Original Article

Breast Cancer Deaths Averted Over 3 Decades

R. Edward Hendrick, PhD [1]; Jay A. Baker, MD[2]; and Mark A. Helvie, MD[3]

BACKGROUND: From 1975 to 1990, female breast cancer mortality rates in the United States increased by 0.4% per year. Since 1990, breast cancer mortality rates have fallen between 1.8% and 3.4% per year, a decrease that is attributed to increased mammography screening and improved treatment. **METHODS:** The authors used age-adjusted female breast cancer mortality rate and population data from the Surveillance, Epidemiology, and End Results (SEER) program to estimate the number of breast cancer deaths averted by screening mammography and improved treatment since 1989. Four different assumptions regarding background mortality rates (in the absence of screening mammography and improved treatment) were used to estimate deaths averted for women aged 40 to 84 years by taking the difference between SEER-reported mortality rates and background mortality rates for each 5-year age group, multiplied by the population for each 5-year age group. SEER data were used to estimate annual and cumulative breast cancer deaths averted in 2012 and 2015 and extrapolated SEER data were used to estimate deaths averted in 2018. **RESULTS:** The number of single-year breast cancer deaths averted ranged from 20,860 to 33,842 in 2012, from 23,703 to 39,415 in 2015, and from 27,083 to 45,726 in 2018. Breast cancer mortality reductions ranged from 38.6% to 50.5% in 2012, from 41.5% to 54.2% in 2015, and from 45.3% to 58.3% in 2018. Cumulative breast cancer deaths averted since 1989 ranged from 237,234 to 370,402 in 2012, from 305,934 to 483,435 in 2015, and from 384,046 to 614,484 in 2018. **CONCLUSIONS:** Since 1989, between 384,000 and 614,500 breast cancer deaths have been averted through the use of mammography screening and improved treatment. ***Cancer* 2019;125:1482-1488**.

KEYWORDS: breast cancer, female, mortality rate, screening mammography, therapy, treatment, United States.

INTRODUCTION

Since 1969, the National Cancer Institute (NCI)'s Surveillance, Epidemiology, and End Results (SEER) program has collected breast cancer incidence and mortality data for the United States.[1] The most recent data extend to 2015. Analysis by the NCI indicates that breast cancer mortality rates for US females of all ages increased by a statistically significant 0.4% per year from 1975 to 1990.[2] Mortality rates then decreased by a statistically significant 1.8% per year from 1990 to 1995, 3.4% per year from 1995 to 1998, and 1.8% per year from 1998 to 2015.[2] From 1989 to 2015, age-adjusted female breast cancer mortality rates among women aged 40 to 84 years are reported to have decreased by 41.6% (Fig. 1).[3] This decrease has been attributed to the increased use of screening mammography combined with improved breast cancer treatment.[4-6]

Screening mammography became widely available in the mid-1980s, and its use increased until the early 2000s.[4-7] According to self-reported data collected in the Center for Disease Control and Prevention's National Health Interview Survey,[7] in 1987, approximately 29% of women aged >40 years reported having undergone mammography within the previous 24 months. This figure rose to 70% in 2000, and then dropped to 64% in 2015. The National Health Interview Survey overestimates screening mammography use for 2 reasons. First, it does not distinguish between screening and diagnostic mammography. According to data from the US Breast Cancer Surveillance Consortium that were collected between 1994 and 2009, approximately 17% of mammographies were performed for reasons other than screening.[8] Second, according to the study by Cronin et al,[9] self-reported mammography use in the previous 2 years overestimated screening mammography use in that period by 14% to 27%. Adjusting for such factors, Berry et al estimated that when screening mammography use was at its peak in the year 2000, approximately 25% of US women aged >40 years received annual screening mammography, another 25% received biennial screening mammography, and the remaining 50% of women underwent irregular screening or no screening at all.[4]

The Cancer Intervention and Surveillance Modeling Network (CISNET), a consortium of NCI-sponsored investigators, has attempted to use models of breast cancer incidence and mortality, along with mammography screening and treatment trends, to separate the effects of screening mammography and adjuvant therapy on the reduction in breast

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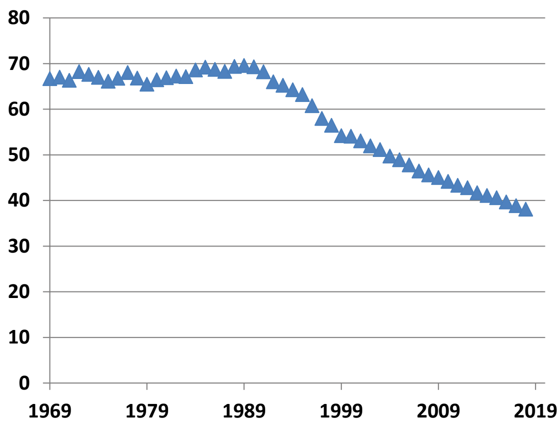

Figure 1. Age-adjusted US breast cancer mortality rates (per 100,000 women) for women aged 40 to 84 years by year from 1969 through 2015 from the Surveillance, Epidemiology, and End Results (SEER) database.

cancer deaths.[4-6] Their models estimated that screening mammography was responsible for 28% to 65% of the reduction in breast cancer deaths in the year 2000, with a median estimate of 46%, and the remainder of the reduction was due to advances in treatment.[4] These estimates assumed that nearly all women diagnosed with breast cancer underwent treatment, but only approximately one-half of women aged >40 years underwent screening mammography annually or biennially.[4,5] Based on 2 CISNET models, Munoz et al estimated that in the year 2000, with 100% compliance to screening mammography, screening would be responsible for 69% to 74% of breast cancer deaths averted.[6] A 2018 CISNET update by Plevritis et al, based on an assumed compliance rate of 50% to 55% with either annual or biennial screening mammography, estimated that in 2012 screening mammography was responsible for 37% of the estimated mortality reduction (range over 6 models, 26%-51%).[5] Clearly, the relative contribution of screening to mortality reduction estimates depends strongly on assumed screening mammography (and treatment) compliance rates.

DeSantis et al estimated the number of female breast cancer deaths averted because of screening and improved treatment from 1989 to 2012 to be 249,000, based on the assumption that, absent increased screening or improved treatment, the death rate would have remained at 1989 levels.[10] Although this assumption is the simplest in assessing changes since 1989, it ignores the steadily increasing background mortality trends prior to 1989. Just as estimates of overdiagnosis over the past 30 years are highly sensitive to assumptions of background breast cancer incidence rates,[11,12] estimates of breast cancer deaths averted since 1989 are similarly sensitive to assumptions regarding breast cancer mortality rates in the absence of screening mammography and improved treatment, referred to herein as background mortality rates.

The goal of the current study was to estimate the number of breast cancer deaths averted since 1989 due to the collective effects of both screening mammography and improved treatment. The current analysis extended the estimates of DeSantis et al[10] by using several different methods to estimate background breast cancer mortality rates, including methods based on mortality rate trends prior to 1989. We also estimated percentage mortality reductions for US women overall and by 5-year age groups. The current analysis did not attempt to estimate the separate contributions of mammography screening and adjuvant treatment with regard to breast cancer deaths averted.

MATERIALS AND METHODS

All data used in the current analysis were anonymized, publicly available data, and therefore required no institutional review board approval. Breast cancer deaths averted in US women since 1989 were estimated using age-specific 5-year breast cancer mortality data and female population data for US women aged 40 to 84 years. Female age-adjusted breast cancer mortality rates (Fig. 2) and population data for each 5-year age group are available from 1969 to 2015 from the latest SEER database mortality tables (SEER*Stat Software, Version 8.3.5).[3] For the years 2016 through 2018, a linear least squares fit to breast cancer mortality rates from the previous 10 years, 2006 through 2015, was used to extrapolate mortality rates for 3 additional years, 2016 to 2018, for each 5-year age group. Analysis of residuals was performed to establish that linear fits were appropriate. Extrapolated mortality rates were included as the last 3 data points for each age group in Figure 2. Female population data for 2016 for each 5-year age group aged 40 to 84 years were taken from US Census estimates as of July 1, 2016,[13] and for 2017 and 2018 from US female population estimates by age.[14]

Four different methods were used to estimate background mortality rates for female breast cancer from 1990 through 2018:

First, following the study by DeSantis et al,[10] background mortality rates were assumed to be flat since 1989. This simple assumption assesses changes since 1989, when breast cancer mortality rates were at their peak, but ignores background mortality rate trends prior

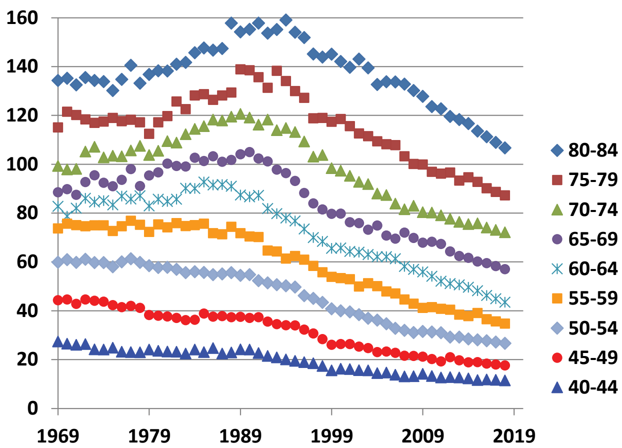

Figure 2. Age-adjusted breast cancer mortality rates (per 100,000 women) by year for each 5-year age group of women aged 40 to 84 years. Rates shown for 2016 through 2018 in each age group are linear extrapolations of mortality rate trends for that age group from 2006 to 2015.

to 1989. Prior to 1989, background mortality rates increased overall, most likely due to preceding increases in breast cancer incidence rates. The 3 assumptions that follow attempt to account for those increasing background mortality trends, although in different ways.

The second method was to assume that background mortality rates after 1989 continued their previously steady increase of 0.4% per year as was observed from 1975 to 1990, based on joinpoint analysis by Noone et al.[2] The extrapolation of joinpoint trends to estimate mortality rates has precedent in the peer-reviewed literature.[15,16]

In the third method, background mortality rates after 1989 were estimated for each 5-year age group using the change in mortality rates for that age group prior to 1990. Specifically, for each 5-year age group from ages 40 to 84 years, the trend over the previous 11 years, 1979 through 1989, was determined by a best linear fit to SEER mortality rate data and the resulting background trend was assumed to persist from 1990 to 2012, 2015, and 2018.[15,16]

Following the study by Cronin et al,[17] which used 7 CISNET models to estimate background mortality rates in the absence of screening or treatment, the fourth method was to assume that background mortality rates increased by 0.94% per year since 1989. The 7 models used by Cronin et al[17] estimated that between 1975 and 2000, in the absence of screening or treatment, breast cancer mortality rates would have increased by a mean of 12.7 deaths per 100,000 women (median, 14.7 deaths per 100,000 women [range, 5.6-15.9 deaths per 100,000 women]) compared with a 1975 breast cancer mortality rate of 48.2 deaths per 100,000 women. Their mean background mortality rate estimate was an increase of 26.2% over 25 years or 0.94% per year. We extrapolated this result to extend to 2012, 2015, and 2018.

Figure 3 illustrates these 4 different background mortality rate assumptions for a single 5-year age group, women aged 65 to 69 years. For each of these 4 methods, we assumed that the background mortality rate change continued from 1989 to different end dates of 2012, 2015, and 2018. Estimates for 2012 and 2015 are based entirely on SEER breast cancer mortality rate and population data. Estimates for 2018 are based on extrapolations of SEER breast cancer mortality rates and census projections of US female population data from 2016 to 2018.

Breast cancer deaths averted in a given year for each 5-year age group were determined by taking the difference between background mortality rates and measured rates for the years 1990 through 2015 (or extrapolated rates for years 2016-2018) per 100,000 women and multiplying by the US female population that year (in 100,000 populations) in that 5-year age group. Breast cancer deaths averted in a given year were determined by summing over all 5-year age groups between ages 40 and 84 years. Cumulative breast cancer deaths averted since 1989 were determined by summing deaths averted in each year from 1990 to the endpoints of 2012, 2015, and 2018.

Percentage mortality reductions in 2012, 2015, and 2018 were determined by dividing the estimated breast cancer deaths averted in a given year by the total estimated breast cancer deaths without screening or improved treatment (the sum of known breast cancer deaths in a given year plus the estimated breast cancer deaths averted in that year) multiplied by 100%:

$$\% \text{ mortality reduction} = (\text{breast cancer deaths averted} \times 100\%) / (\text{known breast cancer deaths} + \text{breast cancer deaths averted})$$

Known breast cancer deaths each year for women aged 40 to 84 years were taken from the SEER mortality database up to 2015.[3] For the year 2018, breast cancer deaths in each 5-year age group were estimated by multiplying the linearly extrapolated breast cancer death rate for 2018 for each 5-year age group by the 2018 estimated female population for each 5-year age group.[13]

RESULTS

Single-year breast cancer deaths averted in US women aged 40 to 84 years by both mammography screening

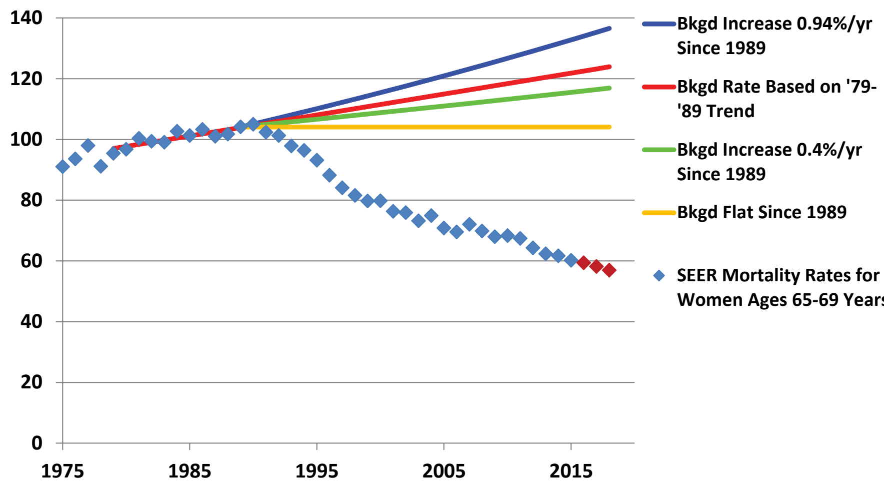

Figure 3. Surveillance, Epidemiology, and End Results (SEER) age-adjusted mortality rates (per 100,000 women) for women aged 65 to 69 years by year from 1975 through 2015 (blue data points). Dark red data points represent linear extrapolation of the mortality rate to 2016 through 2018 based on the trend from 2006 through 2015. Solid lines represent the 4 different assumptions regarding background (Bkgd) mortality rate trends since 1989. Blue indicates increasing by 0.94% per year since 1989; red, based on a linear fit to mortality rates from 1979 through 1989; green, increasing by 0.4% per year since 1989; orange, constant since 1989.

TABLE 1. Single-Year Breast Cancer Deaths Averted and Percentage Mortality Reduction in US Women Aged 40 to 84 Years

	Background Mortality Rate Assumption			
Year	Background Mortality Rate Flat Since 1989	Background Mortality Rate Increase of 0.4% per Year Since 1989	5-Year Age Group Background Mortality Rate Trends: 1979 to 1989	Background Mortality Rate Increase of 0.94% per Year Since 1989
2012	20,860	26,060	27,801	33,842
	38.6%	44.0%	45.6%	50.5%
2015	23,703	29,943	32,329	39,415
	41.5%	47.3%	49.2%	54.2%
2018	27,083	34,424	37,769	45,726
	45.3%	51.3%	53.6%	58.3%

and improved treatment since 1989 are shown in Table 1 for the years 2012, 2015, and 2018. In 2018, estimates ranged from 27,083 to 45,726 breast cancer deaths averted. Also shown in Table 1 are percentage mortality reductions for 2012, 2015, and 2018 based on SEER-reported breast cancer deaths specific to each of those 3 years. In 2018, the percentage mortality reduction estimates for women aged 40 to 84 years ranged from 45.3% to 58.3%.

Cumulative breast cancer deaths averted in US women aged 40 to 84 years by both screening and improved treatment beginning in 1990 and ending in 2012, 2015, and 2018 are shown in Table 2. In 2018, estimates ranged from 384,046 to 614,484 breast cancer deaths averted. Figure 4 illustrates the estimated cumulative breast cancer deaths averted by year since 1989 for the 4 different assumptions about background breast cancer mortality trends. Table 2 and Figure 4 show that the assumption of a flat background since 1989 yields the lowest estimate of breast cancer deaths averted by screening and improved treatment. Table 2 and Figure 4 show approximately similar results for breast cancer deaths averted since 1989 based on a background trend of a 0.4% per year increase and a background trend based on individual 5-year age group mortality trends prior to 1990.

Table 3 shows percentage mortality decreases for each 5-year age group and the entire age range of women aged 40 to 84 years based on our 4 different

TABLE 2. Cumulative Breast Cancer Deaths Averted in US Women Aged 40 to 84 Years Since 1989

	Background Mortality Rate Assumption			
Year Range	Background Mortality Rate Flat Since 1989	Background Mortality Rate Increase of 0.4% per Year Since 1989	5-Year Age Group Background Mortality Rate Trends: 1979-1989	Background Mortality Rate Increase of 0.94% per Year Since 1989
1990-2012	237,234	291,579	312,788	370,402
1990-2015	305,934	377,933	405,499	483,435
1990-2018	384,046	476,947	513,320	614,484

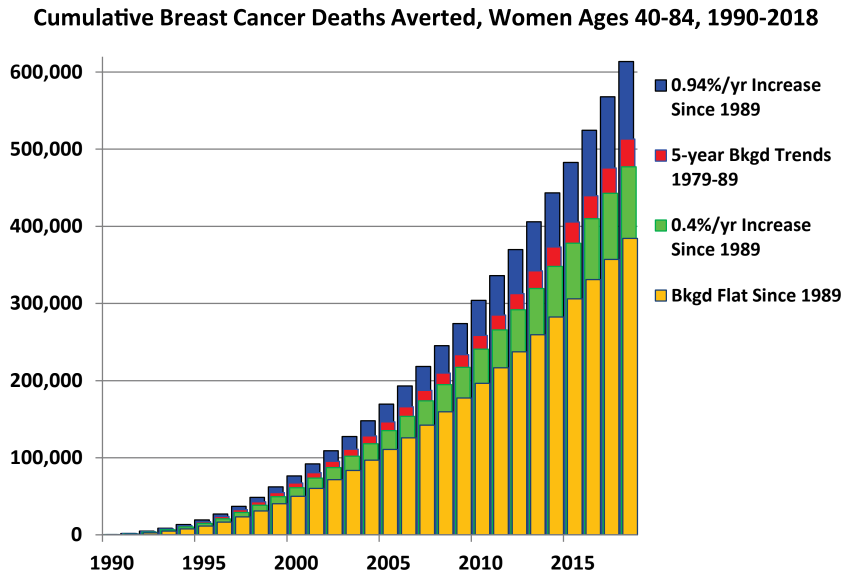

Figure 4. Cumulative breast cancer deaths averted for women aged 40 to 84 years under 4 different assumptions regarding background (Bkgd) mortality rate trends since 1989.

TABLE 3. Percentage Mortality Reduction in 2012, 2015, and 2018 by 5-Year Age Groups and Ages 40 to 84 Years Based on 4 Different Assumptions Regarding Expected Background Mortality Rates in the Absence of Screening and Advances in Treatment

	Background Flat Since 1989			Background Increase of 0.4% per Year Since 1989			Background With 5-Year Age Group Trends			Background Increase of 0.94% per Year Since 1989		
Age Range, Years	2012	2015	2018[a]	2012	2015	2018[a]	2012	2015	2018[a]	2012	2015	2018[a]
40-44	47.0%	51.9%	52.7%	51.6%	56.7%	57.8%	44.5%	49.7%	50.3%	57.2%	62.3%	63.9%
45-49	43.9%	49.4%	53.0%	48.8%	54.4%	58.1%	42.9%	48.4%	52.0%	54.8%	60.4%	64.2%
50-54	46.4%	48.4%	50.9%	51.1%	53.5%	56.3%	36.2%	37.0%	38.6%	56.8%	59.5%	62.6%
55-59	43.6%	45.5%	51.5%	48.6%	50.9%	56.8%	40.6%	42.1%	48.0%	54.6%	57.3%	63.1%
60-64	41.5%	44.8%	50.2%	46.6%	50.3%	55.6%	52.8%	56.4%	61.4%	52.8%	56.7%	62.0%
65-69	38.3%	42.2%	45.3%	43.7%	47.9%	51.3%	46.3%	50.6%	54.1%	50.2%	54.7%	58.3%
70-74	35.6%	37.2%	40.1%	41.2%	43.4%	46.7%	51.7%	54.4%	57.8%	48.0%	50.7%	54.4%
75-79	30.4%	33.2%	37.1%	36.5%	39.8%	44.0%	46.2%	50.0%	54.3%	43.9%	47.6%	52.0%
80-84	22.5%	26.3%	30.8%	29.3%	33.6%	38.4%	39.7%	44.3%	49.1%	37.5%	42.2%	47.3%
40-84	38.6%	41.5%	45.3%	44.0%	47.3%	51.3%	45.6%	49.2%	53.6%	50.5%	54.2%	58.3%

[a]Percentage mortality decreases for 2016 through 2018 are based on linear extrapolations of mortality rate trends from 2006 to 2015.

assumptions regarding expected background mortality in the absence of screening or advances in treatment. The first assumption of mortality rates being unchanged since 1989 represents the known mortality decrease since 1989 in 2012 and 2015, and the estimated decrease since 1989 in 2018.

DISCUSSION

The current study demonstrates that estimates of the number of breast cancer deaths averted due to screening and improved treatment depend strongly on specific assumptions regarding background mortality rate trends in the absence of screening and advances in treatment. For example, estimates of mortality reduction in 2015 ranged from 41.5% to 54.2% and estimates of breast cancer deaths averted in that single year ranged from 23,703 to 39,415 across the 4 different assumptions regarding background mortality rates. Likewise, the cumulative breast cancer deaths averted from 1990 to 2015 ranged from >305,000 women to >483,000 women depending on background mortality assumptions. Extrapolating results to 2018 shows that the cumulative breast cancer deaths averted since 1989 ranged from >384,000 to >614,000.

The assumption that background mortality rates are flat in the absence of screening mammography and improved treatment since 1989 likely underestimates the number of breast cancer deaths averted. This is because, similar to breast cancer incidence rates, US breast cancer mortality rates were increasing prior to 1990.[2] Background mortality rate estimates of the second and third methods also may underestimate the background rate because modern treatment advances with adjuvant chemotherapy and hormonal therapy already had entered clinical practice in the 1980s.[4,5] Both treatments had likely begun to suppress mortality rates by 1989. The successful application of hormonal therapy and adjuvant chemotherapy in the 1980s likely began to reduce mortality shortly after their introduction among women already diagnosed with breast cancer. Screening mammography, although entering widespread clinical practice in the mid-1980s, was shown by randomized controlled trials to require 5 to 7 years to demonstrate an evident mortality reduction due to the longer interval between screen detection and prevented death.[18]

The majority of other developed countries also experienced increasing breast cancer mortality rates prior to the adoption of widespread screening mammography in the 1980s and 1990s.[19] We believe the best estimates of breast cancer deaths averted are those that take into account these background increases. Thus, we estimate that over the last 3 decades, in excess of one-half million breast cancer deaths have been averted by screening mammography and improved treatment.

CISNET modeling results reported in the study by Plevritis et al estimated that in 2012, the mortality reduction due to both mammography screening and advances in treatment for US women aged 30 to 79 years was 49%.[5] Our estimate for the mortality reduction in 2012 for women aged 40 to 84 years based on 5-year age group background trends was 45.6%, which we believe is in reasonable agreement with the estimate of Plevritis et al.[5] If we assume the same background mortality increase of 0.94% per year that was the mean estimate by CISNET models in the study by Cronin et al,[17] our estimated mortality reduction in women aged 40 to 84 years in 2012 is 50.5%, which is in good agreement with the CISNET estimate for women aged 30 to 79 years. Our estimate of 237,234 deaths averted from 1990 through 2012, assuming a flat background, also is in good agreement with the study of DeSantis et al, which had an estimate of 249,000 deaths averted during the same period.[10] The difference between these 2 estimates is that DeSantis et al[10] estimated breast cancer deaths averted in US women of all ages, whereas we restricted our estimate to women aged 40 to 84 years.

One limitation of the current study is that SEER breast cancer incidence data do not specify whether a woman attended mammography screening within 1 year of her breast cancer diagnosis. Although nearly all US women diagnosed with breast cancer receive treatment, only approximately one-half of those aged >40 years undergo either annual or biennial screening.[4,5,9] Thus, the current analysis did not estimate breast cancer deaths averted from screening all age-eligible US women, as other studies have.[6,20] In addition, the current analysis made no attempt to estimate the separate contributions of screening versus advances in treatment, as others have.[4-6]

Another limitation of the current study is that it estimated the number of breast cancer deaths averted and percentage mortality reduction since 1989, not the full number of breast cancer deaths averted by screening mammography and treatment. Although the onset of widespread screening mammography in the mid-1980s did not begin to affect breast cancer mortality rates until the early 1990s, treatment improvements such as tamoxifen and advances in surgical therapy were ongoing and averting breast cancer deaths prior to 1989.

However, based on SEER mortality data and the estimates in the current study, we believe that hundreds of thousands of women's lives, likely in excess of one-half million by 2018, have been saved by the use of screening mammography and new developments in breast cancer treatment since 1989.

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CONFLICT OF INTEREST DISCLOSURES

R. Edward Hendrick has acted as a paid consultant for GE Healthcare for work performed outside of the current study. Mark A. Helvie was supported by institutional grants from GE Healthcare and IBM Watson for work performed outside of the current study.

AUTHOR CONTRIBUTIONS

R. Edward Hendrick: Conceptualization, methodology, data curation, formal analysis, software, writing–original draft, and writing–review and editing. **Jay A. Baker**: Conceptualization, methodology, and writing–review and editing. **Mark A. Helvie**: Conceptualization, methodology, and writing–review and editing.

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