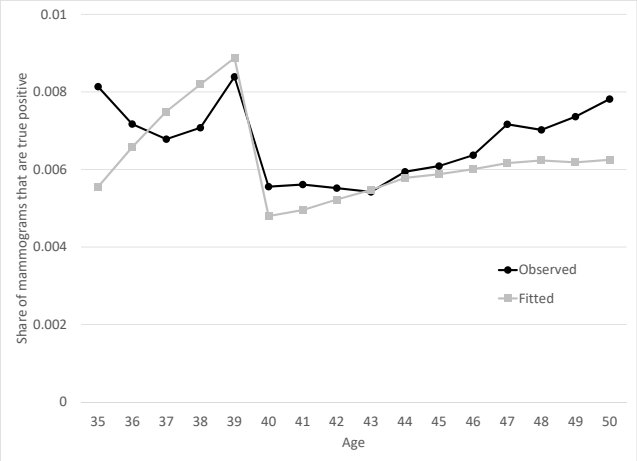


Notes: Figure shows 5-year mortality for diagnosed breast cancer tumors in the SEER (2000-2014) data. Mortality rates are shown separately by age of diagnoses and by tumor stage (in situ and invasive). Error bars reflect 95% confidence intervals. N = 147,243 diagnoses with non-missing 5-year mortality.

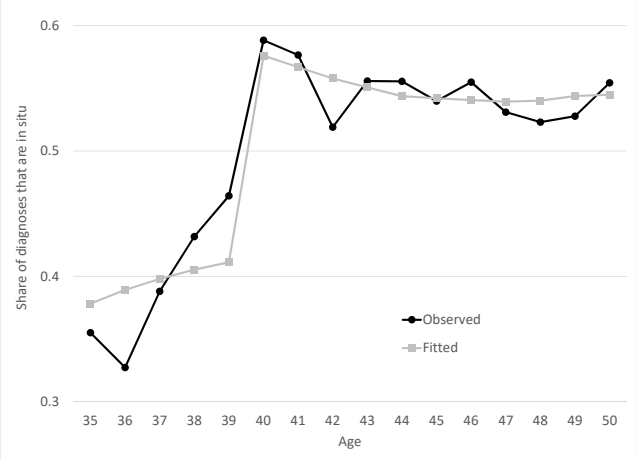
Figure 6: Model fit



(a) Share with mammogram



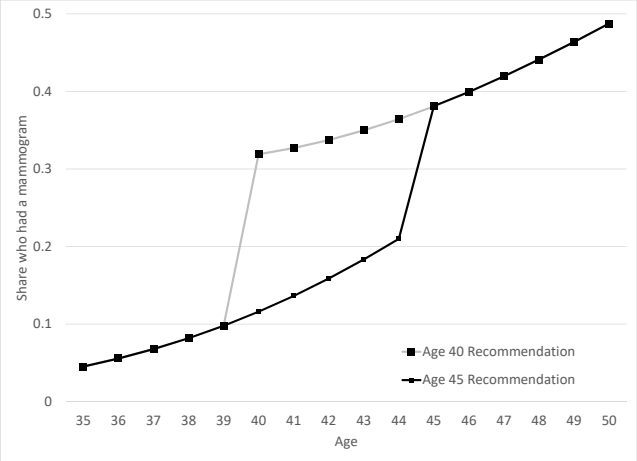
(b) Share of mammograms that are true positive



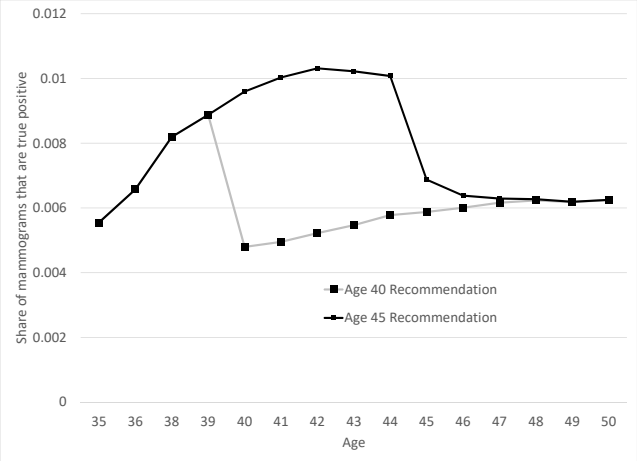
(c) Share of diagnoses in situ

Notes: Figures show model fit by comparing the observed patterns of mammogram rates, outcomes, and types of diagnoses by age to the fitted values from the model based on the parameter estimates from Table 2. The observed data on mammograms (Panel A) was previously shown in Figure 1; the observed data on share of mammograms that are true positives was previously shown in Figure 2; the observed data on the share of diagnoses that are in situ is a modified version of the data shown in Figure 3. While Figure 3 presented the share of all diagnosed cancers that are in situ, we match the share of *mammogram-diagnosed cancers* that are in situ, as shown in Panel C. Appendix C provides more detail.

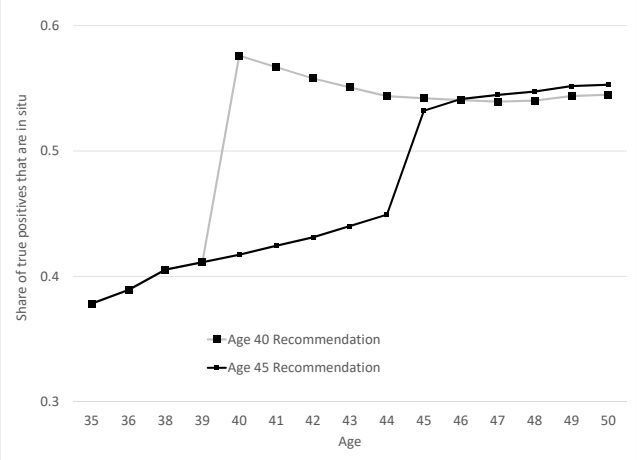
Figure 7: Impact of changing the mammogram recommendation age from 40 to 45, by age



(a) Share with mammogram by age



(b) Share of mammograms that are true positive by age



(c) Share of diagnoses in situ by age

Figure reports the model predictions - by age - for mammogram rates, mammogram outcomes, and the share of diagnoses that are in situ, based on the parameter estimates from Table 2. As in Table 3, we report the model predictions both under the status quo recommendation that mammograms begin at age 40 and the counterfactual recommendation that mammograms begin at age 45.

Table 1: Summary statistics

	No. of Observations		Health Care Spending	
	N (000s)	Share	Total	Out-of-pocket
No mammogram	5,166.2	0.701	$4,300	$625
Mammogram	2,206.9	0.299	$4,985	$751
Conditional on mammogram:				
Negative	1,977.8	0.896	$4,552	$715
False positive	214.6	0.097	$6,106	$952
True Positive	14.4	0.007	$47,639	$2,821

Notes: Table shows summary statistics from insurance claims data on a set of 35-50 year old privately insured women in 2009-2011. Each observation is a woman-year. 12-month spending measures healthcare spending in the 12 months after the mammogram (including the mammogram itself) for those with a mammogram. For those without a mammogram, we draw a reference date from the distribution of actual mammograms in that year. All reference dates are set to be the first of the given month. Spending is measured in the 12 months after this reference date.

Table 2: Parameter estimates

Parameter	Estimate	Std. Err.
α^o	-5.21	0.30
γ^o	0.10	0.01
$\delta^o_{\text{in-situ}}$	0.36	0.18
$\delta^o_{\text{invasive}}$	1.13	14.96
α^r	0.29	0.50
γ^r	-0.03	0.01
$\delta^r_{\text{in-situ}}$	-0.01	0.24
$\delta^r_{\text{invasive}}$	-4.67	33.38

Notes: Table shows the parameter estimates from the mammogram decision model. Standard errors are calculated using 100 repetitions of the bootstrap.

Table 3: Impact of changing the mammogram recommendation age from 40 to 45

	Rec at Age 40	Rec at Age 45	Change
A. Screening and spending (per woman)			
Mammograms	4.70	3.80	-0.90
	(0.06)	(0.14)	(0.08)
Negative	4.22	3.42	-0.81
	(0.05)	(0.12)	(0.07)
False positives	0.46	0.36	-0.09
	(0.01)	(0.02)	(0.01)
True positives	0.0208	0.0204	-0.0004
	(0.0024)	(0.0024)	(0.0001)
In-situ diagnoses	0.0063	0.0060	-0.0004
	(0.0005)	(0.0005)	(0.0001)
Invasive diagnoses	0.0145	0.0145	0.0000
	(0.0019)	(0.0019)	(0.0001)
Total healthcare spending ($)	71,326	71,007	-319
	(128)	(155)	(29)
B. Mortality (per 1,000 women by age 50)			
Dead	15.98	16.03	0.05
	(0.53)	(0.53)	(0.03)
Dead from breast cancer	8.23	8.28	0.05
	(0.53)	(0.53)	(0.03)
Dead from other reason	7.75	7.75	0.00
	(0.00)	(0.00)	(0.00)
Years alive, per woman	15.87	15.87	-0.0002
	(0.00)	(0.00)	(0.0001)

Notes: Table reports model predictions for various outcomes under the status quo recommendation that mammograms begin at age 40 (column 1) and the counterfactual recommendation that mammograms begin at age 45 (column 2). The predictions are generated using the parameter estimates from Table 2, and simulated women's life histories under a non-screening regime based on the clinical oncology model. Panel A reports the average number of mammograms and different mammogram outcomes per woman over ages 35-50. Panel B shows the share of women dead (and from different causes) by age 50, as well as the number of years alive on average between 35 and 50. Standard errors are calculated using 100 repetitions of the bootstrap.

Table 4: Impact of changing mammogram recommendation age from 40 to 45, under alternative assumptions about selection

	Recommendation at Age 40	Recommendation at Age 45	Difference
A. Estimated Selection			
Mammograms (per woman)	4.70	3.80	-0.90
	(0.06)	(0.14)	(0.08)
Total healthcare spending ($ per woman)	71,326	71,007	-319
	(128)	(155)	(29)
Dead by age 50 (per 1,000 women)	15.98	16.03	0.05
	(0.53)	(0.53)	(0.03)
B. No Selection			
Mammograms (per woman)	4.70	3.80	-0.90
	(0.06)	(0.14)	(0.08)
Total healthcare spending ($ per woman)	71,364	71,024	-340
	(111)	(147)	(37)
Dead by age 50 (per 1,000 women)	15.84	16.02	0.18
	(0.47)	(0.53)	(0.06)
C. Consistent Selection			
Mammograms (per woman)	4.70	3.80	-0.90
	(0.06)	(0.14)	(0.08)
Total healthcare spending ($ per woman)	71,450	71,068	-382
	(87)	(134)	(48)
Dead by age 50 (per 1,000 women)	15.54	15.99	0.45
	(0.39)	(0.52)	(0.13)

Notes: Table reports model predictions under the status quo recommendation that mammograms begin at age 40 (column 1) and the counterfactual recommendation that mammograms begin at age 45 (column 2). Each panel reports results under different assumptions about the nature of selection both in the absence and presence of a recommendation. Panel A reports results based on the estimated selection patterns; these results repeat findings shown previously in Table 3. Panel B repeats the same exercises as in Panel A, but instead of using the estimated selection (i.e. δ^r and δ^ovectors shown in Table 2), we instead assume "no selection" - i.e. we set $\delta^r = \delta^o = 0$. Panel C also repeats the exercises in Panel A but now assumes "consistent selection" - i.e. we set δ^requal to our estimates of δ^o in Table 2. In both Panel B and C, we hold the overall mammogram rate fixed at Panel A's predicted age-specific mammogram rates (which of course varies in column 1 and column 2), so that the counterfactuals across panels consider differences in selection, not in levels. To do this we adjust the intercept α_r for each age and counterfactual to match the age-specific mammogram rates in Panel A, assuming the simulated life histories and cancer status remains constant. The small differences in mammograms in Panel A and Panel C are due to changes in the denominator of simulated life histories. Specifically, since fewer women die in Panel C, there are more years where they could potentially obtain a mammogram. Standard errors are calculated using 100 repetitions of the bootstrap.

Table 5: Sensitivity checks for impact of changing mammogram recommendation age from 40 to 45

	A. Estimated Selection			B. No Selection			C. Consistent Selection		
	Dead by age 50 (per 1,000 women)			Dead by age 50 (per 1,000 women)			Dead by age 50 (per 1,000 women)		
	Recommendation at		Diff	Recommendation at		Diff	Recommendation at		Diff
	Age 40	Age 45		Age 40	Age 45		Age 40	Age 45	
Baseline Estimate	15.98	16.03	0.05	15.84	16.02	0.18	15.54	15.99	0.45
Decrease cancer incidence to:									
(1) Erasmus original level	10.66	10.68	0.02	10.67	10.68	0.01	10.65	10.68	0.03
Decrease share of in-situ tumors that become invasive:									
(2) from 62.5% to 28%	15.20	15.22	0.02	15.06	15.21	0.15	14.78	15.18	0.41
(3) from 62.5% to 14%	14.89	14.90	0.01	14.75	14.89	0.14	14.48	14.86	0.39
Increase share of non-malignant tumors:									
(4) from 6% to 19%	15.08	15.12	0.03	14.90	15.10	0.20	14.63	15.07	0.44
(5) from 6% to 42%	12.69	12.70	0.02	12.53	12.68	0.15	12.36	12.66	0.30

Notes: Table reports model predictions under alternate sensitivity assumptions. The first three columns in the first row replicate the results from Table 4 Panel A on the impact of changing the mammogram recommendation age from 40 to 45 based on the estimated selection patterns. We report only the impact on the death rate by age 50. The second three columns replicate the results from Table 4 Panel B where we instead assume "no selection" - i.e. we set $\delta^r = \delta^o = 0$. The last set of columns reflect Table 4 Panel C where we assume "consistent selection" - i.e. we set δ^requal to our estimates of δ^o in Table A.10. Each row tests the sensitivity of these estimates under alternate natural history assumptions, as discussed in Section 5.2.3.

Appendix

A Coding Mammograms and Outcomes in Claims Data

We follow Segel, Balkrishnan,, and Hirth (2017) in coding the incidence of screening mammograms (hereafter "mammograms") and the results of those mammograms in the HCCI claims data.

We code a woman as having a screening mammogram on a given date if she has a claim with ICD-9 procedure code V76.12 or CPT codes 77057 or G0202 on that date, but no claims for any other mammogram within the previous 12 months and no prior claims for breast cancer treatment.[18] Previous work has documented that claims-based measures of mammogram rates tend to be lower than mammogram rates in self-reported survey data. For example, Freeman et al. (2002) document this pattern in Medicare data, and Cronin et al. (2009) document similar evidence in a study of Vermont women. Consistent with these studies, Appendix Figure A.1 documents the age profile of the annual screening mammogram rate, as measured by both the Behavioral Risk Factor Surveillance System (BRFSS) survey and the algorithm described above using the HCCI claims data. Between ages 39 and 41, the mammogram rate jumps by approximately the same amount - 25 percentage points - by both measures, but the survey data describe mammogram rates as being approximately 10 to 20 percentage points higher than the claims data rate at all ages. Of course the samples are not perfectly comparable, as the BRFSS sample is of all women with health insurance (public or private) from 2002-2012, while the HCCI sample is of women privately insured by Aetna, Humana or United between 2008 and 2012.

We code the outcome of a screening mammogram as negative if there are no subsequent claims for either follow-up testing or breast cancer treatment within the next twelve months. We code the outcome as a false positive if there is at least one claim for follow-up testing in the following three months (i.e. a subsequent mammogram, a breast biopsy, a breast ultrasound, or other radiologic breast testing) in the following three months, but no claims for breast cancer treatment in the next 12 months. We code the outcome of a mammogram as true positive if, within twelve months following the mammogram, there is at least one claim for breast cancer. We consider a women to have a subsequent mammogram if she has a claim with ICD-9 procedure code V76.12 or CPT codes 77057 or G0202. A women has a breast biopsy if she has a claim with ICD-9 procedure code 85.11, 85.12, 85.20, or 85.21 or CPT codes 19100, 19101, or 19120. A breast ultrasound is coded with ICD-9 procedure code 88.73 or CPT code 76645. Radiologic breast testing is coded with ICD-9 procedure code 87.35, 87.36, 87.73, or 88.85 or CPT codes 76003, 77002, 76095, 77031, 76086, 76087, 76088, 77053, 77054, 76355, 76360, 76362, 77011, 77012, 77013, 76098, 76100, 76101, 76102, 76120, 76125, 76140, 76150, 76350, or 76365. Breast cancer is coded with ICD-9 procedure code 233.0, V103.0, or 174.0 through 174.9 or CPT code 19160, 19162, 19180, 19200, 19220, 19240, 19301, 19303, 19305, 19307, 38740, or 38745.The codes used to identify these claims are provided in Appendix Table A.1, along with their references.

The linked SEER-Medicare data allows us to cross validate this claims-based coding process against

[18] Segel, Balkrishnan,, and Hirth (2017) focused on data from 2003-2004, so used the CPT code 76092. In 2007 this code was replaced by 77057. In addition, Hubbard et al. (2015) identify CPT code G0202 as indicating a screening mammogram claim. Segel, Balkrishnan,, and Hirth (2017) provide codes for "other" (non-screening) mammograms, which we omit.

cancer diagnoses in the cancer registry. The results are very encouraging. Appendix Tables A.2 and A.3 describe the concordance of true positive mammograms as coded using this algorithm with actual diagnoses as recorded in the SEER-Medicare data. For those who were diagnosed with breast cancer and had a mammogram in the year of diagnosis, 99.8% of mammograms were coded as true positive using our algorithm. Meanwhile, 93% of mammograms for patients who were never diagnosed with breast cancer were negative, while 6.5% were false positives. Most patients with true positive mammograms were diagnosed with breast cancer in the year of or the year following the mammogram, while 83% of those without true positive mammograms were never diagnosed and a further 13% were not diagnosed until more than 1 year after the mammogram (4% were diagnosed in the year following the mammogram, but none in the year of the mammogram).

B Clinical model: the Erasmus model

We use the Erasmus model to generate estimates of the underlying onset rate by age of cancer and cancer type, as well as the evolution of (untreated) cancers. We adjust the model to better match certain key moments of the SEER data. This (modified) Erasmus data, together with assumed parameters from the mammogram decision model (specifically, equations 1 and 2) and the observed policy recommendation (40 and above), generates an age-specific share of women who are screened, as well as the tumor characteristics (in situ and invasive rates) conditional on getting screened, which we then attempt to match by method of moments to the observed data on the age-specific share of women who are screened and the tumor characteristics conditional on getting screened.

As described in the main text, the Erasmus model is one of seven models developed for the Cancer Intervention and Surveillance Modeling Network (CISNET) as part of a project decomposing breast cancer mortality reductions from 1975-2000 into effects from the dissemination of mammography versus the development of advanced treatment techniques (Clarke et al. 2006). Each of the groups participating in the project wrote a model of breast cancer incidence and mortality in the US over this time period and then compared the mortality rates under scenarios with and without mammography and advanced treatment. For convenience, we focus on one of these models, the Erasmus model (Tan et al., 2006).

In what follows we describe our implementation of the Erasmus model. This implementation directly follows Tan et al. (2006), with all the assumptions we describe being theirs. We then describe the calibration changes we make to the model based on some of our own external data and assumptions.

B.1 Model details

Tumor incidence

The model allows us to simulate a cohort of women i, each with a year of birth b_i and a year of death from other causes d_i which is randomly determined and dependent on the year of birth. Specifically, it assumes that in each year y the probability that a person born in year b (such that $y \geq b$) dies of causes other than breast cancer is Q_y^b. A woman's year of death is defined as the lesser of 110 and the first year in which a

random draw from a uniform distribution on [0,1] falls below Q_y^b. It assumes that no woman dies from other causes before age 30.

The model further assumes that there exists a probability C_b that any woman from cohort b will get cancer before age 85. It defines age $a_y^b = y - b$ as the age in year y of an individual born in year b and assumes that for every cohort b and year y such that $20 \leq a_y^b \leq 85$ there exists S_a, the probability that a woman experiences tumor onset at age a conditional on eventually getting cancer. For each woman i with any cancer, we can therefore construct the year of tumor onset t_i as the lesser of the year in which she turns 85 and the first year in which a random draw from a uniform distribution on [0, 1] falls below S_{y-b_i}.

Tumor type and in situ characteristics

At onset, cancer type is defined to be either an invasive tumor or one of three types of non-invasive tumors. Non-invasive tumors are also known as as ductal carcinoma in situ (DCIS), which we refer to in the text as in situ. Invasive tumors are assigned a minimum size and other tumor characteristics (as described in Appendix Table A.4) at onset and immediately begin growing. DCIS-regressive tumors eventually disappear without causing any harm; DCIS-invasive tumors eventually transform into a harmful invasive tumor but do no harm in the meantime, and DCIS-clinical tumors do no harm but are eventually clinically detected. The model assumes that the outcome of each DCIS tumor (regression, invasion, or detection) occurs w_i years after onset, where w_i is generated by random draws from an exponential distribution with mean W. None of the three types of DCIS tumors can be clinically detected during the duration of this "dwell time", but they can be screen-detected with a screening-year-specific probability E_y if screening occurs. The type of tumor is defined at onset subject to age-specific probabilities I_a (invasive), V_a (DCIS-invasive), R_a (DCIS-regressive), and C_a (DCIS-clinical) such that $I_a + V_a + R_a + C_a = 1$. Values for these and other Erasmus parameters are given in Appendix Table A.5.

For DCIS tumors that become invasive, onset of invasive disease is defined as the moment when the tumor size reaches the minimum value of the screening threshold diameter; this threshold varies with the woman's age as well as over time (to reflect improvements in screening technology). The dwell time for DCIS tumors was calibrated in the MISCAN breast cancer model based on the duration from onset of DCIS to the 1975 screening threshold diameter.

Invasive tumor characteristics

The model assumes that the fundamental characteristic of invasive tumors is their year-dependent size s_i^y. For all invasive tumors, it defines s_i^0 (the size in the year of onset) to be equal to 0.01 cm. It assume that all invasive tumors grow exponentially. Tumor size in year y is therefore given by $s_i^0 (1+g_i)^y$ where g_i is the individual-specific growth rate (drawn from a lognormal distribution at tumor onset). It further assumes that diagnosis depends on tumor size and the individual's "screen detection diameter" r_i^{ay} (drawn at the time of screening from an age- and detection-year-specific Weibull distribution) and "clinical diagnosis diameter" c_i (log normally distributed and set at tumor onset). If the patient undergoes screening, the tumor can be detected if $s_i^y > r_i$. Alternatively, if the tumor grows so large that $s_i^y > c_i$, the patient will certainly detect it due to the appearance of clinical symptoms. Tumor size also determines mortality: if a patient diagnoses

her tumor before it reaches its "fatal diameter" f_i (drawn at onset from a year-specific Weibull distribution), she will receive treatment and survive, but if not, she will die regardless of treatment.

The model defines for each invasive tumor the length of time the patient will survive after the tumor reaches its fatal diameter, called the "survival duration since fatal diameter" and denoted u_i (log normally distributed). It assumes that if the tumor has not been clinically detected by the time $0.9*u_i$ years have passed since the fatal diameter was reached, it will be clinically detected due to distant metastases at that time.

Finally, it assumes that the growth rate g_i, clinical diagnosis diameter c_i, and survival duration u_i are correlated with coefficients ρ_{gc}, ρ_{gu}, and ρ_{cu}. The variables described in this section ($s_i^y, r_i^{ay}, f_i\ g_i, c_i, u_i$) , combined with the woman's age and the year of initiation, fully specify the course of the disease for an invasive tumor, subject to potential screening regimens.

B.2 Parameterizing the Erasmus model

We begin by choosing certain population-specific parameters required as inputs for the Erasmus model: the other-cause death probability, the overall tumor incidence, and the tumor incidence by age. As in Tan et al. (2006), the other-cause death probability follows the approach of Rosenberg (2006). However, we adjusted the tumor incidence parameters (overall cohort incidence and quadratic incidence by age) that are given in Tan et al. (2006) in order to match the SEER data's share of diagnoses that are in situ and invasive for those under 40 and over 40. After establishing these population-specific parameters, we simulate individual life histories under a no-screening assumption, and use the tumor sizes and types to determine the population cancer rate by age.

Other-cause death probability

Following Rosenberg (2006), we computed probability of death due to other causes as the difference between the all-cause mortality and breast cancer specific mortality. We obtained all-cause mortality for ages 0-110 and years 1933-2010 from the Human Mortality Database. Using breast cancer death totals from the National Center for Health Statistics and female population totals from the Human Mortality Database, we calculated breast-cancer-specific mortality for ages 0-110 and years 1959-2010. To impute values for previous years, we assumed that the age-specific breast cancer mortality rate in any year before 1958 was equal to the rate in 1958. We combined these data to calculate non-breast-cancer mortality rates for all years between 1933 and 2010.

Age profile of cancer incidence

The Erasmus model provided a CDF of tumor incidence in 5-year increments, implying a step function of yearly incidence that produces spikes in tumor onset within a cohort every 5 years (see Appendix Table A.6, first column reproduced from Tan et al. (2006), based on estimates of US population in 1975). We constructed a smoothed CDF of tumor incidence by fitting to the Erasmus CDF using a constrained polynomial

(quadratic) fit: $y = ax^2 + bx + c$. We fitted a, b, c, the start age x_{start} (at which the CDF should be zero), and the end age x_{end} (at which the CDF should be one). Restrictions included:

$$ax_{start}^2 + bx_{start} + c = 0$$

$$ax_{end}^2 + bx_{end} + c = 1$$

$$2ax_{start} + b \geq 0$$

The values that minimize the error $\sum(\hat{y} - y)^2$ across each of the fourteen ages in Appendix Table A.6 are $x_{start} = 24$, $x_{end} = 85$, $a = 0.000268$, $b = -0.01282$, $c = 0.15327$. We assume that the incidence before age 24 is 0. The fit is shown in Appendix Figure A.5.

Adjusting cancer incidence rates

Tan et al. (2006) calculate cumulative tumor incidence by birth cohort based on observed (i.e. diagnosed) incidence in the US from 1975-1979. Implicitly, this assumes that all tumors are diagnosed. It will therefore miss any undiagnosed tumors. Not surprisingly, therefore, when we use the original Erasmus parameters and our calibrated screening policy described below, the model substantially under-predicts observed diagnoses. To rectify this, we allowed the cohort tumor incidence to vary with a multiplicative shift α which uniformly affects each cohort's tumor incidence.

We calibrate α as follows. We define the parameters $\theta = (\alpha, pscrn_{inv}, pscrn_{dcis})$ where $pscrn_{inv}$ is the probability of a mammogram conditional on having an invasive tumor and $pscrn_{insitu}$ is the probability of a mammogram conditional on having an in situ tumor. We then estimate θ by maximum likelihood. Specifically, we maximize the log likelihood of observing SEER tumor types (1973-2013, for women 25-34). The model's original incidence and the incidence multiplicatively shifted by α are plotted against the SEER diagnosis rates in Appendix Figure A.6. We also plot the model's diagnosis rates with no screening; with the multiplicative shift this roughly matches with the SEER diagnosis levels.

B.3 Visual representation and results from Erasmus model: Underlying cancer rate

The first panel of Appendix Figure A.7 visualizes the Erasmus model using a flow chart. The second panel shows example sequences of progression for each of the four types of tumors, in the absence of screening. The first two rows show the progress of DCIS-regressive and DCIS-clinical tumors, which are harmless and differ only in their behaviors at the end of their dwell time: DCIS-regressive tumors disappear, while DCIS-clinical tumors are detected clinically, for example at a routine physical exam. If these tumors are screened, they will be diagnosed with a probability equal to the "sensitivity" as described in Appendix Table A.5. Likewise, before it switches to its invasive phase, the DCIS-invasive tumor can also be detected by a screening mammogram in the same way. After it becomes invasive, the DCIS-invasive tumor (row 3) and the invasive tumor (row 4) can only be detected if the size exceeds the year- and age-specific screening diameter

of the year in which it is screened. If a woman's tumor is screened (or clinically diagnosed) before it reaches the fatal diameter, her life is saved, but if not, she will eventually die, regardless of detection or treatment in later years. In most cases, when a woman's tumor reaches the fatal diameter without being diagnosed, she will be clinically diagnosed before death. The flow chart omits deaths due to other causes.

Appendix Figure A.8 plots the share of women in each of five categories when the Erasmus model is calculated with no screening. The calculation is based on birth cohorts from 1950-1975, and focuses on women aged 30-50 in 2000-2005. At any given age, the share of women with detectable invasive or DCIS cancer is substantially smaller than the share of women who have already been diagnosed clinically, indicating that there is a small window of time during which a cancer can be screened before it is clinically detected.

Using the calibrated other-cause death probabilities and incidence rates, we solve the Erasmus model assuming that there is no screening for birth years 1950-1975. We restrict to years 2000-2005 and ages 30-50, producing a set of individual life-histories that can be categorized in every year as dead due to breast cancer, dead due to other causes, clinically diagnosed, currently undiagnosed invasive cancer, currently undiagnosed DCIS, or no cancer. (We consider invasive cancer that is too small to be detectable, and regressed DCIS tumors, to be the same as "no cancer.")

We take the "population cancer rate" at each age, or the share of women who have a tumor by a certain age, from the Erasmus model. The Erasmus model assumes that cancers can only be detected by mammogram once they have reached a certain size, so we assume the screening diameter is 1.09 cm – the average screen-detectable size in the Erasmus model – and count the share of women with detectable invasive cancer as the share of women with tumors above that size in the Erasmus model. We also count 80% of the women with DCIS tumors, under the assumption in the Erasmus model that about 80% of technically "detectable" in situ tumors will be detected in any given year. We do not count DCIS-regressive tumors after they have regressed, and after a DCIS-invasive tumor has transitioned to an invasive tumor we determine its detectability based on the rules for invasive cancers.[19]

C Estimation of mammogram model

We estimate our model of mammogram demand by method of moments. The moments are generated from the Erasmus model combined with our model of screening decisions. We first use the Erasmus model to generate cancer incidence and tumor growth under a no-screening assumption, as described above. Specifically, we simulate a panel of ten million women born between 1910 and 1974. We start at age 20 and model cancer incidence and tumor growth using the Erasmus model, assuming no screening. We use the tumor sizes and types to determine the population cancer rate by age.

Then, for a given set of parameters $\alpha^o, \gamma^o, \delta^o, \alpha^r, \gamma^r, \delta^r$, we apply the mammogram decision model (by

[19] Note that this leads to an unintuitive model behavior in which DCIS tumors are detectable at smaller sizes than invasive tumors. In the Erasmus model, invasive tumors are initialized at 0.01 mm and are not considered screen-detectable (by us) until they reach 1.09 cm. DCIS-invasive tumors are initialized at the screening threshold of the year and age in which they become invasive. Since this is sometimes smaller than 1.09 (1.09 is just the average of the distribution of screening thresholds in 2010), the model could simulate a DCIS-invasive tumor which is detectable for several years, then becomes undetectable, then becomes detectable again.

age and recommendation status) to the cancer rate age profile from the Erasmus model to generate the main moments by age.

Although the model is static, it does have a dynamic element in it, as we calculate the model-generated moments only for the women who were not diagnosed with cancer in previous years, or those who did not die (from breast cancer or other causes) prior to the given age. To do this, we must make an assumption about what fraction of clinically-diagnosed women under the no-screening assumption overlap with the screen-diagnosed population when the mammogram decision model is applied. One extreme would be to assume that there is no overlap (perfect negative correlation between clinical and screen diagnosis), so that if 0.01 of the population were clinically-diagnosed under the no-screening assumption, and 0.02 of the population were screen-diagnosed for a given set of parameters, a total of 0.03 of the women would be diagnosed with cancer. We chose to make the other assumption, that there was perfect positive correlation between clinical and screen diagnosis. In this case, if 0.01 of the population were clinically-diagnosed and 0.02 were screen-diagnosed, only 0.02 of the women would be diagnosed with cancer. This likely produces an underestimate of the effects of screening, because it minimizes the number of women who are diagnosed each year.

With this simulated population of women, an assumed value of parameters associated with the mammogram decisions with and without recommendation (equations 1 and 2) and the observed policy recommendation (40 and above), the model generates an age-specific share of women who are screened, and the tumor characteristics (in situ and invasive rates), conditional on getting screened.

As mentioned in the main text (footnote 13), the in situ rate moment differs from Figure 3 in the main text. Figure 3 shows the in situ rate of all diagnosed cancers that appear in the SEER database, but the moment we match with the model is the in situ rate of *screen-detected* cancers. Cancers that are clinically diagnosed are highly unlikely to be in situ, so the SEER value likely underestimates the true value of share in situ for screening mammogram-diagnosed cancers. We adjust the SEER moment at each age using Bayes' rule:

$$P(M) * P(insitu|M) + (1 - P(M)) * P(insitu| \sim M) = P(insitu),$$

where M is the event that a diagnosed tumor was screen-detected. We assume that $P(M)$, the share of diagnoses detected by screening mammogram, is 0.2 for ages 35-39 and 0.34 for ages 40-49 (following Roth et al. (2011)). We assume that $P(insitu| \sim M)$ = 0.08, following Ernster et al. (2002). $P(insitu)$ is given by the SEER moments in Figure 3, allowing us to back out $P(insitu|M)$, our object of interest, which is the moment we actually match. The results for $P(insitu|M)$ for ages 40-49 range from 52% to 55%, which is in line with the 56% reported in this age group by Ernster et al. (2002).

With our 48 moments in hand (16 moments for each of 3 types), we then search for the parameters that minimize the (weighted) distance between these generated moments and the observed moments. We apply a linear weight that decreases on each side of age 40, so that the weight on moments associated with ages 39 and 41 is 10/11 of the weight on the age 40 moment, the weight on moments associated with ages 38 and 42 is 9/11 of the weight on the age 40 moment, and so on. To achieve a reasonable fit, we also weight the moments by the inverse of their standard deviation. We chose 2,000 random starting values in the parameter

space defined as follows:

$$\alpha^o \in [-10,10], \gamma^o \in [-0.2,0.2], \delta^o_{insitu} \in [-2,2], \delta^o_{invasive} \in [-2,2]$$
$$\alpha^r \in [-2,2], \gamma^r \in [-0.2,0.2], \delta^r_{insitu} \in [-2,2], \delta^r_{invasive} \in [-2,2]$$

and applied the Nelder-Mead algorithm to each of these starting vectors. We then iteratively applied the Nelder-Mead algorithm to the best starting value to further minimize the objective function.

D Counterfactual simulations of mammogram model

Our counterfactuals analyze the impact of changing the recommendation age as well as the selection response. In both cases, we first model the underlying onset rate of cancer and the evolution of cancers using the Erasmus model described in Section 4.2 and Appendix B. Since we are interested in analyzing the impact of potential future recommendation changes, we apply the most recent year's value of any time-varying parameters of the Erasmus model. In practice, this means we use the breast-cancer-specific and non-breast-cancer mortality for 2010, the scale parameter for fatal diameter β_F^y from 1975 (see Appendix Table A.5), the screening sensitivity E_y from 2000, the screening diameter scale parameters from 2000 (see Appendix Table A.7), and the tumor incidence for the 1970 cohort (see Appendix Table A.8). We simulate this model for 10 million women's life histories, and in particular from ages 35-50.

We then apply the screening decision as described in Section 4.2 for each women and year. The baseline model uses the parameter values given in Table 2, with the recommendation applied starting at age 40. We change the age of the recommendation in Table 3 and the selection parameters δ^r in Table 4.

In all counterfactuals that retain the age-40 recommendation (i.e. the ones that aim to isolate a counterfactual selection responses), we specify that the age-specific mammogram rates must be the same as in the baseline specification, while the type of women who respond to the recommendation is allowed to change. This allows the counterfactuals to consider only differences in selection, not levels. After imposing the counterfactual selection coefficients, we add an age-specific constant so that the age-specific mammogram rates are unchanged relative to the baseline. In all counterfactuals that both use the age-45 recommendation (i.e. the ones that consider a counterfactual policy recommendation) and impose alternative selection patterns, we make a similar adjustment so that the age-specific mammogram rates match those produced by the age-45 counterfactual with the baseline estimated selection parameters. The screening decisions along with underlying natural history in the Erasmus model determine whether a given mammogram screen results in a negative test, a false positive, or true positive based on the cancer type of the screened woman.

The Erasmus model parameters also reveal whether a mammogram detects a cancer early enough to prevent breast-cancer-related morality. If an invasive tumor is detected before it reaches the fatal diameter (see Appendix Table A.5 on Erasmus parameters), the person survives to die of natural causes. If the invasive tumor is detected after the tumor is larger than the fatal diameter, the person dies of breast cancer after some stochastic period determined by survival duration parameters (see Appendix Table A.5 on Erasmus parameters). Breast cancer related mortality is driven by invasive tumors; in situ tumors are only fatal if

they progress to an invasive tumor.

To estimate total spending under different counterfactuals, we first calculated in the HCCI data, the total age-specific spending in the twelve months following no mammogram, a negative mammogram, a false positive mammogram, and a true positive mammogram. At each age, each simulated woman falls into one of these categories. We add up the spending for a given woman across ages 35-50 based on her relevant mammogram outcomes in each year. For example, suppose a woman had a true positive mammogram at age 42, and no mammograms at any other age. We would add the average spending in the HCCI data for women with no mammograms for ages 35-41, the average spending for a woman in the twelve months following a true positive mammogram at age 42, and the average spending for women with no mammograms at ages 43-50. Note that the screening decision only applies to women who are alive and have never been diagnosed with breast cancer; once a women receives a true positive diagnosis she is not longer screened.

E Sensitivity Analysis

We explore the robustness of our estimates to changing features of our clinical model. In particular, we focus on statistics that can be compared with other sources, such as the share of in-situ tumors that become invasive, and the share of tumors that are non-malignant.

Two specifications test sensitivity to decreasing the share of in-situ tumors that become invasive. The Erasmus model assumes that 62.5% of in-situ tumors will become invasive, while estimates for the fraction of DCIS tumors that would become invasive over 10 years if left untreated ranges from 14-60% (Burstein et al., 2004), putting the Erasmus model at the most conservative end of the spectrum. Alternate estimates suggest that the share of DCIS-tumors that become invasive is 14% (Eusebi et al., 1994) or 28% (Page et al., 1995). In these checks, we also shift the tumor type distribution to match these estimates at age 40. This sensitivity proportionally reduces the share of DCIS-invasive tumors at all ages, and proportionally increases the share of tumors that are DCIS-regressive and DCIS-clinical at all ages. The share of invasive tumors remains the same.

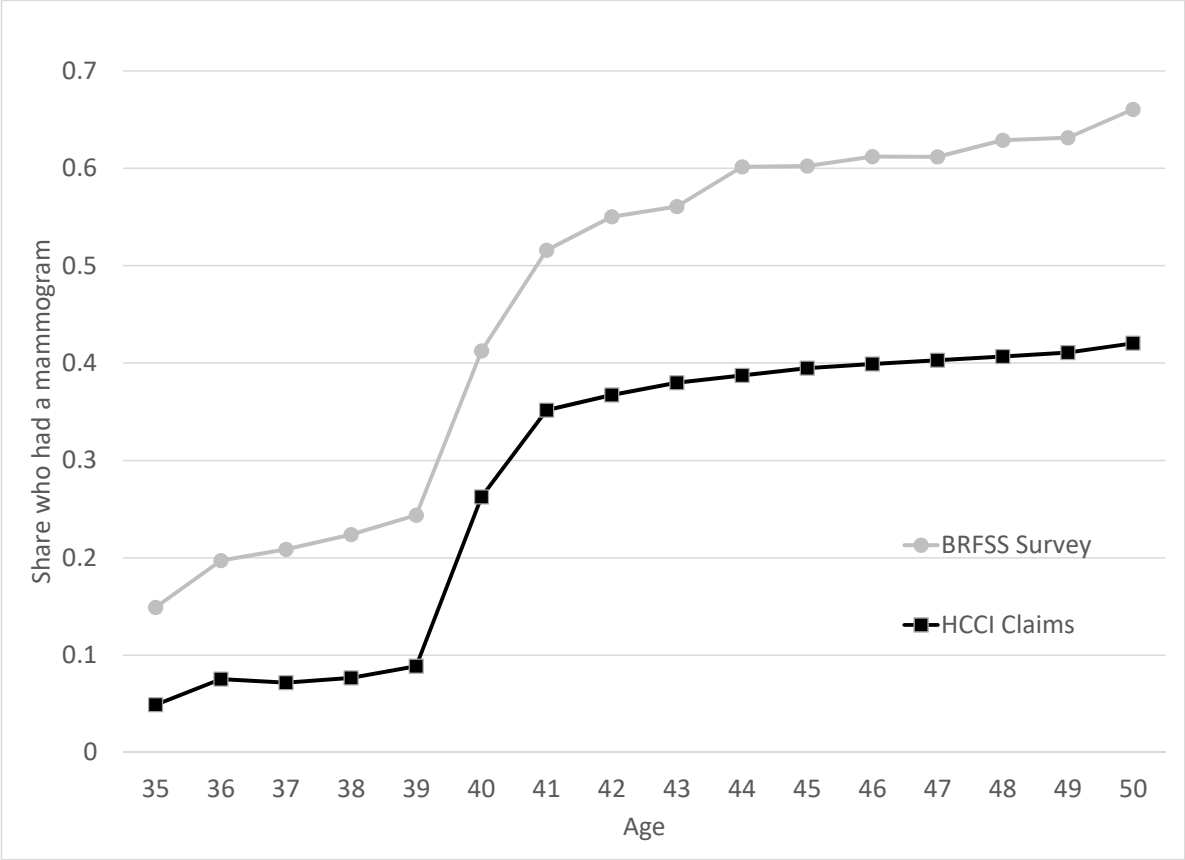
Similarly, two specifications test sensitivity to increasing the share of non-malignant tumors. Non-malignant refers to tumors that have no potential to be invasive and therefore would never result in a breast cancer mortality. Specifically, in our natural history model, recall that there are invasive tumors as well as three types of non-invasive tumors (also known as DCIS or in situ): DCIS-regressive, DCIS-clinical and DCIS-invasive. The invasive and DCIS-invasive tumors are referred to as "malignant" due to their potential to cause harm, while the DCIS-regressive and DCIS-clinical tumors will never become invasive and are therefore referred to as "non-malignant". The Erasmus model's parameters (see Appendix Table A.9) imply that 3-9% of all tumors are non-malignant.[20] In contrast, estimates of over-diagnosis, or the diagnosis of a cancer that would not harm a woman in her lifetime, vary from <5% to >30% (American Cancer Society, 2017a). Compared to other models, the Erasmus model seems to have a low estimate of non-malignancy, or equivalently a high estimate of the share of cancer that is invasive or could become invasive. Therefore,

[20]The share of cancer that is in situ of any kind (DCIS-clinical, DCIS-regressive, or DCIS-invasive) with no screening is approximately 15% at age 35 and 9% at age 50 (see Appendix Figure A.4). The age gradient is because some of the DCIS invasive becomes invasive and some of the DCIS regressive regresses.

each of our sensitivity analysis decreases the amount of invasive or potentially invasive tumors.

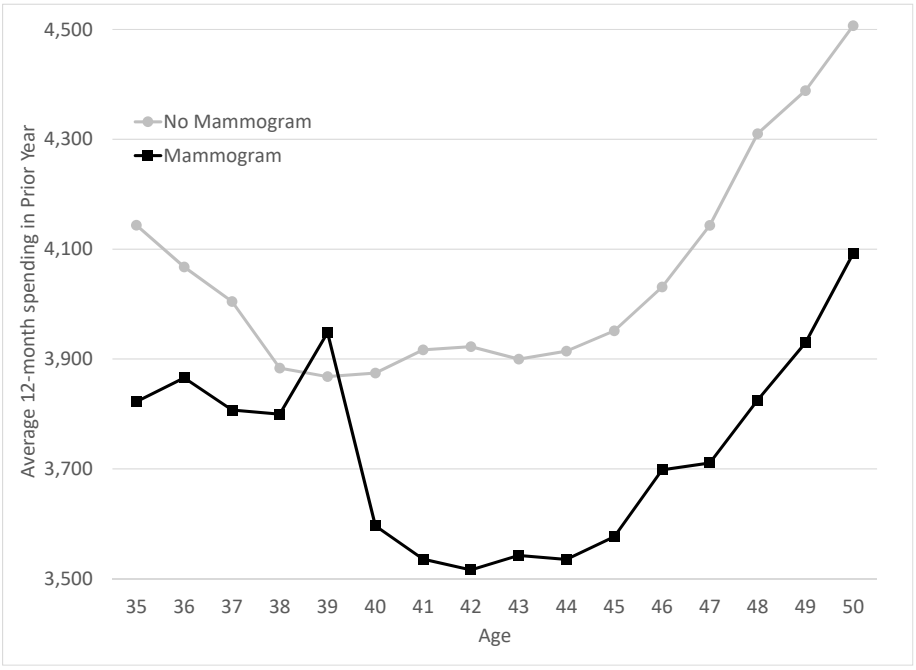
In an alternate natural history model (Fryback et al., 2006), the share of tumors with "non-malignant potential" was 42%. Alternate estimates of over-diagnosis are provided by three trials in which women in the control group were not invited to be screened at the end of the active trial period. In a meta-analysis, estimates of the excess incidence was 19% when expressed as a proportion of the cancers diagnosed during the active screening period (Marmot et al., 2013). We therefore increase the share of non-malignant tumors from approximately 8% at age 40 to (separately) 19% and 42% at age 40. In each of these sensitivity analyses, we increase the share of DCIS-regressive and DCIS-clinical at all ages in a proportional shift so that the share of non-malignant tumors at age 40 is either 19% or 42%. We separately decrease the share of tumors that are invasive or DCIS-invasive by a proportional shift so that the total tumor types sum to 100%.

Figure A.1: Mammogram rate in survey and claims data, by age

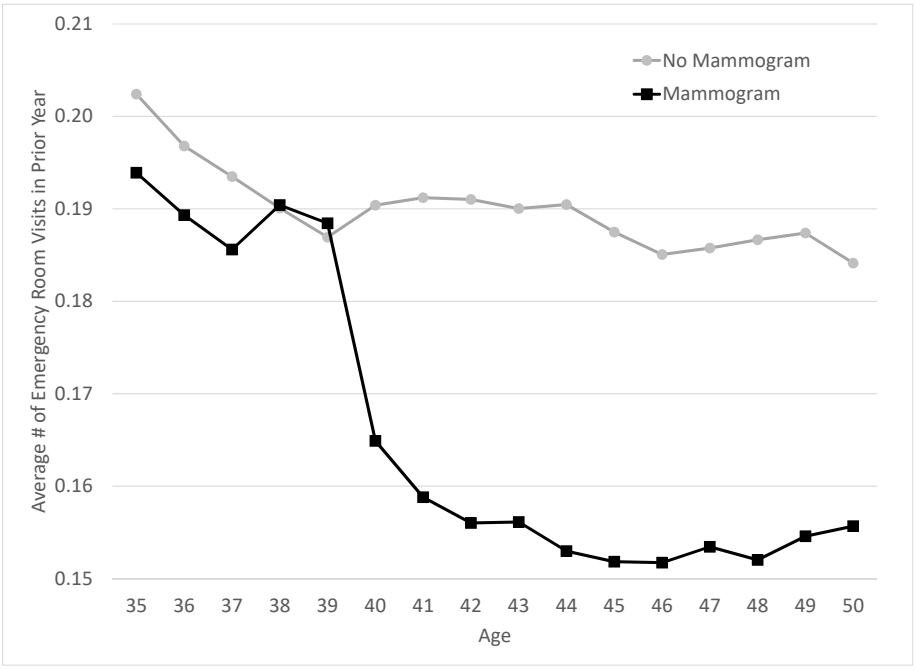


Notes: This figure shows the share of women who received a screening mammogram each year, by age. Source for survey data: Behavioral Risk Factor Surveillance System Survey (BRFSS), even years 2000-2012, restricted to women with health insurance (public or private). Source for claims data: HCCI data from 2008-2012, for mammograms between 2009-2011. Mammograms are coded in the HCCI claims data using the algorithm described in Segel, Balkrishnan,, and Hirth (2017). Mammograms are coded in the BRFSS data based on self-reports. The approximately 15-ppt discrepancy between surveyed and observed mammogram rates is consistent with the finding of Cronin et al. (2009), who document that self-reported screening rates overstated actual screening rates by 15 to 27 percentage points in a study of Vermont women.

Figure A.2: Health care spending and emergency room use prior to mammogram, by age



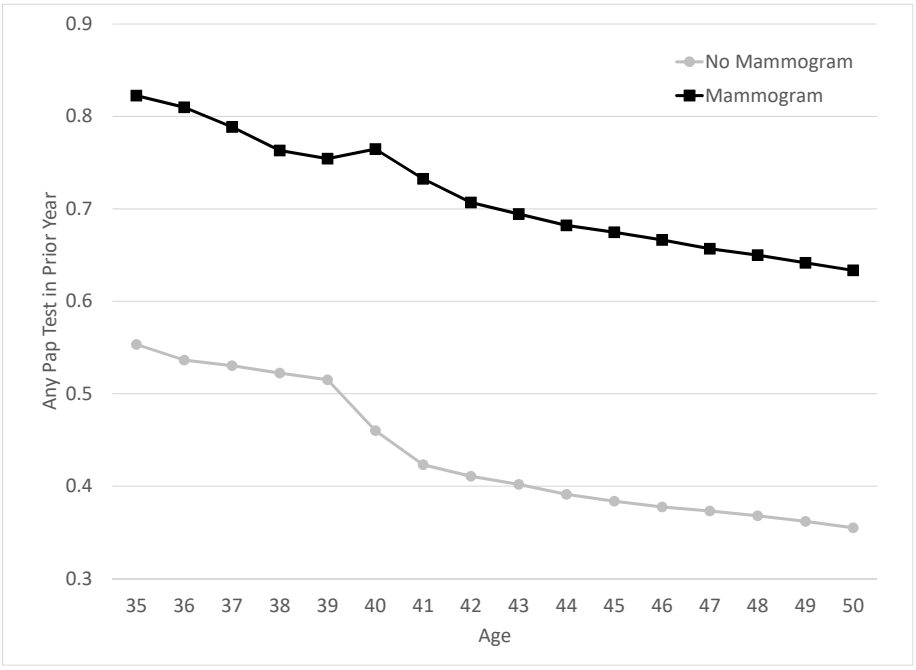
(a) Annual spending in year prior to mammogram



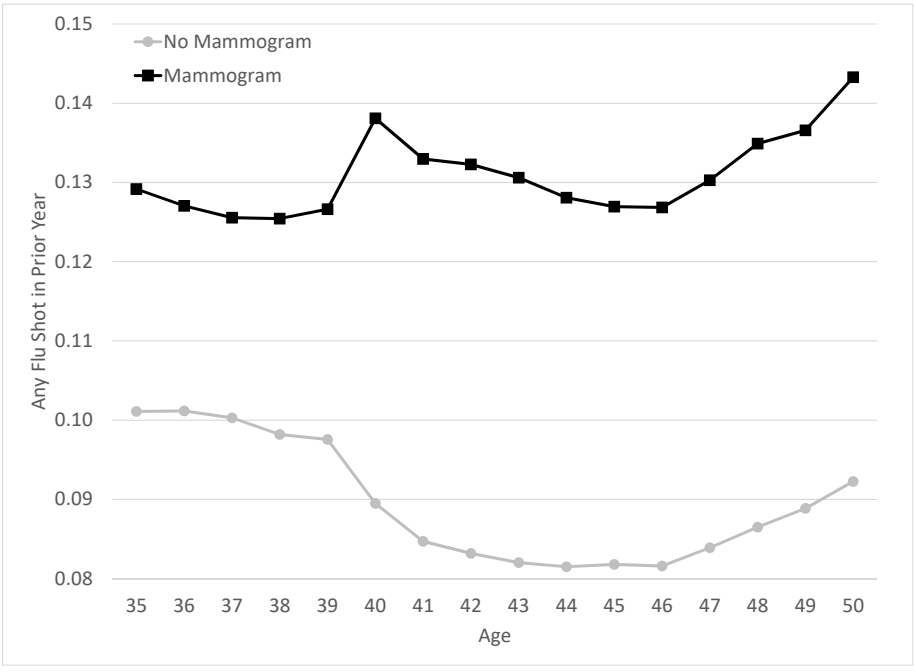
(b) # of emergency room visits in year prior to mammogram

Notes: Sample is insurance claims data on a set of privately insured woman-years from 2009- 2011. The x-axis plots the women's age at the time of the mammogram. Panel A presents average total spending in the 12 months prior to the mammogram, not including the mammogram date. Panel B presents average number of emergency room visits in the 12 months prior to a mammogram. For those without a mammogram, we draw a reference date from the distribution of actual mammograms in that year. All reference dates are set to be the first of the given month. N = 5,140,371 woman-years.

Figure A.3: Preventive care prior to mammogram by age



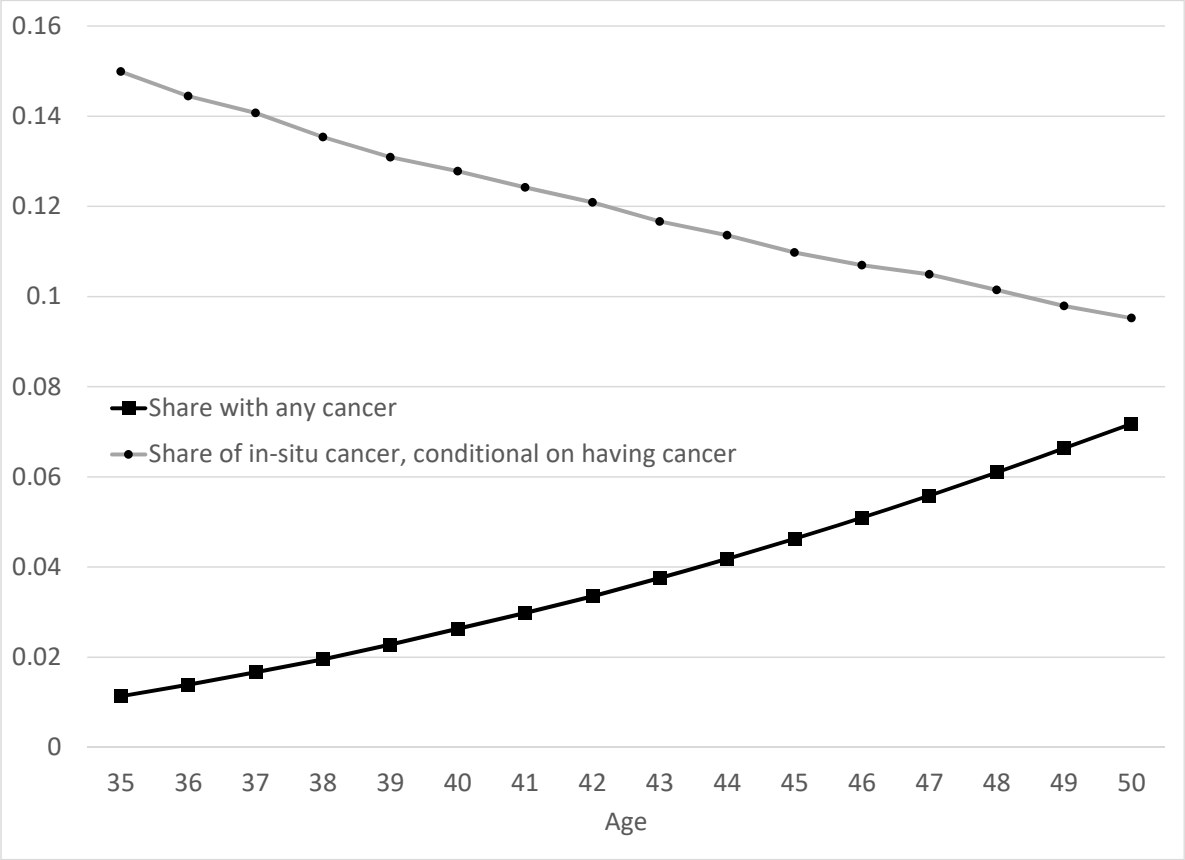
(a) Any pap test in year prior to mammogram



(b) Any flu shot in year prior to mammogram

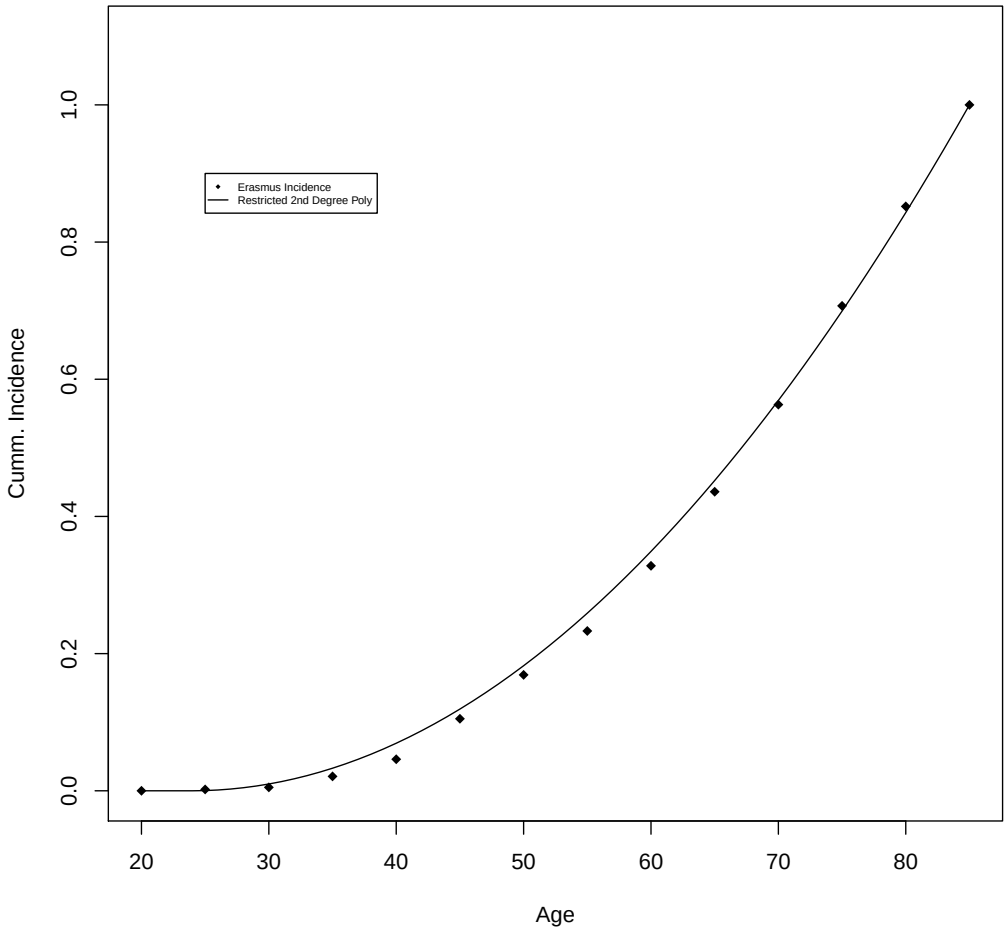
Notes: Sample is insurance claims data on a set of privately insured woman-years from 2009- 2011. In panel A, for each age at the time of the mammogram, we report the average share of women who obtained a pap test in the 12 months prior to the mammogram. We do not include tests done on the day of the mammogram. Panel B presents the analogous results for any flu shot. For those without a mammogram, we draw a reference date from the distribution of actual mammograms in that year. All reference dates are set to be the first of the given month. Spending is measured in the 12 months prior to this reference date. N = 5,140,371 woman-years.

Figure A.4: Erasmus model predictions for share with cancer and share in situ (no screening)



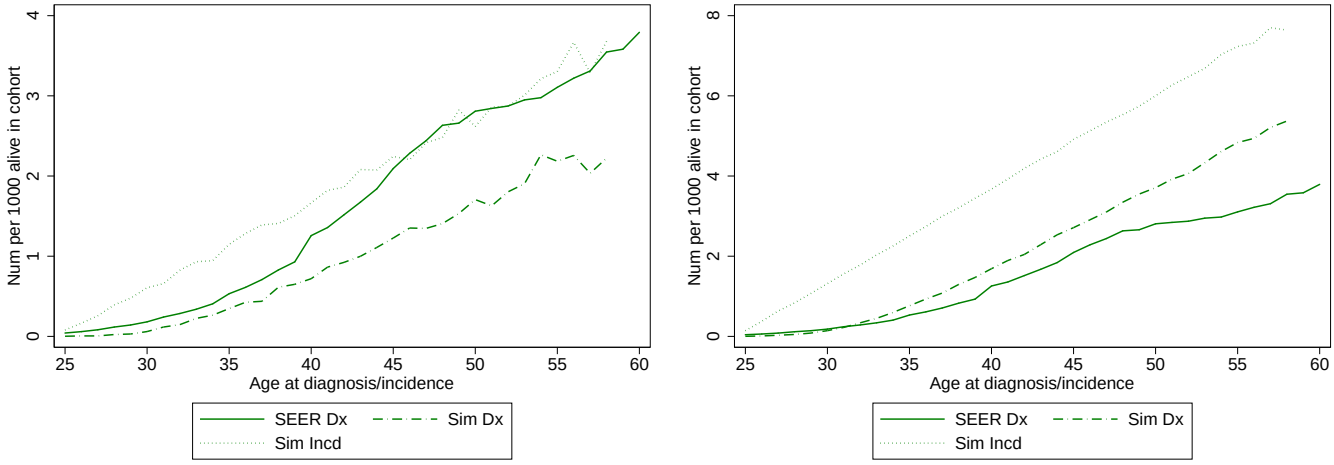
Notes: Figure presents the share with any cancer and the share of cancer in situ in the Erasmus model, with no screening.

Figure A.5: Fitted tumor incidence by age



Notes: Figure presents the smoothed CDF of tumor incidence by age, fitted to the original Erasmus incidence in 5-year intervals.

Figure A.6: Multiplicative incidence adjustment

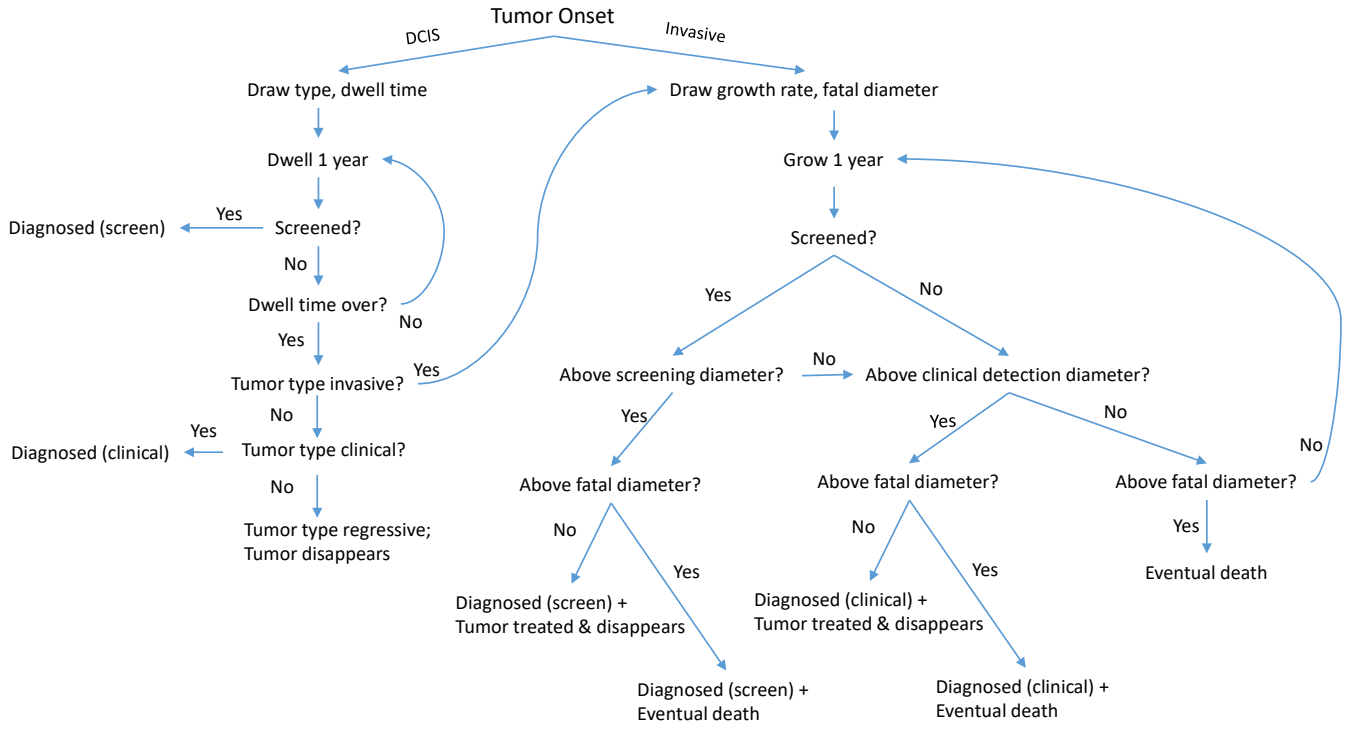


(a) Original incidence

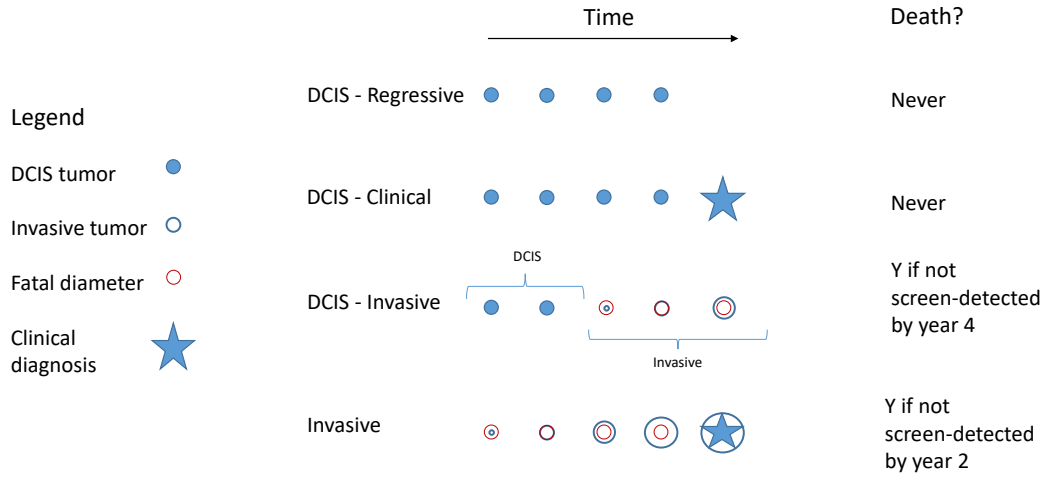
(b) Incidence multiplicatively shifted by α

Notes: Figure presents the simulated incidence and diagnosis rates compared with the SEER diagnosis rates. These are presented for both the original incidence in panel (a), and for the incidence shifted by α in panel (b). This simulation assumes no screening.

Figure A.7: Erasmus model



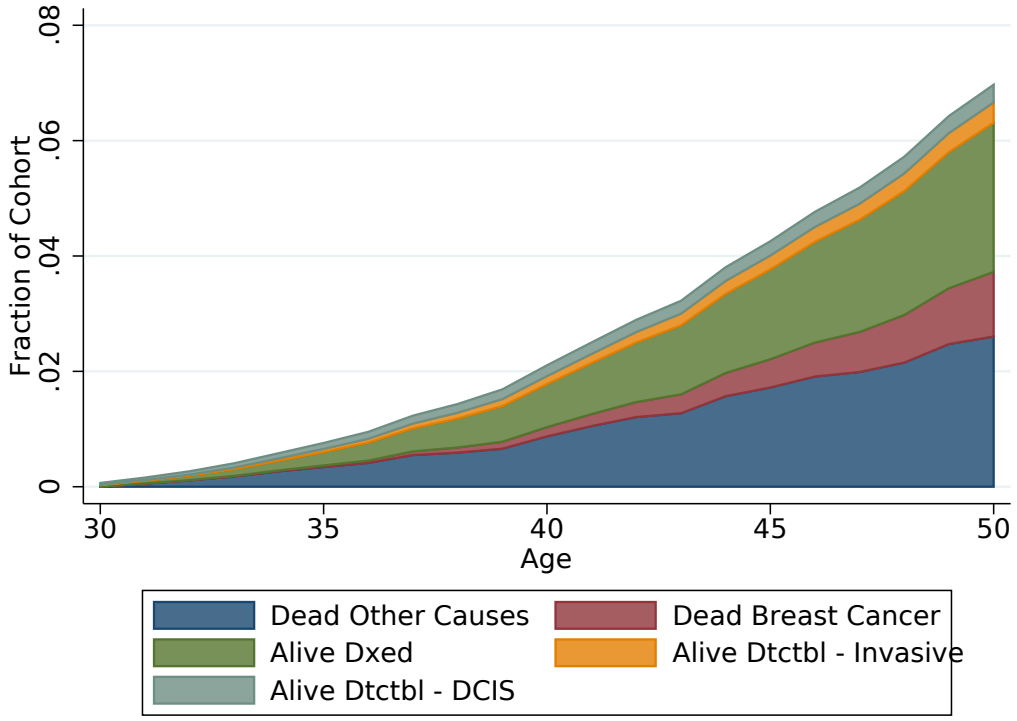
(a) Flow chart



(b) Example sequences

Notes: Panel (a) shows the flow chart of a tumor's natural history according to the Erasmus model. Panel (b) shows example sequences of progression for each different type of tumor, in the absence of screening.

Figure A.8: Cancer histories in Erasmus model



Notes: Figure shows the share of women in different categories when the Erasmus model is run without screening for birth cohorts 1950-1975, and focuses on years 2000-2005. The categories represented are "Dead Other Causes" (died due to other causes), "Dead Breast Cancer" (died due to breast cancer), "Alive Dxed" (alive and with clinically diagnosed cancer), "Alive Dtctbl - Invasive" (alive and with detectable but not yet detected invasive cancer), and "Alive Dtctbl - DCIS" (alive and with detectable but not yet detected DCIS cancer). The remainder of the population is cancer-free or has invasive or DCIS cancer that is too small to be detectable yet.

Table A.1: Codes used to identify claims

Event	Code type	CPT Codes	ICD-9 Codes
Screening mammogram	CPT procedure	77057*, G0202**	V76.12
Breast biopsy	CPT procedure	19100, 19101, 19120	85.11, 85.12, 85.20, 85.21
Breast ultrasound	CPT procedure	76645	88.73**
Radiologic breast testing	CPT procedure	76003, 77002*, 76095, 77031*, 76086, 76087, 76088, 77053*, 77054*, 76355, 76360, 76362, 77011*, 77012*, 77013*, 76098, 76100, 76101, 76102, 76120, 76125, 76140, 76150, 76350, 76365	87.35, 87.36, 87.73, 88.85
Breast cancer treatment	CPT procedure	19160, 19162, 19180, 19200, 19220, 19240, 19301**, 19303**, 19305**, 19307**, 38740, 38745	233.0, V103.0, 174.0-174.9

* indicates this code was not provided by Segel, Balkrishnan,, and Hirth (2017) but is the post-2007 analog of such a code. See http://provider.indianamedicaid.com/ihcp/Bulletins/BT200701.pdf.
** indicates this code was provided by Hubbard et al. (2015) rather than Segel, Balkrishnan,, and Hirth (2017).
Notes: This table provides the codes used to define mammograms in the HCCI and SEER-Medicare claims data. "CPT codes" are also known as "HCPCS codes".

Table A.2: Results of mammograms by diagnosis

	Diagnosed in SEER-Medicare	
	Yes	No
Negative	0.001	0.226
False Positive	0.001	0.014
True Positive	0.501	0.002
No Mammogram	0.497	0.759
N	80,408	3,327,642

Notes: This table summarizes the outcomes of mammograms for SEER-Medicare patients who are diagnosed with breast cancer in that year (column 1) and not diagnosed with breast cancer in that year (column 2). Breast cancer diagnoses are recorded in the SEER linked data. Mammogram outcomes (negative, false positive, true positive, and no mammogram) are coded using the Segel algorithm as described in Appendix A. We restrict to those who were diagnosed between 2007 and 2013. Sample includes both 65+ and disabled.

Table A.3: Diagnosis status by true positive result

	True positive mammogram (Conditional on screened)	
Time of Diagnosis	Yes	No
Prior to mammogram	0.001	0.000
In year of mammogram	0.722	0.000
In year following mammogram	0.145	0.022
More than 1 year after mammogram	0.016	0.142
Never diagnosed	0.116	0.836
N	55,799	952,292

Notes: This table summarizes the time of diagnosis in the linked SEER data for patients who were coded as having a true positive mammogram in the SEER-Medicare data. We restrict this analysis to patients who received a screening mammogram in the SEER-Medicare data, as coded in the Segel algorithm as described in Appendix A. For these patients, we use the SEER-Medicare claims and the Segel algorithm to determine whether the patient had a true positive mammogram. We then compare the timing of this claims-related diagnosis with the SEER diagnosis, if any occurred. The rows refer to the year the patient was coded as having breast cancer in the SEER linked data. Source: SEER-Medicare data, diagnoses between 2007-2013.

Table A.4: Tumor characteristics

Invasive	DCIS
Size s_i^y (cm)	Dwell time w_i (years)
Growth rate g_i (1/years) *	
Screen detection diameter r_i^{ay} (cm)	
Clinical diagnosis diameter c_i (cm) *	
Fatal diameter f_i (cm)	
Survival duration since fatal u_i (years) *	

Note: This table lists the tumor characteristics for invasive and DCIS tumors. Starred variables (*) have correlated distributions - see Table A.5. Parameter values listed in Appendix Table A.4 to A.7 are taken from Tan et al. (2006) or the extended CISNET description of the same model.

Table A.5: Model parameters

All women	Notation	Values
Probability of death from other causes	Q_y^b	Derived following Rosenberg (2006)
Probability of any breast cancer	C_b	Quadratic fit to Table A.8 plus further optimization
Age-specific probability of onset (given any onset)	S_a	Quadratic fit to values in Table A.6
Probability of invasive tumor (given tumor onset)	I_a	See Table A.9
Probability of DCIS tumor sub-type (summing to 1 - I_a)	V_a, R_a, C_a	See Table A.9
Invasive Tumors		
Mean of log of growth rate g_i	μ_G	0.062
SD of log of growth rate g_i	σ_G	0.87
Scale parameter for screen detection r_i^{ay}	β_R^{ay}	see Table A.7
Shape parameter for screen detection r_i^{ay}	η_R	2.95
Mean of log of clinical diagnosis diameter c_i	μ_C	0.97
SD of log of clinical diagnosis diameter c_i	σ_C	0.63
Scale parameter for fatal diameter f_i	β_F^y	Linear between 1915 and 1975 (0.8 in 1915; 4.0 in 1975); 4.0 after 1975
Shape parameter for fatal diameter f_i	η_F	0.95
Mean of log of survival duration u_i	μ_U	2.43
SD of log of survival duration u_i	σ_U	1.13
Correlation between g_i and c_i	ρ_{gc}	+0.41
Correlation between g_i and u_i	ρ_{gu}	-0.90
Correlation between c_i and u_i	ρ_{cu}	-0.43
DCIS Tumors		
Mean of tumor dwell time w_i[21]	W	5.22 - (time to grow from 1975 to current year screening diameter)
Screening sensitivity	E_y	Linear from 1975-2000 (0.4 in 1975, 0.8 in 2000) and 0.8 from 2001-2010

Note: This table lists the parameters of the tumor growth model, along with their values where applicable.

[21] Dwell time w_i (time from in situ onset to invasive onset) is calculated by subtracting the time it takes the invasive tumor to grow from the 1975 screening threshold to the current screening threshold from a random draw from an exponential distribution with mean 5.22.

Table A.6: Tumor incidence by age

Age	Cumulative incidence	Age	Annual probability of incidence
25	0.002	20-24	0.0004
30	0.005	25-29	0.0006
35	0.021	30-34	0.0032
40	0.046	35-39	0.0050
45	0.105	40-44	0.0118
50	0.169	45-49	0.0128
55	0.233	50-54	0.0128
60	0.328	55-59	0.0190
65	0.436	60-64	0.0216
70	0.563	65-69	0.0254
75	0.707	70-74	0.0288
80	0.852	75-79	0.0290
85	1.00	80-85	0.0247

Note: This table shows the age distribution of the incidence of the onset of pre-clinical breast cancer (including ductal carcinoma in situ). Source: Tan et al. (2006); author's calculations.

Table A.7: Screening diameter scale parameter

	Parameter value for age and year screened			
	30-49	50-59	60-69	70-85
1975	2.2	1.7	1.3	1.0
		(linear interpolation)		
2000	1.5	1.1	0.9	0.6

Note: This table shows the age- and screening-year-dependent values of the scale parameter for the screening diameter Weibull distribution. Linear interpolation is applied between years 1975 and 2000.

Table A.8: Tumor incidence by birth cohort: original Erasmus values

Birth cohort	Cumulative incidence
1900-04	0.122
1905-09	0.132
1910-14	0.141
1915-19	0.154
1920-24	0.169
1925-29	0.176
1930-34	0.182
1935-39	0.200
1940-44	0.220
1945-49	0.223
1950-54	0.204
1955-59	0.198
1960-64	0.193
1965-69	0.189
1970	0.187

Note: This table shows the cumulative probability (up to age 85) of the onset of pre-clinical breast cancer by birth cohort. Source: Tan et al. (2006)

Table A.9: Tumor type distribution

Age at onset	Invasive	DCIS-invasive	DCIS-regressive	DCIS-clinical
20-34	0.76	0.15	0.03	0.06
35-79		(linear interpolation)		
80-85	0.92	0.05	0.01	0.02

Note: This table shows the age-dependent proportions of incident tumor types. Linear interpolation is applied between ages 35 and 79.

Table A.10: Sensitivity checks for parameter estimates

		Sensitivity Checks				
		(1)	(2)	(3)	(4)	(5)
	Baseline		Share In-situ to Invasive		Share Non-Malignant	
Parameter	Estimate	Incidence	28%	14%	19%	42%
α^{o}	-5.21	-4.81	-5.20	-5.20	-4.67	-3.33
γ^{o}	0.10	0.09	0.10	0.10	0.09	0.05
$\delta^{o}_{\text{in-situ}}$	0.36	1.15	0.36	0.36	0.09	-0.16
$\delta^{o}_{\text{invasive}}$	1.13	10.89	1.13	1.13	1.15	1.58
α^{r}	0.29	-0.06	0.26	0.26	0.03	-0.73
γ^{r}	-0.03	-0.02	-0.02	-0.02	-0.02	0.00
$\delta^{r}_{\text{in-situ}}$	-0.01	0.58	-0.01	0.00	-0.55	-1.06
$\delta^{r}_{\text{invasive}}$	-4.67	22.28	-5.10	-12.80	-6.67	-13.67

Notes: Table shows the parameter estimates from the mammogram decision model under alternate sensitivity assumptions. Specifics for each of the columns are discussed in Section 5.2.3.