SPECIAL ARTICLES

PROGRESS AGAINST CANCER?

JOHN C. BAILAR III AND ELAINE M. SMITH

Abstract We assessed the overall progress against cancer during the years 1950 to 1982. In the United States, these years were associated with increases in the number of deaths from cancer, in the crude cancer-related mortality rate, in the age-adjusted mortality rate, and in both the crude and the age-adjusted incidence rates, whereas reported survival rates (crude and relative) for cancer patients also increased.

In our view, the best single measure of progress against cancer is change in the age-adjusted mortality rate associated with all cancers combined in the total population. According to this measure, we are losing the war against cancer, notwithstanding progress against several uncommon forms of the disease, improvements in palliation, and extension of the productive years of life. A shift in research emphasis, from research on treatment to research on prevention, seems necessary if substantial progress against cancer is to be forthcoming. (N Engl J Med 1986; 314:1226-32.)

THE primary purpose of this article is to assess the overall progress against cancer during the years 1950 to 1982, the most recent year for which reliable data are available. During this time there was very rapid and extensive growth of private and governmental support of research on cancer, and toward the end of the period there was also substantial emphasis on the effective delivery of research results to physicians, patients, and the public. It is time for an open debate to take stock of past achievements and to consider what levels of funds should be invested in what kinds of future efforts. We offer some observations and interpretations relevant to such a debate.

In 1962, cancer was the recorded cause of death for 278,562 Americans. In 1982, just 20 years later, 433,795 persons died of cancer — a 56 percent increase (Table 1). But the population was growing, and the proportions of persons in older age categories were changing. Crude mortality rates, which adjust for population size, increased by 25 percent (from 151.0 to 188.8 per 100,000) in this 20-year period, and age-adjusted mortality rates, which adjust for changes in age distributions as well as population size, increased by only 8.7 percent (from 170.2 to 185.0 per 100,000).

Mortality data do not tell the whole story. We might ask, not how many Americans die of cancer, but how many contract the disease. From 1973 to 1981 the crude incidence rate for all neoplasms combined rose by 13.0 percent, and the age-adjusted incidence rate by 8.5 percent (Table 1).

Or, we might focus on neither incidence nor mortality, but on the long-term survival of patients who have had a diagnosis of cancer. Unadjusted five-year survival rates for patients with all forms of cancer combined increased by 4.2 percent from 1973 to 1978 (from 38.5 to 40.1 percent), while rates adjusted for "expected" mortality from all other causes of death rose by 5.1 percent (from 46.8 to 49.2 percent).

From the Harvard School of Public Health, Boston, and the University of Iowa Medical Center, Iowa City. Address reprint requests to Dr. Bailar at the Department of Biostatistics, Harvard School of Public Health, Boston, MA 02115.

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Which of these conflicting pictures of change, if any, captures the "truth" about recent advances in the control of cancer? More specifically, what yardstick should we use to measure the overall success of the long and intense effort to control and eventually eliminate these diseases? Interest in this matter is sharpened by the recent announcement that the goal of the National Cancer Institute is a 50 percent reduction in cancer-related mortality (on an age-adjusted basis) by the year 2000.[3] To answer these questions, we first discuss the kinds of data that are available and the methods used to reduce them to simple index figures.[4,5] We then give our views on which measures are most appropriate and what they indicate.

MORTALITY DATA

In the United States, nearly all national cancer-related mortality data are derived from death certificates submitted through local and state channels to the National Center for Health Statistics. The Death Registration Area has included the entire United States since 1933. Major changes since then include five revisions of the standard system for coding causes of death, as well as continual improvement in medical procedures for antemortem diagnosis.[6-8] However, these changes have had less effect on the certification of deaths from cancer than on certification of deaths from other major causes.

Mortality records can be used in many ways, each of which is best suited for specific purposes. Sometimes there is a need for information about changes in mortality that are independent of demographic changes such as shifts in the age distribution of the population or shifts in place of residence (for geographically related cancers). "Adjusted" rates may be used to remove the effects of the variable or variables adjusted, so that other effects can be more easily detected and measured.[4,5]

One common method of adjustment for age is the "direct" method, which is a simple weighted average of observed age-specific rates, with weights determined by some fixed "standard" population, such as the U.S. population of 1980. For this paper all adjustments were made by the direct method with reference

Table 1. Cancer in the United States: Selected Measures of Recent Changes.*

Measure	Year		Total % Change	Average % Change/Yr
	1962	*1982*		
Mortality				
No. of deaths	278,562	433,795	55.7	+7.8
Crude rate†	151.0	188.8	25.1	+1.3
Age-adjusted rate†	170.2	185.1	8.7	+0.4
	1973	*1981*		
Incidence				
Crude rate†	365.2	412.7	13.0	+1.6
Age-adjusted rate†	368.2	399.4	8.5	+1.1
	1973	*1978*		
Five-year survival (%)‡				
Absolute survival rate	38.5	40.1	4.2	+0.8
Relative survival rate§	46.8	49.2	5.1	+1.0

*Sources: McKay et al.,[1] the National Center for Health Statistics,[2] and unpublished data from the SEER Program, National Cancer Institute.

†Rates are per 100,000 population. Age adjustments are to the 1980 U.S. population. Incidence data for 1981 include two areas not in the 1973 data; the base population reflects this change.

‡White population only.

§Relative to survival of the U.S. white population with the same age distribution.

to the U.S. population of 1980. There has been recent discussion about whether, in view of diagnostic errors at older ages, age-adjusted mortality rates should include the entire age span.[9,10] Ours do, because cancer is a common cause of death and because (contrary to the situation with some other causes of death) the available data do not suggest that net errors are so high as to make the figures unreliable for overall evaluation. Furthermore, changes in mortality rates for persons in specific age categories may be useful for understanding causes of cancer, but cannot measure progress against cancer in all age groups.

We believe that to study overall trends in cancer-related mortality (how they have changed in recent years and how they could change by the year 2000), the best single measure of mortality is the age-adjusted death rate associated with all cancers combined, supplemented by age-adjusted rates and sometimes age-specific rates, for specific sex and broad racial categories. These measures remove the effect of changing population size and changing distribution according to age, sex, and race.

Figure 1 shows age-adjusted mortality rates for all forms of cancer from 1950 to 1982 in the entire population and according to sex and race, with age adjusted to the 1980 population. Cancer-related mortality, measured in this way, rose steadily among white males; fell slightly, plateaued, and recently began to rise again among white females; rose rapidly and steadily among nonwhite males; and declined slightly and recently plateaued among nonwhite females. In all race and sex groups combined, there was a moderate increase in age-adjusted mortality. (The small discontinuity in 1957 is a result of a change in methods of classifying a cause of death on death certificates; more recent changes have had only a minor influence on cancer-related mortality rates.[6-8])

Site-Specific Mortality Data

Although mortality from all forms of cancer combined provides the most important information, study of specific sites (Fig. 2) can both illuminate the overall changes and show why the site-specific analyses alone may be misleading. To preserve comparability across sites, Figure 2 shows rates of each cancer (including the sex-specific cancers) relative to the total population. Rates of breast cancer among women only and rates of prostatic cancer among men only are approximately twice the rates given in this graph.

There has been no apparent change in mortality from breast cancer among white or nonwhite women since 1950. Rates among nonwhites (not shown) vary about their mean more than the rates among whites, but this appears to be due to the effect of smaller numbers of deaths and, hence, larger random variability.

The sharp and continuing rise in deaths from lung cancer (Fig. 2), nearly all from cigarette smoking, is now widely recognized as a medical, social, and political scandal. The increase was evident before 1950 among white and nonwhite men, and it has been evident among white and nonwhite women since the late

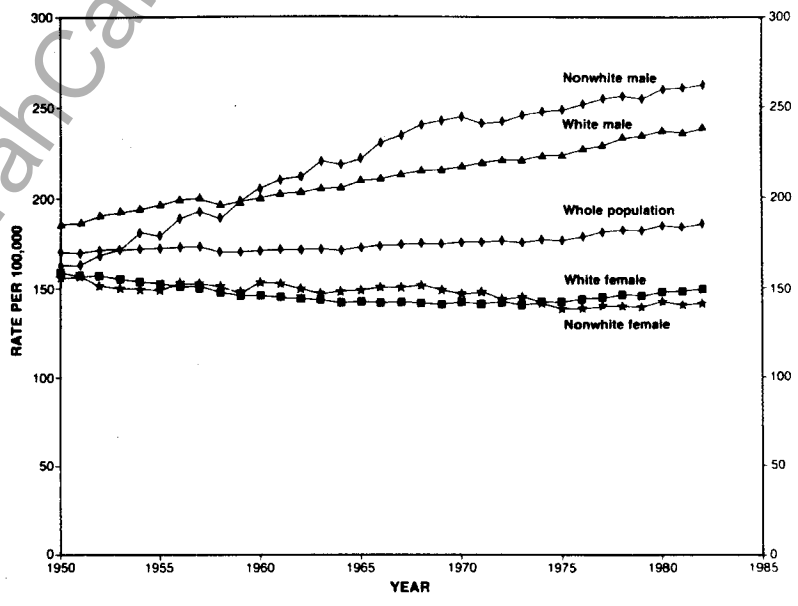

Figure 1. Mortality from All Malignant Neoplasms, 1950 through 1982, in the U.S. White Population and According to Race (White or Nonwhite) and Sex. Age was adjusted to the U.S. population of 1980.

1960s. These changes in death rates from lung cancer have substantially affected mortality rates from all cancers combined (Fig. 1). (Later on we will discuss the effect of excluding lung and other cancers from the trends shown in Figure 2.) Data on nationwide mortality trends with smokers and nonsmokers separated are not available.

Mortality from cancer of the prostate (Fig. 2) has not changed appreciably in the entire male population, despite continual increases among nonwhite men since 1950.

Mortality from stomach cancer (Fig. 2) has steadily declined in all four race and sex groups. This decline reflects changes in incidence rather than better methods of treatment, earlier diagnosis, or changes in definition.[6-8] Mortality from cervical cancer (not shown) has also declined dramatically as a result of widespread screening programs, improved standards of living, and a high rate of hysterectomy.[11]

Mortality from colorectal cancer (Fig. 2) has been declining slowly and steadily for reasons not fully understood but probably including better diagnostic procedures and improvements in treatment.

These data, taken alone, provide no evidence that some 35 years of intense and growing efforts to improve the treatment of cancer have had much overall effect on the most fundamental measure of clinical outcome — death. Indeed, with respect to cancer as a whole we have slowly lost ground, as shown by the rise in age-adjusted mortality rates in the entire population (Fig. 1). This is not to say that without these efforts at treatment the trends would have been the same, but overall, the effort to control cancer has failed — so far — to attain its objectives.

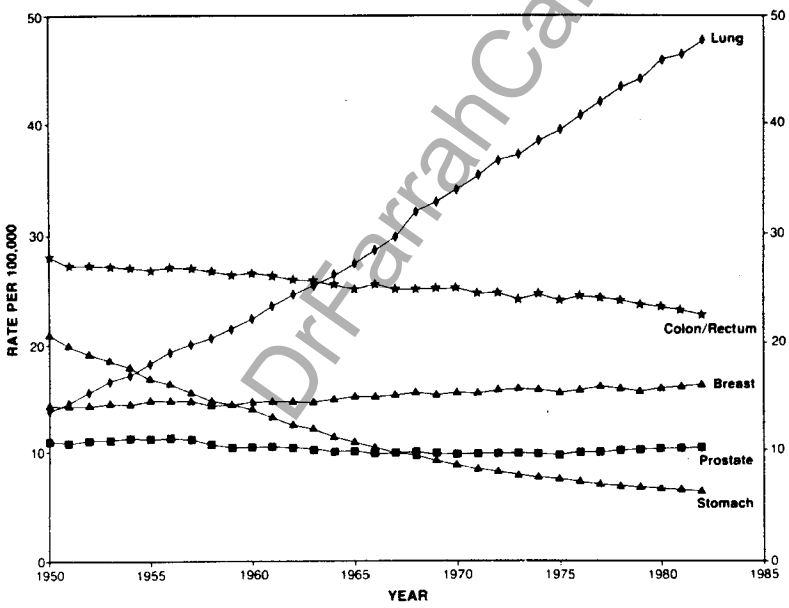

Figure 2. Mortality from Cancer of Selected Sites, 1950 through 1982, in the Total U.S. Population.
Age was adjusted to the U.S. population of 1980.

This generally dismal picture obscures some striking successes, however. For example, age-adjusted mortality from all cancers combined has dropped notably in patients under the age of 30, though such deaths account for only about 1 to 2 percent of total mortality from cancer.[12,13] In older persons, mortality from small-cell lung cancer and from non-seminoma testicular cancer has also decreased (data not shown).

Incidence Data

The possible measures for the incidence of cancer are similar to those for mortality from the disease — counts, crude rates, and several kinds of adjusted rates, each of which may be limited to particular demographic segments or particular forms of cancer.[4,5] The incidence statistic that we chose for a measure of overall progress against cancer is the direct age-adjusted rate for all cancers combined (U.S. 1980 standard), but supplemented by rates for certain narrower segments that illuminate specific problems.

Table 1 shows cancer incidence data from the SEER (Surveillance, Epidemiology, and End Results) Program, which was developed under the auspices of the National Cancer Institute. One can compare these statistics with the mortality data in Table 1, but keeping in mind that most superficial skin cancers are excluded, that the SEER data are for a nonrandom sample of about 10 percent of the U.S. population from 10 diverse geographic areas (4 states, 5 metropolitan areas, and Puerto Rico), that the series begins only in 1973 for 8 of 10 areas (the others were added in 1974 and 1975), and that the incidence data are subject to substantial shifts in diagnosis and reporting during that time.[14] Data on cancer incidence are limited to the white population because the number of nonwhites in the SEER population was too small to provide reliable estimates of risks and because the distribution of nonwhites across specific racial categories was substantially different from that in the United States as a whole.

Cancer incidence rates are shown in Figure 3. Overall trends are upward among both white males and white females, suggesting a failure to prevent or control new or current causes of cancer.

Site-Specific Incidence Data

The reported incidence rates for breast cancer show a distinct one-year peak in 1974 and a slower rise in more recent years (Fig. 4). The reported incidence of cancer of the prostate (Fig. 4) has increased slightly among white men and more sharply among nonwhite men (data not shown). Incidence rates for lung cancer have been ris-

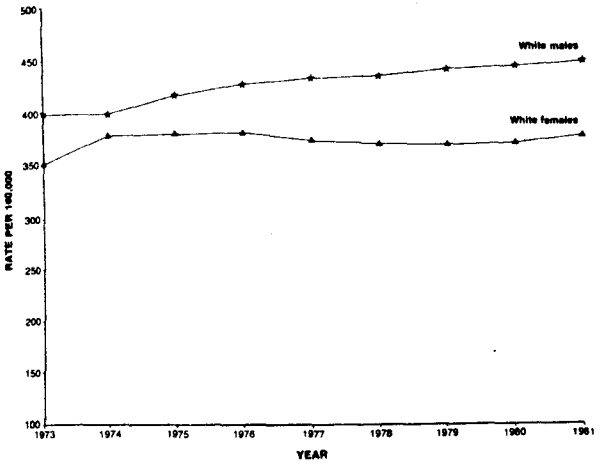

Figure 3. Incidence of All Cancers, 1973 through 1981, According to Sex, in the White Population of the SEER Registry Area.
Age was adjusted to the U.S. population of 1980.

ing rapidly in white men and white women, largely in response to changes in tobacco smoking in recent decades.

Again, we see no reason for optimism about overall progress during recent years. There is no reason to think that, on the whole, cancer is becoming any less common.

Survival Data

There are many divergent measures of case survival, just as there are for mortality and incidence. One can count a group of patients with cancer, then count the number who are alive at some specific time after diagnosis (e.g., 2, 5, or 10 years) and calculate the percentage surviving at that time. However, that mixes the lethal effects of cancer with deaths from unrelated causes. One might instead compute the percentage who are alive and appear to be free of cancer at five years, or exclude those who have died of causes other than cancer during the period, or try to calculate the lifetime probability that someone with cancer will eventually die of it. A common device is to avoid difficult judgments about the presence of recurrent cancer or the cause of death and, instead, adjust for "expected" survival estimated from rates in the general population with the same age and sex distribution. The ratio of observed survival (cancer patients) to expected survival (general population), called the relative survival rate, is a commonly reported measure of case survival.[15]

Any of these survival measures can be applied to cancer overall, to specific forms of cancer, or to specific demographic groups of patients. Again we have many measures, with none of them clearly best. The difficulty in interpreting survival rates after cancer is illustrated by recent congressional testimony stating that the United States is on the verge of attaining a five-year survival rate of 50 percent. News stories did not always make it clear that the computation of such a high rate required exclusion of the nonwhite population and the use of relative rather than absolute survival rates.[16]

Problems in Interpreting Recent Incidence and Survival Data

Changing standards of diagnosis and medical care of patients with cancer may affect incidence and survival rates substantially more than they affect mortality rates. At one time, a cancer was a cancer, and it could be assumed that a truly malignant neoplasm would eventually appear in hospital records (for treatment) or in death records (if treatment was unsuccessful or not attempted). The major exception, most forms of superficial skin cancer, could be excluded from the registry system by definition (the biologic behavior of superficial skin cancer is unlike that of other neoplasms because metastatic spread, the main reason for death from cancer, is uncommon). Other neoplasms lacking metastatic behavior used to be considered infrequent and were not regarded as a source of serious bias in the interpretation of trends. That assumption can no longer be made. The implications are substantial.

The 1974 peak in the incidence of breast cancer (Fig. 4) corresponded to the occurrence of public disclosures that the wives of the U.S. President and Vice President had breast cancer and a major public effort to promote screening for the disease by mammography. Although the 1974 peak was well beyond the limits of random variation, there has been no apparent corresponding change in mortality from breast cancer (Fig. 2) or in case survival rates (Table 2). We believe that the 1974 peak in incidence is spurious and reflects the inclusion of a proportion of benign and borderline lesions that in other years would not have been detected and reported. That such shifts in diagnostic criteria do occur, and specifically for breast cancer, is well documented.[7,17,18] After the 1974 peak the

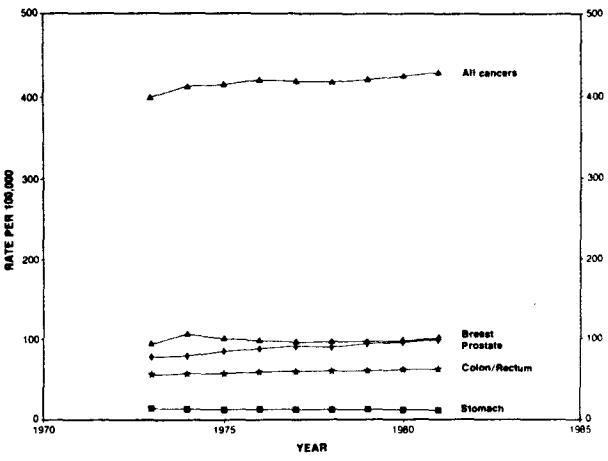

Figure 4. Incidence of All Cancers and Cancers of Selected Sites, 1973 through 1981, in the White Population of the SEER Registry Area.
Age was adjusted to the U.S. population of 1980.

rates plateaued at a lower level, then started to rise slowly but steadily among both white and nonwhite women. A recent resurgence of screening programs may account for some of this latest increase, but present data do not permit a definitive conclusion about whether it is artifactual or represents a true increase in incidence.

Cancer of the prostate is a common incidental finding when unselected tissue specimens of old men are examined, whether at autopsy (after death from another cause) or biopsy (at surgery for a benign condition). Reports of prevalence rates in the 25 percent range are not rare.[7] It is less widely recognized that such lesions, especially those found incidentally at prostate surgery, are commonly reported as cancer in the incidence statistics. There appear to be no data on what proportion of these prevalent prostatic "cancers" had shown evidence of malignant behavior. Incidence rates for this disease do not exceed 1.2 percent per year even in the oldest age groups, including some proportion of patients with incidental diagnoses; the incidence of clinically apparent prostatic cancer must be lower, and mortality rates are lower still. We must conclude that the prevalence rates are seriously inaccurate and that most of the tumors found, which do have the microscopical appearance of malignancy, do not have the behavior we associate with the word "cancer." Such an interpretation, combined with an increasing frequency of incidental tissue diagnosis, would be consistent with the rapid changes in survival after prostatic cancer shown in Table 2.

Lung cancer has increased rapidly in all major population segments. As a result, several kinds of screening programs have been developed and tested. Findings tend to be that in comparison to a randomized control group, the screened group has more cancers detected, the cancers are in earlier stages, more are considered suitable for curative treatment, and case survival rates are substantially higher. However, overall mortality is little affected.[19-21] This again seems to be a result of detecting and reporting lesions that have the microscopical appearance of cancer but not its biologic behavior. As a result of adding these benign conditions, the pool of real "cancers" is diluted, and we find high detection rates, early stage, resectability, and improved case survival, but with little or no change in outcome as measured by deaths.

Thus, the incidence and case survival data for three major forms of cancer may not mean what they at first suggest. Because of these uncertainties about the current meaning of "cancer" of the breast, prostate, and lung, neither incidence rates nor case survival rates for these diseases can be taken as reliable indicators of change in the overall progress against cancer. One must wonder whether similar problems affect the data on other forms of cancer. Mortality data do, in contrast, measure biologic behavior rather directly. That is mainly why we believe that mortality rates, age-adjusted to a current standard, are the best single measure of overall progress. Specifically, we disagree with the decision of the National Cancer Institute to emphasize survival (and the short-range goal of a five-year overall relative case survival rate of 50 percent), because it is subject to substantial bias from changing standards of diagnosis and reporting. A reported survival rate of 50 percent, if many of the patients do not have the biologic disease in question, would only mislead and confuse the public, the news media, governmental representatives, and health professionals who are not sophisticated in biostatistical and epidemiologic analysis.

Enstrom and Austin[22] have also discussed the problems of interpreting cancer survival rates. Although this matter needs further study, the uncertainties are great enough to make case survival an inappropriate measure of progress.

Colleagues have argued that the overall picture of cancer mortality is dominated by rising rates of death from lung cancer and that this disease should therefore be omitted from any summary measure of progress against cancer. Reasons for such an omission have not been clearly stated, although it conveniently reverses the overall rise in mortality from cancer. Lung cancer is in fact the best illustration of our primary conclusion that despite great effort over many years, research on cancer treatment has failed to deal effectively with

Table 2. Absolute and Relative Survival Rates.*

Five-Year Survival	Year of Diagnosis					
	1973	1974	1975	1976	1977	1978
	percent					
Absolute rate†						
All neoplasms	38.5	40.6	41.0	41.2	40.8	40.1
Colorectal cancer	36.2	37.8	38.2	39.6	39.4	38.7
Lung cancer	9.0	9.8	9.7	10.3	10.6	11.0
Breast cancer	64.3	65.2	67.0	66.0	66.0	65.0
Prostate cancer	41.2	43.9	45.9	47.7	47.8	47.4
Hodgkin's disease	57.7	63.3	66.6	71.9	69.5	67.3
Non-Hodgkin's disease	34.3	37.9	40.0	41.0	39.0	39.0
Relative rate†						
All neoplasms	46.8	49.3	50.0	50.3	50.0	49.1
Colorectal cancer	46.4	48.8	49.4	51.1	51.3	50.3
Lung cancer	11.0	11.9	11.8	12.5	13.0	13.4
Breast cancer	72.3	73.6	75.8	74.7	75.1	74.1
Prostate cancer	60.7	65.0	67.6	70.2	69.9	69.4
Hodgkin's disease	61.5	67.6	71.0	76.5	74.3	72.0
Non-Hodgkin's disease	40.9	45.1	47.3	48.6	46.8	47.1

*Source: Unpublished data from the SEER Program, National Cancer Institute.

†Rates are for white males and white females only, relative to survival of the U.S. white population with the same age distribution.

the cancer problem. We have nevertheless calculated age-adjusted mortality rates excluding lung cancer; with this exclusion the change in overall age-adjusted mortality from cancer since 1950 shifts from an 8 percent increase to a 13 percent decrease. If one also excludes cancer of the stomach and cervix, whose rates have also been changing for reasons largely unrelated to treatment (Fig. 5), age-adjusted mortality shifts from 130.1 in 1950 to 128.9 in 1980 — a change of less than 1 percent. It is difficult to claim success in the war against cancer on the basis of these figures.

In Figure 5 the time scale is extended to the year 2000. We have marked on the figure the National Cancer Institute goal of a 50 percent reduction in mortality by that year. It is clear that the goal will not be attained unless the present upward trend is reversed very soon and there is a precipitous and unprecedented decline. We do not believe that hopes for such a change are realistic.

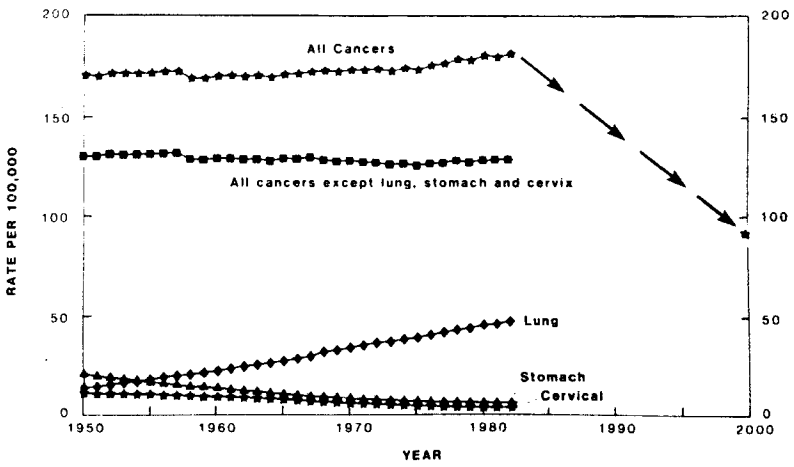

Figure 5. Mortality from Cancer of All Sites and Selected Sites, 1950 through 1982, in the U.S. Population.

Age was adjusted to the U.S. population of 1980. Extension to the year 2000 is shown to reflect the stated goal of the National Cancer Institute.

Conclusions

Some measures of efforts to control cancer appear to show substantial progress, some show substantial losses, and some show little change. By making deliberate choices among these measures, one can convey any impression from overwhelming success against cancer to disaster.

Our choice for the single best measure of progress against cancer is the mortality rate for all forms of cancer combined, age-adjusted to the U.S. 1980 standard. This measure removes the effects of changes in the size and age composition of the population, prevents the selective reporting of data to support particular views, minimizes the effects of changes in diagnostic criteria related to recent advances in screening and detection, and directly measures the outcome of greatest concern — death. The National Cancer Institute has also adopted this standard for its prospective goal of halving cancer mortality by the year 2000, but continues to use relative case survival rates to assess progress in years past.[3,16]

Age-adjusted mortality rates have shown a slow and steady increase over several decades, and there is no evidence of a recent downward trend. In this clinical sense we are losing the war against cancer. Substantial increases in our understanding of the nature and properties of cancer have not led to a corresponding reduction in incidence or mortality. On the basis of the age-adjusted trends that we have presented, it is unlikely that the National Cancer Institute will attain its stated goal of reducing age-adjusted mortality from cancer by 50 percent by the year 2000 — just 14 years from now.

These comments about lack of progress are in no way an argument against the earliest possible diagnosis and the best possible treatment of cancer. The problem is the lack of any substantial recent improvement in treating the most common forms.

Cairns[23] has also discussed the results of the effort to develop cures for cancer. His approach is largely clinical and biologic; ours is largely epidemiologic and statistical, yet we come to similar conclusions about the poor rate of success to date and the need to reconsider present directions in both research and applications. His paper should be read in conjunction with ours for a more comprehensive view of the matter.

The main conclusion we draw is that some 35 years of intense effort focused largely on improving treatment must be judged a qualified failure. Results have not been what they were intended and expected to be. We think that there could be much current value in a comprehensive, consolidated, objective review of the technical reasons for this failure. What forces led to overlapping waves of interest and program emphasis, such as chemotherapy screening, virology, immunology, and perhaps now molecular biology, that have appeared to hold more promise than they have fulfilled? Why were hopes so high, what went wrong, and can future efforts be built on more realistic expectations? Why is cancer the only major cause of death for which age-adjusted mortality rates are still increasing?[24]

A full analysis of current program plans and directions would require substantial expertise, time, and support. On the basis of past medical experience with infectious and other nonmalignant diseases, however, we suspect that the most promising areas are in cancer prevention rather than treatment. Although no one can be certain about the benefits of preventive efforts, history suggests that savings in both lives and dollars could be great. For example, opinions that attempts to prevent smoking have been discouraging are wrong. In scarcely 20 years of half-hearted effort, this country

has reversed historic trends in smoking and altered its casual tolerance of smokers. Societal antismoking norms have changed, and those who use tobacco are now on the defensive. Research opportunities in other areas of cancer prevention may well merit sharp increases in support, even if this requires that current treatment-related research must be substantially curtailed. Certainly, the background of past disappointments must be dealt with in an objective, straightforward, and comprehensive manner before we go much further in pursuit of the cure that always seems just out of reach.[24]

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