

The American Cancer Society 2035 Challenge Goal on Cancer Mortality Reduction

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Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Abstract: A summary evaluation of the 2015 American Cancer Society (ACS) challenge goal showed that overall US mortality from all cancers combined declined 26% over the period from 1990 to 2015. Recent research suggests that US cancer mortality can still be lowered considerably by applying known interventions broadly and equitably. The ACS Board of Directors, therefore, commissioned ACS researchers to determine challenge goals for reductions in cancer mortality by 2035. A statistical model was used to estimate the average annual percent decline in overall cancer death rates among the US general population and among college-educated Americans during the most recent period. Then, the average annual percent decline in the overall cancer death rates of college graduates was applied to the death rates in the general population to project future rates in the United States beginning in 2020. If overall cancer death rates from 2020 through 2035 nationally decline at the pace of those of college graduates, then death rates in 2035 in the United States will drop by 38.3% from the 2015 level and by 54.4% from the 1990 level. On the basis of these results, the ACS 2035 challenge goal was set as a 40% reduction from the 2015 level. Achieving this goal could lead to approximately 1.3 million fewer cancer deaths than would have occurred from 2020 through 2035 and 122,500 fewer cancer deaths in 2035 alone. The results also show that reducing the prevalence of risk factors and achieving optimal adherence to evidence-based screening guidelines by 2025 could lead to a 33.5% reduction in the overall cancer death rate by 2035, attaining 85% of the challenge goal. *CA Cancer J Clin* 2019;69:351-362. © 2019 American Cancer Society.

Keywords: breast cancer, cancer, colorectal cancer, lung cancer, mortality, prostate cancer, risk factor

Introduction

Over the years, public health organizations have conducted futuring activities and issued cancer challenge goals in attempts to motivate and guide cancer control activities. In 1981, Doll and Peto published a now classic article on the causes of cancer, stressing the influence of tobacco on cancer death rates, which they estimated to account for approximately 30% of cancer deaths in the United States.¹ This led the US National Cancer Institute (NCI) in 1986 to call for an effort to halve the cancer death rate between 1985 and 2000.²

In 1996, the American Cancer Society (ACS) Board of Directors issued a challenge goal to halve what appeared to be possible peak cancer mortality in 1990 by 2015.³ In 2016, Byers et al published a summary evaluation of the ACS 2015 challenge goal.³ Overall US mortality from all cancers combined declined 26% over the period from 1990 to 2015. Mortality rates declined over the 25-year period for lung cancer (45% among men and 8% among women), colorectal cancer (47% among men and 44% among women), female breast cancer (39%), and prostate cancer (53%). Declines for all other cancers were 13% among men and 17% among women.³ These declines are thought to reflect a reduction in tobacco use and improvements in early detection and treatments.⁴⁻⁹

Over the past decades, however, ACS scientists and researchers from other agencies have reported substantial disparities in progress against cancer among populations defined by race/ethnicity,¹⁰⁻¹³ region of residence,¹⁴⁻¹⁷ and socioeconomic status (SES).^{11,18-20} These findings suggest that not all segments of the US population have benefitted equally from advances in cancer prevention, early detection, and treatments and that the US cancer mortality can be lowered considerably by applying known interventions equitably and broadly.²¹⁻²³

In light of the above findings, the ACS Board of Directors commissioned researchers from the ACS Intramural Research Department to make cancer mortality projections for the United States to the year 2035 and determine challenge goals. The questions to be addressed were:

- What will cancer death rates look like in 2035 if current trends continue?
- What can cancer death rates look like in 2035 by accelerating progress in reducing cancer mortality (a challenge goal)?
- What is a pathway toward attaining the 2035 challenge goal?

It is hoped that a glimpse at what is possible in terms of cancer prevention and control, as outlined in this article and in the other ACS cancer control blueprint articles,^{8,24-27} will motivate Americans and American institutions to intensify cancer prevention and control efforts.

Methods

Corresponding to the 3 questions proposed above, this article includes a 3-part analysis. The objective of the first part was to project cancer death rates for the general population in 2035. The objective of the second part was to estimate challenge goals based on cancer mortality trends among college graduates in the United States. The objective of the third part was to estimate what reductions in risk factors and increases in uptake of recommended cancer screening would be needed to achieve the challenge goals.

Data Sources

For part 1 of the analysis, mortality and population data from 1969 through 2015 for the general US population were obtained from the Surveillance, Epidemiology, and End Results (SEER) program's SEER*Stat database.²⁸ For part 2 of the analysis, mortality data by education for 2001 through 2015 were obtained from public-use, multiple-cause-of-death data files, which were published by the National Center for Health Statistics.²⁹ Corresponding population denominator data were obtained from the public-use microdata sample files of the American Community Survey.³⁰

For part 3 of the analysis, the 2005 and 2015 National Health Interview Survey (NHIS) data³¹ were used to estimate the prevalence of smoking. The 2005 and 2006 NHIS data were used to estimate average alcohol intake in 2005 to 2006, and the 2015 and 2016 NHIS data were used to estimate average alcohol intake in 2015 to 2016. Because alcohol intake is generally underreported in surveys, we adjusted NHIS alcohol intake using per capita alcohol consumption³² according to a method suggested by Rey et al.³³ Data from the National Health and Nutrition Examination Survey (NHANES)³⁴ were used to estimate the prevalence of excess body weight, fruit and vegetable intake, red meat and processed meat consumption, dietary fiber and dietary calcium intake, and physical inactivity. To obtain more stable estimates, the 2003 to 2004 and 2005 to 2006 NHANES data were combined to estimate average prevalence during 2003 through 2006 (representing 2005), and the 2013 to 2014 and 2015 to 2016 NHANES data were combined to estimate average prevalence during 2013 through 2016 (representing 2015). Breast cancer and colorectal cancer screening rates were obtained from the 2010 and 2015 NHIS survey. Screening for cancers of the prostate (no consensus on recommendation), cervix (relatively small number of deaths), and lung (limited data) were not included in the analysis. The prevalence of tamoxifen/raloxifene use for breast cancer risk reduction in 2005 was directly obtained from previous reports.^{35,36}

Statistical Analysis

Part 1: Projecting Cancer Death Rates for the General Population in 2035

By using SEER*Stat,²⁸ we calculated age-standardized (to the 2000 US standard population) death rates from 1969 to 2015 among the US general population for all cancers combined and for major cancer sites. Then, we performed joinpoint regression modelling (trend analysis) based on these age-standardized death rates with a maximum of 3 joinpoints allowed. The resulting annual percent changes for the last trend segment, representing the current trends, were then used to project cancer death rates for the general population in 2035.

Part 2: Estimating Challenge Goals

On the basis of the 2000 US standard population, we first calculated age-standardized death rates from 2001 through 2015 by education for all cancers combined and for major cancer sites. We then performed joinpoint analyses based on these age-standardized death rates with a maximum of 2 joinpoints allowed in modelling to obtain average annual percent changes (AAPCs) in death rates during 2001 through 2015 for college-educated Americans (see Supporting Table 1). We then applied these AAPCs to the US general population beginning in 2020 to project the

2035 cancer deaths rates, which were set as the ACS 2035 challenge goals. Of note, this approach is not seeking to equalize the rates for everyone to the rates of those with a college education but to accelerate the decreasing trends during 2020 through 2035 among the general population to the levels of college graduates during 2001 through 2015.

Part 3: Pathways to Achieving the Challenge Goal: Defining the Roadmap

The ACS challenge goal of reducing mortality by 50% between 1990 and 2015 was aspirational. However, one lesson of that ACS goal, an NCI goal for the same reduction between 1985 and 2000, and a 2002 goal set by the NCI Director to eliminate death and suffering from cancer by 2015 is that a challenge goal should be potentially achievable. In addition, a path toward achieving the goal should be laid out. Herein, we estimated the extent to which cancer death rates can be reduced by decreasing the prevalence of known, modifiable risk factors and increasing cancer screening uptake rates, such that we can lay out the pathways to achieving the challenge goals. The method is described below.

On the basis of risk factor exposure (including lack of screening), the death rate from each cancer site can be expressed as:

$$\text{Death rate} = \text{Death rate of the unexposed group} * \sum_0^I P_i \times RR_i,$$

where I denotes the number of exposure groups (including the unexposed group), P_i denotes the prevalence of exposure group I , and RR_i denotes the relative risk of death for group i compared with the unexposed group. A 10-year lag period (latency period) between reductions in risk factor prevalence and in cancer mortality and a 5-year lag period between increases in screening rates and reductions in cancer mortality were considered in this analysis. This means that the 2015 cancer death rate reflects the risk factor prevalence in 2005 and the screening level in 2010, and the 2035 cancer death rate will only be affected by changes in risk factor prevalence before 2025 and by changes in screening before 2030.

By using smoking and lung cancer as examples, the lung death rate in 2015 could be expressed as: $D_{2015} = D_{\text{never}} \times (P_{\text{never},2005} \times 1 + P_{\text{former},2005} \times RR_{\text{former}} + P_{\text{current},2005} \times RR_{\text{current}})$, where D represents the death rate, P represents prevalence, *never* represents never smokers, *former* represents former smokers, and *current* represents current smokers. Similarly, the lung cancer death rate in 2035 could be expressed as: $D_{2035} = D_{\text{never}} \times (P_{\text{never},2025} \times 1 + P_{\text{former},2025} \times RR_{\text{former}} + P_{\text{current},2025} \times RR_{\text{current}})$. Assuming that lung cancer death rates of the never smokers are stable over time, the reduction of lung cancer death rates from 2015 to 2035

could be estimated as: $\text{reduction}(\%) = 1 - (P_{\text{never},2025} \times 1 + P_{\text{former},2025} \times RR_{\text{former}} + P_{\text{current},2025} \times RR_{\text{current}}) / (P_{\text{never},2005} \times 1 + P_{\text{former},2005} \times RR_{\text{former}} + P_{\text{current},2005} \times RR_{\text{current}})$. The 2025 prevalence here represents the targeted level for the general population to attain by 2025.

To estimate the reductions for all cancer death rates, we first estimated the percent reduction in the overall cancer death rates caused by individual risk or protective factors as the weighted sum of the cancer-specific percent reduction, with the ratios of the number of cancer-specific deaths to the number of all cancer deaths as weights (see Supporting Information). Then, we summed over the individual risk or protective factor proportions. Because of a lack of stable data for college graduates, we did not estimate the effects of infections and radiation on cancer death rates. Relative risks used in the calculation are listed in Supporting Tables 2 through 5.

To produce a range of estimates of future changes in cancer death rates, we used 2 sets of targeted risk factors and screening profiles for the general population. The lower bound targets are the risk factors and screening profiles (levels) of college-educated Americans observed in 2015. Even among college-educated adults, the prevalence of major risk factors and screening is suboptimal; thus, we defined upper bound prevalence and screening targets as: smoking prevalence at the level of those with a master's degree; body mass index distribution at the level of the 1970s; on the basis of 2015 levels for adult Americans, increasing their daily consumption of fruits and vegetables on average by 100 g, dietary fiber by 10 g, and dietary calcium by 200 mg; reducing their daily consumption of red meat and processed meat on average by 50 g; reducing their alcohol beverage consumption on average by 1 drink per day; increasing their moderate/vigorous physical activities on average by 250 metabolic equivalent task minutes per week; increasing the prevalent use of tamoxifen/raloxifene for breast cancer prevention among women age 35-79 years to 5%; and increasing the uptake rate of colorectal and breast cancer screening to 90%. The prevalence of risk factors and screening uptake rates are shown in Table 1.³⁶

The prevalence of risk factors and the screening uptake rates were estimated using SAS-Callable SUDAAN version 11.0 (RTI International), accounting for complex survey designs. The percent reduction in cancer death rates was calculated using SAS version 9.4 (SAS Institute Inc).

Results

What Is Cancer Mortality Likely to Look Like in 2035?

Figure 1 shows observed (1969-2015) and projected (2016-2035; represented by the blue line) overall cancer death rates for both sexes combined in the United States. The projection through 2035 represented by the blue line assumes that

TABLE 1. Distribution of Risk Factors by Sex Among Adults Aged ≥30 Years and Uptake Rate of Recommended Screenings

RISK FACTOR/SCREENING	2005 PREVALENCE, %		2015 PREVALENCE AMONG COLLEGE GRADUATES, %		OPTIMAL PREVALENCE, % ^a	
	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
Cigarette smoking						
Never	48.2	61.6	69.2	73.7	78.5	81.1
Former	29.4	21.0	24.6	20.8	17.5	14.9
Current	22.3	17.3	6.2	5.5	4.0	4.0
Body mass index, kg/m ²						
<18.5	0.8	1.5	1.0	1.8	1.6	3.3
18.5-24.9	24.1	33.7	23.7	41.0	41.6	49.5
25.0-29.9	41.6	28.4	42.8	26.8	43.1	27.8
30.0-34.9	22.4	18.9	22.6	15.4	11.2	11.9
35.0-39.9	7.7	10.1	6.0	8.1	2.0	5.1
≥40.0	3.3	7.4	4.0	6.9	0.4	2.5
Fruit/vegetable intake, g/d						
0-99	19.6	23.5	13.8	18.3	0.0	0.0
100-199	23.8	26.5	24.2	23.2	23.8	26.3
200-299	22.1	21.2	22.6	20.9	25.2	25.9
300-399	13.6	12.6	17.2	17.9	19.4	19.7
≥400	20.9	16.3	22.2	19.7	31.5	28.1
Fruit intake, g/d						
0-49	46.0	45.0	39.2	37.6	0.0	0.0
50-99	9.7	11.4	12.1	11.3	50.2	45.9
100-149	10.6	12.4	13.1	12.6	10.4	12.3
150-199	8.5	9.8	8.0	11.4	9.9	11.0
200-249	6.1	6.4	6.0	7.8	6.8	9.0
≥250	19.0	15.0	21.7	19.2	22.7	21.7
Red meat consumption, g/d						
0-9	44.1	53.2	52.3	60.1	64.1	77.6
10-99	30.6	34.0	28.0	28.4	24.5	18.5
≥100	25.3	12.8	19.7	11.5	11.4	4.0
Processed meat consumption, g/d						
0-5	52.4	63.5	57.4	65.3	74.6	83.9
5-49	21.3	21.9	19.3	18.5	13.1	10.7
≥50	26.4	14.6	23.3	16.3	12.3	5.4
Dietary fiber intake, g/d						
0-9	22.2	34.0	9.8	18.9	0.0	0.0
10-19	45.0	47.6	42.7	45.7	19.6	28.7
20-29	21.8	14.0	29.9	26.2	41.9	45.6
≥30	11.1	4.4	17.5	9.2	38.5	25.7
Dietary calcium intake, mg/d						
0-199	2.2	4.3	0.7	1.3	0.0	0.0
200-399	10.3	14.4	8.1	8.1	2.0	2.5
400-599	15.1	21.8	11.9	18.3	9.6	13.0
600-799	17.1	20.1	16.3	18.5	13.5	19.0
800-999	14.7	13.1	14.8	18.9	14.7	18.3
≥1000	40.7	26.3	48.2	34.9	60.2	47.3

TABLE 1. Continued

RISK FACTOR/SCREENING	2005 PREVALENCE, %		2015 PREVALENCE AMONG COLLEGE GRADUATES, %		OPTIMAL PREVALENCE, % ^a	
	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
Moderate/vigorous physical activity, MET min/wk						
0-249	46.1	50.8	37.5	38.6	0.0	0.0
250-499	9.1	10.5	8.9	10.2	53.6	57.1
500-749	8.5	8.1	7.5	8.6	7.9	8.6
750-999	5.4	5.9	7.4	6.8	5.5	7.4
≥1000 MET	31.0	24.7	38.7	35.7	33.0	27.0
Vigorous physical activity, MET min/wk						
0-249	72.9	76.8	61.5	65.6	0.0	0.0
250-499	5.0	3.6	5.5	3.3	75.2	80.4
≥500	22.1	19.6	33.0	31.0	24.8	19.6
Alcohol intake, drinks/d						
0	32.7	45.8	20.3	25.5	67.5	83.5
0.1-0.9	35.6	40.3	42.1	50.4	9.4	6.4
1.0-3.9	20.6	10.6	26.9	19.8	13.0	7.2
≥4.0	11.0	3.3	10.6	4.3	10.0	3.0
Tamoxifen/raloxifene						
Use of tamoxifen/raloxifene	—	0.1 ^b	—	0.5 ^b	—	5.0 ^b
Screening						
Colorectal cancer screening	58.8	58.8	71.6	69.5	90.0	90.0
Mammography	—	69.5	—	76.7	90.0	90.0

Abbreviations: MET, metabolic equivalent task.

^aOptimal levels: smoking prevalence drops to the level of those with a master's degree; body mass index drops to the level of the 1970s; on the basis of 2015 level, adult Americans increases their daily consumption of fruits and vegetables on average by 100 g, dietary fiber by 10 g, and dietary calcium by 200 mg; reduces their daily consumption of red meat and processed meat on average by 50 g each; reduces alcohol beverage consumption on average by 1 drink per day; increases moderate/vigorous physical activities by 250 MET minutes per week; the use of tamoxifen/raloxifene among women age 35-79 years increases to 5%; and the uptake rates of both colorectal and breast cancer screening increase to 90%.

^bAdapted from Waters EA, Cronin KA, Graubard BI, Han PK, Freedman AN. Prevalence of tamoxifen use for breast cancer chemoprevention among U.S. women. *Cancer Epidemiol Biomarkers Prev.* 2010;19:443-446.³⁶ The prevalence of tamoxifen use in 2005 was 0.08% among US women aged 40 to 79 years without a personal history of breast cancer and was assumed to be 0.5% in 2015 for college graduates and 5% at the optimal level.

mortality will continue to decline at rates similar to those of the most recent time period in the general population. Between 2015 and 2035, overall cancer death rates are projected to decline by 26.4% in both sexes combined. During the corresponding period, death rates are projected to decline by 30.3% in males and by 24.6% in females (Fig. 2, represented by the blue line) if sex-specific declines in cancer mortality rates over the next 20 years continue at the current pace.

Table 2 shows observed (1990 and 2015) and projected (2035) death rates and percent changes in the rates for the 4 most common cancers (lung, colorectum, prostate, and female breast cancers) and for 3 cancers (pancreas, liver, and uterus) with increasing death rates. The 4 common cancers account for nearly one-half of all cancer deaths and are the main driver for the steady decline in the overall cancer death rates over the past 25 years because the rates for each of the 4 cancers declined by 31% to 51% since 1990.

What Can Cancer Mortality Look Like in 2035 (A Challenge Goal)?

Progress in reducing cancer death rates is steeper and death rates are lower among Americans with at least a college degree compared with the US population as a whole. From 2001 to 2015, for example, overall cancer death rates in the United States decreased by 2.6% per year in college-educated persons versus 1.5% per year in all populations. If overall cancer death rates from 2020 to 2035 in the US general population decline at the pace of college graduates, overall cancer death rates in 2035 will drop by 38.3% from the 2015 level and by 54.4% from the 1990 level (Fig. 1) (Table 2). The corresponding percent declines by sex from 2015 are 39.3% in males and 37.7% in females, and those from 1990 are 58.8% in males and 51.6% in females (Fig. 2) (Table 2). We estimate that expeditiously moving toward this goal could lead to approximately 1.3 million fewer

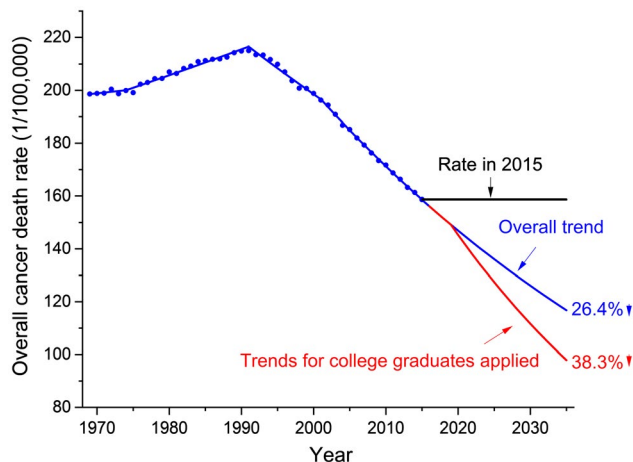


FIGURE 1. Observed (1969–2015) and Projected (2016–2035) Cancer Death Rates in the United States. Rates were age standardized to the 2000 US standard population. Blue dots represent observed death rates; the blue line after 2015 represents projected death rates (2016–2035) based on current trends among the general population and the red line after 2019 represents projected death rates (2020–2035) based on the average annual percent change in overall cancer death rates during 2001 through 2015 for college graduates.

cancer deaths from now to 2035 and 122,500 fewer deaths in 2035 alone.

Table 2 also shows the challenge goals for common cancer sites from the levels of 1990 and 2015. The goal of mortality reduction between 2015 and 2035 is 49.3% (about 50%) for lung cancer, 54.2% (about 55%) for colorectal cancer, 40.9% (about 40%) for female breast cancer, and 53.4% (about 55%) for prostate cancer.

The Pathway Toward Achieving the Goal

We estimated that, if the prevalence of some major risk factors (smoking, excess body weight, low fruit and vegetable consumption, red meat consumption, processed meat consumption, low dietary fiber consumption, low dietary calcium consumption, alcohol intake, physical inactivity, and nonadherence to evidence-based use of tamoxifen/raloxifene for breast cancer prevention), and colorectal cancer and breast cancer screening rates among all Americans can reach the levels of college graduates in 2015 by 2025 and 2030, respectively, we will see a 20.5% drop in the overall cancer death rate in 2035 compared with the rate in 2015 (Table 3).

If risk factor prevalence and screening rates become more optimal (smoking prevalence drops to the level of those with a master’s degree; body mass index levels drop to the level of the 1970s; on the basis of 2015 levels, adult Americans increase their daily consumption of fruits and vegetables on average by 100 g, dietary fiber by 10 g, and dietary calcium by 200 mg; reduce their daily consumption of red meat and processed meat on average by 50 g; reduce their alcohol beverage consumption on average by 1 drink per day; increase their moderate/vigorous physical activities by 250 metabolic equivalent task minutes per week; increase the use of tamoxifen/raloxifene among women age 35–79 to 5%; and increase the uptake rate of colorectal and breast cancer screening to 90%), then the overall cancer death rate between 2015 and 2035 will drop by 33.5%.

Table 3 also shows the percent of death rate reduction from 2015 to 2035 by achieving these risk factor and

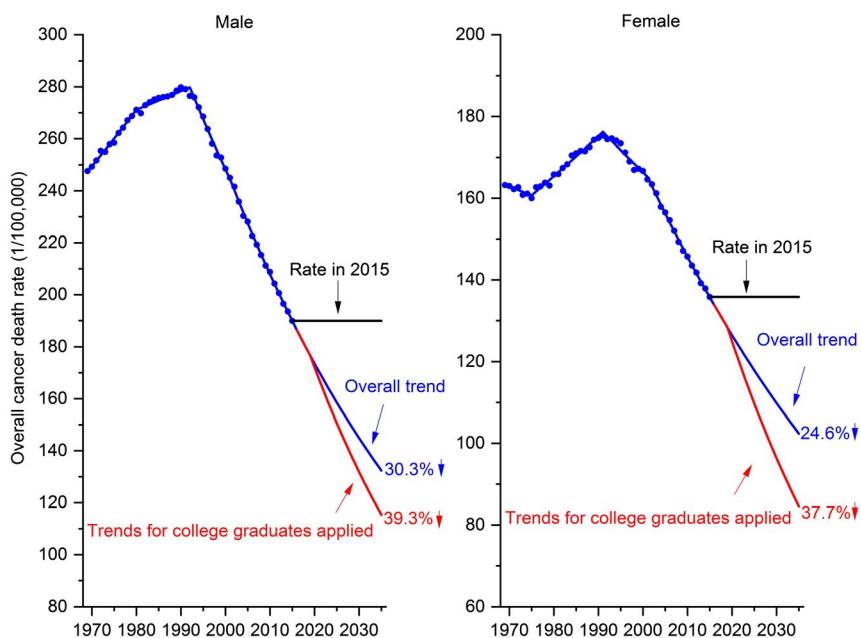


FIGURE 2. Observed (1969–2015) and Projected (2016–2035) Cancer Death Rates by Sex in the United States. Rates were age standardized to the 2000 US standard population. Blue dots represent observed death rates; the blue line after 2015 represents projected death rates (2016–2035) based on current trends among the general population and the red line after 2019 represents projected death rates (2020–2035) based on the average annual percent change in overall cancer death rates during 2001 through 2015 for college graduates.

TABLE 2. Observed and Projected Cancer Death Rates (per 100,000 Population) by Cancer Site

CANCER SITE	OBSERVED DEATH RATE			PROJECTED DEATH RATE ^a			CHALLENGE GOAL ^b		
	1990 RATE	2015 RATE	% CHANGE FROM 1990	2035 RATE	% CHANGE FROM 2015	% CHANGE FROM 1990	2035 RATE	% CHANGE FROM 2015	% CHANGE FROM 1990
All cancers	214.9	158.7	−26.2	116.8	−26.4	−45.7	97.9	−38.3	−54.4
Male	279.8	189.9	−32.1	132.3	−30.3	−52.6	115.3	−39.3	−58.8
Female	174.7	135.8	−22.3	102.4	−24.6	−41.6	84.6	−37.7	−51.6
Lung	58.9	40.6	−31.1	24.5	−39.7	−58.5	20.6	−49.3	−65.0
Colorectum	24.6	14.0	−43.1	9.0	−35.7	−62.5	6.4	−54.2	−74.0
Female breast	33.1	20.3	−38.7	14.8	−27.1	−54.7	12.0	−40.9	−63.7
Prostate	38.6	18.9	−51.0	9.8	−48.1	−75.1	8.8	−53.4	−77.2
Liver	3.6	6.6	83.3	10.4	57.6	181.1	7.7	16.0	113.9
Pancreas	10.7	11.0	2.8	11.6	5.5	8.4	10.2	−7.1	−4.7
Uterus	4.3	4.8	11.6	7.0	45.8	66.7	5.3	9.8	23.3

^aThe projected death rates are the rates assuming current mortality trends continue until 2035.

^bThe challenge goals for 2035 are the rates if all Americans experience the mortality trends of college-educated Americans during 2001 through 2015 starting in 2020.

screening targets for some major cancer sites. The reduction ranges from 50% to 66% for lung cancer, from 32% to 81% for colorectal cancer, from 6% to 18% for female breast cancer, from 10% to 17% for pancreatic cancer, and from 15% to 36% for liver cancer.

Discussion

The ACS 2035 Challenge Goals

By applying the AAPC in overall cancer death rates of college-educated Americans during 2001 through 2015 to the US general population beginning in 2020, we projected that the 2035 overall cancer death rate will drop by 38.3% from the 2015 rate and by 54.4% from the 1990 rate. For ease of communication, we set the ACS 2035 challenge goal as a 40% reduction in the overall cancer death rate between 2015 and 2035. Achieving this goal could lead to approximately 1.3 million fewer cancer deaths during 2020 through 2035 and 122,500 fewer deaths in 2035 alone.

One lesson from the previous goal-setting practices is that a challenge goal should be potentially achievable. In setting the 2035 goal, we decided to use a reference cohort—a well defined population with better cancer outcomes than the US population as a whole. The future outcomes for the United States based on cancer trends in the reference population and in the entire US population can be projected and compared. Race/ethnicity and educational attainment (as a marker of SES) are the 2 indicators that we considered in selecting the reference cohort. Compared with race/ethnicity, educational attainment is a better indicator of exposure to cancer risk factors, adherence to cancer screening guidelines, and access to cancer care. In addition, a substantial extent of racial/ethnic disparity is because of SES. Therefore, the cohort chosen for reference was the US population aged 25 years or older with a college degree. This cohort comprises 32% of all Americans older than

25 years.¹¹ Previous studies reported that progress in reducing cancer mortality in the United States is greatest in persons with a college degree^{19,20,37} and that eliminating education-related inequalities would have a greater effect on reducing disparities in cancer mortality than eliminating racial/ethnic inequalities.¹¹ Of note, historically, death rates for all cancers combined and for most major cancer sites (lung, colorectum, and female breast) were higher in high SES populations, which included highly educated persons, than in low SES populations, because the former had higher prevalence of risk factors, such as smoking and an unhealthy diet.³⁸ The reversal of this SES and cancer mortality association in addition to the subsequent widening socioeconomic disparities in cancer mortality suggest that high SES populations have benefited more from cancer interventions than low SES populations. To mitigate cancer disparities and eventually reduce cancer burden among the entire population, tailored interventions are needed among low SES populations as some socioeconomic constraints may limit their abilities to change health behaviors and their access to care.

Consistent with previous studies,^{19,20,39} we found that progress in reducing cancer death rates was steeper and death rates were lower in Americans with at least a college degree compared with the US population as a whole. From 2001 to 2015, the overall cancer death rate in the United States decreased by 2.6% per year in college-educated persons versus 1.5% per year in all populations. These differential trends between college graduates and the general population largely reflects differences in the prevalence of known risk factors and uptake of cancer screening, as well as access to and utilization of high-quality care.³⁸ Although the prevalence of known risk factors is lower and the rates of receipt of standard of cancer care are higher in college graduates compared with noncollege graduates, the patterns in

TABLE 3. Proportional Reduction (%) in Death Rates From Improvement in Cancer Risk Factor and Screening to Optimal Levels^a

RISK FACTOR	PROPORTIONAL REDUCTION IN DEATH RATE, %						
	LUNG	COLORECTUM	BREAST (FEMALE)	PANCREAS	LIVER	OTHER RELATED CANCER SITES	ALL CANCERS
Tobacco	47.9-59.3	6.4-8.3		8.7-10.3	13.7-17.2	Oral cavity and pharynx, 32.7-39.4; esophagus, 25.6-33.6; stomach, 10.4-13.5; larynx, 51.3-60.5; cervix, 8.6-11.9; kidney, 8.4-11.5; urinary bladder, 24.2-31.7; leukemia, 7.9-10.5	17.0-21.1
Excess body weight		0.3-2.0	1.4-4.3	1.1-6.7	1.6-13.7	Esophagus, 1.0-12.9; stomach, 0.1-1.2; gallbladder, 3.2-14.5; corpus uteri, 6.0-20.6; ovary, 0.5-1.5; kidney, 1.6-13.2; thyroid, 0.8-4.4; multiple myeloma, 0.7-4.4	0.4-2.6
Physical inactivity		2.2-3.2	0.7-1.4			Corpus uteri, 5.1-7.3	0.3-0.5
Alcohol use		0.0-3.6	0.0-5.6		0.0-4.9	Esophagus, 0.0-4.1; lip, oral cavity, pharynx, 0.0-13.2; larynx, 0.0-3.3	0.0-1.3
Fruit/vegetable	2.1-6.7					Oral cavity, pharynx, larynx, 2.2-7.8	0.6-1.9
Red meat/ processed meat		1.9-8.3				Stomach, 0.9-5.3	0.2-0.8
Dietary fiber		2.8-7.9					0.2-0.7
Dietary calcium		2.2-4.7					0.2-0.4
Nonuse of tamoxifen/ raloxifene			0.2-1.9				0.0-0.1
Lack of screening		16.3-43.1	1.7-4.7				1.6-4.1
All factors	50.0-66.0	32.1-81.1	5.5-17.9	9.8-17.0	15.3-35.8		20.5-33.5

^aThe lower bound of the proportion was calculated based on the levels of college-educated Americans in 2015; the upper bound was calculated based on the optimal levels listed in the last column of Table 1.

college graduates are far from optimal. For example, 7% of college graduates in the United States are current smokers, 28% are obese, and 17% are physically inactive.^{40,41} Therefore, concerted efforts to promote healthy behaviors (quitting smoking, achieving and maintaining a healthy body weight, being physical active) and increasing access and utilization of known, evidence-based medical interventions (screening, diagnostics, and treatment) in all populations, including college graduates, are essential to achieving the 2035 challenge goal.

In addition to the overall cancer mortality goal, we estimated challenge goals for cancers of the lung, colorectum, prostate, and female breast, which together account for nearly one-half of all cancer deaths. These 4 major cancer sites were the main drivers for the steady decline in the overall cancer death rates over the past 25 years and will continue to be the focus of the 2035 challenge goal. The targeted percent decreases from 2015 to 2035 are 50% for lung cancer, 55% for colorectal cancer, 40% for female breast cancer, and 55% for prostate cancer.

Lung cancer mortality rates peaked in 1991 and likely will continue declining during the next 2 decades because of declines in smoking prevalence over the past several decades and expected declines in the future. It is well established that screening and modern treatment reduce colorectal cancer incidence and mortality. Colorectal cancer death rates

were declining before screening became common, since the 1980s in men and the 1950s in women, in part because of changes in dietary patterns, reductions in smoking, and increased use of anti-inflammatory drugs and of hormone replacement therapy (women only).^{42,43} It is noteworthy that, historically, colorectal cancer death rates were higher in high-SES than in low-SES groups but were reversed in the 1950s.³⁸ Despite the long-term mortality decline, however, colorectal cancer death rates have increased slightly among adults aged 20 to 54 years over the past decade.⁴³ Reasons for this increase are unknown, but it may in part reflect the obesity epidemic and unhealthy diet.^{43,44} Because the obesity epidemic and increasing unhealthy diet are likely to continue, targeted interventions are needed to slow down or reverse these unfavorable trends.

Breast cancer screening and treatment have improved dramatically over the past 40 years. Previous studies suggested that adjuvant chemotherapy and screening each have contributed to about one-half of the decline in mortality in this disease.⁴⁵ However, similar to colorectal cancer, the decline in breast cancer mortality because of treatment and screening may have been attenuated by the obesity epidemic. Adulthood obesity has been linked to an increasing risk of postmenopausal breast cancer.²¹ The high prevalence of childhood obesity is a recent phenomenon and may transition to a higher rate of adulthood obesity in the United States.

Prostate cancer death rates have dropped significantly since the early 1990s. Screening and treatment each likely contributed to some of the decline.⁴⁶ Prostate cancer death rates, however, have declined in 20 or more countries without screening.⁴⁷ There are data suggesting a link between high-grade, deadly prostate cancer and tobacco use,^{48,49} but the contribution of the decline in smoking prevalence to the declining prostate cancer mortality rate is unknown. A recent study, however, found that the pace of decline in prostate cancer death rates in the United States is slowing during the most recent period.⁵⁰

Mortality rates are increasing for cancers of the pancreas, liver, and corpus uterus (endometrial). However, they are not expected to rise such that they will substantially affect the overall cancer mortality trend. The age-adjusted pancreatic cancer death rate has risen from 10.6 per 100,000 population in the early 1980s to 11.0 per 100,000 population in 2015 and is projected to be 11.6 per 100,000 population in 2035 (Table 2). Pancreatic cancer is associated with smoking and obesity.^{21,51} The increasing number of Americans who are obese throughout adulthood may have contributed to the increase in pancreatic cancer incidence and death rates.

The age-adjusted liver cancer death rate per 100,000 population rose from 2.8 in 1975 to 6.6 in 2015. Factors that are thought to contribute to this increase include the obesity epidemic, the high prevalence of chronic hepatitis C virus (HCV) infection among baby boomers, and an increase in alcohol consumption.⁵² The relatively new treatments for HCV infection can attenuate or reverse the rising liver cancer rates, although the drugs have yet to be disseminated widely because of their high cost.⁵³ It is estimated that less than 20% of Americans diagnosed with HCV infection are treated, and the majority of those with HCV infection have not been diagnosed.^{53,54} Cancer of the uterine corpus is the malignancy most associated with obesity and physical inactivity,^{21,55} and there is an opportunity to halt or reverse the unfavorable mortality trend of pancreatic, liver, and endometrial cancers through individual and community actions to promote healthful lifestyles, such as achieving and maintaining a healthy body weight, being physically active, and consuming a healthy diet.

The Pathways Toward Achieving the Goals

It is estimated that known, modifiable risk factors of cancer are responsible for 45.1% of all cancer deaths in 2014 in the United States.²¹ This indicates that a substantial proportion of cancer deaths could be prevented by a broader adoption of more healthful habits.

We estimate that, if the prevalence of some major risk factors and colorectal cancer and breast cancer screening rates among all Americans can achieve the levels of college graduates in 2015 by 2025 and 2030, respectively, we will see a 20.5% drop in the overall cancer death rate in 2035

compared with the 2015 rate, attaining about one-half of the challenge goal. As previously noted, the risk factor and cancer screening profiles among college graduates are still far from optimal. If risk factor prevalence and screening rates in 2025 for the general population become more optimal than those of college graduates in 2015 (as listed in Table 1),³⁶ then the overall cancer death rate will drop by 33.5% between 2015 and 2035, attaining 85% of the challenge goal.

These results suggest that intensified, coordinated efforts by civil societies, policy makers, and community leaders for the broad application of known interventions tailored to different socioeconomic groups have the potential to reduce cancer mortality to a level close to the 2035 ACS challenge goal. Furthermore, wider dissemination of existing targeted therapies and immunotherapies^{56,57} and of new discoveries in prevention and early detection methods and treatments within the next decade could further accelerate the reduction in cancer death rates and lead to achieving or even exceeding the challenge goal. Clinicians will play a critical role in achieving the 2035 goals by helping their patients adhere to recommended preventive services. Previous studies have shown that provider-based interventions are effective in both primary prevention and promoting cancer screening.⁵⁸⁻⁶⁰

Limitations

As with any projections, there are limitations. First, we used log-linear extrapolation to predict future cancer death rates. Without modelling changes in risk factors, screening, and treatments, our projected rates are subject to some levels of uncertainty. Second, the racial composition of the US population is also expected to change. Between 2015 and 2035, the shares of the Hispanic and Asian populations, the 2 populations with the lowest cancer death rates, are projected to increase from 17.4% to 22.8% and from 5.4% to 7.0%, respectively.⁶¹ However, we did not account for the change in racial composition in the projection of rates, which are likely to be overestimated. Third, because of a lack of stable data for college-educated Americans, we did not include some known risk factors, including hepatitis virus infections and ultraviolet radiation exposure, which collectively account for nearly 4% of total cancer deaths.²¹ Fourth, we selected 5% as the target level of tamoxifen/raloxifene use for breast cancer prevention among women age 35-79 years. It is estimated that although about 15% of US women age 35-79 years are eligible for breast cancer chemoprevention, less than 5% of women age 35-39 years may have a favorable risk-benefit profile.⁶² In addition, because of limited data, we did not examine the potential effect of cervical cancer screening (because of the relatively small numbers of cervical cancer deaths), human papillomavirus vaccination, lung cancer screening, and advances in cancer treatment on future cancer mortality reduction.

Therefore, the mortality reductions from decreasing risk factors and increasing cancer screening are likely to have been underestimated in our study.

Conclusions

Over the past 6 decades, cancer research has yielded significant knowledge concerning its causes, screening, diagnosis, and treatment. Unfortunately, that knowledge has not been put into practice consistently and equitably throughout the entire population. Consequently, every year, the American public loses over \$80 billion for direct medical costs and hundreds of thousands of lives because of premature cancer deaths. Indeed, this futuring exercise demonstrates that we can significantly reduce cancer mortality if all sectors of society enjoy good preventive and therapeutic care. Future progress in the “war on cancer” depends on the extent to which policy makers and the American public can join together to create systems to provide adequate health care to all.

Previous articles in this ACS cancer control blueprint series have summarized knowledge, opportunities (including the proportion of potentially preventable cancer cases and deaths),²¹ and unanswered questions in cancer control,⁸ including the prevention²⁴ and early detection of cancer.²⁵ The blueprint series includes an article about the strengths and shortcomings of our current health care system,²⁶ as well as an article outlining current knowledge, opportunities, and research questions that must be answered to improve the delivery of survivorship care.²⁷ The ACS will continue the cancer control blueprint series by publishing an article about addressing the social determinants of health. The final entry will provide a cancer research blueprint

based on an in-depth series of interviews with leading cancer researchers.

The greatest pay-off in terms of cancer deaths prevented is through continued work on tobacco control, followed by an effort to control excess body weight. This would require a change in the behavior of the US population and culture of a magnitude very similar to that of the changes regarding smoking since the mid-1960s. Such a change would reduce cancer incidence and death rates toward the 2035 goals and also would reduce incidence, morbidity, and mortality from several other chronic diseases, including cardiovascular disease, diabetes, and orthopedic conditions. It also has the potential to substantially reduce America’s health care costs.

Previous studies showed that a substantial number of Americans receive less than optimal care.⁶³⁻⁶⁸ Widespread and equitable access to and utilization of high-quality care (both preventive and therapeutic) is necessary to achieve the 2035 challenge goal of reducing cancer mortality from the 2015 level. A 33.5% reduction in age-adjusted cancer mortality can only be achieved if the entire community acts urgently to ensure that everyone in the United States has the opportunity to benefit from the interventions described in the ACS cancer control blueprint series. Accelerating research progress will be needed to meet or even exceed our challenge goal of a 40% reduction in cancer mortality. Indeed, perhaps the most important and pertinent research question in cancer control is: “How can we provide adequate high-quality care, including preventive care, to as many Americans as possible while also continuing the basic, translational, and clinical research that will improve tomorrow’s standard of care?” ■

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