Special Article

CANCER UNDEFEATED

JOHN C. BAILAR III, M.D., PH.D., AND HEATHER L. GORNIK, M.H.S.

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-

From the Department of Health Studies, University of Chicago, 5841 S. Maryland Ave., MC 2007, Chicago, IL 60637-1470, where reprint requests should be addressed to Dr. Bailar.

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-

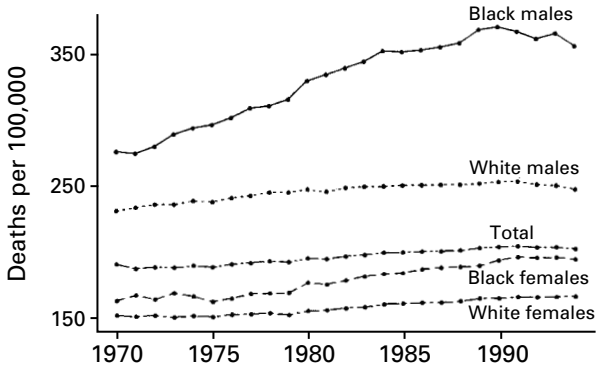

Figure 1. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population and According to Race and Sex.

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

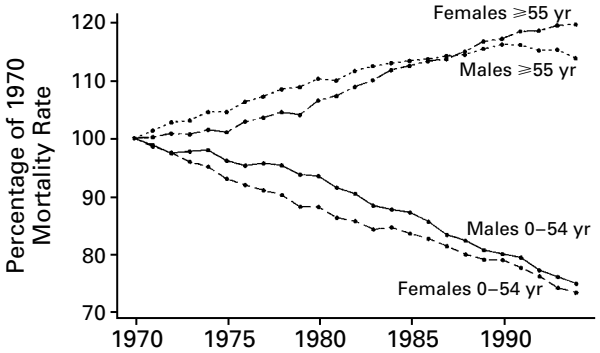

Figure 2. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

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

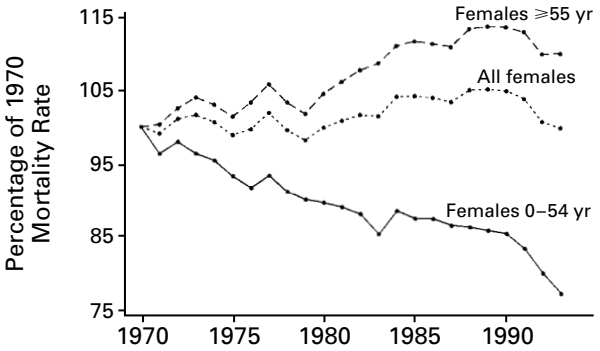

Figure 3. Mortality from Breast Cancer, 1970 through 1993, in the Total U.S. Female Population as a Percentage of the Rate in 1970, According to Age.

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

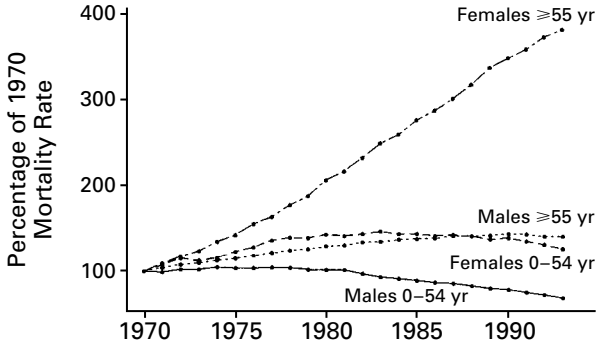

Figure 4. Mortality from Cancer of the Trachea, Bronchus, or Lung, 1970 through 1993, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

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

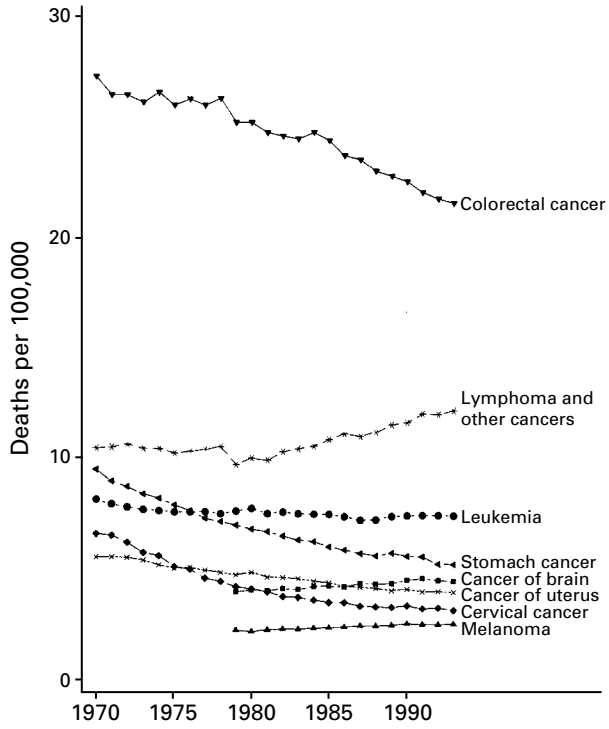

Figure 5. Mortality from Cancer at Selected Sites, 1970 through 1993, in the Total U.S. Population.

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.

We are indebted to the National Center for Health Statistics for supplying most of the data used in this study; to the National Cancer Institute and the Bureau of the Census for the remainder; and to Dr. Samuel Broder for kindly suggesting the title.

REFERENCES

1. Bailar JC III, Smith EM. Progress against cancer? N Engl J Med 1986; 314:1226-32.
2. National Cancer Act, P. L. No. 99-158 (1971).
3. Bailar JC. Rethinking the war on cancer. Issues Sci Technol 1987; 4:16-21.
4. *Idem.* Cancer in Canada: recent trends in mortality. Chronic Dis Can 1992;13:Suppl:S2-S8.
5. *Idem.* Deaths from all cancer: trends in sixteen countries. Ann N Y Acad Sci 1990;609:49-56.
6. Progress against cancer? N Engl J Med 1986;315:963-8.
7. More on progress against cancer. N Engl J Med 1987;316:752-4.
8. The war on cancer: views from the front. Issues Sci Technol 1988; 4:14-6.
9. Extramural Committee to Assess Measures of Progress Against Cancer. Measurement of progress against cancer. J Natl Cancer Inst 1990;82: 825-35.
10. Ries LAG, Kosary CL, Hankey BF, Harras A, Miller BA, Edwards BK, eds. SEER cancer statistics review, 1973-1993: tables and graphs. Bethesda, Md.: National Cancer Institute (in press). (For preliminary edition see <http://www-seer.ims.nci.nih.gov>.)
11. National Center for Health Statistics. Vital statistics of the United States, 1970–1994. Vol. 2. Mortality. Part A. Washington, D.C.: Government Printing Office, 1974-1996 (1993 and 1994 in press).
12. Bureau of the Census. Preliminary estimates of the population of the United States, by age, sex, and race: 1970-1981. Current population reports. Series P-25. No. 917. Washington, D.C.: Government Printing Office, 1982.
13. *Idem.* U.S. population estimates, by age, sex, race, and Hispanic origin: 1980-1991. Current population reports. Series P-25. No. 1095. Washington, D.C.: Government Printing Office, 1993.
14. Breslow NE, Day NE. Statistical methods in cancer research. Vol. 2. The design and analysis of cohort studies. Lyon, France: International Agency for Research on Cancer, 1987. (IARC scientific publications no. 82.)
15. Shalala DE. New cancer mortality rates. Washington, D.C.: Department of Health and Human Services, 1996 (press conference).
16. Cole P, Rodu B. Declining cancer mortality in the United States. Cancer 1996;78:2045-8.
17. National Cancer Institute. Cancer control: objectives for the nation, 1985–2000. NCI monographs. No. 2. Washington, D.C.: Government Printing Office, 1986. (NIH publication no. 86-2880.)
18. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst 1981; 66:1191-308.
19. Financial Management Branch. NCI fact book. Bethesda, Md.: National Cancer Institute, 1993–1996.

Correspondence

Winning the War on Cancer

To the Editor: In their Special Article, provocatively entitled "Cancer Undefeated," Bailar and Gornik (May 29 issue)[1] acknowledge the substantial changes in mortality due to cancer during the past 20 years in men and women under the age of 55 years. The authors note that for this age group, there has been a 25 percent decrease in all cancer-related deaths, a 23 percent reduction in deaths from breast cancer, and a slight but definite decline in mortality from lung cancer; for persons of all ages, there has been approximately a 15 percent drop in deaths from colorectal cancer. Bailar and Gornik believe these changes reflect changes in the incidence of cancer or early detection, discount entirely the impact of therapeutic intervention, and argue that progress will occur only through a national commitment to prevention.

Nobody disputes the merits of cancer prevention. By now, eliminating the use of tobacco products — particularly among the young — has become a social and legislative issue; sufficient research has already been performed to justify the needed behavioral changes. Reducing exposure to known carcinogens such as ultraviolet light, hepatitis B and hepatitis C viruses, asbestos, and excess ethanol has received widespread attention, as has the importance of screening for breast, cervical, and colorectal cancers. The recent development of germ-line genetic-testing techniques will probably identify people at very high risk for breast, colorectal, and ovarian cancers in whom prophylactic medical or surgical interventions, or both, may be of value. A major component of the National Cancer Institute's budget is for cancer prevention, and in 1996, a distinguished panel of experts in this area was commissioned by the institute's director, Dr. Richard D. Klausner, to provide an external critique of this effort.

Bailar and Gornik reveal their underlying bias by choosing to ignore the influence of treatment on the reduction in cancer-related mortality among persons under the age of 55 years. During the past 25 years, previously fatal conditions, such as advanced testicular cancer,[2] Hodgkin's disease,[3] and childhood leukemia,[4] have become curable in more than 70 percent of cases, and up to 50 percent of patients with non-Hodgkin's lymphomas may now be cured.[5] Prospective, randomized trials have shown that postoperative (i.e., adjuvant) therapy leads to a 25 to 30 percent reduction in mortality among patients with locally advanced breast cancer[6] or colorectal cancer.[7] Reductions in cancer-related mortality clearly have multifactorial explanations, but for Bailar and Gornik to dismiss widely used, well-accepted advances in treatment is not only absurd but also potentially damaging to patients with newly diagnosed malignant conditions, who may be influenced by the publicity surrounding this extreme view to reject life-saving treatment. . . .

ROBERT J. MAYER, M.D.
LOWELL E. SCHNIPPER, M.D.
American Society of Clinical Oncology
Alexandria, VA 22314

1. Bailar JC III, Gornik HL. Cancer undefeated. N Engl J Med 1997;336:1569-74.
2. Williams SD, Birch R, Einhorn LH, Irwin L, Greco FA, Loehrer PJ. Treatment of disseminated germ-cell tumors with cisplatin, bleomycin, and either vinblastine or etoposide. N Engl J Med 1987;316:1435-40.
3. Canellos GP, Anderson JR, Propert KJ, et al. Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Engl J Med 1992;327:1478-84.
4. Pui C-H. Childhood leukemias. N Engl J Med 1995;332:1618-30.
5. Fisher RI, Gaynor ER, Dahlberg S, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. N Engl J Med 1993;328:1002-6.
6. Bonadonna G, Valagussa P, Moliterni A, Zambetti M, Brambilla C. Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer — the results of 20 years of follow-up. N Engl J Med 1995;332:901-6.
7. Moertel CG, Fleming TR, Macdonald JS, et al. Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. Ann Intern Med 1995;122:321-6.

INSTRUCTIONS FOR LETTERS TO THE EDITOR

Letters to the Editor are considered for publication (subject to editing and abridgment) provided they do not contain material that has been submitted or published elsewhere. Please note the following: •Your letter must be typewritten and triple-spaced. •Its text, not including references, must not exceed 400 words (please include a word count). •It must have no more than five references and one figure or table. •It should not be signed by more than three authors. •Letters referring to a recent *Journal* article must be received within four weeks of its publication. •Please include your full address, telephone number, and fax number (if you have one). •You may send us your letter by post, fax, or electronic mail.

Our address: Letters to the Editor • *New England Journal of Medicine* • 10 Shattuck St. • Boston, MA 02115

Our fax numbers: 617-739-9864 and 617-734-4457

Our e-mail address: letters@nejm.org

We cannot acknowledge receipt of your letter, but we will notify you when we have made a decision about publication. We are unable to provide prepublication proofs. Please enclose a stamped, self-addressed envelope if you want unpublished material returned to you. Financial associations or other possible conflicts of interest must be disclosed. Submission of a letter constitutes permission for the Massachusetts Medical Society, its licensees, and its assignees to use it in the *Journal*'s various editions (print, data base, and optical disk) and in anthologies, revisions, and any other form or medium.

To the Editor: Bailar and Gornik express gratitude to me "for kindly suggesting" the title of their article, "Cancer Undefeated." I did not suggest this title, and I respectfully decline the acknowledgment. I did, as part of a dialogue with Dr. Bailar, refer him to a 1960 article by Sir John Crofton, entitled "Tuberculosis Undefeated."[1] This article offers many parallels for our discussions about cancer today.

SAMUEL BRODER, M.D.
Miami, FL 33137

1. Crofton J. Tuberculosis undefeated. BMJ 1960;2:679-87.

To the Editor: The results of treatments for cancer may be better than Bailar and Gornik suggest. Any improvement in survival will increase the age at death. The number of deaths below any given age will therefore fall, and the number above it will rise. This will cause a divergence between the mortality rates for the old and those for the young. Indeed, Figures 2 and 3 in the article by Bailar and Gornik show a marked divergence in the rates at the age of 55 years — probable evidence of steadily increasing survival.

T.H. HUGHES-DAVIES, F.R.C.P.
Breamore Marsh
Fordingbridge, Hampshire SP6 2EJ, United Kingdom

To the Editor: Although Bailar and Gornik clearly demonstrate the failure of current treatment efforts in many areas, I fail to see how their article supports the conclusion that more money should be spent on prevention, since prevention has not been very effective either. . . .

TOM S. RAND, M.D.
Wilson Orthopaedic Surgery and Neurology Center
Wilson, NC 27895-3148

To the Editor: Bailar and Gornik report that the age-adjusted rate of mortality from all cancers in the United States declined by 1 percent from 1991 through 1994. Our estimate for the same interval[1] was 2.2 percent, and we also reported a 3.9 percent decline during the period from 1990 to 1995. The discrepancy in the data for the 1991–1994 period stems from the use of different populations for age adjustment. Bailar and Gornik used the relatively elderly 1990 U.S. population and by doing so, minimized striking reductions in mortality that occurred among young and middle-aged persons. We used the U.S. "standard million" population, the basis for all national reports. Use of this population, which is essentially the relatively young 1940 population, reveals the full downturn in cancer-related mortality. We used the standard million not for impact but of necessity to describe a current trend; the latest data are available only in this form. Thus, our 1996 report includes findings for 1995, whereas the report by Bailar and Gornik is limited to 1994. Data for the period from January to October 1996[2] show a further 0.7 percent reduction in mortality from cancer, bringing the decline for the period from 1990 to 1996 to 4.6 percent.

Our more important difference with Bailar and Gornik concerns their view that improvements in treatment resulted in little reduction in mortality from cancer. We reported that one half of the decline we observed reflected advances in medical care and access to it. This statement was based on data showing long-term gains in the survival of patients with cancer even after a correction had been made for the effect of earlier diagnosis.

There are three more reasons for our opinion. First, many aspects of the diagnosis and treatment of cancer have improved greatly, as Bailar and Gornik acknowledge. Second, virtually all oncologists believe that cures and long-term palliation of cancer are much more common now than previously. Finally, several national trends seem explicable only in terms of treatment gains. For example, the mortality rate for all cancers except lung cancer has declined since the mid-1970s, whereas the incidence has remained the same or increased.[3]

PHILIP COLE, M.D.
BRAD RODU, D.D.S.
University of Alabama at Birmingham
Birmingham, AL 35294

1. Cole P, Rodu B. Declining cancer mortality in the United States. Cancer 1996;78:2045-8.
2. National Center for Health Statistics. Births, marriages, divorces, and deaths for November 1996. Mon Vital Stat Rep 1997;45(11).
3. Devesa SS, Blot WJ, Stone BJ, Miller BA, Tarone RE, Fraumeni JF Jr. Recent cancer trends in the United States. J Natl Cancer Inst 1995;87:175-82.

To the Editor: . . . The cavalier attitude of Bailar and Gornik toward the remarkable reduction of deaths due to childhood cancer is wrong. Although the numbers of cured children may be small, each child's life affects many people — the family, the school, the community, and the parent's workplace. Moreover, without a cost–benefit analysis of curative childhood cancer effects, there can be no complete evaluation of the "war on cancer." The number of deaths from cancer is just one outcome to be reckoned with.

SETH COREY, M.D., M.P.H.
Children's Hospital of Pittsburgh
Pittsburgh, PA 15213

To the Editor: An analysis of the effect of the U.S. research effort on cancer that is based entirely on mortality rates, with no consideration of incidence rates, is flawed. Bailar and Gornik conclude that research funds should be diverted from treatment to prevention. They provide no analysis of the effectiveness of preventive strategies and summarily dismiss gains from nonpreventive approaches. Data from the Surveillance, Epidemiology, and End Results (SEER) study show that from 1973 to 1993, the increases in mortality and incidence rates for cancer were 5.8 and 27.3 percent, respectively.[1] Mortality rates decreased in 14 of the 23 cancer sites assessed. For six of the remaining nine sites, the increase in mortality was smaller than the increase in the incidence of cancer.

There are many points of attack in the effort to defeat

cancer, and we have seen valuable gains in the quality of life and knowledge of cancer biology, as well as reductions in mortality. For example, there have been major advances in preserving anatomy or function in treating cancers of the eye (uveal melanoma), esophagus, breast, larynx, anus and rectum, extremities, and prostate.

Significant improvement in survival has been demonstrated in recent phase 3 clinical trials for cancer of the testis, breast, rectum, colon, and esophagus, as well as osteogenic sarcoma and cancers in children. These improvements are largely due to the use of multidisciplinary treatment strategies (combinations of surgery, chemotherapy, and radiation therapy).

Finally, a remarkably rapid increase in our knowledge of cancer biology at the most basic level has occurred since 1970. Cancer is now known to be a genetic disease. We have gained great insight into the multistep process of cancer through research on tumor-suppressor genes, oncogenes, programmed cell death, DNA repair, angiogenesis, and the process of metastasis. These diverse research successes will make it possible for oncologists to begin using molecular diagnostics, individualizing management strategies, and planning gene therapy.

We support research on prevention, but it should not be undertaken at the expense of early detection and treatment.

HERMAN SUIT, M.D.
KURT ISSELBACHER, M.D.
BRUCE CHABNER, M.D.
Massachusetts General Hospital
Boston, MA 02114

1. Ries LAG, Kosary CL, Hankey BF, Harras A, Miller BA, Edwards BK, eds. SEER cancer statistics review, 1973–1993: tables and graphs. Bethesda, Md.: National Cancer Institute (in press).

To the Editor: As a practicing medical oncologist, I agree with Bailar and Gornik that the progress we have made in the treatment of cancer over the past number of years is disappointingly small. However, as both an oncologist and a patient with cancer, I vehemently disagree with the widely publicized opinion of the authors that "in an age of limited resources this may well mean curtailing efforts focused on therapy." Why? Are we putting up a white flag?

War is hell, including the war against the diseases called cancer. In war, progress may not be evident immediately. If the cause is just, one does not quit because of a few lost battles. Some wars last six days, others a hundred years. The war against cancer has been fought for a relatively short time and only very recently with the most modern laboratory techniques. Science is by nature a slow process with an occasional breakthrough. Twenty-five or 30 years is too short a period for a declaration of failure against such a difficult foe.

ALAN FELDMAN, M.D.
Coney Island Hospital
Brooklyn, NY 11235

To the Editor: Bailar and Gornik state, "35 years of intense effort focused largely on improving treatment must be judged a qualified failure," and they believe the emphasis should therefore be shifted toward a preventive approach. In truth, the effort has been far less than intense. As Donald Coffey, president of the American Association for Cancer Research, has noted, "A real war against cancer has never been mounted. To date, available federal funds have supported only a small, intense skirmish by a limited number of investigators."

Although political leaders pay lip service to stopping a disease that will attack one of every four Americans alive today, the fact is that the government's commitment has not changed substantially. During the past 10 years, federal funding for research on cancer, adjusted for inflation, has increased by just 1 percent. Today, research on cancer represents just 0.1 percent of the federal budget. . . .

RICHARD N. ATKINS, M.D.
PHILIP A. ARLEN
CHRISTOPHER L. NOXON
CaP CURE
Santa Monica, CA 90401

To the Editor: Cancer is "undefeated"; the "war against cancer" has not been won. These are military allusions, initially used by a political figure and too readily adopted as snappy media language by the medical and scientific communities in the United States and elsewhere.

In wars there are the victors and the vanquished (not always easily distinguished), and collateral damage is all too common. Wars delay and obfuscate problems but do not often solve them. Wars encourage simplistic and jingoistic attitudes — us versus them. But cancer is so much more complex than this. There is no invading army, no call to arms, no enemy — the trouble is within.

It is time to redefine the problem. Although we should continue our exploration of the biology of cancer, trials of new therapies, and population-based preventive strategies, we also need to face the inevitability of cancer. Cancer is the price we pay for being sophisticated organisms, and there are only so many times we can faithfully replicate the genome with each cell division before making a critical mistake. In addition, the rising incidence of some cancers needs to be seen in context: overall life expectancy in the Western world continues to increase. Although better prevention and early detection should reduce mortality, metastatic cancer will develop in many people and is likely to remain largely incurable. For these people, the emphasis should be on living with cancer rather than dying in battle.

The war-on-cancer metaphor distracts attention from the complexity of the disease and inevitably identifies winners and losers. We should tell the world that we are working at understanding cancer and that knowledge is power.

NICHOLAS WILCKEN, M.D., PH.D.
Westmead Hospital
Sydney, NSW, 2145, Australia

The authors reply:

To the Editor: Several letters and the Sounding Board article by Kramer and Klausner in this issue of the *Journal*[1] distort our position and divert attention from the critical issues. None of the authors, however, question the finding

that cancer-related mortality is higher now than at the time of the National Cancer Act of 1971, even after adjustment for aging in the population and declines in other lethal diseases.

Kramer and Klausner[1] charge that we extrapolate the future from the past. A very long history of great effort by great scientists, marked by great ballyhoo and very spotty progress, *should* engender some skepticism about today's claims of wonderful things to come. We acknowledged that there are successes, but not enough, in palliation and treatment for childhood cancers and some adult cancers. Our argument is that new efforts should be made to advance cancer prevention, already shown to be fruitful, and the examples Kramer and Klausner cite actually support our conclusion. Fleming's discovery of penicillin was a product of acute observation, not basic science; iron lungs disappeared because of prevention, not treatment; tamoxifen is indeed useful in treatment but also has potential for prevention; the delay in federal efforts to reduce smoking (prevention again) was due to political pressures, not lack of knowledge or will at the National Cancer Institute; and the discovery of the roles of human papillomavirus, *Helicobacter pylori,* and nicotine addiction reinforces the need for greater attention to cancer prevention.

Kramer and Klausner ask whether cancer is sufficiently homogeneous to emphasize a single path. We do not claim so, but note that some preventive approaches, such as chemoprevention and strengthening of internal defenses, may have a broader spectrum of benefit than specific treatment regimens. We are not content with a 0.6 percent decrease per year in cancer-related mortality, since at that rate, it would take 115 years for mortality to decline to half the present level. Kramer and Klausner also dispute our contention that the present program is lopsided but fail to mention that prevention and control accounted for about 6 percent of the National Cancer Institute's budget from 1973 (the first year the budget was presented in the current form) until 1994 and that the recent expansion to 10 percent was at the direction of Congress. Furthermore, some of that money is for improved screening and treatment, not prevention.

Mayer and Schnipper say we ignore the influence of treatment on cancer-related mortality in people under the age of 55 years. This is not so; Figure 2 of our article shows trends for people 55 years or older and for those younger than 55, and we specifically mention improved treatment for Hodgkin's disease and childhood neoplasms. Whether adjuvant therapy for breast and colorectal cancer will have effects demonstrable at the population level is not yet known.

The point raised by Hughes-Davies applies to trends in crude rates. We presented only age-adjusted rates to avoid such problems.

We refer Rand to the substantial decline in tobacco use among adults; the effective control of asbestos, benzene, and many other industrial carcinogens; reductions in radiation doses per exposure; and the dietary changes adopted by increasing numbers of Americans — all initiated with little support from basic-science investigators or the government. We need to know how much more we could achieve with a vigorous program of prevention encompassing research and practice.

If cancer-related mortality rates for people of different ages were moving in parallel, the choice of a standard for age adjustment would make little difference, but the rates are not parallel. Declines are greatest at the youngest ages, and increases are greatest at the oldest ages, with a gradual change between these extremes and a crossover from declines to increases at about the age of 55 years. We chose the 1990 standard as the midpoint of the critical recent period; the National Cancer Institute chose the 1970 standard, with somewhat more favorable results; and Cole and Rodu prefer the even more favorable findings with the 1940 standard. If we had used a medieval population, with half the population under the age of 6 years and almost nobody over the age of 50, the trend would have looked wonderful. But only the 1990 standard is appropriate for comparisons of U.S. trends over a period centered on the year 1990.

In response to Cole and Rodu and to Suit et al.: we gave good reasons for not using incidence rates or case survival rates. Furthermore, the argument that better treatment is balancing the rapid increase in incidence supports our conclusion that prevention — reversing the increases in incidence — is crucial.

JOHN C. BAILAR III, M.D., PH.D.
HEATHER L. GORNIK, M.H.S.
University of Chicago
Chicago, IL 60637-1470

1. Kramer BS, Klausner RD. Grappling with cancer — defeatism versus the reality of progress. N Engl J Med 1997;337:931-4.

Anticoagulation and Elective Surgery

To the Editor: In their review of the management of anticoagulation before and after elective surgery, Kearon and Hirsh (May 22 issue)[1] assert that in patients with mechanical heart valves, anticoagulation should be discontinued perioperatively. They assume that the "temporary discontinuation of warfarin . . . exposes patients to a risk of thromboembolism equivalent to one day without anticoagulation before surgery and another day without anticoagulation after surgery." Although this may be possible when patients have an international normalized ratio (INR) between 2.0 and 3.0, it does not seem likely for patients with an INR between 2.5 and 3.5. At this higher level, patients will need a longer time without warfarin preoperatively and a longer time with warfarin postoperatively, thus increasing the length of their time at risk for thromboembolism.

Patients with mechanical valves in the mitral position are considered to have a high risk of thromboembolism and therefore require an INR between 2.5 and 3.5. Two studies, both retrospective reviews, have examined how these patients fare without anticoagulation in the perioperative period. In their report of patients with prosthetic valves who required surgery, Katholi et al. noted that 2 of 10 patients with mitral or combined mechanical valves had fatal strokes when anticoagulation was discontinued three to five days preoperatively.[2] Tinker and Tarhan noted that among 74 patients with mitral or combined mechanical valves, none had embolic events in the absence of anticoagulation.[3] But interpreting the results of the latter study