Fax Transmittal

NATIONAL CANCER INSTITUTE

Office of Cancer Communications
Office of the Associate Director

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301-496-6631
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Date 7-14-97

To Jerry Mande

Fax Number 202-456-6027

From Paul Van Nevel

Cover Sheet plus 3 Pages Transmitted

Message

Information about the Cancer Genome Anatomy Project is being sent at Dr. Richard Klausner request.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

July 14, 1997

NOTE TO JERRY MANDE

Dr. Klausner asked me to fax to you some background information about the new Cancer Genome Anatomy Project and its new website. When the National Cancer Institute unveils the new CGAP website during the last week of July, scientists will have a real-time index to the expression patterns of thousands of genes that might be involved in the development of cancer.

Over the past two decades, scientists made important strides in their understanding of cancer. We know now that cancer is not one disease but many, and that a common thread of all cancers is that they result from the gradual accumulation of changes in our genes. Through the efforts of the international research community, we now know the identity of several key genes that are involved in the development of various cancers. However, many of the important genes in cancer development are not yet known, making it difficult to optimize strategies to prevent, diagnose, and treat cancer.

The Cancer Genome Anatomy Project aims to place in the hands of researchers information about all genes that might be involved in the development of cancer. This project is a national partnership of government, academic, and industrial laboratories. Data from the project, and relevant medical information, are being loaded into a real-time website, so that cancer researchers will be able to look at the data and direct their creative energies toward the development of new ways to prevent, diagnose, and treat cancer.

Attached is a recent news article from *Science* magazine that provides an excellent overview of CGAP.

Paul Van Nevel

J. Paul Van Nevel
Associate Director for
Cancer Communications
National Cancer Institute
301-496-6631

cc: Dr. Klausner

Attachment

GENOMICS

A Catalog of Cancer Genes At the Click of a Mouse

Webster Cavenee can't wait to start doing cancer research on the Web. Like thousands of other biologists, Cavenee, a cancer geneticist at the Ludwig Institute for Cancer Research in San Diego, has already come to depend on a burgeoning array of online databases to help search for new genes and understand what they do. But sometime next month, Cavenee and his colleagues will be able to take their computer queries to a new level, thanks to the Cancer Genome Anatomy Project (CGAP)—an ambitious effort that aims at nothing less than a complete catalog of all the genes expressed in cancer cells.

Starting with five big killers—breast, colon, lung, prostate, and ovarian cancers—CGAP will classify tumor genes by the type of cancer cell they came from and the degree of the cell's malignancy. "We want to achieve a comprehensive molecular characterization of cancer and precancerous cells," says National Cancer Institute (NCI) molecular biologist Robert Strausberg, who is coordinating the CGAP project. With just a click of the mouse, researchers should be able to determine how gene expression changes as a cancer progresses and ultimately begin to understand how tumors arise in the first place—all for no charge. "CGAP will be a national resource that all can tap into via the World Wide Web," says NCI director Richard Klausner. "It's a wonderful, farsighted thing to do," says Cavenee. "It will accelerate cancer research beyond anything [else] they could have done."

The project is the latest example of how a marriage between computer science and genetics—creating a brand-new field called "genomics"—is transforming whole areas of biology. It's also an example of fleet-footedness on the part of NCI. Klausner began talking about the project in mid-1996, even before some of the key technologies were in place. But they made their debut before the end of the year, and about the same time, Klausner got the go-ahead to fund CGAP (*Science*, 29 November 1996, p. 1456). NCI is putting $20 million into the effort this year, and it's also being supported by contributions from the National Library of Medicine's National Center for Biotechnology Information (NCBI), the Department of Energy (DOE), and several pharmaceutical companies.

And all that is just for starters. CGAP funds will also support the development of technologies for rapid analysis of gene activity patterns in the thousands of tumors likely to be seen in a hospital pathology lab. The hope is that, eventually, the tumor gene index and these new technologies will enable physicians to base a patient's diagnosis, prognosis, and treatment on the status of a particular tumor's genes and proteins rather than on its appearance under the microscope. "The notion that one can identify all the genes altered in a given cancer is very exciting," comments cancer geneticist Louise Strong at the M. D. Anderson Cancer Center in Houston. "It should [provide] really good information [for] classifying tumors and identifying targets for therapy."

Cell removal. Laser-based dissection lifts small groups of cells *(right)* from a prostate tumor, leaving the rest of the tumor intact *(left)*.

Despite all this enthusiasm, however, this vision could take years to realize. Although various companies and academic researchers have begun developing methods for wholesale analysis of gene expression patterns, the methods have not yet been shown to work on anything near the large scale envisioned. And plans to expand the tumor gene index to include other cancers are still vague. A similar effort currently getting under way in Europe may, however, help out here (see sidebar). In time, NCI expects its Web site to be linked to the one the Europeans are planning.

Key techniques. The expectations are bold for a program that's still taking shape. But, as Klausner reported last month at the annual meeting of the American Association for Cancer Research, a team led by NCI pathologist Lance Liotta has already demonstrated the feasibility of constructing a gene index for one tumor: prostate cancer. The success of that work depended on two new techniques: one for pulling specific cells out of tumors, which are a heterogeneous mix of normal cells and cells in various stages of malignancy, and the other for analyzing the very tiny amounts of RNA present in the isolated groups of cells.

The melange of cell types in a typical tumor has long been a problem for researchers analyzing gene expression in cancer cells. They can't get an accurate picture by looking at RNAs extracted from a whole tumor, because it will be a mix of molecules from all the different cell types. And standard methods for dissecting out individual cells are not only tedious but also unreliable except in the most experienced hands, says Ramon Parson, a cancer geneticist at Columbia University College of Physicians and Surgeons in New York City. But last year, Liotta, Michael Emmert-Buck, also of NCI, and their colleagues developed a technique called laser capture microdissection that enables researchers to pick out just the cells they want to analyze in about one-tenth the time that standard microdissection requires (*Science*, 8 November 1996, p. 998).

The procedure starts with a thin slice of tumor tissue, placed on a glass microscope slide and covered with a transparent cap from a tiny vial, the underside of which is lined with a thin layer of plastic. A researcher simply scans the sample through a microscope to find a uniform group of cells and, when they are in the scope's cross hairs, squeezes a trigger, zapping that spot with a weak laser. The laser heats the plastic so it becomes sticky and adheres to the cells just underneath. When the cap is lifted from the sample, it pulls off the targeted cells with it. The rest of the sample remains intact, so by moving to a different section, a researcher can obtain cells in various stages of tumor development, all from one piece of tissue.

Emmert-Buck used this technique to collect four sets of cells—normal prostate tissue, cells just starting to transform, fully transformed cells, and invasive cancer cells—from a single frozen prostate tumor. Each set contained about 5000 cells.

The investigators' next challenge was to show that they could use these cells to generate libraries of complementary DNA—DNA from expressed genes—that accurately reflect the full complement of the cells' active genes. Making such libraries requires copying messenger RNA sequences into cDNAs that can then be cloned separately in bacteria. A big problem is that when there is too little RNA, the scarcest sequences can get lost. As a result, sequences of the more common messenger RNAs are overrepresented and others are underrepresented in the library.

Europe's Cancer Genome Anatomy Project

Not long after the Cancer Genome Anatomy Project (CGAP) goes online next month (see main text), the plan is to have it hook up with a similar project now taking shape in Europe. Eleven European academic and clinical laboratories have teamed up to create the Cancer Gene Expression Program, which is also intended to study gene expression in cancer "in a very comprehensive manner," says Charles Auffray, a cancer geneticist at the National Center for Scientific Research in Villejuif, France. Auffray and colleagues from Germany, Sweden, and the Netherlands will focus first on prostate, colorectal, breast, lung, skin, kidney, and pediatric brain cancers.

Once it raises the funding needed, the European team's first goal is to make libraries of full-length complementary DNAs (the DNA from active genes)—as opposed to shorter DNA fragments called expressed sequence tags, or ESTs—from these cancers. They will then select the subsets of sequences that appear to be specific to each of the tumor types. Each subset will be used to screen large numbers of that type of tumor to verify that indeed those genes are either aberrantly expressed (as in the case of oncogenes) or not expressed (as in tumor-suppressor genes) in that cancer, Auffray explains. He expects to make this information publicly available as quickly as possible.

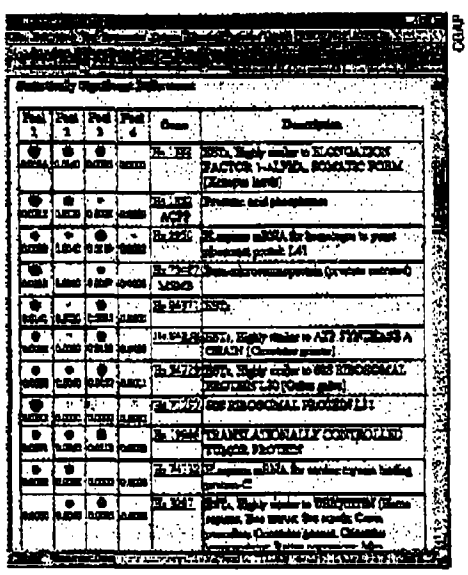
The project is still in the planning stages, but already Auffray has been talking with CGAP folks about collaborating and linking the European project's Web site to CGAP's. At first glance, the projects seem to be trying to accomplish the same goals. But both are needed, says Auffray, because "there are so many genes, so many different cancer types, and so many stages." He hopes even more teams will become involved in cataloging the cancer genes. –E.P.

Another method developed last year by Emmert-Buck, NCI molecular biologist David Krizman, and their colleagues seems to have solved that problem. It combines an efficient cloning technique with a few cycles of the polymerase chain reaction to increase the number of copies of each bit of sequence. When Krizman used this procedure on the cells Emmert-Buck obtained by laser capture microdissection, he found, he says, that "the diversity was really quite good [and] all the genes are kept in a good balance." Genes common in the prostate, such as the one encoding prostate-specific antigen, were well represented in the library, as would be expected. Moreover, there appeared to be some 360 new genes not previously described.

Creating a tumor index. Emmert-Buck, Krizman, and their colleagues will spend the next few months making similar cDNA libraries for normal, precancerous, and cancerous cells from lung, colon, breast, and ovarian tumors, as well as from more prostate cancers. Robert Waterston's team at Washington University in St. Louis will then spend 6 months sequencing several thousand bits of cDNA called expressed sequence tags, or ESTs—unique sequences useful for identifying active genes—from each of these 45 libraries. After that, the task will fall to a yet-to-be-named NCI grantee.

As fast as these EST sequences come in, NCBI researchers will post them in GenBank where they can be accessed from the CGAP Web site along with data about both the tumors and the libraries. This information is not currently available for ESTs in GenBank's database. "We want to present the ESTs in the context of the biology," says NCI's Strausberg.

A program developed at NCBI will enable any Web visitor to look at differences in the patterns of gene expression between any two libraries. Those differences could point researchers to genes important to the progression of cancer, or that could serve as markers of disease. "The hope is that what we'll find are patterns of gene expression that will define much better the subpopulations of cancers," says NCI's Kenneth Katz.



Web-site preview. A CGAP program computes the relative expression of genes from different stages of a tumor, displaying differences by dot size and shading.

That information might help clinicians identify diagnostic markers that can distinguish between normal and cancerous cells or aid in determining a patient's prognosis. Being able to predict a particular tumor's metastatic potential "would be of tremendous benefit," says molecular biologist Claire Fraser of The Institute for Genomic Research in Rockville, Maryland. An oncologist could then tailor the follow-up radiation or chemotherapeutic treatment according to how likely the tumor was to have spread.

In addition to building EST libraries, CGAP investigators will start constructing libraries with longer stretches of cDNA that contain more of an active gene's coding region. These will come from several dozen different types of cancers. Because larger amounts of starting material are needed to generate libraries with longer cDNAs, the RNA will be extracted from bulk rather than microdissected samples. A researcher finding an EST that appears to be unique to, say, precancerous tissue can then look for a match among the longer sequences in these libraries and, upon finding one, possibly isolate the gene faster.

Toward these ends, the NCI is putting $4 million this year into the tumor gene index. Several companies are kicking in additional support for the generation of ESTs. And DOE is allocating $1 million to help set up the bacterial clones in which the ESTs and longer clones are maintained. The IMAGE consortium at Lawrence Livermore National Laboratory in California will make these clones available to any researcher who wants them.

Another $6 million of NCI funds is slated to be distributed to grantees to develop new technologies for analyzing many genes at a time or to improve upon techniques for generating long, potentially full-length cDNAs. Several companies are already working on either DNA chips or microarrays, which arrange many thousands of bits of DNA in a small space. Once these companies have automated the process and sufficiently expanded the numbers of bits of DNA squeezed into an array or onto a chip, these devices can be used for rapid screening of large numbers of cDNA samples to detect expressed genes, Strausberg says. Finally, NCI will spend about $10 million on grants for researchers to come up with ways to put these basic data to use in the clinic.

All this should quickly produce a rich Web site. "The potential for data mining is just great," Emmert-Buck notes. And researchers not involved in CGAP couldn't agree more. "It will generate new directions for investigators," says cancer geneticist Kenneth Kinzler of Johns Hopkins University School of Medicine. All that potential has Cavenee's research team "salivating," he says. "We're checking the Internet daily to see if the [CGAP] home page has come up."

–Elizabeth Pennisi

Erikson
484-636-8562

7-7-97
Klausner 2/2

- Don't know if there would be added costs to moving patients to trials.

Friends of Ca Research
= Ellen Segal

Principle barriers to adult participation in clinical trials
- Financial
- Information – Information system

Last wk – blue ribbon rpt on clinical trials.

ACS surgeons diagnose 80% of all Ca — NCI funding ACS for testing new information.

In kids all diagnoses by oncologist – because so many cancers are hematological

NCI only spend 9¢ on M on Cooperative groups need 5x more.
↳ more studies – faster
↳ funded at higher level
↳ large clinical trial

* funded only at 30-70% of recommended level of funding

NCI runs 9 coop groups
SW oncology group
Semi-regional
10-11K oncologists
8,500 members of NCI
17 adult
2 ped

- Managed care limiting free time.

- Prevention trials – drugs – anti-estrogens
  Tamoxifen
  Vaccines against infectious agents that lead to Ca.
  Vaccines that mobilize immune system against Ca

Framework is there for adults, but needs to be filled in.

① ~~Getting~~ Link into drug discovery infrastructure

② Informatics

③ Funding to ~~#~~ # and speed.

Jerold R. Mande

07/14/97 10:50:49 AM

Record Type: Record

To: Ron Klain/OVP @ OVP, Donald H. Gips/OVP @ OVP, Toby Donenfeld/OVP @ OVP

cc:

Subject: Cancer Initiative

I met with Rick Klausner last week to seek his advice. He was very enthusiastic about the possibility of the VP stepping forward on cancer and offered to help. He also raised an immediate opportunity (week of 7/14 or 7/21) for the VP to announce the Cancer Genome Anatomy Project -- a top NCI priority. It is a natural fit for the VP -- it involves biotechnology, the internet, a partnership for funding involving DoE and industry. It would also allow the VP to put his marker down on cancer, pointing toward a major speech in the fall.

I also wanted to call your attention to a 7/2 request from the Friends of Cancer Research (Valenti & Lansing) for a meeting with the President sometime in the next two weeks to discuss the President's position on biomedical research in general and his stand on the FY97 NIH appropriations, which is currently being marked up in the House, in particular. Public Liaison indicated that the President is likely to do this meeting.

Fax Transmittal

Office of Cancer Communications
Office of the Associate Director

NATIONAL CANCER INSTITUTE

Building 31, Room 10A31
Bethesda, Maryland 20892

301-496-6631
Fax 301-402-4945

Date 7-14-97

To Jerry Brandt

Fax Number 202-456-6027

From Paul Van Nest

Cover Sheet plus 2 Pages Transmitted

Message

Add. transl information about the Cancer Genome Anatomy Project

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

July 14, 1997

NOTE TO JERRY MANDE:

Earlier today I faxed you some background information on the Cancer Genome Anatomy Project. Here is some additional information about the issue, and the event being planned to launch the CGAP website. Dr. Klausner will be away for a couple of weeks beginning in early August and we would like to hold the event in the last week in July. If the Vice President is able to participate, his schedule, of course, would dictate the date and time of the event. Please let us know as soon as possible about his decision and the best possible date for him.

ISSUE

Please see the note I faxed to you earlier today. The CGAP website will provide scientists with the first real-time index to the expression patterns of thousands of genes that might be involved in the development of cancer. CGAP is at the intersection of genomics and informatics, where gene discovery and computer technology will come together to develop new ways to combat this disease. Already, scientists know the identity of several key genes that are involved in the devlopment of cancer, but many of the important genes involved in cancer development are not known yet. CGAP ultimately will give scientists information about all of the genes involved in the development of cancer. As the Project develops data about the expression genes involved in the development of cancer, that data will be loaded onto the real-time website where scientists can study it and begin to develop new ways to prevent, diagnose, and treat cancer.

EVENT

The National Cancer Institute plans to hold a media briefing that will feature demonstrations of two key elements of the Cancer Genome Anatomy Project: 1) A new technology (called laser microdissection technology) that allows a pathologist to dissect a tumor sample into a few cells for gene analysis; and 2) the new Cancer Genome Anatomy Project website, where data from the project are being displayed so that scientists worldwide can examine existing information and use that information in their research to prevent, diagnose, or treat cancer. At the event, the Vice President could operate the laser that enables individual cells to be plucked from the tumor sample to be analyzed for their genes, and operate the computer, whose

screen will be projected, to surf through the website. DHHS Secretary Donna Shalala has also been invited to participate. Dr. Klausner and the staff from NCI and from the National Library of Medicine, which will operate the website, will also participate to handle the technical and scientific aspects of the project.

J. Paul Van Nevel
Associate Director for
Cancer Communications
National Cancer Institute
301-496-6631

cc: Dr. Klausner

Ron Klain @ OVP
07/02/97 09:18:21 PM

Record Type: Record

To: Jerold R. Mande/OSTP/EOP

cc:
Subject: Cancer Strategy

The VP asked me where this stands. He is anxious to start to move ahead. And one other point: he wants to get Hodding Carter involved in this as well. He met with Carter last year, and thought Carter had some great ideas.

Specifically, what the VP wants is: (1) a BRIEF memo from you, ASAP, outlining where we stand and what we might do; (2) a call sheet for the VP to call Carter, solicit his advice, and then pass him off to you; and (3) then a final meeting with you and Carter to sign off on a plan that the VP would begin to sell internally.

Let me know how this sounds, and when you think you can be ready for step one.....Thanks.

Elizabeth Drye
07/21/97 06:57:12 PM

Record Type: Record

To: Jerold R. Mande/OSTP/EOP

cc:
Subject: cancer

This doesn't transfer well from POTUS to VPOTUS, but here it is.

National Cancer Institute and National Cancer Act

President Roosevelt signed the National Cancer Institute Act in 1937, establishing the NCI. The law mandated the new institute "to provide for, foster, and aid in coordinating research relating to cancer."

President Nixon signed the NCA on December 23, 1971. His statement on the bill, attached, notes that he had called for the legislation in his January '71 State of the Union address. In July of '71 Congress also approved his request to dramatically increase NCI's budget by $100 million (to $337.5 million). The NCA, among other things:

- made the NCI Director a presidential appointee and expanded the Director's mandate;
- established two advisory boards appointed by the President;
- initiated the **National Cancer Program**, calling on NCI's Director to "plan and develop and expanded, intensified, and coordinated cancer research program encompassing . . . NCI research, related programs of other research institutes, and other Federal and non-Federal programs;
- authorized the first cancer centers; and
- required NCI to submit its budget directly to the President.

Nixon noted in his statement that these provisions "place the full weight of the Presidency behind the national cancer program . . . the President will be able to take personal command of the Federal effort to conquer cancer."

7-7-97

O: 301-496-5615

H: 301-469-5931

Klausner 1/2

2,513,000

FY 1999 ~ 2000 M add

- Incredible to even have the VP speak out.

- Science thriving. Sense of nat'l Ca program not.

- New vision - major increase in progress.

20% of infrastructure for 1% of Ca funding tried

kids - 90% treated according on NCI ~~bad~~ protocol - 70% ~~cure~~ 5% - 70-80% over 35 yrs.

adults - 2% on NCI protocols.

5 yr survival 40% to 60%

Colorectal - ~~over 35 yr~~ brought down 35%

think 20 yrs of clinical trials - should have taken 3-5 yrs

curve rate 2-5 yrs out without disease adults different

Pass through budget -

Think tank — 100's involved - Anatomy Project.

1-2 wks — Ca genome - DoE, Industry partnership.

Internet

Transform oncology - until optimal therapies are available - get more people in protocols

Fall

- Nat'l Ca Informatics Infrastructure - still using pencil.

John Silva - DARPA Larry NCSA $20M

Can cut mortality 10-20% if everyone treated with optimal protocol

Natl Mtg: Natl Coalition Ca Survivorship

- More robust surveillance & data base.

Reinvention Lab

Ca Info - Customer Survey - OMB paperwork takes months - questionnaires - 6 mos.

PDQ - basic

March

Payers - clinical trials.

Reference #1

ROUTING & REQUEST

Please...

- [x] Read
- [x] Handle
- [x] Approve

And...

- [x] Forward
- [ ] Return
- [ ] Keep or Recycle
- [ ] Review with Me

To: Jerry

I am still working on Refs. 4 and 5 but there Items which makes me believe its one of these

From: Christine

Date: 6/19/97

Post-it® 7664 ©3M 1995

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.

Supported in part by grants from the Alfred P. Sloan Foundation, the Mobil Corporation, and the University of Iowa Research Foundation.

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.?	185.1	8.7	+0.4
	1973	*1981*		
Incidence				
Crude rate†	365.?	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

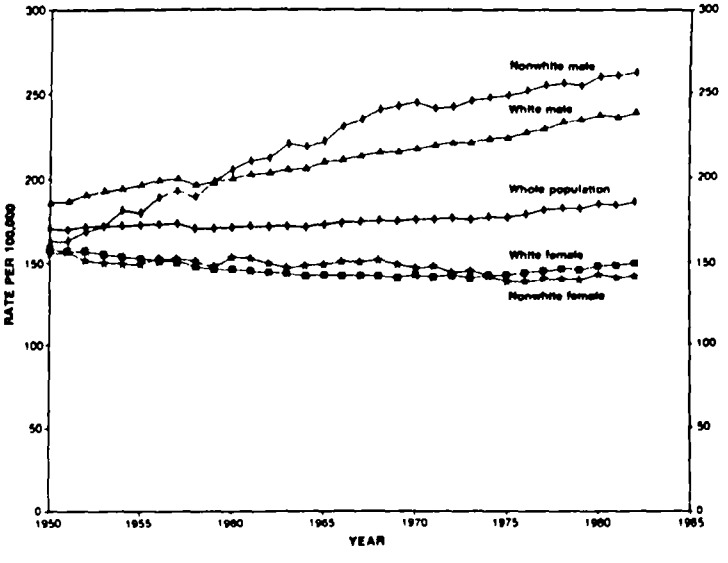


Figure 1. Mortality from All Malignant Neoplasms, 1950 through 1982, in the U.S. White Population and According to Race (White or Nonwhite) and Sex. Age was adjusted to the U.S. population of 1980.

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.

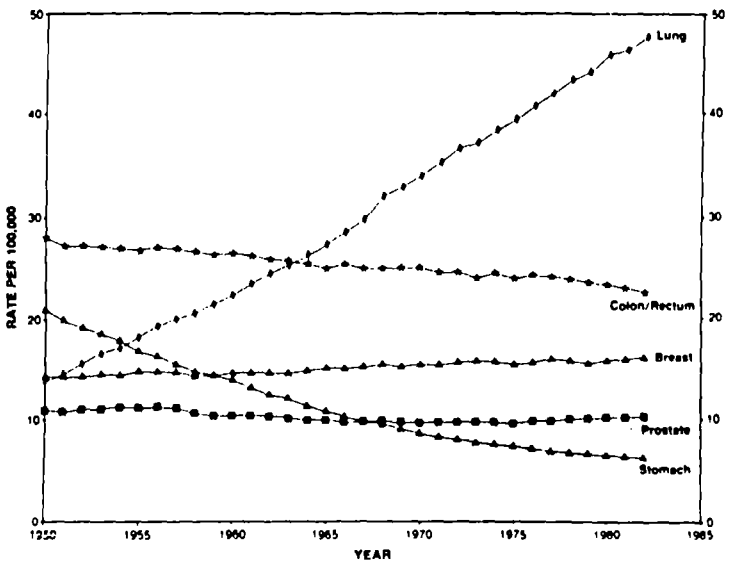


Figure 2. Mortality from Cancer of Selected Sites, 1950 through 1982, in the Total U.S. Population.
Age was adjusted to the U.S. population of 1980.

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-

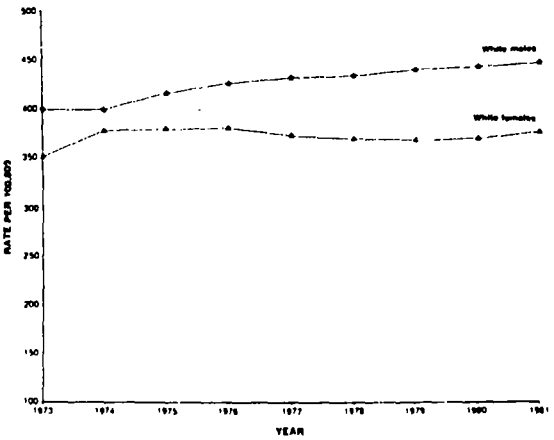


Figure 3. Incidence of All Cancers, 1973 through 1981, According to Sex, in the White Population of the SEER Registry Area.
Age was adjusted to the U.S. population of 1980.

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

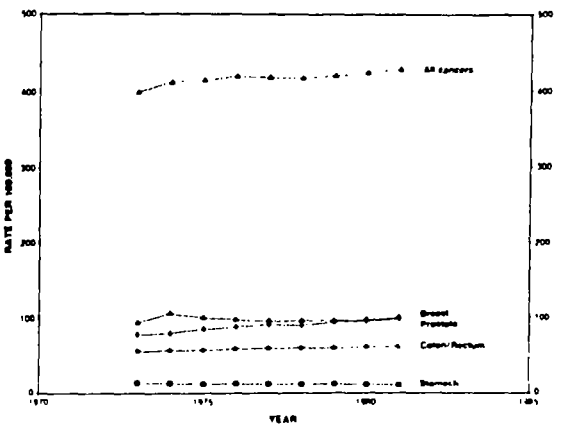


Figure 4. Incidence of All Cancers and Cancers of Selected Sites, 1973 through 1981, in the White Population of the SEER Registry Area.
Age was adjusted to the U.S. population of 1980.

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.

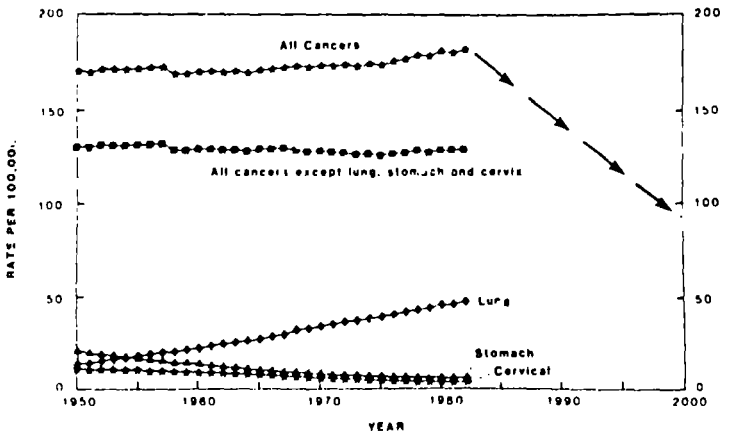


Figure 5. Mortality from Cancer of All Sites and Selected Sites, 1950 through 1982, in the U.S. Population.

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.

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.

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]

We are indebted to Jesse Berlin and Julia Bailey for help in processing the data presented here, to Dr. Michael Shimkin for encouragement, and to many colleagues for helpful comments on earlier drafts.

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Reference #6

of accelerated coronary artery disease in the transplanted heart.

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CORRESPONDENCE

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PROGRESS AGAINST CANCER?

To the Editor: The report by Bailar and Smith (May 8 issue)* certainly provoked a great deal of discussion among American oncologists. I think it is clear from the data they provided that mortality from lung cancer in the United States continues to be a serious health problem. Lung cancer is increasing in incidence and appears to be reaching epidemic proportions. I disagree with the authors' conclusion that wholehearted efforts to prevent lung cancer will substantially change the mortality figures. Incidence rates for lung cancer have been rising in both white men and white women. To date, there is nothing to suggest that the halfhearted efforts of government and society to modify smoking behavior will change incidence figures in the future. Rather, I believe that in addition to fruitless attempts to educate society about the evils of smoking, the most expedient way of changing smoking habits is to tax cigarettes more heavily. The revenues generated could be used to fund primary prevention studies, and there would also be a monetary incentive to stop smoking.

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To the Editor: The pessimistic review of cancer-mortality statistics from 1950 to 1982 presented by Bailar and Smith does not reflect the lag between improvements in breast cancer treatment since 1975 and their effect. Since median survival after breast cancer (Stages I and IV) is at least seven years, the authors' conclusion that improved treatment must be judged a "qualified failure" may be invalid. Although adjuvant chemotherapy was initiated in the mid-1970s, it was not widely employed until the 1980s, and it is still not being recommended even for high-risk postmenopausal patients, according to the September 1985 National Institutes of Health (NIH) Consensus Conference.

A survey of the practice patterns of 634 oncologists by the Chemotherapy Foundation[1] in the summer of 1985 indicates that most oncologists use only the mild convenience regimen consisting of cyclophosphamide, methotrexate, and fluorouracil (CMF) for premenopausal women and less than 35 percent employ the more aggressive (Cooper-type) regimen consisting of cyclophosphamide, methotrexate, fluorouracil, vincristine, and prednisone or regimens containing doxorubicin. For postmenopausal cancer, a study begun in 1980 by Bonadonna et al.[2] in high-risk patients with Stage I breast cancer has recently shown that an intensified CMF regimen is highly effective in prolonging long-term survival. Bailar and Smith's data cannot indicate the effect of the potential curability of chemotherapy in breast cancer, even though it is now firmly established by several 8- to 19-year-old studies indicating increased disease-free survival of 12 to 27 percent.[3-5] Early perioperative and aggressive curative programs are virtually ignored by the profession. The current conservative trend has even extended to chemoprevention, since the NIH Consensus Conference failed to encourage the use of tamoxifen in Stage I postmenopausal breast cancer. The effect of tamoxifen for Stage II breast cancer, although its use has been established since 1979, has yet to be felt on American mortality statistics. I estimate that 10,000 lives could be saved by the early aggressive use of polychemotherapy in breast cancer, as compared with the negligible number of lives, perhaps several thousand, now being saved. At the recent meeting of the American Society of Clinical Oncologists, DeVita estimated" that 4000 patients with lymphoma annually are not achieving 10-year disease-free survival as a result of inadequate dosages of otherwise good treatment regimens.

Before condemning current treatment as futile, one needs to examine the extent to which improved treatments are actually being employed.

The paper by Bailar and Smith may perhaps rouse us from our lethargy. But, unfortunately, it is reminiscent of Bailar's study[7] a decade ago emphasizing the negative risk–benefit ratio involved in mammography, which was based on the use of antiquated radiologic equipment. What good are improved methods not optimally applied?

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To the Editor: The article "Progress against Cancer?" does not aim at stimulating discussion of the progress of research in the United States. Rather, it attempts to summarize some 35 years of the cancer-research experience (including the most recent 15 years, since the National Cancer Institute launched its current intensive effort) in an elementary manner. It refers to only a single measure of progress. On this basis the article concludes that "we are losing the war against cancer." This is an erroneous view.

The article contains glaring weaknesses. For example, the use of the age-adjusted mortality rate as the sole measure of progress addresses only one of many dimensions of the accomplishments of the national cancer program and deserves to be questioned. Even if one examines treatment results to the exclusion of all other progress in the cancer program, the use of mortality data that measure old events is not a good assessment of the state of the art today. The intensive effort, referred to by Bailar and Smith as "the war against cancer," began with special funding in 1972. The mortality data cited for 1982 measure events in diagnosis and treatment for many cancers that occurred between 1972 and 1975 and sometimes earlier. Reports on curative therapies for some cancers and the definitive adjuvant-treatment studies in breast cancer, for example, were not even published at that time.

The article fails even to mention the types and magnitude of prevention research now in progress. And although we agree that prevention research merits increasing support, so too do research on treatment and basic research on the mechanisms that determine normal cell division and differentiation and on the failure of these mechanisms that leads to neoplasia. Basic research, research on prevention, and research on treatment need not be considered competitors and should not compete, given adequate levels of financial support. We need to stimulate all these areas of scientific inquiry, and current programming reflects those directions.

The progress of a scientific program of the scope and dimensions of the national cancer program cannot be assessed in a Special Article by two authors with a unidimensional approach and a limited knowledge of the extent of the research effort supported by the National Cancer Institute. It is a complex program constantly open to scrutiny, criticism, advice, and public debate. It is, however, a program based in science, and it deserves a valid scientific assessment. This article does not provide such an assessment.

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To the Editor: The suggestion that the age-adjusted mortality rate is the appropriate standard for evaluating success in cancer treatment may be as erroneous as the more positive data reported by the National Cancer Institute. The use of death-certificate diagnosis as the basis for statistical studies is pragmatic but not reliable or precise enough to justify the negative conclusions of the paper. In the 25 years referred to in this article there have been many changes in cancer diagnostic techniques and in the attitudes toward cancer of physicians and patients that could have altered the reported incidence of cancer or mortality data.

Physicians who critically analyze the results of cancer treatment do not rely on data based on death certificates. We have learned how to assess the statistics of treatment results, such as those regularly reported in the *Journal*. Specific mortality and detailed morbidity evaluations are both important considerations in cancer treatment.

I have to reject the conclusions of Bailar and Smith that emphasis in cancer research should be switched from treatment to prevention. Certainly, prevention should be an important priority in cancer research and educational efforts. The inaccuracies of the data-collection technique used in this article do not justify our abandoning treatment-based research efforts. Indeed, "progress against several uncommon forms of the disease, improvements in palliation, and extension of the productive years of life"* argue in favor of the expansion of these efforts.

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*Bailar JC III, Smith EM. Progress against cancer? N Engl J Med 1986; 314:1226-32.

To the Editor: Bailar and Smith noted an 8 percent increase in the age-adjusted cancer mortality rates since 1950 and concluded that there has been no progress against cancer in patients over 30 years of age. However, their use of summary age-adjusted rates to examine cancer mortality trends has obscured important age-specific differences. When the 1980 age-specific rates are compared with the corresponding 1950 rates[1] (Table 1, columns 1 through 4), marked decreases in cancer mortality are apparent in all five-year intervals under age 50, although the age categories over 50 show substantial increases. Bailar and Smith claimed further support for their conclusion when, after excluding deaths from lung, stomach, and cervical cancer in order to remove the effects of cancers whose rates have changed for reasons unrelated to treatment, they found a trivial decrease of less than 1 percent. However, inspection of the deflated age-specific rates (Table 1, columns 5 through 7) reveals a material decline in cancer mortality in all age groups under 65. Rate increases persist in the age categories over 65. The comparison of the 1980 and 1950 age-specific rates reveals a classic crossover phenomenon, a severe type of interaction that precludes the use of age adjustment as a valid means of summarizing data.[2] Changes in the age-specific cancer mortality rates since 1950 suggest that progress may in fact have been achieved in the treatment of cancer patients under the age of 65.

Table 1. Age-Specific Cancer Mortality Rates for 1950 and 1980.*

Age Group	All Cancer Mortality			All Cancer Mortality Except Lung, Stomach, and Cervix		
	1950 Rates	1980 Rates	Percent Change	1950 Rates	1980 Rates	Percent Change
30–34	25.1	17.3	−31.1	19.9	14.9	−25.1
35–39	45.6	33.5	−26.5	35.1	26.4	−24.8
40–44	80.9	66.7	−17.6	60.6	47.7	−21.3
45–49	136.5	128.3	−6.0	99.6	84.9	−14.8
50–54	216.3	228.9	+5.8	157.4	148.1	−5.9
55–59	328.7	358.1	+8.9	239.0	230.8	−3.4
60–64	467.4	525.8	+12.5	341.8	336.7	−1.5
65–69	597.6	722.7	+20.9	445.0	475.5	+6.9
70–74	828.3	940.9	+13.6	631.5	646.7	+2.4
75–79	1065.4	1142.6	+7.3	823.9	835.8	+1.4
80–84	1321.4	1378.7	+4.3	1047.9	1086.0	+3.6
>85	1451.0	1594.6	+9.9	1176.1	1326.3	+12.8

*Rates are per 100,000 person-years.

Before one accepts the concomitant interpretation that treatment efforts over the past 35 years have actually hastened rather than retarded cancer mortality in the older age groups, two alternative hypotheses deserve consideration. First, the apparent increase in cancer mortality in the older age groups, even after the deletion of deaths from lung, stomach, and cervical cancer, may be due to the inclusion of deaths from other cancers attributable to tobacco use. Epidemiologic studies have shown that cancers of the larynx, esophagus, oral cavity, bladder, kidney, and pancreas are also associated with cigarette smoking.[3] Second, the 1950 cancer mortality rates may have been underestimated in the older age strata. The accuracy of the primary cause of death as stated on the death certificate has certainly improved since 1950.[4,5] That the most dramatic improvement has occurred in the older age groups is suggested by reductions in the age-specific mortality rates for deaths due to senility and other ill-defined conditions,[1] which more than offset the increases in cancer mortality (data available on request). Explanations for improvements in the accuracy of assigning cause of death include the expansion of elderly people's access to health care through Medicare, as well as advances in physicians' diagnostic acumen. The alternative hypotheses we have proposed are not mutually exclusive, and we suspect that both factors have contributed to the peculiar age-dependent trends in cancer mortality since 1950.

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1. Vital Statistics in the United States. Vol. 2. (Mortality, Parts A and B.) Rockville, Md.: National Center for Health Statistics, 1950 and 1980.
2. Fleiss JL. Statistical methods for rates and proportions. 2nd ed. New York: John Wiley, 1981:246-7.
3. Wynder EL, Hoffman D. Tobacco. In: Schottenfeld D, Fraumeni JF Jr, eds. Cancer epidemiology and prevention. Philadelphia: WB Saunders, 1982: 277-92.
4. Kircher T, Nelson J, Burdo H. The autopsy as a measure of accuracy of the death certificate. N Engl J Med 1985; 313:1263-9.
5. Bauer FW, Robbins SL. An autopsy study of cancer patients. I. Accuracy of the clinical diagnoses (1955 to 1965) Boston City Hospital. JAMA 1972; 221:1471-4.

To the Editor: Bailar and Smith have done a public service with their thoughtful analysis of cancer mortality in the United States.

Many scientific advances with practical applications have been achieved with the use of funds allocated to cancer research. Monoclonal antibodies serve well as a recent example. The total mortality from cancer, however, has not been reduced; it has climbed slowly but steadily. The reduction of cancer mortality among younger patients is an important advance, but it applies to about 10 percent of the total cancer burden of the population. The big killers — cancers of the lung, colorectum, breast, and prostate — are more resistant.

The Bailar–Smith analysis should not be considered a criticism of cancer research, although it questions its allocations. And its implications do militate against the promotion of cancer research through public relations based on wishful thinking or worse.

Bailar and Smith put their confidence in the ability of physicians and the general public to reach correct conclusions when they are confronted with facts that are uncomfortable. Congratulations.

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To the Editor: The lack of progress against cancer, as described by Bailar and Smith, is not confined to the United States alone. In 1985 the World Health Organization (WHO) reported its study of cancer-mortality trends covering the period 1960 to 1980 in 28 countries, including the United States, representing 75 percent of the population of the developed world.[1,2] The conclusions were essentially the same and are summarized in Table 1.

The cancer that had the steepest rise in mortality and that was the dominant factor in the overall increase was lung cancer. It is primarily a self-induced, preventable cancer. Sadly, if there had been an active commitment to reduce tobacco consumption, this increase could have been avoided.

Table 1. Age-Adjusted Increase (or Decrease) in Cancer Mortality in 28 Developed Countries from 1960 to 1980.*

Cancer	Males	Females
	percent	
Lung	76	135
Stomach	(45)	(58)
Breast	—	22
Cervical	—	(30)
All cancers	19	(2)

*Parentheses indicate a decrease in mortality.

Stomach cancer is decreasing in nearly all countries, and although the specific reasons for this effect are unknown, the most plausible explanation appears to be changes in diet and food preparation and not improved therapy.

Cancer of the cervix uteri is virtually the only common tumor in which there has been a substantial decrease in mortality due primarily to action taken by the medical community. Reductions in mortality from cervical cancer were seen in countries that had clear screening policies and a well-organized cytologic screening system.

In the WHO analysis, the important role of preventive measures and the value of carefully designed screening programs were clear. The influence of therapeutic treatment on overall mortality for the common cancers was very limited, although there has been dramatic progress in therapy for some less common cancers.

Contrary to common belief, there are more cases of cancer in absolute numbers in the developing countries than in the industrialized countries. Although accurate time-trend information is not available from most developing countries, sufficient data exist to permit the conclusion that the relative increase in cancer has occurred at a faster rate than in developed countries.[3,4] The primary reasons for this are an increase in life expectancy and a dramatic increase in the consumption of tobacco. For example, in Shanghai County, an area near the city of Shanghai in China, cancer was the sixth leading cause of death in 1960. By 1980 cancer had become the leading cause of death.[5]

In accordance with these and other findings, WHO advises member states to plan national cancer-control programs with the primary focus on prevention — especially education and legislation concerning tobacco — early detection, and treatment of the disease and on the provision of pain relief.[6]

The need to establish new priorities and strategies in cancer comes not only from analyses such as the one outlined above, but also from cost-effectiveness investigations that clearly point to the value of preventive programs, especially regarding tobacco control.[7] Experience in the Scandinavian countries (tobacco smoking) and in India (tobacco chewing) has shown that life styles can be changed in a positive fashion.[8] To win the war against cancer we must also win the battle against tobacco.

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1. Cancer increases in developed countries. WHO Wkly Epidemiol Rec 1985; 17:125-9.
2. Cancer in developed countries: assessing the trends. WHO Chron 1985; 39:109-11.
3. Cancer as a global problem. WHO Wkly Epidemiol Rec 1984; 59:125-6.
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5. Gu XY, Chen ML. Health services in Shanghai County: vital statistics. Am J Public Health 1982; 72:Suppl 9:19-23.

6. Stjernswärd J, Stanley K, Eddy DM, et al. Cancer control: strategies and priorities. World Health Forum 1985; 6(2):160-4.
7. Eddy DM. Setting priorities for cancer control programs. JNCI 1986; 76: 187-99.
8. Control of oral cancer in developing countries: a WHO meeting. Bull WHO 1984; 62:817-30.

To the Editor: Although I agree with Bailar and Smith that some success claims may be exaggerated and some future goals unrealistic and I support increased efforts to prevent cancer, I believe that their article presents an unfairly bleak picture of the effort against cancer.

The inevitability of death should, one feels intuitively, create some linkage among death rates for various diseases. From 1964 to 1979, death rates (age-adjusted to the 1970 population) for heart disease and stroke (together, nearly 50 percent of all deaths) fell 25.9 and 42.2 percent, respectively, while cancer mortality increased 6.9 percent.[1] Perhaps falling cardiovascular mortality has "unmasked" cancer mortality, and persons who formerly died with cancer now die of cancer. In this context, a small percentage increase in cancer mortality may well represent progress.

Inevitable mortality also makes it unrealistic to expect the prevention of eventual death; at best, only premature death can be prevented or reduced. From this perspective, progress has been made against cancer: Age-specific cancer mortality decreased from 1964 to 1979 for all 5-year age groups below the age of 50 (Table 1).[1] Although such deaths represent a small fraction of total cancer mortality, the decrease represents an important reduction in the number of premature deaths.

Table 1. 1979 Age-Specific Mortality Rates (per 100,000) for All Cancers in the Total Population and Percentage Changes since 1964.*

Age Group	Rate	Change	Age Group	Rate	Change
0–4	4.5	−47.1	45–49	129.0	−3.8
5–9	4.8	−32.4	50–54	231.2	+2.5
10–14	4.2	−30.0	55–59	355.4	+5.8
15–19	5.5	−28.6	60–64	539.3	+13.0
20–24	7.0	−23.9	65–69	708.5	+6.3
25–29	10.4	−26.2	70–74	928.7	+12.9
30–34	17.4	−29.6	75–79	1227.1	+21.5
35–39	33.0	−23.4	80–84	1414.2	+16.3
40–44	66.5	−15.1	>85	1434.7	−2.2

*Data from *Vital Statistics in the United States*.[1]

The data excluding lung cancer (Table 2)[2] suggest that, except for nonwhite males, cancer mortality among nonsmokers decreased or remained constant from 1962 to 1977. The cervical-cancer data and the data on rectal as compared with nonrectal colon cancer illustrate the benefits of treatment when early detection is possible. The differences in changes in mortality according to race and sex for total cancer and nonrectal colon cancer suggest that some of the limitation of progress against cancer is due to failure to apply knowledge, not failure to develop or discover it.

Although Bailar and Smith imply that emphasis on prevention will yield large results, more cautious expectations are in order. If, as the authors state, lung cancer is the best example of the failure of treatment, it is also the best example of the failure of prevention (especially among women). We have known for 22 years how to prevent this disease. Just as treatment has had limited success because of the failure to discover a "cancercillin," so too gains in prevention may be limited in the absence of a "tumovax." In such a case, prevention will require the compliance of an asymptomatic population, always difficult to achieve. A balanced approach is needed: research on prevention and on new methods of cure, and — what is most likely to yield rapid results — improved implementation of current knowledge and research on improved early detection. The two last-mentioned capitalize on the limited but real progress in cancer treatment.

Table 2. 1977 Age-Adjusted Mortality Rates (per 100,000, Adjusted to the 1970 Population) for Selected Cancers, According to Race and Sex, and Percentage Changes since 1962.*

Site	White Female	Nonwhite Female	White Male	Nonwhite Male
	rate (% change)			
All	133.0 (+0.3)	148.1 (+5.0)	207.8 (+13.6)	258.2 (+32.3)
Lung	17.7 (+179.9)	17.1 (+187.9)	67.6 (+61.4)	80.9 (+100.2)
All except lung	115.3 (−8.7)	131.0 (−3.1)	140.2 (−0.6)	177.3 (+14.5)
Cervix	3.5 (−53.4)	9.6 (−47.7)	—	—
Colon (not rectum)	16.4 (−5.4)	16.4 (+28.1)	20.7 (+18.3)	18.5 (+41.6)
Rectum	3.0 (−39.5)	3.0 (−34.5)	5.2 (−34.6)	5.5 (+3.0)

*Data from McKay et al.[2]

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1. Vital statistics in the United States. Vol. 2 (Mortality, Part B.) Rockville, Md.: National Center for Health Statistics, 1979 and 1964.
2. McKay FW, Hanson MR, Miller RW. Cancer mortality in the United States: 1950–1977. Bethesda, Md.: National Cancer Institute, 1982. (NIH publication no. 82-2435.)

To the Editor: I have the good fortune to belong to the class of oncologists that is dealing with a subset of cancer wherein success is real; in pediatrics cure is the norm. That claim can be demonstrated by the measure that Bailar and Smith advocate — the decline in mortality from cancer in children in the general population.* The results achieved by pediatric oncologists represent a major contribution to the decrease of all cancers in patients under the age of 30 years, as acknowledged by Bailar and Smith. Even in pediatrics, however, the very success rate makes the current approach to cure through large-scale clinical trials less effective. Furthermore, the victory is often a Pyrrhic one, since the threat of second malignant neoplasms is ever increasing, and serious physical, developmental, and psychosocial iatrogenic sequelae are inevitable.

Prevention is always better than treatment of established disease, though physicians can treat quite effectively, both empirically and symptomatically. Whatever success the war on cancer has had has been achieved through objectively verified empiricism. Prevention cannot be approached as readily that way. One has to understand in order to prevent. A great deal of research on prevention is in fact research on causation. Much prevention can be accomplished when cause and effect are understood, as in the case of lung cancer and smoking. Preventive efforts without an understanding of cancer's causes are either too broad or miss the mark entirely; as a result they are costly and often ineffective.

Large-scale funding of research on therapy has not been a uniform failure, although the areas of success contribute only a small percentage to the improvement of treatment of all cancers. However, it either has failed or has become less promising in every area of success achieved. A rethinking of funding priorities is indeed in order. I strongly urge the redistribution of funds to favor once again fundamental research into the malignant process. In that way we will be able to prevent an understandable disease.

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*Miller RW, McKay FW. Decline in US childhood cancer mortality: 1950 through 1980. JAMA 1984; 251:1567-70.

To the Editor: As a medical oncologist familiar with the barrenness and futility of so many published studies of cancer treatment (including some conducted by national cooperative groups), I found much with which I could agree in Bailar and Smith's article. Despite the undoubted successes of chemotherapy in the treatment of particular tumors, such as lymphomas and breast cancer, the claim "We are winning" is hardly justified by the facts. The source of this inappropriate emphasis on treatment seems to me to be the American health care community's excessively pragmatic stress on curing disease whose pathogenesis is still not understood. But shifting the emphasis to prevention, as these authors propose, reflects the same ill-directed pragmatism. Aside from lung cancer, how many neoplastic diseases can be considered preventable on the basis of present knowledge?

The authors are also in error, I believe, in equating recent progress in the elucidation of the molecular genetics of cancer (i.e., oncogenes) with previous fads in this field. This work has given us the first specific data on the biochemical abnormalities of neoplastic cells. The national approach to cancer should be redirected not to yet another blind, empirical enterprise, however popular, but to basic research, which alone holds out the hope of real progress.

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To the Editor: Recently, Bailar and Smith[1] and DeVita[2] faced off on the progress we have made in the war against cancer. In their article in the *Journal*, Bailar and Smith stated that mortality figures indicate we have not made progress, whereas DeVita, current director of the National Cancer Institute (NCI), pointed to the success of clinical research in advancing survival.[2] This could be a case of "where you sit is where you stand."

Perhaps they both have their facts right but not their interpretations. There are several obstacles to preventive activities, to the rapid dissemination of research results, and to the use of appropriate state-of-the-art treatment. The U.S. government is a major culprit in this problem, with inappropriate reimbursement policies and the lack of a coordinated NCI program to communicate information to primary care physicians.

Reimbursement for preventive activities is appalling. Breast mammography, Hemoccult tests, and the Pap test are not regularly reimbursed. Federally funded research may have proved their efficacy, but no one told the reimbursers. Reimbursement by third-party insurers and the diagnosis-related-group (DRG) payment program are altering the patterns of treatment, pushing chemotherapy treatment out of the hospital, for example, and establishing serious barriers to the treatment of adult patients with leukemia. Recently, the Prospective Payment Assessment Commission recommended that the adult leukemia DRGs be recalculated and increased on the basis of information provided by the Association of Community Cancer Centers, but action has yet to be taken. New forms of therapy are also facing an uphill battle for reimbursement, despite their efficacy and cost effectiveness. For example, VP-16 for small-cell lung cancer has been denied by Blue Cross–Blue Shield in some parts of the country, since the research on which its use is based is still considered "experimental" (e.g., not listed on the package insert).

At NCI over the past decade, only four programs have allocated any money for "technology transfer," most aimed at tertiary care community hospitals. Since a great many decisions in cancer therapy are made by primary care physicians in rural areas and since "the first decision in cancer management most often determines whether the outcome will be successful,"[3] this inattention to ensuring that physicians are aware of the importance of prevention and of diagnostic and staging procedures is a serious concern.

We spend 10 percent of the gross national product on health care bills, billions for important basic and clinical research, 25 percent of the current NCI budget for research on prevention, and less than 2 percent of the NCI budget to get the word out to the people who manage 85 percent of the care. As if to emphasize this lack of interest in the providers of care, the recent appointments to the National Cancer Advisory Board completely ignored the need for community-physician representation. Is it so surprising that we are not affecting the bottom line?

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1. Bailar JC III, Smith EM. Progress against cancer? N Engl J Med 1986; 314:1226-32.
2. Bailar NEJM article "irresponsible, purposefully misleading," ignored facts, DeVita tells NCAB. The Cancer Letter. May 23, 1986:1-2.
3. Rubin P. Clinical oncology: a multidisciplinary approach. 6th ed. Rochester, N.Y.: American Cancer Society, 1983:vi.

To the Editor: Bailar and Smith concluded from total mortality data that we are losing ground against cancer. Their method may be dominated by the numerous deaths at advanced ages, thereby masking progress in terms of prolonged survival of patients or of delayed onset or prevention of incident cases. Therefore, a complementary approach, free of these problems, might employ years of potential life lost (YPLL) before age 65.[1] This summary measure highlights the leading causes of death among younger persons (Wise RP, et al.: unpublished data).

Application of this YPLL measure to mortality from all causes between 1979 and 1984, with use of the 10 percent current mortality sample from the National Center for Health Statistics, revealed a 12.8 percent decrease in the rate of YPLL per 1000 persons under the age of 65. This reduction in mortality at younger ages was broadly based, with decreases in the YPLL rate for 10 of the 12 leading causes during this period (Fig. 1).

The decrease in the YPLL rate for cancer was 4.1 percent. However, the YPLL rate for cancers other than lung cancer fell faster, decreasing 6.2 percent during this interval. Most of this progress was due to the reduced death rate from cancer (excluding lung cancer) in 45-to-54-year-olds, which decreased from 126.7 to 117.6 per 100,000 persons. In striking contrast, the lung cancer mortality rate in the group 55 to 64 years old increased (146.5 to 156.1 per 100,000), thus reducing the overall improvement for cancer. Bailar and Smith's emphasis on tobacco's role in causing increased cancer is clearly appropriate.

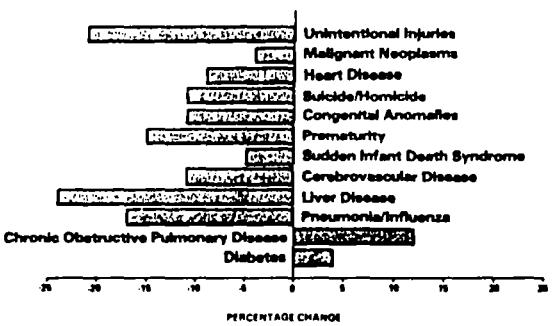

Figure 1. Percentage Change in the YPLL Rate for the Ranked Leading Causes of Premature Mortality in the United States, 1979 to 1984.

The percentage change is calculated as (1984 rate − 1979 rate) × 100/1979 rate. The YPLL rate is the number of years of potential life lost before age 65 per 1000 persons under age 65. Causes of mortality are defined and ranked in conformity with data from *Morbidity and Mortality Weekly Report.*[2] (Source, Centers for Disease Control; unpublished data.)

These data are consistent with a general trend among Americans to live longer that is due to progress (defined in terms of reduced mortality before age 65) against a wide array of diseases, not including chronic obstructive pulmonary disease and diabetes mellitus. As deaths from causes that compete with cancer decrease, more people are at risk of death from malignant conditions. With the reduction of mortality from cardiovascular disease, for example,[3] a larger proportion of deaths at older ages may now be due to cancer.

In addition, some increment in cancer death rates at older ages could also be due to prolonged survival of patients with cancer, which must also be credited as "progress against cancer." Again, the YPLL method would be more likely to reflect such progress than total mortality.

In summary, we suggest that the public health struggle against cancer should also be evaluated in terms of lengthened survival.

The views expressed in this letter do not necessarily reflect any policy or official position of the Food and Drug Administration.

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1. Changes in premature mortality — United States, 1983-1984. MMWR 1986; 35:29-31.
2. Estimated years of potential life lost before age 65 and cause-specific mortality, by cause of death — United States, 1984. MMWR 1986; 35:365.
3. Thom TJ, Epstein FH, Feldman JJ, Leaverton PE. Trends in total mortality and morbidity from heart disease in 26 countries from 1950 to 1978. Int J Epidemiol 1985; 14:510-20.

The above letters were referred to the authors of the article in question, who offer the following reply:

To the Editor: We welcome this interest in the accomplishments and future course of cancer research. We can comment here on only four points raised by these letters.

A cancer-research program that does not reduce overall death rates is not successful, whatever its other accomplishments. Thus, mortality data are critical, despite short delays from diagnosis to death and further short delays in publication. Cancer research was a major activity long before the National Cancer Act of 1971, and most cancer deaths occur within two to three years after diagnosis. (The main exception, breast cancer, accounts for only 9 percent of all cancer deaths.) Major improvements in survival by 1981 should be clearly visible in the 1983 data now available; they are not there.

If the evaluation of progress against cancer should not reflect our failure to contain the rise in deaths from lung cancer, neither should it reflect the fall in cancer of the stomach, cervix, and perhaps other organs for which recent trends are largely unrelated to treatment. We know of no good argument for any omissions at all, and certainly not for lung cancer alone.

Two letters point to percentage drops at younger ages that are larger than percentage rises at older ages, but the pattern is reversed for absolute risks. For the evaluation of progress, a fall from 25.1 per 100,000 to 17.3 (the 31.1 percent decrease at ages 30 through 34) is fundamentally much smaller than a rise from 597.6 to 722.7 (the 20.9 percent increase at ages 65 through 69), even after weighting for population size.

Should progress be measured according to years of life lost before age 65? To do so implies that some lives are worth less than others and that some should not be counted at all. Evaluation should not be based on years of life lost without full public understanding and acceptance of its implications.

The ugly fact remains that overall cancer mortality is rising; if one omits cancer of the lung, stomach, and cervix, it has been essentially unchanged for some 35 years. This cannot be explained away as a statistical artifact, obscured by the clear evidence of progress here and there, or submerged by rosy rhetoric about research results still in the pipeline. And it cannot be ignored.

We repeat our call for a full inquiry into the past, present, and future course of cancer research.

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MORE ON OPEN-CHEST CARDIAC MASSAGE AFTER CARDIAC ARREST

To the Editor: The results of the prospective clinical trial of open-chest cardiopulmonary resuscitation (CPR) reported by Geehr and his associates (May 1 issue)[1] are important, but predictable from data on animals.[1-3] Previously published clinical and animal studies have shown that open-chest CPR provides better hemodynamics than closed-chest compression.[2-5] It remains uncertain, however, whether improvements in hemodynamics result in improved resuscitation and long-term survival. We approached this question in an animal model of cardiac arrest and found that after 15 minutes of closed-chest massage, open-chest CPR improved resuscitation, as compared with continued efforts by closed-chest techniques.[2] However, there was no improvement in resuscitation by open-chest CPR after 25 minutes of closed-chest massage, in spite of improved hemodynamics with open-chest massage.[3] The clinical implications of our study are that open-chest resuscitation will improve survival only if it is begun within 15 to 20 minutes of the onset of cardiac arrest, but will not improve survival if begun after 25 minutes.[3] Geehr et al. have confirmed this latter finding in humans.[1] Further clinical studies are needed to determine if the earlier application of open-chest massage will improve survival.

We believe that open-chest CPR will have a limited but definite role in the treatment of patients in cardiac arrest. Of all the proposed alterations of the standard technique of CPR investigated by our group and others, open-chest CPR results in the most dramatic hemodynamic improvement. Despite this, three important questions remain: Are there newer techniques of closed-chest CPR that are more effective than standard CPR? What features can tell us whether continued efforts with closed-chest CPR will be ineffective? Will open-chest cardiac massage, when applied early (within 15 minutes of arrest), improve resuscitation and result in improved long-term survival without neurologic defects?

We agree with Geehr and his associates that open-chest CPR is not appropriate as a "last-ditch" effort in patients with arrest times of 25 minutes or longer. Such use will only reinforce the negative impression that many physicians now have about open-chest CPR. The exact role of open-chest CPR needs to be determined by appropriate clinical trials firmly based on good experimental data.

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To the Editor: We must be careful not to draw unjustified conclusions from the interesting report of Dr. Geehr and his colleagues.

Reference #7

after menopause. Women whose cancer is diagnosed when they are entering menopause at 54 have a better prognosis than either 54-year-old women who are several years past menopause or 49-year-old menopausal women. The prognosis of middle-aged women with breast cancer probably depends jointly on the chronological relation of diagnosis to menopause and the age at diagnosis.

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1. Rochman H, Conniff ES, Kuk-Nagle KT. Age and incidence of estrogen receptor positive breast tumors. Ann Clin Lab Sci 1985; 15:106-8.
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The above letters were referred to the authors of the article in question, who offer the following reply:

To the Editor: Dr. Daniell suggests that there is a relation between age at diagnosis and the pattern of tumor dissemination. A predominance of visceral spread in older women might contribute to a shorter survival. However, since no curative treatment is available for patients with any type of systemic dissemination, differences in survival time should not translate into a more favorable long-term survival and a higher cure rate among patients with distant metastases first demonstrated at nonvisceral sites. The findings of Daniell thus do not explain the Swedish survival data.

Professor Lindegård has seemingly misunderstood our methods. Our analyses were based on patients available for follow-up only. A bias due to lack of follow-up in patients who emigrated after having had a breast cancer diagnosis reported to the Cancer Registry is unlikely. This hypothesis would require (1) that such women constituted a considerable proportion of all patients, (2) that they were unevenly distributed among the age groups, and (3) that their prognosis differed considerably from that of patients in the same age group who were available for follow-up. None of these requirements is sufficiently met by our data. The differences in the prevalence of breast cancer between Swedes and immigrants have no bearing on our conclusions. They are reasonable in view of the differences in age-specific incidence rates between Sweden and the low-risk and intermediate-risk countries from which most immigrants came.

Gore and Pocock suggest that the "clinical profile" acts as a confounder in the analysis of age–survival relations. Clinical covariates are complex measures, dependent on the biologic features of the tumor, the tumor–host relations, and the temporal progress of tumor growth and dissemination. Our primary aim was to analyze the biologic properties in relation to age. It seems far from clear whether adjustment for "clinical profile" is preferable in this context; it might decrease the power of the analysis without any meaningful gain in internal validity.

Our claim that age has an effect on relative survival beyond the 10th year of follow-up was based not on cumulative rates, but on the persistent difference in annual hazard rates and the consequent continued change in difference between age groups even later than 10 years after diagnosis. This finding probably cannot be refuted by data from the relatively small Western General series, which have been grouped into only three categories.

We do not agree with Dr. Klawansky that hormone-dependent and hormone-independent tumors constitute two distinct populations. Receptor concentration is a continuous — not a dichotomous — variable, and many observations indicate that its clinical correlates behave accordingly. Dr. Klawansky's hypothesis that hormone dependence is related both to age at diagnosis and to survival is reasonable from several points of view, but it does not account for the relations between age and survival observed in our study, which were more pronounced and longer lasting than the difference in survival prospects between patients with receptor-rich and those with receptor-poor tumors.

Our conclusion that "biologic mechanisms other than the hormone dependence of the tumor" may account for the relation between age and survival has been erroneously interpreted to mean that the mechanisms are necessarily of a "nonhormonal" nature. For instance, hormonal regulation of the metastatic process would be a possible explanation for the findings.

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MORE ON PROGRESS AGAINST CANCER

To the Editor: Letters from Bitran[1] and Mann[2] (Oct. 9, 1986, issue) in response to the article by Bailar and Smith[3] (May 8, 1986, issue) imply that prevention is unlikely to have an important impact on mortality from cancer, at least with respect to lung cancer. Much evidence suggests the contrary. Physicians can certainly do more with regard to promoting healthier practices by their patients,[4] but the potential rewards of prevention extend beyond the practitioner's office. Specifically, community health promotion studies have demonstrated a beneficial impact on a wide range of health behaviors (including smoking)[5]; work-site health promotion efforts have shown beneficial effects in hypertension control,[6] exercise,[7] and other health behaviors[8]; and school health education programs offer another promising venue for promoting healthier life styles.

Prevention can work and has. Those seeking progress against cancer might well heed the example of the undisputed progress against cardiovascular disease, which has resulted in a decline in mortality of approximately 25 percent in the United States from 1964 to 1979.[9] One analysis ascribes more than half the decline to changes in life style.[10]

The comment by Bitran regarding rising incidence rates of lung cancer among both white men and women is incorrect. The incidence of lung cancer among white males actually declined by 4 percent between 1982 and 1983[11] — a result of the decline in the prevalence of smoking among males, from 52 percent in 1963 to about 35 percent in 1983.

Although biomedical research is essential to progress in both treatment and prevention and much remains to be learned about the cause of many cancers, present knowledge warrants a stronger attack on the preventable cause of approximately one third of all cancer mortality — cigarette smoking. The failure to reduce the prevalence of smoking further speaks less to the efficacy of prevention than to our failure to fund and promote it adequately.

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To the Editor: Although Bailar and Smith minimize the importance of incidence rates, an examination reveals that increases in cancer rates cannot be ascribed exclusively to tobacco use. Overall cancer incidence has increased sharply, at the rate of 1 percent annually since 1970 and at similar rates as that for lung cancer alone.[1] Incidence rates have also risen sharply for cancers unrelated to smoking, including breast and colon cancer and acute adult nonlymphatic leukemia; only about one third of the overall increase is due to respiratory cancer. For some cancers, the rising incidence rates contrast with constant mortality, as increases appear to have been offset by small improvements in treatment. Moreover, substantial recent increments in mortality rates of cancers not related to smoking have been masked by focusing on overall mortality data alone.[2] For example, from 1979 to 1983 there were marked increases in mortality rates among blacks for cancers of the prostate, lymphatic–hematopoietic system, and breast; lung cancer accounts for, at most, half the recent increase in cancer mortality among black males. Similarly, for the entire U.S. population from 1979 to 1983, there were major increases in cancer-associated mortality rates for cancer of the lymphatic–hematopoietic system and in the category of "all other causes," including malignant diseases such as soft-tissue sarcoma; there were also increases for melanoma and for cancers of major sites such as the colon from 1969 to 1976,[1] although new site categorization by the National Center for Health Statistics makes it difficult to obtain recent comparative data.

Furthermore, there is substantial evidence that occupational and community exposures to carcinogens are major factors in increasing lung cancer rates that cannot be attributed exclusively to smoking. Lung cancer rates are higher among blacks than whites, although a smaller proportion of blacks have ever smoked and black smokers smoke less than white smokers.[3] Increasing proportions of lung cancers are adenocarcinomas, which are either weakly related or unrelated to smoking.[4] Rates for cancers other than lung cancer that are associated with high relative risks among smokers, such as cancer of the buccal cavity, are declining.[5] Geographic patterns of lung cancer closely follow those of petrochemical and other industries and have recently shifted to reflect their migration to the south-central United States, and studies have also incriminated community exposure to atmospheric emissions from industries manufacturing or using industrial carcinogens.[3] High lung cancer rates that are largely insensitive to smoking levels have been identified among various occupational groups.[6] Also, case–control studies have demonstrated an occupational cause in 30 to 40 percent of lung cancers in Norway and Italy.[7]

There is ample support for the growing perception that we have lost the war against cancer and that national policies and priorities, including those of the major concerned institutions — the National Cancer Institute and the American Cancer Society — must be redirected from currently imbalanced and overly optimistic emphasis on chemotherapy and treatment into more promising areas of prevention and control.

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1. Pollack ES, Horm JW. Trends in cancer incidence and mortality in the United States, 1969–76. JNCI 1980; 64:1091-103.
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The above letters were referred to the authors of the article in question, who offer the following reply:

To the Editor: We heartily agree with Gemson that prevention works. We also note, however, that the recently reported small decreases in the incidence of lung cancer are not yet reflected in age-adjusted death rates.[1] Although a drop in mortality from lung cancer will surely follow the fall in incidence, increased efforts to curtail smoking will cause it to come sooner. This triumph of prevention, when it occurs, will far outweigh all the advances in treatment since 1950.

Epstein and Swartz state that cancer incidence rates have been rising sharply, at an annual rate of 1 percent since 1970. We said in our article why we have reservations about the meaning of trends in incidence rates, and more recent data from the National Cancer Institute indicate a smaller increase — about 5 percent for the nine years from 1975 through 1984.[1] Also, there may be a problem in using the 1970 data because they refer to a population base that is different from that of the 1975–1984 rates. Of course, there would be no basis for complacency even if the incidence rate had been declining, and Epstein and Swartz correctly note that the trend (if any) for all cancers combined may mask contrary trends for some specific kinds of cancers.

The 1975–1984 data[1] show welcome and statistically significant decreases in the reported age-adjusted incidence of cancer of the stomach, cervix, and uterine corpus (and unspecified uterine cancer), and of leukemia (all types), as well as significant increases in cancer of the colon–rectum, liver, lung–bronchus, breast, prostate, testis, urinary bladder, and kidney, and in non-Hodgkin's lymphoma and melanoma of the skin.

Epstein and Swartz comment only on the apparent increases in the incidence of some cancers, as well as the clear increases in cancer-associated mortality in black males and in some kinds of cancer in the whole population. This is the converse of the tendency of the National Cancer Institute and others to emphasize the positive.[2,3] We are glad of the support of Epstein and Swartz in promoting a shift of emphasis toward cancer prevention, but we believe that arguments for such a shift must include a strictly evenhanded and objective reading of the situation as a whole. The rate of progress against cancer is discouraging enough even when all the successes are included. The overall rate of death from cancer is rising, and if lung cancer is excluded, the rate has been essentially unchanged for a decade. We see no evidence of any recent change in these patterns. The need for a comprehensive external review of the

entire U.S. national cancer program is more acute now than it was at the time our paper was published.

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1. Sondik EJ, Young JL, Horm JW, Gloeckler LA, eds. Annual cancer statistics review. Washington, D.C.: National Cancer Institute, December 1985.
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"I ACCUSE" THE *JOURNAL* OF UNFAIR JOURNALISM

To the Editor: On January 13, 1898, in an open letter to President Félix Faure on the Dreyfus case, Émile Zola started each paragraph with the words "J'accuse" (I accuse). In this letter I continue this practice.

I accuse the *New England Journal of Medicine* of not providing an equal forum for the debate of issues. Fair journalism calls for equal coverage.

I accuse the *Journal* of publishing, without a balancing view, the article by Bailar and Smith that concluded "we are losing the war against cancer."

I accuse the *Journal* not merely of publishing such controversial views but of issuing press releases to help publicize them. The resultant flood of secondary articles reached the deserts of Arizona.

I accuse the *Journal* of burying balancing views such as those of DeVita (from the National Cancer Institute) and Korn (from Stanford University) (Oct. 9, 1986, issue)* among a welter of letters to the Editor. Neither their views nor any other balancing views have permeated these lay hinterlands.

I accuse the *Journal* of thoughtless weighting of views. Concurrent opposing views should be sought for simultaneous publication. Press releases should be balanced from the start.

I accuse the *Journal* of potentially jeopardizing health care and research in the United States by such practices. I look forward to your rebuttal.

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*DeVita VT Jr, Korn D. Progress against cancer? N Engl J Med 1986; 315:964.

Editor's reply: The *Journal* rarely publishes countervailing opinions on controversial articles in the same issue with the original article. Our usual practice is to rely on our Correspondence section for expressions of opposing views, and that is what we did in the case of the Bailar and Smith article.

Because we received so many letters, both pro and con, we published more than the usual number and devoted five pages in our October 9 issue to that purpose. Far from "burying balancing views," as Dr. Hecht claims, we included among the 12 published letters no less than 6 that were critical of the Bailar and Smith article, including the letter from DeVita and Korn.

In view of their strong criticisms of the Bailar and Smith article, DeVita and his colleagues were invited to submit a full-length article presenting their view of the subject, but they declined.

As for the "balanced" press releases Dr. Hecht demands from us, he needs to know that the *Journal* issues no press releases of any kind. We don't believe that is our job. We let the media decide whether any of our articles are newsworthy and how they are to be interpreted to the public.

On this subject (progress against cancer), as on any other controversial health topic, we remain open to responsible views from all sides. The Bailar and Smith article was unsolicited. We do not set the agenda, nor do we influence what our contributors choose to say. If Dr. Hecht can think of a better way for us to deal with scientific debate, we would welcome his suggestions.

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HERPES SIMPLEX VIRUS INFECTIONS

To the Editor: In their excellent review of the clinical spectrum of herpes simplex virus (HSV) infections, Corey and Spear (March 13, 1986, issue)[1] neglected to discuss the less commonly acknowledged HSV infections involving just the skin. Although cutaneous involvement by HSV is associated with concomitant lesions of the mucous membranes or a disseminated HSV infection, it may also occur alone as an initial manifestation of an HSV infection. We recently evaluated a patient with cutaneous involvement by HSV that occurred without known exposure to the virus or other identifiable risk factors usually associated with HSV infections.

A 23-year-old woman had a vesicular eruption on the left knee that was associated with generalized malaise, fever, paresthesias, and inguinal adenopathy. Five weeks earlier she had had a second-degree burn on the same site and had intermittently "picked off" the eschar. The vesicular lesions resolved without therapy in about 10 days. Six months later a similar eruption developed on the same site; the patient sought medical care and was treated with oral cephalosporins for a presumed cellulitis. The lesions resolved in about seven days. After a third outbreak, the patient was seen at the University of Connecticut Health Center and was found to have clusters of vesicles on an erythematous base (Fig. 1), with associated tenderness and localized erythema. A Tzanck smear revealed

Figure 1. Cutaneous Herpes Simplex Virus Type 2 Infection of the Left Knee.

Reference #8

implications for educating consumers. The error rate for this test is approximately 4 percent when using large families for linkage analysis, but it is still unknown when smaller families are used. This error rate means that there will be a certain percentage of false positive and false negative tests. Until closer markers are discovered, or until the gene for Huntington's Disease is found, we have no way of knowing which persons will be incorrectly advised of their marker status until either they begin to show signs of this disease or have outlived their period of risk. Thus, individuals need to understand not only the genetic aspects of these tests, but the concepts of risk and probability, and how to interpret their personal risk to make decisions about their futures. These latter topics are notoriously difficult to understand, and they present a major educational challenge.

A second concern is the possible misuse of information available through genetic testing. Previous experience with insurance companies denying coverage to those testing positive for exposure to the AIDS virus and with employment discrimination based on screening for the sickle-cell trait has shown that concern for privacy and confidentiality is justified. One fear is that when these tests become clinically available, only those wealthy enough to pay for them outright, thus avoiding third-party involvement, will be able to keep private their genetic status. In the absence of any clear sense of how insurance companies and employers are going to handle this information, individuals desiring genetic testing are well advised to be cautious about disclosing either their participation in testing or the results.

On a positive note, those who present themselves for voluntary testing are likely to be those who have decided that the advantages of knowing what is in store for them outweigh the disadvantages. Knowing that one is likely to develop a disease can give one time to prepare for it and thus reduce its impact. In fact, much of the fear that accompanies diagnoses such as Huntington's Disease or Alzheimer's Disease has to do with our present inability to deal adequately with disorders requiring long-term care. Those who know their fate in advance may be motivated to work for changes in the health care system.

This new technology by its very nature will undoubtedly stir controversy in a country such as ours, with its pluralism of values. At this stage of its introduction, it would be tragic to interfere with the ability of many individuals to benefit because of the mishandling of a few.

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The war on cancer: views from the front

Dr. John Bailar's article, "Rethinking the War on Cancer" (*Issues*, Fall 1987), is a challenge to current cancer research policy. Bailar believes that a major shift in priorities toward prevention of cancer is necessary. He is partially correct. Prevention of disease is probably the only way to substantially reduce morbidity and mortality.

Only cigarette smoking, radiation, alcohol consumption, sunlight, and a few occupational risks have been clearly identified as important risk factors potentially amenable to intervention, at least within the United States. Bailar is wrong in believing that there are a large number of preventive strategies sitting on the shelf waiting to be implemented.

Bailar is also correct in suggesting that the "magic bullet" approach to cancer research may be good publicity but not good policy. The belief that a cure for cancer is only an oncogene away results in a false promise for the future and failure to implement what we already know today.

For example, more than 10 years after the National Cancer Institute (NCI) sponsored important clinical trials and demonstration projects of early detection of breast cancer, only a very small number of women at risk are being screened. It is hard to compare NCI's efforts in promoting breast cancer detection with the tremendous efforts of the National High Blood Pressure Education Program and the remarkable decrease in stroke mortality. The failure is not with NCI but rather with the organization of medical care in the United States. In order to develop effective community-based, high-quality cancer care, the efforts of NCI and those that pay the bills for medical care of cancer patients must be coordinated.

Bailar urges a reorganization of personnel and projects. He may be correct. Certainly, there must be new approaches to cancer epide-

miology and etiological research. Clinical trials and community intervention programs in primary and secondary prevention need to be implemented much more aggressively and effectively. And Bailar's initial premise that prevention is the cornerstone of cancer control is correct. Unfortunately, we need better science, even more than a change in policy, to give us the tools necessary for major successes.

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John Bailar's basic premise ignores both the mandate given to the National Cancer Institute by the Cancer Act of 1971 and the structure of the National Cancer Program.

The Cancer Act mandated support for basic research as its first priority. It also identified specific programs to apply the results of basic research, but qualified the support for these programs by the words "insofar as feasible," an indication of the uncertainty that existed in 1971 as to how much research could be applied effectively. We have adhered to these priorities and directed over two-thirds of our budget to support for basic research.

Only 15 percent of our budget now supports the maintenance and continued development of a network of programs to make it "feasible" to apply the results of basic research in prevention, diagnosis, and treatment. Part of this network is the Surveillance, Epidemiology and End-Results program (SEER) established in 1973 to monitor progress against cancer as well as the process of technology transfer. The other essential elements of this network—the Cancer Prevention and Control Program, some 58 Cancer Research Centers, over 50 Community Clinical Oncology Programs, the Cancer Information Service (1-800-4-CANCER), the PDQ Computer-Based Cancer Information System, and the network of organizations that conduct cooperative clinical trials in prevention, diagnosis, and treatment—were completed in 1984. It was then that the Institute articulated goals we thought could be achieved based on the full application of knowledge then at hand.

The support for basic research has been an extraordinary success. Many of the advances in molecular genetics we herald today can be traced to the infusion of resources from NCI-supported research programs that Dr. Bailar deprecates directly or by implication. If the "war on cancer" is defined in terms of the advances in our understanding of the cascade of molecular and genetic events that lead the normal cell to become malignant—knowledge whose main value will be felt most in cancer prevention programs—or in our knowledge of events that allow the cell to migrate and kill the host, we have come further in this battle than even the most optimistic scientist would have imagined a mere 16 years ago, when the metaphoric "war" actually began. Any poll of the scientific community will bear out this observation, which is why so few bother to respond to Dr. Bailar's unidimensional assessment of scientific progress using age-adjusted death rates. We make no apologies to anyone for this investment and point proudly to these achievements in fundamental science. This is the main battlefront of the war on cancer and all other diseases.

Dr. Bailar chooses to ignore the large investment we have made in prevention since the beginning of the National Cancer Program, and, moreover, the continuing success of this program as evidenced by the reduction in the percentage of the public who smoke; the development of a network of federally sponsored programs that now deal with applied studies in chemoprevention and in workplace and environmental safety; the development of knowledge about the links between diet and cancer (such as the potential for reducing risks by lowering dietary fat and calories and by increasing dietary fiber); and the identification of causal relationships between asbestos and lung cancer, between sun exposure and melanoma, and between chlorinated water and bladder cancer, to cite just a few. He also fails to mention the advances in early detection of breast cancer, which, if fully applied, could reduce the mortality from this disease by more than 30 percent, and the research under way to validate methods for the early detection of colon and rectal cancer.

We are quite optimistic that intervention programs in prevention will work. Half of the reduction in mortality we see for the year 2000 can be achieved by effective prevention.

Dr. Bailar sees a failure in the long continuing rise in the incidence of lung cancer "stemming

from our limited success in reducing tobacco smoking." In fact, this view is too pessimistic. Since the Surgeon General's Report 22 years ago, over 40 million Americans have stopped smoking. But because the damage done by smoking takes some 10 to 15 years to repair, only now do we see significant impact as a result of smoking cessation programs. Lung cancer incidence in white males is headed downward for the first time in 50 years and, in addition, the increasing incidence trend in black males has leveled off. Both of these changes are due to major reductions in the percentage of men who smoke. Progress in reducing smoking among women, however, has been slower and reflects, no doubt, the tremendous amounts spent on advertising by the cigarette companies targeted for the female share of the market.

National clinical trials groups already existed in 1971, when the Cancer Act was passed, to develop and apply the results of treatment research. Their effort was devoted primarily to treatment research in children with cancer and young adult patients with hematologic malignancies. These studies have reduced cancer death rates, showing that, when tracked over an adequate period of time, treatment advances do influence national statistics. The clinical trials groups required expansion so that investigators could be added who would study the more common visceral tumors. As a result of this expansion, new treatments have been developed that reduce mortality as well as morbidity within the study populations in breast, colon, rectal, lung, bladder, and ovarian cancers and sarcomas of soft tissue—tumors that make up the vast majority of cancers.

The first positive clinical trials (in breast cancer) were reported in 1975; the most recent in colon and bladder cancer this year. These clinical advances are not a wish list, as they were in 1971, but programs that exist, have been published, and represent new leads that can be applied while they are being improved. They should have an impact when widely used, just as past advances did.

Our SEER program tells us and Dr. Bailar that the impact of many of these advances has not yet been felt nationwide. However, a substantial part of the age-specific decline in mortality, especially that seen in the 45–54 age group, has appeared since 1980 and is due to the application of some of those treatments. In most cases, the advances are too recent to be felt beyond the population captured in the clinical trials, which, for common cancers, is often less than one percent of the total. In other cases (breast cancer and diffuse large cell lymphomas) we would have expected to see a greater national impact from this research by now. In those two tumors, our data indicate problems in technology transfer, which gives us the opportunity to solve these problems.

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The author replies:

Most of what Drs. DeVita and Sondik say is quite true—and quite irrelevant.

The point at issue is not what we have learned, but what we have accomplished. Our cancer death rate is still going up (as a rate per 100,000 population, age-adjusted), our cancer incidence rate is going up (also age-adjusted), and our cancer case survival rate (adjusted for "normal" expected mortality) has been essentially unchanged for some years.

Drs. DeVita and Sondik refer to "extraordinary success" in basic research (and I agree), but they go on to define the "war on cancer" in terms of basic research findings. I do not.

I know of no knowledgeable person who thinks that any of the three most basic broad measures of cancer—death rate, incidence rate, case survival rate—will be markedly different in two years, or five, and few who would bet very much on even the year 2000, now just 12 years away, when the National Cancer Institute's goal of cutting the cancer death rate by 50 percent is supposed to have been realized.

I fervently hope, like Dr. DeVita, Dr. Sondik, and everyone else involved in the effort to conquer cancer, that success will come at least as soon, and at least as abundantly, as NCI's goal projects. But hope, already often disappointed in this matter, can make only a crumbling base for public policy.

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NATIONAL CANCER INSTITUTE

Fax Transmittal

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Cancer Information Service Branch

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301-496-5583, ext. ____
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Date 6/10/97

To CHRISTINE CONGLETON

Fax Number 301-594-6777

From LINDA SLAN

Cover Sheet plus ____ Pages Transmitted

Message

Public Law 92-218
92nd Congress, S. 1828
December 23, 1971

An Act

To amend the Public Health Service Act so as to strengthen the National Cancer Institute and the National Institutes of Health in order more effectively to carry out the national effort against cancer.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

The National Cancer Act of 1971.

SHORT TITLE

SECTION 1. This Act may be cited as "The National Cancer Act of 1971".

FINDINGS AND DECLARATION OF PURPOSE

SEC. 2. (a) The Congress finds and declares—

(1) that the incidence of cancer is increasing and cancer is the disease which is the major health concern of Americans today;

(2) that new scientific leads, if comprehensively and energetically exploited, may significantly advance the time when more adequate preventive and therapeutic capabilities are available to cope with cancer; 85 STAT. 778 85 STAT. 779

(3) that cancer is a leading cause of death in the United States;

(4) that the present state of our understanding of cancer is a consequence of broad advances across the full scope of the biomedical sciences;

(5) that a great opportunity is offered as a result of recent advances in the knowledge of this dread disease to conduct energetically a national program against cancer;

(6) that in order to provide for the most effective attack on cancer it is important to use all of the biomedical resources of the National Institutes of Health; and

(7) that the programs of the research institutes which comprise the National Institutes of Health have made it possible to bring into being the most productive scientific community centered upon health and disease that the world has ever known.

(b) It is the purpose of this Act to enlarge the authorities of the National Cancer Institute and the National Institutes of Health in order to advance the national effort against cancer.

NATIONAL CANCER PROGRAM

SEC. 3. (a) Part A of title IV of the Public Health Service Act is amended by adding after section 406 the following new sections: 58 Stat. 707; 62 Stat. 464. 42 USC 281.

"NATIONAL CANCER PROGRAM

"SEC. 407. (a) The Director of the National Cancer Institute shall coordinate all of the activities of the National Institutes of Health relating to cancer with the National Cancer Program.

"(b) In carrying out the National Cancer Program, the Director of the National Cancer Institute shall: National Cancer Institute Director, duties.

"(1) With the advice of the National Cancer Advisory Board, plan and develop an expanded, intensified, and coordinated cancer research program encompassing the programs of the National Cancer Institute, related programs of the other research institutes, and other Federal and non-Federal programs.

"(2) Expeditiously utilize existing research facilities and personnel of the National Institutes of Health for accelerated exploration of opportunities in areas of special promise.

"(3) Encourage and coordinate cancer research by industrial concerns where such concerns evidence a particular capability for such research.

"(4) Collect, analyze, and disseminate all data useful in the prevention, diagnosis, and treatment of cancer, including the establishment of an international cancer research data bank to collect, catalog, store, and disseminate insofar as feasible the results of cancer research undertaken in any country for the use of any person involved in cancer research in any country.

85 STAT. 779
85 STAT. 780

"(5) Establish or support the large-scale production or distribution of specialized biological materials and other therapeutic substances for research and set standards of safety and care for persons using such materials.

"(6) Support research in the cancer field outside the United States by highly qualified foreign nationals which research can be expected to inure to the benefit of the American people; support collaborative research involving American and foreign participants; and support the training of American scientists abroad and foreign scientists in the United States.

"(7) Support appropriate manpower programs of training in fundamental sciences and clinical disciplines to provide an expanded and continuing manpower base from which to select investigators, physicians, and allied health professions personnel, for participation in clinical and basic research and treatment programs relating to cancer, including where appropriate the use of training stipends, fellowships, and career awards.

"(8) Call special meetings of the National Cancer Advisory Board at such times and in such places as the Director deems necessary in order to consult with, obtain advice from, or to secure the approval of projects, programs, or other actions to be undertaken without delay in order to gain maximum benefit from a new scientific or technical finding.

"(9)(A) Prepare and submit, directly to the President for review and transmittal to Congress, an annual budget estimate for the National Cancer Program, after reasonable opportunity for comment (but without change) by the Secretary, the Director of the National Institutes of Health, and the National Cancer Advisory Board; and (B) receive from the President and the Office of Management and Budget directly all funds appropriated by Congress for obligation and expenditure by the National Cancer Institute.

President's Cancer Panel. Membership.

"(c)(1) There is established the President's Cancer Panel (hereinafter in this section referred to as the 'Panel') which shall be composed of three persons appointed by the President, who by virtue of their training, experience, and background are exceptionally qualified to appraise the National Cancer Program. At least two of the members of the Panel shall be distinguished scientists or physicians.

Term.

"(2)(A) Members of the Panel shall be appointed for three-year terms, except that (i) in the case of two of the members first appointed, one shall be appointed for a term of one year and one shall be appointed for a term of two years, as designated by the President at the time of appointment, and (ii) any member appointed to fill a vacancy occurring prior to the expiration of the term for which his predecessor was appointed shall be appointed only for the remainder of such term.

"(B) The President shall designate one of the members to serve as Chairman for a term of one year.

Compensation.

"(C) Members of the Panel shall each be entitled to receive the daily equivalent of the annual rate of basic pay in effect for grade

GS–18 of the General Schedule for each day (including traveltime) during which they are engaged in the actual performance of duties vested in the Panel, and shall be allowed travel expenses (including a per diem allowance) under section 5703(b) of title 5, United States Code. 5 USC 5332 note.

"(3) The Panel shall meet at the call of the Chairman, but not less often than twelve times a year. A transcript shall be kept of the proceedings of each meeting of the Panel, and the Chairman shall make such transcript available to the public. 80 Stat. 499; 83 Stat. 190. Meetings. Transcripts, availability.

"(4) The Panel shall monitor the development and execution of the National Cancer Program under this section, and shall report directly to the President. Any delays or blockages in rapid execution of the Program shall immediately be brought to the attention of the President. The Panel shall submit to the President periodic progress reports on the Program and annually an evaluation of the efficacy of the Program and suggestions for improvements, and shall submit such other reports as the President shall direct. At the request of the President, it shall submit for his consideration a list of names of persons for consideration for appointment as Director of the National Cancer Institute. Reports to President.

"NATIONAL CANCER RESEARCH AND DEMONSTRATION CENTERS

"SEC. 408. (a) The Director of the National Cancer Institute is authorized to provide for the establishment of fifteen new centers for clinical research, training, and demonstration of advanced diagnostic and treatment methods relating to cancer. Such centers may be supported under subsection (b) or under any other applicable provision of law.

"(b) The Director of the National Cancer Institute, under policies established by the Director of the National Institutes of Health and after consultation with the National Cancer Advisory Board, is authorized to enter into cooperative agreements with public or private nonprofit agencies or institutions to pay all or part of the cost of planning, establishing, or strengthening, and providing basic operating support for existing or new centers (including, but not limited to, centers established under subsection (a)) for clinical research, training, and demonstration of advanced diagnostic and treatment methods relating to cancer. Federal payments under this subsection in support of such cooperative agreements may be used for (1) construction (notwithstanding any limitation under section 405), (2) staffing and other basic operating costs, including such patient care costs as are required for research, (3) training (including training for allied health professions personnel), and (4) demonstration purposes; but support under this subsection (other than support for construction) shall not exceed $5,000,000 per year per center. Support of a center under this section may be for a period of not to exceed three years and may be extended by the Director of the National Cancer Institute for additional periods of not more than three years each, after review of the operations of such center by an appropriate scientific review group established by the Director of the National Cancer Institute. 58 Stat. 708. 42 USC 285.

"CANCER CONTROL PROGRAMS

"SEC. 409. (a) The Director of the National Cancer Institute shall establish programs as necessary for cooperation with State and other health agencies in the diagnosis, prevention, and treatment of cancer.

"(b) There are authorized to be appropriated to carry out this Appropriation.

section $20,000,000 for the fiscal year ending June 30, 1972, $30,000,000 for the fiscal year ending June 30, 1973, and $40,000,000 for the fiscal year ending June 30, 1974.

"AUTHORITY OF DIRECTOR

"SEC. 410. The Director of the National Cancer Institute (after consultation with the National Cancer Advisory Board), in carrying out his functions in administering the National Cancer Program and without regard to any other provision of this Act, is authorized—

"(1) if authorized by the National Cancer Advisory Board, to obtain (in accordance with section 3109 of title 5, United States Code, but without regard to the limitation in such section on the number of days or the period of such service) the services of not more than fifty experts or consultants who have scientific or professional qualifications;

80 Stat. 416.

"(2) to acquire, construct, improve, repair, operate, and maintain cancer centers, laboratories, research, and other necessary facilities and equipment, and related accommodations as may be necessary, and such other real or personal property (including patents) as the Director deems necessary; to acquire, without regard to the Act of March 3, 1877 (40 U.S.C. 34), by lease or otherwise through the Administrator of General Services, buildings or parts of buildings in the District of Columbia or communities located adjacent to the District of Columbia for the use of the National Cancer Institute for a period not to exceed ten years;

19 Stat. 370.

"(3) to appoint one or more advisory committees composed of such private citizens and officials of Federal, State, and local governments as he deems desirable to advise him with respect to his functions;

"(4) to utilize, with their consent, the services, equipment, personnel, information, and facilities of other Federal, State, or local public agencies, with or without reimbursement therefor;

"(5) to accept voluntary and uncompensated services;

"(6) to accept unconditional gifts, or donations of services, money, or property, real, personal, or mixed, tangible or intangible;

"(7) to enter into such contracts, leases, cooperative agreements, or other transactions, without regard to sections 3648 and 3709 of the Revised Statutes of the United States (31 U.S.C. 529, 41 U.S.C. 5), as may be necessary in the conduct of his functions, with any public agency, or with any person, firm, association, corporation, or educational institution; and

"(8) to take necessary action to insure that all channels for the dissemination and exchange of scientific knowledge and information are maintained between the National Cancer Institute and the other scientific, medical, and biomedical disciplines and organizations nationally and internationally.

"SCIENTIFIC REVIEW; REPORTS

Regulations.

"SEC. 410A. (a) The Director of the National Cancer Institute shall, by regulation, provide for proper scientific review of all research grants and programs over which he has authority (1) by utilizing, to the maximum extent possible, appropriate peer review groups established within the National Institutes of Health and composed prin-

cipally of non-Federal scientists and other experts in the scientific and disease fields, and (2) when appropriate, by establishing, with the approval of the National Cancer Advisory Board and the Director of the National Institutes of Health, other formal peer review groups as may be required.

"(b) The Director of the National Cancer Institute shall, as soon as practicable after the end of each calendar year, prepare in consultation with the National Cancer Advisory Board and submit to the President for transmittal to the Congress a report on the activities, progress, and accomplishments under the National Cancer Program during the preceding calendar year and a plan for the Program during the next five years. Report to Congress.

"NATIONAL CANCER ADVISORY BOARD

"SEC. 410B. (a) There is established in the National Cancer Institute a National Cancer Advisory Board (hereinafter in this section referred to as the 'Board') to be composed of twenty-three members as follows: Membership.

"(1) The Secretary, the Director of the Office of Science and Technology, the Director of the National Institutes of Health, the chief medical officer of the Veterans' Administration (or his designee), and a medical officer designated by the Secretary of Defense shall be ex officio members of the Board.

"(2) Eighteen members appointed by the President.

Not more than twelve of the appointed members of the Board shall be scientists or physicians and not more than eight of the appointed members shall be representatives from the general public. The scientists and physicians appointed to the Board shall be appointed from persons who are among the leading scientific or medical authorities outstanding in the study, diagnosis, or treatment of cancer or in fields related thereto. Each appointed member of the Board shall be appointed from among persons who by virtue of their training, experience, and background are especially qualified to appraise the programs of the National Cancer Institute.

"(b)(1) Appointed members shall be appointed for six-year terms, except that of the members first appointed six shall be appointed for a term of two years, and six shall be appointed for a term of four years, as designated by the President at the time of appointment. Term.

"(2) Any member appointed to fill a vacancy occurring prior to expiration of the term for which his predecessor was appointed shall serve only for the remainder of such term. Appointed members shall be eligible for reappointment and may serve after the expiration of their terms until their successors have taken office.

"(3) A vacancy in the Board shall not affect its activities, and twelve members thereof shall constitute a quorum.

"(4) The Board shall supersede the existing National Advisory Cancer Council, and the appointed members of the Council serving on the effective date of this section shall serve as additional members of the Board for the duration of their terms then existing, or for such shorter time as the President may prescribe. National Advisory Cancer Council, supersedure.

"(c) The President shall designate one of the appointed members to serve as Chairman for a term of two years.

"(d) The Board shall meet at the call of the Director of the National Cancer Institute or the Chairman, but not less often than four times a year and shall advise and assist the Director of the National Cancer Institute with respect to the National Cancer Program.

"(e) The Director of the National Cancer Institute shall designate a member of the staff of the Institute to act as Executive Secretary of the Board.

"(f) The Board may hold such hearings, take such testimony, and sit and act at such times and places as the Board deems advisable to investigate programs and activities of the National Cancer Program.

Report to President and Congress.

"(g) The Board shall submit a report to the President for transmittal to the Congress not later than January 31 of each year on the progress of the National Cancer Program toward the accomplishment of its objectives.

Compensation.

"(h) Members of the Board who are not officers or employees of the United States shall receive for each day they are engaged in the performance of the duties of the Board compensation at rates not to exceed the daily equivalent of the annual rate in effect for GS-18 of the General Schedule, including traveltime; and all members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703, title 5, United States Code, for person in the Government service employed intermittently.

5 USC 5332 note.

80 Stat. 499; 83 Stat. 190.

"(i) The Director of the National Cancer Institute shall make available to the Board such staff, information, and other assistance as it may require to carry out its activities.

"AUTHORIZATION OF APPROPRIATIONS

"SEC. 410C. For the purpose of carrying out this part (other than section 409), there are authorized to be appropriated $400,000,000 for the fiscal year ending June 30, 1972; $500,000,000 for the fiscal year ending June 30, 1973; and $600,000,000 for the fiscal year ending June 30, 1974."

Ante, p. 781.

(b)(1) Section 402 of the Public Health Service Act is amended by adding at the end thereof the following:

58 Stat. 707; Infra. 42 USC 282.

"(b) Under procedures approved by the Director of the National Institutes of Health, the Director of the National Cancer Institute may approve grants under this Act for cancer research or training—

"(1) in amounts not to exceed $35,000 after appropriate review for scientific merit but without the review and recommendation by the National Cancer Advisory Board prescribed by section 403(c), and

"(2) in amounts exceeding $35,000 after appropriate review for scientific merit and recommendation for approval by such Board as prescribed by section 403(c)."

(2) Section 402 of such Act is further amended—

(A) by inserting "(a)" immediately after "SEC. 402."; and

(B) by redesignating paragraphs (a), (b), (c), (d), (e), (f), and (g) as paragraphs (1), (2), (3), (4), (5), (6), and (7), respectively.

42 USC 283.

(3) Section 403(c) of such Act is amended by striking out "In carrying out" and inserting in lieu thereof "Except as provided in section 402(b), in carrying out".

Supra.

REPORT TO CONGRESS

SEC. 4. (a) The President shall carry out a review of all administrative processes under which the National Cancer Program, established under part A of title IV of the Public Health Service Act, will

58 Stat. 707; 62 Stat. 464. 42 USC 281.

operate, including the processes of advisory council and peer group reviews, in order to assure the most expeditious accomplishment of the objectives of the Program. Within one year of the date of enactment of this Act the President shall submit a report to Congress of the findings of such review and the actions taken to facilitate the conduct of the Program, together with recommendations for any needed legislative changes. Report to Congress.

(b) The President shall request of the Congress without delay such additional appropriations (including increased authorizations) as are required to pursue immediately any development in the National Cancer Program requiring prompt and expeditious support and for which regularly appropriated funds are not available. Additional Appropriations.

PRESIDENTIAL APPOINTMENTS

SEC. 5. Title IV of the Public Health Service Act is amended by adding after part F the following new part: 58 Stat. 707; 82 Stat. 771. 42 USC 281.

"PART G—ADMINISTRATIVE PROVISIONS

"DIRECTORS OF INSTITUTES

"SEC. 454. The Director of the National Institutes of Health and the Director of the National Cancer Institute shall be appointed by the President. Except as provided in section 407(b)(9), the Director of the National Cancer Institute shall report directly to the Director of the National Institutes of Health." Ante, p. 780.

CONFORMING AMENDMENTS

SEC. 6. (a)(1) Section 217 of the Public Health Service Act is amended (A) by striking out "National Advisory Cancer Council," each place it occurs in subsection (a), and (B) by striking out "cancer," in subsections (a) and (b) of such section. 64 Stat. 446. 42 USC 218.

(2) Sections 301(d), 301(i), 402, and 403(c) of such Act are each amended by striking out "National Advisory Cancer Council" and inserting in lieu thereof "National Cancer Advisory Board". 42 USC 241, 282. Ante, p. 784.

(3) Section 403(b) of such Act is amended by striking out "National Cancer Advisory Council" and inserting in lieu thereof "National Cancer Advisory Board". 58 Stat. 707. 42 USC 283.

(4) Section 404 of such Act is amended— 42 USC 284.

(A) by striking out "council" in the matter preceding paragraph (a) and inserting in lieu thereof "National Cancer Advisory Board", and

(B) by striking out "COUNCIL" in the section heading and inserting in lieu thereof "BOARD".

EFFECTIVE DATE

SEC. 7. (a) This Act and the amendments made by this Act shall take effect sixty days after the date of enactment of this Act or on such prior date after the date of enactment of this Act as the President shall prescribe and publish in the Federal Register. Publication in Federal Register.

(b) The first sentence of section 454 of the Public Health Service Act (added by section 5 of this Act) shall apply only with respect to appointments made after the effective date of this Act (as prescribed by subsection (a)).

(c) Notwithstanding the provisions of subsection (a), members of the National Cancer Advisory Board (authorized under section 410B of the Public Health Service Act, as added by this Act) may be appointed, in the manner provided for in such section, at any time after the date of enactment of this Act. Such officers shall be compensated from the date they first take office, at the rates provided for in such section 410B.

Ante, p. 783.

Approved December 23, 1971.

LEGISLATIVE HISTORY:

HOUSE REPORTS: No. 92-659 accompanying H.R. 11302 (Comm. on Interstate and Foreign Commerce) and No. 92-722 (Comm. of Conference).
SENATE REPORTS: No. 92-247 (Comm. on Labor and Public Welfare) and No. 92-565 (Comm. of Conference).
CONGRESSIONAL RECORD, Vol. 117 (1971):
July 7, considered and passed Senate.
Nov. 15, considered and passed House, amended in lieu of H.R. 11302.
Dec. 9, House agreed to conference report.
Dec. 9, 10, Senate agreed to conference report.
WEEKLY COMPILATION OF PRESIDENTIAL DOCUMENTS, Vol. 7, No. 52:
Dec. 23, Presidential statement and remarks.

- Met c Hamilton Jordan in Atlanta during campaign.
- Organizing survivors.
- Short mtg.
- Political potential of linking to them, talking to them, working in gov't.
- A gift to the VP.

At EK suggestion to follow-up on their mtg. - Scheduling.

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-

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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-

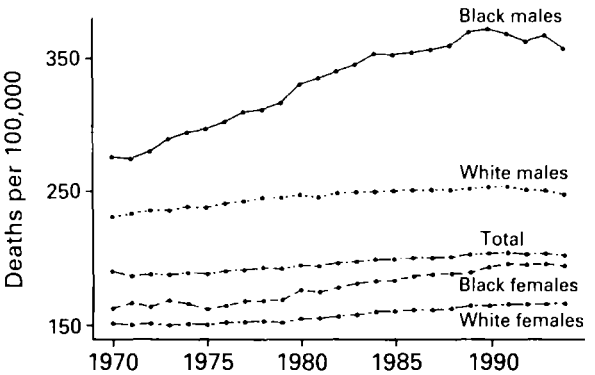

Figure 1. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population and According to Race and Sex.

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

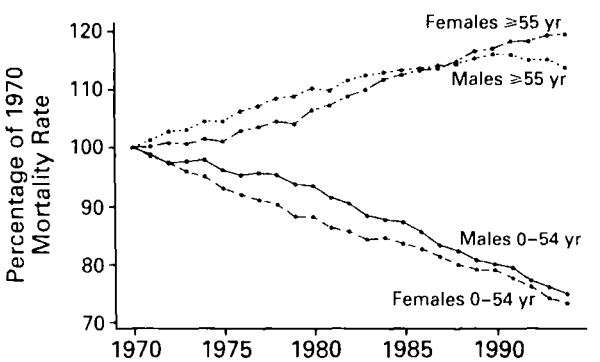

Figure 2. Mortality from All Malignant Neoplasms, 1970 through 1994, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

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

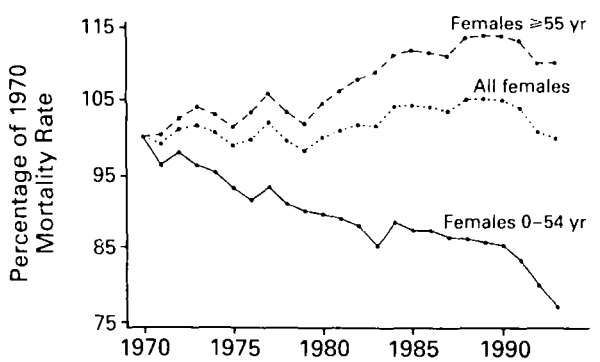

Figure 3. Mortality from Breast Cancer, 1970 through 1993, in the Total U.S. Female Population as a Percentage of the Rate in 1970, According to Age.

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

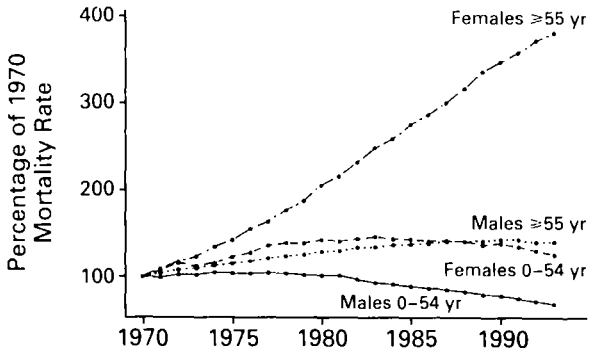

Figure 4. Mortality from Cancer of the Trachea, Bronchus, or Lung, 1970 through 1993, in the Total U.S. Population as a Percentage of the Rate in 1970, According to Age and Sex.

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

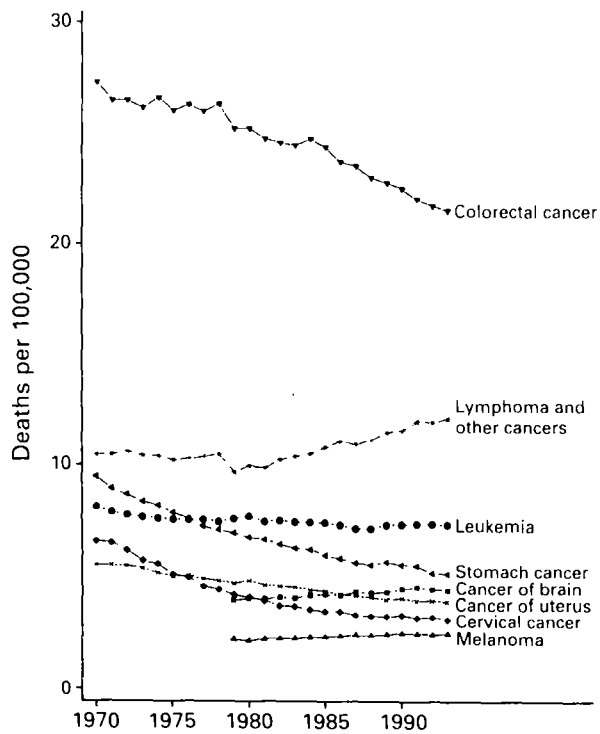

Figure 5. Mortality from Cancer at Selected Sites, 1970 through 1993, in the Total U.S. Population.

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.

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.

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October 21, 1998

REMARKS BY THE PRESIDENT AT NATIONAL BREAST CANCER AWARENESS EVENT

THE WHITE HOUSE

Office of the Press Secretary

For Immediate Release October 21, 1998

REMARKS BY THE PRESIDENT
AT NATIONAL BREAST CANCER AWARENESS EVENT

The East Room

4:15 P.M. EDT

THE PRESIDENT: Thank you very much. I'm delighted to be here with this distinguished panel of people, and I hope I can communicate a little bit of what we've tried to do in this area in just a few moments. As all of you know I think, I have been spending most of the last week in the Middle East peace talks at Wye Plantation on the Eastern Shore. And when I conclude my remarks, I have to go take a call from Secretary Albright and see if I'm going back. So I hope you'll forgive me for leaving.

Let me say I'm delighted to be here with all of you. I thank all of you for your work. I am glad to see Senator Jeffords here. I used to refer to Senator Jeffords as my favorite Republican, and then I was informed that I had endangered his committee chairmanship and his physical well-being. (Laughter.) So I never do that anymore, but I'm honored to have you back in the White House, Senator. And Mayor Beverly O'Neill, from Long Beach, California, thank you for coming. And to all the rest of you.

Twenty-five years ago, America declared war on cancer. Twenty-five years from now, we have a good chance to have won the war. I hope the war on cancer 25 years from now will have about as much meaning to children in school as the War of 1812. I hope school children don't even know what chemotherapy means.

For nearly six years, we have worked hard to bring us closer to that day. We've helped cancer patients to keep their health coverage when they change jobs, accelerated the approval of cancer drugs while maintaining high standards of safety; continually

increased funding for cancer research.

Recently, I named Dr. Jane Henney the first woman, and the first oncologist, to be the Commissioner of the Food and Drug Administration. And I am pleased to report that about two hours ago she was actually confirmed by the United States Senate. (Applause.)

Thanks to the work of a lot of you in this room, we have made genuine process. We're closing in on the genetic causes of breast cancer, colon cancer, prostate cancer, and now testing medicines to actually prevent those cancers. New tools for screening and diagnosis are returning to many patients the promise of a long and healthy life. From 1991 to 1995, cancer death rates actually dropped for the first time in history.

I'm especially proud of the five years of progress we've made in prevention, detection and treatment of breast cancer. Not one day goes by that I don't think about my mother and, through her, all the other women in this country who have had that dreaded disease. It requires more than courage to deal with it. We all owe it to ourselves and our future to make the sustained commitment to research that once and for all can win this war.

Without research there would be no mammography. Without research there would be no genetic testing for vulnerability to breast cancer. Without research there would be no -- how do you pronounce that -- tamoxifin. I practiced this twice this morning --(laughter.) But since then, my chain of thought has been interrupted. (Laughter.) Anyway, we wouldn't have it without research. (Laughter.)

This afternoon, before I came over here, I signed the balanced budget that we fought so hard in the last days of this Congress. It has, among other things, breakthrough funding for cancer research and a general, large increase in research funding for our country's future -- a part of the commitment that Hillary and I made when we ask Americans to honor the millennium by honoring our past and envisioning our future.

I'm pleased that the new budget includes a record increase of $400 million in new support for the National Cancer Institute. With nearly $3 billion in funding, NCI now will be able to fund critical new research, including a trial to expand the use of Herceptin to treat breast cancer earlier, and 10 more new clinical trials for breast cancer treatment. This is an important victory for women's health. It reflects a balanced budget that honors our values. And this, as in so many other things, I also would like to thank the Vice President, who spearheaded our drive to get the research funding into the budget.

If you will, I'd like to mention just a couple of other ways that this budget strengthens our nation. First, it honors our duty of fiscal responsibility. It is a budget surplus that we now enjoy for the first time in nearly three decades, the largest in our history. And despite the temptations here just before an election to spend it on tax cuts and new spending programs, the budget actually meets my challenge to set aside the surplus until we safe Social Security for the 21st century.

It also provides funding within the balanced budget to begin to hire 100,000 new teachers to reduce class size in the early grades; thousands of tutors to help children read; up to 100,000 mentors to help poor children prepare for college; after-school programs to give a quarter of a million children someplace to learn

instead of the streets; a half a million summer jobs to teach young people the discipline and joy of work.

The budget strengthens our nation in other ways as well. It will bolster our own prosperity and help us to meet our responsibilities to deal with the global economy turmoil by meeting our obligations to the International Monetary Fund. It actually strengthens the protection of the environment. It guarantees safer water, cleaner air, more pristine public lands. It will help struggling farmers who face natural disasters and dramatically declining markets as a result of the trouble in Asia.

We had to fight for each of these priorities, and the budget is not perfect. You know, I lost the line item veto in our court case, and there's a lot of little things tucked away there that I wish weren't in that budget. But, on balance, it honors our values and strengthens our country and looks to the future.

Now, I believe that it's important to point out, too, that if we had the right sort of spirit throughout the year we wouldn't have had to cram a year's worth of work into a 4,000-page, 40-pound document passed several days after the budget year had run out. There are still some elements of partisanship that I would like to note in the hope that they can be removed.

In the past few days the Congress persisted in tying our United Nations' dues to unrelated and controversial social provisions, which endanger the health of women and deny them even basic information about family planning, even though studies show that countries where women have access to strong family planning actually have fewer abortions.

I've made it clear many times that I will veto such provisions. Congress sent me the bill to fund our arrears to the United Nations, knowing full well I would do so. So today I did. I regret that. I regret, too, that the 105th Congress leaves town with unfinished business, challenges that must be met in the coming months and years to strengthen our families and our nations.

The next Congress must pass the patients' bill of rights. (Applause.) I might say there is bipartisan support for this, just not enough to get it by. Our plan says to cancer patients and all Americans: You should have the right to a specialist, such as an oncologist. You should not have to worry that you will have to change doctors in the middle of a cancer treatment if your employer changes health care providers. You should have a right to an independent appeals process if critical treatment is delayed or denied. Managed care or traditional care, every American should have quality care.

The next Congress should act in other ways to strengthen the health of women. This year I asked Congress to cover clinical trials for Medicare beneficiaries so they, too, can get cutting edge treatment. (Applause.) And I asked Congress to outlaw discrimination based on the results of genetic screening. (Applause.) Both these measures failed to pass; the next Congress should pass them. The next Congress should also meet our obligations to our children by modernizing our schools. And above all, the next Congress must be the Congress that acts to save Social Security.

This year we had a series of bipartisan forums around the country on how to reform Social Security to meet the burdens that will be there when the baby boomers retire and we'll only have about two people working for every one person drawing Social Security. We're going to have a national conference in December. We were

successful in saving the surplus until we could consider the cost in future years of reforming Social Security.

Social Security lifted a generation of elderly Americans from poverty. Today, even though most Americans have other sources of income who draw Social Security, fully one half of our seniors would be in poverty without it. So here at the White House on Friday we will talk about the vital importance of Social Security, especially to women, who have fewer pensions and smaller savings.

If we want to keep this commitment as strong for our children as it was for our parents, and if we want to see the baby boomers retire in dignity without imposing unfair burdens on our children and their ability to raise our grandchildren, we must act now.

I must say, I was disappointed a couple of days ago that the Senate Majority Leader said he may not now want to join me in reforming Social Security next year. If we don't, then there will be more pressure to squander this money on tax cuts or spending programs. I think that is unhelpful. We know that we can make modest changes now that have a huge impact down the road, in much the way that modest investments in research now have a huge impact down the road on health care. And I believe this is an issue which really binds the American people not only across generations, but across political parties. None of us -- none of us -- wants to leave a legacy of burdening our children to support our retirement or risking that those of us who -- unlike me, won't have a good pension -- will face an undignified and impoverished old age just because the demographics are changing in America. So we need progress, not partisanship, on Social Security.

Now, there are 436 days left in this millennium. It can -- it should -- be a time when we redouble our efforts to honor our parents, to strengthen our nation, to prepare for our children's future, and to honor the tenacity and courage that those of you here have shown every day in dealing with this great challenge.

Again, let me say, I am very proud of what this budget did for cancer research. I'm very proud of what we are doing together to deal with the challenge of breast cancer. I want you to know that I believe that we are within reach of genuine cures and genuine prevention strategies of stunning impact. And we have to remember that on the things that really count, whether it's cancer research, or saving Social Security, or educating our children, this country needs to be united. This country needs to be reconciled to one another -- all of us -- across all the lines that divide us.

There are plenty of things to fight about. But on the fundamental things, we need to be one. That is, parenthetically, the argument I've been making for a week out at the Middle East peace talks.

The only way that life ever really works is when we understand that the only victories that have lasting impacts are not victories over other people, but victories for our common humanity. And that's what I'm going to work for now. To me, that's what every day your struggle against breast cancer symbolizes. And I'm very grateful to all of you.

Thank you, and God bless you. (Applause.)

END 4:27 P.M. EDT

THE CLINTON/GORE ADMINISTRATION: LEADING THE FIGHT AGAINST BREAST CANCER

October 21, 1998

"If we do what we must, if we act together and press our advances against the scourge of cancer, then the dawn of a new century can be a dawn of a new era of human health."

President Bill Clinton
October 21, 1998

Today, President Clinton joins First Lady Hillary Rodham Clinton at a White House event in honor of Breast Cancer Awareness Month. During the event, the President will announce the passage by Congress of the budget agreement and discuss the increased investments made in cancer research and new clinical trials of drugs to reduce the risk of breast cancer. The First Lady will unveil an expanded mammography outreach campaign and release a five-year report from the Federal Coordinating Committee on Breast Cancer that outlines the progress made in breast cancer research, prevention, and treatment.

Standing With America's Families. Today, the Congress passed a fiscally responsible budget that reflects the President's commitment to invest in our people and strengthen our economy as we move into the 21st Century. This budget honors our duty of fiscal responsibility and meets the President's challenge to save the surplus until Social Security is reformed. This budget will also expand opportunity by: beginning to hire 100,000 new teachers, reducing class sizes in grades 1-3, and providing thousands of tutors to help children read. The budget also recognizes our commitment to environmental protection, our obligations to the International Monetary Fund, and helps struggling farmers who face natural disasters and declining export markets.

Providing Critical Resources For Cancer Research. As part of the budget agreement, Congress granted a significant down-payment on the President's 21st Century Research Fund. The National Cancer Institute (NCI) will receive a total budget of $2.9 billion this fiscal year. This funding will enable NCI to fund critical new research activities, including one to expand the use of Herceptin to treat breast cancer earlier. The First Lady will also announce a new clinical trial to examine tamoxifen, a drug that has been show to reduce the risk of breast cancer, and raloxifene, which researchers believe may also reduce the risk of breast cancer. The unique STAR trial will involve 22,000 women at increased risk of breast cancer and is scheduled to open at approximately 400 sites around the country and Canada next year.

Progress In The Fight Against Breast Cancer. The First Lady will release a report from the Federal Coordinating Committee on Breast Cancer that underscores the critical progress that has been made since the Administration took office:

- A significant investment in research that has led to historic advances in breast cancer research, including the identification of new breast cancer genes, and promising new treatments;
- Improved quality and availability of prevention tools, including mammograms;
- Enhanced access to treatment and quality of care for women with breast cancer by increasing access to cancer trial clinics, and new projects to improve detection and

care among low-income and minority women;

- Innovative interagency and public-private partnerships to apply the latest in defense and space technology to better detect cancerous tissues and develop less intrusive surgery methods for patients.

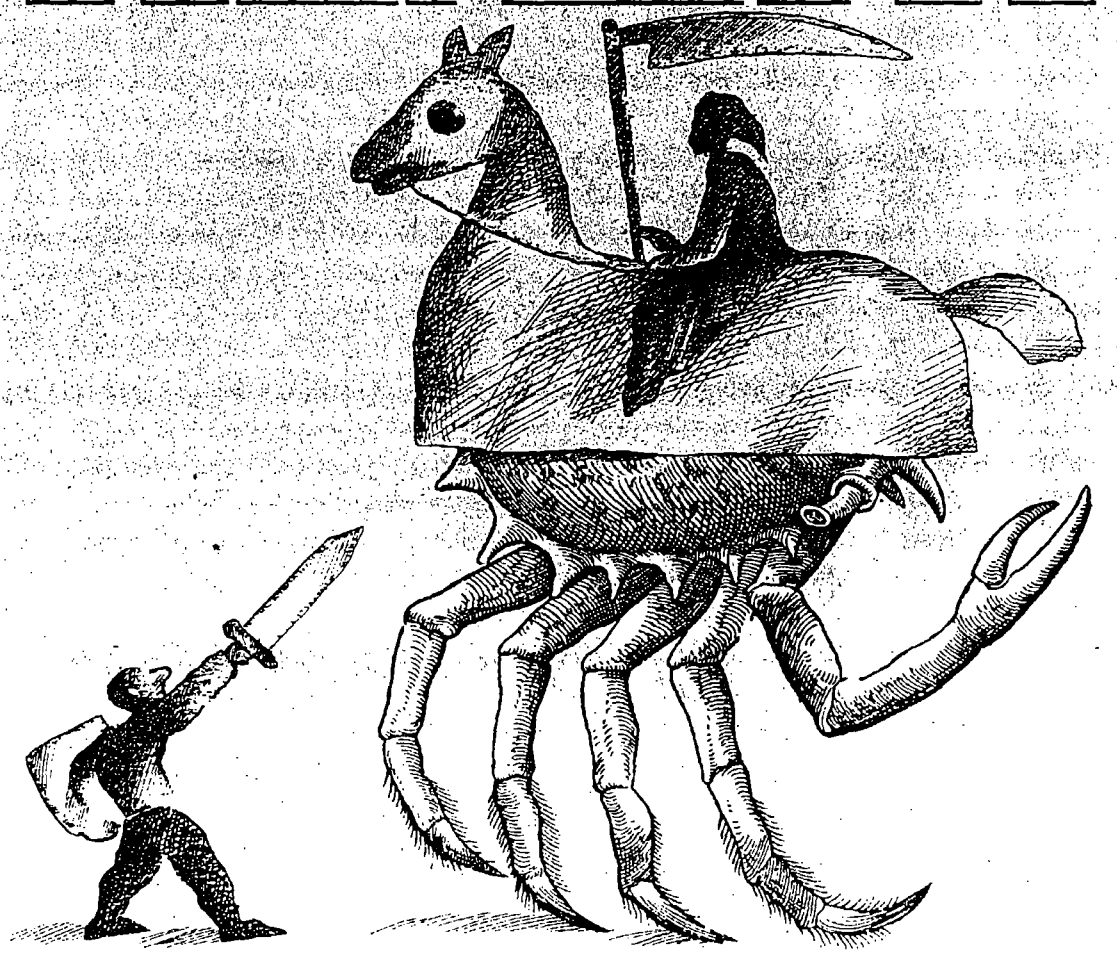
Encouraging Older Women To Get Mammograms. The First Lady will unveil an expanded outreach and education campaign to encourage women ages 65 and over to get regularly scheduled mammograms. This year's campaign will emphasize the new mammography Medicare benefit that the President fought for and signed into law that covers annual mammograms and makes them more affordable.

Family Planning -- We Must Put Progress Ahead Of Partisanship. Although the President fought for and won victories in the budget negotiations, Congress has persisted on the path of partisanship. A Congressional bill to reauthorize the State Department contains unacceptable restrictions on international family planning -- even though women in countries with strong family planning have fewer abortions. Congress has even attempted to tie meeting our United Nations obligations to this unrelated and controversial provision. Today, the President vetoed this bill for a second time.

The Washington Post

TUESDAY, FEBRUARY 14, 1995

HEALTH



How Goes the War on Cancer?

Are Cases Going Up? Are Death Rates Going Down?

What the Statistics Really Tell Us

How the United States Compares With Other Countries

HOW GOES THE WAR ON CANCER?

Are Cases Going Up? Are Death Rates Going Down?

BY RICK WEISS

Cancer news seems destined to confuse.

One week breast cancer has reached epidemic proportions; the next week all is explained away as a statistical fluke, attributable to improved mammography. ne study shows that cancer deaths are steadily rising; anoth- chalks it up to an aging population and shows that age-ad- sted death rates actually have dropped.

Despite a glut of information on cancer these days—or per- ips p / because of that glut—the question lingers unan- vered in most Americans' minds: How goes the war?

Researchers sought to answer the question this month by l the latest and most complete analysis of cancer ends in the United States. Painstakingly collected and com- led from doctors and hospitals all across the country, the fig- es offer a cold tallying of the numbers of white men and omen of different ages who were diagnosed with or died from rious cancers during a recent five-year period, with compari- n to a five-year period 20 years ago.

Yet clear as the figures are, there is still wide disagreement out what they really mean.

On one side are those who are heartened by the news that ath rates have declined for several of the most common and adliest cancers. "We are at the turning point," asserted Phil- Cole and Warren Sateren, University of Alabama epidemiol- gists, in an editorial accompanying the data in the Feb. 1 Jour- l of the National Cancer Institute. "Early in the new century, ncer's primacy will fade."

On the other side are those who detect in the figures a wor- some trend of increased cancer incidence or death rates for veral kinds of tumors, including those of the kidney, brain d testicles. To them the latest numbers suggest an escalat- g public health crisis that may be due to some as yet unrec- nized environmental or occupational hazards. These scien- sts say victory against cancer is by no means assured, and they point to a recent spate of disturbing studies to support their downbeat convictions.

"We are going to see increases," said Brenda K. Edwards, associate director of the NCI's cancer surveillance program. "Cancer is going to take a growing share of our health concerns, and I don't want to gloss over that."

Many Diseases

Such differing views reflect both the inherent pliability of statistics in general and the politically charged nature of cancer numbers in particular. Today everyone has a stake in how cancer statistics play: researchers in need of funding, politicians responsible for federal expenditures, environmental activists seeking attention for their cause, companies not wanting to spend fortunes on pollution controls, physicians who don't want to discourage their patients unduly.

But most fundamentally, the confusion over cancer statistics is rooted in cancer's multiplicity as a disease: Cancer is not a single ailment and cannot be counted as such.

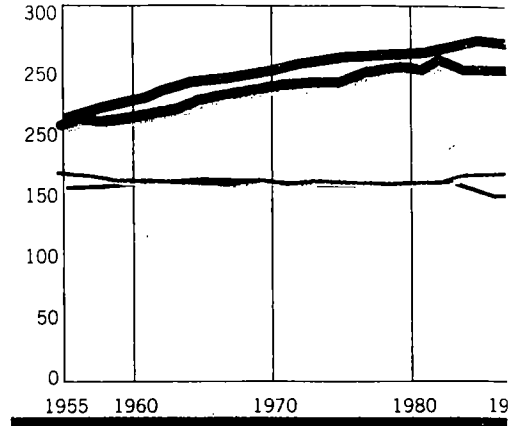
To be sure, all cancers have a lot in common, notably their obsession with cell division and growth, said Aaron Blair, chief of NCI's occupational safety section. But they also differ widely in their causes, their growth patterns and their susceptibility to various treatment strategies. "In reality," he said, "we're dealing with a huge collection of diseases."

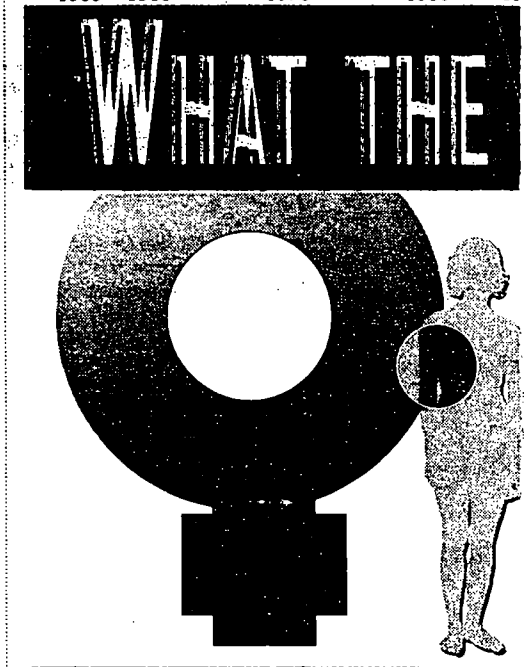
This variability was the motivation that drove NCI epidemiologist Susan S. Devesa and her colleagues to analyze the incidence and mortality data for 30 different cancers and delineate their respective trends over a 12-year period. The team parsed data from a national cancer registration program according to type of cancer, patient gender and patient age, to reveal the specific dynamics underlying the more widely reported—and disputed—cancer statistics.

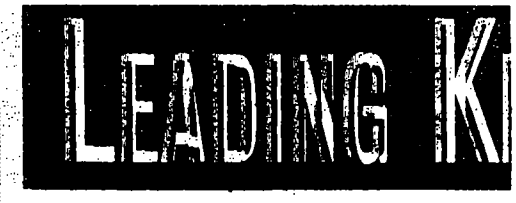
See CANCER, Page 16

U.S. DEATHS PER 100,000 PEOPLE COM

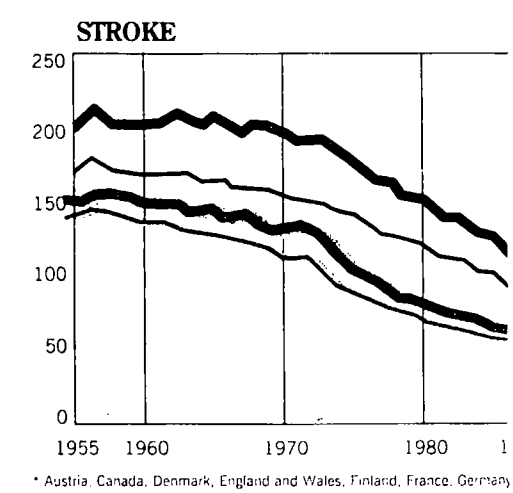
CANCER







STROKE



* Austria, Canada, Denmark, England and Wales, Finland, France, Germany

Cancer Gaining On Heart Disease as Number One Killer

BY CRISTINE RUSSELL

Around much of the industrialized world, the leading cause of death is steadily shifting from heart disease to cancer, according to an extensive new analysis of international statistics released this month y U.S. federal health officials.

The 191-page report by the National Center for Health tatistics shows that cancer now "rivals or at times clearly urpasses" heart disease in several European nations and arts of Asia and Latin America.

"There is a clear trend in many industrialized countries, vith the exception of Eastern Europe, that a continued de- line in heart disease coupled with no major improvements in ancer mortality results in cancer becoming the leading ause of death," said Alvan O. Zarate, an analyst at the Na- ional Center for Health Statistics.

"That trend is correct," said Thomas Thom, a statistician vith the National Heart, Lung and Blood Institute who has tudied heart and cancer mortality patterns. "Cancer is or is lose to being the number one cause of death" in many countries, he said, largely because of the drop in heart disease deaths and increases in lung cancer.

The report also provides a compelling view of other health conditions in the United States. It shows that the United States has the lowest death rate from stroke in the industrialized world for males and among the lowest for females and has significantly lowered mortality from heart disease and car crashes in the past two decades. But the United States rates poorly against other top killers: Smoking-related lung cancer rates for women and murder rates are among the highest of the developed countries.

"We've made a lot of progress in circulatory diseases, like heart disease and stroke. We're looking better than we used to compared to other countries. But there has not been much progress overall regarding cancer. It hasn't moved much," said Zarate.

Zarate said the new report is the most comprehensive look at international death rates ever done by his agency. It

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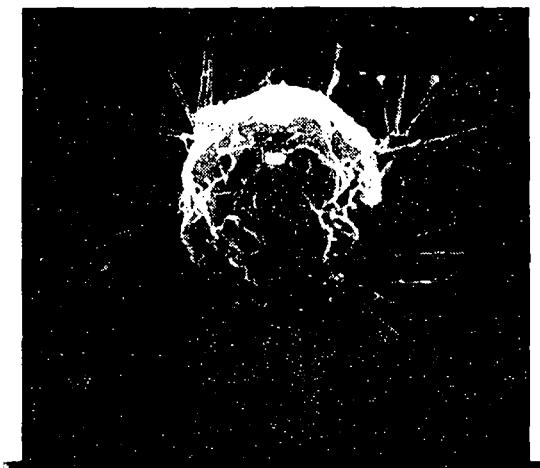
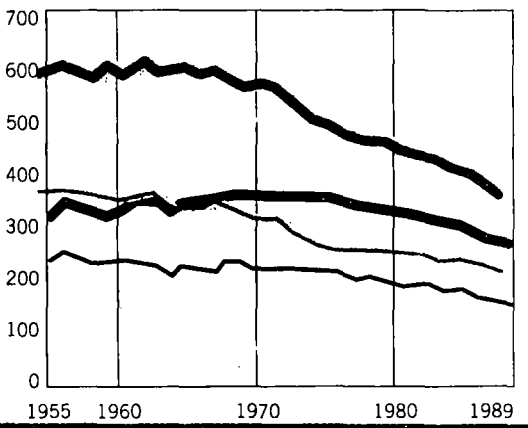
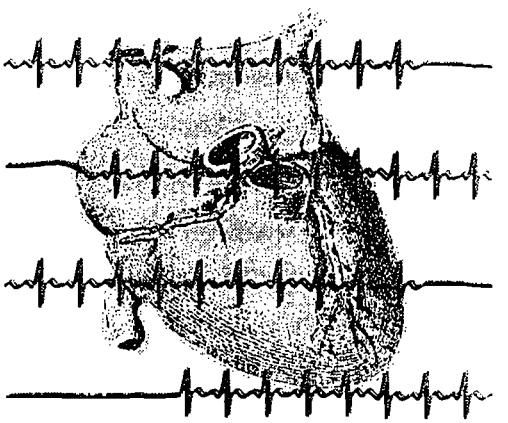
RED TO A GROUP OF 20 OTHER DEVELOPED COUNTRIES*: U.S. MALE — U.S. FEMALE — OTHER COUNTRIES, MALE — FEMALE —



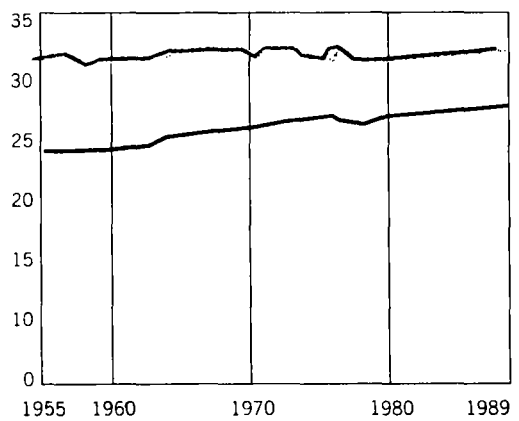
HEART DISEASE

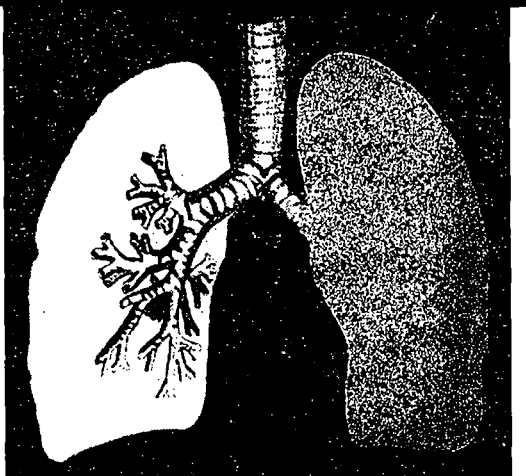




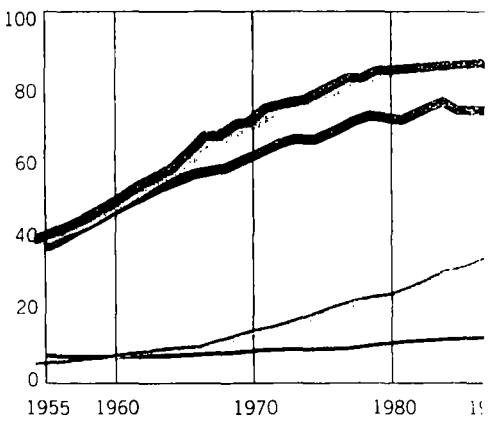
STATISTICS TELL US ABOUT SOME

BREAST CANCER

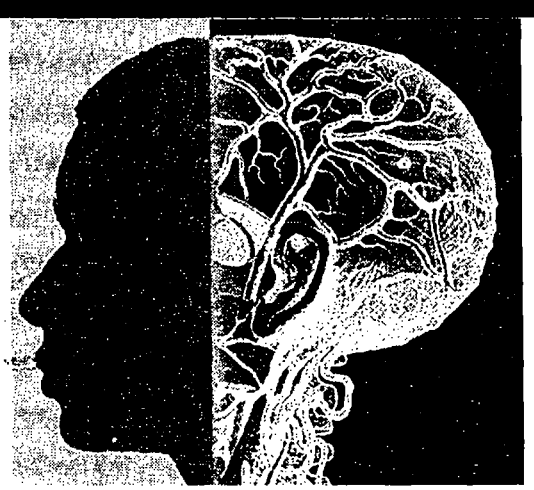




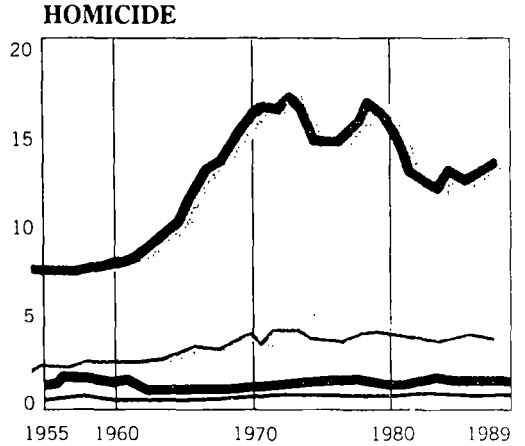
LUNG CANCER

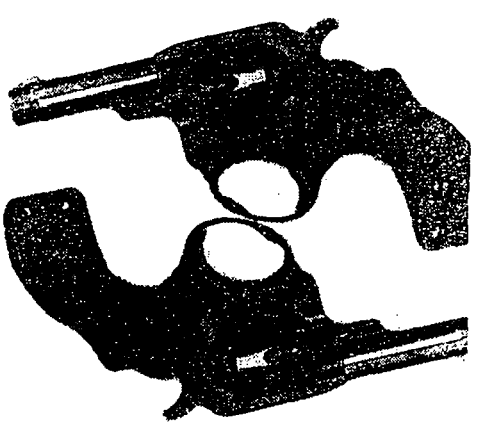


LLERS IN THE INDUSTRIALIZED WORLD



HOMICIDE





eral Republic of), Hungary, Ireland, Italy, Japan, Netherlands, New Zealand, Norway, Northern Ireland, Portugal, Scotland, Spain, Sweden, Switzerland

A Cancer Survivor Discusses Her Experiences

Ellen Stovall, 48, is executive director of the National Coalition for Cancer Survivors, a group that promotes the interests of those who are living with the illness. In 1971, she was diagnosed with Hodgkin's disease, a cancer of the lymph nodes. Stovall was 24 then and had given birth to her first child just three weeks before.

Stovall was successfully treated but experienced a recurrence in 1984. Since then, she has remained symptom-free. She worked for years as a volunteer for various cancer organizations, then became executive director of the national coalition in 1992. She spoke with Washington Post staff writer Sally Squires about her experiences.

How has being a cancer survivor changed over 10 years?

First of all, you cannot pick up the New York Times, The Washington Post or the Wall Street Journal and not find an article or some attention made to a new advance made in cancer. Women with breast cancer have really raised the consciousness by bringing attention to this as a public-policy issue. There have been a lot of high-profile people who have come out with cancer: Happy Rockefeller. Betty Ford. Gilda Radner. Jill Ireland. People can identify with these people. They went public about their cancer, and that helps. Every little bit helps.

What do you tell someone who has recently been diagnosed with cancer?

The first thing that I like to say to them is "I have had cancer too." Then I tell them that there is always something that they can do. Not that this is a walk in the park, but [I tell them that] everything is not as bad as it seems right now, and there is always something that you can do to make things better. It is hard to convince someone who is living in a project, or has no insurance, or has a festering stage IV breast cancer, that there is always something to do, but there is.

I don't want people to mistake that for, "We can cure you." I think that the word is preposterous. Life is a death sentence.

What were your thoughts when you were first diagnosed?

My first thought was, you know, cancer? I am 24 years old. This is a disease of old people. Disbelief. Absolute, abject terror that I wouldn't be here to be with my family, to raise my son—and absolute determination that I had to be here. There were no answers, only questions.

For four years, I had symptoms that we now know are related to Hodgkin's. I would itch. I had itching all over my body. I was treated for allergies. I had three miscarriages. I was very anemic. There was a friend of my husband's family who was a physician. He took my husband aside and said, "She is really crazy. There is nothing wrong with her." He put me on Valium, patted me on the head and said, "Go home, little girl." Neurotic I was and am, but crazy I wasn't. So when I did get the diagnosis, I was relieved on one level.

What was your prognosis?

Uncertain. I asked one doctor, "When will you know if I will be okay, whether I will be cured?" The American Cancer Society said five years. The doctor said if it hadn't recurred in two years, which he didn't believe, because the tumor was so big, he would give me a 50 percent chance of being alive in five years. So I held on to those statistics. Another doctor said to me: "Why do you want statistics? It's either 100 percent or nothing for you." I made a bargain. I have a tremendous sense of spirituality. I promised myself that if I was still alive in two years that I would devote whatever was left of the rest of my life to helping people with cancer. And so, 23 years later, I am doing that.

BY JAMES M. THRESHER—THE WASHINGTON POST

ELLEN STOVALL

Looking back, what has it been like to be a cancer survivor?

The first time was a shock. I lost my innocence, I lost my naivete about cancer. All the stigmas and myths that I had heard about cancer no longer applied. It wasn't a death sentence. I didn't lose all my hair and not get it back [from radiation treatments]. I wasn't rejected by a lot of people that I knew, although I did have a family member who used to give me a kiss when she saw me [before the cancer] and then stopped doing that. Because it happened to me before AIDS, I have this perception of being a cancer survivor at a time when it was the plague.

What does it mean—cancer survivor?

Survivorship became what I did. I lived with the cancer, I lived through the cancer, and I lived beyond the cancer. Survivorship became a way that I lived my life after the cancer. I live with the fact that I had cancer and that knowledge has been empowering for me, which is really what this organization is about.

Patient support was almost anathema in 1971. Really, if people have just been diagnosed with cancer, they should have a mirror of what their life might look like in a few years. Something to hold on to—that yes, you may be bald today, or yes, you may feel dreadful today, but somewhere two years from now, there is a person who survived. I always felt like a survivor. I never felt like a patient.

From the moment of diagnosis and for the rest of life, that person is a cancer survivor. The idea that you can survive two weeks, 22 days or 22 years, we are talking about quality of life. Society is just beginning to recognize that survivorship is a very important concept.

Fitzhugh Mullan [chairman of the board of the coalition and director of the Bureau of Health, Public Health Service] identified stages that people go through with cancer survival: acute stage, extended stage and permanent stage of survival. It's really a continuum. Somewhere along there, people live and people die. It is also important to define the quality of life.

How is having cancer different from having other kinds of life-threatening, chronic illnesses?

There is a fear and the stigma. I also think that cancer is so commonplace, we all know someone who has had cancer. It makes it a universal metaphor for chronic illness.

The fear, the fear of recurrence is just an overwhelming fear, even if they have been told that there is just this very good chance that they will be here for a long time. You never lose it. There isn't a day that I don't wake up and be very grateful just to be alive.

Have you ever encountered discrimination?

My husband decided to go out on his own in January 1992 to start his own architectural practice. We had [insurance coverage] for 18 months [from his old job]. [Looking for new insurance] was the only time that I experienced direct discrimination. I applied to nine different companies and got turned down by nine different companies.

One insurance company was even stupid enough to tell me that they were not denying me because I had cancer, they wanted me to know that, but because I had sought mental health coverage. I sought therapy for the first time in my life when I had cancer the second time, in 1984. I think that psychosocial services are so, so important for people with cancer.

I finally got insurance for huge, huge premiums.

How has cancer affected your view of life?

I am very impatient. And I also don't plan. I used to joke about the fact that I didn't take out magazine subscriptions, I would cross out one year and put in six months. I wouldn't plan a trip a year in advance. On the other hand, I have thrown caution to the wind. If somebody had said to me before I had cancer, "Do you want to go white-water rafting or bungee jumping?" I would have said forget it. Now I would like to try it. I have more of a spirit of adventure. I am not as cautious.

I could walk out on the street and get hit by the Number 52 bus. I am probably going to die of cancer, but maybe not. So why not try some things? ■

DEATH, *From Page 12*

compares age-adjusted death rates from 41 industrialized countries for the years from 1955 through 1991 using U.S. and World Health Organization statistics.

Among the report's findings:

■ The United States ranks somewhere in the middle of all industrialized countries in life expectancy and overall mortality or death rate, the annual number of deaths for each 100,000 people. But the statistics show some dramatic differences when sex and race are taken into account.

■ The overall death rate for white American men and women is better than in two thirds of 36 industrialized countries studied. Among black American males and females the death rate, however, ranks among the highest, as it does in most Eastern European countries. Across the world, male death rates from various causes tend to be far higher than women's.

■ Homicide deaths among U.S. men have increased dramatically since the mid-1950s compared with the rates in other developed countries, with black American men in 1991 having by far the highest death rate. The rate for American women is also among the highest in the industrialized world.

■ Cancer deaths are particularly high among American blacks: The death rate for prostate cancer is the highest for any industrialized nation studied, and the death rate for breast cancer is also high.

■ U.S. blacks have the highest rates of death from diabetes.

■ The death rate for lung cancer is "extremely high," said Zarate, among both U.S. white and black women.

The shift from heart disease to cancer was found in both total deaths and the age-adjusted mortality rate, which takes into account differences in the size and composition of the total population, including aging, and makes it easier to make comparisons, said Zarate and Thom.

Cancer is the leading cause of death among men in France, Italy, Portugal, Spain, Belgium, Japan, Hong Kong and Uruguay, and death rates from heart disease and cancer are virtually tied in the Netherlands and Chile. Among women, cancer is the top-ranked killer in France, Belgium, the Netherlands, Denmark, Japan, Hong Kong, and Chile, and it is roughly equal to or slightly behind heart disease deaths in Canada, the United Kingdom, Switzerland, Portugal, Italy, Norway, Uruguay and Costa Rica, according to the report.

In the United States, heart disease death rates have long been far higher than in other countries, particularly among men, and heart disease is still the top killer here. But American experts predict that a continuing decline in heart disease will move cancer into the number one cause of death by the end of this decade.

In other English-speaking and Scandinavian countries heart disease continues to have a significant lead over cancer as the

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NCER, *From Page 12*

Devesa knew, for example, that taken as a whole the long-ar g increase in U.S. cancer *mortality* (the percentage of ner , who die from cancer) has been flattening out. In-ed, when figures are properly adjusted to account for the ing of the American population and the increase in cancer aths that would be expected with such aging, it turns out e percentage of people dying from cancer actually dropped little in 1993 for the first time on record.

The simplest interpretation: Decades of work in the areas cancer prevention, diagnosis and treatment are finally pay-g off.

But Devesa also knew that much of that drop was due to ie dec in a single huge category, lung cancer deaths in oung men, as a result of the decline in cigarette smoking mong these men. Might other cancers be expanding just as uch or more, their growth largely hidden by the simulta-e drop in lung cancer rates?

To find out, Devesa's team collected cancer incidence and ortality rates from the period 1987 to 1991—the latest peri-d for which statistics were available—and compared them to ie rates from 1975 to 1979. (They focused on data for whites; gures for blacks were roughly equivalent but were different nough to be considered separately in a report yet to be pub-ished.) What emerged is both good news and bad: For some ypes of cancer it seems the war is indeed being won, but for thers there appears to be trouble on the horizon.

■ **The good news:** Lung cancer, the nation's number one ancer killer, and tumors of the mouth, throat and voice box re declining among men in their thirties, forties and fifties, reflective of that group's shunning of cigarettes, researchers aid. That alone is a major victory; nearly 170,000 cases of ung cancer are diagnosed each year, and 87 percent of those eople die within five years of their diagnosis.

Looking at the gastrointestinal tract, cancer of the stom-ach, colon and rectum are declining for both men and wom-en. That's probably the result of improved diet, researchers suggest, and better methods for finding and removing pre-cancerous growths in the colon.

Cancers of the uterus also have declined steadily since the mid-1970s, mostly because doctors stopped prescribing so-called unopposed estrogens to menopausal women. (Instead, they are giving estrogen along with the female hormone pro-gestin, a combination that offers the same benefits without the added risk of uterine cancer.)

■ **The news that might not be that bad:** The incidence of breast cancer in women and prostate cancer in men rose dramat-ically during the 20-year period covered by the study. But in both cases the increase seems largely due to improved diagnostic techniques, the researchers concluded. Put simply, better mam-mography and new tests for detecting early prostate tumors are finding next year's cancers this year, generating a bookkeeping glitch that shows up as a temporary increase in incidence that should cancel itself out later on.

Lung cancer rates increased dramatically in women over 35, but even this bad news has a silver lining of sorts. The in-crease is almost entirely attributable to the growing popular-ity of cigarettes among women during the past few decades, and so is at least in theory reversible should the antismoking message get through to this group.

Similarly, steeply rising rates of melanoma, the potentially fa-tal skin cancer, can largely be blamed on the growing popularity of sunbathing and other outdoor activities, experts said. Some-thing as simple as increased use of protective clothing and sun-screen would probably blunt the deadly trend.

■ **The bad news:** Several types of cancer are becoming more common for no apparent reason. Most of these cancers are not household words, like renal carcinoma (cancer of the kidneys) and non-Hodgkin's lymphoma (a cancer of the lymph nodes). But researchers say it's possible that before long they could play the role that lung cancer did in the 1950s and '60s—taking big tolls on the population while their cause re-mains a mystery.

"There is a lot that we can't account for," Devesa said. Of particular concern, she said, is increased incidence of brain cancers (above and beyond the increase that is due to im-proved brain imaging technology), non-Hodgkin's lymphoma (above and beyond the increase that is due to the growing number of people with AIDS, many of whom develop this cancer), kidney cancer and testicular cancer.

Also of concern is the increase in certain types of breast cancer that cannot be explained by better mammographic screening. Specifically, most of the apparent increase in breast cancer involves the type of breast tumors that grow in response to estrogen, so-called ER-positive tumors. If the increase in breast cancer were solely an artifact of improved mammographic screening, the increase would be seen equally among ER-positive and ER-negative tumors, since mammograms are no better at picking up one type than the other. But that's not happening. And the imbalance, Devesa said, suggests that some of the increase in breast tumors is real.

Nobody knows why this handful of varied cancers are becoming more common, but some epidemiologists strongly suspect that environmental toxins are to blame. They point in part to studies of American farmers to back up their claim.

Deadly Harvest?

American farmers are far healthier than the typical American; for the most part they don't smoke and they have impressively low rates of cancer, heart disease and other ailments. Oddly, however, for decades they have exceeded the national average for several cancers, including leukemia, non-Hodgkin's lymphoma and cancers of the brain and prostate.

"You ask yourself, 'What do those sites have in common?' " said Blair, of the NCI. "And the first thought is, 'Nothing.' "

But in fact there are two things notable about that collection of tumors, he said: They are cancers that are in many cases just now starting to become more common in city people. And they are cancers that tend to appear in people whose immune systems are damaged, either because they have a disease like AIDS or because they've been given immune-suppressing drugs.

"So a working hypothesis is that in agriculture there may be environmental factors that impinge on the immune system, giving cancer a boost," Blair said. "And these undetermined factors may also be getting into the general population and may be contributing to some extent to the rise in these tumors."

What kind of immune-suppressing carcinogens have farmers long been exposed to that are only now becoming common in the Big City?

Pesticides are a perfect example, Blair said. "Farmers have been handling pesticides since the 1960s, but only since the '70s and '80s did you see this in the urban environment" with the rise in lawn care services and home-use weed killers and insecticides. Similarly, Blair said, "30 years ago, you didn't fill your own tank with gas and breathe the fumes. Farmers have been filling there own tanks forever."

No one knows whether these types of exposures are causing significant numbers of cancers in people, Blair said. But animal and epidemiological studies have shown an association between non-Hodgkin's lymphoma, brain and kidney cancer, he said, and exposure to pesticides or solvents such as gasoline products.

Taking a different tack, some scientists have proposed that plastics, pesticides and other environmental contaminants—many of which are chemical mimics of the hormone estrogen—may be bathing people and animals in a dilute sea of female hormones, triggering estrogen-sensitive breast cancers and testicular tumors.

Studies in animals indicate that environmental estrogens can cause testicular abnormalities similar to those now on the rise in men, which include not only testicular cancers but undescended testicles and defective sperm. Some scientists have reported a dramatic drop in sperm quantity and quality worldwide in recent decades. And while one recent report disputed a sperm count drop, researchers at the University of South Paris reported in the New England Journal of Medi-

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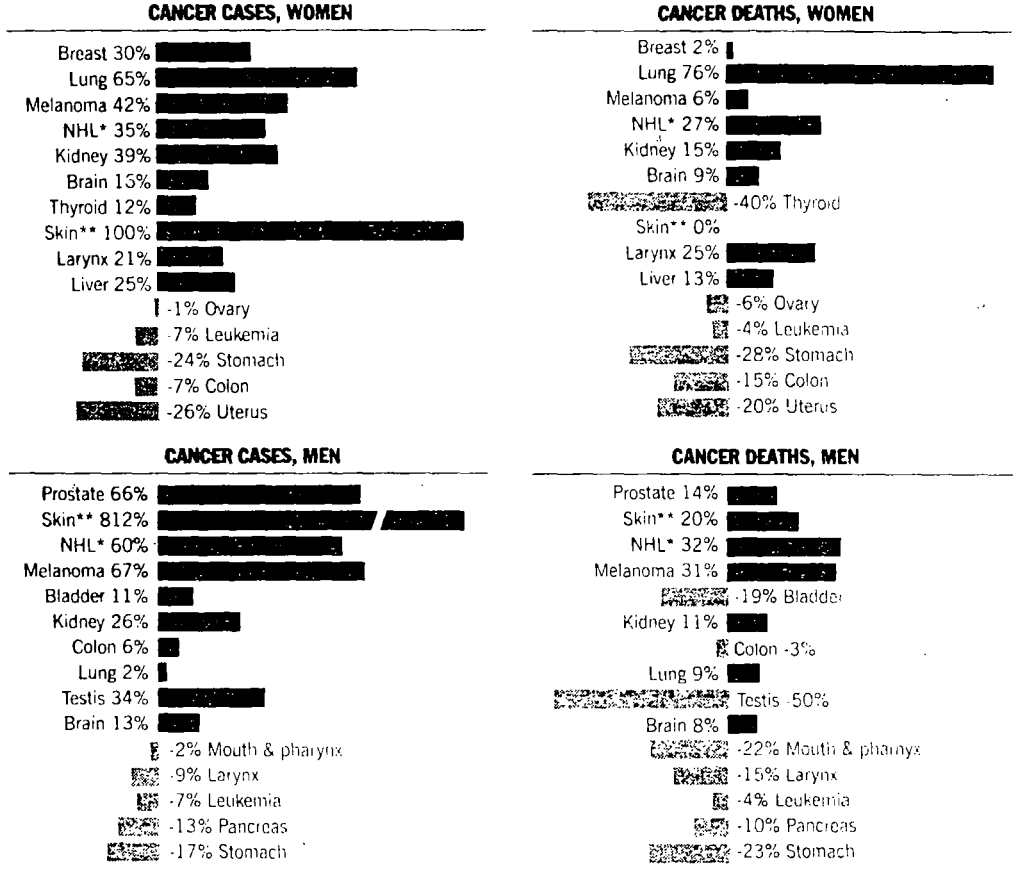
PERCENT CHANGE IN CASES AND DEATHS FOR SOME CANCERS IN WHITE MEN AND WOMEN

Between 1975-1979 and 1987-1991



*NHL: Non-Hodgkin's Lymphoma. **Skin cancer refers to non-melanoma type; increase is mostly due to Kaposi's sarcoma cases in people with AIDS.

CANCER, *From Page 16*

cine this month that sperm counts in Parisian men clearly have fallen in the past two decades, while the percentage of gimpy sperm has increased.

The link between estrogen-mimicking pollutants and breast cancer remains controversial, with some studies finding correlations between breast cancer incidence and exposure to pesticides and chlorine-containing chemicals, while other studies do not. The most comprehensive study yet to look at the issue, the four-year Long Island Breast Cancer Study Project, sponsored by the National Cancer Institute, will be launched in April.

The list of other potential cancer culprits is endless and difficult to interpret. Animal studies have found a link between common antihistamines and cancer. Studies in people have suggested that diuretic drugs ("water pills") may increase the risk of kidney cancer. And some epidemiological studies with people have suggested a link between electromagnetic radiation and cancers of the brain or leukemia. But no study has yet found any single factor clearly responsible for any of the cancer increases now being tallied. And some researchers don't expect to find one.

Cole and Sateren, of the University of Alabama, for example, don't deny that some environmental factors may eventually turn out to be causing some cancers, but they chide those who foresee a tumorous Armageddon. It's easy to come up with hypotheses, they write in their Feb. 1 editorial, and to predict an impending cancer disaster. "In reality, the disaster has remained impending for more than 20 years, and Devesa's findings suggest that it will not occur."

Devesa disagrees. Although she does not believe that environmental hazards are overwhelming contributors to cancer right now, neither does she think that the war on cancer is in the home stretch. "That sounds great, but it's not that simple," she said.

One thing that Devesa, Cole and practically everyone else in the field of cancer research agree on: The best way to make progress against this deadly collection of diseases is to find out what is causing them and keep them from cropping up in the first place.

"We spend close to $100 billion a year on cancer treatment in this country," said Devra Lee Davis, senior adviser to the assistant secretary for health and human services. "If we are going to get on top of this problem, we absolutely have to focus more on prevention." ■

Scientist's Funding Raises Eyebrows

An editorial by two University of Alabama researchers in the Feb. 1 issue of the Journal of the National Cancer Institute has stirred controversy because of its mostly upbeat tone in the face of new cancer statistics that some researchers perceived as worrisome. Several cancer experts have quietly questioned whether a source of one of the scientist's funding may have influenced his conclusions.

Philip Cole, one of the authors of the recent JNCI editorial, said in an interview that some of his research has in the past been funded by various oil and chemical companies and he is currently conducting research supported by the International Institute of Synthetic Rubber Producers.

Cole said industrial support is common at universities, and he noted that in his case the monies went to his university department, not to him directly. He called any suggestion that he might be influenced by funding sources "a distraction" from the scientific facts, which are, he said, that cancer mortality is dropping and lifespans increasing.

"I don't make up the national statistics," Cole said. "This is nothing but an *ad hominem* attack. It causes people to focus on the perception rather than fact."

Adding to the controversy is the journal's failure to mention Cole's funding source. That information should have been noted, JNCI's managing editor Julianne Chappell said in an interview, since some readers might suspect that such associations could soften Cole's views about the role of environmental toxins in cancer. Unfortunately, Chappell said, the journal mistakenly failed to ask Cole for the information, so it never appeared.

"We were at fault," Chappell said. Since 1993 the journal has intended to update the forms it sends to authors, she said, to include new instructions requiring such information. But the task had slipped through the cracks. "Our information to authors is inadequate when it comes to conflict of interest," she said, adding that the forms will now be updated.

Chappell emphasized that the opinions expressed in invited editorials do not necessarily represent those of the journal, which is completely independent of the National Cancer Institute. Indeed, she said, some authors are selected to provoke controversy.

Mission accomplished.

—Rick Weiss

DEATH, *From Page 15*

major cause of death. And in most Eastern European countries heart disease remains far and away the leading killer.

The shift toward cancer as a top killer is "a relatively recent phenomenon," said Zarate, although in Japan and France cancer death rates have been ahead of heart disease for several decades. "I expect that it will occur in more countries over the next decade."

Healthful lifestyles, including lower-fat diets, more exercise and less smoking, control of high blood pressure, and better treatment are widely credited for reducing deaths from heart disease and stroke.

The lack of progress in reducing cancer death rates results from a variety of factors, from prevention to treatment. Health officials point out that there is a lag time of perhaps 10 to 20 years between exposure to cancer-causing agents like cigarettes and diagnosis of cancer. For example, the worldwide epidemic of lung cancer deaths in recent decades followed the increase in popularity of cigarette smoking from the 1930s and 1940s on.

In the United States, lung and other breathing-related cancer death rates ranked higher than a group of 20 industrialized countries studied in the report. But recently the rates among men have leveled off, while female lung cancer deaths have risen more steeply here than elsewhere.

A recent National Cancer Institute study of long-term trends found that overall cancer deaths rose slightly in the United States through 1991, largely because of the rise in lung cancer. In an editorial in the Journal of the National Cancer Institute this month, University of Alabama epidemiologist Philip Cole noted that cancer is soon expected to surpass heart disease as the top U.S. killer, but he contended that there are signs that a long-term gradual decline in cancer deaths may be starting.

Others are not so sure. "There is no clear evidence that a [cancer] mortality decline is occurring yet", said Zarate.

But in other areas, the health outlook is more positive. Stroke, which ranks as the third most prevalent killer in most industrialized countries, has been declining steadily among both men and women around the world for two decades, in part because of efforts to control high blood pressure. The fourth leading cause of death in most of the industrialized world was unintentional injuries, largely from motor vehicle crashes, which ranked just ahead of chronic obstructive lung diseases, problems largely linked to smoking.

In the United States, however, the two switched places in the early 1990s. Unintentional injuries, which have been declining most rapidly among men, dropped to fifth place as a leading killer of Americans. Chronic obstructive lung diseases, rising in American women, moved to fourth place.

The highest death rates among industrialized nations are in Eastern Europe and the former Soviet Union, while northern European and Scandinavian countries are among the leaders in long lives. Life expectancy at birth in Hungary is 65 years for boys and 73.8 for girls, compared with 72.7 years for boys and 79.5 years for girls in the United States. A Swedish male can expect to live 74.7 years, females 80.4 years.

"Eastern Europe fares poorly as far as mortality compared to other industrialized countries across the board," said Zarate. "We're seeing health habits in those regions with regard to smoking, alcohol consumption and highway safety in some cases worsening. And the health care systems are in economic chaos."

A 1993 report on international health statistics by the Office of Technology Assessment (OTA) sought to look beyond death rates to other health indicators in 12 industrialized countries. It concluded that the United States generally has higher death rates among infants, children, and young to middle-aged adults than the other countries studied. In terms of key behaviors that affect both disease and death, the U.S. record was mixed. Fewer Americans today, particularly men, smoke compared with Canadians or Europeans, and more Americans than Canadians or Europeans undergo some tests for cancer, such as Pap smears for cervical cancer. However, Americans weigh more, exercise less and use seat belts less frequently than Canadians.

The OTA report concluded that it was difficult to get agreement on how to compare overall health status in various countries.

Zarate said that death statistics were the most reliable data for comparing health in various countries but emphasized that they "document only the final outcome, but don't necessarily provide a measure of overall health status. It's only one part of the picture. Lots of people have arthritis but don't die from it." ■

THE WAR ON CANCER

Twenty-five years after the war was declared, new insights are plentiful, but the death toll has mounted

Imagine declaring war when you know little about your enemy's firepower, strategies or tactics. That's what happened on Jan. 22, 1971, when President Richard Nixon proclaimed war on cancer in his State of the Union address. Many anticipated swift victory, with the taming of the dread disease likened to a moon landing. Even as recently as 1984, the National Cancer Institute's director predicted that cancer deaths could be halved by the year 2000 in America.

In the quarter century since Nixon launched the battle against cancer, the NCI has invested $29 billion in what some critics have called a "medical Vietnam." This year, 555,000 Americans are expected to die of cancer—215,000 more than in 1971. As for the former NCI director's prediction, current trends suggest that cancer might overtake heart disease as the nation's No. 1 killer by 2000. The overall death rate may have stopped its annual climb, but the absolute numbers will still rise.

Yet the news from the front isn't en-

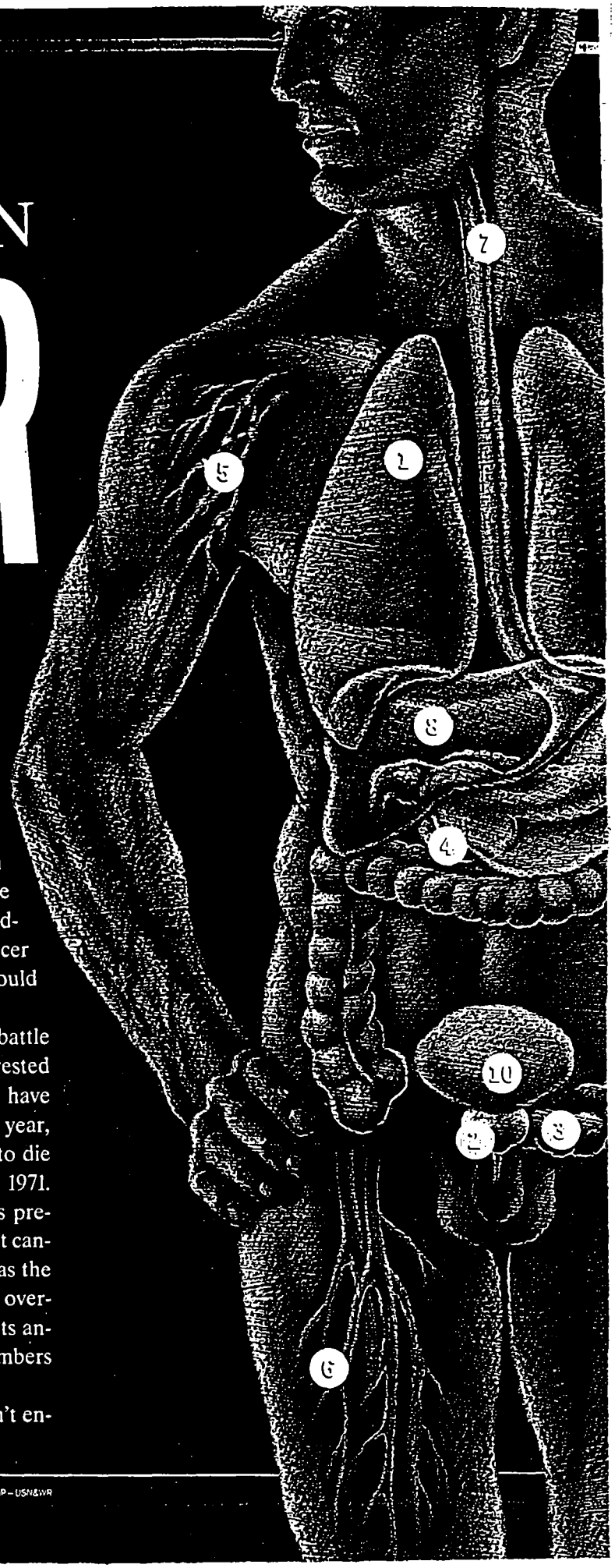
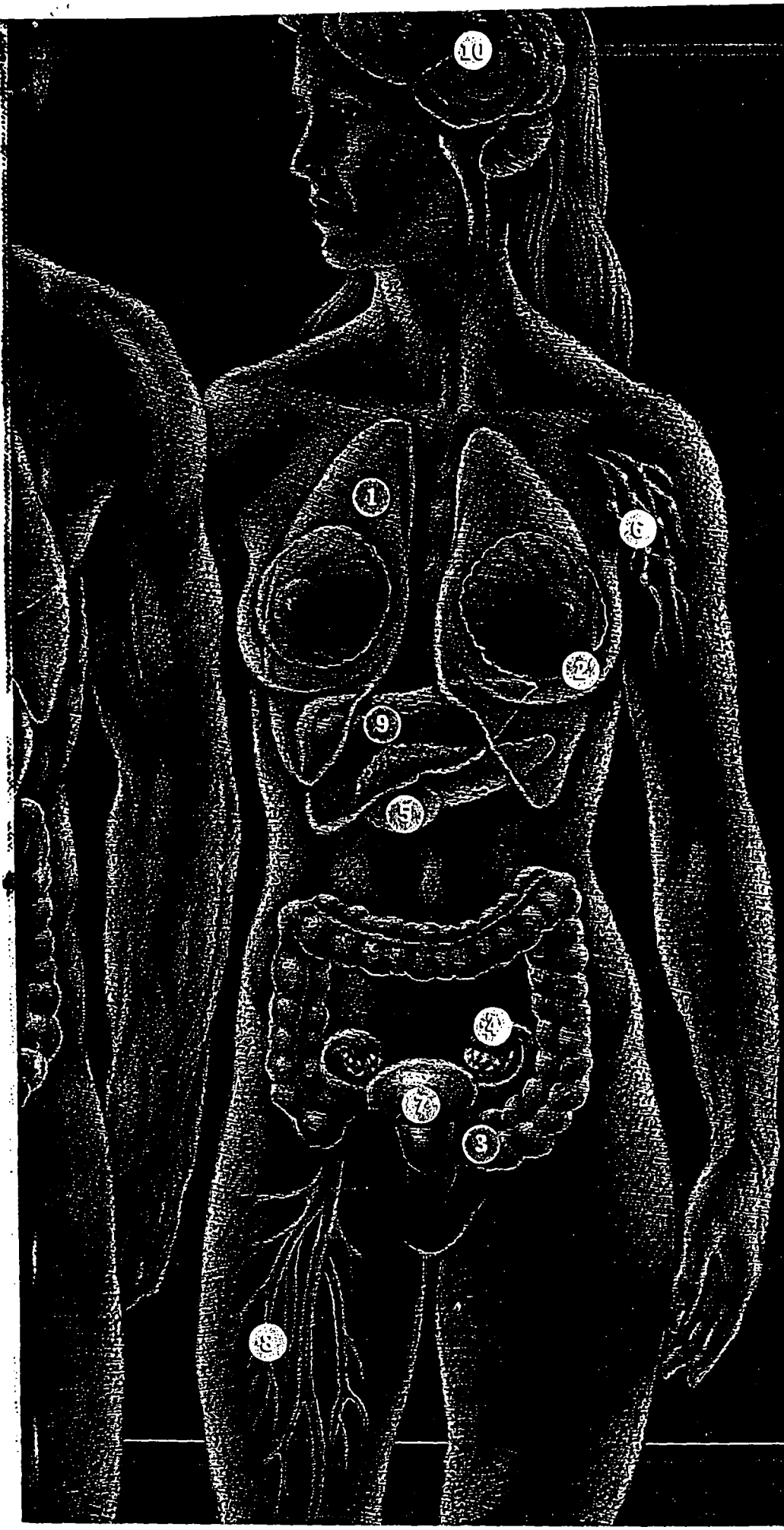


ILLUSTRATION BY ROBERT KEMP—USN&WR



TOP 10 CANCER KILLERS

In all but a few instances, the number of cancer deaths has risen markedly since 1971 compared with what is expected this year.

MEN	1971	1996
1. LUNG	54,931	94,400
2. PROSTATE	17,772	41,400
3. COLON/RECTUM	22,410	27,400
4. PANCREAS	9,967	13,600
5. LYMPHOMA	7,577	13,250
6. LEUKEMIA	8,206	11,600
7. ESOPHAGUS	4,599	8,500
8. LIVER	4,711	8,400
9. STOMACH	9,421	8,300
10. BLADDER	6,075	7,800

WOMEN	1971	1996
1. LUNG	13,686	64,300
2. BREAST	29,969	44,300
3. COLON/RECTUM	23,924	27,500
4. OVARY	9,978	14,800
5. PANCREAS	7,945	14,200
6. LYMPHOMA	6,016	11,560
7. UTERUS*	12,216	10,900
8. LEUKEMIA	6,263	9,400
9. LIVER	7,945	6,800
10. BRAIN	3,518	6,100

*INCLUDES ENDOMETRIAL AND CERVICAL

USN&WR—BASIC DATA: AMERICAN CANCER SOCIETY

OLIVIER LAUDE FOR *USN&WR*

JERRY STAFFORD, 34.
BRAIN CANCER SURVIVOR

A SAVING SEIZURE

Neida Stafford feared that one of their few fights had triggered her husband's grand mal seizure. But the real cause was much worse: Jerry Stafford had an extremely rare type of brain tumor. A month after his June 1993 diagnosis, he underwent a 5½-hour operation at the University of California at San Francisco Medical Center, near the couple's home. From mid-September to mid-November that year, he had daily radiation treatments to destroy bits of tumor that couldn't be removed surgically. Stafford still takes antiseizure medication, but all indications are he's tumor-free.

tirely dismal. Quality of life has improved for cancer patients, thanks to less disfiguring operations like lumpectomies for breast cancer; drugs to minimize nausea, infections and other treatment side effects; and better pain control. Death rates have dramatically fallen for relatively uncommon malignancies such as childhood leukemia, Hodgkin's disease and testicular cancer, often fatal 25 years ago. (The stories of people surviving thanks to treatment advances are chronicled in the pictures and captions that accompany this article.)

When it comes to leading killers, progress in cutting deaths has been modest. Between 1973 and 1991, the death rate from colon and rectal cancer dropped about 15 percent, at least in part because of improved early detection and treatment. Breast cancer death rates appear to have leveled off, and a higher percentage of women diagnosed with advanced as well as early breast cancer are surviving, says Harmon Eyre, deputy vice president for research and medical affairs at the American Cancer Society.

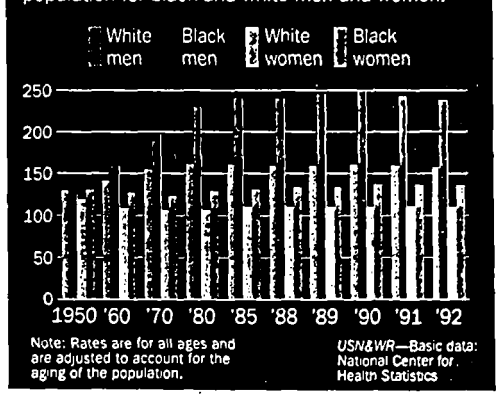
Such gains pale, however, next to lung cancer's growing toll. From 1973 to 1991, the lung cancer death rate shot up 42 percent and was accompanied by a 34 percent rise in the rate of new diagnoses. Most of the increase was in women, who started smoking in large numbers much later than men. The rates of lung cancer deaths and new diagnoses appear to have peaked in men.

Part of the overall rise in cancer cases in recent years stems from the aging of the population. Another part comes from wider use of screening tests like mammography and prostate specific antigen, or PSA, blood tests that pick up tiny tumors in people who previously might have died of other causes before their cancer was diagnosed. Yet better detection and aging can't explain the entire increase in new cases of these tumors. And other cancers, such as brain tumors and non-Hodgkin's lymphoma, are becoming more common. These increases might reflect changes in exposures to unidentified carcinogens.

So the question persists: Why can't the country make great strides in halting cancer deaths, as it has in combatting heart disease? It's an unwarranted comparison. Most heart disease deaths are due to blockages of the arteries. Cancer, by contrast, is perhaps 100 different diseases. "We haven't reached where we would like to be in cancer—not because of misplaced strategies, not because of ill-conceived policies—but because cancer is extraordinarily complex," says Richard Klausner, National Cancer Institute director. Overcoming cancer, Klausner says, requires basic research as well as appropriate

Race and cancer

Overall cancer death rates per 100,000 population for black and white men and women:



Note: Rates are for all ages and are adjusted to account for the aging of the population.

USN&WR—Basic data: National Center for Health Statistics

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PAULA LERNER - WOODFIN CAMP FOR USN&WR

NIKKI DRINKWATER, 10, BONE CANCER SURVIVOR

A NEW OPTION

Thanks to advances in the treatment of bone cancer, Nikki still has two legs to stand on. In September 1994, X-rays taken after a fall revealed a tumor in her left leg. In December 1994, doctors at Children's Hospital in Boston replaced her cancerous thighbone with a donor bone. A year of chemotherapy followed. "Ten years ago, you really didn't have any options," says mom Cynthia Drinkwater, of Plymouth, Mass. "They just used to amputate." Nikki had to undergo the operation again last October after breaking the donor bone. She has to wear a brace for a year.

public policies to take advantage of what is learned.

WHY CANCER IS DIFFERENT

Back in 1971, oncology was a relatively new, low-prestige discipline. Trial and error was the general treatment strategy, since scientists had little inkling of how a normal cell becomes a tumor cell or how a tumor cell multiplies and spreads. One theory of that era blamed cancer on a disruption in how the body broke down carbohydrates. "We were pretty brazen to declare war," recalls Francis Collins, director of the National Center for Human Genome Research.

If cancer were an infectious disease like smallpox or diphtheria, scientists could have developed effective vaccines or better treatments. Vaccines and antibiotics capitalize on the differences between human cells and viruses and bacteria. But cancer cells *are* human cells, with a few minor changes. That's why they escape the immune system's wrath. That's why a "magic bullet" that will destroy only cancer cells, leaving normal cells unscathed, has been so elusive.

Molecular biologists have unlocked many of the workings of tumor cells, but few findings have translated into better treatments or preventive measures. "The kind of biological information that is being generated today is just astounding," says Joseph Simone, physician in chief at the Memorial Sloan-Kettering Cancer Center in New York. "One hopes that among all this wonderful science there is going to be some information that can be applied practically."

The fundamental revelation has been that cancer stems from a series of genetic alterations. As cells divide in the body, thousands of errors occur every day, including some in genes that dictate how cells reproduce. The reason people aren't riddled with tumors is that cells have a mechanism that searches out and eliminates mutated genes. The cell either repairs the defective gene or commits suicide. In cancer, this fail-safe mechanism breaks down; cells are unable to recognize or get rid of genetic mistakes.

Genetic alterations can cause a cell to begin dividing wildly by turning off genes that serve as emergency brakes or by turning up the genes involved in normal division. But such changes aren't enough to cause a life-threatening cancer. Most human tumors at first lack blood vessels to nourish them, so they can't grow bigger than a pea. Barely existing off of nearby blood vessels, they remain that size for several years, often escaping detection. This type of tumor is described as *in situ*, or in place. It's not going anywhere or hurting anyone. Autopsy studies suggest that about 40 percent of women in their 40s have such tiny tumors in their breasts. Now that screening tools are picking up breast and prostate tumors ever earlier, molecular biologists are trying to distinguish ones likely to remain dormant for a long time from more aggressive cancers. With this information, patients could be spared unnecessarily intensive treatments.

Tumor cells become threatening when, for reasons not yet totally understood, they begin developing their own blood vessels—a phenomenon called angiogenesis. With nutrients pouring in from its new blood supply, the tumor swells to marble-size or larger.

Angiogenesis often leads to the first symptom of a tumor—blood in urine, sputum or a stool. Unfortunately, by that time the tumor's new blood vessels have likely enabled some cancer cells to spread to other parts of the body. If a renegade cell was angiogenic before it broke away, a second tumor will soon show up at its new home. If not,

it will develop only into a dormant tumor, harmless until some of its cells become angiogenic and the process begins anew. As a result, cancer survivors can suffer recurrences years after they were first treated.

"MAGIC BULLETS"?

This new understanding of how tumors grow and spread has spurred the search for "magic bullets" that could halt cancer before it becomes deadly, without hurting normal tissue. Such treatments would be used to control breakaway cancer cells, or metastases, after conventional therapies have vanquished a primary tumor.

One target of therapy is the genes that, when altered, lift off the brakes or step on the gas of cell growth. For example, when a gene called ras is mutated, it goes into overdrive, causing the creation of excessive levels of a protein that promotes cell division. But the protein can work only if it's anchored inside a cell membrane. Using the first of a new class of drugs, scientists have successfully broken that bond in mice with ras mutations. Such a drug could prove useful in colon and bladder cancers.

If unregulated cell growth can't be nipped in the bud, perhaps angiogenesis can be blocked. Nine "angiogenesis inhibitors" are now being tested on patients, says angiogenesis pioneer Judah Folkman of Children's Hospital in Boston. In the *Journal of the National Cancer Institute* last April, Folkman and his research team reported that a protein compound called interleukin-12 stopped the growth of tumor blood vessels. Interleukins belong to a group of substances, normally produced in tiny quantities by cells, that had been thought to shrink tumors only by arousing the immune system. Patients would have to take angiogenesis inhibitors for years, if not indefinitely, but most of the drugs seem to be well tolerated.

If tumor blood vessels continue to grow, another treatment approach would single them out for destruction. Researchers in several labs are looking for a molecule present only on the cells of proliferating tumor blood vessels, not normal vessels, which rarely grow. An antibody against the molecule could be chemically attached to a poison, forming a type of treatment called an immunoconjugate. The idea is to target the poison so it only attacks tumor blood vessels.

THE ROLE OF FAMILY

With an increasing number of the "hows" of tumor development answered, researchers are struggling with the "whys." Nearly all tumors are thought to arise from the interplay between inherited genetic alterations and the environment—that is, anything that can mutate genes, from radiation to a woman's estrogen. "Cancer is virtually 100 percent a genetic disease, but it's not 100 percent a hereditary disease," says Collins.

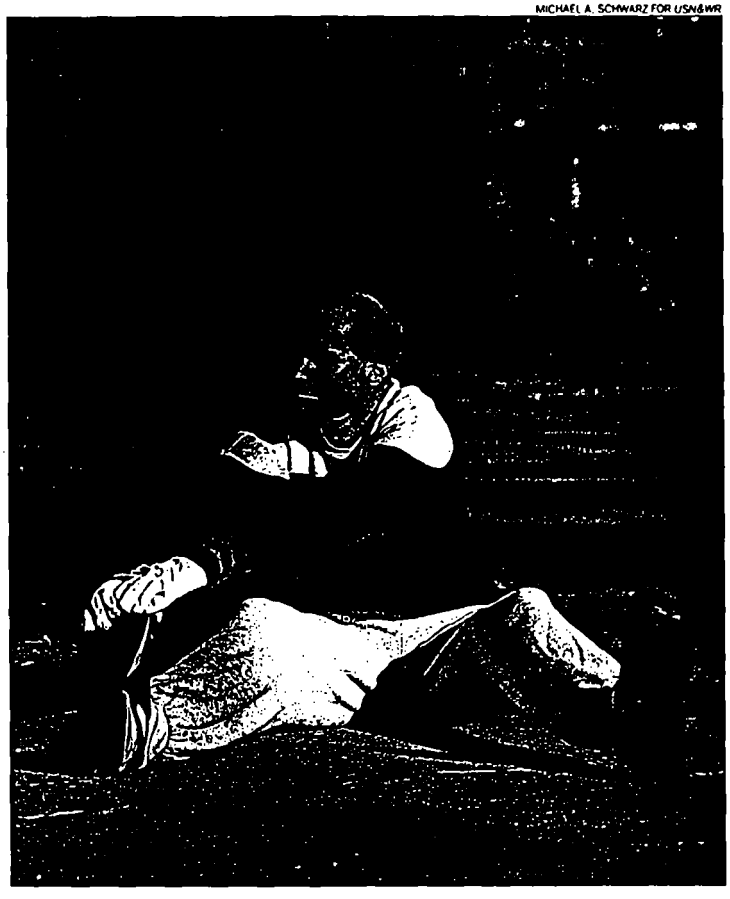
Between 20 and 30 "cancer susceptibility" genes have been identified, and most greatly raise the risk of getting the disease. One in 300 Americans carries an altered form of one of a family of genes called HNPCC, which hikes the chance of developing colon cancer at some time in their lives to 75 percent. In families with a strong history of breast and ovarian cancers, women who inherit a flawed BRCA-1 gene have up to an 85 percent risk of developing breast tumors and up to a 50 percent risk of developing ovarian tumors sometime in their lives.

Scientists suspect many as-yet unidentified genes have a more modest impact on specific cancers. For instance, Collins's team is studying families with an abundance of prostate cancer. The work is tricky. Prostate tumors are so common that it is difficult to be sure whether a large number of cases is a biological heirloom or simply a terrible coincidence.

Within a decade, predicts Collins, testing for altered genes that increase the risk of specific, common tumors will become routine. That raises concerns about whether those who test positive for a flawed gene will get adequate counseling and whether they might be subject to workplace and insurance discrimination. But the benefits for some cancers are obvious. For example, those who inherited a gene that raises their chance of developing colon cancer could begin having regular colonoscopies at an early age.

If there was a simple test today for BRCA-1 alterations, though, doctors would have little advice for carriers. "This is some of the most exciting basic research that's being done, but it's also some of the most frustrating when it comes to public policy," says Devra Lee Davis, an epidemiologist at the World Resources Institute in Washington,

MICHAEL A. SCHWARZ FOR USN&WR



JOHN BROWNLEE, 39, HODGKIN'S SURVIVOR

STRETCHING LIFE

In June 1983, a lump in this engineer's neck led to a diagnosis that he had this lymph cancer. A combination of chemotherapy drugs called MOPP put him in remission for nearly a year. Eight months of an experimental mix of four drugs followed, but his second remission lasted only six months. Brownlee's last option, intensive chemotherapy and radiation followed by a bone marrow transplant, cured him. It has been 10 years since he received his brother's marrow at the Fred Hutchinson Cancer Research Center in Seattle. Today, he lives in Tucker, Ga.

D.C., once a policy adviser in the Department of Health and Human Services.

NEW PREVENTION STRATEGIES

If you can't pick your parents, there are steps you can take to reduce your inherited cancer risk. As evidence, scientists point to dramatically lower cancer death rates in other countries. If America had the same breast cancer death rate as Japan, for example, 11,000 American women would have died of the disease last year instead of 46,000. Are the Japanese hiding some wondrous cancer cure? Are they made of tougher stock? Of course not. Granddaughters of women who move from Japan to the United States have breast cancer death rates right in line with those of other Americans.

Pinpointing exact causes is a big challenge. But the sharp differences among nations may stem partly from lifestyle, particularly diet, which might be linked to a third of all U.S. cancer cases. Asians typically consume more soy products and less fat than Americans, a diet researchers think reduces breast cancer risk. A major federal trial is studying the role of a low-fat diet in reducing breast cancer risk for middle-aged and older women.

The NCI is conducting or sponsoring nine major trials of possible preventive measures. One nutritional intervention for lung cancer, tested in three other trials, didn't meet expectations. Researchers from one of the studies announced last month that smokers who took beta carotene and vitamin A supplements had higher rates of lung cancer, not lower. A second trial found no benefit or increased risk from beta carotene. Researchers in the third, which hadn't announced any results yet, told participants to stop taking beta carotene supplements. The nutrient looked promising because smokers and others who eat lots of fruits and vegetables, which are loaded with it, tend to have less cancer. Perhaps other substances in produce with a lot of beta carotene are protecting consumers.

The more controversial NCI prevention studies involve giving potent drugs to healthy people. In one, women are taking tamoxifen, known to prevent breast cancer relapses, in hopes of reducing their risk of developing the disease in the first place. But tamoxifen appears to raise uterine cancer risk slightly. In the other study, men are taking finasteride, used to treat benign enlarged prostates, to see if it can prevent prostate cancer.

Such prevention trials would provide answers more quickly and cheaply if scientists didn't have to wait until people developed cancer to assess a particular measure. The NCI and the National Institute for Environmental Health Sciences, an arm of the National Institutes of Health, are involved in dozens of studies looking for guideposts along the road of tumor development. An analogy in heart disease would be cholesterol and blood pressure levels—two easily measurable and treatable warning signs.

While some intestinal polyps and abnormal cell growths in the breast, prostate and cervix "are clearly on the pathway" to cancer, most such markers haven't yet been confirmed in clinical trials, says Peter Greenwald, director of the Division of Cancer Prevention and Control at the NCI. And none of them are as easy to detect as high cholesterol or hypertension. To assess breast cells, for example, scientists have to remove tissue with a fine needle or aspirate fluid from the nipple. Eventually, though, says Greenwald, "we think that what are now fancy, sophisticated tests in laboratories will be kits in doctors' offices. When we find individuals at risk, the aim will be to bring down that risk."

The reality is that people often won't do what's good for them. Scientists have documented conclusively that nicotine is addictive and that smoking causes about 30 percent of U.S. cancer deaths,

JIM LO SCALZO—USN&WR

DAYLE LEMKE, 33, TESTICULAR CANCER SURVIVOR

A LONG SIEGE

By the time he was diagnosed in September 1987, cancer had spread to his lungs and liver. "An X-ray looked like somebody had thrown a handful of change in my lungs," he recalls. After his testicle was removed, Lemke remained in the University of Texas M. D. Anderson Cancer Center in Houston for nine months of aggressive chemotherapy. It took several years to recover from the treatment. Last summer, he returned to full-time work on a cotton-and-corn farm in Victoria, Texas.

but millions still smoke. "We have not learned how to prevent most lung cancers and all the other tobacco-related cancers, because we don't know how to give help to all the people who want to quit smoking and can't," laments John Bailar III, chairman of health studies at the University of Chicago, who has long criticized the NCI for not investing more in prevention research.

HOW SYNTHETIC CHEMICALS FIT IN

The compounds in cigarette smoke aren't the only ones connected to increased cancer risk. Arsenic and asbestos are among others associated with lung cancer. Benzene, present in lead-free gasoline, has been linked with leukemia. And exposure to chemicals that mimic the effects of estrogen, such as some pesticides, has come under scrutiny as a potential risk factor for breast cancer.

Increasingly, research has pointed to a woman's lifetime exposure to estrogen as a factor in whether she'll develop breast cancer. Breast cancer diagnoses may be increasing because women are postponing or deciding against having children, lengthening their exposure to the hormone. But Devra Lee Davis and others suspect pesticides are at least partly to blame. Experiments have shown that large amounts of some compounds that mimic estrogen can cause breast tumors in animals. "The evidence is not hard and fast; it's suggestive," says Ken Olden, director of the environmental health institute. "It does make some sense."

Decades could pass between exposure to a cancer-triggering compound and the diagnosis of a malignancy. On-the-job contact with possible carcinogens is easier to measure than is exposure outside the workplace. That's why much of what has been learned about cancer-causing chemicals comes from certain occupations with strikingly high cancer rates. Shipbuilders in Norfolk, Va., helped tip scientists off to the connection between asbestos and lung cancer.

Researchers now are turning to communities known to have come in contact with exceedingly high levels of possible carcinogens. This spring, NCI scientists will begin studying women in tiny Triana, Ala., site of a factory that made the pesticide DDT and related compounds from the mid-1940s to the early 1970s. In the late 1970s, fat samples taken from residents had some of the highest levels ever recorded of DDE, produced when DDT is broken down in the body. NCI researchers want to see whether breast cancer patients have higher levels of DDE than women who don't have the disease.

Before the study even begins, NCI researchers know that many Triana residents run a higher-than-average risk of dying from a variety of cancers because they are poor. Poor Americans lack access to screening tests that would catch cancers early and to treatments once diagnosed. If every American had such access, the overall five-year survival rate would jump from around 50 percent to 75 percent, argues Harold Freeman, a cancer surgeon at Harlem Hospital Center in New York and head of the President's Cancer Panel.

Cervical cancer is a good example. Since the Pap test's introduction in the 1950s, it has dramatically cut deaths by catching cervical cancer in its earliest stage. Still, nearly 5,000 American women will die of cervical cancer this year, mainly because they did not get regular Pap tests or could not get treated for lack of insurance, says Freeman. "It's a misconception to say that research cures cancer," he says. "You've got to cure cancer in the neighborhoods of America where people are living and dying." ■

BY RITA RUBIN

A listing of the best U.S. hospitals for cancer treatment and lists for each state and 10 metropolitan areas are available on the Internet on U.S. News Online at http://www.usnews.com.

CHRIS USHER FOR USN&WR

LITA BRANCO, 18, CHILDHOOD LEUKEMIA SURVIVOR

FREE OF DOCTORS

No way is she going to pursue a health care career. Marine biology maybe, but no more doctors or hospitals. She had her fill after she was diagnosed with acute lymphocytic leukemia at age 3. Nearly four years of chemo left her cancer free. She stops back at Johns Hopkins Hospital in Baltimore to see her doctor, Cindy Schwartz, who directs a program to monitor and treat long-term complications from therapies for childhood cancers—the one downside to improved cure rates.