Annals of Internal Medicine ORIGINAL RESEARCH

Continuation of Annual Screening Mammography and Breast Cancer Mortality in Women Older Than 70 Years

Xabier García-Albéniz, MD, PhD; Miguel A. Hernán, MD, DrPH; Roger W. Logan, PhD; Mary Price, PhD; Katrina Armstrong, MD, MSCE; and John Hsu, MD, MBA, MSCE

Background: Randomized trials have shown that initiating breast cancer screening between ages 50 and 69 years and continuing it for 10 years decreases breast cancer mortality. However, no trials have studied whether or when women can safely stop screening mammography. An estimated 52% of women aged 75 years or older undergo screening mammography in the United States.

Objective: To estimate the effect of breast cancer screening on breast cancer mortality in Medicare beneficiaries aged 70 to 84 years.

Design: Large-scale, population-based, observational study of 2 screening strategies: continuing annual mammography, and stopping screening.

Setting: U.S. Medicare program, 2000 to 2008.

Participants: 1 058 013 beneficiaries aged 70 to 84 years who had a life expectancy of at least 10 years, had no previous breast cancer diagnosis, and underwent screening mammography.

Measurements: Eight-year breast cancer mortality, incidence, and treatments, plus the positive predictive value of screening mammography by age group.

Results: In women aged 70 to 74 years, the estimated difference in 8-year risk for breast cancer death between continuing and stopping screening was −1.0 (95% CI, −2.3 to 0.1) death per 1000 women (hazard ratio, 0.78 [CI, 0.63 to 0.95]) (a negative risk difference favors continuing). In those aged 75 to 84 years, the corresponding risk difference was 0.07 (CI, −0.93 to 1.3) death per 1000 women (hazard ratio, 1.00 [CI, 0.83 to 1.19]).

Limitations: The available Medicare data permit only 8 years of follow-up after screening. As with any study using observational data, the estimates could be affected by residual confounding.

Conclusion: Continuing annual breast cancer screening past age 75 years did not result in substantial reductions in 8-year breast cancer mortality compared with stopping screening.

Primary Funding Source: National Institutes of Health.

Ann Intern Med. 2020;172:381-389. doi:10.7326/M18-1199 **Annals.org**
For author affiliations, see end of text.
This article was published at Annals.org on 25 February 2020.

Randomized trials have shown the effectiveness of screening mammography in reducing breast cancer incidence and mortality. The most recent meta-analysis found that initiating screening between ages 50 and 69 years and continuing it for 10 years prevents 21.3 (95% CI, 10.7 to 31.7) breast cancer deaths per 10 000 women (1). An unanswered question is whether to continue screening at older ages. None of the screening trials included women older than 74 years (1), and all had few women aged 70 to 74 years, such that the 95% CI ranged from preventing 32.1 deaths to causing 17.2 deaths. Given the existing evidence base, a future randomized trial to study when to stop screening may be infeasible and potentially unethical.

Because of the lack of evidence on the effectiveness of screening mammography in older women, current guidelines contain cautious and noncommittal language. The U.S. Preventive Services Task Force states that "the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older" (2); the American Cancer Society recommends performing screening in all women older than 45 years and continuing it "as long as their overall health is good and they have a life expectancy of 10 years or longer" (3); and the American Geriatrics Society, which has identified breast cancer screening as 1 of its targets for the "Choosing Wisely" campaign, generally recommends considering life expectancy and the risks of testing, overdiagnosis, and overtreatment before recommending screening (4).

Despite the lack of evidence, many older women continue to have screening mammography—52% of U.S. women aged 75 years or older had mammography within the past 2 years (5), and more than a third of all breast cancer deaths occur in women diagnosed after age 70 years (6). In this study, we used the experience of a large random sample of Medicare beneficiaries to estimate the effect of continuing screening on breast cancer mortality among women aged 70 to 74 years and those aged 75 to 84 years.

Methods

In principle, the effect of continuing breast cancer screening at older ages could be evaluated in a pragmatic randomized trial (7, 8). Because this hypothetical target trial is not available, we used observational data to emulate it. To focus the clinical question and justify our methods, we first characterize the target trial.

See also:

Editorial comment 427
Summary for Patients I-22

Web-Only
Supplement

Table 1. Abbreviated Protocol of the Pragmatic Target Trial and Its Emulation Using U.S. Medicare Data From 1999 to 2008

Component	Target Trial	Emulation
Eligibility	Women aged 70–84 years who have no history of breast cancer, have had no breast symptoms in the previous 9 months, have a perceived life expectancy of ≥10 years, and have screening mammography the day they enter the trial. Because information will be collected via Medicare claims, only women with continuous enrollment in Medicare Parts A and B (not Medicare Advantage) for ≥12 months are eligible.	Same as target trial A combined comorbidity score <1 was used as a proxy for perceived life expectancy of ≥10 years (10).
Treatment strategies	*Stop screening:* Women do not have further screening after baseline *Continue screening:* Women continue annual screening mammography (with a 3-month grace period [i.e., women can have mammography in the 12th, 13th, or 14th month after their last one]) and are excused from further screening after a breast cancer diagnosis Under both strategies, diagnostic mammography is allowed when clinically indicated (under the second strategy, the diagnostic mammography date becomes the new starting point for the next screening interval)	Same as target trial
Treatment assignment	Eligible women are randomly assigned to 1 of the strategies. Randomization is done separately for women aged 70–74 years and those aged 75–84 years. Women are aware of the strategy they are assigned to.	We assumed that women were randomly assigned within levels of the following baseline variables: age, race, previous use of health resources (visits to the emergency department and days admitted), long-term care residency, combined comorbidity score, previous use of preventive services, Census Bureau division, calendar year, and Chronic Conditions Data Warehouse comorbidities (Table 2).
Follow-up	For each woman, follow-up starts at the time of assignment to a strategy and ends at death, disenrollment from fee-for-service Medicare, or 8 years, whichever comes first.	Same as target trial
Primary end point	Breast cancer mortality	Same as target trial
Causal contrast	Intention-to-treat effect Per protocol effect	Observational analogue of the per protocol effect
Statistical analysis	Intention-to-treat analysis Per protocol analysis (9): Women are censored when they deviate from their assigned strategy as follows: *Stop screening:* Censored when they have screening mammography *Continue screening:* Censored at the 14th month after the last mammography if no screening mammography (if no breast cancer diagnosis) The analysis is adjusted for baseline variables and, using inverse probability weighting, for the time-varying variables: time since last mammography; type (screening or diagnostic) and number of mammographies; acute myocardial infarction, hip fracture, stroke, and use of preventive services in the previous 12 months; breast symptoms, visits to the emergency department, and days admitted in the previous 6 months; combined comorbidity score; institutionalization in a long-term care facility; and new diagnosis of any of the Chronic Conditions Data Warehouse comorbidities in Table 2. All analyses are stratified by age group.	Same as per protocol analysis, except that we created 2 individuals (clones) per eligible woman and assigned 1 to each screening strategy.

Table 1 outlines the protocol for our pragmatic target trial and the emulation procedure. In brief, the trial would randomly assign women aged 70 to 74 or 75 to 84 years who have favorable life expectancy and recently had screening mammography to 1 of 2 strategies: stop screening, or continue screening mammography every 12 months (with a 3-month grace period) until a diagnosis of breast cancer or death. In a sensitivity analysis, a modified strategy in which women stopped screening when they developed a serious condition (such as Alzheimer disease or lung cancer) did not materially change any estimates.

This target trial could estimate both the intention-to-treat effect and the per protocol effect (9) (that is, the effect if all women had adhered to the protocol for their assigned strategy). The per protocol effect is arguably of greater clinical interest (9, 11).

Per Protocol Analysis of the Target Trial

The per protocol analysis would estimate the hazard ratio for breast cancer mortality for the "continue screening" strategy versus the "stop screening" strategy via a discrete hazards model, approximated using a pooled logistic regression model (12, 13) that includes an indicator for the screening strategy, a flexible function of time (cubic splines), and the baseline covariates in Table 2. Our approach would censor women if they deviate from their assigned strategy. To adjust for potential selection bias due to censoring (9, 14), each woman would receive a time-varying inverse probability weight that depends on the baseline and time-varying variables in Table 1 (see the Appendix, available at Annals.org, for a description of the weighting procedure). A critical assumption is that the adjustment

Table 2. Baseline Characteristics of Eligible Women, by Age Group*

Characteristic	Aged 70–74 Years (*n* = 1 235 459)	Aged 75–84 Years (*n* = 1 403 735)
Race		
White	91.1	92.3
Black	5.9	5.0
Other	3.0	2.8
Census Bureau division		
New England	6.0	6.6
Middle Atlantic	11.8	12.5
East North Central	18.9	19.2
West North Central	9.5	9.7
South Atlantic	21.8	21.2
East South Central	7.0	6.3
West South Central	10.0	9.2
Mountain	5.5	5.3
Pacific	9.1	9.8
Non–Census Bureau division	0.3	0.2
Calendar year		
2000	8.1	8.2
2001	15.1	15.0
2002	14.8	14.6
2003	14.2	14.1
2004	14.1	14.2
2005	13.9	14.0
2006	13.5	13.6
2007	6.3	6.3
Emergency department visits in previous 6 mo		
1	6.0	6.7
≥2	0.9	1.0
Days admitted in previous 6 mo		
1–5	3.0	3.4
6–10	0.5	0.6
<11	0.2	0.3
Medicare-covered preventive services received in previous 12 mo		
Influenza vaccination	54.0	58.6
Bone mass measurement	14.7	14.5
Cardiovascular screening	64.8	64.3
Diabetes screening	10.5	10.7
Annual wellness visit	8.1	7.2
Colorectal cancer screening	28.2	27.6
Pelvic screening	21.5	17.4
Long-term care resident	1.3	2.7
Combined comorbidity score		
<0	44.4	45.5
0	55.6	54.5
Chronic Conditions Data Warehouse comorbidities		
Alzheimer disease and related disorders	1.3	2.7
Acute myocardial infarction in previous 12 mo	0.1	0.2
Atrial fibrillation	1.8	3.1
Anemia	20.8	25.6
Asthma	3.9	3.7
Cataracts	63.6	75.1
Chronic heart failure	3.9	5.7
Chronic kidney disease	1.6	1.9
Chronic obstructive pulmonary disease	6.3	7.1
Colorectal cancer	0.9	1.4
Depression	12.0	12.5
Diabetes	16.0	16.0
Endometrial cancer	0.5	0.7
Glaucoma	17.3	21.7
Hip fracture in previous 12 mo	0.1	0.3
Hypertension	69.1	76.7
Hypothyroidism	16.2	18.2
Ischemic heart disease	22.0	27.2
Hyperlipidemia	63.1	63.6
Lung cancer	0.1	0.2
Osteoporosis	21.1	28.1
Rheumatoid arthritis/osteoarthritis	38.2	45.3
Stroke in previous 12 mo	1.0	1.5
Women diagnosed with breast cancer at baseline screening, *n* (%)	9755 (0.8)	13 035 (0.9)
Treated with surgery†	80.5	77.7
Lumpectomy†	53.3	49.4
Simple mastectomy†	9.9	9.8
Radical mastectomy†	17.4	18.5
Treated with radiotherapy†	53.3	45.1
Treated with chemotherapy†	15.9	9.0

* Data are percentages unless otherwise indicated.
† Among women diagnosed with breast cancer.

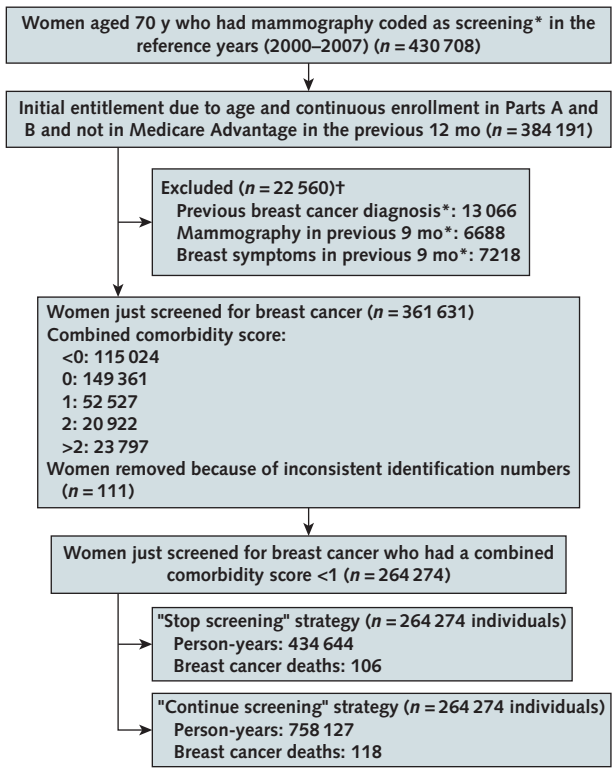
variables include all important baseline and postbaseline risk factors that predict adherence to the assigned strategy. We also would censor women if they die of causes other than breast cancer, which are not expected to be affected by breast cancer screening.

To produce estimates of cumulative incidence curves standardized to the distribution of the baseline variables in the study population, we would include product ("interaction") terms for screening strategy and time variables in the pooled logistic model (15). The predicted probabilities from this regression model would be used to estimate the 8-year predicted probability of breast cancer death. Because the use of weights induces within-subject correlation, we would use nonparametric bootstrap resampling (for example, based on the percentiles from 500 individual-level resamplings) to obtain valid estimates of 95% CIs.

Medicare Data

To emulate the target trial, we used data from a random 20% sample of fee-for-service Medicare beneficiaries enrolled in Parts A and B between 1999 and 2008. We extracted information on demographic characteristics (age, race, original reason for enrollment, and Census Bureau division) and Medicare Chronic Conditions Data Warehouse condition categories (in-

Figure 1. Selection of eligible women enrolled in Medicare and aged 70 y, 1999 to 2008.



* Required by the screening mammography extraction algorithm.
† Women could be excluded for >1 reason.

cluding breast cancer diagnosis, both invasive and in situ) from the denominator files. We used the outpatient and carrier files (to identify physician services) to extract information on use of preventive services (for example, annual wellness visits; influenza vaccination; bone mass measurements; screening for cardiovascular disease, diabetes, and colorectal cancer; and screening pelvic examinations) and screening mammography (using a validated algorithm for Medicare claims) (16). We then computed a combined comorbidity score (10) using inpatient hospital claims and data on stays in long-term care facilities and a validated algorithm for the skilled-nursing facility encounters file (17). We used these data to evaluate the presence of breast cancer symptoms or signs (using International Classification of Diseases, 9th Revision, codes for mastodynia, lump or mass in breast, induration, inversion or retraction of nipple, and nipple discharge) and treatments (18). We classified the most extensive breast surgery within the first year of diagnosis as the definitive surgery (19) and breast histologic examinations (biopsy or lumpectomy) as having positive results if they were followed by a breast cancer diagnosis in the next 6 months. We used a Medicare-specific comorbidity score that ranges from −2 to 26 (better to worse) to include only women with a high probability of living 10 additional years (that is, those with a score <1) (10).

Cause of death was obtained from the National Death Index (1999 to 2008). Cause-of-death codes have been edited and audited by the National Center for Health Statistics using parts I and II of the cause-of-death section on death certificates, which contain "immediate and underlying causes of death" and "other significant conditions contributing to death," respectively. We did not evaluate the effect of screening on all-cause mortality because of concerns about intractable confounding with this outcome (20).

Emulation of the Target Trial

We first emulated a trial among women who met the eligibility criteria on the day they had screening mammography at age 70 years (8, 21). Because all women had baseline data consistent with both the "continue screening" and "stop screening" strategies, we needed to create 2 identical individuals (clones) for each woman, assign each to 1 of the strategies, and censor them when data became inconsistent with that strategy (see the **Appendix** for more details and a sensitivity analysis in which, instead of cloning, women in the database were randomly assigned to 1 of the strategies) (22, 23). We then followed each individual until death, disenrollment from fee-for-service Medicare, or December 2008, whichever came first.

We repeated the process separately for women between ages 71 and 84 years, creating 15 total cohorts. Each woman could contribute an eligible individual in multiple cohorts as she aged as long as she satisfied the cohort-specific eligibility criteria (8, 24, 25). We then conducted the per protocol analysis described earlier for the target trial to estimate the effect of the screening strategies on breast cancer mortality and described diagnoses and treatments in each group during follow-up. A critical assumption was that the adjustment variables included all important baseline and postbaseline risk factors that also predicted assignment and adherence to the strategy.

We computed the positive predictive value (PPV) of mammography (conducted for any reason) by dividing the number of histologic examinations with positive results by the number of mammograms that prompted a histologic examination. We used SAS, version 9.4 (SAS Institute), for all analyses. The Partners Human Research Committee and the Institutional Review Board at Harvard T.H. Chan School of Public Health approved the study.

Role of the Funding Source

This research was supported by the National Institutes of Health. The funders had no role in the study design, data collection and analysis, manuscript preparation, or the decision to publish the manuscript.

RESULTS

Among women aged 70 years, 264 274 were eligible for our emulated trial. **Figure 1** shows the selection process. These women contributed 434 644 person-years to the "stop screening" strategy and 758 127 person-years to the "continue screening" strategy. **Sup-**

plement Figure 1 (available at Annals.org) shows the selection process for those aged 71 to 84 years. Each woman was eligible for an average of 2.5 age-specific emulated trials. Therefore, after pooling over all age groups, 2 639 194 individuals contributed 4 656 465 person-years to the "stop screening" strategy and 7 170 142 person-years to the "continue screening" strategy. Median follow-up was 16 months (interquartile range, 14 to 32 months) (Supplement Figure 2, available at Annals.org).

Table 2 shows the baseline characteristics of eligible women by age group. Compared with younger women, older ones had more frequent visits to the emergency department and higher frequency of Medicare Chronic Conditions Data Warehouse conditions at baseline. Older women diagnosed with breast cancer at baseline were also less likely to have surgery or receive radiotherapy or chemotherapy.

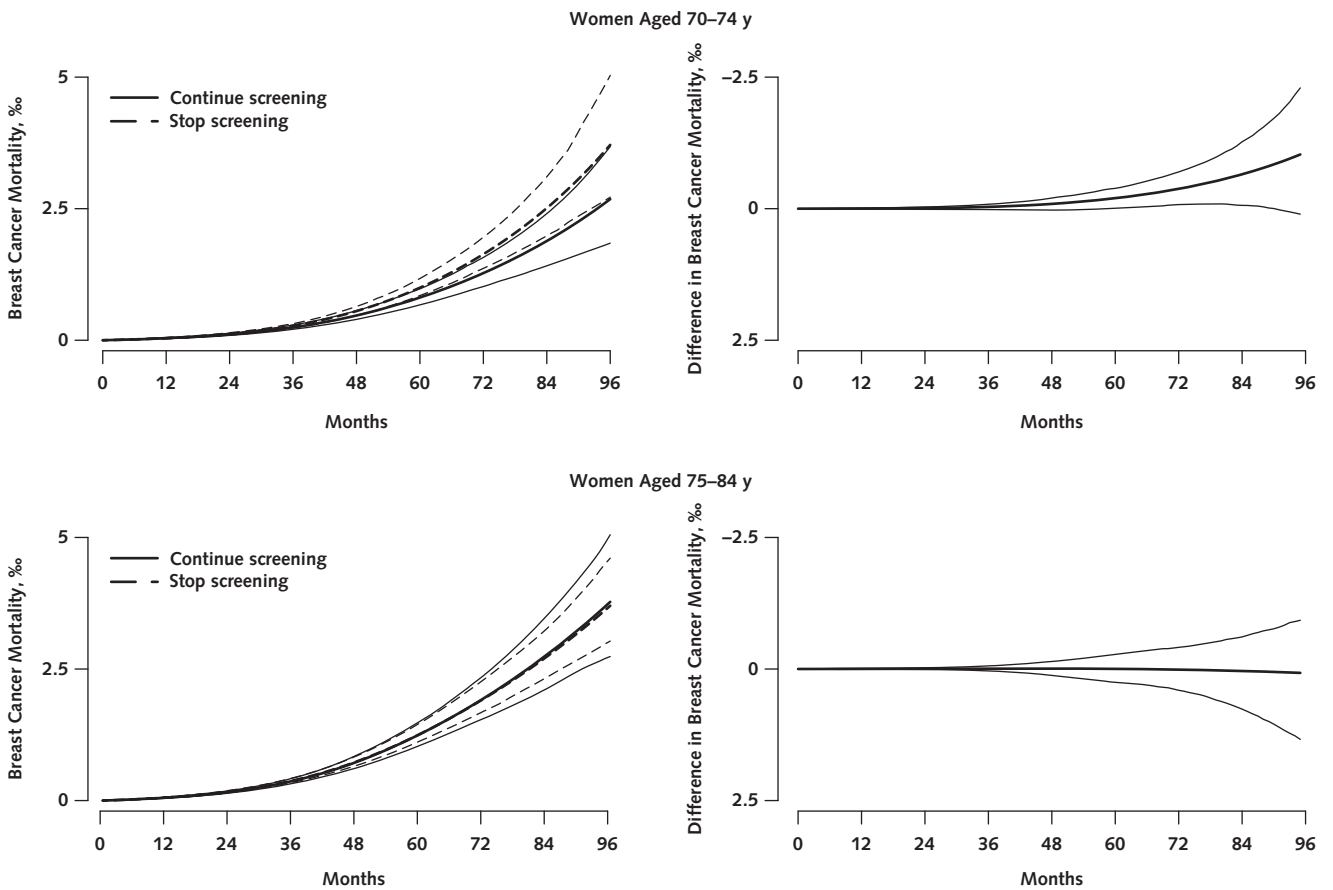
Breast Cancer Outcomes

During follow-up, there were 1533 deaths due to breast cancer under the "continue screening" strategy and 1304 under the "stop screening" strategy. Among women aged 70 to 74 years, the estimated 8-year risk for breast cancer death was 2.7 (CI, 1.8 to 3.7) deaths per 1000 women with the "continue screening" strategy and 3.7 (CI, 2.7 to 5.0) deaths per 1000 women with the "stop screening" strategy, which corresponds to a risk difference of −1.0 (CI, −2.3 to 0.1) death per 1000 women and a hazard ratio of 0.78 (CI, 0.63 to 0.95). Among women aged 75 to 84 years, the estimated 8-year risk for breast cancer death was 3.8 (CI, 2.7 to 5.1) deaths per 1000 women with the "continue screening" strategy and 3.7 (CI, 3.0 to 4.6) deaths per 1000 women with the "stop screening" strategy, which corresponds to a risk difference of 0.07 (CI, −0.93 to 1.3) death per 1000 women and a hazard ratio of 1.00 (CI, 0.83 to 1.19) (Figure 2). Supplement Table 1 (available at Annals.org) shows estimates by 5-year age groups.

Sensitivity analyses that excluded women who had previous cancer diagnoses, had serious comorbidities, or resided in long-term care centers or that defined breast cancer death as a death with "breast cancer" as any of the underlying causes (rather than using the cause of death provided by the National Death Index) did not materially change the results.

Adjustment for confounders had a large effect on the estimates. For example, in women aged 70 to 74 years, the unadjusted 8-year risk difference was −5.6

Figure 2. Standardized cumulative incidence curves for breast cancer mortality, by screening strategy and age group.



Thinner lines represent 95% CIs. The 2 curves in the 75- to 84-y age group are indistinguishable from each other.

Table 3. Treatments Received by Women Diagnosed With Breast Cancer Under Each Screening Strategy in the Emulated Target Trial*

Treatment	Proportion (95% CI)			
	Aged 70–74 Years (n = 1 235 459)		Aged 75–84 Years (n = 1 403 735)	
	Continue Screening	Stop Screening	Continue Screening	Stop Screening
Lumpectomy	52.6 (51.8–53.4)	36.5 (35.2–38.0)	48.8 (47.9–49.5)	32.6 (31.5–33.8)
Simple mastectomy	11.3 (10.8–11.8)	10.4 (9.5–11.3)	10.8 (10.3–11.2)	10.1 (9.4–10.9)
Radical mastectomy	13.9 (13.4–14.5)	18.2 (17.0–19.4)	14.2 (13.7–14.6)	17.0 (16.0–17.9)
Radiotherapy	51.0 (50.3–51.8)	39.9 (38.6–41.3)	41.2 (40.4–41.9)	31.9 (30.7–33.1)
Chemotherapy	15.2 (14.7–15.8)	21.1 (20.0–22.1)	8.6 (8.3–9.1)	11.5 (10.6–12.3)

* Percentages are standardized to the age group–specific distribution of age; comorbidity score; new diagnosis of Alzheimer disease, acute myocardial infarction, chronic heart failure, chronic kidney disease, chronic obstructive pulmonary disease, hip fracture, stroke, or cancer (lung, endometrial, or colorectal); and institutionalization in a long-term care center.

deaths per 1000 women. Adjustment for baseline variables changed it to −4.9 deaths per 1000 women, and adjustment for time-varying variables changed it to −1.0 death per 1000 women. Adjustment for time-varying screening history and time-varying comorbidities had the greatest effect (**Supplement Figure 3** and **Supplement Table 2**, available at Annals.org). In sensitivity analyses (26, 27), we explored scenarios under which our effect estimates would not be substantially affected by unmeasured confounding (**Supplement Tables 3** and **4** and the "Unmeasured Confounding" section of the **Supplement**, available at Annals.org). In addition, we used corpus uteri cancer mortality as a negative control outcome to assess the presence of unmeasured confounding. The results suggest that unmeasured confounding, if it exists, would result in overestimation of the beneficial effect of continuing screening on breast cancer mortality (**Supplement Table 5** [available at Annals.org] and the "Unmeasured Confounding" section of the **Supplement**).

Breast Cancer Diagnoses and Treatments

The estimated 8-year risk for breast cancer was 5.5% with the "continue screening" strategy (5.3% in women aged 70 to 74 years and 5.8% in those aged 75 to 84 years) and 3.9% with the "stop screening" strategy (3.9% in women aged 70 to 74 years and 3.9% in those aged 75 to 84 years) (**Supplement Figure 4**, available at Annals.org).

The PPV of mammography done for any reason after baseline was 38.5% with the "continue screening" strategy (35.8% in women aged 70 to 74 years and 41.5% in those aged 75 to 84 years) and 45.3% with the "stop screening" strategy (42.2% in women aged 70 to 74 years and 48.4% in those aged 75 to 84 years). **Table 3** describes the treatments received after a postbaseline breast cancer diagnosis. Differences in treatments among strategies were similar across age groups. Women diagnosed under the "stop screening" strategy (that is, those whose breast cancer was detected by means other than a screening mammogram) were more likely to receive chemotherapy but less likely to receive radiotherapy, lumpectomies, or any other type of surgery.

DISCUSSION

There is limited trial evidence and dim prospects for future trials to address the important clinical question of how long women should continue with breast cancer screening. In female Medicare beneficiaries aged 70 years or older who had a high probability of living another 10 years and had undergone screening mammography, we compared 2 screening strategies: continuing annual breast cancer screening, or stopping it. Our estimates suggest that continuing to screen women aged 70 to 74 years would reduce 8-year breast cancer mortality by 1 death per 1000 women, with the 95% CI ranging from 2 deaths to none. In contrast, continuing to screen women aged 75 years or older does not seem to affect 8-year breast cancer mortality. The estimated benefit for women aged 70 to 74 years in our observational study was similar to those estimated in randomized clinical trials (1). The reduced benefit in older women is consistent with the hypothesis that competing causes of death, such as cardiovascular or neurologic conditions, overtake breast cancer mortality with increasing age.

Previous observational studies of breast cancer screening in older women (28–31) have been criticized for the presence of lead time and length time biases (32). Our observational design mitigates these by emulating a target trial that explicitly aligns eligibility and assignment to screening strategies at baseline and adjusts for both baseline and postbaseline prognostic factors (8, 33). A previous simulation study (34) highlighted the importance of a long life expectancy for screening benefit and proposed screening cessation at ages similar to those in our study. However, unlike that study, our study used real-world data to emulate a pragmatic target trial (35). The target trial emulation approach has been used in several research fields (21, 23, 25, 36, 37), and a detailed exposition of the methods can be found elsewhere (7, 22, 33).

Although breast cancer prognosis depends on the extent (nodes and distant spread) and biology of the tumor rather than its size (38), the justification for annual mammography is that treatment is more effective for the small asymptomatic tumors detected at screening than for the larger symptomatic tumors detected in

the absence of screening (39). In our study, as expected, women who continued screening were more likely to receive a breast cancer diagnosis. The excess diagnoses in this group were either aggressive asymptomatic tumors or tumors that would not have become clinically apparent in the absence of screening (overdiagnosis). Consequently, in our study, women were treated more aggressively under the "stop screening" strategy, as we expected. Of note, women aged 75 to 84 years were less likely to receive radiotherapy or chemotherapy than those aged 70 to 74 years (differences in surgery were smaller). The lower use of radiotherapy in the older age group is consistent with clinical recommendations (40), and the lower use of chemotherapy probably reflects judicious use of this aggressive treatment in an elderly population (41).

All women included in our analysis had health insurance through Medicare and therefore probably had access to screening and treatment. However, like every observational analysis, ours relies on the assumption that all important prognostic factors that affect screening and treatment decisions were included. Our analyses adjusted for many of these factors, including time-varying comorbidities and screening, which had a profound effect on the estimates because newly diagnosed comorbidities can determine screening choices as well as cancer treatments and because one of the reasons to stop screening is a breast cancer diagnosis, which of course affects breast cancer mortality. Although we could not adjust for postmenopausal hormone therapy use, family history of breast cancer, age at menarche, and age at first completed pregnancy, these factors have not been found to be strongly associated with breast cancer in older women (42). The Supplement includes an extended discussion of unmeasured confounding.

Our study did not include women enrolled in Medicare Advantage, which is administered by private plans. In our study period, 13% to 21% of the total Medicare population was enrolled in Medicare Advantage (43). During this period, Medicare Advantage enrollees tended to be healthier on average than traditional fee-for-service beneficiaries, although these differences have lessened considerably in recent years (43–46).

The observed PPVs were on the scale of modern performance metrics and increased with age (47). Estimates of PPV for women who continued screening were worse than for those who stopped and might have been better had we studied biennial screening mammography, which is currently recommended by the U.S. Preventive Services Task Force (1). Nevertheless, during the years used for this analysis (1999 to 2008), many guidelines recommended annual or biennial mammography (48), and annual screening also was the most frequent pattern in Medicare (data not shown). Our estimates are restricted to 8 years of follow-up because the most current available linkage between Medicare and the National Death Index covers only 1999 to 2008. Although 10-year estimates are frequently reported in the literature, our 8-year estimates can still inform practice in an elderly population in the absence of clinical trials of breast cancer screening.

In conclusion, among women who have had at least 1 screening mammography, our estimates suggest that continuing screening past age 75 years results in no material difference in cancer-specific mortality over the following 8-year period compared with screening cessation.

From Harvard T.H. Chan School of Public Health and Massachusetts General Hospital, Boston, Massachusetts, and RTI Health Solutions, Barcelona, Spain (X.G.A.); Harvard T.H. Chan School of Public Health and Harvard-MIT Division of Health Sciences and Technology, Boston, Massachusetts (M.A.H.); Harvard T.H. Chan School of Public Health, Boston, Massachusetts (R.W.L.); Massachusetts General Hospital, Boston, Massachusetts (M.P., K.A.); and Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts (J.H.).

Grant Support: By grants K99-CA207730, P01-CA134294, R01-CA164023, and R01-HS023128 from the National Institutes of Health.

Disclosures: Dr. Hsu reports grants from the National Institutes of Health and the Agency for Healthcare Research and Quality during the conduct of the study; other support from the American Association for the Advancement of Science, the University of California, DaVita, Sidley Austin LLP, Delta Health Alliance, and Community Servings outside the submitted work; and employment at Massachusetts General Hospital, which provides medical care and cancer screening for Medicare beneficiaries. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M18-1199.

Reproducible Research Statement: *Study protocol:* See the Appendix. *Statistical code:* Available from Dr. García-Albéniz (e-mail, xabi@post.harvard.edu). *Data set:* Available from the Centers for Medicare & Medicaid Services (www.cms.gov).

Corresponding Author: Xabier García-Albéniz, MD, PhD, Department of Epidemiology, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA 02115; e-mail, xabi@post.harvard.edu.

Current author addresses and author contributions are available at Annals.org.

References

1. **Nelson HD, Fu R, Cantor A, et al.** Effectiveness of breast cancer screening: systematic review and meta-analysis to update the 2009 U.S. Preventive Services Task Force recommendation. Ann Intern Med. 2016;164:244-55. [PMID: 26756588] doi:10.7326/M15-0969

2. **Siu AL; U.S. Preventive Services Task Force.** Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2016;164:279-96. [PMID: 26757170] doi:10.7326/M15-2886

3. **Oeffinger KC, Fontham ET, Etzioni R, et al; American Cancer Society.** Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. JAMA. 2015;314:1599-614. [PMID: 26501536] doi:10.1001/jama.2015.12783

4. **Choosing Wisely.** American Geriatrics Society: Breast, Colorectal and Prostate Cancer Screening in Older Adults. Philadelphia: ABIM

Foundation; 2014. Accessed at www.choosingwisely.org/clinician-lists/american-geriatrics-society-breast-colorectal-prostate-cancer-screening-in-older-adults on 8 March 2016.
5. **National Center for Health Statistics.** Health, United States, 2018. Hyattsville, MD: Centers for Disease Control and Prevention; 2019. Accessed at www.cdc.gov/nchs/data/hus/hus18.pdf on 19 January 2020.
6. **Smith RA, Andrews K, Brooks D, et al.** Cancer screening in the United States, 2016: a review of current American Cancer Society guidelines and current issues in cancer screening. CA Cancer J Clin. 2016;66:96-114. [PMID: 26797525] doi:10.3322/caac.21336
7. **Hernán MA, Robins JM.** Using big data to emulate a target trial when a randomized trial is not available. Am J Epidemiol. 2016;183:758-64. [PMID: 26994063] doi:10.1093/aje/kwv254
8. **García-Albéniz X, Hsu J, Hernán MA.** The value of explicitly emulating a target trial when using real world evidence: an application to colorectal cancer screening. Eur J Epidemiol. 2017;32:495-500. [PMID: 28748498] doi:10.1007/s10654-017-0287-2
9. **Hernán MA, Robins JM.** Per-protocol analyses of pragmatic trials. N Engl J Med. 2017;377:1391-8. [PMID: 28976864] doi:10.1056/NEJMsm1605385
10. **Gagne JJ, Glynn RJ, Avorn J, et al.** A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64:749-59. [PMID: 21208778] doi:10.1016/j.jclinepi.2010.10.004
11. **Hernán MA, Scharfstein D.** Cautions as regulators move to end exclusive reliance on intention to treat. Ann Intern Med. 2018;168:515-6. [PMID: 29554689] doi:10.7326/M17-3354
12. **Thompson WA Jr.** On the treatment of grouped observations in life studies. Biometrics. 1977;33:463-70. [PMID: 911970]
13. **D'Agostino RB, Lee ML, Belanger AJ, et al.** Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. Stat Med. 1990;9:1501-15. [PMID: 2281238]
14. **Hernán MA, Hernández-Díaz S, Robins JM.** A structural approach to selection bias. Epidemiology. 2004;15:615-25. [PMID: 15308962]
15. **Cole SR, Hernán MA.** Adjusted survival curves with inverse probability weights. Comput Methods Programs Biomed. 2004;75:45-9. [PMID: 15158046]
16. **Fenton JJ, Zhu W, Balch S, et al.** Distinguishing screening from diagnostic mammograms using Medicare claims data. Med Care. 2014;52:e44-51. [PMID: 22922433] doi:10.1097/MLR.0b013e318269e0f5
17. **Yun H, Kilgore ML, Curtis JR, et al.** Identifying types of nursing facility stays using Medicare claims data: an algorithm and validation. Health Serv Outcomes Res Methodol. 2010;10:100-10. doi:10.1007/s10742-010-0060-4
18. **Smith GL, Xu Y, Buchholz TA, et al.** Association between treatment with brachytherapy vs whole-breast irradiation and subsequent mastectomy, complications, and survival among older women with invasive breast cancer. JAMA. 2012;307:1827-37. [PMID: 22550197] doi:10.1001/jama.2012.3481
19. **Smith BD, Jiang J, Shih YC, et al.** Cost and complications of local therapies for early-stage breast cancer. J Natl Cancer Inst. 2017;109. [PMID: 27678203] doi:10.1093/jnci/djw178
20. **García-Albéniz X, Hsu J, Bretthauer M, et al.** Estimating the effect of preventive services with databases of administrative claims: reasons to be concerned. Am J Epidemiol. 2019;188:1764-7. [PMID: 30869122] doi:10.1093/aje/kwz049
21. **García-Albéniz X, Hsu J, Bretthauer M, et al.** Effectiveness of screening colonoscopy to prevent colorectal cancer among Medicare beneficiaries aged 70 to 79 years: a prospective observational study. Ann Intern Med. 2017;166:18-26. [PMID: 27669524] doi:10.7326/M16-0758
22. **Cain LE, Robins JM, Lanoy E, et al.** When to start treatment? A systematic approach to the comparison of dynamic regimes using observational data. Int J Biostat. 2010;6:Article 18. [PMID: 21972433]
23. **Garcia-Albeniz X, Chan JM, Paciorek A, et al.** Immediate versus deferred initiation of androgen deprivation therapy in prostate cancer patients with PSA-only relapse. An observational follow-up study. Eur J Cancer. 2015;51:817-24. [PMID: 25794605] doi:10.1016/j.ejca.2015.03.003
24. **Hernán MA, Robins JM, García Rodríguez LA.** Discussion on "Statistical Issues in the Women's Health Initiative." Biometrics. 2005;61:922-30.
25. **Hernán MA, Alonso A, Logan R, et al.** Observational studies analyzed like randomized experiments: an application to postmenopausal hormone therapy and coronary heart disease. Epidemiology. 2008;19:766-79. [PMID: 18854702] doi:10.1097/EDE.0b013e3181875e61
26. **Schneeweiss S.** Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. Pharmacoepidemiol Drug Saf. 2006;15:291-303. [PMID: 16447304]
27. **Lash TL, Fox MP, Fink AK, eds.** Applying Quantitative Bias Analysis to Epidemiologic Data. New York: Springer-Verlag; 2009. doi:10.1007/978-0-387-87959-8
28. **Badgwell BD, Giordano SH, Duan ZZ, et al.** Mammography before diagnosis among women age 80 years and older with breast cancer. J Clin Oncol. 2008;26:2482-8. [PMID: 18427152] doi:10.1200/JCO.2007.12.8058
29. **McPherson CP, Swenson KK, Lee MW.** The effects of mammographic detection and comorbidity on the survival of older women with breast cancer. J Am Geriatr Soc. 2002;50:1061-8. [PMID: 12110066]
30. **McCarthy EP, Burns RB, Freund KM, et al.** Mammography use, breast cancer stage at diagnosis, and survival among older women. J Am Geriatr Soc. 2000;48:1226-33. [PMID: 11037009]
31. **Van Dijck JA, Verbeek AL, Beex LV, et al.** Mammographic screening after the age of 65 years: evidence for a reduction in breast cancer mortality. Int J Cancer. 1996;66:727-31. [PMID: 8647640]
32. **Walter LC, Schonberg MA.** Screening mammography in older women: a review. JAMA. 2014;311:1336-47. [PMID: 24691609] doi:10.1001/jama.2014.2834
33. **Hernán MA, Sauer BC, Hernández-Díaz S, et al.** Specifying a target trial prevents immortal time bias and other self-inflicted injuries in observational analyses. J Clin Epidemiol. 2016;79:70-5. [PMID: 27237061] doi:10.1016/j.jclinepi.2016.04.014
34. **Lansdorp-Vogelaar I, Gulati R, Mariotto AB, et al.** Personalizing age of cancer screening cessation based on comorbid conditions: model estimates of harms and benefits. Ann Intern Med. 2014;161:104-12. [PMID: 25023249] doi:10.7326/M13-2867
35. **Visvanathan K, Levit LA, Raghavan D, et al.** Untapped potential of observational research to inform clinical decision making: American Society of Clinical Oncology research statement. J Clin Oncol. 2017;35:1845-54. [PMID: 28358653] doi:10.1200/JCO.2017.72.6414
36. **Danaei G, Rodríguez LA, Cantero OF, et al.** Observational data for comparative effectiveness research: an emulation of randomised trials of statins and primary prevention of coronary heart disease. Stat Methods Med Res. 2013;22:70-96. [PMID: 22016461] doi:10.1177/0962280211403603
37. **Cain LE, Saag MS, Petersen M, et al; Antiretroviral Therapy Cohort Collaboration, the Centers for AIDS Research Network of Integrated Clinical Systems, and the HIV-CAUSAL Collaboration.** Using observational data to emulate a randomized trial of dynamic treatment-switching strategies: an application to antiretroviral therapy. Int J Epidemiol. 2016;45:2038-49. [PMID: 26721599] doi:10.1093/ije/dyv295
38. **Sparano JA, Gray RJ, Makower DF, et al.** Prospective validation of a 21-gene expression assay in breast cancer. N Engl J Med. 2015;373:2005-14. [PMID: 26412349] doi:10.1056/NEJMoa1510764
39. **Welch HG, Prorok PC, O'Malley AJ, et al.** Breast-cancer tumor size, overdiagnosis, and mammography screening effectiveness. N Engl J Med. 2016;375:1438-47. [PMID: 27732805]
40. **Biganzoli L, Wildiers H, Oakman C, et al.** Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA). Lancet Oncol. 2012;13:e148-60. [PMID: 22469125] doi:10.1016/S1470-2045(11)70383-7

41. **Loibl S, von Minckwitz G, Harbeck N, et al.** Clinical feasibility of (neo)adjuvant taxane-based chemotherapy in older patients: analysis of >4,500 patients from four German randomized breast cancer trials. Breast Cancer Res. 2008;10:R77. [PMID: 18796139] doi:10.1186/bcr2144
42. **Vacek PM, Skelly JM, Geller BM.** Breast cancer risk assessment in women aged 70 and older. Breast Cancer Res Treat. 2011;130:291-9. [PMID: 21604157] doi:10.1007/s10549-011-1576-1
43. **Neuman P, Jacobson GA.** Medicare Advantage checkup. N Engl J Med. 2018;379:2163-72. [PMID: 30428276] doi:10.1056/NEJMhpr1804089
44. **McWilliams JM, Hsu J, Newhouse JP.** New risk-adjustment system was associated with reduced favorable selection in Medicare Advantage. Health Aff (Millwood). 2012;31:2630-40. [PMID: 23213147] doi:10.1377/hlthaff.2011.1344
45. **Newhouse JP, Price M, Huang J, et al.** Steps to reduce favorable risk selection in Medicare Advantage largely succeeded, boding well for health insurance exchanges. Health Aff (Millwood). 2012;31:2618-28. [PMID: 23213145] doi:10.1377/hlthaff.2012.0345
46. **Newhouse JP, Price M, McWilliams JM, et al.** How much favorable selection is left in Medicare Advantage? Am J Health Econ. 2015;1:1-26. [PMID: 26389127]
47. **Lee CS, Sengupta D, Bhargavan-Chatfield M, et al.** Association of patient age with outcomes of current-era, large-scale screening mammography: analysis of data from the National Mammography Database [Letter]. JAMA Oncol. 2017;3:1134-6. [PMID: 28426842] doi:10.1001/jamaoncol.2017.0482
48. **U.S. Preventive Services Task Force.** Screening for breast cancer: recommendations and rationale. Ann Intern Med. 2002;137:344-6. [PMID: 12204019]

Current Author Addresses: Drs. García-Albéniz, Hernán, and Logan: Department of Epidemiology, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA 02115.
Drs. Price and Hsu: Mongan Institute, Massachusetts General Hospital, 50 Staniford Street, 9th Floor, Boston, MA 02114.
Dr. Armstrong: Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114.

Author Contributions: Conception and design: X. García-Albéniz, M.A. Hernán, J. Hsu.
Analysis and interpretation of the data: X. García-Albéniz, M.A. Hernán, J. Hsu.
Drafting of the article: X. García-Albéniz, M.A. Hernán.
Critical revision of the article for important intellectual content: X. García-Albéniz, M.A. Hernán, K. Armstrong, J. Hsu.
Final approval of the article: X. García-Albéniz, M.A. Hernán, R.W. Logan, M. Price, K. Armstrong, J. Hsu.
Statistical expertise: X. García-Albéniz, M.A. Hernán, R.W. Logan.
Obtaining of funding: X. García-Albéniz, M.A. Hernán, J. Hsu.
Administrative, technical, or logistic support: R.W. Logan, M. Price, J. Hsu.
Collection and assembly of data: R.W. Logan, M. Price, J. Hsu.

Appendix: Technical Appendix

Comparing Sustained Interventions

Assignment of Follow-up Consistent With Both Screening Strategies

Comparison of screening strategies that are sustained over time requires use of statistical methods that can appropriately adjust for time-varying confounders, such as the g-formula (49) or inverse probability weighting preceded by cloning and censoring (50). We describe in detail our implementation of the latter approach for the comparison of the "stop screening" and "continue screening" strategies during 8 years in the absence of a breast cancer diagnosis.

Appendix Table 1 shows data for 4 hypothetical women in our study. Only the first 3 years of follow-up are shown for simplicity.

The first step is cloning each woman into 2 identical individuals, each of whom is assigned to 1 strategy. The second step is censoring the clones when they deviate from their assigned strategy. Appendix Figure 1 depicts this approach, and Appendix Table 2 shows this process for the 4 women. In the "stop screening" group, individuals 2A and 4A are censored because individual 2 had screening mammography 1 year after her baseline screening mammography and individual 4 had screening mammography 1 year after diagnostic mammography (note that diagnostic mammography is allowed at any time in both groups). In the "continue screening" group, individual 1B is censored because she did not have mammography 1 year after baseline. Individual 3 is not censored under either strategy because in our target trial, patients are not required to adhere to a specific strategy after a breast cancer diagnosis. Of note, censoring is needed to estimate the observational analogue of the per protocol effect; otherwise, the comparison of women assigned to each group would be the analogue of an intention-to-treat analysis with extreme nonadherence, which would be uninformative.

Inverse Probability Weighting to Adjust for Informative Censoring

Because the censoring in the previous step can introduce selection bias, the next step is adjustment via inverse probability weighting. Briefly, uncensored individuals receive a weight equal to the inverse of their probability of being uncensored, conditional on their screening and covariate history. Appendix Table 3 describes the contribution to the weights for each strategy as a function of the probability of having screening mammography conditional on screening and covariate history. We truncated the weights at the 99th percentile to avoid undue influence of outliers (51). Nontruncated weights yielded similar point estimates.

To estimate the time-varying probability of having mammography, we fit a pooled logistic model for the monthly probability of having screening mammography to the original data before cloning. The model included a time-varying intercept (which we estimated using a restricted cubic spline as a flexible function of time), baseline covariates (age, race, calendar year, geographic region), and the following time-varying covariates: visits to the emergency department and admissions in the previous 6 months; comorbidity score; use of annual preventive services (cardiovascular screening, colorectal cancer screening, diabetes screening, pelvic screening, influenza vaccination, bone mass measurement, wellness visit); diagnosis of atrial fibrillation, Alzheimer disease and related disorders, acute myocardial infarction in the previous year, anemia, asthma, cataracts, chronic heart failure, chronic kidney disease, chronic obstructive pulmonary disease, colorectal cancer, depression, diabetes, endometrial cancer, glaucoma, hip fracture in the previous year, hypertension, hypothyroidism, ischemic heart disease, hyperlipidemia, lung cancer, osteoporosis, osteoarthritis, or stroke in the previous year; admission to a long-term care center; breast symptoms in the previous 6 months; number of diagnostic and screening mammographies received to date; and time since last mammography. The estimates from this model are shown in Appendix Table 4.

The probabilities estimated by this model were used to construct the inverse probability weights as described in Appendix Table 3. The distribution of the weights, truncated at the 99th percentile, is summarized in Appendix Table 5 by study group and age group.

Sensitivity Analysis: Random Assignment of Treatment Strategies as an Alternative to Cloning

In our example, all women have baseline data consistent with both screening strategies, so we cloned women and assigned each clone to 1 of the strategies. An alternative approach is to randomly assign individuals to a single strategy. We did this analysis by randomly assigning half of the 1 235 459 women aged 70 to 74 years to continue screening for 8 years and the other half to stop screening and then proceeded as in our main analysis (censoring when a woman's data became inconsistent with her assigned strategy and fitting an inverse probability–weighted model). The hazard ratio of breast cancer mortality was 0.82 (CI, 0.60 to 1.12) for continuing versus stopping screening. When we repeated the procedure 100 times, the hazard ratios varied from 0.58 (CI, 0.44 to 0.76) to 0.97 (CI, 0.70 to 1.35), with an average hazard ratio of 0.79 and a mean robust SE of 0.153 (Appendix Figure 2). Using the cloning approach, the corresponding hazard ratio was 0.78 (CI, 0.63 to 0.97) and the robust SE was 0.113.

Web-Only References

49. **Robins JM, Hernán MA.** Estimation of the causal effects of time-varying exposures. In: Fitzmaurice G, Davidian M, Verbeke G, et al, eds. Longitudinal Data Analysis. Boca Raton, FL: Chapman & Hall/CRC; 2009:553-99.

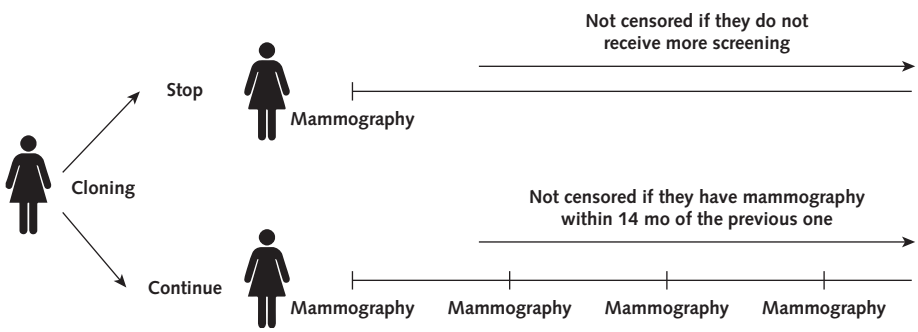
50. **Hernán MA.** How to estimate the effect of treatment duration on survival outcomes using observational data. BMJ. 2018;360:k182. [PMID: 29419381] doi:10.1136/bmj.k182

51. **Cain LE, Logan R, Robins JM, et al; HIV-CAUSAL Collaboration.** When to initiate combined antiretroviral therapy to reduce mortality and AIDS-defining illness in HIV-infected persons in developed countries: an observational study. Ann Intern Med. 2011;154:509-15. [PMID: 21502648] doi:10.7326/0003-4819-154-8-201104190-00001

Appendix Table 1. Four Hypothetical Women in Our Study

Identifier	Type of Mammography at Baseline	Breast Cancer Diagnosis by End of First Year	Deceased at End of First Year	Type of Mammography at Start of Second Year	Deceased at End of Second Year	Type of Mammography at Start of Third Year	Deceased at End of Third Year
1	Screening	No	No	None	No	None	No
2	Screening	No	No	Screening	No	Screening	No
3	Screening	Yes	No	None	No	None	Yes
4	Screening	No	No	Diagnostic	No	Screening	No

Appendix Figure 1. Schematic representation of the process of cloning and censoring.



Appendix Table 2. Cloning and Censoring of 4 Hypothetical Women in Our Study

Identifier	Study Group	Type of Mammography at Baseline	Breast Cancer Diagnosis by End of First Year	Deceased at End of First Year	Type of Mammography at Start of Second Year	Deceased at End of Second Year	Type of Mammography at Start of Third Year	Deceased at End of Third Year
1A	Stop screening	Screening	No	No	None	No	None	No
2A	Stop screening	Screening	No	No	Screening	Censored	–	–
3A	Stop screening	Screening	Yes	No	None	No	None	Yes
4A	Stop screening	Screening	No	No	Diagnostic	No	Screening	Censored
1B	Continue screening	Screening	No	No	None	Censored	–	–
2B	Continue screening	Screening	No	No	Screening	No	Screening	No
3B	Continue screening	Screening	Yes	No	None	No	None	Yes
4B	Continue screening	Screening	No	No	Diagnostic	No	Screening	No

Appendix Table 3. Contribution to the Weights at Each Time Point, by Screening Strategy*

Strategy	Time Point	Contribution to Weights†
Stop screening	$t > 0$	$1/(1 - p)$
Continue screening	$0 < t \leq 13$	1
	$t = 14$	$1/p$

* t is the time since the last mammography (for any reason; resets to 0 the month of the examination), and p is the probability of having screening mammography (conditional on screening and covariate history).
† In the absence of a breast cancer diagnosis.

Appendix Table 4. Estimated Log Odds Ratios of Receipt of Screening Mammography

Variable	Coefficient (SE)
Baseline	
Age	−0.42 (0.0081)
Age squared	0.0025 (0.000054)
Calendar year	−0.11 (0.0014)
Calendar year squared	0.014 (0.00023)
Race	
White	Reference
Black	−0.32 (0.0034)
Other	−0.22 (0.0046)
Census region	
Northeast	0.036 (0.0021)
Midwest	0.070 (0.0019)
South	Reference
West	0.016 (0.023)
≥1 emergency department visit in previous 6 mo	−0.0055 (0.0030)
Days admitted in previous 6 mo	
0	Reference
1–5	0.046 (0.0043)
>5	0.057 (0.0084)
Combined comorbidity score	
<0	−0.020 (0.0020)
0	Reference
Long-term care resident	0.25 (0.0083)
Use of preventive services in previous 12 mo	
Cardiovascular screening	0.025 (0.0018)
Colorectal cancer screening	0.10 (0.0017)
Diabetes screening	0.014 (0.0024)
Pelvic screening	0.038 (0.0020)
Influenza vaccination	0.071 (0.0016)
Bone mass measurement	0.094 (0.0022)
Annual wellness visit	0.0070 (0.0030)
Alzheimer disease and related disorders	0.18 (0.0082)
Acute myocardial infarction in previous 12 mo	−0.054 (0.019)
Atrial fibrillation	0.051 (0.0068)
Anemia	0.0041 (0.0026)
Asthma	0.0062 (0.0063)
Cataracts	0.040 (0.0020)
Chronic heart failure	0.019 (0.0050)
Chronic kidney disease	0.026 (0.0082)
Chronic obstructive pulmonary disease	−0.020 (0.0046)
Colorectal cancer	0.055 (0.011)
Depression	0.018 (0.0037)
Diabetes	−0.077 (0.0036)
Endometrial cancer	0.052 (0.015)
Glaucoma	0.014 (0.0033)
Hip fracture in previous 12 mo	−0.085 (0.018)
Hypertension	−0.0079 (0.0025)
Hypothyroidism	0.0055 (0.0033)
Ischemic heart disease	−0.023 (0.0027)
Hyperlipidemia	0.018 (0.0021)
Lung cancer	0.49 (0.025)
Osteoporosis	0.020 (0.0027)
Stroke in previous 12 mo	−0.28 (0.0065)
Time-varying	
≥1 emergency department visit in previous 6 mo	−0.099 (0.0026)
Days admitted in previous 6 mo	
0	Reference
1–5	−0.21 (0.0035)
>5	−0.55 (0.0056)
Combined comorbidity score	
<0	−0.17 (0.14)
0	Reference
1	−0.015 (0.0022)
≥2	−0.016 (0.0033)
Use of preventive services in previous 12 mo	
Cardiovascular screening	0.19 (0.0018)
Colorectal cancer screening	0.16 (0.0017)
Diabetes screening	−0.0086 (0.0025)

Continued on following page

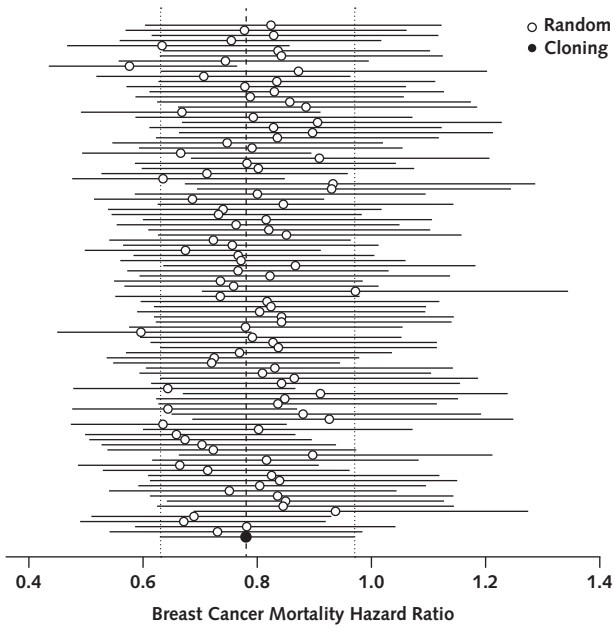
Appendix Table 4–Continued

Variable	Coefficient (SE)
Pelvic screening	0.33 (0.0020)
Influenza vaccination	0.15 (0.0016)
Bone mass measurement	−0.016 (0.0020)
Annual wellness visit	0.17 (0.0030)
Atrial fibrillation	0.0057 (0.0042)
Alzheimer disease and related disorders	−0.43 (0.0043)
Acute myocardial infarction in previous 12 mo	−0.20 (0.013)
Anemia	−0.0071 (0.0022)
Asthma	0.045 (0.0046)
Cataracts	0.082 (0.0024)
Chronic heart failure	−0.067 (0.0032)
Chronic kidney disease	−0.023 (0.0042)
Chronic obstructive pulmonary disease	−0.047 (0.0032)
Colorectal cancer	−0.016 (0.0079)
Depression	−0.11 (0.0028)
Diabetes	−0.043 (0.0030)
Endometrial cancer	0.066 (0.011)
Glaucoma	0.043 (0.0029)
Hip fracture in previous 12 mo	−0.33 (0.012)
Hypertension	0.012 (0.0026)
Hypothyroidism	0.018 (0.0027)
Ischemic heart disease	−0.025 (0.0024)
Hyperlipidemia	0.021 (0.0024)
Lung cancer	−0.43 (0.014)
Osteoporosis	0.050 (0.0022)
Rheumatoid arthritis/osteoarthritis	0.029 (0.0020)
Stroke in previous 12 mo	−0.17 (0.0060)
Long-term care resident	−0.29 (0.0057)
Breast symptoms in previous 6 mo	0.17 (0.012)
Number of diagnostic mammographies	
0	Reference
1	0.030 (0.024)
2	0.25 (0.0043)
3	0.59 (0.0056)
≥4	0.68 (0.0079)
Number of screening mammographies	
1	Reference
2	1.02 (0.0034)
3	1.83 (0.0052)
4	2.54 (0.0066)
5	3.20 (0.0079)
6	3.83 (0.0094)
7	4.52 (0.012)
8	5.23 (0.020)

Appendix Table 5. Distribution of Inverse Probability Weights

Age Group	Strategy	Mean	SD	Minimum	Maximum
70–74 y	Stop screening	2.6	3.9	1	27.0
	Continue screening	1.5	1.7	1	12.7
75–84 y	Stop screening	2.5	3.4	1	23.8
	Continue screening	1.6	2.1	1	15.4

Appendix Figure 2. Hazard ratios for breast cancer mortality using different approaches of baseline treatment assignment in women aged 70 to 74 y.



Horizontal lines represent 95% CIs.