Five Strategies for Accelerating the War on Cancer in an Era of Budget Deficits

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ABSTRACT
In recent years, the National Institutes of Health’s largest institute, the National Cancer Institute (NCI), has adapted to difficult economic conditions by leveraging its robust infrastructure—which includes risk factor surveillance and population monitoring, research centers (focused on basic, translation, clinical, and behavioral sciences), clinical trials and health care research networks, and rigorously validated statistical models—to maximize the impact of scientific progress on the public health. To continue advancement and realize the opportunity of significant, population-level changes in cancer mortality, the NCI recommends that five national-level actions be taken: (1) significantly increase enrollment of Medicare patients into cancer clinical trials through adequate physician reimbursement, (2) increase NCI/Centers for Medicare and Medicaid Services collaboration on clinical trials research to evaluate the therapeutic efficacy of anticancer drugs, (3) establish a national outcomes research demonstration project to test strategies for measuring and improving health care quality and provide an evidence base for public policy, (4) leverage existing tobacco-control collaborations and possible new authorities at the U.S. Food and Drug Administration to realize the outstanding health gains possible from a reduction in tobacco use, and (5) increase colorectal cancer screening rates through intensified collaboration between federal agencies working to address barriers to access and use of screening. These cost-effective strategies provide the opportunity for extraordinary results in an era of budget deficits. Of the chronic diseases, cancer has the strongest national research infrastructure that can be leveraged to produce rapid results to inform budget prioritization and public policy, as well as mobilize new projects to answer critical public health questions.

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INTRODUCTION
Following the doubling of the National Institutes of Health’s (NIH) budget between 1998 and 2003, the NIH has seen increased financial pressures, and has struggled to maintain rapid innovation with a flat or, in some years, even a reduced budget. This sudden cut in available financial resources has affected all of the institutes, including the National Cancer Institute (NCI), whose budget had increased 80% between 1998 and 2003.

Fortunately, the NCI has maintained reasonable momentum in the postbudget-doubling period, thanks to its robust infrastructure for supporting basic, clinical, and population sciences. This has enabled the NCI to begin new projects to answer important clinical and public health questions using only modest, highly targeted increases in funding.

The unique features of the cancer research enterprise provide an excellent model for how to leverage changes in policy, funding, and research infrastructure to maximize the...
impact of scientific progress. Among the chronic diseases that confer the greatest burden on the population, cancer has the strongest national research infrastructure—including risk factor surveillance and population monitoring; research centers focusing on basic, translational, clinical, and behavioral sciences; clinical trials networks; health care research networks; and rigorously validated statistical models. This remarkable research infrastructure can be leveraged to produce rapid research results to prevent cancer, diagnose it earlier, treat it more effectively, and inform budget priorities and policy change.

Significant population-level changes in cancer incidence and mortality have already been achieved through improved screening and treatment, and reductions in tobacco use. But, much more is possible. With this in mind, we have identified a short list of actions that can be taken at the national level that can be implemented rapidly and will yield dramatic benefits to patients and the public, at only modest cost. The specific recommendations are the following:

1. Significantly increase enrollment of Medicare patients into cancer clinical trials.
2. Increase NCI/Centers for Medicare and Medicaid Services (CMS) collaboration on clinical trials research to determine the effectiveness of new cancer drugs.
3. Undertake a national outcomes research demonstration project.
4. Leverage existing tobacco-control collaborations and possible new authorities at the U.S. Food and Drug Administration (FDA).
5. Disseminate and implement colorectal cancer screening.

**Significantly Increase Enrollment of Medicare Patients into Cancer Clinical Trials**

Although individuals >65 years of age account for >60% of new cancer cases in the U.S. [1, 2], they make up less than a third of participants in oncology clinical trials. This underrepresentation makes it difficult to provide evidence-based treatment guidelines for this population, because results from clinical trials that enroll an overwhelmingly younger group of patients may not be clinically applicable to older patients.

A major barrier to increasing enrollment for older patients comes not from the patients themselves but from the current, insufficient Medicare reimbursement rate for the type of office visits required for patients entered into clinical trials. Today, physicians receive the same reimbursement for a standard chemotherapy consultation as they do for a patient visit in which they must explain the scientific rationale for a clinical trial and obtain written informed consent from the patient for the study. This process is critical to research trials, but may take twice the time as a standard patient encounter. This harsh financial reality explains why many practicing oncologists have opted out of the clinical trials enterprise.

On June 7, 2000, President Clinton signed an Executive Order, later reconfirmed by President Bush, requiring Medicare reimbursement for the routine costs associated with both federally sponsored and FDA-approved clinical trials. Contrary to expectations, however, this has not produced an increase in enrollment of patients >65 years old [1, 3].

Many believe that the Executive Order did not increase clinical trial enrollment because it did not address the inadequacy of current reimbursement rates to cover the actual professional costs associated with the complexities of clinical trial enrollment. The current choice for oncologists is to either enroll a patient in a federally sponsored study and be guaranteed a monetary loss on every visit or treat the patient with a standard, noninvestigational therapeutic regimen that requires less than half the time, and receive the same level of reimbursement. This is simply not a choice that can be expected to support the active participation of oncologists in cancer clinical trials.

We propose that a modest increase in physician reimbursement from the CMS for the professional component of the patient visit for those individuals entered into clinical trials would dramatically (up to twofold) increase the enrollment of Medicare patients into new and existing NCI-sponsored clinical trials. This increase would substantially speed up the completion of critical clinical studies of therapeutic effectiveness, in particular, those trials that address the question of which therapies actually benefit elderly patients. We estimate that the potential cost of such a reimbursement increase—which would not require Congressional action—is <$100 million dollars a year. Ultimately, this modest increased expense would save the CMS many times this amount in pharmaceutical costs alone, by definitively determining which cancer treatments benefit the Medicare population the most.

**Increase NCI/CMS Collaboration on Clinical Trials Research to Determine the Effectiveness of New Cancer Drugs**

Another collaborative effort between the NCI and CMS that could potentially produce savings far surpassing its initial investment would be an Executive Order instructing the CMS and NCI to cosponsor collaborative effectiveness clinical trials for cancer drugs newly approved by the FDA. If a drug receives FDA approval, the CMS is required to pay for it. Because almost two thirds of all cancers are diag-
nosed in patients eligible for Medicare, new chemotherapy drugs and biologics represent a large and growing financial burden for the CMS. The costs of these drugs have grown exponentially more expensive over the past decade, often reaching levels of $75,000 to $150,000 a year, for a single patient. For example, bevacizumab (Avastin®; Genentech, Inc., South San Francisco, CA) for the treatment of advanced non-small cell lung cancer can add >$80,000 to the cost of a full course of therapy [4]. Although approved for specific cancer types, such as non-small cell lung cancer, these drugs are often only effective in a subset of patients with the diagnosis. It is crucial that we better understand how to target patients who will truly benefit from these costly, but highly effective, new treatments through research on biomarkers (properties of the tumor) that will help identify those patients whose cancers will respond to these cutting-edge treatments. Without research trials to develop and assess biomarkers of clinical benefit, we cannot predict who will benefit from these agents.

The NCI has the existing scientific capability to evaluate which patients will benefit from the new “targeted” therapeutic agents. For example, the NCI recently launched the Marker Validation for Erlotinib (Tarceva®; OSI Pharmaceuticals, Inc., Melville, NY) in Lung Cancer (MARVEL) clinical trial, which is the first trial to test a potential predictive biomarker of a new, targeted therapy for lung cancer. Erlotinib blocks tumor cell growth by targeting aberrant production of a protein called the epidermal growth factor receptor (EGFR). The drug is currently approved by the FDA for the treatment of patients with locally advanced or metastatic non-small cell lung cancer. However, the abnormal expression of the EGFR protein is not consistent from tumor to tumor and patient to patient.

In the MARVEL trial, patients with non-small cell lung cancer will have their levels and molecular characteristics of EGFR in their tumor measured upon enrollment in the trial. Patients will then be randomly assigned to receive either erlotinib or the standard therapy (pemetrexed). The trial will examine whether or not measurable features of the EGFR gene can predict response to treatment with erlotinib or the standard chemotherapy.

The CMS now supports the enormous cost of erlotinib treatment for seniors with advanced lung cancer (>8,000 per month per patient). This is despite the fact that, in unselected populations, the drug is effective, at best, only about 10% of the time [5]. Based on current data, it is likely that the MARVEL study will demonstrate that a modestly priced and easily available biomarker test can determine which patients will benefit from treatment with erlotinib and which will not. The total research funding for the MARVEL trial, borne completely by the NCI, is estimated to be $10 million. CMS investment in clinical research studies, such as the MARVEL trial, could reap enormous financial savings to the agency, by determining in advance which patients will actually benefit from drugs such as erlotinib. Equally important, patients could be spared the side effects of drugs that will not benefit them.

The MARVEL trial is the first biomarker study to be conducted by the Oncology Biomarkers Qualification Initiative (OBQI), a collaboration among the FDA, NCI, and CMS that began in 2006. Similar trials could be conducted rapidly and relatively inexpensively using the existing OBQI expertise and infrastructure, with the potential financial benefit to Medicare far exceeding the costs of the research. To do this, however, would require an Executive Order instructing the CMS to expand its activities to include funding the clinical research costs of studies that evaluate the therapeutic efficacy of anticancer drugs.

A NATIONAL OUTCOMES RESEARCH DEMONSTRATION PROJECT

The clinical trials that the NCI supports, its Comprehensive Cancer Centers Program, and other special programs, such as the Special Programs of Research Excellence (SPORES), have and continue to develop cutting-edge, highly effective, and targeted cancer therapies. Nevertheless, many patients do not receive optimal care, and wide disparities in the quality of cancer care and health outcomes exist. The NCI provides leadership in understanding, addressing, and ameliorating these disparities in health outcomes after a cancer diagnosis. For example, since 2000, the NCI has led the interagency Quality of Cancer Care Committee, which has supported several pilot projects to test strategies for measuring and improving quality of care across a wide range of contexts, including the Veteran’s Health Administration and the Health Resources and Services Administration’s (HRSA) Bureau of Primary Health Care. More recently, a pilot program called the NCI Community Cancer Centers Program has awarded contracts to nonprofit hospitals across the country to support community cancer centers to expand the reach of clinical research and high-quality health care to underserved populations.

The quality of cancer care and differences in health outcomes experienced by patients with a similar cancer are the result of a complex interaction of factors such as patient factors (such as presence of other illnesses), physician factors (such as training), and health care system factors. Important roles of the NCI are to understand these complex interrelationships; develop, assess, and disseminate interventions—from public policy to training health care providers to helping family caregivers help their relatives with cancer; and inform the larger health policy debate about the most

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cost-effective methods for cancer prevention, early detection, treatment, and surveillance.

Critical to the success of these research infrastructures is the linkage of medical records and other data systems that together collect, assemble, and facilitate the analysis of data on the multiple dimensions and factors that contribute to cancer outcomes, because no one source of data captures all of the contributors to cancer outcomes. The NCI already has successful research models designed not only to investigate the determinants of cancer outcomes but also to project the impact of policy and other interventions to change those outcomes. The NCI’s well-established cooperative clinical trials networks—providing critical evidence concerning treatment efficacy—must be coupled with a new national network for the generation of data concerning treatment effectiveness and outcomes to ensure that the benefits of cancer research are experienced by all Americans.

Expanding these established cancer outcomes projects will vastly improve the capacity to understand and address population disparities in cancer outcomes and contribute to a comprehensive, national research infrastructure for research on cancer outcomes.

One of these projects includes a research infrastructure called the Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium, which has followed cohorts of 5,000 lung and 5,000 colorectal cancer patients through the continuum of care across a wide variety of health care settings [6]. CanCORS has shown how data from multiple sources (including medical records, patient-reported outcomes, physician surveys, caregiver surveys, and claims data) can be linked to identify the many factors that explain variations in the quality of cancer care patients receive and their health outcomes.

There is a formidable gap between the rapid pace of innovation in biomedicine and our ability to harness it to improve population health. While contemporary science has enabled the collection of data from randomized controlled trials, observational studies, surveys, cancer registries, claims data, and other health-related sources, it remains a challenge to integrate these sources of information into optimal decision-making tools to inform public policy. The Cancer Intervention and Surveillance Modeling Network (CISNET) is a consortium of NCI-supported investigators who use simulation modeling of breast, prostate, colorectal, and lung cancers to understand the impact of cancer control interventions (i.e., screening, treatment, and prevention) on past trends, to project future trends, and to help determine optimal cancer control policies and guidelines.

The group uses a comparative modeling approach, in which reproducibility across models adds credibility to the results, while differences point out areas for further system-atic study. Examples of CISNET collaborations include the U.S. Preventive Services Task Force (USPSTF) in support of new screening guidelines for breast and colorectal cancers; the CMS for technology assessments to support National Coverage Determinations of new cancer screening tests; the Centers for Disease Control and Prevention (CDC) to provide guidance in designing new cancer control programs and enhancing existing ones; and the American College of Radiology Imaging Network on a cost-effectiveness study as part of the National Computed Tomography Colonography Trial [7, 8].

Launched in 1999, the NCI health maintenance organization (HMO) Cancer Research Network (CRN) uses large managed care systems as a platform for basic, clinical, and population sciences research. The CRN has access to nearly 11 million HMO enrollees nationwide, with an overall age and sex distribution accurately reflecting the general U.S. population [9]. Since 1999, both researchers within the CRN and external collaborators have used this diverse population to answer questions about the efficacy of targeted smoking cessation efforts, breakdowns in the screening process, ways of improving the monitoring of the quality of care delivered to patients newly diagnosed with lung or colorectal cancer, and hospice referral and palliative care in the managed care environment, among dozens of other successful projects.

An investment of $10 million allocated to the CRN would permit the NCI to leverage this infrastructure to pilot one critical element of the national infrastructure: linking data from the NCI’s clinical trials network with other data systems with cancer outcomes data to enable the more rapid identification of rare side effects of treatment as well as the impact of comorbidities that typically disqualify patients from participating in clinical trials.

The pace of new developments in cancer control technologies, molecular determinants of cancer risk and treatment effectiveness, and results from screening and treatment trials will continue to accelerate. A modest investment of $5 million would augment existing CISNET models to expand CISNET to additional cancer sites and support collaborations with colleagues in the fields of public health, public policy, legislative affairs, cancer control planning, and clinical science. This investment would guide us in determining the best strategies to achieve the maximum public health benefit.

LEVERAGE EXISTING TOBACCO-CONTROL COLLABORATIONS AND POSSIBLE NEW AUTHORITIES AT THE FDA

Reducing tobacco use—the nation’s leading cause of cancer death—remains the greatest unmet potential for im-
proving control of cancer and many other chronic diseases. Currently, about one in five adult Americans smokes cigarettes, and by the 12th grade, nearly 45% of teenagers have tried cigarette smoking [10]. However, these overall figures mask tremendous disparities in tobacco use by level of educational attainment, income, race/ethnicity, and other variables; the fact that tobacco use is increasingly limited to certain populations contributes heavily to the health disparities that so burden our nation.

The experience of California, which has had a model tobacco control program since 1989, illustrates what is possible. Since the program’s inception, adult smoking prevalence in the state has gone from approximately 11% lower than the rest of the nation in 1988 to 20% lower in 1996, and exposure to secondhand smoke has plummeted [11]. Additionally, a recent analysis of the impact of California’s state tobacco control program on aggregate personal health care expenditures in the state found that the first 5 years of the program were associated with $86 billion lower health care expenditures than would have been expected without the program [12]. These remarkable results complement a wealth of evidence demonstrating the tremendous health and economic gains that can be achieved if we tackle tobacco control with the seriousness and energy it deserves.

In recent years, the nation’s investment in tobacco control has been meager, and state-level efforts have suffered from budget cuts and the diversion of tobacco settlement funds to nontobacco-control-related projects. Fortunately, there exists an extensive and systematic collaboration between nonprofit, state, and federal entities to enable a rapid scale-up of efforts should funds become available.

In 2004, a task force commissioned by the Secretary of the Department of Health and Human Services determined that millions of premature deaths caused by smoking could be prevented by implementing several evidence-based strategies, including increasing tobacco excise taxes and improving access to cessation services [13]. Additionally, it is critical to ensure more widespread adoption of measures to protect the public from secondhand smoke, a cause of lung cancer and coronary heart disease [14]. Congress has recently considered whether to grant the FDA the authority to regulate tobacco products. The bill under consideration has broad support among medical and public health organizations; it would restrict the marketing and sales of tobacco products to youth, require larger and stronger tobacco package warning labels, ban the use of misleading descriptors such as “light” and “mild” on packages or advertising, and require the tobacco companies to provide the FDA with detailed information on the constituents of their products. In addition, it would strictly regulate the marketing of tobacco products purported to reduce harm, and allow the FDA to require changes in current and future tobacco products to protect the public health. Importantly, funds for the FDA’s tobacco regulatory activities would be provided by fees on tobacco manufacturers.

If the FDA is granted authority to regulate tobacco products, there will be many important opportunities to leverage existing evidence and research capacity. The NCI and CDC currently support a broad portfolio of tobacco control research, including research to study tobacco products purported to reduce harm. These research efforts can be rapidly expanded to inform the FDA’s regulatory mission. Additionally, the NCI’s Centers of Excellence in Cancer Communications can provide guidance to the FDA on the most effective ways to design effective and compelling tobacco warning messages, and on other critical tobacco control communication strategies.

Although most smokers want to quit, few use evidence-based smoking cessation methods, and accessing such services can be difficult [15]. The National Network of Smoking Cessation Quitlines (1–800-QuitNow), supported in part by the NCI’s Cancer Information Service, can be greatly strengthened by increasing the capacity to handle calls, adding coverage hours, providing services in additional languages, and extending coverage for medications. Enactment of FDA regulatory authority will increase the demand for cessation services, and the public health agencies, along with the states, need to be ready to provide evidence-based services to those who need it. Quitlines are a cost-effective strategy, especially when they include the provision of medications and follow-up counseling.

A recent NCI monograph highlighted that cigarettes are one of the most heavily marketed products in the U.S., and determined that tobacco advertising and promotion are causally related to increased tobacco use [16]. Additionally, the research described in the monograph found that youths’ exposure to depictions of smoking in the movies promotes youth smoking initiation. To begin to “level the playing field,” there is a critical need for a national media campaign focusing on the tobacco industry’s efforts to promote tobacco use, the importance of quitting as early in life as possible, and the need to eliminate nonsmokers’ exposure to secondhand smoke.

All of these efforts in tobacco control research and programs could be supported with a $60 million investment.

**DISSEMINATION AND IMPLEMENTATION OF COLORECTAL CANCER SCREENING**

Strong evidence shows that screening for colorectal cancer reduces both the incidence of and mortality from this disease [17]. Since 1996, the USPSTF has recommended that
all adults aged ≥50 years at average risk for colorectal cancer undergo regular colorectal cancer screening [7]. But the rates of colorectal cancer screening for this population—estimated at only 50% [17]—lag far behind the current rates for breast and cervical cancer screening.

Raising awareness of the need for and rates of colorectal cancer screening is a sensible focus for difficult economic times; models have shown that a 49% reduction in the risk of colorectal cancer death could be achieved by the year 2020 simply by decreasing the prevalence of lifestyle risk factors, increasing the rate of colorectal cancer screening to 70%, and implementing widespread use of the current best available chemotherapy across all age groups [18]. Of these, increasing screening can be expected to have the largest effect on reducing colorectal cancer mortality.

Fortunately, we already understand many of the barriers to screening—not just at the personal level, but at the provider, health system, and community levels as well [19]. Lack of adequate health insurance coverage is a major barrier to preventive care in general, and colorectal cancer screening in particular [20].

Intensified collaboration among the federal agencies working on these issues would help to overcome these barriers. The NCI has previously collaborated with the CDC on pilot programs to encourage and financially support colorectal cancer screening for underserved populations, such as the CDC’s Screen for Life National Colorectal Cancer Action Campaign and Colorectal Cancer Screening Demonstration Program and the NCI-CDC-HRSA Regional Cancer Collaborative project [20]. With minimal additional funds, these existing, successful relationships could easily be expanded, and would have the advantage of bringing together experts from different organizations representing diverse areas of public health focus to address deficiencies in access to and use of colorectal cancer screening.

Some of the ways to build on this experience of federal collaboration to support local work would include working with the CMS to create a mandate for colorectal cancer screening as an explicit component of the Welcome to Medicare benefit. Doing so would instantly reach tens of thousands of people at average risk for colorectal cancer each year. The experience in the NCI Community Cancer Centers Program and the Cancer Collaborative could be leveraged to help disseminate knowledge and methods for increasing the use of colorectal cancer screening and guideline recommendations in cancer control through Federally Qualified Health Centers and community care networks. Such an effort would take advantage of collaboration that could serve millions of our most vulnerable populations. Collectively, these efforts could be supported with an investment of $25 million.

CONCLUSION

This short list of actions has the potential for substantial clinical and public health impact at minimal cost. Some actions can be implemented using existing authorities; others will need new congressional or federal Executive Office authorities. All of these can be implemented quickly because they build directly on existing research, clinical, and public health models.

Taken together, the total cost would be $210 million. This investment would be highly leveraged because all five projects build on the NCI’s already existing strong research infrastructure. In some cases the potential cost savings are estimable and considerable, and the public health benefits would be substantial. Finally, these actions build upon strong collaborations and partnerships that the NCI already has with its sister Health and Human Services agencies the FDA, CMS, and CDC.

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