Original Article

Reduction in Late-Stage Breast Cancer Incidence in the Mammography Era

Implications for Overdiagnosis of Invasive Cancer

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BACKGROUND: Mammographic screening is expected to decrease the incidence of late-stage breast cancer. In the current study, the authors determined the decrease in late-stage cancer incidence and the changes in invasive cancer incidence that occurred in the mammographic era after adjusting for prescreening temporal trends. **METHODS:** Breast cancer incidence and stage data were obtained from the Surveillance, Epidemiology, and End Results program. The premammography period (1977-1979) was compared with the mammographic screening period (2007-2009) for women aged ≥ 40 years. The authors estimated prescreening temporal trends using 5 measures of annual percentage change (APC). Stage-specific incidence values from 1977 through 1979 (baseline) were adjusted using APC values of 0.5%, 1.0%, 1.3%, and 2.0% and then compared with observed stage-specific incidence in 2007 through 2009. **RESULTS:** Prescreening APC temporal trend estimates ranged from 0.8% to 2.3%. The joinpoint estimate of 1.3% for women aged ≥ 40 years approximated the 4-decade long APC trend of 1.2% noted in the Connecticut Tumor Registry. At an APC of 1.3%, late-stage breast cancer incidence decreased by 37% (56 cases per 100,000 women) with a reciprocal increase in early-stage rates noted from 1977 through 1979 to 2007 through 2009. Resulting late-stage cancer incidence decreased from 21% at an APC of 0.5% to 48% at an APC of 2.0%. Total invasive breast cancer incidence decreased by 9% (27 cases per 100,000 women) at an APC of 1.3%. **CONCLUSIONS:** There is evidence that a substantial reduction in late-stage breast cancer has occurred in the mammography era when appropriate adjustments are made for prescreening temporal trends. At background APC estimates of ≥ 1%, the total invasive breast cancer incidence also decreased. ***Cancer* 2014;000:000-000.** © *2014 American Cancer Society.*

KEYWORDS: mammography, screening, overdiagnosis, breast cancer, late-stage disease.

INTRODUCTION

Breast cancer is a major worldwide health problem and the most common cause of female cancer death. In 2008, 1.4 million women were diagnosed with breast cancer and 458,000 died of the disease worldwide.[1] Mammographic screening can reduce breast cancer mortality. A recent meta-analysis of 8 randomized trials demonstrated a 14% to 32% mortality reduction among women invited to be screened compared with women who were not invited.[2] A meta-analysis of women participating in organized clinical screening programs showed a 49% mortality reduction.[3] The Cancer Intervention and Surveillance Modeling Network (CISNET) models of annual screening beginning at age 40 years demonstrated a 40% average reduction in breast cancer mortality.[4] Even with these substantial benefits, however, mammographic screening remains controversial and trade-offs between benefit and harms are debated.

Successful screening programs are expected not only to detect small early-stage cancer but to decrease the incidence of higher-mortality late-stage disease. Many organized mammographic screening programs have demonstrated a shift from late-stage to early-stage disease detection.[5-10] Results from the United States, which lacks a national screening program, have shown a greater increase in early-stage disease incidence compared with late-stage disease reduction in breast cancer.[11-13] Recently, Bleyer and Welch used Surveillance, Epidemiology, and End Results Program (SEER) breast cancer incidence data, which included both screened and unscreened women, to demonstrate a 69% increase in localized disease but only an 8% decrease in late-stage disease over a 30-year interval from 1976 through 1978 to 2006 through 2008.[13]

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Questions were raised whether screening mammography had met the fundamental requirement of decreasing late-stage disease. However, stage-specific incidence results were not adjusted for the underlying temporal trend of increasing breast cancer incidence that existed before the introduction of widespread screening mammography in the United States in the mid-1980s. Breast cancer incidence increased 1% to 3% per year in the United States and Europe before the advent of mammography screening.[14-20] In the United States, the annual incidence increased approximately 1.2 % (annual percentage change [APC]) in the long-standing Connecticut Tumor Registry from 1940 to 1982.[16-18,21,22] More rapid increases, up to 5% per year, have been documented in the absence of screening mammography in Asia, Africa, and Eastern Europe.[1,14,23,24]

Although these underlying temporal trends absent screening mammography may appear small on an annual basis, their impact on expected future incidence over many decades is profound, independent of interventions such as screening mammography. These trends directly influence calculations of late-stage disease changes and estimates of overdiagnosis. Over 30 years, a 1% annual increase results in an incidence increase of 33% and a 2% annual increase results in an overall incidence increase of 78% due to compounding. The projected incidence of early-stage and late-stage disease as well as total breast cancer incidence will be much larger in the future given those underlying temporal trends, independent of screening.

In the current study, we sought to determine the effect on late-stage breast cancer incidence and total invasive breast cancer incidence in the United States after adjusting for temporal trends by comparing SEER registry data from the prescreening era of 1977 through 1979 to the screening era of 2007 through 2009. Baseline incidence values in 1977 through 1979 were projected to the period from 2007 through 2009 using a range of APCs. We then compared the projected values with actual observed values in 2007 to 2009. We used 5 different APC estimates derived from the following sources: historic female premammographic screening data from the Connecticut Tumor Registry from 1940 to 1982, SEER data for women aged ≥ 40 years from 1977 to 1982, SEER data for men aged ≥ 40 years from 1977 to 2009, SEER data for women aged < 40 years from 1977 to 1984, and United Kingdom female cancer registry data from 1975 to 1987. We calculated changes in early-stage, late-stage, and total invasive breast cancer rates between 1977 through 1979 and 2007 through 2009 after making these underlying temporal trend adjustments.

MATERIALS AND METHODS

Determinations of Annual Percentage Change in Breast Cancer Incidence

Previous analyses of Connecticut Tumor Registry incidence trends from 1940 through 1982 have shown an APC of 1.16%[18] with age-specific APC values ranging from 0.8% for women aged 40 years to 49 years to 1.51% for women aged 60 years to 69 years.[21] When adjusted for period and cohort effect, the APC was 1.67%.[16] Age-adjusted breast cancer incidence increased from 83.4 per 100,000 women in 1936 through 1940 to 131.2 per 100,000 women in 1976 through 1978.[17]

Breast cancer incidence data in the United States from 1977 to 2009 were obtained from the population-based registries that participate in the National Cancer Institute's SEER program.[25] We extracted reported breast cancer cases by age and stage of disease in 18 SEER geographic areas, which captured cancer data from 27.8% of the US population.[26] Tumor stage was categorized as localized, regional, and distant. Individuals with ductal carcinoma in situ (DCIS) were determined using 14 codes from the 3rd edition of the *International Classification of Diseases for Oncology* (8500/2, 8501/2, 8502/2, 8503/2, 8504/2, 8507/3, 8508/2, 8510/2, 8521/2, 8522/2, 8523/2, 8540/2, 8541/2, and 8543/2) for in situ groups, but we excluded lobular carcinoma in situ. United States breast cancer incidence trends were analyzed and categorized into 3 groups: women aged ≥ 40 years, women aged < 40 years, and men aged ≥ 40 years. In addition, female breast cancer incidence in the United Kingdom from Cancer Research UK was reviewed.[27]

Statistical Analysis

To characterize trends in age-adjusted incidence rates, we performed joinpoint regression analyses using Joinpoint statistical software (version 3.5; Surveillance Research Program, National Cancer Institute, Bethesda, MD). Joinpoint regression allows for the identification of statistically significant changes in trends and the estimation of the annual percentage rate of change in each trend interval. Joinpoint analysis was performed by group (women aged ≥ 40 years, women aged < 40 years, and men aged ≥ 40 years) and stage of disease (DCIS, localized, regional, and distant). We analyzed joinpoint trends and APCs from the prescreening era: 1977 through 1982 for women aged ≥ 40 years, 1977 through 1984 for women aged < 40 years (1984 was used instead of 1982 because the joinpoint result demonstrated a natural breakpoint at 1984), and 1975 to 1987 for women in the United Kingdom (national screening began in 1988 in the UK) overall

TABLE 1. Breast Cancer Temporal Trends Prior to Mammographic Screening

Group	Years	Initial Incidence[a]	Final Incidence[a]	APC	95% CI
Connecticut Tumor Registry	1940-1982	Literature[b]		1.2	—
SEER: women aged ≥40 y	1977-1982	212.6	226.7	1.3	0.2-2.4
SEER: men aged ≥40 y	1977-2009	2.3	3.1	0.8	0.5-1.1
SEER: women aged <40 y	1977-1984	13.4	14.9	1.9	0.4-3.4
United Kingdom: women aged >15 y	1976-1987	71.8	89.7	1.7	1.4-2.0
15-39 y		15.8	17.9	1.1	0.7-1.6
40-49 y		118.5	130.5	0.7	0.4-1.0
50-64 y		152.8	195.1	2.1	1.9-2.3
65-69 y		192.4	235.1	1.8	1.6-2.0
≥70 y		227.5	286.1	2.3	2.1-2.4

Abbreviations: 95% CI, 95% confidence interval; APC, annual percent change; SEER, Surveillance, Epidemiology, and End Results.
[a] Incidence indicates the number of cases per 100,000 women.
[b] See text.

and by age group.[28] We used 1977 through 2009 for men aged ≥ 40 years. Male incidence trends were reviewed because they represented the longest-duration unique SEER population that had never been recommended for screening. The APC in age-adjusted incidence was calculated from joinpoint analyses. Based on the obtained APC estimates, we assumed 4 APCs of 0.5%, 1.0%, 1.3%, and 2.0% for underlying temporal trend adjustments in incidence.

Incidence Estimates

Unadjusted trends for stage-specific SEER breast cancer incidence values were averaged over the 3-year period of 1977 through 1979 for each stage of disease to produce baseline prescreening values. Similarly, unadjusted stage-specific incidence values from the screening period of 2007 through 2009 were averaged to produce an observed value. We then adjusted the baseline value for 1977 through 1979 for APC values of 0.5%, 1.0%, 1.3%, and 2.0% to produce a "projected" incidence value by applying the APC for 30 years for each disease stage. These would be the expected incidence values for each breast cancer stage if only the underlying trend in APC continued for 30 years. We compared the projected values with observed values in 2007 through 2009 and reported the change in the number of cases per 100,000 women as well as the percentage change, defined as the change in incidence divided by projected incidence multiplied by 100%. We grouped DCIS and localized breast cancer as early-stage disease and regional and distant breast cancer as late-stage disease. Finally, we compared the projected incidence versus the observed incidence for each APC for invasive breast cancer alone and for all breast cancer (invasive cancer plus DCIS).

TABLE 2. Incidence[a] of Stage-Specific Breast Cancer Among Women Aged ≥40 Years, Unadjusted for Underlying Breast Cancer Temporal Trends Increase

	1977 to 1979	2007 to 2009	Absolute Change	% Change
Early stage				
DCIS	6.3	58.4	52.1	827
Localized disease	106.6	181.2	74.7	70
Total	112.9	239.6	126.8	112
Late stage				
Regional	86.5	77.2	−9.3	−11
Distant	16.8	17.7	0.9	5
Total	103.3	94.9	−8.4	−8
Total invasive cancer	209.9	276.2	66.3	32
Total breast cancer	216.2	334.6	118.4	55

Abbreviation: DCIS, ductal carcinoma in situ.
[a] Incidence indicates the number of cases per 100,000 women.

RESULTS

The APC estimates for each of the 5 methods are shown in Table 1. The 1.3% APC for women aged ≥ 40 years approximates the 4-decade historic Connecticut Tumor Registry trend of 1.2% and is considered a central estimate. Overall, APC values ranged from 0.8% for men aged ≥ 40 years to 2.3% for UK women aged ≥ 70 years. The 1.3% APC for US women is less than the APC of 1.7% for UK women, the annual rate of incidence increase observed overall in UK women from 1976 to 1987.

Table 2 provides mean age-adjusted SEER breast cancer incidence rates, unadjusted for underlying temporal trend increase, for the periods of 1977 through 1979 and 2007 through 2009 for women aged ≥ 40 years. When unadjusted for underlying temporal trend increase, these rates demonstrated a marked increase in early-stage disease (DCIS and localized breast cancer) with an

TABLE 3. Projected Incidence[a] of Stage-Specific Breast Cancer Among Women Aged ≥40 Years From 1977 Through 1979 to 2007 Through 2009, Adjusted for Underlying Temporal Trends

	1977 to 1979	Projected 2007 to 2009			
	Baseline	APC of 0.5%	APC of 1.0%	APC of 2%	APC of 1.3%
Early stage					
DCIS	6.3	7.7	8.4	11.2	9.2
Localized disease	106.6	121.3	144.0	186.4	152.6
Total	112.9	129.0	148.4	197.6	161.8
Late stage					
Regional	86.5	100.7	116.3	154.8	126.8
Distant	16.8	19.1	22.0	29.3	24.0
Total	103.3	119.8	138.4	184.1	150.8

Abbreviations: APC, annual percent change; DCIS, ductal carcinoma in situ.
[a] Incidence indicates the number of cases per 100,000 women.

associated small decrease in late-stage disease (regional and distant breast cancer). Localized disease was found to increase by 74.7 cases per 100,000 women or 70%, whereas late-stage disease decreased by 8.4 cases per 100,000 women or 8%. In addition, there was an increase in the incidence of invasive and total cancer noted when no adjustment was made for prescreening temporal trends.

The projected stage-specific incidence rates derived from Table 2 after adjusting for prescreening temporal trends are shown in Table 3. These would be the expected incidences if no factor other than the prescreening temporal trends continued over the 30-year period. At an APC of 1.3%, the regional disease incidence value for 1977 through 1979 would be projected to increase from 86.5 to 126.8 cases per 100,000 women exclusively due to continuation of the premammography underlying temporal trend. Similarly, at an APC of 1.3%, the projected localized disease incidence value would increase from 106.6 cases per 100,000 women to 152.6 cases per 100,000 women.

Table 4 shows stage-specific differences between projected and observed incidence values for 2007 through 2009 for various APCs. At an APC of 1.3%, late-stage disease decreased 37% from the projected rate (150.8 cases to 94.9 cases per 100,000 women). There were 55.8 cases per 100,000 fewer women with late-stage disease noted between 2007 and 2009 than at the baseline of 1977 through 1979. There was a similar but reciprocal increase in the incidence of early-stage disease of 48% (difference of 77.9 cases per 100,000 women). It is interesting to note

TABLE 4. Projected Change in Stage-Specific Breast Cancer Incidence[a] Among Women Aged ≥40 Years From 1977 Through 1979 to 2007 Through 2009 by APC Estimates

	2007 to 2009	APC of 0.5%			APC of 1.0%			APC of 2.0%			APC of 1.3%		
	Observed	Projected	Change	% Change	Projected	Change	% Change	Projected	Change	% Change	Projected	Change	% Change
Early stage													
DCIS	58.4	7.7	50.7	657	8.4	50.0	595	11.2	47.2	422	9.2	49.2	537
Localized disease	181.2	121.3	60.0	50	140.0	41.2	29	186.4	−5.1	−3	152.6	28.6	19
Total	239.6	129.0	110.7	86	148.4	91.2	61	197.6	42.1	21	161.8	77.9	48
Late stage													
Regional	77.2	100.7	−23.5	−23	116.3	−39.1	−34	154.8	−77.6	−50	126.8	−49.6	−39
Distant	17.7	19.1	−1.4	−7	22.0	−4.3	−20	29.3	−11.6	−40	24.0	−6.3	−26
Total	94.9	119.8	−24.9	−21	138.4	−43.4	−31	184.1	−89.2	−48	150.8	−55.8	−37
Total invasive cancer	276.2	241.1	35.1	15	278.4	−2.2	−1	370.5	−94.3	−26	303.4	−27.2	−9
Total breast cancer	334.6	248.8	85.8	35	286.8	47.8	17	381.7	−47.1	−12	312.6	22.0	7

Abbreviations: APC, annual percent change; DCIS, ductal carcinoma in situ.
[a] Incidence indicates the number of cases per 100,000 women.

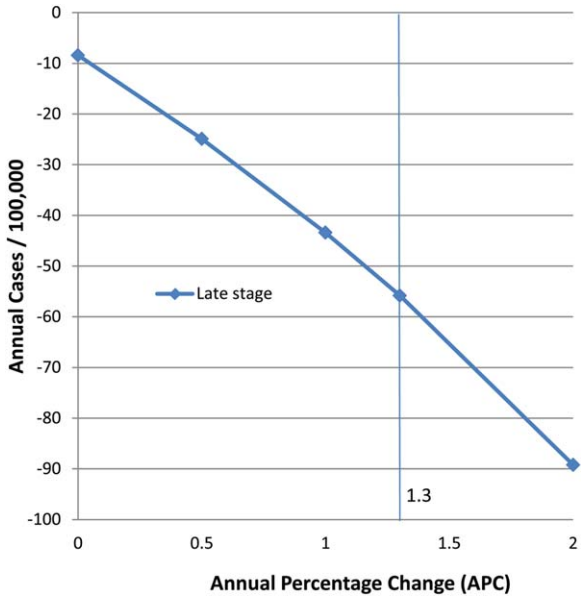

Figure 1. Reduction in late-stage breast cancer incidence is shown among women aged ≥ 40 years from 1977 through 1979 to 2007 through 2009 by annual percent change (APC) estimates of prescreening temporal trends.

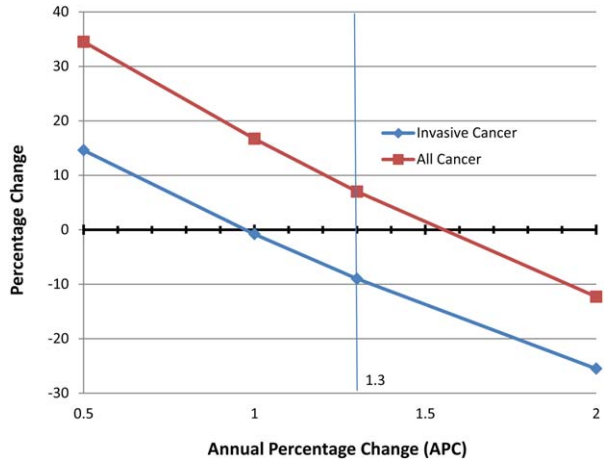

Figure 2. Percent change of breast cancer incidence between 1977 through 1979 and 2007 through 2009 by annual percent change (APC) estimate is shown for invasive breast cancer and all breast cancers among women aged ≥ 40 years.

that the majority of the early-stage increase is due to an increase in the incidence rate of DCIS (49.2 cases per 100,000 women compared with a localized breast cancer rate increase of 28.6 cases per 100,000 women). Across all APC estimates, decreases in late-stage disease ranged from 21% at an APC of 0.5% to a 48% decrease at an APC of 2.0%. Figure 1 shows the marked decline in late-stage breast cancer incidence with increasing estimates of APC.

Table 4 also provides estimates of changes in invasive cancer incidence in the mammographic era. At an APC of 1.3%, there were 9% (27.2 cases per 100,000 women) fewer women with invasive breast cancer between 2007 through 2009 than expected. Even at an APC of 1%, a value below all APC estimates except for males, there were 1% fewer invasive breast cancer cases than expected. At an APC of 2%, which approximates the UK trend, there were 26% fewer invasive breast cancer cases in 2007 through 2009 than expected. Total breast cancer incidence (invasive cancer plus DCIS) demonstrated a 7% increase over the 30-year period for an APC of 1.3% and a 12% decrease for an APC of 2%. Figure 2 shows the relationship between the percentage changes for invasive cancer and all breast cancer between 1977 and 1979 and 2007 and 2009 by APC estimates. At background APC estimates of ≥ 1%, a decrease in the incidence of invasive breast cancer was noted. The total breast cancer (invasive breast cancer plus DCIS) incidence increase noted between 1977 and 1979 and 2007 and2009 is entirely accounted for by the background incidence trend for an APC of > 1.5%.

DISCUSSION

The results of the current study demonstrate a substantial reduction in the incidence of late-stage breast cancer in US women in the mammography era when adjusted for temporal trends in incidence observed in the prescreening era. Increases in the incidence of early-stage disease are associated with the decrease in late-stage incidence, the expected finding of mammographic screening. At a central APC of 1.3%, a 37% reduction in late-stage disease was observed, with a reciprocal increase in early-stage disease. This decrease in late-stage disease approximates the breast cancer mortality reduction observed among women in the United States from 1990 through 2009.

The current study results also demonstrate an overall decrease in the incidence of invasive cancer at APC estimates of ≥ 1%. At first inspection, the data in Table 2, which does not adjust for underlying temporal trends, would suggest there was a good deal of excess breast cancer incidence from 2007 through 2009 compared with 3 decades earlier. However, an adjustment for underlying temporal trends is essential in making such a comparison and conclusion. After appropriate APC adjustments based on 5 different methods, we demonstrated that the conclusion of a large excess invasive cancer incidence drawn from unadjusted breast cancer incidence values is not supported. To the contrary, at the central APC estimate of 1.3%, there was a 9% reduction (27 cases per 100,000

women) in invasive cancer incidence. This means 27 of every 100,000 women were potentially spared the development of invasive cancer and its associated morbidity and mortality in each year from 2007 through 2009. The reduction in invasive cancer incidence is consistent with disruption of the nonobligatory pathway from DCIS to invasive breast cancer through the detection and treatment of DCIS in some women. At an APC of 1.3%, the total breast cancer incidence increased by 7% over 30 years but this small overall incidence increase should not be construed to represent an overdiagnosis rate, because the change in overall breast cancer incidence would be reduced when adjusted for lead time.[29] This observation of a low rate of potential overdiagnosis is consistent with a recent Euroscreen analysis of 13 overdiagnosis studies that demonstrated a low level of overdiagnosis (1%-10%) when appropriate adjustments for temporal trends, risk factors, and lead time were considered.[30] The results of the current study differ distinctly from those of Bleyer and Welch, who estimated overdiagnosis at a rate of 31% but used an APC value of only 0.25%.[13] The APC they used is less than the various estimates of APC we obtained in the absence of screening mammography. At APC values of $>1.5\%$, such as the incidence trends observed in the United Kingdom in the 1980s, there is an overall reduction in the total breast cancer burden.

The shift from late-stage to early-stage disease in the current analysis has been reported in many organized screening programs.[5-10] Foca et al recently reviewed the Italian screening experience and demonstrated a 29% reduction in the diagnosis of pT2 to pT4 tumors at 7 to 8 years after the introduction of organized screening.[7] In the United States, studies have demonstrated a marked increase in early-stage disease with disproportionately small decreases in late-stage disease using tumor registry data over 60-year and 30-year periods but have not adjusted for temporal trends.[12,13]

Breast cancer incidence had increased 1% to 3% per year in the United States and Western Europe before mammography screening.[14,15,18] The longest-standing US tumor registry shows an APC of 1.2% from 1940 through 1982.[18] In the United Kingdom, APC values of 1% to 2% were reported, a finding that is in keeping with the current analysis.[6,19,28] Larger incidence increases have occurred in regions of Eastern Europe, Asia, Africa, and Latin America without mammographic screening.[1] From 1973 through 1999, Hong Kong had an age-standardized APC increase of 3.6%.[23] Zimbabwe observed a 4.9% APC increase from 1991 through 2010.[24] Longstanding reproductive, dietary, and environmental factors associated with increased breast cancer risk are commonly cited as reasons for the increases now observed globally.[1,14]

An accurate APC estimate is critical for determining projected incidence and overdiagnosis. We have provided a range of APC values (with a central value of 1.3%) rather than a single number, because to the best of our knowledge direct measures of age-matched control APC values during the study period between 1977 and 2009 are not available. Each APC estimate has strengths and limitations. The 4-decade APC trend of 1.2% from the Connecticut Tumor Registry is unique in its long duration and quality and is frequently cited as a US trend line. The joinpoint trend for women aged ≥ 40 years noted between 1977 and 1982 is relatively short in duration but includes the target population and uses complete SEER data. The calculated 1.3% APC for this target group of women closely approximates the historic Connecticut Tumor Registry APC but is lower than more recent UK trends of 1.7%, which extended to the late 1980s. The longest SEER trend line for unscreened individuals is for men, but obvious differences in biology limit its use as an exclusive measure. Even for males, an APC of nearly 1% was observed. The trend lines for women aged <40 years showed a joinpoint APC of 1.9% for the premammographic screening period (1977-1984), but there was heterogeneity in later-year trends, including a -1.3% APC from 1984 through 1994 and a 0.7% APC from 1994 through 2009. The trend among young females may not be directly applicable to older women due to different cancer biology. Results from the United Kingdom have demonstrated significantly lower APC values for women aged <40 years (an APC of 1.1%) compared with older women (with APCs of 1.8%-2.3%). Also confounding the analysis for younger US women, mammographic screening was recommended to begin at age 35 years by some organizations during the study period. The prescreening UK data from 1976 through 1987, which overlap the first decade of our study period, may reflect more recent temporal trends but are not matched to the US population. The possibility of accelerating background temporal trends for disease of distant stage in more recent years is supported by a study that demonstrated an overall APC of 2.1% from 1973 through 2009, but a greater APC of 3.6% during 2000 to 2009 for US women aged <40 years.[31] We applied APC projections equally across all stages of disease. It is possible that APC trends may vary by disease stage.

The initiation of large-scale opportunistic mammographic screening in the United States in the mid-1980s is the most probable cause for the decrease in late-stage

disease and the corresponding increase in early-stage disease. However, it is unlikely that mammography is the sole etiology. Because SEER does not track the mode of detection, we can only postulate the correlation with screening mammography. Breast self-examination, clinical breast examination, and an overall heightened awareness of breast cancer may also have contributed. Mammographic screening use increased rapidly in the late 1980s from $< 5\%$ before 1984 to 17% in 1987 and 33% by 1990.[18,32] More recently, 52% to 70% of women aged ≥ 40 years have self-reported having had a mammogram within the last 2 years. It is worth noting that the actual use of screening mammography has been shown to be 15% to 25% lower due to overestimates from self-reporting.[33]

The results of the current study may underestimate the positive impact of screening, which is not captured by the broad SEER stage categories due to SEER's inclusion of both screened and unscreened women along with changes in methods of diagnosis and stage determination. Downsizing within stage of disease occurs by screening mammography.[10] Within the localized stage, downsize migration and not treatment advances was responsible for 61% of the observed improvement in disease stage specific survival over a 20-year period.[34] Sentinel lymph node sampling, which began during the 1990s, resulted in upstaging of lymph node disease. Imaging improvements can now detect more distant disease at the time of presentation. These factors would increase more recent rates of regional and distant disease incidence and cause underestimation of late-stage incidence declines.

Conclusions

There is evidence of a substantial reduction in the incidence of late-stage breast cancer, with a corresponding shift toward early-stage disease, in the mammographic era when appropriately adjusted for prescreening temporal trends. At central APC estimates, a reduction in total invasive breast cancer incidence is observed. Because mammographic screening is underused in the United States, there may be the potential to reduce the incidence of late-stage disease and invasive cancer further with the increased use of screening mammography.

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CONFLICT OF INTEREST DISCLOSURES

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