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When Should We Stop Screening?

CONTEXT. Although the age at which screening should be started is the subject of considerable debate, the question of when to stop has received little attention.

COUNT. Days of life lost by stopping screening at various ages.

CALCULATIONS. For each of three types of cancer (breast, cervical, and colon), we used life tables to calculate life expectancy at various ages for stopping screening and for continuing screening until death. The days of life lost by stopping screening is the difference in life expectancy between the two life tables for a specified age.

DATA SOURCES. All-cause and cancer-specific mortality were obtained from the National Center for Health Statistics and Surveillance Epidemiology and End Results Survey (SEER).

ASSUMPTIONS ABOUT BENEFIT. On the basis of randomized trial data, we used a 30% reduction in cancer-specific mortality for breast and colon cancer screening. Because there are no comparable data for cervical cancer, we assumed a 30% reduction in the mortality rate for the “best-guess” analysis and a 70% reduction in the mortality rate for the “best-case” analysis. We assumed that these benefits persisted for the elderly.

ASSUMPTIONS ABOUT HARM. We assumed that there was no harm with screening.

RESULTS. Given a starting age of 50 years, screening throughout life has a maximum potential life expectancy benefit of 43 days for breast cancer and 28 days for colon cancer. The average 75-year-old who stops either mammography or fecal occult blood testing would give up a maximum of 9 days. By stopping at age 80, she would give up a maximum of 5 days. Given a starting age of 20, Pap smear screening has a maximum potential benefit of 47 days in the best-case analysis and 7 days in the best-guess analysis. The average 75-year-old who forgoes Pap smear screening would give up a maximum of 3 days (best case) or 0.5 days (best guess). By stopping at age 80, she would give up a maximum of 1.5 days and 0.2 days, respectively.

CONCLUSIONS. Even assuming that the mortality reduction with screening persists in the elderly, 80% of the benefit is achieved before 75 years of age for breast cancer, 80 years for colon cancer, and 65 years for cervical cancer. The small benefit of screening in the elderly may be outweighed by the harms: anxiety, additional testing, and unnecessary treatment.

In recent years, one of the more contentious aspects in establishing guidelines for cancer screening has been the age at which to begin testing. Nowhere has this been more true than for breast cancer screening. The debate about the starting age was fueled by different interpretations of data collected in several randomized trials.¹ By comparison, the question of the age at which screening should be stopped has received little attention.

Perhaps as a consequence of the scarcity of experimental data in the elderly, the recommendations by different professional organizations have been inconsistent. For example, for screening mammography, the American College of Physicians–American Society of Internal Medicine recommends against routine breast cancer screening for

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women older than 75 years of age, the U.S. Preventive Services Task Force states that evidence for or against routine screening in women over 70 is insufficient, and the American Cancer Society and the American Medical Association cite no upper age limit.² The recommendations of various professional organizations regarding an upper age limit for cervical and colon cancer screening are similarly ambiguous.²

Because benefits of screening are delayed, the expected value of screening decreases as the risk for dying of other causes increases. At some point for the elderly, the reality of these “competing” risks for death means that the expected value of screening will become very small (or even negative if there are associated harms). To help inform decisions about when to stop cancer screening, we created life tables to model screening for breast, colon, and cervical cancer and to calculate the days of life lost by stopping screening at various ages.

Methods

Basic approach

Our primary outcome is the number of days of life lost by stopping screening at various ages. For each stopping age, we built two life tables: one for no further screening and one for regular screening until death. **Figure 1** is our back-of-the-envelope calculation of days of life lost by stopping screening; this number is the difference between the life expectancies calculated in the two tables. Life expectancy is, in turn, determined by the age-specific all-cause mortality rates for each table. We modeled the benefit of screening by reducing the cancer-specific mortality rate by a fixed percentage, thereby reducing the all-cause mortality in the life table for screening throughout life. We performed separate analyses for breast, cervical, and colon cancer.

Data

All-cause and cancer-specific mortality data were obtained from DevCan,³ a software package from the National Cancer Institute. Although DevCan is primarily designed to convert incidence and mortality data to probabilities of developing and dying of cancer, we used the program only to obtain its input data.

Cancer-specific mortality rates in DevCan are from the 1994 to 1996 Surveillance, Epidemiology and End Results Survey (SEER). SEER data represent the government’s effort to collect and report on cancer incidence, initial treatment, and mortality. This database consists of information from population-based cancer registries in various areas of the country, including Connecticut, Iowa, New Mexico, Utah, and Hawaii and Detroit, San Francisco, Seattle–Puget Sound, and Atlanta. The all-cause mortality data in DevCan are from the National Center for Health Statistics and are specific to the same geographic areas as SEER.

Because all-cause and cancer-specific rates are reported for 5-year age groups and we needed annual inputs for the life tables, we interpolated between the reported values to estimate annual rates. The rate for any 5-year age group was assigned to the midpoint of that interval (e.g., the breast cancer mortality rate for the 50- to 54-year-old age group was assigned to age 52; the 55- to 59-year-old age group was assigned to 57). Annual rates were then estimated by performing a linear interpolation between successive base-case values (e.g., between 52 and 57). The pattern of age-specific mortality for the three types of cancer is shown in **Figure 2**.

Assumptions about Benefit

Benefit was modeled as a reduction in cancer-specific mortality by a fixed percentage at each age. Future bene-

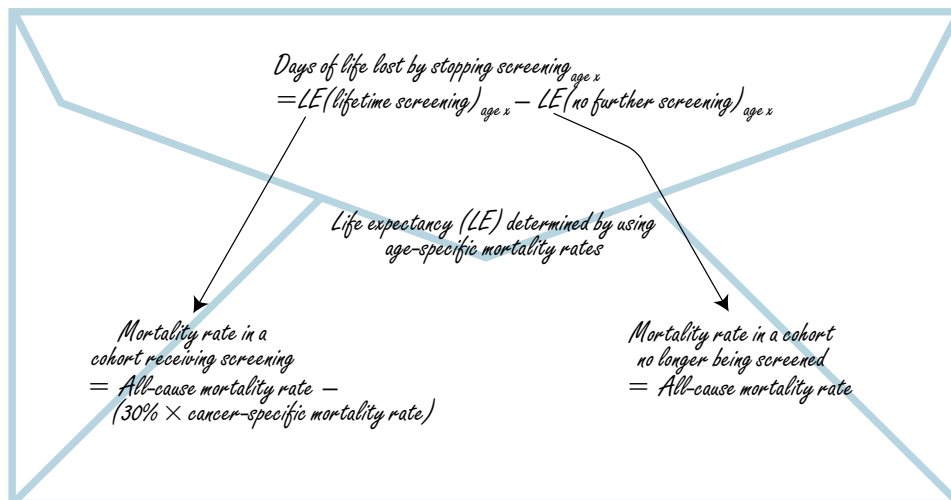


FIGURE 1. Back-of-the-envelope calculation for days of life lost by stopping screening at various ages.

fits from screening were not discounted. We assumed that the mortality benefit of screening persists for 5 years after screening is stopped (e.g., if screening stops at age 70, cancer mortality does not return to baseline until age 75).

Breast Cancer. Eight randomized, controlled trials and a meta-analysis have evaluated screening mammography.⁴ The relative reduction in the mortality rate estimated from the meta-analysis is 26% (95% CI, 17% to 34%) in women aged 50 to 74 years.⁴ On the basis of these data, we chose a relative mortality reduction of 30%. Our starting age for screening is 50 years of age. Although no data indicate that the breast cancer mortality rate is reduced beyond 74 years of age, we assumed that the benefit of screening extends to the elderly (i.e., that the reduction in mortality persists at every age).

Colon Cancer. Three randomized trials have examined screening with fecal occult blood testing in 45- to 80-year-old men and women.⁵⁻⁷ The relative reduction in the mortality rate in these studies ranged from 16% to 33%.⁵⁻⁷ In our model of colon cancer, we chose a relative reduction of 30%. As in the breast cancer analysis, we assumed a starting age of 50 and that the benefits of screening extend to the elderly.

Cervical Cancer. We faced two problems in modeling the benefits of screening in cervical cancer. First, because no randomized trials exist, the relative reduction in the mortality rate with screening is not known. Second, unlike the other two types of cancer, the mortality rate for cervical cancer has decreased dramatically in the past 50 years.⁸ Because this decrease coincides with

the introduction of Pap smears, it is possible that the low mortality rate is the result of screening. However, it is also possible that other factors (e.g., better control of infectious disease) are responsible for the decline. Thus, the mortality rate for cervical cancer in an unscreened U.S. population is unknown. To gauge the effect of these uncertainties, we performed two analyses with vastly different assumptions about the effectiveness of screening and the mortality rate in an unscreened population. In both cases, we used a starting age of 20 and assumed that benefits extend to the elderly.

For our “best-guess” analysis (i.e., our best estimate given current data), we assumed a relative reduction in mortality rate of 30% and that observed cervical cancer mortality rates (i.e., those currently reported by SEER) are from a population that is midway between universal screening and no screening. Thus, if the observed mortality rate was 100, we assumed that the unscreened mortality rate would be 118 and that the screened rate would be 82 (the change from 118 to 82 represents a 30% reduction).

For our “best-case” analysis, we assumed a 70% reduction in the mortality rate and that observed mortality rates for cervical cancer (i.e., those currently reported by SEER) are from a population that is universally screened. Thus, if the observed mortality rate for cervical cancer was 100, we assumed that the unscreened rate would be 333 and that the screened rate would be what is currently observed—100 (the change from 333 to 100 represents a 70% reduction).

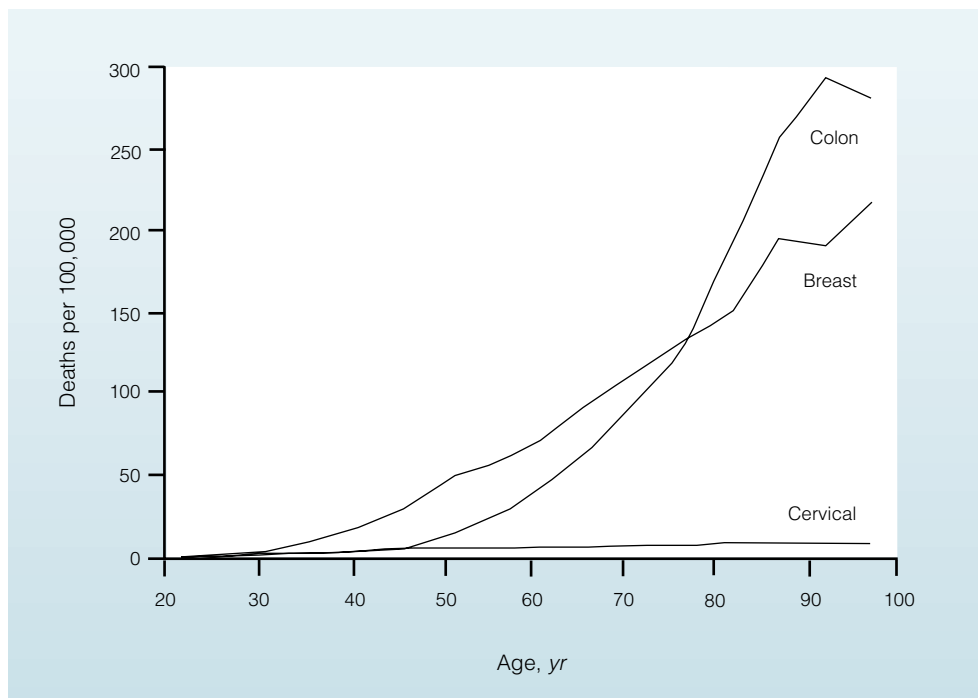


FIGURE 2. Age-specific mortality rates for breast, colon, and cervical cancer. The rates of breast and cervical cancer are for women only; the rates for colon cancer are for both sexes.

Assumptions about Harm

In our models, we assumed no harm with screening. This assumption simplifies our model; however, we recognize that screening may have many undesirable consequences, including anxiety,⁹ false-positive results that lead to subsequent unnecessary testing,¹⁰ and detection of disease that is either nonprogressive or unlikely to affect survival but leads to subsequent therapy and its attendant risks.¹ Because these effects were ignored, our results can only show persistent benefit and are therefore biased in favor of screening.

Analysis

To tabulate life expectancy, annual mortality rates were converted to survival probabilities. A cumulative probability of survival was calculated for each age interval by multiplying the probability of survival *to the preceding* interval by the probability of survival *in the current* interval. The sum of the cumulative survival probabilities from a specified age to the bottom of the table (age 97, the last year for which data are available) determined life expectancy. A detailed example of our spreadsheet is provided in the **Appendix**.

Results

To determine the maximum potential benefit from a lifetime of screening, we calculated the difference in life

expectancy between screening throughout life and a lifetime without screening. Given a starting age of 50, our approach produces a maximum potential benefit of 42.7 days for lifetime screening in breast cancer and 28.1 days for colon cancer. Given a starting age of 20, screening throughout life for cervical cancer has a maximum potential benefit of 46.6 days in the best-case analysis and 7.1 days in the best-guess analysis.

Figure 3 shows that the days of life lost by stopping screening decreases dramatically as the stopping age increases. For each stopping age shown, the days of life lost are greater for breast and colon cancer screening than for cervical cancer screening, reflecting the relative magnitude of cancer-specific mortality shown in **Figure 2**. **Figure 3** also highlights the effect of the uncertainty about the benefit of Pap smears on our estimate of the days of life lost with stopping screening.

Table 1 displays the proportion of the maximum potential benefit of screening achieved at specified stopping ages ($[\text{maximum days} - \text{days lost at stopping age}] / \text{maximum days}$). For example, a woman who began screening mammography at 50 years of age and decides to stop at age 80 has achieved 89% ($[42.6 - 4.6] / 42.6 = 0.89$) of the maximum potential benefit. As shown in **Table 1**, 80% of the maximum benefit is achieved before 75 years of age with mammography, before 80 years with fecal occult blood testing, and before 65 years with Pap smears. Somewhat surprisingly, the uncertainties of the benefit of Pap smears had no effect on this finding.

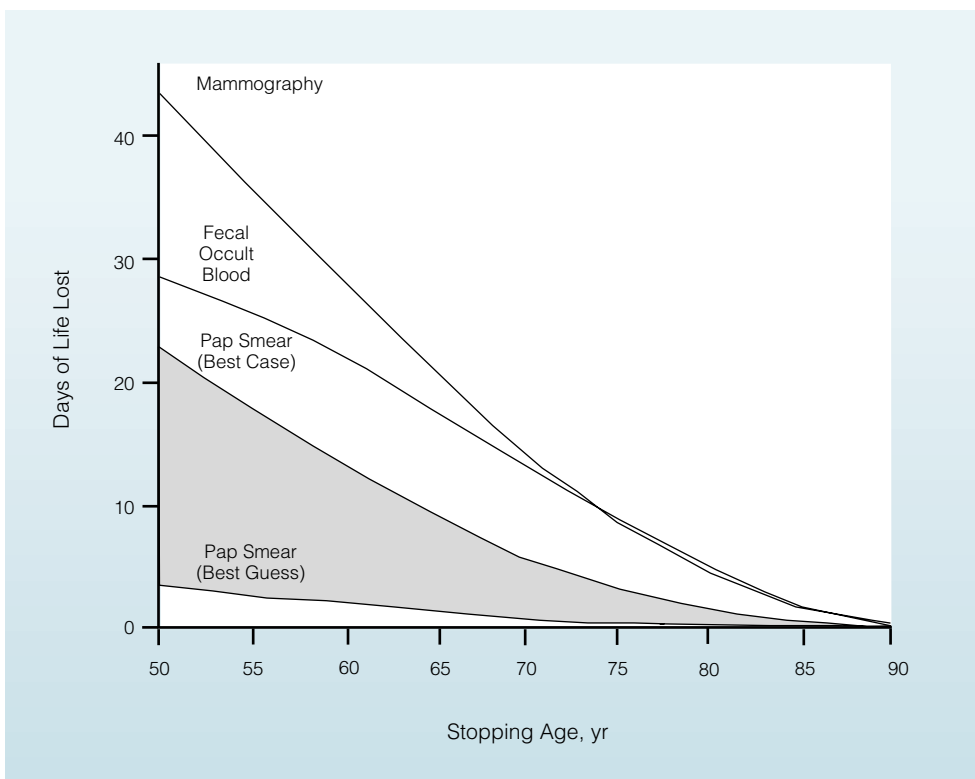


FIGURE 3. Days of life lost by stopping screening at various ages.

TABLE 1

Proportion of the Maximum Potential Benefit of Screening Achieved at Different Stopping Ages*

STOPPING AGE	MAMMOGRAPHY	FECAL OCCULT BLOOD TEST	PAP SMEAR	
			BEST GUESS	BEST CASE
65 yr	52% (20.5)	37% (17.6)	80% (1.4)	80% (9.1)
70 yr	68% (13.9)	53% (13.1)	88% (0.9)	88% (5.6)
75 yr	80% (8.5)	68% (8.9)	93% (0.5)	93% (3.4)
80 yr	89% (4.6)	83% (4.8)	97% (0.2)	97% (1.5)
85 yr	96% (1.8)	94% (1.7)	99% (0.1)	99% (0.5)

*The number of days lost by stopping screening is shown in parentheses. Blue indicates the point at which at least 80% of the benefit of screening has been achieved.

Discussion

By using a simple method, we have illustrated the effect of stopping three common screening tests at various ages. As expected, we found that the days of life lost from stopping screening decrease rapidly with increasing age. Even assuming that the mortality reduction with screening persists in the elderly, most of the benefit of cancer screening occurs before 70 years of age. Finally, regardless of the assumptions about the magnitude of the reduction in mortality rate for cervical cancer, we found the benefit of Pap smear screening in the elderly to be particularly small.

Our analysis has several limitations. The first is that our method is simple. It ignores many of the complexities of screening and considers only one outcome: mortality. Second, our method undoubtedly overestimates benefit. We do not discount future benefits, and we assume that benefits persist throughout life and that there is no harm with screening. These assumptions help explain why our estimates of the benefit of mammography in the elderly are higher than those previously reported.¹¹ Nevertheless, our results do not differ drastically from those of other analyses for breast and colon cancer screening.^{12, 13} Third, we had to make assumptions both about the benefit of cervical cancer screening and the mortality rate in an unscreened U.S. population. In choosing best-guess and best-case assumptions, our intention was to provide bounds within which the true state probably exists.

Finally, our results only apply to an “average” patient. Our input data are population based, and our primary outcome measure is average life expectancy. Thus, our results represent the expectation for individuals in average health. Because individuals at either end of the spectrum of health status may have different age-specific all-cause mortality rates (and hence life

expectancies) than average individuals of similar age,¹⁴ our estimate of forgone days of life is an underestimate for individuals in extremely good health and an overestimate for those who are ill.

On the other hand, the simplicity of our analysis may also be a strength. First, this analysis can be readily reproduced with spreadsheet software and easily accessible data (we encourage others to do so).³ Second, because our method uses the same simplifying assumptions for each type of cancer, it is a particularly useful tool for comparing the relative benefits of screening across various types of cancer. Our results are driven solely by the simple relation between cancer-specific mortality and all-cause mortality—in other words, the relation between dying of a specific type of cancer and dying of all other causes. Because these competing risks become so great in the elderly, even completely successful therapy for a specific type of cancer may not affect life expectancy.¹⁵ This information may be useful to patients who are prioritizing among screening tests. For example, if women are informed of the comparatively little benefit to be achieved with continuing cervical cancer screening relative to screening mammography after age 70, some may comfortably decide to forgo further Pap smears.

The decision to undergo screening has been compared with placing a bet.¹⁶ An individual who decides to screen is willing to risk the immediate and more probable consequences of testing (e.g., anxiety, false-positive results, and unnecessary treatment) for a potentially large, although unlikely, payoff: a gain in life expectancy. When the expected payoff becomes small, some individuals may view the immediate costs as excessive and not place the bet. Others may still want to gamble. Rather than defining an upper age limit for cancer screening, we hope that the information communicated here will facilitate this decision for elderly patients.

Take-Home Points

- Although the age at which to start screening has been the subject of considerable debate, the question of when to stop has received little attention.
- We assumed that the reduction in cancer-specific mortality rate from screening persists in the elderly and used life tables to calculate life expectancy for stopping screening and for continuing screening at various ages; we also assumed that there was no harm with screening.
- The average 75-year-old who stops either mammography or fecal occult blood testing would reduce life expectancy by a maximum of 9 days. By forgoing Pap smears, she would lose a maximum of 3 days.
- Eighty percent of the life-expectancy benefit achieved with screening occurs before 75 years of age in breast cancer, 80 years in colon cancer, and 65 years in cervical cancer.
- Because the small benefit of screening in the elderly may be outweighed by its harms (anxiety, additional testing, and unnecessary treatment), older individuals may reasonably choose not to be screened for cancer.

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Disclaimer

The views expressed herein do not necessarily represent the views of the Department of Veterans Affairs or the United States Government.

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Appendix: Construction of Life Tables*

Life tables have been used for centuries to determine the life expectancy of individuals as a function of age (thus informing decisions about premium schedules for life insurance companies). The technique makes use of cross-sectional data (i.e., the observed mortality rate in specific age groups) and translates them into longitudinal information (i.e., life expectancy).

In this analysis, two life tables (one for stopping screening and one for continued screening) were constructed in a spreadsheet for each stopping age for each type of cancer. An abridged version of the two life tables for a stopping age of 65 in breast cancer is shown below.

Stopping Screening				Continuing Screening			
AGE, yr	ALL-CAUSE MORTALITY (acm)	ANNUAL PROBABILITY OF SURVIVAL (e^{-acm})	CUMULATIVE PROBABILITY OF SURVIVAL	BREAST CANCER MORTALITY (bcm)	REVISED ALL-CAUSE MORTALITY ($acm' = acm - 0.3 bcm$)	ANNUAL PROBABILITY OF SURVIVAL ($e^{-acm'}$)	CUMULATIVE PROBABILITY OF SURVIVAL
65	0.0120	0.9881	0.9881	0.00087	0.0120	0.9881	0.9881
:	:	:	:	:	:	:	:
:	:	:	:	:	:	:	:
75	0.0309	0.9695	0.8006	0.00125	0.0306	0.9699	0.8023
76	0.0335	0.9670	0.7742	0.00128	0.0331	0.9674	0.7762
77	0.0361	0.9645	0.7468	0.00132	0.0357	0.9649	0.7489
78	0.0409	0.9599	0.7168	0.00135	0.0405	0.9603	0.7192
79	0.0458	0.9552	0.6848	0.00139	0.0454	0.9556	0.6873
80	0.0506	0.9506	0.6509	0.00142	0.0502	0.9510	0.6536
:	:	:	:	:	:	:	:
:	:	:	:	:	:	:	:
97	0.2541	0.7756	0.0620	0.00215	0.2535	0.7761	0.0628
Sum			18.8181				18.8743

The first column in the *Stopping Screening* life table (*left*) is the age interval, meaning that each row contains information specific to a given year of life. (Only selected years appear above.)

The second column is the annual age-specific all-cause mortality rate, which was taken from the National Center for Health Statistics for the SEER areas. From 65 to 69 years of age, all-cause mortality is reduced by the same amount as in continuing screening. All-cause mortality is reduced to account for the delayed effect of screening in earlier periods (e.g., screening from age 60 to 64 will continue to reduce cancer-specific mortality for another 5 years—that is, ages 65 to 69 years).

The third column is the annual probability of survival. This column conceptually involves two steps: 1) calculating the probability of dying in that year by using an annual mortality rate ($1 - e^{-\text{mortality rate}}$), and 2) obtaining the complementary probability: the probability of survival ($1 - \text{probability of dying}$). The calculation thus simplifies to $e^{-\text{mortality rate}}$.

The fourth column is the cumulative probability of survival, which is the product of the probability of survival in the current year and the cumulative probability of survival in the previous year. The sum of this column is the life expectancy from the age in the first row (in this case, 18.818 years for a 65-year-old woman).

The first column of the *Continuing Screening* life table (*right*) contains additional data: the age-specific mortality rate for the specific type of cancer, which came from SEER. The second column is the revised all-cause mortality with screening. In this case, 30% of breast cancer mortality is subtracted from the reported all-cause mortality. The third and fourth columns contain the annual and cumulative probability of survival as described above. As before, the sum of the final column is the life expectancy (in this case, 18.874 years for a 65-year-old woman).

The difference between the life expectancies from the two tables is the days lost by stopping breast cancer screening at 65 years of age (in this case, $18.874 - 18.818 = 0.056$ years or 20.5 days).

*e = the base of natural logarithms, or about 2.718; SEER = Surveillance, Epidemiology, and End Results.