Special Article

CANCER UNDEFEATED

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ABSTRACT

Background Despite decades of basic and clinical research and trials of promising new therapies, cancer remains a major cause of morbidity and mortality. We assessed overall progress against cancer in the United States from 1970 through 1994 by analyzing changes in age-adjusted mortality rates.

Methods We obtained from the National Center for Health Statistics data on all deaths from cancer and from cancer at specific sites, as well as on deaths due to cancer according to age, race, and sex, for the years 1970 through 1994. We computed age-specific mortality rates and adjusted them to the age distribution of the U.S. population in 1990.

Results Age-adjusted mortality due to cancer in 1994 (200.9 per 100,000 population) was 6.0 percent higher than the rate in 1970 (189.6 per 100,000). After decades of steady increases, the age-adjusted mortality due to all malignant neoplasms plateaued, then decreased by 1.0 percent from 1991 to 1994. The decline in mortality due to cancer was greatest among black males and among persons under 55 years of age. Mortality among white males 55 or older has also declined recently. These trends reflect a combination of changes in death rates from specific types of cancer, with important declines due to reduced cigarette smoking and improved screening and a mixture of increases and decreases in the incidence of types of cancer not closely related to tobacco use.

Conclusions The war against cancer is far from over. Observed changes in mortality due to cancer primarily reflect changing incidence or early detection. The effect of new treatments for cancer on mortality has been largely disappointing. The most promising approach to the control of cancer is a national commitment to prevention, with a concomitant rebalancing of the focus and funding of research. (N Engl J Med 1997;336:1569-74.)

IN 1986, when one of us reported on trends in the incidence of cancer in the United States from 1950 through 1982,[1] it was clear that some 40 years of cancer research, centered primarily on treatment, had failed to reverse a long, slow increase in mortality. Here we update that analysis through 1994. Our evaluation begins with 1970, both to provide some overlap with the previous article and because passage of the National Cancer Act of 1971 marked a critical increase in the magnitude and vigor of the nation's efforts in cancer research.[2]

The 1986 report and follow-up articles[1,3-5] were criticized,[6-8] primarily on the grounds that research already completed had not yet been incorporated into practice and that new research findings were on the way. Critics also argued that data for all cancers combined are not meaningful and that the study of age-adjusted mortality rates is not appropriate when the rates in different age groups exhibit different trends, as they do for cancer.

The Senate asked the National Cancer Institute to convene a committee to consider how to measure progress against cancer, and it published its report in 1990.[9] The committee recommended that progress be assessed in three general areas: direct measures (mortality, incidence, and survival, including the quality of life), portents of change (such as reductions in tobacco use), and advances in knowledge that may have an effect in the future.[9] Direct measures were taken to be central to the assessment of progress.

The most basic measure of progress against cancer is age-adjusted mortality. The use of rates removes the effect of changes in the overall size of the population. Adjustment for age further removes the effect of changes in the age distribution of the population, and with it the effect of changing mortality from causes other than cancer. The use of mortality as the chief measure of progress against cancer, rather than incidence or survival, focuses attention on the outcome that is most reliably reported and is of greatest concern to the public: death. The use of rates for all types of cancer combined, though difficult to interpret in biologic terms, usefully supplements site-specific rates because it prevents selective reporting of data to support particular views and minimizes the effects of changes in the diagnosis and reporting of specific types of cancer.

Briefly summarized, the reason for not focusing on the reported incidence of cancer is that the scope and precision of diagnostic information, practices in screening and early detection, and criteria for re-

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porting cancer have changed so much over time that trends in incidence are not reliable.[1] For example, the development and vigorous commercial promotion of the test for prostate-specific antigen occurred at the same time as a doubling of the reported incidence of cancer of the prostate between 1974 and 1990 (from 65.6 per 100,000 population to 131.8 per 100,000),[10] without visibly affecting mortality. Few knowledgeable observers believe that either the true frequency or the lethality of the disease has changed much. A similar but smaller trend has affected rates of breast cancer, and there are reasons for concern about the incidence of other cancers.[1]

Trends in survival rates are also suspect, because they are based on the same series of patients as incidence rates, and any inflation of incidence due to the inclusion of less malignant or nonmalignant diseases creates a spurious increase in case survival rates.

METHODS

Sources of Data

Numbers of deaths according to year, age, race, sex, and cancer site were obtained from the National Center for Health Statistics.[11] Population data came from the Bureau of the Census and the National Center for Health Statistics[12,13] (and Rosenberg H, Mortality Statistics Branch: personal communication). Other data were obtained from the National Cancer Institute.[10]

Age-specific mortality rates, the building blocks of age-adjusted rates, are simple ratios of numbers of deaths to the size of the population. The numerators are the numbers of deaths from a specific cancer or group of cancers among people in specific age ranges and, often, with specific demographic characteristics. The denominator is the corresponding U.S. population, as estimated by the Bureau of the Census. Data adjusted for age by the "direct" method (which we use throughout) are weighted sums of these age-specific rates, with the weights determined by reference to some fixed population, such as the total U.S. population in the 1990 census.[14] For example, age adjustment of rates for each of the years from 1984 through 1994 to the 1990 standard entails the estimation of mortality as if the actual population in each of those years had the same age distribution as the 1990 U.S. population.

If we want to examine recent changes in overall mortality due to cancer, the most appropriate reference population for adjustment is one that falls within, or very close to, the period of study. Because we are focusing largely on events in recent years, we have used the U.S. population as reflected in the 1990 census.

When trends in different age groups diverge, the choice of a reference population can make a substantial difference in estimated trends. For example, the population of the United States was much younger in 1940 than in 1990, and hence the use of the 1940 population as the reference group gives greater weight to mortality rates among younger persons, which have been declining, whereas rates in older persons have been increasing. Therefore, the 1940 standard gives an unduly favorable picture of recent trends in mortality due to cancer; rates adjusted to the 1970 standard lie between those adjusted to 1940 and those adjusted to 1990. Data presented at a recent press conference by the Department of Health and Human Services and the American Cancer Society, and in a related publication, reported rates that were adjusted to the 1970 and 1940 populations.[15,16]

RESULTS

Table 1 shows age-adjusted death rates for all malignant neoplasms, year by year, since 1986. For the U.S. population as a whole, the long-sustained annual increase in mortality due to cancer ceased in about 1991. Between 1991, when the highest rate was reported, and 1994, the most recent year for which data are available, mortality decreased by 1.0 percent (from 203.0 to 200.9 per 100,000 population). This drop may well portend larger improvements to come. Even if rates turn upward again, the decline will surely resume within the next few years as a result of reductions in smoking over recent decades.

For historical perspective, U.S. cancer mortality rates, age adjusted to 1970 by the National Cancer Institute, increased by an estimated 0.3 percent annually from 1975 through 1993, as compared with an increase of 0.1 percent per year from 1950 through 1975.[10] This accelerated increase in mortality due to cancer occurred despite the enlarged scope of cancer research since 1971.

Figure 1 presents trends in mortality from all malignant neoplasms since 1970, according to race and sex. After decades of rather steady increases in each demographic group, mortality rates plateaued or declined slightly in the 1990s, most notably in the black male population, among whom the recent downward trend follows years of rapidly increasing mortality.

Figure 2 shows trends since 1970 for males and females in two broad age groups. The population under 55 years of age is much larger than the older population, whereas rates of mortality due to cancer are much higher among older people than in the younger age group. As a result, the smaller percentage increase in mortality observed in the smaller, older group represents more deaths than the larger percentage decrease in the younger group. The interplay of these factors determines the population-wide rate, which has changed much more slowly than rates within these two broad age groups.

Among older persons, both men and women, mortality due to cancer increased by 15 to 20 percent between 1970 and 1994, with a recent decline among older men. During the same period, mortality due to cancer among people younger than 55 decreased by about 25 percent for both sexes. The close parallels between the rates for males and females in each age category seem coincidental, since the rates for the two sexes reflect distinct patterns of cancer sites.

We turn now to some specific forms of cancer. Mortality due to breast cancer has increased by approximately 10 percent since 1970 among women 55 years of age or older, with a recent plateau, but has decreased by almost 25 percent among younger women (Fig. 3). The recent and substantial increase in the use of mammography among women over 50, for whom annual examination is known to be effective, has not prevented this increase. These data suggest that a true increase in incidence may have been

TABLE 1. RECENT TRENDS IN MORTALITY DUE TO CANCER IN THE UNITED STATES.*

YEAR	TOTAL	MALES	FEMALES
		deaths/100,000	
1986	199.0	256.4	161.3
1987	199.2	256.7	161.3
1988	199.8	256.8	162.3
1989	201.6	258.4	164.1
1990	202.4	259.6	164.6
1991	203.0	259.3	165.7
1992	201.8	256.7	165.3
1993	202.1	256.5	165.7
1994	200.9	253.2	165.7

*The rates shown are numbers of deaths from all malignant neoplasms per 100,000 population. Rates have been adjusted for age, with standardization to the age distribution of the U.S. resident population in 1990.

only partially offset by the effectiveness of screening. Although mammography before the age of 50 is controversial, these data suggest that declines in mortality were well established before mammography became widely used. Overall, the decrease among younger women and the increase among older women have left population-wide mortality almost unchanged.

For lung cancer, death rates for women 55 or older have increased to almost four times the 1970 rate, whereas rates among males younger than 55 have decreased slightly (Fig. 4). Rates for older men and younger women have risen since 1970, but with some recent downturn. These trends reflect delayed effects of changes in smoking habits that occurred decades ago.

Figure 5 shows trends in mortality for additional types of cancer from 1970 through 1993. Age-adjusted rates for several important types of cancer declined steadily. The decrease in cancer of the stomach, observed worldwide over many decades, is not well understood, but it is largely or entirely a result of decreasing incidence rather than earlier detection or improved therapy. The sharp decline for cancer of the cervix is also not fully explained but reflects a combination of reduced incidence and improvements in the detection of premalignant lesions by means of the Papanicolaou smear and their subsequent removal; earlier detection of invasive cervical neoplasms may also be important. Deaths from cancer of the uterus (including uterine neoplasms not specified as of the cervix) are primarily due to endometrial cancers, but they include a small proportion of deaths from cervical cancer reported as nonspecific cancer of the uterus and a few malignant myometrial neoplasms. Here, too, there has been a sustained de-

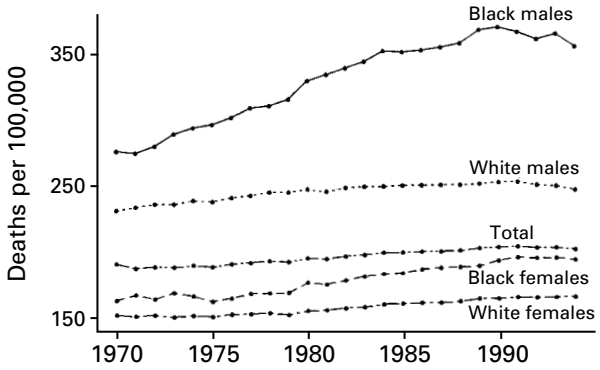

Figure 1. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population and According to Race and Sex.

The rates have been age-adjusted to the U.S. resident population of 1990.

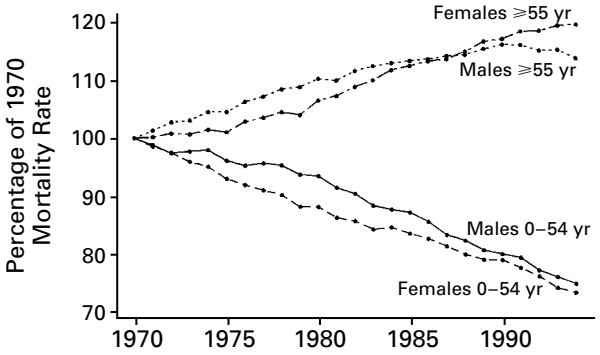

Figure 2. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

The rates have been age-adjusted to the U.S. resident population of 1990.

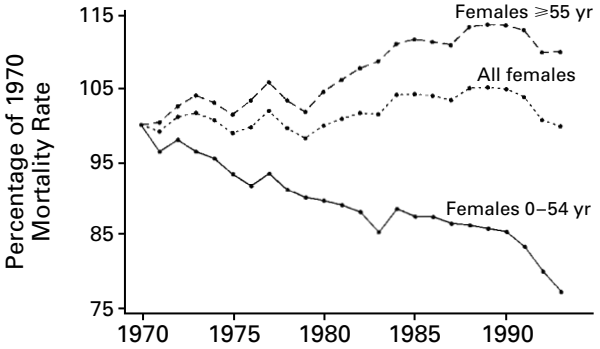

Figure 3. Mortality from Breast Cancer, 1970 through 1993, in the Total U.S. Female Population as a Percentage of the Rate in 1970, According to Age.

The rates have been age-adjusted to the U.S. female resident population of 1990.

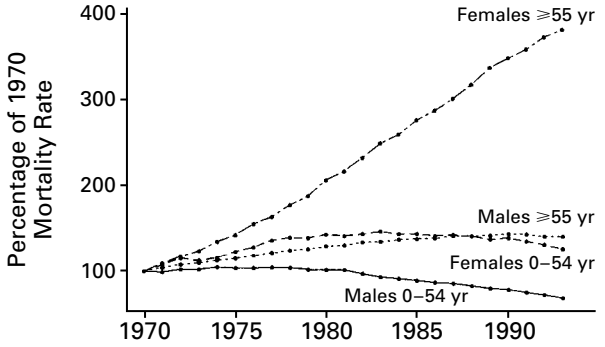

Figure 4. Mortality from Cancer of the Trachea, Bronchus, or Lung, 1970 through 1993, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

The rates have been age-adjusted to the U.S. resident population of 1990.

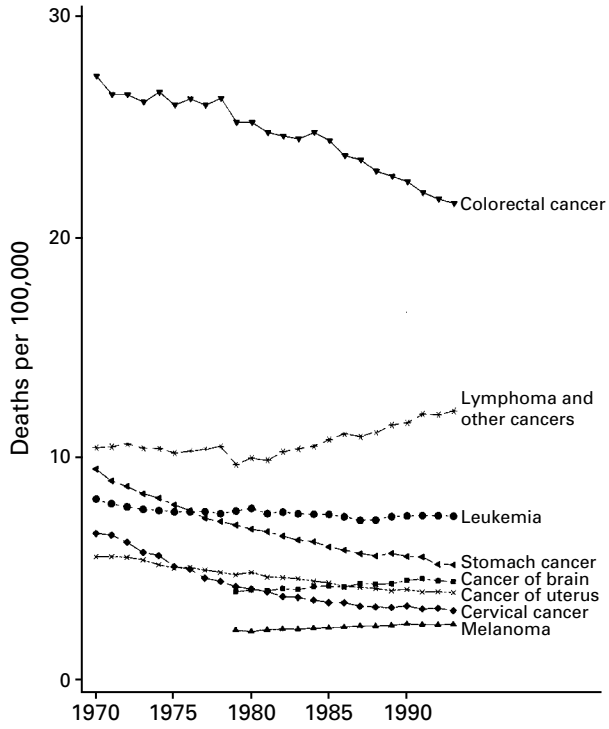

Figure 5. Mortality from Cancer at Selected Sites, 1970 through 1993, in the Total U.S. Population.

The rates have been age-adjusted to the U.S. resident population of 1990.

cline, though not as great as for cervical cancer, and at least a part of this improvement is due to earlier detection.

Mortality from leukemia (all types and in all age groups) has also decreased. Deaths from colorectal cancer (including anal cancer) decreased substantially for reasons that are not entirely clear, but they may include earlier detection as well as a reduction in incidence.[10] Improved treatment has contributed little.

Small increases have been reported for malignant brain tumors and malignant melanoma, shown here since 1979, when the National Center for Health Statistics introduced a new format for reporting mortality data.[11] Mortality from lymphomas and other lymphoid neoplasms (including Hodgkin's disease, non-Hodgkin's lymphoma, and multiple myeloma) increased by 17.3 percent from 1970 to 1993, despite reductions in mortality from Hodgkin's disease alone.[10]

Trends in mortality due to cancer among children require special comment. Death rates for each major category of childhood cancer have declined by about 50 percent since the 1970s (data not shown). The decline is continuing, and the percentage drop in the most recent 10-year period is slightly greater than that for the previous 10 years. To put this finding in perspective, however, cancer accounted for only 1699 deaths among children under 15 years of age in the United States in 1993, among a total of 529,904 deaths due to cancer in all age groups.[11] Even the complete elimination of deaths due to childhood cancer would have little effect on the national death toll.

DISCUSSION

It is worth reviewing probable reasons for these changes in mortality due to cancer. Some declines are clearly a result of reduced incidence or earlier detection (cancer of the cervix, other cancers of the uterus, and cancers of the colon, rectum, and stomach). Similarly, recent changes in mortality from lung cancer are certainly due to changes in smoking patterns over the past few decades. The smaller increases in mortality from melanoma and cancer of the brain, the prostate, and perhaps the breast (in older women) can hardly be due to a decline in the effectiveness of treatment; they must reflect rising incidence. Thus, the observed trends largely reflect changing incidence or earlier detection, rather than improved therapy.

Despite numerous past claims that success was just around the corner, mortality due to cancer continued to increase, until quite recently. The death rate in 1994 was 2.7 percent higher than in 1982, the last year covered in the 1986 paper,[1] but it is likely that the recent downturn will be confirmed and substantially extended as a result of improved prevention

and earlier detection and, especially, past reductions in tobacco use.

In 1986, we concluded that "some 35 years of intense effort focused largely on improving treatment must be judged a qualified failure."[1] Now, with 12 more years of data and experience, we see little reason to change that conclusion, though this assessment must be tempered by the recognition of some areas of important progress. These include the much-improved outlook for children and young adults with cancer, which is entirely the result of improved treatment; better treatment for Hodgkin's disease; far better palliation of many kinds of advanced cancer; a better understanding of cancer, which as a by-product has improved the medical management of nonmalignant immunologic, metabolic, and viral diseases, including the acquired immunodeficiency syndrome; and great improvements in imaging technology. Though these benefits must not be discounted, their effects on overall mortality due to cancer have been largely disappointing.

The argument that rising incidence has just balanced rising case survival rates, so that mortality is roughly constant, seems unlikely to be true but is irrelevant anyway. However one analyzes and interprets the present data, the salient fact remains that age-adjusted rates of death due to cancer are now barely declining. Hopes for a substantial reduction in mortality by the year 2000 were clearly misplaced.[17] The effect of primary prevention (e.g., reductions in the prevalence of smoking) and secondary prevention (e.g., the Papanicolaou smear) on mortality due to cancer indicates a pressing need for reevaluation of the dominant research strategies of the past 40 years, particularly the emphasis on improving treatments, and a redirection of effort toward prevention.

Unfortunately, the means to prevent most cancers have not yet been elucidated, adequately tested, and shown to be effective and feasible. For example, we need to know more about how to help the smoker who wants to quit, and much of the evidence that diet is related to one third or more of cancers[18] must be reduced to findings about specific dietary components. The needed research on prevention may demand as much in time, effort, and resources as has already been invested in studies of treatment. We emphatically do not propose that research on treatment be stopped; there should, however, be a substantial realignment of the balance between treatment and prevention, and in an age of limited resources this may well mean curtailing efforts focused on therapy.

Prevention is much broader than the elimination of carcinogens. For example, recent progress in understanding the roles of dietary modification, chemoprophylaxis (e.g., with retinoic acid and tamoxifen), and genetic predispositions to cancer (in order to reduce exposure to carcinogens and to increase surveillance with the goal of earlier detection) holds intriguing promise for substantial reductions in mortality due to cancer, although much critical research remains to be done. Also part of "prevention" research is the investigation of risk factors for cancer in order to determine which factors can be modified and investigations in the behavioral sciences aimed at improving the application of findings relevant to prevention. The role of basic research is unclear, partly because what is called "basic" is highly subjective and can be rapidly redefined in response to threatened budget cuts. However, we support the expansion of basic-science research that is not so basic as to have no clear, direct, and specific link to prevention.

Will we at some future time do better in the war against cancer? The present optimism about new therapeutic approaches rooted in molecular medicine may turn out to be justified, but the arguments are similar in tone and rhetoric to those of decades past about chemotherapy, tumor virology, immunology, and other approaches. In our view, prudence requires a skeptical view of the tacit assumption that marvelous new treatments for cancer are just waiting to be discovered.

We, like others, earnestly hope that such discoveries can and will be made, but it is now evident that the worldwide cancer research effort should undergo a substantial shift toward efforts to improve prevention. Will this shift mean that prevention research will ultimately succeed in the way that treatment research was expected to succeed? There is no guarantee that it will. The ultimate results may be as disappointing as those to date from treatment efforts, but it is time to find out.

There are also questions of implementation. Prevention is likely to be more difficult and costly than treatment, which can be rather narrowly focused on persons in need during a limited time and can be provided without major changes in the ambient environment, workplace, diet, or consumer products. Treatment, if it could be made to work, would obviously be much simpler.

The public seems to understand the need for the shift in attitude and emphasis toward prevention. The evidence includes the large and continuing reduction in smoking, widespread individual efforts to change diet to prevent cancer, and the use of sunscreens to reduce exposure to sunlight. The government has had little role in these changes. However, to leave this matter entirely to the public is to risk faddism, on the one hand, and a turning away from orthodox therapy, on the other.

Aside from overstatement of the decline in mortality due to cancer in the United States in recent years, the recent joint press conference[15] held by the Department of Health and Human Services and the American Cancer Society was notable for its public

recognition of the importance of prevention in the effort to control cancer. According to Secretary of Health and Human Services Donna Shalala,

> We must continue to work for the day when our children must turn to the history books to learn about a disease called cancer. . . . It will take better research, better treatments, better detection, and most important, it will take better education. . . . From tobacco to poor diet to lack of reproductive screenings, we must give the American people the information they need to prevent cancer and make the best choices with their lives.[15]

We hope that this statement, as well as the recent increase in support of prevention activities in the National Cancer Institute budget,[19] represents an early step in the commitment to prevention, rather than lip service obscuring blind faith in treatment-based approaches.

The best of modern medicine has much to offer to virtually every patient with cancer, for palliation if not always for cure, and every patient should have access to the earliest possible diagnosis and the best possible treatment. The problem is the lack of substantial improvement over what treatment could already accomplish some decades ago. A national commitment to the prevention of cancer, largely replacing reliance on hopes for universal cures, is now the way to go.

Presented in part as the Ramazzini Lecture, given by Dr. Bailar on October 26, 1996, in Carpi, Italy, as part of the annual Ramazzini Days of the Collegium Ramazzini.

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