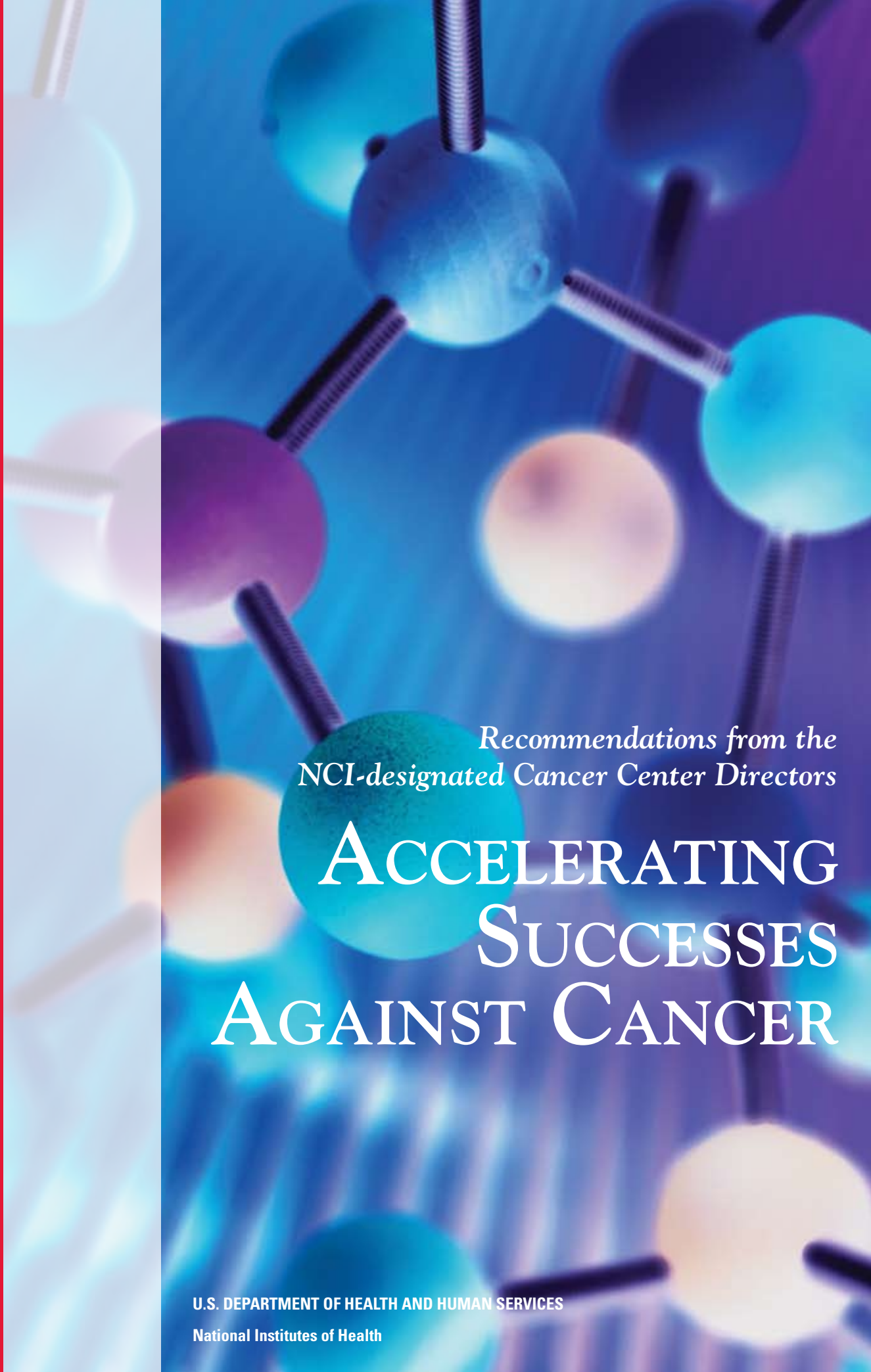
National Cancer Institute



Recommendations from the NCI-designated Cancer Center Directors

Accelerating Successes Against Cancer

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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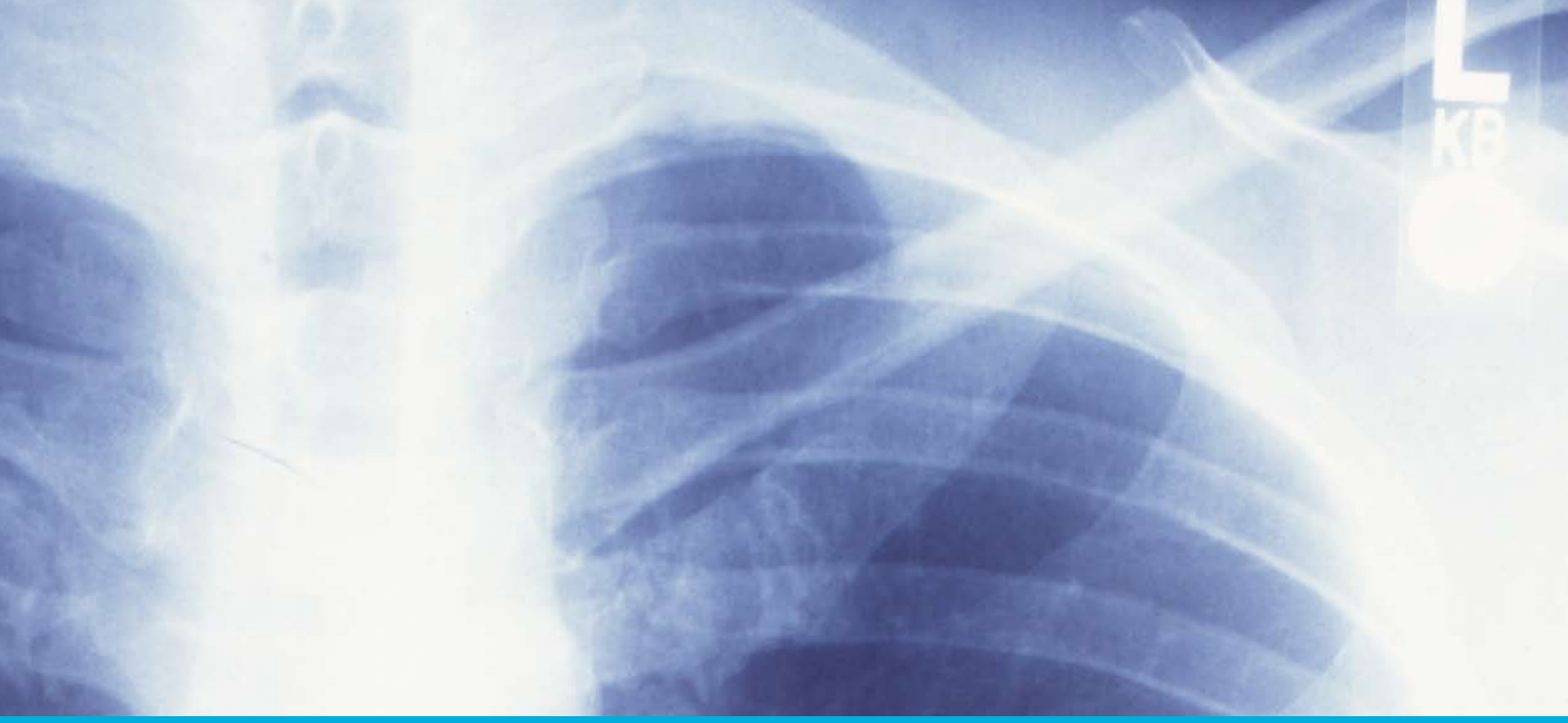


Statement of Purpose

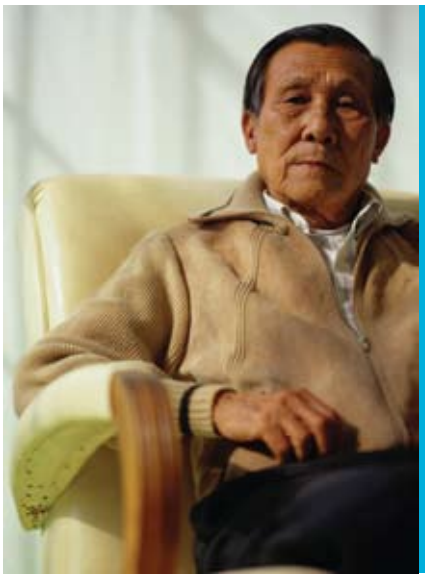
Never has there been such opportunity and promise for improving outcomes for patients with cancer. The human genome project and other recent accomplishments in molecular biology and technology development have made it possible to revolutionize the way physicians and researchers can address the challenge of preventing and curing cancer.

In 1971, with the passage of the National Cancer Act, the National Cancer Institute (NCI) initiated creation of centers of excellence and charged them with gathering together the expertise to greatly expand research on understanding the causes of cancer and improving its treatment. Initially the centers of excellence consisted of three NCI-designated Cancer Centers. Today there are 61 Centers, spread widely across the United States.

As a result of the government's increased investment in research over a period of more than three decades, we now know that cancer is caused by mutations or abnormal functioning of critical genes which control the replication and behavior of the cells in our bodies. This statement could not have been made in 1971.

The National Institutes of Health (NIH) Director Dr. Elias Zerhouni's new NIH Roadmap Initiative contains three key concepts: 1) exploring new pathways to discovery focusing on molecular networks associated with disease, imaging technologies, and nanomedicine; 2) creating interdisciplinary research teams of the future;

and 3) re-engineering the clinical research enterprise and incorporating community-based physicians, in order to place more patients in innovative clinical trials. The Nation's Cancer Centers and academic cancer research programs are leading the way in all three of these areas, and have been doing so for decades. By their very nature, research programs in NCI-designated Cancer Centers bring together basic, clinical, and population scientists to focus on cancer. Since their inception, the Cancer Centers have been peer-reviewed and scored by NCI based upon the strength of their intra- and interprogrammatic interactions. This model has contributed significantly to the successes that have been achieved in understanding the molecular basis of cancer and in developing targeted therapies and new imaging modalities. The nationwide program of clinical trials investigating new cancer treatments on many thousands of patients is a model of clinical investigation.



While our knowledge of cancer will never be complete, we have reached the point where medical researchers can at last envision ways to greatly improve our ability to reduce death and suffering from cancer. The age-adjusted rate of cancer mortality has been falling for a decade. Recently, it was reported that in 2003, for the first time, the absolute number of cancer deaths in the United States was reduced from the previous year. This is despite the fact that as a whole the U.S. population is living longer and cancer is a disease whose risk increases with aging. We can substantially reduce deaths from cancer just by broadening the application of knowledge we have today. By expanding our knowledge through further research, even greater gains are well within our reach.

The Cancer Centers Directors working group, described below, was not in a position to pursue an independent economic analysis of the benefits of improving cancer care. However it is worth making a few points from the available literature. The cost of caring for patients with cancer reached $40 billion in 1996. Medicare bears over one-third of these costs. This figure has increased during the past decade to $72 billion. This does not include the cost of screening and the value of time lost from work during treatment, as well as the cost of premature death with loss of productivity. As an example, the cost of treating an early stage breast cancer patient over her lifetime is over $70,000. There were 213,000 new cases of this disease alone in 2006.

The total impact of cancer on health is high. It was recently reported that for Americans under the age of 85, cancer is the leading cause of death. The American Cancer Society reported that last year there were 1,399,790 new cases of cancer and 564,830 deaths. Economists at the University of Chicago estimate that a 1% reduction in cancer deaths would be worth over $400 billion.

NCI was created as a governmental agency to lead cancer research, not to deliver health care. In contrast, most of the Nation's NCI-designated Cancer Centers are imbedded in academic medical centers which have the dual missions of leading the fundamental study of disease and translating new knowledge to change the delivery of health care. The NCI's Strategic Plan published in January 2006 outlines a bold vision of strategies to investigate cancer in the laboratory, in the clinic, and in the community, and states clearly that dissemination and application of research discoveries are required for success. The Nation's Cancer Centers are

uniquely positioned to both lead in cancer research and lead in this dissemination process.

The Cancer Centers Directors' Working Group

At the November 7, 2005 meeting of the NCI Director with the directors of the NCI-designated Cancer Centers, a small working group – chaired by Dr. John Mendelsohn, President, University of Texas, MD Anderson Cancer Center – was asked to write a report providing a blueprint on how the Cancer Centers can contribute to achieving the following goals:

1. Reduce the burden of cancer through research in the areas of prevention, detection, treatment, and survivorship, and create a strategy for success.

2. Identify ways in which NCI-designated Cancer Centers can enhance collaboration with each other and with other stakeholders in the pursuit of our shared mission.

3. Suggest initiatives that will enable the Cancer Centers to extend their research beyond their local communities and to provide leadership in the wide dissemination of best practices in cancer care and prevention.

4. Create a realistic vision of the potential for future successes and identify the roadblocks that must be dealt with.

The working group was subdivided into six subcommittees concentrating on the outlined goal areas: prevention, detection, treatment, survivorship, collaboration, and dissemination. The subcommittee reports were presented and discussed at the NCI Cancer Center Directors Retreat in May 2006 and the final report of recommendations was reviewed by all of the Cancer Center directors.

We Have Made Progress

Progress has been made during the 35 years since passage of the National Cancer Act in 1971. During the 10 years between 1990 and 2002, the age-adjusted death rate from cancer declined 1% per year. This translates into over 315,000 lives saved or prolonged beyond that period of time. In 2004, the total deaths from cancer, which had been leveling off for a number of years, fell to levels slightly below the previous year's figures.

The American Cancer Society recently published a midpoint analysis of progress towards its goal of reducing cancer deaths by 50% over the 25 year period between 1990 and 2015. If trends over the first 12 years continue, the projection is for a 23% reduction in cancer deaths by 2015. However, for breast cancer, colon cancer, and lung cancer in males, the trends predict a 50% reduction.

It is worthwhile considering why these significant levels of reduction are being achieved and what more can be expected. For breast cancer, the improvement is attributed to a combination of early detection due to mammography and manual palpation and improved therapy. Significantly, only 58% of women had mammograms in 1970 while by 2002 the number reached 76%. That leaves room for helping the 24% of women who currently do not receive the benefits of early detection.

For colon cancer, the 50% trend for reduced deaths is attributed almost entirely to colon endoscopy with polypectomy. Polypectomy reduced the incidence of cancer by 80% in two large studies. Only about 50% of Americans over the age of 50 undergo colon examination, so there is high potential for further improvement in death rates.

For male lung cancer, the 50% trend for reduced death is attributed primarily to reduced tobacco use. There is likely to be a downward trend in lung cancer death rates for women, because lung cancer incidence rates have begun to fall for women in recent years, paralleling the earlier fall for men. These gains have resulted from an enlightened behavior on the part of the public, supported by educational campaigns, clean indoor air laws, cigarette taxes, improved access to counseling and pharmacologic aids, and increased commitment of time and effort by the medical profession. Obviously, a great deal more can be accomplished. It must be emphasized that nearly one-third of all cancer deaths in the United States (over 180,000 people last year) are directly attributed to tobacco, with lung cancer leading the list.

It is apparent that most of the substantial reduction in cancer deaths over the past 12 years has resulted from prevention and increased use of effective diagnostic studies. This report will present measures to further enhance prevention and early detection of cancer, as well as new

approaches to the treatment of cancer, and management of survivors. While it is impossible to precisely quantify the anticipated impact on death rates, it is reasonable to predict that if research efforts and use of evidence-based clinical practices are increased in the areas we outline, we will reduce the burden of cancer far more rapidly and come closer to achieving the American Cancer Society's goal for 2015.

Conclusion

We conclude that the Nation's 35-year-old cancer plan can be re-energized to increase the pace of discovery and dissemination of improvements in cancer care. This document is presented as a blueprint for accelerating successes against cancer, both by expanding knowledge of cancer and by applying these discoveries expeditiously to improving the care of cancer patients. Our report of recommendations builds on and expands the NCI Strategic Plan.

NCI-designated Cancer Centers are in the privileged position of being able to contribute to both research and patient care goals, and we make a renewed commitment to do so in partnership with the NCI. We invite collaborators from the many sectors of our society with an interest in reducing the burden of cancer to join in this endeavor with renewed commitment of their efforts and resources.

We wish to emphasize that this must be a joint effort, involving academia, medical care providers, professional organizations, governmental agencies and the U.S. Congress, pharmaceutical and biotechnology companies, and – most importantly – patient advocacy groups and the public. These stakeholders will need to synchronize their goals and actions. From the beginning of planning the National Cancer Act, and continuing up to the present, patient advocacy groups have played a critical role in bringing together the public, the government, and the biomedical research community, and reminding us all to focus on the patient.

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Executive Summary

The following is a summary of the major recommendations in each of the six areas targeted for review by the working group of the Cancer Center directors.

Prevention

In addressing the challenge of reducing the burden of cancer, prevention is the most desirable goal. Population studies have identified lifestyle changes that can reduce the risk of cancer, the most prominent of which is avoidance of tobacco use and exposure. We also have discovered that molecular and biological changes in blood and tissue specimens from patients can serve as markers, identifying individuals who bear higher risk for developing certain cancers, including those who show the very earliest biological

changes in the development of cancer. These individuals may benefit from active interventions in their lifestyle and behavior and, in the future, from treatment with agents that can retard or prevent the development of cancer.

We endorse the recommendations of the National Cancer Policy Board on cancer prevention and early detection, which are summarized in this report.

Strategies that Can Immediately Begin to Reduce the Risk of Cancer

- Implement known methods and investigate improved methods for preventing initiation and enabling discontinuation of tobacco use. If successful, this measure alone can reduce the incidence of cancer by more than 30%, after an estimated lag time of about two decades.
- Implement other evidence-based changes in lifestyle that will reduce the incidence of cancer, including a healthy diet, avoidance of obesity, and increased physical activity.
- Implement scientifically established medical strategies, including administration of tamoxifen or raloxifene to prevent breast cancer in high-risk postmenopausal women and HPV vaccination to prevent cervical cancer in young females.
- Utilize rapidly developing knowledge of inherited and environmentally induced mutations to begin to establish risk profiles for high-risk populations, to set the stage for rational chemoprevention and other strategies.

Cancer Centers can partner with governmental agencies and health care providers to extend these measures to the entire U.S. population through improved delivery and targeted education. Vaccination against certain cancers should eventually become as standard in medical practice as vaccination against serious viral infections.

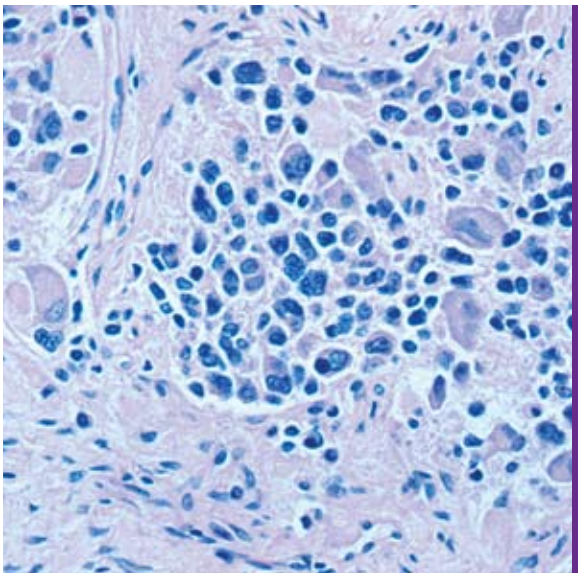
Strategies Involving Either Change in Policies or Further Research and Requiring a Decade or More Before Clinical Application

- Perform research on the application of "personalized medicine" to intraepithelial neoplasias (IENs) and precancerous conditions, by carrying out clinical trials to discover molecular targets for both early detection of high-risk lesions and targets for chemoprevention treatments.
- Increase clinical research in the behavioral sciences that will identify improved methods for changing personal lifestyles and promote informed decisions about health-related behaviors.
- Continue to pursue chemoprevention clinical trials, based on the successes with anti-estrogen agents in preventing or postponing breast cancer in high-risk groups.

While Cancer Centers can collaborate in carrying out these large-scale and long duration clinical studies, funding will be needed from governmental agencies or from companies willing to partner in these efforts.

Early Detection

Early detection of cancer can enhance the chances of achieving



cure or prolonging life for individuals diagnosed with cancer. In spite of the great interest in identifying markers in blood or cells that can identify the presence of cancers at the earliest possible time, progress in research has been slow. This is due to limitations in available technology and lack of adequate funding to support the large-scale and expensive clinical trials required to first identify and then validate these markers.

The effort and expense involved are highly worthwhile. This is because the chances for cure of most early stage cancers is typically higher than 90%, whereas cure rates for advanced stage cancers can be lower than 5% for most, but not all, solid tumors. Detection at an early stage can yield tremendous benefits in reducing death rates in cancers of the breast, colon, lung and prostate, which together account for nearly two thirds of all cancers.

Strategies that Can Immediately Increase Early Detection of Cancer

- Cancer Centers should partner with governmental agencies and health care providers to expand the use of currently validated screening methods for early detection, especially in underserved populations. These methods include colonoscopy, Pap tests, mammography, and the PSA test.
- Cancer Centers should join advocacy groups in pursuing payment for validated early detection tests by Centers for Medicare and Medicaid (CMS), insurance companies and health plans, and for extending access to uninsured Americans.
- Cancer Centers should partner with state departments of health and medical provider systems to disseminate information on the benefits of early detection of cancer and on locations where access to these measures are available.
- Cancer Centers should partner with each other to develop collaborative networks and cross-disciplinary teams that can share tissue resources and advanced technology platforms.

Strategies Involving Further Research and Requiring Up to a Decade or More Before Clinical Application

- Cancer Centers should perform large-scale, collaborative clinical trials designed to identify potential markers, using the expanding technologies of genomics, proteomics, immunohistochemistry and molecular imaging. These must be followed by clinical trials validating the capacity of these markers to accurately predict the presence of cancer. This research will require large-scale funding from the NCI or other sources.
- Fundamental research investigating specific genetic and molecular abnormalities that contribute to the malignant phenotype must continue full force because this approach will continue to contribute importantly to identification of markers that predict risk, prognosis, and appropriate therapy.
- With guidance and support from the NCI, Cancer Centers should develop and adopt a standardized and secure web-based tool for collecting and querying histories of patients and their families in a uniform way that will enable informed communication between patients and families and their health care providers, and provide data for researchers seeking to identify high-risk populations.
- Standardized and uniformly utilized electronic medical records would support initiatives in detection, treatment, and survivorship and should be a national priority. Collection, storage, and annotation of tissue specimens from each patient in a standardized way would also support these initiatives. Both initiatives will require substantial funding, collegiality, and visionary leadership.

Treatment

There has been tremendous progress in research leading to an understanding of the fundamental genetic and molecular causes of cancer and the development of new therapies that target these abnormalities. This has been accompanied by advances in surgery, radiation therapy, and systematic therapies which have already improved outcomes for cancer patients.

Because it already is uniformly acknowledged that fundamental research must continue to be pursued and funded, this report focuses primarily on the need for collaboration, coordination, standardization, and infrastructure support in clinical investigation. This will require participation by all stakeholders, including oncology specialists, providers, payers, regulatory agencies, government sponsors (e.g., NCI),

and patients. It also will require adequate funding specifically designated for these purposes. Cancer Centers are in an optimal position to lead in this effort, but the funding for clinical research must come from outside sources.

We endorse the findings of NCI's Clinical Trials Working Group (CTWG) entitled "Restructuring the National Cancer Clinical Trial Enterprise," which was adopted by the National Cancer Advisory Board in 2005. The CTWG action items are summarized below.

Strategies that Can Be Implemented Immediately to Improve Treatment Research

- Activate the recommendations of the CTWG for improving the NCI's capacity to lead in coordinating and supporting innovative clinical research.
- Place a top priority on supporting clinical investigators and funding the clinical research infrastructure needed for Cancer Centers, academic medical centers, and practicing physicians to carry out innovative and timely clinical trials.
- Increase collaborations between Cancer Centers in designing and performing clinical trials, sharing specialized core services and new technologies, and exchanging tissue specimens.
- Increase collaboration in new drug development between Cancer Centers and pharmaceutical/biotechnology companies. This will be greatly enhanced by agreement on both sides to reach compromise with regard to control of intellectual property, while protecting the interests of the inventors.

Strategies for Implementation in the Long Term

- Implement the extensive CTWG recommendations, which will lead to more efficient investigation of new treatments and more timely regulatory approval.
- Investigate new technologies and targeted therapies for the treatment of cancer, alone and in combination.
- Continue intensive research on the genetics and biology of cancer, which will provide increased understanding of the malignant process and identify promising targets for anticancer agents.
- Collaborate with the NCI, FDA, CMS and pharmaceutical/biotechnology companies in creating a unified and standardized web-based clinical trials information technology system for recording, reporting, and analyzing clinical research data.

Survivorship

Today there are over 10 million Americans who have survived cancer. A risk of recurrence continues beyond 5 years for some types of cancer. In addition, cancer survivors have a higher than average risk of a second malignancy. In fact, approximately 16% of cancers occur in survivors of the disease. Survivors also are subject to long-term sequellae caused by either their cancer or the therapy they received.

With the increasing mobility of the U.S. population and the frequency with which patients change their health care providers, there is a serious need for uniform guidelines and electronic summaries of medical records to enable appropriate follow up for cancer survivors. In addition, research is needed on ways of preventing the late side effects of cancer treatments and for dealing with them when they occur.

The result of these activities will be a decrease in deaths from second cancers due to earlier detection, and improved duration and quality of life due to control or elimination of late sequellae of the cancer or its therapy.

Strategies

- Cancer Centers should collaborate with the NCI Office of Cancer Survivorship to establish and populate a data warehouse containing clinical information, research protocols, educational materials, and descriptions of outreach activities for the public and for medical professionals.
- Cancer Centers should collaborate with the American Society of Clinical Oncology (ASCO) and other organizations in developing clinical practice guidelines for long-term follow up of cancer survivors and mobilizing adoption of these guidelines by the states and health care providers.
- Cancer Centers should take leadership in designing collaborative clinical trials that explore ways of avoiding late complications of cancer therapy or evaluate treatments which can control them.

Collaborations

The Cancer Center directors agree with the statement in the NCI Strategic Plan that: "Our success will depend on our ability to integrate our activities across a seamless continuum of discovery, development and delivery." The academic, commercial, and governmental sectors each have critical contributions to make. The effectiveness and efficiency of their interfaces need to be addressed with creativity and compromise.

Chemoprevention

Chemoprevention trials involve large, lengthy, and extremely expensive studies of both high-risk and healthy populations, requiring large infrastructures to access and monitor data for many years. Collaborations between industry and clinical investigators – both academic and in the community – must be long term, with careful prioritization and planning, and thorough scientific review in order to optimize the use of scarce human and financial resources.

Strategy

- Form a collaborative chemoprevention trial consortium of Cancer Centers and academic medical centers with centralized infrastructure and data management, funded by the NCI and pharmaceutical companies.

Biomarkers and Imaging

The discovery and validation of useful biomarkers and imaging tests are under-explored at companies and Cancer Centers because of limited available funding, in spite of the critical role of markers in plans to speed up drug development and personalize cancer care. Multiple markers are likely to be required for early detection and for selection of therapies for each type of cancer. The economic case has not been made adequately for the utility of biomarkers for both patient care and drug development.

Strategies

- A consortium of companies should be encouraged to jointly invest in the discovery of new technologies in proteomics, marker identification, and imaging agents as a pre-competitive activity, much like the successful SNP Consortium.
- Research on biomarkers can be expedited by exploring many candidate markers at the same time in a comprehensive validation trial that provides long-term follow up of a number of surrogate markers and predictors, until mortality endpoints are reached.
- Regulatory agencies could provide financial and fast-track review incentives for companies to encourage early exploration and identification of markers that predict the efficacy of new therapies.
- For each of the topics covered in this report, research can be strengthened by bringing together expertise across Cancer Centers. Sharing of specialized, high-tech core facilities will also enhance the quality of research.

Treatment

Therapeutic clinical trials require a series of contractual partnerships between companies and clinical investigators which must last for a number of years. The timeline for preclinical and clinical studies leading to possible FDA approval is typically 10-15 years. Shortening this timeline will require increased collaboration in new drug development between companies and academia, collaborative efforts to validate and implement use of biomarkers and imaging technologies as endpoints in clinical trials, elimination of redundancy in the numerous reviews required for approval of trials, and the use of standardized licensing contracts that create agreed upon sharing of intellectual property.

Strategy

- Facilitate collaboration between companies and academic institutions, by developing shared licensing agreements which can be used to speed up contract negotiations.

Survivorship

Research on the factors influencing the health of cancer survivors requires expensive, long-term studies of many patients. As with prevention research, the requirement for funding of these extensive studies and for collaboration between institutions serving cancer patients must be acknowledged and dealt with effectively.

Strategies

- Collaborations led by Cancer Centers should develop and implement standardized databases for collecting and analyzing information on cancer survivors.
- Research to identify the problems experienced by large cohorts of cancer survivors and to explore treatments and interventions that predict or manage these problems should

be carried out collaboratively between Cancer Centers, and must be funded adequately from external sources.

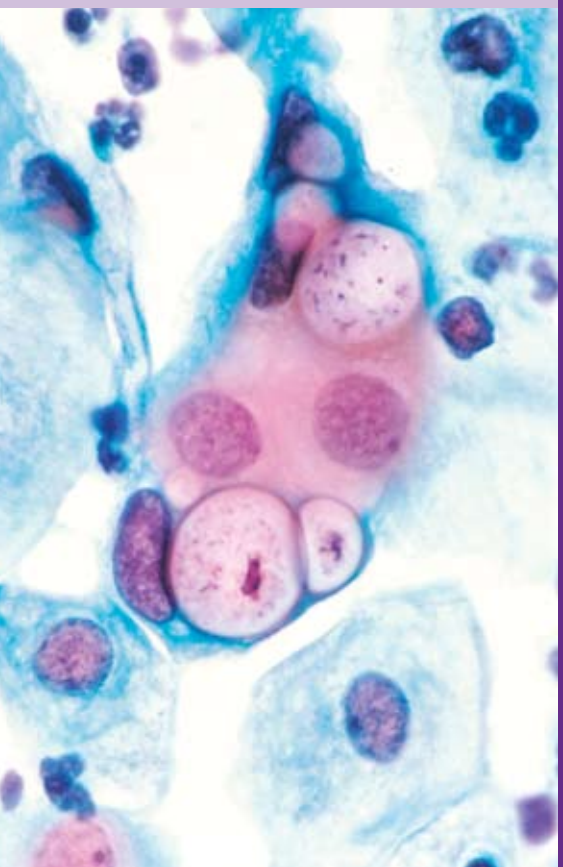
Dissemination

Advances in diagnostic tests and treatments for cancer usually are made available to patients rapidly by Cancer Centers, academic medical centers, and major health care providers. However, reaching all patients with cancer and their health care providers is a goal obtainable only through concerted efforts in education and widespread adoption of best practices, especially by physicians for underserved populations. The Cancer Centers should insure that opportunities to participate in clinical trials of new cancer treatments are made available to greater numbers of individuals, including underserved and diverse populations.

Strategies

- The Federal government needs to designate a lead agency within the Department of Health and Human Services (HHS) to coordinate funding and dissemination of cancer control efforts to the entire U.S. population, by bringing together the fragmented efforts of NCI, CDC, CMS, and other HHS agencies.
- Cancer Centers should take the lead in disseminating cancer care guidelines throughout their states, in collaboration with state health departments and state cancer plans.
- Cancer Centers should work with state cancer registries to convert them into outcomes registries, and should use them to identify populations with disproportionate needs for cancer prevention and care.
- Demonstration of the medical and financial benefits of best cancer control practices should be accomplished by establishing demonstration projects in regions served by Cancer Centers, funded by CMS and led by the Cancer Centers.

Prevention



Summary

In addressing the challenge of reducing the burden of cancer, prevention is the most desirable goal. Population studies have identified lifestyle changes that can reduce the risk of cancer, the most prominent of which is avoidance of tobacco use and exposure. We also have discovered that molecular and biological changes in blood and tissue specimens from patients can serve as markers, identifying individuals who bear higher risk for developing certain cancers, including those who show the very earliest biological changes in the development of cancer. These individuals may benefit from active interventions in their lifestyle and behavior and, in the future, from treatment with agents that can retard or prevent the development of cancer.

We endorse the recommendations of the National Cancer Policy Board on cancer prevention and early detection, which are summarized in this report.

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- Implement other evidence-based changes in lifestyle that will reduce the incidence of cancer, including a healthy diet, avoidance of obesity, and increased physical activity.
- Implement scientifically established medical strategies, including administration of tamoxifen or raloxifene to prevent breast cancer in high-risk postmenopausal women and HPV vaccination to prevent cervical cancer in young females.

Cancer Centers can partner with governmental agencies and health care providers to extend these measures to the entire U.S. population through improved delivery and targeted education.

Strategies Involving Either Change in Policies or Further Research and Requiring a Decade or More Before Clinical Application

- Perform research on the application of "personalized medicine" to intraepithelial neoplasias (IENs) and precancerous conditions, by carrying out clinical trials to discover molecular targets for both early detection of high-risk lesions and chemoprevention treatments.
- Increase clinical research in the behavioral sciences that will identify improved methods for changing personal lifestyles and promote informed decisions about health-related behaviors.
- Implement a strong, molecularly-targeted detection and chemoprevention drug development program.

Continue to pursue promising agents in chemoprevention clinical trials, based on the successes with anti-estrogen agents in preventing or postponing breast cancer in high-risk groups.

While Cancer Centers can collaborate in carrying out these large-scale and long duration clinical studies, funding will be needed from governmental agencies or from companies willing to partner in these efforts.

Introduction

The goals of cancer prevention are to reduce the incidence, morbidity, and mortality due to cancer by preventing initiation of primary tumors (primary prevention), intraepithelial neoplasias (secondary prevention), or second cancers or disease-related complications (tertiary prevention). The incidence and mortality from cancer has been decreasing slowly during the past decade. Unfortunately, our aging population will reverse this trend in the next decade, despite recent advances in the understanding of the genetic and molecular bases of the common cancers and the development of molecularly-targeted biological therapies.

The cancer patient is not well one day and the next day diagnosed with cancer. It is estimated that in most cases there is an average lag of at least 20 years between the development of the first cancer cell and the onset of metastatic disease for a broad range of solid tumors. In fact, using sensitive molecular genetic methods, there is now evidence that potentially neoplastic cell populations can exist at the time of birth and that only in some cases is there progression to full-blown malignancy later in life. Based on the fact that there were more than 570,000 cancer deaths in the United States in 2005, and given the estimated 20-year lag time, more than 10 million currently "healthy" Americans may harbor ultimately deadly cancers.

It is increasingly apparent that virtually all cancers proceed from the first initiated tumor cell (through somatic mutations); to mild, moderate, and severe dysplasia; invasive carcinoma (invasion of cells through the basement membrane); and metastatic disease (Figure 1). Precancerous lesions are termed intraepithelial neoplasias (IENs) and can often be identified through increasingly sensitive screening technologies, both histologically and molecularly, using a variety of analytical methods (e.g., cDNA microarrays).

The best cancer is that which never occurs, so primary prevention (e.g., preventing and treating tobacco use, reducing sun exposure, promoting healthy diets and exercise) is both the most effective and least costly approach because it can reduce the likelihood that the first initiated tumor cell will occur. Thus, given the average 20-year cancer lag time, secondary, and tertiary prevention strategies represent effective and cost-effective opportunities to dramatically reduce cancer mortality in the next decades (Figure 2). Unfortunately, a pervasive problem in the United States is poor access to health care, including prevention measures, because of a lack of health insurance. In 2001, an estimated 15% of the U.S. population

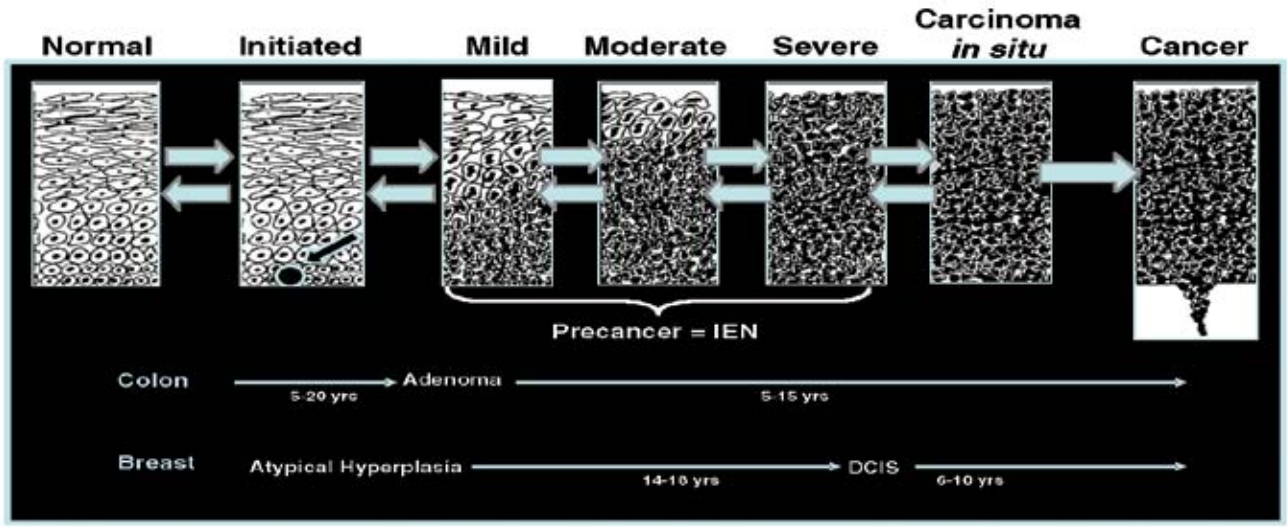


Figure 1. Progression of precancer to cancer in humans is a multi-year process, adapted from O'Shaughnessy et al. (O'Shaughnessy, Kelloff et al. 2002)

(41.2 million individuals) was uninsured during the entire year.

Current Knowledge, Issues and Problems

The development of effective cancer prevention strategies has the potential to impact more than 8 million cancer diagnoses and to prevent more than 5.2 million cancer-related deaths each year worldwide. The American Cancer Society (ACS) has estimated that 564,830 cancer deaths will occur in the United States in 2006, and that half of all cancer deaths could be prevented. Tobacco use alone, which represents the greatest preventable cause of cancer death by far, is predicted to cause 30% (170,000) of the cancer deaths in the United States this year. It is thought that one of the primary reasons why current knowledge and information about cancer and its prevention is not applied to the general public is due to an overload of complicated information. The dissemination of complicated information is problematic, but comprehensive information is essential to reduce the burden of cancer.

There are many factors known to reduce overall cancer incidence, such as minimizing exposure to carcinogens (e.g., avoiding tobacco), vaccination for some cancers, dietary modification, reducing body weight, increasing physical activity, or through medical intervention (e.g., surgery and/or chemoprevention) (Table 1).

However, research on developing and implementing effective cancer prevention and control interventions lags in funding relative to its potential impact on reducing the cancer burden in the United States. For example, only one non-nicotine medication is currently approved by the Food and Drug Administration (FDA) for smoking cessation, though others are in the pipeline, and the existing medications achieve smoking cessation quit rates of 25% at best. Since many health care organizations do not include smoking cessation medications as a covered benefit, the incentive for pharmaceutical companies to prioritize the development of smoking cessation medications is not high – thus fostering a negative feedback loop that discourages health care organizations from covering medications

Table 1. Factors associated with cancer risk, adapted from Giovannucci (Giovannucci 1999)

Factor	Association to Cancer Risk
Height	Increases prostate, colon, and breast cancer risk
Obesity	Increases colon, breast, kidney, endometrial, and gallbladder cancer risk; may increase ovarian cancer risk
Physical inactivity	Increases colon cancer risk; may increase breast and prostate cancer risk

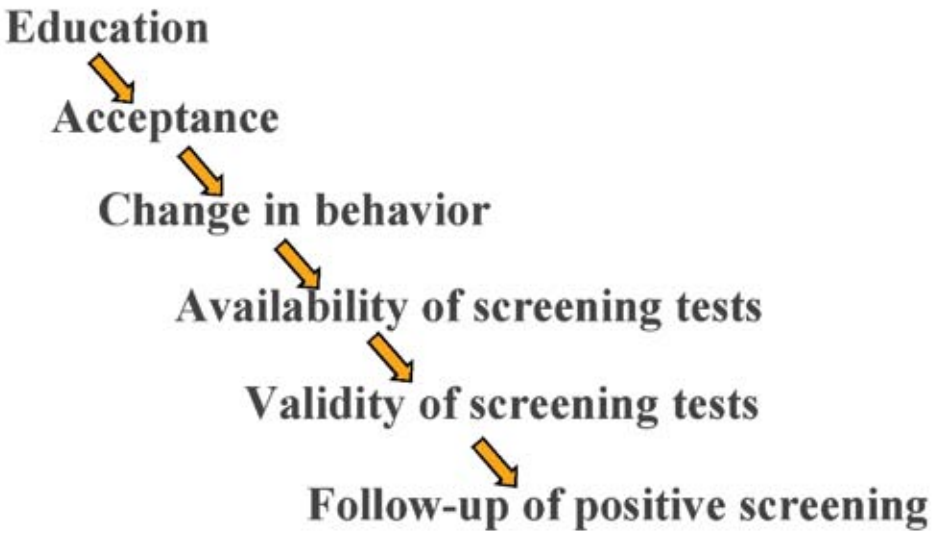


Figure 2. Issues in secondary prevention for physicians and the public

because the effectiveness of those medications is low.

Similarly, pharmaceutical companies have traditionally been unwilling to invest in the development of chemopreventive agents, because of the required length of time and the size and cost of Phase III confirmatory trials. Furthermore, these companies are concerned about the uncovering of unexpected, life-threatening toxicities that may be observed with the long-term exposure required for many cancer prevention intervention strategies. This can have an extremely negative impact on safety profiles of approved drugs (e.g., celecoxib twice-daily dosing increased cardiovascular events in at least two blinded, prospective trials by 4-5%).

The high "cost" of cancer prevention trials and the need to develop reliable and meaningful intermediate endpoints are significant barriers that must be overcome. Cancer prevention clinical trials, like the recently completed STAR (Study of Tamoxifen and Raloxifene to reduce the risk of breast cancer in post-menopausal women) and the ongoing SELECT (Selenium and Vitamin E to reduce the risk of prostate cancer) take between 5 and 10 years or more to complete, and require thousands of participants. The cost to complete such large-scale trials is in the $100- to $200 million range and, of course, a positive outcome may not be achieved – e.g., the recently announced unsuccessful results of intervention with calcium plus Vitamin D in the Women's Health Initiative (WHI) to reduce the risk of colorectal cancer.

Obviously, the need to develop risk-reducing preventive strategies for large populations who may develop common solid cancers remains a high priority for NCI and the Cancer Centers. To reduce the need for large populations in chemoprevention studies, there must be a clear identification of high-risk populations for prevention efforts. This will reduce the size of the study population and will likely reduce the risk of attrition by accruing individuals likely to be highly motivated to prevent cancer. However, by reducing the study population, there is a risk of insufficient statistical power if the risk is overestimated, and the results of these trials will not be generalizable to the overall population that is potentially at risk.

An alternative solution is the development of intermediate biomarker endpoints – whether molecular, biochemical, or image-based – that can serve to reduce the size, duration, and cost of cancer prevention trials. One illustrative example relates to a 2,297 participant trial of oral Vitamin A standard dose (25,000 IU daily) for up to 5 years (versus placebo) in individuals with moderate to severe actinic keratosis (i.e., a cutaneous IEN associated with a high risk for squamous cell cancer of the skin). The primary endpoint for this trial was the risk of developing a squamous cell skin cancer. This Phase III chemoprevention trial – funded by NCI in the middle

Disease site	1975	2005	Modalities responsible
Breast	50%	90%	Screening, Education, Adjunct Therapy
Colon	40%	55%	Screening, Education, Adjunct Therapy
Cervix	60%	90%	Screening, Education, Adjunct Therapy
Prostate	50%	99%	Screening, Education
Melanoma	50%	90%	Screening, Education
Head/Neck	40%	50%	Education, Early Neoadjuvant Therapy

Table 2. Increase in 5-year cancer survival, 1975-2005

1980s and concluded in the middle 1990s – documented a statistically significant, nearly 30% reduction in the risk of developing a squamous cell cancer of the skin associated with prolonged Vitamin A dosing (HR=0.74; 95% confidence interval, 0.56-0.99; p = 0.04).

Knowing that standard dose Vitamin A can reduce the risk of developing a squamous cell cancer of the skin, there was additional interest to determine if doubling or tripling the Vitamin A dose further enhanced its skin cancer preventive activity. Thus, a Phase IIb, placebo-controlled trial was designed to compare the relative activities of three different doses of Vitamin A (i.e., 25,000 IU, 50,000 IU, and 75,000 IU per day). The primary endpoint of the follow-up study was an evaluation of Vitamin A effects on sun-damaged skin of the lateral forearm, using skin biopsy nuclear chromatin pattern abnormality at one year of Vitamin A dosing versus baseline. A quantitative efficacy endpoint was obtained through karyometric analysis of formalin-fixed, paraffin-embedded, hematoxylin and eosin (H & E) stained biopsies. The results documented that the placebo group's skin damage worsened while there was a clear dose-related response between 25,000 and 50,000 IU/day of Vitamin A. This 1-year trial required only 130 participants, cost approximately one-twentieth as much as the original Phase III trial, and successfully established a 50,000 IU/day dose of Vitamin A as both safe and possibly more effective than standard dose Vitamin A. There is an absolute need to identify and validate markers that can be integrated into chemoprevention research to reduce the cost and duration of these trials while assuring that sufficient statistical power to detect change is not compromised. Biomarkers must be necessary steps in the pathway of carcinogenesis, assays must be accurate, precise and reproducible, and biomarkers must be validated.

Accomplishments

As stated earlier, barriers to accelerated success in cancer chemoprevention include: the relative impotency of chemopreventive agent drug discovery and early phase drug development programs in academia, NCI, and in the pharmaceutical industry; the long duration and high cost of Phase III cancer chemopreventive clinical trials; and the shrinking NCI budget, coupled with a relatively lower priority for cancer prevention, as compared to research funding for cancer treatments. Despite these barriers, cancer prevention efforts have contributed substantially to the reduction of morbidity and mortality due to cancer (Table 2).

Cancer chemoprevention and dietary intervention Phase III trials have been limited by relatively small amounts of funding for drug discovery, preclinical pharmacology, and toxicology available in NCI's Division of Cancer Prevention (DCP). There has also been an almost total lack of interest by the pharmaceutical industry. Nevertheless, there have been an increasing number of high-impact intervention trials targeting intermediate- to high-risk populations for breast, cervix, colorectal, prostate, and skin cancers. Listed in Appendix A are the primary results of paradigm-shifting trials funded by the NCI and/or the U.S. pharmaceutical industry that have been reported over the past 10 years. As this table demonstrates, there is increasing evidence that chemoprevention strategies are increasingly effective in pre-empting the pathway of carcinogenesis in intermediate to high-risk populations for many common cancers.

Medications, new screening technologies, and chemoprevention agents are critically important tools to prevent and control cancer, but their effectiveness depends on behavioral and psychosocial factors that are also, by themselves, important factors in the prevention of cancer. Patient-provider communications, for example, play a critical role in determining who will engage in health-enhancing lifestyles that reduce cancer risk. They impact the likelihood that a person at risk for cancer will seek and engage in appropriate screening, and they

also determine whether appropriate pharmacotherapies are used, and used appropriately to effectively blend with critical behavioral and lifestyle changes. As new genetic and molecular discoveries improve our ability to develop personalized treatments, similar advances are needed to tailor behavioral and psychosocial interventions so that they are individually and culturally appropriate, work to eliminate disparities, and assure that personal responsibility for sustaining and improving health is not outweighed by the perception that cancer prevention and control is assured via the medicine cabinet.

It is important for primary caregivers, as well as the research community, policy–makers, and government agencies to take a multidisciplinary approach to investigating, understanding, and improving the success of cancer prevention.

Emerging Therapeutic and Interventional Strategies

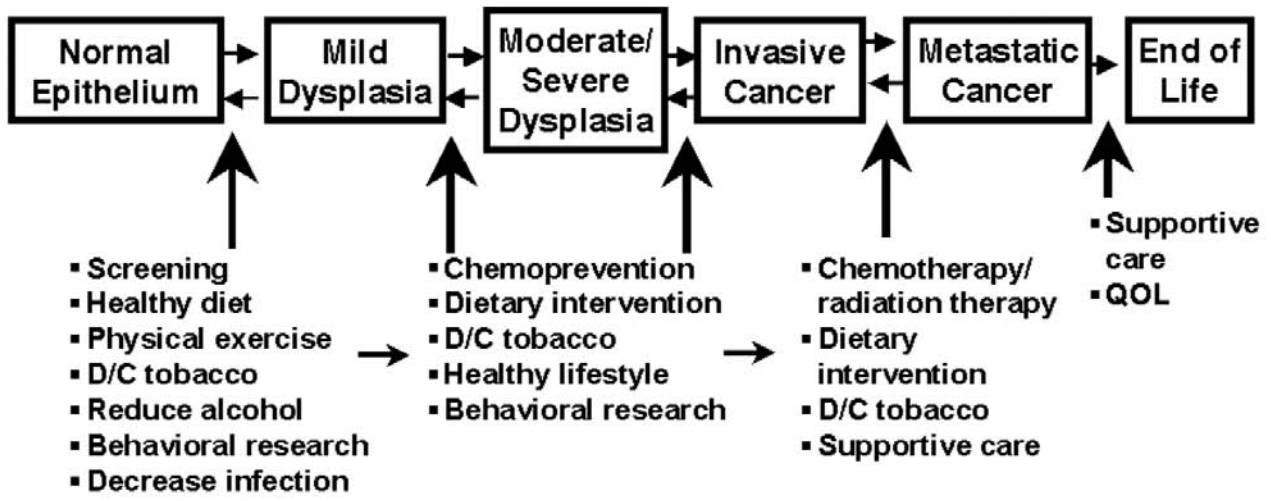
In the United States, approximately 44.5 million adults (21% of the U.S. population) continue to smoke, despite current prevention and cessation efforts. Tobacco use is the leading cause of cancer and the greatest leading cause of preventable death. Tobacco use causes over 440,000 premature deaths – 198,000 of which are cancer deaths from smoking and environmental tobacco exposure.

According to a 2002 report from the International Agency for Research on Cancer (IARC), tobacco exposure is a direct causal factor of at least 13 different cancers, such as cancers of the lung, pancreas, cervix, liver, stomach, head/neck, and leukemia. Nearly 90% of all lung cancers are directly due to tobacco exposure (tobacco use or environmental exposure). As a noted researcher pointed out, if we are able to prevent just 10% of all lung cancer deaths, it would be equivalent to preventing all deaths from glioma or ovarian cancer.

Each year, approximately 5 million people worldwide die prematurely due to tobacco exposure and that number is expected to exceed 10 million by 2020 if current tobacco exposure rates remain unchanged. In the United States, most smokers become dependent before the age of 18, and once dependence occurs, the chances of quitting on any one occasion is approximately 5%. Use of the most effective treatments increases that percentage to 15-25%, thereby demonstrating that more effective treatment for tobacco dependence is needed.

A recent NIH State of the Science conference on tobacco identified the following priority research areas to reduce tobacco exposure: (1) developing new pharmacological and behavioral treatments; (2) community-based interventions; (3) assessing cancer risks of various smokeless tobacco products; (4) implementing policy interventions that will increase cessation;

Figure 3. Multi-step carcinogenesis pathway, adapted from Alberts, et al. (Alberts 1999)



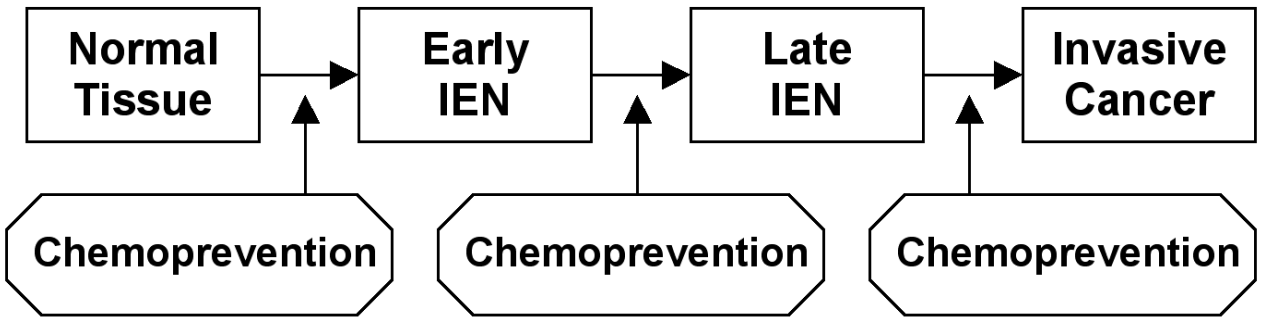


Figure 4. Chemoprevention of intraepithelial neoplasia (IEN)

and (5) studying genetic predisposition to tobacco dependence.

Many cancers are also now known to be directly attributable to viral infections. The family of infectious agents most closely linked to cancer are viruses such as: human papillomavirus infection (HPV), which is a necessary factor in the development of cervical cancer and possibly squamous cell carcinomas of the oropharynx or anus; hepatitis B and C virus infection which are initiators and promoters for hepatocellular carcinoma; human T lymphotropic virus (HTLV-1) which has been implicated in the development of T-cell leukemia; human herpes virus type 8 (HHV8) which has been implicated in Kaposi's sarcoma; Epstein Barr Virus (EBV) which has been implicated in Burkitt's lymphoma, as well as other B-cell malignancies and nasopharyngeal cancer; and simian virus 40 (SV40) which may be implicated in mesothelioma.

Less commonly, other infectious agents may lead to cancer, such as bacterial infections of Helicobacter pylori (H. pylori), which may be an initiator and promoter for gastric cancer, and helminth infections such as Schistosoma haematobium which is associated with urinary bladder cancer.

A number of primary prevention efforts exist or are being developed such as vaccines against HPV (see sidebar, "Cervix Cancer Prevention with HPV Vaccines") and hepatitis B and C, and vaccines against H. pylori to prevent the development of cervical, liver, and gastric cancers respectively. In some cases, eradication of chronic viral or bacterial infections by immunotherapy, antiviral therapy, or antibiotic therapy may be viewed as a form of secondary prevention. For example, administration of anti-EBV specific T-cells in transplant patients known to be high risk for post-transplant lymphoproliferative disorders can reduce the circulating EBV viral load, and reduce the rate of lymphoproliferative disorders. Research into the biology of these cancers, strategies to prevent infection, and therapies to eliminate chronic infection will all play a role in preventing such cancers. Because prevention depends on unambiguously understanding the cause of the disease, basic cancer research efforts impact cancer prevention research in important ways.

The vast majority of current treatment modalities are used to treat advanced or metastatic cancers. However, now that it is possible to identify IENs for many solid tumor types, lifestyle changes, simple surgical procedures, and chemopreventive agents may be used to impede the development and progression of potentially dangerous precancerous lesions (Figure 3).

Furthermore, multiple lifestyle changes, taken together, could profoundly reduce the risk of the first initiated cell progressing to mild dysplasia. This would include severely reducing dietary fat intake (e.g., as demonstrated by a 25% reduction in the risk of breast cancer recurrence rates in the Women's Interventional Nutrition Study), increasing the number of servings of fruits and vegetables, minimizing alcohol intake, tobacco exposure cessation, and markedly increasing physical activity. These changes may potentially reduce risk for several cancers by up to 60%.

Furthermore, the addition of an effective chemoprevention agent, such as tamoxifen for moderately or severely dysplastic IENs such as ductal carcinoma in situ, can reduce cancer risk by as much as

50%. Figure 4 presents the concept that an effective chemopreventive agent could prevent IEN growth, progression, or ultimately, invasion through the tissue basement membrane (as did Proscar in the 18,000 participant Prostate Cancer Prevention). Thus, the concept of cancer prevention is now entering the mainstream of cancer therapeutics. Of course, any chemopreventive agent intervention may be associated with toxicity and the risk to benefit ratio for any of these agents must be taken into consideration at both the individual person and larger population levels.

The National Cancer Policy Board of the Institute of Medicine (IoM) concluded that to save the most lives from cancer, health care providers, health plans, insurers, employers, policy-makers, and researchers should be concentrating their resources on helping people to stop smoking, maintain a healthy weight and diet, exercise regularly, keep alcohol consumption at low to moderate levels, and to follow recommendations for breast, prostate, skin, cervical, and colorectal cancer screening. Additionally, these efforts might also help alleviate the disproportionate burden of cancer borne by members of racial and ethnic minority groups.

Identification and Prioritization of Opportunities for Advancement

IoM's National Cancer Policy Board recommended that several steps be taken to increase the rates of adoption, the reach, and the impact of evidence-based cancer prevention and early detection interventions. We have adapted these recommendations to identify and prioritize opportunities to advance cancer prevention efforts.

(1) Congress and state legislatures should enact and provide funding for enforcement of laws to substantially reduce and ultimately eliminate the adverse public health consequences of tobacco use and exposure.

- Reduction in tobacco use offers the greatest opportunity to reduce the incidence, morbidity, and mortality of cancer.
- Efforts to increase the cost of tobacco, and to eliminate environmental tobacco smoke exposure in public places and worksites, and by children in homes, are effective in reducing cancer risk and in encouraging a lifestyle that is tobacco free.
- Tobacco consumption reduction efforts by Cancer Centers, the health care community, policy-makers, and government agencies should apply to U.S. tobacco products marketed and sold internationally.
- Although tobacco exposure causes more than 30% of all cancer deaths, only about 3% of the current NCI budget is directed to tobacco control efforts. There is a tremendous need for behavioral and social research and intervention.

(2) A national strategy should be developed and coordinated by the U.S. Department of Health and Human Services (HHS) to address the epidemic of obesity, unhealthy diet, and physical inactivity in America. Effective interventions need to be identified and broadly applied to reduce cancer risk among the general population and among populations at higher risk.

- Obesity and physical activity have recently joined unhealthy diet as leading risk factors for cancer.
- Efforts to maintain a healthy weight that start early in childhood and continue throughout adulthood are likely to be more successful than efforts to achieve and maintain weight loss once obesity is established.
- Over time, even a small decrease in the number of calories consumed and a small increase in physical activity can help prevent weight gain or facilitate weight loss.

(3) Sufficient Federal appropriations should be made to fund NCI-designated Cancer Centers to support innovative public and private partnerships to develop, implement, and evaluate comprehensive community-based programs in cancer prevention and early detection. Every state should have and implement a comprehensive cancer control plan.

A) Federal Efforts

- The Centers for Disease Control and Prevention (CDC), as the Federal link to the Nation's public health infrastructure, needs to build the capacities of states - and, in turn, their local partners (Cancer Centers, academic medical centers, and health care systems) - to develop and implement comprehensive cancer control plans.
- Support for the CDC's National Breast and Cervical Cancer Early Detection Program

Cervix Cancer Prevention with HPV Vaccines

The dramatic reduction in the incidence and mortality from cervical cancer in the United States over the past 50 years is a direct result of the widespread and effective screening using cervicovaginal (or Pap) smears. Yet, despite a greater than 70% reduction in death in the U.S., as many as 10,000 women each year who fail to be screened adequately develop cervical cancer and nearly 4,000 women still die annually of this disease. Worldwide, deaths from cervical cancer could reach 1 million per year unless effective screening and prevention programs are implemented.

In the past 25 years, tremendous research advances have demonstrated that virtually all cases of cervical cancer are caused by infection with human papillomavirus (HPV). A recent series of clinical trials testing HPV vaccines have yielded dramatic results. As a result, on June 8, 2006, Merck's quadrivalent HPV vaccine, Gardasil™, targeting HPV types 6, 11, 16 and 18, was approved by the FDA for vaccination of females aged 9 to 26 years of age. In clinical trials, Gardasil was 100% effective in preventing HPV 16- or 18-related cervical, vulvar, or vaginal intraepithelial neoplasia (IEN) grades 2-3 or adenocarcinoma in situ (AIS) among women who had not been exposed to HPV. However, there was no clear evidence of protection from disease caused by HPV types for which subjects were PCR or seropositive at study entry. The efficacy of Gardasil was 39% for the protection of HPV 16- or 18-related cervical IENs and AIS and 69.1% for the prevention of HPV 16- or 18-related vulvar or vaginal IENs grades 2-3 among women with any HPV status at baseline who received at least one vaccine dose. A second HPV vaccine, Cervarix™, manufactured by GlaxoSmithKline, is currently being tested in Phase III clinical trials.

While the development of HPV vaccines has the potential to eliminate the majority of cervical cancer cases worldwide, a number of critical questions remain that provide particular opportunities for research in cancer surveillance, prevention, dissemination, communication, HPV persistence and progression – all of which have a tremendous public health impact. Furthermore, there is a need to be engaged in areas of investigation related to co-factors (such as cigarette smoking) that play a role in viral persistence and progression to cervical cancer.

(NBCCEDP) should be increased. The NBCCEDP has succeeded in improving screening rates among medically underserved populations, but the program reaches only 15% of eligible women because of limited financial support. Under funding of CDC's NBCCEDP contributes to lost opportunities for prevention.

- Because screening for colorectal cancer is a proven strategy for reducing cancer mortality in people over 50 years of age, a CDC program similar to NBCCEDP is needed to provide colorectal cancer screening to people who are uninsured and underinsured.

B) State Efforts

- State efforts in cancer prevention and early detection should be reformed because in many cases current programs are piecemeal and organized around categorically-funded programs.

(4) Public and private insurers and providers should consider evidence-based cancer prevention and early detection services to be essential benefits and should provide reimbursement for them. These services at a minimum should include interventions recommended in the U.S. Public Health Services' 2000 clinical practice guideline on treating tobacco use and dependence, screening for breast cancer among women age 50 and older, screening for cervical cancer among all

sexually-active women with an intact cervix, and screening for colorectal cancer among adults age 50 and older.

- Public and private health insurers and providers should include in their benefit packages coverage for evidence-based interventions for cancer prevention and early detection.
- Nicotine replacement therapy and treatment (e.g., Bupropion SR) and counseling, for example, are effective in helping individuals quit smoking.

(5) Congress should increase support for programs that provide primary care to uninsured and low-income people. These programs increase the use of cancer prevention and early detection services among medically underserved populations.

- The differences in morbidity and mortality from cancer among various racial and ethnic groups and among the under- and uninsured present both a challenge to understand the reasons for and an opportunity to reduce the burden of cancer.
- In a Nation of increasing diversity, interventions to improve cancer prevention and early detection must accommodate different languages, cultural values, and beliefs.
- Public and private initiatives to reduce disparities in the cancer burden (e.g., programs at NCI and the American Cancer Society) should be supported.

(6) HHS should complete a comprehensive review to assess whether evidence-based prevention services are being offered and successfully delivered in Federal health programs.

- The Federal government administers or funds programs that do not always reflect best practices in cancer prevention and early detection.
- The evidence is clear that disease prevention is not only effective, but highly cost effective. Thus, investments in supporting healthy lifestyles and appropriate screening will have not only improved the quality and quantity of life, but will save money for the U.S. health care systems. Additional research is needed to optimize and disseminate cancer prevention and early detection approaches to achieve the broadest implementation nationally. Support for programs like the NCI's Cancer Research Network, and collaboration between organizations like NCI, Veterans Administration (VA), the Agency for Healthcare Research and Quality (AHRQ), and CMS to improve and expand health care services research, will improve cancer prevention and control implementation.
- The lack of coverage for effective prevention services in public programs introduces a significant barrier to those most burdened by cancer: the uninsured population and members of racial and ethnic minority groups who often depend on government-funded programs for care.

(7) Programs are needed for health care providers to improve their education and training, monitor their adherence to evidence-based guidelines, and enhance their practice environments to support the provision of cancer prevention and early detection services.

- Primary care providers in health care settings are effective agents of behavioral change. When counseled about smoking in clinical settings, 5-10% of individuals are able to quit.
- Evidence suggests that physicians and other practitioners are not providing effective clinical interventions such as counseling and screening tests as often as would be beneficial.

(8) Congress should provide sufficient support to HHS for the U.S. Preventive Services Task Force and the U.S. Task Force on Community Preventive Services to conduct timely assessments of the benefits, harms, and costs associated with screening tests and other preventive interventions. Summaries of recommendations should be made widely available to the public, health care providers, and state and local public health officials and policy-makers.

- Evidence-based guidelines for clinical and community practice provide maps for action.
- Assessments of prevention services (such as those by the U.S. Preventive Services Task Force) are needed on a continual basis to ensure that public health recommendations incorporate the latest scientific evidence.
- As state efforts to implement comprehensive cancer control plans gain momentum, guidance on the effectiveness of public health interventions (such as those identified by the U.S. Community Services Task Force) will be critically needed.

(9) Public and private organizations should take steps to improve the public's understanding of cancer prevention and early detection with a focus on promoting healthy lifestyles and informed decision-making about health behaviors and cancer screening.

- Raising public awareness of the benefits of cancer prevention and early detection is central to reducing the cancer burden.
- One barrier to effective communication is the contradictory and sometimes questionable research reported by the news media.
- Expanded health communications research, particularly via the Health Communications and Informatics Branch at NCI, is needed to improve understanding of which communications approaches – both individual (e.g., patient-provider) and community-based (e.g., news media) – are most effective with specific populations to prevent and control cancer.

(10) Public and private sponsors of research should expand their support of studies that integrate cancer control and behavioral research with advanced imaging and systems biology technologies. Such integrated strategies more rapidly advance understanding of some key barriers to the development of healthy behaviors and other risk-reducing strategies in children and adults, and will foster personalized medicine approaches that take into consideration not just unique genetic characteristics of individuals but also the unique behavioral and social characteristics of those individuals.

- The culture of clinical cancer research has been dynamically influenced by advances in imaging, molecular validation studies, the human genome project, and systems biology so that it is now possible to discover underlying mechanisms for environment-diet-behaviors-health. Companion studies are common today in the conduct of clinical trials and molecular profiling is also being applied to drug discovery and development.
- Integration of such studies in the field of cancer prevention has not been given the prominence it deserves in NCI's Division of Cancer Prevention (DCP) and Division of Cancer Control and Population Sciences (DCCPS) or extramurally in the Cancer Centers and Specialized Programs of Research Excellence (SPOREs).
- NCI should invest in a long-term, coordinated national program that specifically supports transdisciplinary, integrated research in cancer prevention and control which brings together the biological and behavioral sciences in a way that reflects the critical roles that each play in preventing cancer.
- DCP and DCCPS have been chronically under funded by NCI. This has greatly diminished and slowed progress in cancer prevention and control. NCI should increase funding for both divisions by at least 100% over the next 5 years. We recognize that in an environment of flat or decreasing NCI budgets, such a recommendation means reduced funding elsewhere, but the evidence is clear that the greatest advances in reducing cancer morbidity and mortality are likely to be achieved by rapidly reducing or eliminating preventable causes of cancer. More specifically, we recommend major expanded collaboration between DCP and DCCPS, particularly via NCI's Rapid Access to Preventive Intervention Development (RAPID) program, to assure that $50 million is invested per year for 10 years with the goal of discovering, developing, and implementing new medications to prevent and/or treat tobacco dependence.
- To further strengthen cancer prevention and control research activities within the Cancer Centers, we recommend that to obtain short-term or long-term comprehensive cancer center designated status by NCI, that all comprehensive cancer center members must work for the common good, and thus establish a major wellness and cancer survivorship site within the scope of their clinical trials.

(11) Public and private sponsors of research should expand their support of applied behavioral research and how best to disseminate evidence-based prevention interventions. Effective strategies are especially needed to encourage healthy behaviors among children and their families, medically underserved populations, and the public at large through multicomponent interventions.

- Tobacco use, physical activity, and diet are among the most significant lifestyle behaviors related to cancer risk. In addition, alcohol, sun safety, and sexual practices are also important contributors to cancer risk.
- Unfortunately, minimal research resources have been allocated to understanding the details of behavioral risk as it relates to cancer. This includes the environmental and societal aspects of individual behavior and population-wide norms.
  - It is critical to focus not on the basic question of whether interventions work, but how they work, for whom, and under which circumstances. This can be achieved through better research questions and improved measures. Doubling the funding to DCCPS (see above) is needed to expand the dissemination research PAR into a funded RFA mechanism.
  - Cancer Centers must address primary prevention at the community level and must be given greater resources, and this focus must be given greater attention. Moreover, cancer prevention and control clinical trial accruals should not only be considered equal to therapeutic accruals in cancer center core grant renewals, but should be considered for special merit in the review process as a means of increasing prevention and control research at Cancer Centers in order to speed efforts to prevent cancer more effectively. At present, there is minimal incentive for Cancer Centers to expand their cancer prevention and control portfolio.
  - For a number of years, behavioral neuroscientists have used systems biology approaches in assessing the genetic basis of behavioral risks (e.g., studies on alcohol and drug addiction). Cancer Centers should be encouraged to integrate such analyses collaboratively in their studies on behavioral and cancer risk.

(12) Governmental health care policy-makers and professional and educational organizations should institute programs to educate both the public and medical professionals that certain persons, families, groups and even subpopulations are at significantly increased familial and inherited risk for cancer and constellations of cancers, and thus need more aggressive screening and surveillance.

- Familial and inherited predispositions to cancers of various types account for a significant fraction of the overall burden of cancer and represent a population at significantly higher risk of certain cancers.
- Evidence-based studies document remarkable decreases of both incidence and mortality of cancer in high-risk groups with appropriate surveillance.
- The knowledge of the risk groups, the recommended screening and surveillance strategies, and the appropriate application of genetic testing when indicated are very poorly appreciated or understood by the public and medical community.

Action Items for NCI-designated Cancer Centers

(1) Reducing the rate of smoking toward levels of the recently reported California adult smoking rate of 14% through comprehensive efforts to stop tobacco use. Recent data from the California Department of Health Services document that smoking among 45 to 64 year olds declined from 15.3% in 2004 to 13.8 % in 2005. This is 25% lower than that rest of the Nation.

(2) Implement outstanding compliance with the newly FDA-approved HPV vaccine for young girls and recommendations for the use of raloxifene to reduce the risk of breast cancer in high-risk, post-menopausal women. There have been two remarkable cancer prevention breakthroughs in the past year. First is the FDA approval of a safe vaccine for HPV types 16 and 18 – which cause most cervical cancers – to be used in adolescent girls. Second was documentation that raloxifene was equally as active as tamoxifen in reducing incidence of breast cancer among high-risk women, but with reduced incidences of endometrial cancers, pulmonary emboli, and cataracts compared to tamoxifen. The Cancer Centers must be heavily engaged in methods to enforce compliance to these extremely important prevention methods.

(3) Strongly support research on the application of "personalized medicine" to IENs for the purpose of identifying high-risk lesions and specific molecular targets for both early detection and personalized chemoprevention. Molecular profiling of IENs and determination of susceptibility through genetic testing, family history, and lifestyle for the purpose of personalized medicine may have an even stronger rationale than molecular profiling for early and advanced cancers, because the critical molecular targets are likely better defined and the long-term impact on cancer outcomes more dramatic.

Anticipated Outcomes and Potential Impact

IoM's National Research Council has stated, "The nation needs new strategies to prevent cancer and, when cancer occurs, to catch it at its earliest stages. Smoking, unhealthy diet, obesity, sedentary lifestyles, and failure to get screened all contribute to the excess burden of cancer. Failure to implement proven methods of cancer prevention leads to avoidable disease and death. A 19% decline in the rate at which new cancer cases occur and a 29% decline in the rate of cancer deaths could potentially be achieved by 2015 if efforts to help people change their behaviors that put them at risk were stepped up and if behavioral changes were sustained. This would equate to the prevention of approximately 100,000 cancer cases and 60,000 cancer deaths each year by the year 2015. The possible reductions in cancer incidence are particularly striking for certain cancers: accelerated changes in risk behavior could halve the number of smoking-related cancers such as lung cancer and reduce the numbers of cases of colorectal cancer by up to one-third."

The United States is at a crossroads in cancer prevention research. Discoveries in basic biological and behavioral science, along with epidemiology and surveillance, are advancing knowledge in a number of areas, from the relationship between cancer and modifiable behavioral risk factors all the way to the molecular pathways that mediate the actions of those risk factors.

At the same time, applied research is illustrating how the already vast amount of available evidence can be better used to more rapidly reduce cancer rates. To effectively reduce the national cancer burden, there needs to be greater emphasis on two key strategies: action-oriented research and interdisciplinary research that takes best advantage of advances in informatics, human genetics, functional genomics, imaging and systems thinking (biology and social interaction), and behavioral sciences.

The first strategy addresses the problem that scientific knowledge about the solutions to health problems and their causes do not automatically guarantee that appropriate steps are taken in our clinics and communities to implement the changes required for the conversion of research to practice. The second strategy addresses the overarching principle that best practices in cancer prevention will evolve only when etiological knowledge is linked to cancer prevention research projects in an iterative way such that the results from basic research informs clinical and community practice, and that clinical and community practices inform basic science. Furthermore, it reflects the need to implement, whenever possible, community participatory approaches to discovery so that the public better understands and supports science and to foster incorporation of science into practice whenever feasible. Once programs of support evolve from these strategies, our potential to reduce the burden of cancer will be very substantially improved.

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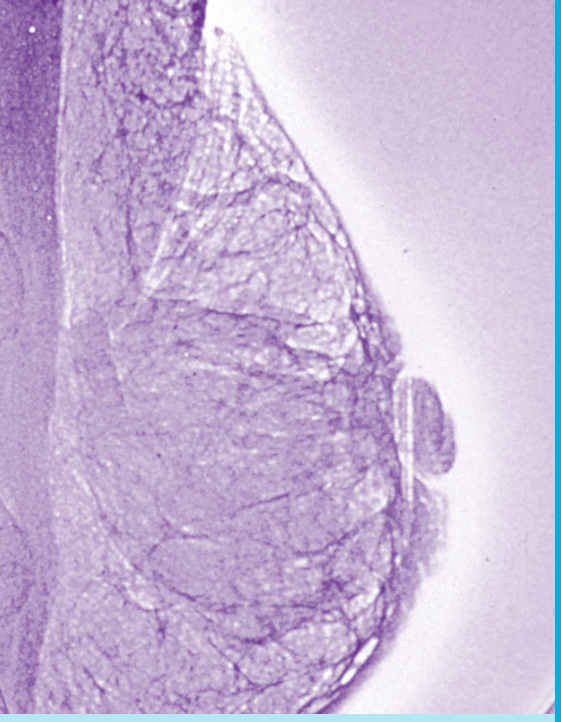


Early Detection

Summary

Many, but not all cancers are curable through medical and surgical intervention after early diagnosis. While methods for early detection of cancer, including mammography, PSA testing, PAP smear, and colonoscopy, have been counted as important public health approaches to reducing the burden of cancer, much remains to be done. Most cancers cannot be detected early by conventional techniques. Use of screening methodologies for early detection is far below recommended levels. New methodologies for early detection have not been introduced broadly into the population, while others have yet to be validated. Nonetheless, early detection leading to cure of cancer is likely to be the most powerful and cost-effective method of reducing the burden and death rate from cancer in our lifetime.

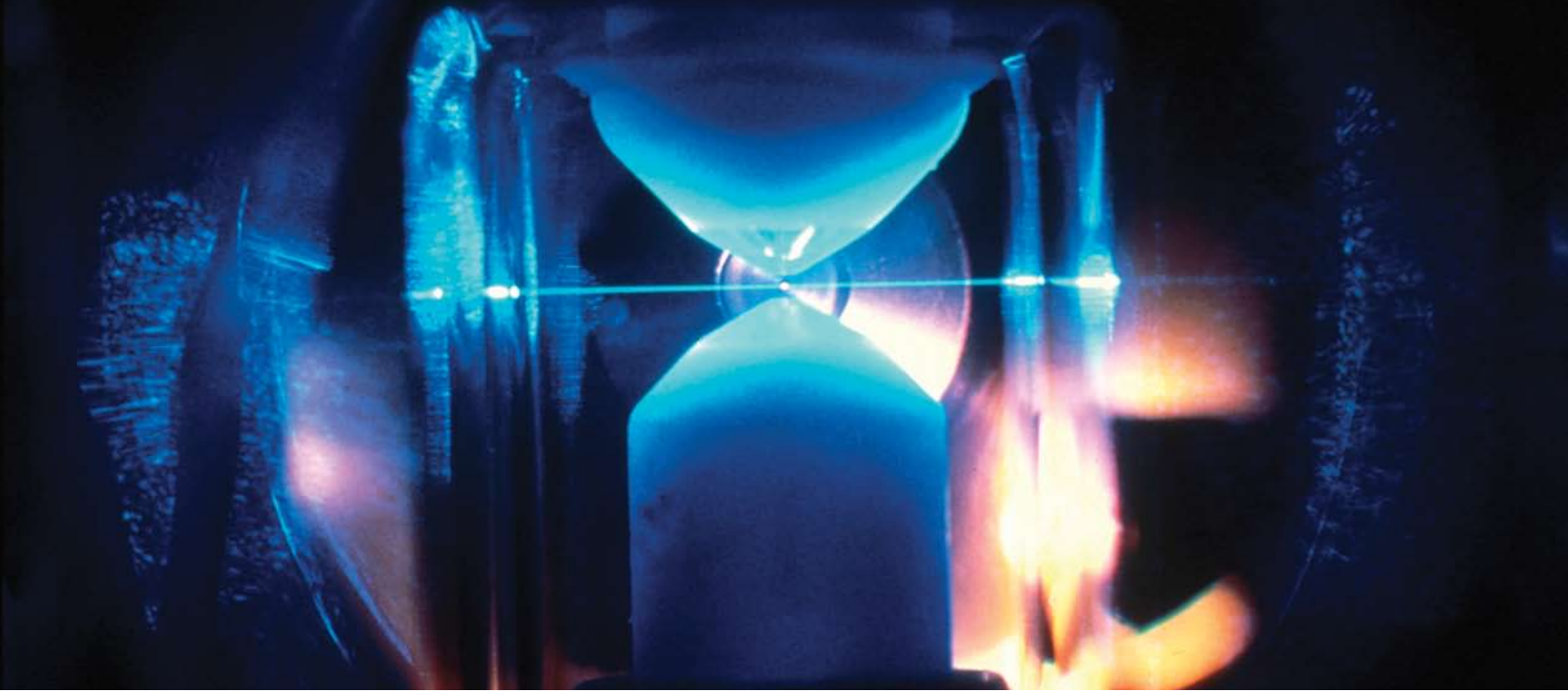
The key opportunities for early detection include:

- Improve use of existing detection approaches including mammography, colonoscopy, PSA, and PAP smear
- Promote new technologies in imaging, proteomics, and genomics through biomarker identification, test population validation, and population-wide screening to define biomarkers of early disease
- Concentrate on high-risk populations to evaluate the most cost-effective new technologies in early detection by identifying and validating these technologies in cancer survivors, those with a genetic predisposition, and those with either an environmental or lifestyle exposure or high-risk family history of cancer

NCI-designated Cancer Centers have led the discovery of new markers of cancer, improved image-based detection, and the development of genomic and proteomic approaches. Providing resources for this discovery effort and supporting the large-scale validation in high-risk populations will lead to improved early detection, improved cancer cure rates, and decreased rates of suffering from cancer. The cost-effectiveness of current detection strategies is clear, while that of new technologies will need to be defined.

NCI-designated Cancer Center Action Plan

- Cancer Centers should develop collaborative efforts for screening new early detection technologies
- Cancer Centers should coordinate evaluation of genetic early detection markers for colorectal, lung and pancreatic cancers, because preclinical detection will increase the potential of curative surgery
- Cancer Centers should promote development of registries of high-risk populations for colorectal, breast, ovary, prostate and lung cancers who would benefit from early detection screening. Examples include: breast MRI in carriers of BRCA1 and 2 genes, and mismatch repair



protein mutation analysis in families with colon, gastric and endometrial cancers

Introduction

Many, but not all cancers are curable through medical and surgical intervention after early diagnosis. While methods for early detection of cancer, including mammography, PSA testing, Pap smears, and colonoscopies, have been counted as important public health approaches to reducing the burden of cancer, much remains to be done. Most cancers cannot be detected early by conventional techniques. In addition, usage levels of proven screening methodologies for early detection are far below recommended levels. New methodologies for early detection have not been introduced broadly into the population, while others have yet to be validated. Nonetheless, early detection leading to the cure of cancers is likely to be the most powerful and cost-effective method of reducing the burden and death rate from cancer in our lifetime.

We are at an exciting crossroad in cancer research. The ability to align outstanding basic discovery of genetic and molecular causes of cancer; imaging, protein and genetic discovery technologies; and population-based research, combine to provide a compelling capability to rapidly translate and disseminate these discoveries towards early detection of cancer in at-risk populations.

The potential impact is enormous. Today, early cancers of the skin, breast, colon, and bladder can be controlled by surgery, chemotherapy, and/or radiation therapy. Early stage disease can be cured by rapid intervention. Validating the most cost effective new methods for cancer detection will have extraordinary impact reducing the burden of cancer in the population.

Current Knowledge, Barriers, and Opportunities

Stage I and Stage II breast cancer, colorectal cancer, small solitary lung cancers, localized prostate cancers, early cervical cancer, and many cutaneous malignancies – basal cell, squamous cell, and melanoma – are cured through early detection, intervention, and medical therapy.

However, many other cancers need further investigation into their etiology, which would allow early screening to have an effective impact on overall outcome and suffering. For instance, many early stage ovarian cancers are not cured even with early surgical intervention. Likewise, most pancreatic carcinomas, even when localized, cannot be cured by surgical and medical techniques. Gliomas are almost never cured, even when diagnosed early. Prognoses for leukemias and lymphomas do not appear to be primarily influenced greatly by stage at the time of diagnosis, but rather by the biology and molecular characteristics of molecular abnormalities associated with the diseases.

Therefore, efforts at early detection should be focused on those tumors in which early detection makes a current difference in patient outcome and survival (see sidebar,

"Optimizing Current Screening Technologies"). With this in mind, however, patients with deep tissue tumors, such as ovarian cancer and pancreatic cancer, which are normally diagnosed later, may still have an improved survival and outcome were they to be diagnosed early in the course of the tumor progression, even though curative impact is less likely to be achieved.

Colonoscopy Colonoscopy is considered by most experts to be the most accurate available procedure for the diagnosis of colonic neoplasia and is the only test that allows for simultaneous removal of lesions. However, population-based data from the Behavioral Risk Factor Surveillance System indicate that as recently as 2005, only 53.1% of adults aged 50 and older had ever undergone sigmoidoscopy or colonoscopy. In addition, as currently practiced, colonoscopy is associated with a "miss rate" for large polyps of as high as 12.5% and up to 0.9% of patients develop interval cancer following a colonoscopy with removal of adenomatous polyps. Thus, improvements in colonoscopic practice and technology are needed, with the net result of providing thorough examinations to a greater proportion of the population at risk. Although Medicare has provided coverage for screening colonoscopy since 2001, fewer than half of the states have laws that requires this coverage from private insurers.

Advances in imaging technology are also being applied to enhance detection of colorectal neoplasia. Variations on standard techniques that have been proposed include high magnification devices and chromo-endoscopy with spraying of the mucosa with stains, which highlight and thereby facilitate detection of flat or depressed neoplastic lesions. Imaging technology is developing "virtual" colonoscopy as a new technology.

Pap Testing Pap testing has been widely used for several decades, and currently approximately 86% of women aged 18 and older have been examined within the past 3 years. This represents the highest delivery of all cancer screening services. Despite widespread screening, approximately 10,000 American women will be newly diagnosed with cervical cancer annually and 3,700 deaths will be attributed to this disease. Inci-

Optimizing Current Screening Technologies

Breast MRI screening is more sensitive than mammography and has been shown to have value. For high-risk populations, such as Ashkenazi Jewish women who have a 45% to 65% lifetime risk of developing breast cancer, breast MRI screening is more cost-effective for BRCA1 carriers than BRCA2 carriers, who have mammographically dense breasts.

MRI screening is at least 10 times more expensive than standard screening and generates higher diagnostic costs. Adding annual MRI screening tests for women aged 25 to 69 years in this high-risk population would cost $88,651 per year of life gained for BRCA1 carriers and $188,034 per year of life gained for BRCA2 carriers. As a general rule, breast MRI, as with other technologies, becomes more cost-effective as risk of breast cancer increases and is less cost-effective as the risk decreases. Genetic screening in this population may increase average survival and may also be cost-effective.

A second technology for breast cancer is digital mammography. However, fixed costs may be one-and-a-half to four times more expensive than film-based systems. While overall the advantage is unclear, digital screening has advantages for women under the age of 50 years with radiographically dense breasts. Improved detection using digital mammography has reduced cancer mortality in select populations by more than 15%.

PSA screening of men for prostate cancer has lead to early detection, down-staging of early lesions, a lower rate of radical prostatectomies, and a better understanding of the impact of a rising PSA in an asymptomatic male. Nonetheless, PSA screening is not uniform and many high-risk populations are not routinely screened. African American males have lower screening rates, higher PSA at screening, and a higher incidence of prostate cancer. Research into the proper management of the isolated rising PSA, the impact of false negatives using the current PSA cut off of 4 ng/ml, and long-term follow-up of individuals identified during screening will help to define the value of population-wide screening of asymptomatic individuals. Refined PSA testing will likely reduce the need for biopsies and improve accuracy.

dence rates are highest in African American and Latino women and death rates are almost twice as high in African American women compared to Caucasians.

As currently practiced, approximately 7% of all Pap tests – or 3.5 million per year – are abnormal and require further evaluation. Screening intervals can be increased from every 1 to every 2 years if liquid-based Pap tests are used. HPV testing identifies high risk individuals since virtually all cases of cervical intraepithelial neoplasia (IEN) are associated with HPV infection. More frequent testing is still recommended for members of high risk groups such as immune suppressed and HIV-positive women and those with *in utero* exposure to DES. It is recognized that certain subtypes of HPV, specifically types 16 and 18, are associated with most cases of cervical neoplasia. The recently approved HPV vaccine will impact the rate of cervical cancer but is not effective in women already infected with HPV.

With respect to cervical cancer, mortality rates have declined by up to 46% in the United States over the past four decades. This success is due to the widespread use of the Pap smear screening programs. Recently, the FDA approved HPV DNA testing with cytology screening for women more than 30 years of age. Every three year screening with liquid-based cytology and screening using HPV DNA testing provided economic benefits greater than those provided by annual tests with costs of $95,300 and $228,700 per year of life gained.

In comparison, these same tests conducted annually only provide a few hours of additional life expectancy and had costs of more than $2 million per year of life gained. Screening every two years is slightly more costly and has a cost-effectiveness estimate of $257,400 per year of life saved. Of available options, liquid-based cytology may be most inexpensive although, when coupled with the HPV test, it is more accurate.

Mammography Breast carcinoma remains the most commonly diagnosed cancer and second leading cause of cancer death in women. Consistent with a greater detection of early stage cancer, incidence rates have increased since the 1980's, but death rates have decreased over that time interval. Although African American women have a lower breast cancer incidence than Caucasians, mortality rates are higher which may relate to a more aggressive genetic signature of the tumors.

Population-based rates of mammography within the previous two years has increased from 61.5% in 1990 to 75.9% in 2002, but almost one-fourth of women age 40 and older have not been screened. Rates of mammography in the previous year are especially low among uninsured women younger than age 65 (33.2%).

As currently practiced, mammography is associated with defined false positive and false negative rates. For example, in a recent large clinical trial of screening mammography, standard film mammography had an overall sensitivity of 66%, a specificity of 92%, and a positive predictive value of only 5% when a 5-point scoring system (BIRADS score) was used to quantify mammographic findings.

PSA Screening PSA screening to detect prostate cancer has lead to down-staging of early lesions, a lower rate of radical prostatectomies, and a better understanding of the impact of a rising PSA in an asymptomatic male. Nonetheless, many high-risk populations are not routinely screened. African American males have lower screening rates, higher PSA at screening, and a higher incidence of prostate cancer than the general population. Research into the proper management of the isolated rising PSA, the impact of false negatives using the current PSA cut off of 4 ng/ml, and long-term follow-up of individuals identified during screening will help to define the value of population-wide screening of asymptomatic individuals. Refined PSA testing will likely reduce the need for biopsies and improve accuracy.

Emerging Technologies

Imaging for Early Detection

Imaging and Cancer Detection
The use of ultrasound, x-ray computer tomography, MRI, positron emission tomography (PET), and more recently combined imaging systems, have been the backbone of early detection of cancer. With completion of the sequencing of the human genome (and the ongoing cancer genome project), there is little question that the emerging development of molecular and cellular imaging will further revolutionize the way we treat and manage cancer in the next few decades.

Cellular and Molecular Imaging Molecular imaging techniques must be designed to detect a molecular signature of cancer, in which the combination of multiple molecular biomarkers provide sufficient accuracies to identify tumor tissues and likely therapeutic responses, especially at the earliest stages. Molecular imaging probes must be designed for high throughput, high sensitivity, and specificity to differentiate tumor tissues and normal or inflammatory tissues.

Nanodetectors The most promising technologies for early cancer detection will be new developments in both *in vitro* diagnostics and *in vivo* molecular imaging. For example, in the area of *in vitro* diagnostics, the development of new nanosensors utilizing the latest advances in nanotechnology (e.g., magnetonano and nanowire) should allow very sensitive detection of low levels of serum proteins. It still remains to be seen which serum proteins are relevant for early detection, but they will likely be discovered over the next 5-10 years. Nanosensors, coupled to good reagents (e.g., antibodies and aptamers), should allow for other reliable clinical tools for early detection. *In vivo* molecular imaging with optical and other technologies could then also be used to localize disease.

Imaging Early Cancers

Biomarkers of Disease Altered metabolism detected by PET and altered blood flow detected by DC-MRI represent two promising approaches to imaging early cancers. An emerging approach and intensive area of study is directed towards the role of tissue remodeling in the growth and metastasis of tumors. The enzymatic breakdown of extracellular matrix is believed to be an essential step in both the production of new blood vessels to support tumor growth (angiogenesis) and the migration of tumor cells to distant locations (metastasis). Recent attention has focused on inhibiting matrix-degrading enzymes in order to halt the progress of cancer. The activity of these enzymes can be detected by high molecular weight contrast agents or blood flow.

Imaging of Tumor-Targeted Peptides The emerging identification of tumor-homing peptides for both therapeutic and imaging purposes offers exciting opportunities to develop novel peptides and small molecules for early cancer detection. Attachment of tumor-homing molecules to nanoparticles and radioactive labels offers excellent potential for using multimodality imaging approaches to detect precancerous and cancerous lesions prior to existing imaging approaches.

Novel Development of Imaging Technologies

Advances in imaging will continue to be made through investment in discovery and validation of cancer specific imaging. Promising areas include the following:

- "Smart" MR probes
- New optimized reporter genes (PET, BLI, SPECT, MRI)
- Agents targeted to the cell surface
- Optimizing agents for intracellular targets
- Incorporating imaging into therapy trials for the purpose of identifying response and predictive biomarkers
- Hardware development (i.e., PET/MR, SPECT/MR systems), integration of imaging agents, biomarker identification/qualification, and informatics

Proteomics for Early Detection

Proteomics involves the detection of novel peptides in bodily fluids that provide specific fingerprints of various tumors. Advances for early detection currently require improvements in both methodologies and applications of technology to noninvasively screen for colon and ovarian cancer, as well as other cancers. At many NCI-designated Comprehensive Cancer Centers, active screening programs are underway to discover new peptide markers and improve sensitivity and specificity of existing markers in colon, ovarian, pancreatic, prostate, and other cancers. The availability of robust biobanks with consistent collection and annotation is critical to this effort. This highlights the importance of these resources to the development of novel early detection approaches. Also, critical to these systems biology approaches are the use and continual improvement of bioinformatic pathway tools to annotate and organize the targets identified to be up- and down-regulated.

Validation Research of Proteomic Biomarkers The goal of these research efforts is to define the capacity of proteomics approaches to identify novel biomarkers that will provide better and cost-effective risk assessments in screening both high-risk patients and the general patient population as well as guide therapeutic decision-making for patients undergoing treatment. All of these promising leads need to be validated in retrospective and prospective cohort trials. The availability of screening and validation sets of blood samples will be needed, with

attention to proper collection and storage of material, selection of patients, and broad distribution of cohorts across populations. Current barriers exist in the availability of these samples, and the lack of collected samples in populations not yet diagnosed with cancer.

Genomics in Early Detection

Single nucleotide polymorphisms (SNPs) are variations in DNA sequences that occur within the 3 billion base pairs of the human genome. Although 99% of human gene sequences are the same, it is the subtle variations that contribute to individuality, predispose to cancer, and impact response to treatments. By identifying those who are predisposed, interventions can be carried out to prevent or delay the onset of cancer, thereby ultimately reducing the national cancer burden.

Current Knowledge, Issues, and Problems in Cancer Genomics The NIH Human Genome Project and the SNP Consortium – formed by collaborating pharmaceutical companies – are mapping the SNPs in the human genome. It is estimated that there are 3 million SNPs and that these make up 90% of human genomic variation. The ultimate location of these SNPs will serve as useful sequence landmarks and begin to help define susceptibility to disease and response to treatment. Researchers have found SNPs in 40 candidate genes that appeared to predispose Japanese men to habitual smoking and drinking. Other investigators found SNPs that alter the metabolism of carcinogenic components of tobacco smoke, thereby helping to define smokers at high risk for cancer who would be prime targets for intensive screening and prevention.

Investigators at the Institute for Advanced Studies and the Cancer Institute of New Jersey identified a common variant in the promoter region of the murine double minute gene (mdm2) that blunts the normal physiological response to cellular damage. In collaboration with investigators at MD Anderson Cancer Center, they found that individuals with inherited p53 mutations (Li Fraumeni Syndrome) – who also harbor the mdm2 SNP – were prone to the onset of multiple cancers at younger ages when compared with those with wild-type mdm2 alleles. This likely represents one of many SNPs that might be strong predictors of predisposition to particular malignancies and who would be identified as at high risk and in need of intense cancer screening.

Opportunities for Advancement in Genomics for Early Detection The significance of the SNPs will ultimately depend on their impact on individuals. This will require the formation of research teams that will include statistical geneticists, epidemiologists, molecular biologists, pathologists, informatics experts, pharmacologists, and clinicians. No better place exists than the NCI-designated Cancer Centers to bring these groups together.

Thus, it will be critical for NCI to provide incentives for the formation of these collaborative teams, through award mechanisms and review panels that are familiar with the complexities of this research. Potential problems exist whenever genetic information is being requested from patients. Therefore, it will be incumbent upon Federal, state, and local policy-makers to clarify current regulations that have hampered the approval of research protocols and the enrollment of patients into these cohorts.

Validation Process for New Technologies

Any new technology in the area of early detection needs to provide accurate, cost-effective screening for cancer and to be capable of dissemination to a broad population. Mammography and colonoscopy have emerged as effective methods for screening of large populations despite their need for advanced technology, imaging, and informatics. With these as examples, there is a high-cost barrier for a new technology, which could become a commonplace cancer-screening device.

A major barrier remains in the area of population validation for sensitivity and specificity of cross populations and particularly for high-risk populations (see below). Methods for such validation are not commonly employed in academic laboratories and require complex cross-disciplinary teams including medical technology experts, physicians, epidemiologists, statisticians, human geneticists, and clinical laboratory pathology, radiology, and public health experts. Among available technologies, we would anticipate that validation of a novel early detection screen would take 2 years at the level of Phase II validation, 3-4 years for Phase III validation, and 5-7 years to validate across populations.

New Screening Methods

The NCI-designated Cancer Centers will continue to be a nidus for discovery of new technologies. Efforts are ongoing among the Centers to establish the value

of a number of different approaches towards early detection using lead discoveries in genomics, imaging technology, colonoscopy, ultrasound, and advances in minimally-invasive technologies – such as CCD color bronchoscopy, MRI of the breast, and proteomics. New scientific discoveries in cancer etiology and cancer detection will lead to new approaches for early detection. These areas include:

- Novel colon cancer blood tests based on novel gene expression
- Proteomics screening for ovarian, prostate, lung, and head and neck cancers
- DNA methylation analysis of peripheral blood circulating tumor cells for colon, pancreas, and perhaps gliomas
- Glycomics and metabolomics as blood screens for a number of cancers

High-Risk Populations for Early Detection Screening

Cancer Survivors Patients who have survived a diagnosis of cancer, and now are in clinical remission, have a risk of recurrence and are the single group at the highest risk for developing another primary cancer. While this population is often followed either by their medical oncologist or internist, broad-based screening of this population for all cancer types is often suboptimal. National standards for long-term screening of these individuals are not established. For instance, patients with lymphoma and chronic lymphocytic leukemia (CLL) are at increased risk for skin tumors, while patients with hereditary nonpolyposis colorectal cancer (HNPCC) are at risk for endometrial and ovarian carcinoma.

Underserved Populations While the overall incidence of cancer in underserved populations is only slightly higher than the general population, cancers are often detected much later in the course of the disease leading to a much worse prognosis, higher rates of metastatic disease, increased pain and suffering, increased need of medical treatment, higher costs of treatment, and higher death rates from cancer. Thus, underserved populations are targets for early detection with the potential for considerable financial and socioeconomic benefits. Underserved populations include minorities, the poor, urban inner city populations, the medically uninsured, rural populations, and older individuals.

Ethnic Groups With Increased Risk for Specific tumors These include African American males who are at increased risk of prostate cancer and American Indians who are at increased risk for gallbladder cancers.

Behavioral, Environmental, and Work Place Risk Groups These include obese patients, smokers, those exposed to secondary smoke, and environmental exposures to pesticides, benzene, and organic molecules.

Family Cancer History Family history has also been identified as a demonstrable risk, however, only a few genes accounting for this have been identified. One of the most important aspects of early detection is to identify the target population. Some early detection studies should be performed on all individuals in an age-dependent fashion. For instance, all women over the age of 40 with such histories should have mammograms. In other instances, the optimal target populations still need to be defined.

Genetic Risk Easy Assessment Tool (GREAT)

The Genetic Risk Easy Assessment Tool (GREAT) has been developed at Case Comprehensive Cancer Center to facilitate systematic collection, interpretation, and communication about the family history of cancer. The web-based GREAT tool *(https://family.case.edu)* allows people to record a detailed family history via a secure Internet connection at a time and place convenient for them, using a reliable, computerized questionnaire that has been validated by comparison with genetic counselors. The program then automatically constructs and displays a digital family tree (pedigree), and automates risk analysis for breast, ovarian, and colorectal cancer. In 2007, the GREAT system could be made available to multiple NCI Cancer Centers for interest, validation, utility, and for development of identifiable families that would then be approached to participate in early detection clinical trials.

Opportunities to Impact Early Detection and to Reduce the Cancer Burden

Resource Allocations

1. Improve use of current early detection screening especially for underserved populations
2. Increase research funding for:
   - Imaging technologies for early detection
   - Genomics for SNPs and other genomic screening efforts
   - Development of proteomics for screening tests
   - Use of family history to define at risk populations
   - Large-scale, population-based screening initiatives to validate new technology
3. Coordinate regional and statewide initiatives for population dissemination of early detection efforts and technology
4. Develop collaborations with state departments of public health, insurance carriers, medical systems
5. Increase the proportion of the population covered for existing and standard early detection screening including colonoscopy, mammogram, PSA, and Pap test
6. Coordinate and support efforts to identify high-risk populations based on the above criteria
7. Facilitate and expand efforts to identify families with cancer histories and support development of cancer family history registries, allowing such high-risk groups to have more intensive screening

NCI-designated Cancer Centers Action Plan

Cancer Centers should:

1. Develop collaborative efforts evaluating new early detection technologies
2. Coordinate evaluation of genetic early detection markers for cancers because preclinical detection will increase the potential of curative treatment
3. Promote development of registries of high-risk populations for colorectal, breast, ovary, prostate, and lung cancers that would benefit from early detection screening. Examples would include breast MRIs in carriers of BRCA 1 and 2 genes, and mismatch repair protein mutation analysis in families with colon, gastric and endometrial cancers

Anticipated Outcomes and Potential Impact

Colon Cancer Current nationwide screening rates for colon cancer by colonoscopy is approximately 27% and approximately 40% for the use of occult blood testing in patients over age 50. Increasing screening to over 80% of the population would improve early detection of colon cancer and improve survival rates.

Breast Cancer Current methods for detecting breast cancer by mammography are proven to increase early detection, decrease late-stage diagnosis, increase cure rates, and prolong survival. However, mammography in underserved populations is performed in only 47% of women. Increasing annual mammography utilization in women over the age of 40 in underserved populations would improve early detection, intervention, cure, and prolong survival of affected individuals while providing a strong support to underserved populations.

Skin Cancer Skin cancer screening efforts can be improved by increasing primary care physician detection capabilities for visual inspections and increasing referrals to dermatologists for questionable lesions. For cancers like melanoma, this will dramatically decrease progression to local, regional, and metastatic disease in the vast majority of patients.

Prostate Cancer Improved prostate cancer detection methods would allow early intervention against high-grade prostate cancer lesions and reduce the overall morbidity and mortality from this disease.

Cervical Cancer The underserved populations continue to have a reduced rate of cervical Pap smears performed, leading to the diagnosis of advanced cervical cancer and death. Even with the availability of the new HPV vaccine, it is likely that the underserved populations will be the last to receive this vaccine and will receive it at a late date, increasing their overall risk of cervical cancer and making it quite likely that this disease will reseed to the boundaries of the underserved population. Aggressive ongoing efforts to both vaccinate with the new HPV vaccine and to screen underserved patients with the cervical Pap smear will dramatically decrease the impact of this disease.

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Summary

Recent national data indicate that the multimodality treatment of cancer is making a significant contribution to the decline in the overall cancer mortality rate. This is particularly gratifying in that these statistics do not even reflect some of the exciting recent advances due to the application of molecularly-targeted therapies. These encouraging statistics reflect the success of multidisciplinary and multimodality therapies which increasingly include a wide spectrum of combinations of surgery, radiotherapy, chemotherapy, hormonal therapy, and newer targeted therapy – both small and large molecules.

Treatment

There is a substantial basis for optimism for accelerating advances in the treatment of responsive as well as refractory tumors if cancer researchers can more efficiently and effectively move discoveries in cancer biology to clinical trials and to ultimate application in the community at large. The major thrust of this commentary on cancer treatment is to emphasize that an extraordinary level of collaboration – as well as alignment of incentives – will be required by all stakeholders in the cancer therapeutic enterprise if we are to significantly accelerate the rate of progress.

This section on cancer treatment presents a broad outline of such a blueprint and highlights an important new NCI initiative developed by the Institute's Clinical Trials Working Group (CTWG) which aims at restructuring the national cancer clinical trials enterprise. This type of national plan for cancer treatment research – coupled with continued robust support for fundamental science – has the potential of revolutionizing cancer treatment during the next few decades.

Introduction

Recent cancer statistics indicate continued improvement in survival. Between 1991 and 2001, the drop in cancer mortality rate was 10%, translating into as many as 321,000 lives saved. Furthermore, for the first time in over 70 years, the absolute number of cancer deaths dropped in 2003. Certainly, screening, early detection, and a wide range of prevention activities account for a significant amount of this improvement, but it is becoming increasingly clear that cancer treatment, particularly combined with early diagnosis, is having a major impact on cancer mortality.

The goals of cancer treatment are to decrease the mortality and morbidity from cancer by preventing the emergence of clinical metastasis at the time of diagnosis with primary and adjuvant therapy; and to eradicate or significantly reduce metastatic disease which has become clinically significant. At the time of the launching of the National Cancer Program in 1971, there had been considerable improvement and refinement

in surgical and radiation therapy techniques resulting in improved removal and eradication of the primary tumor with decreased morbidity. However, the effectiveness of systemic therapy was largely limited to a relatively small subset of cancers including childhood cancers, choriocarcinoma, Hodgkin and non-Hodgkin lymphoma and certain leukemias. There was little to offer patients with the common solid tumors in either the adjuvant or advanced settings and the explosion in our understanding of the molecular basis of cancer was just in its infancy.

In the ensuing three decades, there has been a tremendous increase in our understanding of the genetic and molecular pathogenesis of cancer, accompanied by new technologies and model systems, leading to a large number of new approaches to cancer treatment. The advent of combination chemotherapy, multidisciplinary therapy particularly in the setting of earlier diagnosis of cancer, newer approaches to endocrine therapy, and the remarkable gains in cellular and molecular biology coupled with the introduction of molecularly-targeted therapy have transformed the entire treatment approach to cancer. This was made possible by the adoption of formal clinical trials of new therapies which are carried out in Cancer Centers and academic institutions, and to some degree by practicing oncologists.

In order to build on these accomplishments and accelerate the rate of progress, we must understand as much as possible about the interventions that have lead to this improvement in survival. There are now data available from the Cancer Intervention and Surveillance Modeling Network (CISNET) – a consortium of NCI-sponsored investigators – whose purpose is to measure the effect of cancer control interventions on the incidence of and risk of death from cancer in the general population. CISNET data indicate that screening and treatment have contributed to the observed decline in the rate of death from breast cancer, and that the decline can be explained by a combination of screening and therapy and not by either one alone. When reviewing the improving survival statistics in breast cancer and

other malignancies, it should be noted that the impressive benefits now being demonstrated with targeted therapy (e.g., Herceptin in the adjuvant therapy of breast cancer) have yet to be represented in the survival statistics.

The opportunities and challenges that now face therapeutic researchers include:

- Building on the recent advances in the therapy of responsive neoplasms
- Beginning to make progress in the cancers refractory to current therapeutic approaches
- Continuing and enhancing fundamental research in order to accelerate translational research in both responsive and nonresponsive cancers
- Significantly improving delivery of advances in therapeutics to the community at large and in particular to underserved, minority populations

Current Knowledge, Barriers and Opportunities

Our current understanding of cancer therapy is in a rapid state of transition. Traditionally, we have employed modalities with minimal or no specificity for a particular cancer (e.g., chemotherapy, radiation, surgery) and often with the inability to avoid damaging normal cells. With the recent stunning advances in molecular genetics, epigenetics, and cell biology, the major task before us over the next decade is to sort out the molecular targets and the drugs that impact them and study their role in the therapy of patients with cancer. This 'translational' aspect of cancer is not solely an engineering problem. It is also a scientific problem.

Our scientific challenge is to maximize the number of studies that identify targets and their inhibitors and to get them to clinical trial as expeditiously as possible. Our engineering task is to find better ways to move the knowledge we already have to the broader and diverse community at every level including early detection, prevention, and therapy. The Cancer Centers have been steadily growing over the past 40 years in their ability to do cutting edge science and translate its discoveries into clinical trials. Their success is a testimony to the wisdom of creating the NCI Centers' Program and enhancing the extent of extramural funding for research.

The Cancer Centers have not, however, been as successful in the role of enhancing care delivery in their respective regions. In part, this is because that role has not been adequately funded by the NCI or other sources. Perhaps an even greater impediment to this critical phase of translational research is the lack of a coherent, effective national health system that is designed to provide quality care to all the citizens. Even if these barriers are removed, there are still fundamental engineering challenges in the process of translational research and its movement into the broader public arena.

These challenges include:

1. The ability of Cancer Centers and industry to more effectively interact. Removal of bureaucratic hurdles, standardization of clinical research and reporting methodologies, and alignment of incentives between industry and academia should be more actively explored to make progress in this area.
2. There is not a clear recognition that our supply of clinical and translational investigators is dangerously low. The "perfect storm" of medical schools relying on faculty practice plans, the Medicare/Medicaid cuts, the impact of medical school costs on career choices, and the excessive regulation of clinical research are making the process of identifying, training, and retaining investigators extremely difficult.
3. Past Federal and state efforts to grow or shrink specific areas of the physician work force are now leading us to an era of critical shortages in several cancer-related specialties.
4. The grant process at the Federal and state level is focused on individual outcomes without recognizing the critical need for broader, more flexible funding that is critical for the institutions that serve as the backbone for the collaborative activities of these investigators.
5. Mentoring and tenure and promotion policies at universities are often focused on individual accomplishments without appropriate recognition of the collaboration required for clinical/translational research.
6. There are limited funds for pursuit of truly innovative, risky research. This is also true for strategies to move knowledge out to the community where it can ultimately impact survival curves.
7. The competition for intellectual property has reached a level which inhibits or greatly slows advancements that require collaborations to move

novel ideas and agents into clinical trials.

Emerging Therapeutic and Interventional Strategies

A thorough understanding of molecular carcinogenesis (genetic and epigenetic) has led to the capacity to identify targets which are most suitable for preventive and therapeutic interventions. These target identification studies need to be undertaken on a large scale cooperative basis and appropriate biomarkers identified in order to evaluate the effectiveness of such interventions in a timely fashion.

Rapidly evolving technologies to sequence the human genome have allowed for the discovery of an abundance of genetic mutations in cancer. Structural analysis of such mutations should result in the discovery and development of drugs that are specific for the defined lesion and nontoxic for the patient. The challenge lies in the heterogeneity of such mutations under the umbrella of specific cancers. Thus, proving the efficacy of molecularly-targeted cancer therapies will depend on comparable advances in molecular diagnostics to ensure that these therapies are tested in cohorts of cancer patients that have the relevant mutation. For successful development of therapeutic strategies, acquisition of tissue through minimally-invasive procedures needs to be combined with outstanding tissue procurement infrastructure and molecular diagnostics. Technological advancements in molecular, cellular, and tissue imaging may provide opportunities for noninvasive discovery of markers and targets for both therapeutic and prevention studies.

Molecularly individualized therapy with its resultant diminished market size has the potential to dampen enthusiasm from the industry's perspective. Current intellectual property concerns also inhibit the use of new agents from different pharmaceutical/biotechnology companies in designing novel combinatorial regimens. A new comprehensive therapeutic development plan that aligns incentives between academia, industry, and government is required to overcome these obstacles.

Taking advantage of these opportunities and surmounting these obstacles are critical if we are to achieve multimodality therapy which is designed and targeted for appropriate cohorts of patients. Currently, the therapeutic options for cancer therapy include:

- Surgery
- Radiation therapy
- Chemotherapy
- Endocrine therapy
- Molecularly-targeted therapy: small molecules that regulate tumor growth, survival, and angiogenesis
- Immunotherapy
  - Monoclonal antibodies
  - Cancer vaccines
  - Cytokines
- Gene therapy

Increasingly, patients receive several of these treatment approaches in combinatorial regimens. Individualizing this combination therapy is now a feasible way of improving the antitumor response while avoiding adverse effects. New methodologies and paradigms must be pursued for designing and evaluating individualized therapy based on the specific molecular abnormalities of a patient's tumor.

Identification and Prioritization of Opportunities for Advancement

In the 2006 NCI strategic plan, the NCI leadership highlights general principles on which to base the overall strategy. These include:

- Discover, develop, and validate cancer biomarkers for cancer prognosis, metastasis, treatment response, and cancer progression. The discovery and application of these markers are now possible through recent advances in biomedical technology such as genomics, proteomics, nanotechnology, molecular imaging; all coupled with bioinformatics.
- Accelerate identification of potential targets for cancer treatments by integrating preclinical and clinical research.
- Develop individualized therapies tailored to the specific characteristics of a patient's cancer to cure or prolong survival with little or no adverse effects.
- Develop more effective symptom management and palliative strategies to better reduce the toxicities of cancer therapy to insure the highest quality of life.

In order to achieve these ambitious translational research goals, Dr. Andrew von Eschenbach, former director of the National Cancer Institute, established in January 2004 the Clinical Trials Working

Group (CTWG) which advised the National Cancer Advisory Board (NCAB) on whether and in what ways the NCI-supported national clinical trials enterprise should be restructured. The CTWG was a broadly constituted panel of experts from academic research institutions, community oncology practices, pharmaceutical and biotechnology industries, cancer patient advocacy groups, NCI, the Food and Drug Administration, and the Center for Medicare and Medicaid Services.

The full report titled "Restructuring the National Cancer Clinical Trials Enterprise" was issued in June 2005 and is available online at http://integratedtrials.nci.nih.gov/ict/CTWG_report_June2005.pdf. The summary vision of the CTWG is to "enhance the best of all the components of the NCI-supported clinical trials system, to develop a cooperative enterprise built on a strong scientific infrastructure and a broadly engaged coalition of crucial stakeholders."

The detailed blueprint for achieving this vision is described in detail in this report in four thematic areas which are summarized below:

Coordination Initiatives

- Create a comprehensive database containing information on all NCI-funded clinical trials to facilitate better planning and management across clinical trial venues.
- Realign NCI and academic incentives to promote collaborative team science.
- Increase cooperation between NCI, FDA, and industry to enhance the focus and efficiency of oncology drug development.
- Expand awareness of the NCI-FDA expedited approval process to speed trial initiation.
- Work with CMS to identify clinical studies that address both NCI and CMS objectives, and for which CMS may be able to reimburse some routine and investigational costs.

Prioritization/Scientific Quality Initiatives

- Create an Investigational Drug Steering Committee to work with NCI to enhance the design and prioritization of early phase drug development trials.
- Create a network of Scientific Steering Committees, which leverage current Intergroup, Cooperative Group, Specialized Programs of Research Excellence (SPOREs), and Cancer Center structures, to work with NCI in the design and prioritization of Phase III trials to better allocate scarce resources, improve scientific quality, and reduce duplication.
- Increase community oncologist and patient advocate involvement in clinical trial design and prioritization to improve the rate of patient accrual, and better address practical and quality of life concerns in the design of trials.
- Develop a funding and prioritization process to ensure that critical correlative science and quality of life studies can be conducted in a timely manner in association with clinical trials.
- Develop a standards-setting process for the measurement, analysis, and reporting of biomarker data in association with clinical trials to enhance data comparisons, reduce duplication, and facilitate data submission for regulatory approval.
- Investigate integration of Phase II trials into the overall prioritization process to further coordinate the national clinical trials system.

Standardization Initiatives

- Create, in partnership with the extramural cancer research community, a national cancer clinical trials information technology infrastructure fully interoperable with NCI's Cancer Bioinformatics Grid (caBIG) to improve cost effectiveness and comparability of results across trials and sites.
- In consultation with industry and FDA, develop standard Case Report Forms incorporating Common Data Elements to improve information sharing among cancer researchers and optimize data requirements.
- Build a credentialing system for investigators and sites recognized by NCI and industry to allow faster trial initiation and keep the investigative community abreast of legal, safety, and regulatory changes.
- Develop commonly accepted clauses for clinical trial contracts with industry to reduce the lead-time needed to open trials.

Operational Efficiency Initiatives

- Restructure the Phase III funding model to promote rapid patient accrual rates and cost-effectiveness.
- Reduce institutional barriers to timely trial initiation.

Table 1. Trends in Cancer Mortality Rates in the U.S. by Cancer Site 1990 to 2002*

	CANCER SITE/GENDER						
Year	All cancer sites	Lung/Men	Lung/Women	Colorectal	Breast/Women	Prostate	All other sites
1990	216.0	91.9	37.1	24.5	33.3	38.4	101.3
1991	215.2	90.0	37.8	23.7	32.7	38.9	101.5
1992	213.5	88.1	38.8	23.4	31.6	38.9	101.0
1993	213.5	87.6	39.4	23.1	31.4	39.0	101.1
1994	211.7	85.6	39.7	22.7	30.9	38.2	100.9
1995	209.8	84.2	40.3	22.4	30.5	37.0	100.1
1996	206.7	82.6	40.4	21.7	29.5	35.7	99.3
1997	203.5	81.2	40.9	21.4	28.2	33.9	98.0
1998	200.7	79.7	41.1	21.1	27.6	32.4	96.9
1999	199.4	78.1	40.9	20.9	26.5	30.9	96.9
2000	198.3	78.2	40.9	20.8	26.6	30.0	95.6
2001	194.3	78.0	42.0	20.1	25.9	28.5	94.3
2002	192.3	76.2	41.7	19.7	25.5	27.5	92.7
Average % decline per year †	1.0	1.6	-1.0	1.8	2.2	2.7	0.7

* Rates are per 100,000 population for all races/ethnicities and were adjusted to the 2000 U.S. age distribution by using the direct method. Rates for the years 1999 to 2002 were adjusted further to account for the change in coding from the International Classification of Disease, 9th Revision (ICD-9) to the ICD-10 (see Anderson et al., 2001[13]).

† The average percent declines per year are the means of the changes across the 12 yearly intervals between 1990 and 2002.

Source: Byers, et al. Cancer, 2006, 107(2) 396-405.

- Increase patient and public awareness and understanding of clinical trials.
- Increase minority patient access to clinical trials to improve the participation of underserved and underrepresented populations.
- Promote adoption of the NCI Central Institutional Review Board facilitated review process to reduce the time and resources needed to open trials at individual sites.

The Cancer Center Directors working group endorses this restructuring effort and would like to highlight the following critical responsibilities and key collaborative efforts of the stakeholders:

1) *Individual Cancer Centers and academic medical centers must work toward achieving the goals of the NCI strategic plan and the restructuring of the national cancer clinical trials enterprise* The individual Cancer Centers must remain the engines of discovery and see that promising laboratory discoveries are promptly taken into early phase clinical studies with the collection of biological materials for appropriate correlative research. Mechanisms must be developed within these individual Cancer Centers and academic medical centers to decrease bureaucracy, reduce legal barriers, overcome potential conflict of interest problems, facilitate necessary preclinical studies, and ensure the expedited filing of INDs with the FDA.
2) *Collaboration between Cancer Centers* Individual Cancer Centers must be encouraged and incentivized to work closely together to implement and complete early clinical trials in an accelerated timeframe. Likewise, an inventory of unique core services at

individual Cancer Centers should be available for access across the entire Cancer Centers network. Mechanisms to share tissue specimens across institutions through biorepositories should be further developed.

3) *Collaboration with other entities* Current relationships between Cancer Centers, cooperative groups, industry, as well as with the FDA and CMS should be improved and streamlined particularly in the area of development and implementation of Phase III trials.
4) *Collaboration with the health care providers and payer systems* Although progress has been made in certain areas of the country and with specific payers, there must be a coherent national approach to approval of the costs of patient care in clinical research approved by the NCI, NIH, VA, cooperative groups as well as trials approved by an NCI-designated Cancer Center with an approved Protocol Review and Monitoring System.
5) *Collaboration with policy-makers and government agencies* The closer ties between FDA and NCI should be further developed. The development of a national clinical trials management system utilized by Cancer Centers, community oncologists, industry, and government agencies would have an enormous effect on the ultimate productivity of translational research in the United States.
6) *Collaboration with pharmaceutical/biotechnology companies* Issues surrounding technology transfer –including intellectual property, confidentiality, conflict of interest, access of drugs for combinatorial regimens – constitute major bureaucratic impediments to timely development of new diagnostics and therapeutics.
7) *Enlightened and responsible behavior of people* Improved education of the public is essential to impact on personal behavior regarding tobacco use, diet, and other lifestyle issues, screening and cancer prevention as well as to enhance the public understanding of research. Cancer prevention should be regarded as the leading edge of a continuum which includes cancer treatment. An educated public will take better care of themselves and can be a highly effective supporter of research.

Anticipated Outcomes and Potential Impact

In 1996, the Board of Directors of the American Cancer Society set an ambitious challenge goal for the United States to reduce cancer deaths rates by 50% between 1990 and the year 2015. An article published in the July 15, 2006 issue of Cancer provides analysis of progress toward that goal through 2002, the mid-point of the challenge. This analysis has shown that if the current rate of decline in death rates continues into the future, the United States will have approximately a 23% lower age standardized death rate from cancer in the year 2015 compared to the year 1990. While this is only approximately half of the ACS' 2015 goal, it is an impressive decrease. The authors further note that if the current overall rate of decrease in death rates continues on the same trajectory, cancer death rates will be 50% lower than 1990 only after the year 2040. It should be noted, however, that the trends for reduction in death rates for cancers of the colorectum, breast, and prostate have been tracking toward the ACS 50% goal while trends for other cancer sites have declined at a much slower rate (Table 1).

To predict the potential impact of advances in cancer treatment on survival statistics, we must be able to assess the current contribution of treatment to improving survival. In the previously quoted CISNET study, the proportion of the decrease in the rate of death from breast cancer that was attributable to adjuvant treatment ranged from 35% to 72% with a median of 54%. The authors of this report point out that in spite of the variability in the quantitative conclusions across the seven independent statistical models of breast cancer incidence and mortality in this study, it demonstrates a significant interplay between screening and treatment. They conclude that screening and treatment appear to have contributed approximately equally to the improvement in survival that has occurred. It does not seem unreasonable to expect that similar conclusions might be reached regarding the analysis of survival improvement in colorectal and prostate cancer.

Given the progress that has been made with currently available treatments in breast, prostate, and colorectal cancer and the advances being made in molecularly-targeted diagnostics and therapeutics, an accelerated decline in the rate of deaths from responsive neoplasms might well be anticipated. As

pointed out in this report's section on Prevention, immediate measures to reduce death rates are available through application of validated screening procedures to underserved and underutilizing populations. The challenges for treatment of cancers that have thus far been largely refractory and more difficult to detect – such as pancreatic cancer – are obviously more difficult and require major investment of resources.

Implementation of the NCI Strategic Plan – with emphasis on a highly coordinated and collaborative national blueprint accompanied by the recommended restructuring of the cancer clinical trials national enterprise – can be expected to accelerate treatment progress in both currently responsive and nonresponsive neoplasms. However, unlike the situation with the successful space exploration projects, these accelerated gains in cancer therapy are dependent not only on skillful application of what we currently know, but also on continued fundamental research into the biologic behavior of cancer.

Three specific action items that should be advocated and promoted during the next year are:

1. Cancer Centers' leadership must play a vital role in prioritizing and implementing initiatives of the CTWG.
2. A unified national cancer clinical trials information technology system must be created with full collaboration of the Cancer Centers, cooperative groups, and pharmaceutical companies, and coordination with the NCI and the FDA.
3. Investment in translational research infrastructure in Cancer Centers should be a high priority, despite budgetary constraints, with recognition that translational research largely originates in Cancer Centers and within cancer programs at academic institutions. For example, funding:
   a. Biorepositories
   b. Easy access to shared resources across centers
   c. Enhancement/improvement of mechanisms like the Rapid Access to Intervention Development (RAID) program

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Survivorship

Summary

With an estimated 10 million cancer survivors in the United States, the demand for addressing the long-term needs of cancer survivors is clear and optimally accomplished through the partnerships of academic medical centers, Cancer Centers in particular, the community, and cancer survivors.

Cancer Centers, through collaborations with other Cancer Centers and community providers, play a critical role in survivorship research, development of evidence-based guidelines for cancer survivors, and education.

Surveys need to be conducted to identify existing resources and deficiencies or gaps that must be addressed to meet the needs of adult survivors, such as those unique needs of survivors with less common forms of cancer, and the gap related to the period immediately following completion of initial treatment. Adopting the pediatric cancer model of survivor programs and clinics may help address the needs of adult cancer survivors.

Partnerships must be developed between various stakeholders including academia, community practices, patient advocacy groups, third-party payers, and industry (e.g., pharmaceutical and biotechnology companies) to provide the necessary infrastructure for research, with an emphasis on the development of biomarkers for early detection and identification of risk factors for common problems, including second primary cancers experienced by cancer survivors.

The Survivorship Subcommittee recommends the following action items be accomplished over the next year:

1. A shared resource warehouse should be established through the NCI Office of Cancer Survivorship. This warehouse would provide for a central source of tools on survivorship. Cancer Centers should collaborate and participate in the establishment and population of this data warehouse, to include the following tools:
   a. Research protocols
   b. Educational materials
   c. Detailed descriptions of clinical, research, educational, and outreach activities being conducted at each Cancer Center
2. Cancer Centers, in collaboration with ASCO and other professional organizations, should take a leadership role in the development and implementation of clinical practice guidelines for survivors and mobilizing adoption of these guidelines as part of their respective states' cancer control plans. This work should also

involve looking at model programs and practices and ways to improve reimbursement for survivorship services.

3. Working groups drawn from the Cancer Centers should be convened to work on implementing the two action items listed above. Consideration should given to having a meeting, hosted by the NCI Office of Cancer Survivorship, that brings together experts on these topics, develops specific plans on how to achieve these objectives, and establishes a process for monitoring and ensuring progress.

Introduction

The Cancer Center Director Working Group Survivorship Subcommittee adopts the NCI definition that "an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life." Consistent with the definition, the domain of cancer survivorship covers the physical, psychosocial, and economic issues of cancer, from diagnosis until the end of life. It includes issues related to the ability to get health care and follow up treatment, late effects of treatment, second cancers, and quality of life. Survivorship programs at Cancer Centers should address the uniqueness of each individual's disease experience, as impacted by:

- Type of cancer
- Stage at diagnosis
- Age or life stage at time of treatment
- Long-term disabilities or impairments, including the risk of second primary malignancies, caused by treatment or disease

Current Knowledge, Issues, and Problems

Over the past 20 to 30 years, Cancer Centers excelled in preparing patients for treatment, but the time has come to move with greater emphasis towards preparing patients for recovery and survivorship. This preparation should include the implementation of early detection protocols since second primary malignancies among this group account for approximately 16% of all cancer incidence.

Cancer survivors, including their families, experience a spectrum of mental and physical problems in transitioning from active treatment to follow-up care. Many find they need assistance in adjusting to their "new normal."

Longitudinal research on quality of life and symptom management is needed to better serve the needs of cancer survivors. This longitudinal research should begin at the point of diagnosis. The ability to follow these individuals and their families throughout their life span would be enhanced by the ability of Cancer Centers to establish affiliations with community practitioners that provide ongoing medical care to cancer survivors once active treatment ends.

According to the Institute of Medicine's (IOM) reports, titled Childhood Cancer Survivorship: Improving Care and Quality of Life and From Cancer Patient to Cancer Survivor: Lost in Transition *(see Appendix B of this report)*, and consistent with the President's Cancer Panel 2003/2004 Annual Report, Living Beyond Cancer: Finding a New Balance *(see Appendix C of this report)*, there is a need for cancer patients to receive a comprehensive care summary and follow-up plan. Such a care plan would summarize critical information needed for the survivor's long-term care.

Moreover, there is a consensus agreement on the need to work toward development of evidence-based clinical practice guidelines for the care of survivors.

Cancer Centers have a substantial number of activities in survivorship. However, for adults in particular, these activities are focused on the most common forms of cancer and on longer-term aspects of survivorship. Therefore, deficiencies or gaps may exist in addressing the needs of survivors of less common forms of cancer and in the period just following completion of initial treatment.

Emerging Therapeutic and Interventional Strategies

Many Cancer Centers have established programs and clinics for survivors of pediatric cancers, recognizing the long-term care needs of this patient population. This comprehensive approach to survivorship research and follow-up care has only recently been applied to populations diagnosed with cancer in adulthood. As a successful model of a multidisciplinary comprehensive cancer survivorship program, we refer to The Lance Armstrong Foundation Living Well After Cancer Program at the Abramson Cancer Center of the University of Pennsylvania (see sidebar).

The adoption and refinement of this pediatric model will allow Cancer Centers to develop multidisciplinary teams that can provide not only a comprehensive array of services to meet the needs of adult survivors, but to do so within a research-based environment. This approach provides a foundation for research efforts, such as the determination of optimal surveillance strategies for survivors and the development of new biomarkers to facilitate the early detection of disease recurrence and second primary cancers, while facilitating continuity of care.

The interventional strategies offered in these multidisciplinary clinics should address the common acute and long-term problems associated with survivorship, such as:

- Fatigue
- Depression
- Sexual problems
- Cognitive problems
- Second cancer risk
- Therapy-related chronic disease (e.g., cardiac, pulmonary, endocrine)
- Psychosocial function (e.g., education, marriage, employment)
- Health behaviors (e.g., tobacco use, diet, exercise, medical screening)
- Reproduction and offspring

Furthermore, as the medical sequellae of treatments become better understood, research to identify useful interventions during cancer treatment should be greatly expanded in the form of cross-institutional clinical trials.

Lance Armstrong Foundation's Living Well After Cancer

A Model Program in Cancer Survivorship

The Lance Armstrong Foundation (LAF) Living Well After Cancer (LWAC) Program at the Abramson Cancer Center of the University of Pennsylvania is a successful model of a multidisciplinary survivorship program in a large, complex Comprehensive Cancer Center. The program consists of specialists from medical oncology (physicians and nurse practitioners), cardiology, rehabilitation medicine, and exercise physiology, psychiatry and behavioral science, social work, nutrition, and primary care – working in a collaborative environment.

The LWAC team determined that a research focus would be critical to its success and sustainability. To facilitate this, they have developed databases and chose tools to evaluate medical and psychosocial aspects of survivorship. During the first 2 years of the program, LWAC developed and refined their practice and consultative models of care. They also developed a transition program for young adult survivors of childhood cancers. LWAC's strategy is to include treatment teams who care for a specific population as sub-protocol PIs responsible for identifying eligible patients. This strategy has been well received by the oncology practice teams at the university.

Developing the LAF LWAC program required that the team members go through a number of cycles of implementing, evaluating, and redesigning their care models and assessment tools. The initial aim was to develop a single clinical care/research center for cancer survivors. However, after piloting this it was evident that more than one model of care was needed; differences in patient populations and the needs of providers meant that a 'one size fits all' approach to program development was unlikely to provide the best care possible.

After careful consideration, the LWAC team developed parallel practice and consultative models. The practice model provides routine follow-up care, surveillance, and an individual risk profile for late effects of treatment based on age, family history, co-morbidities, and cancer treatment history.

In addition to the large volume of survivors that mandates a separate clinical program, the issue of continuity of care with the primary oncology practice teams was an important consideration for patients and oncologists. Consequently, LWAC developed the consultative model to pilot and determine feasibility. LWAC serves as research consultants to the treating teams to allow for continuity of survivorship care while generating useful data for research.

Patients are followed prospectively from diagnosis with yearly mailings of study packets. These data are combined with clinical data to provide a prospective understanding of the survivor experience. This approach may prove particularly useful, as it allows for the use of baseline indicators in the construction of models to predict differing trajectories in the survivorship experience among populations of patients with different cancer diagnoses, which may allow for early identification of individuals at risk for developing difficulties during survivorship.

The goal of the LAF LWAC Program is to improve the care provided to cancer survivors. To accomplish this, stakeholders are included in the design and implementation of programs, focusing on issues that they find pressing, and overcoming identified barriers to uptake of services.

Identification and Prioritization of Opportunities for Advancement

Individual Cancer Centers and Academic Medical Centers

Academic medical centers, and Cancer Centers in particular, have an important role in survivorship research, clinical care, and education. With regard to research, studies are needed that can contribute to evidence-based guidelines for the optimal care of pediatric, adolescent, and adult survivors of cancer. With regard to clinical care, new service delivery models are needed that will allow Cancer Centers to work closely with community providers to provide follow-up care. With regard to education, Cancer Centers need to take the lead in informing patients, families, and the medical community about the common problems experienced by cancer survivors and their management.

As an initial effort to describe the survivorship activities at the Nation's Cancer Centers, we solicited narrative descriptions of research, clinical, and education efforts in this area. These narratives are found in Appendix D of this report which is available at www.cancer.gov/cancercenters/. We subsequently developed a template that provided an opportunity to collect standardized information on these activities. The data submitted by the Cancer Centers were compiled into an extensive grid that provides a basis for further analysis and interpretation of the various categories of survivorship activities currently being provided and what may be lacking and needed to reach the goal of ending the suffering and death from cancer. The grid, found in Appendix E of this report, provides a more effective means of communicating the breadth and depth of activities currently taking place at Cancer Centers, and identifies opportunities to share best practice models, as well as provides focus on survivorship activities that may be lacking.

The Survivorship Subcommittee recommends that systematic data collection occurs using a well-defined, online survey method to gather commonly codified data. This will allow for a deeper analysis of those activities available at Cancer Centers, and identify gaps that exist.

Cancer Center Collaborations

Cancer Centers can generate the knowledge base related to survivorship issues, conduct pilot programs, and coordinate large-scale studies and demonstration projects. In addition to generating new knowledge, Cancer Centers can utilize and disseminate existing knowledge to ensure that best practices become part of routine clinical care.

Community Collaborations

Work in survivorship is seen as a continuum that will require partnerships of Cancer Centers with community care practitioners. Cancer Centers can serve as the hub of networks involved in clinical care, education, and research at it relates to survivorship. These networks can also serve as the foundation for the conduct of multisite demonstration projects. One such demonstration project should be the development of community-based alliance models that evaluate the quality of care provided to cancer survivors through the monitoring of both health outcomes and processes of care.

Health Care Providers and Payer Systems

Reimbursement for psychosocial and palliative care and for symptom management must be integrated into health insurance plans. Cancer Centers can assist advocacy groups in pursuing this activity.

Policy-makers and Government Agencies

The NCI should consider establishment of survivorship programs and survivorship research as an essential element of an NCI-designated Comprehensive Cancer Center. Modest funding of survivorship activities by NCI would leverage the ability of Cancer Centers to attract other funding sources to this area.

Pharmaceutical/Biotechnology Companies

Pharmaceutical and biotechnology companies should be considered among the stakeholders that have a vested interest in survivorship activities. In addition to support for educational efforts, assistance should be sought from pharmaceutical companies for the conduct of clinical trials of pharmacologic agents with the potential to address common problems of cancer survivorship (e.g., depression and fatigue). In addition, support should be sought from the biotechnology industry to support research on development of new biomarkers for early detection and on identification of genetic risk factors for common problems (e.g., second malignancies, cognitive difficulties).

Individual Behaviors

Cancer Centers play a significant role in educating cancer survivors, their families, and health care providers about issues faced by cancer survivors. Most Cancer Centers have already established programs that provide information and support for patients undergoing cancer treatment. This work now needs to be extended to the post-treatment period. In addition, education and service programs are needed that can foster adoption of positive health behaviors (e.g., regular exercise, diets high in fruits and vegetables) among survivors.

Anticipated Outcomes and Potential Impact

These efforts by Cancer Centers should lead to improvements in the quality of care provided to cancer survivors and their families and, by extension, improvements in the quality of their lives. Cancer Centers are uniquely positioned to lead these efforts and in doing so, can galvanize public and medical community support for the view that a comprehensive approach to cancer care should extend throughout a patient's life span.

The Survivorship Subcommittee recommends evaluating the establishment of a shared resource data warehouse containing a single source of resources for patients, academic center faculty, and community practitioners. Such a data warehouse would create a remarkable resource to facilitate research and comparability.

Cancer Centers could provide their information online, within in a public domain, which may include the following examples:

- Follow up procedures
- Common sets of data elements
- Survivorship protocols, especially coordinated with prevention activities relative to tobacco use, obesity, etc.
- Questionnaires
- Definitions
- Educational materials

This warehouse would not only facilitate Cancer Center collaborations, but would also provide an outstanding resource to disseminate information to the community.

References

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Collaborations

Summary

While great progress could be made to reduce cancer mortality, roadblocks to collaborations exist that will be necessary to overcome in four primary areas of consideration – chemoprevention trials, therapeutic trials, deployment of biomarker and imaging agents, and survivorship. Below summarizes these roadblocks, and key action items are proposed that could be undertaken by Cancer Centers to begin to overcome them.

Chemoprevention trials

Difficulties in accruing large patient volumes, a lack of infrastructure within Cancer Centers, declining funding, and the size, complexity, and expense of these trials mandates a need for collaborations between Cancer Centers to conduct large chemoprevention trials. Liability concerns and lack of profitability have made it difficult to engage pharmaceutical and biotechnology companies in large prevention trials.

Action item: We recommend that a Cancer Center consortium be formed to centralize chemoprevention trial infrastructure activities.

Therapy trials

It is difficult for partnerships to remain intact for the 10-15 years required to take a therapeutic from concept to clinical practice. Many industry collaborators are abandoning their traditional academic partners in therapeutic trials due to difficulties of dealing with legal issues and the technology licensing and contracting offices of these institutions.

Action item: Collaborations between institutions would be facilitated by a shared licensing agreement that reduces the burden of individual contract negotiations with each partner.

Biomarkers and Imaging

Technology advancements are acutely needed in the rapid development of assays for proteins in blood and other body fluids for early detection that are inexpensive, sensitive, and quantitative. One major challenge to the use of surrogate biomarkers in clinical trials is the difficulty of establishing a predictive relationship between the surrogate and mortality from the disease.

Scientists involved in the commercial side of diagnostic tests complain of an inadequate source of human samples for marker validation. There is a need for greater understanding of the value added by a good diagnostic test because currently, there is little economic incentive to develop diagnostic tests. For example, the opportunity for early detection and risk assessment is very poor due to the lack

of reimbursement by Medicare and Medicaid for disease prevention.

The necessary interdisciplinary collaborations needed to discover new imaging agents is lacking in most Cancer Centers. Regulatory bodies are often overly restrictive in their application of vague safety and consent requirements to imaging trials that are designed for therapy trials.

Action item: A consortium of companies should be organized to fund a precompetitive academic activity to improve the technology for biomarker discovery, particularly protein biomarkers, much like the SNP Consortium.

Survivorship

Research requires longitudinal studies, multiple sites of care, or studies at multiple institutions to obtain sufficient samples sizes. The lack of uniformity or standardization of quality control can impede combining data from different sources. Provisions of the Health Information Privacy and Accountability Act (HIPAA) inhibit the ability to track and collect data for research.

Action item: A consortium of Cancer Centers should be formed to coordinate research efforts and funding strategies in order to facilitate the conduct of multi-institutional studies and the creation of a comprehensive research infrastructure.

Introduction

The NCI goal as expressed in the 2006 Strategic Plan is to "Reduce the burden and eliminate the adverse outcomes of cancer by leading an integrated effort to advance fundamental knowledge about cancer across a dynamic continuum of discovery, development and delivery." The strategy for meeting this goal depends on successful collaboration across the entire spectrum of stakeholders. "We as a Nation will achieve this vision by optimizing new approaches in interdisciplinary collaborations and transdisciplinary science," NCI explains. "Our success will depend on our ability to integrate our activities across a seamless continuum of discovery, development, and delivery; partner with others to leverage resources, and build synergy." Most of the goals in the NCI Strategic Plan require large-scale collaboration across two or more entities.

Current Knowledge, Issues, and Problems

There are many potential arenas for collaboration for NCI-designated Cancer Centers. Moreover, these collaborations extend from a micro-scale – involving individuals within a Cancer Center collaborating with individuals or organizations outside the Center – to the macro-scale involving institution to institution collaboration and consortia of institutions. In general, micro-scale collaborations are frequent and productive and depend more upon the initiative of the individual than the leadership of the institution. A survey was taken of the NCI-designated Cancer Centers to identify core resources that could be shared among centers (Appendix F). We will focus our consideration for this report in the macro-scale collaborations.

Many areas of medical science are evolving toward larger scale science projects motivated by opportunities to apply the abundance of new knowledge to patient needs. Application of new discoveries into standard medical practice is, by its nature, a much larger undertaking than discovery science, requiring highly organized, systematic activity involving collaborations across research institutions, industry, patient care providers, governmental agencies, and regulatory entities.

The subcommittee was greatly aided by a recent report from National Research Council and Institute of Medicine (NRC / IoM) titled "Large-Scale Biomedical Science." This report is strongly recommended for a much greater depth of consideration of these topics than can be provide here.

Emerging Therapeutic and Interventional Strategies

The NCI Strategic Plan for 2006 lays out a large number of strategic aims, many of which are big science projects requiring collaboration across many sectors of the discovery, commercialization, and implementation pipeline. As part of the academic medical community, Cancer Centers have had limited success with these larger scale collaborations. Four areas described below– prevention, diagnostics, therapeutics, and survivorship – might benefit from more effective large-scale collaboration.

Identification and Prioritization of Opportunities for Advancement

Prevention

Focus on Collaborations in Chemoprevention Trials During the past decade several prominent task forces of national experts have identified chemoprevention as a major area of cancer prevention research that could have a significant impact on the cancer burden. Studies have shown that chemopreventive agents can be effective in preventing cancer in a high-risk population (e.g., the Breast Cancer Prevention Trial, testing tamoxifen in women at high risk for breast cancer that showed a 49% reduction in incidence of invasive breast cancer).

Currently, NCI has about 400 compounds under study and has identified five classes of promising chemopreventive agents that are considered priority. Because the chemoprevention research pipeline is complex and involves large, long-term, expensive studies of high-risk and healthy populations, the collaborations required – among NCI, Cancer Centers, research networks, and industry – are substantial to continue to advance this area of cancer prevention.

NCI's Chemoprevention Program Among the cancer prevention initiatives, the NCI Strategic Plan has identified strategies to advance chemoprevention research that will require broad-scale collaborations within the cancer research community, including supporting a robust cancer prevention agent development program, large-scale clinical trials to evaluate cancer prevention agents, and a consortium of research centers for conducting chemoprevention trials.

At present, there are focused programs within NCI's Division of Cancer Prevent (DCP) that support collaborative work on chemoprevention agents and Phase I clinical trial development, including:

- The Rapid Access to Preventive Intervention Development (RAPID) program provides contract resources to the research community for preclinical and early clinical drug development of potential chemopreventive agents. This facilitates the process of bringing discoveries from the laboratory to clinical trials, potentially enhancing the attractiveness of licensing candidates for industry.
- The Early Detection Research Network (EDRN) is a national network and scientific consortium for the development, evaluation, and validation of biomarkers for early detection and risk assessment for cancer. With relatively small funding, experts note that this mechanism has done a "commendable job" developing collaborations across Cancer Centers, SPORES, and Program Projects.

Clinical trials for chemoprevention agents are currently coordinated through consortium groups of research centers conducting ongoing Phase I and II trials, Cancer Centers, and cooperative groups, with additional participation of community physicians through the Community Clinical Oncology Program (CCOP).

A set of initiatives supported by NCI's National Cancer Advisory Board (NCAB) for revamping the NCI clinical trials system is addressing the need for enhanced scientific quality and clinical trial prioritization, including increased collaboration with the broad oncology community. The plan is to investigate expansion of these initiatives in the future to include studies of new preventive agents.

Key Challenges Requiring Large-Scale Collaborations

Chemoprevention

While there has been significant progress and promising outcomes in the developing chemoprevention field, it faces some significant challenges and an overarching need for large-scale collaborations:

Size, expense, and timeframe Large-scale Phase III clinical trials, involving hundreds to thousands of high-risk and healthy populations, and multi-institutional participation, are required to test whether cancer risk can be reduced by chemoprevention interventions as well as to provide opportunities to validate potential biomarkers. These trials are expensive and require a long timeframe for completion (10 years or more).

Clinical trial infrastructure Within individual Cancer Centers, the infrastructure for supporting large Phase II and Phase III chemoprevention trials is viewed by many experts as "gravely lacking" and a key research barrier. Cancer Center clinical trials offices and data management support are primarily focused on therapeutic

trials involving cancer patients rather than population-based trials requiring specialized support (i.e., data management, statistical, trial recruitment, etc.). Only institutions with large Program Project grants – which have been an effective mechanism for advancing cancer prevention translational research, although such funding is declining – have been able to develop the capacity for Phase IIB or Phase III chemoprevention trials. However, individual Cancer Centers generally do not have the ability to accrue large patient volumes for Phase III trials or to coordinate and conduct large-scale intermediate biomarker endpoints required for translational research success.

The lack of infrastructure within Cancer Centers – coupled with declining Program Project funding and the size, complexity, and expense of these trials – mandates a need for collaborations between Cancer Centers to conduct large chemoprevention trials. Mechanisms need to be considered – potentially centralized or through a consortium arrangement– that most effectively address infrastructure deficiencies for large-scale trials. Collaborations will also be needed with cooperative groups and research networks, which will likely benefit from consortium arrangements comprised of organizations that are best suited for, and interested in, population-based chemoprevention trials.

Safety and trial design The results of some recent large chemopreventive studies have varied significantly from expectations. For example, the Beta-Carotene and Retinol Efficacy Trial (CARET), testing a combination of beta carotene and vitamin A supplements in persons at high risk for lung cancer, showed a 28% increase in lung cancers and 17% higher death rate compared to the placebo group. This has raised concerns about the safety of using chemopreventive agents in otherwise healthy subjects and the need for scientific collaboration to ensure that long-term benefits outweigh major side effects.

Concerns have also been raised about past chemoprevention agents moving into Phase III studies without adequate justification. These concerns have been attributed to issues such as appropriate dose scheduling; single- versus multiple-agent regimens; and inadequate underlying animal pharmacology/mechanistic studies, Phase I and early Phase II studies, and intermediate biomarker endpoints. Some of these concerns are beginning to be addressed through DCP's Phase I/II chemoprevention consortium effort.

Additional challenges include engaging the interest and involvement of pharmaceutical and biotechnology companies. To date, they have had a lack of interest in the cancer chemoprevention field, in contrast to embracing cardiovascular chemoprevention. This has been in part due to safety and liability concerns and the alleged lack of profitability of chemoprevention agents.

Treatment

As discussed in the NCI's 2006 Strategic Plan, the most important scientific strategies for advancing cancer treatment are: understanding the fundamental differences between metastatic and non-metastatic cancers; developing biomarkers and imaging agents to improve monitoring of treatment response; and developing molecularly-targeted agents with fewer toxicities. The Plan emphasizes the importance of integrating preclinical and clinical research and recognizes that collaboration among clinical scientists, cancer modelers, and imaging researchers through public/private partnerships will be an important implementation strategy.

However, NCI's Strategy does not address how these collaborations and partnerships can be facilitated so they are more effective than past NCI efforts to foster partnerships among these groups. Recent examples include the NCI Cancer Genome Anatomy Project (CGAP) program for development of early drugs in clinical trials, SPORE grants, and the AP4 initiative, all of which are popular with the participating institutions, but which have not yet demonstrated their value through promising new therapeutic targets.

A challenge of all of these types of initiatives is the long time frame required to take a therapeutic agent from concept to practice. Therefore, collaboration models must be measured over a 10-15 year time horizon, and it is difficult for partnerships to remain intact for such a long period. Cancer Center directors were surveyed about successful inter-institutional partnerships at their organizations. Two interesting models that were presented for further analysis were: the State of California, the University of California and various industry groups; and the Immune Tolerance Network, which is a nonprofit organization that provides funding, clinical

trials support, and access to assays, agents, and equipment.

Interviews with academic and industry scientists revealed many inherent difficulties with academic/industry partnerships that will require significant leadership in the field to overcome. Although academic institutions bring a wealth of expertise to the table, most industry partners have become extraordinarily wary about dealing with the legal, technology licensing, and contracting offices of these institutions. Agreements can take months or years to negotiate, and many institutional review boards are unsophisticated and cumbersome. Most industry representatives have abandoned academic institutions as a clinical trials venue and try to eliminate them from the drug development process at the earliest possible time.

It is ironic that community hospitals, community oncology groups and overseas health systems are easier to work with than organizations that were created and structured for this very purpose. Furthermore, many of the new technologies that show promise toward shortening the long-term costs of clinical trials – such as biomarkers and new imaging modalities – are very expensive on a cost-per-case basis. Much work remains to be done to communicate the cost effectiveness of these studies to payers and industry representatives.

A discipline that receives little mention in the therapeutics section of the NCI Strategic Plan is health economics. Nonetheless, in these difficult times in the Federal budget, the therapies with the highest likelihood of adoption by Medicare and other payers are those that reduce the total cost of cancer care.

There are two working groups within the NCI that are endeavoring to understand how barriers to partnership in therapeutics can be overcome. The first is the Translational Research Working Group (TRWG) and the second is the Clinical Trials Working Group (CTWG). Both have representation from most of the key stakeholders and their recommendations will help shape the changes that need to be made to create an environment more favorable to partnership. Both groups must assure that their recommendations are reviewed by economists because, in the end, development of translational discoveries must be funded by the financial markets and the health care payers. NCI's ability to fund this development effort is extremely limited and Cancer Centers must look to industry partners for this effort.

In addition, several Cancer Centers are willing to partner with other Centers and with industry to bring together the strengths of each organization. However, many of them will need help to overcome administrative barriers that transcend the creative skills of academic officials. NCI should consider taking some of the key resources that the NIH has invested in – such as the San Diego Center for Chemical Genomics, Harvard's Initiative for Chemical Genetics, the Mouse Model Consortium – and hiring top-tiered intellectual property lawyers to work with the institutions involved on a shared licensing agreement that reduces the burden of individual contract negotiations with each partner. Industry groups and foundations have found ways to manage these licensing issues and nonprofit and governmental organizations must adopt their best practices.

Biomarkers and Imaging

The NCI Strategic Plan relies heavily on advances in biomarkers and targeted imaging for improving the diagnosis, treatment, and prevention of cancer. The pipeline for both biomarkers and targeted imaging agents involves a series of steps from discovery to validation, commercialization, regulatory approval, and implementation. For both there is a continuum of partnerships needed involving research funding from the NIH or foundations, discovery in academic or commercial laboratories, commercialization by companies, approval by FDA and implementation by CMS and other insurers, and adoption by health care agencies and patients. Incentives and bottlenecks along this pipeline were considered, and points at which innovative solutions are needed are identified below.

Need for Protein Biomarkers Many applications of DNA-based biomarkers require direct biopsy of diseased tissue, which requires that the tumor be identified, localized, and accessible, and hence are only applicable between the stages of tumor localization and removal. Biomarkers that can be accessed noninvasively are needed at all stages of disease management, from risk assessment to treatment. The most informative biomarkers are likely to be proteins because of their diversity and proximity to function. They are also likely candidates for imaging targets.

Diagnostics Work in a System Our goals in applying biomarkers to disease management are: to identify persons with potentially life-threatening cancers at the earliest stage possible; to avoid false-positive

tests and unnecessary treatments; and to minimize the overall cost of the program. Since no single test performs perfectly, sensitivity, specificity, and cost become tradeoffs in the application of diagnostics to disease management. Ultimately, the goal will be to optimize overall performance of a system of tests and interventions. The advantage of a systems approach is that biomarkers whose performance may be inadequate when considered at a single stage of the disease continuum may actually be of great value when integrated into a disease management continuum.

Discovery of Protein Biomarkers Although there have been significant advances in proteomics, the discovery of new protein biomarkers appears to be stalled. NCI has recently moved to accelerate the field with programs that foster discovery in mouse models of cancer, provide for informatics support, reagents, and large grants for centers for technology development. Technology advancements are acutely needed in the rapid development of assays for proteins in blood and other body fluids that are inexpensive, sensitive, and quantitative. In the area of collaborations, most of the effort is currently being made between NIH and academic laboratories. A consortium of companies that would invest in discovery technology as a precompetitive activity, much like the SNP consortium, could be highly effective in moving the field forward.

Validation of Biomarkers Protein biomarker validation is currently conducted either via collaborations between NCI and academia (for example, the EDRN program) or as a commercial activity with or without an academic partner. Few protein biomarkers are currently in the validation stage. The bottleneck at discovery means that validation studies are often limited to a single biomarker at a time. If the bottleneck to discovery were solved, biomarkers could be multiplexed by the hundreds in validation studies, dramatically decreasing the cost per marker and increasing the probability that some would be validated. At the other end of the pipeline, the perception of low reimbursement and thus insignificant profits to cover development cost inhibits companies from undertaking validation studies unless the biomarker is necessary for a drug therapy that will yield significant financial return. One major challenge to the use of surrogate markers in clinical trials is the difficulty of establishing a predictive relationship between the surrogate and mortality.

Commercialization of Biomarkers Commercialization of biomarkers for diagnostic tests usually involves a commercial entity to provide the necessary investment and quality control, and an academic partner to provide biological insight, assays, and tissues. Industry scientists complain of an inadequate source of well-annotated human samples for marker validation. Obtaining such samples is the single most expensive aspect of diagnostic test development. New health privacy regulations (HIPAA) and differences in interpretation of what constitutes informed consent further exacerbate this problem.

Another serious impediment to biomarker commercialization stems from intellectual property (IP) issues. Use of panels of biomarkers in the future will be very difficult if different entities own IP rights to different markers.

The total market for a successful diagnostic may be $50-100 million per year but the cost of development can be more than $100 million. As a consequence, there is not enough economic incentive to develop diagnostic tests that will only be used once regardless of their importance in health care. The opportunity for early detection and risk assessment is very poor due to the lack of reimbursement by CMS for disease prevention practices.

Approval of Biomarkers Both the FDA and CMS regulate diagnostic tests. FDA regulates tests that are sold as kits or systems in interstate commerce while CMS oversees laboratory testing services commercially offered at single sites, in-house or "home-brew" or sold commercially to CLIA-approved laboratories as analyte-specific reagents. Several hurdles frequently thwart the FDA approval process. As a result, the CLIA home-brew policy is an easier route to approval and may obtain higher reimbursement by dealing directly with the user. There is concern in some quarters that the home-brew procedures for approval do not assure enough patient protection and that this option should be eliminated. This recommendation would be a disaster for the implementation of biomarkers in cancer.

Given the likelihood that many biomarker tests will be developed for use in guiding molecularly-targeted therapeutic interventions, there are not currently procedures for co-review or co-approval by FDA and CMS, although these are under consideration.

Implementation of Biomarkers The economic incentive for diagnostic tests is low because most tests will be performed infrequently on a patient. Reimbursement is calculated based on the cost of doing the test rather than considering value added by the test or the costs of its development. This is entirely different than reimbursement for therapeutics. There is a need for more understanding of the value added by a good diagnostic test. Two government commissioned reports have recommended a re-evaluation of reimbursement rates for diagnostics.

Three diagnostic companies compete for control of clinical laboratory testing. Tests are standardized utilizing primarily antibody tests and polymerase chain reaction (PCR) technology. Any new technology platform for diagnostics would be difficult to introduce.

The promise of biomarkers for reducing mortality by early detection of cancer is completely undermined by the fact that Medicare does not reimburse for screening tests unless mandated by Congress, as is the case for colonoscopy.

Recommendations for Biomarkers A specific statement from NCI as to the clinical problems for which tests are needed, what performance standards need to be met, and funds to support their development might provide motivation for development of new biomarker tests.

Discovery of Imaging Agents Discovery of new imaging agents seems to be most productive in academic centers that involve collaboration across academic departments and disciplines, with funding from NIH and one of the three large companies that produce imaging instrumentation. The NCI has established a series of such imaging centers. While these provide a strong focus for collaboration, progress is often less than optimal because of the difficulty of collaborating across disciplines. In many academic institutions these collaborations are not effective.

Validation of Imaging Agents Fast-track FDA approval for new agents only works for drugs with known toxicities that are adapted to imaging strategies. Completely new drugs do not fare as well. The preclinical burdens hamper development in terms of cost and time. Medical ethics committees do not understand the low risks imaging studies pose to subjects, and are often overly restrictive in their application of vague safety and consent requirements that are designed for therapy trials.

Commercialization of Imaging Agents The major instrumentation providers will be the likely entities to commercialize new imaging markers that achieve the necessary validation and approval. Reimbursement is good for imaging used in clinical diagnosis and treatment so there is both sufficient resources for commercialization and incentive to do so.

Approval of Imaging Agents Preclinical and validation components for imaging studies should focus on optimally defining the initial human trial. The rules of evidence for prognostic studies are not nearly as well defined as they are for treatment trials or for simple diagnostic measures. These need to be developed through a dialogue involving FDA, NCI, academia, and industry groups and should address the appropriate use of new imaging procedures in early clinical trials of experimental therapies. New imaging agents for targeted therapy cannot be developed and validated independent of the treatment protocols.

Implementation of Imaging Agents Since most new imaging agents will be designed to be used in one of a half dozen instruments that are widely available in health care settings, and since diagnostic imaging tests are well reimbursed, there are both the technical platforms and trained personnel to implement new imaging agents.

However, one of the most important applications of imaging agents – to inform therapeutic outcomes in clinical trials – has not been effectively implemented. More than 80% of drugs entering clinical development do not receive FDA approval, with many failing late in development, often after prolonged Phase III trials, because of unexpected safety issues or difficulties in determining efficacy. This contributes to the high costs of oncology drug development and highlights the need for tools to identify promising candidates early in development. To that end, NCI, FDA, academic researchers, and industry are discussing ways to collaborate with the goal of identifying biomarkers that will provide a clear and timely picture of a patient's cancer and its response to therapy.

In oncology, the gold standard clinical trial endpoint is overall survival, which may require long-term studies and may be confounded by a patient's death from causes other than cancer. Over the years, the oncology community and the FDA

have come to rely on endpoints that are regarded as correlates of clinical benefit or surrogate endpoints (SEP). However, the measurements of SEPs using standard anatomic imaging techniques are often inadequate, especially for monitoring the effects of drugs that do not cause tumor shrinkage or for cancers that progress slowly or metastasize diffusely.

Newer imaging modalities, including volumetric and functional imaging, show high promise as additional biomarkers in cancer. For example, clinical trials in breast cancer and other settings (e.g., non-small cell lung cancer and esophageal cancer) have demonstrated that FDG-PET – a physiologic imaging modality – may provide an early indication of therapeutic response that is well-correlated with clinical outcome. If the use of FDG-PET can be confirmed as a biomarker in such settings, unnecessary chemotherapy may be avoided for some patients and the costs of unnecessary long-term follow up reduced. The FDG-PET imaging modality has the potential to facilitate oncologic drug development by shortening Phase II trials and detecting clinical benefit earlier in Phase III investigations.

Current obstacles to including correlative imaging studies in clinical trials are: cost; the perception that adding a correlative imaging study will make the trial more difficult to implement and may hamper accrual; and the investigators' concerns that the imaging study will not add value in terms of yielding publishable findings or as a validated endpoint that can be used in trial design. Collaborations are needed to define and develop imaging biomarkers based on newer imaging technologies for use in oncology drug development, particularly evaluation of therapeutic response. Ultimately, the outcome of these studies will inform the development FDA guidance and best practices in oncology.

Survivorship

Advances in the ability to detect, treat, and support cancer patients have turned cancer into a chronic or readily managed disease for many. There are 10 million Americans alive today with a personal history of cancer and as of 1997 there were 270,000 survivors of childhood cancer.

Recently, task forces of national experts have evaluated and identified the requirements for a comprehensive approach to addressing the needs of cancer survivors and patients diagnosed or treated for cancer. In accordance with those task force recommendations, the NCI Strategic Plan focuses on the following areas:

- Discovery
  - Expanding research efforts to understand the biological, physical, psychological, and social mechanisms, and their interactions, that affect a cancer patient's response to disease, treatment, and recovery.
  - Expanding the development and use of tools to assess the health-related quality of life and quality of care of cancer survivors and their family members, and tracking outcomes for these populations.
- Delivery
  - Ensuring the delivery of new information, interventions, and best practices in collaboration with other Federal, professional, and nonprofit organizations.
- Development
  - Accelerating intervention research in order to reduce cancer-related chronic or late morbidity and mortality.

Key Challenges The majority of survivors (62%) are 5 years or more post-treatment. Thus research to understand the multiple factors influencing the health of survivors requires longitudinal studies, multiple sites of care, or studies at multiple institutions to obtain sufficient samples sizes.

Funding Strategies Funding for research has traditionally been based on shorter-term projects rather than the longitudinal approach required for the long-term studies fundamental to survivorship research.

Complexities of Conducting Multi-Institutional Studies and Long-term Studies Multi-institutional studies may require data from a variety of sources and the lack of uniformity or standardization of quality control can impede combining data from different sources. Data collected in large-scale projects is often placed in publicly accessible databases, giving rise to issues of patient confidentiality and consent. The provision of HIPAA may inhibit the ability to track and collect data for research. Obtaining appropriate patient consent can be challenging for longitudinal studies and studies

conducted on data collected over a long period of time.

Coordination Among Health Care Providers Given that the majority of follow-up care for survivors is provided in the community, coordination between health specialists at Cancer Centers and community-based providers is critical but underdeveloped.

Infrastructure for a Comprehensive Database on Cancer Survivorship While the NCI has provided statistical information on cancer survivors in the United States, further work is required to improve coordination between existing resources [e.g., the Surveillance, Epidemiology, and End Results (SEER) program], and to develop the infrastructure for large-scale studies.

Successes and Opportunities There are opportunities for further coordination between the NCI, Cancer Centers, foundations, community groups, and advocacy organizations. NCI is successfully partnering with local and national organizations including the American Cancer Society, the Intercultural Cancer Council, and the Lance Armstrong Foundation to provide informational resources on cancer survivorship to patients, family members and medical providers. These collaborations are ideal for the dissemination of educational materials including statistical information about cancer survivors, survivors' second malignancies, quality of life, and other information such as current research grants and post-treatment resources.

Future collaborations to consider include coordination of efforts and funding strategies. For example, the Lance Armstrong Foundation is funding the development of cancer survivorship programs in multiple sites. Coordination of these efforts with NCI can provide efficiencies and contribute to a more comprehensive approach.

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Dissemination

Summary

Advances in diagnostic tests and treatments for cancer usually are made available to patients rapidly by Cancer Centers, academic medical centers, and major health care providers. However, reaching all patients with cancer, and their health care providers, is a goal obtainable only through concerted efforts in education and widespread adoption of best practices, especially by physicians for underserved populations. The NCI-designated Cancer Centers should ensure that opportunities to participate in clinical trials of new cancer treatments, preventative strategies, and early detection tests are made available to greater numbers of individuals, including underserved and diverse populations.

Highest Priority Strategies

- The Federal government needs to designate a lead agency within the Department of Health and Human Services (HHS) to coordinate funding and dissemination of cancer control efforts to the entire U.S. population, by bringing together the fragmented efforts of NCI, CDC, CMS, and other HHS agencies.
- Cancer Centers should take the lead in disseminating cancer care guidelines throughout their states, in collaboration with state health departments and state cancer plans.
- Cancer Centers should work with state cancer registries to convert them into outcomes registries, and should use them to identify populations with disproportionate needs for cancer prevention and care.
- Demonstration projects on the medical and financial benefits of best cancer control practices should be initiated in regions served by Cancer Centers, funded by CMS and led by the Cancer Centers.

Introduction

In order to fulfill as quickly as possible NCI's Challenge Goal to eliminate the death and suffering from cancer – and to realize the potential for known best practices and research advances – it is essential to extend the expertise and infrastructure that has been extraordinarily well developed at the NCI-designated Cancer Centers to all the relevant populations in the United States that are currently beyond the areas and communities that are traditionally serviced by the Cancer Centers.

There is ample evidence that even when advances are made in cancer treatment, early detection, and prevention, the overall populations that can and should benefit have insufficient knowledge of and access to these advances and evidence-based best practices.

Current Knowledge, Barriers and Opportunities

The main focus of the Cancer Centers and NCI support for them has been on basic, translational and clinical research. Participation of Cancer Centers in education and outreach activities has generally not been encouraged, or has taken the form of unfunded mandates. Dissemination of research advances to all appropriate populations – including ethnic minorities and the underserved, uninsured and uninformed – has been suboptimal. There are well known barriers to enlisting various populations into clinical research studies, including cultural and language issues, and adequate dissemination of clinical research access to these populations will require culturally-sensitive approaches.

It is widely recognized that participation in cancer therapeutic trials only involves 3-5% of cancer patients in the United States. There are considerable efforts being made to reduce barriers to participation in the Phase III clinical trials conducted under the auspices of the cooperative groups, CCOPs, and other multicenter collaborative consortia supported by NCI and by the pharmaceutical and biotechnology industries.

Similarly, only a very small proportion of individuals at high risk for cancer participate in clinical research studies of cancer prevention or early detection. A major bottleneck and rate-limiting issue is the low participation in the large number of translational and innovative early phase investigator-initiated trials, which are now performed almost entirely at the Cancer Centers. There currently is little access to such studies by the overall appropriate population. Effective linkages to community hospitals and to clinical oncologists and primary care physicians in the regions served by the Cancer Centers could provide much wider access and also substantially accelerate accrual to such studies.

There is striking heterogeneity in the United States in the knowledge of best practices or evidence-based

approaches to cancer therapy, early detection, prevention, and survivorship issues, and also in their implementation by health care providers. To address these disparities, most of the NCI-designated Cancer Centers have – in addition to their research excellence – developed the expertise, and needed faculty and well-trained staff, to provide to the populations that they serve the best practices and evidence-based approaches for cancer (see sidebar, "UPMC Cancer Centers Network: Dissemination Beyond NCI-designated Cancer Centers"). However, there have been relatively little attention, processes, or resources directed toward the capability of these Cancer Centers to disseminate their knowledge and expertise to most of the communities in the United States, especially those that are not directly proximal to or traditionally linked to the Cancer Centers.

It is very encouraging that national organizations such as the CDC, American Cancer Society, and C-Change – and also a substantial number of the state governors – have promoted the development and implementation of cancer control plans in all of the states in the country. Many of the state plans are very well conceived, comprehensive, and feasible. However, these plans have largely remained only on paper, due to lack of sufficient and effective infrastructure and resources for implementation. Implementation of the cancer control plans is the responsibility of the departments of health in each state, which often lack the needed cancer-relevant expertise to implement the best practices and evidence-based approaches encompassed in the plans. Linkage of the state plans to the NCI-designated Cancer Centers, which often have this expertise, is not supported.

Another major current barrier to effective dissemination of best practices for cancer control is the limited reimbursement by CMS or private payers for cancer prevention, early cancer detection screening, or survivorship issues.

Emerging Dissemination Strategies

The important problems summarized above are clearly multifaceted and will require enhanced collaborative efforts among many organizations and sectors, including the Federal government – not just NCI and other relevant NIH institutes, but even more importantly, CMS, CDC, AHRQ and HRSA – along with state governments, local governments, academic cancer centers, community-based cancer centers, and other health care providers, private insurers, and the business community, especially the pharmaceutical and biotechnology industries.

There is a real opportunity for the network of NCI-designated Cancer Centers across the United States to play a major role in linking together these key stakeholders in order to mount effective dissemination of both research advances and best practices for addressing cancer prevention, early detection, treatment and improved survivorship.

The following specific recommendations are proposed:

- Strengthening of current overall infrastructure for dissemination of research and best practices by clinical and comprehensive Cancer Centers to their region, and also to disseminate to those states that lack NCI-designated Cancer Centers.
- Designation by the Federal government of a lead agency within the Department of Health and Human Services (HHS) for dissemination of cancer control programs to the entire population of the United States and to coordinate what are currently relatively fragmented efforts by various HHS agencies, including NCI and CDC. An appropriate level of resources needs to be provided to the designated lead agency in order to effectively promote dissemination of cancer control throughout the country.
- Provide leadership by the HHS lead agency for cancer control dissemination to forge effective linkages between NCI-designated Cancer Centers and state governments, CDC and CMS to implement action plans to address the areas of greatest need.
- Added support for NCI's Cancer Centers program to allow substantive involvement in, and leadership role for, cancer control plans in states that have one or more Cancer Centers, for working together and with other health care providers in their state. Various mechanisms and processes might be implemented to facilitate a central role by the NCI-designated Cancer Centers in dissemination.
- Development of effective processes for substantive involvement of the Cancer Centers in the CDC-funded cancer control efforts in the states, with the CDC

UPMC Cancer Centers Network

Dissemination Beyond NCI-Designated Cancer Centers

The University of Pittsburgh Medical Center (UPMC) Cancer Centers, one of the largest clinical cancer networks in the United States, provides highly specialized cancer care to patients within their own communities. This truly multifunctional cancer care network is economically integrated and uniformly managed and operated across multiple settings.

In a regional "hub and satellite" structure, inpatients and specialized treatment are provided at UPMC's central hub facility, the Hillman Cancer Center in Pittsburgh. Outpatient care in medical oncology, radiation therapy, and surgery is offered at more than 40 UPMC Cancer Centers' regional satellite sites across western Pennsylvania, eastern Ohio, and northern West Virginia.

UPMC Cancer Centers works in tandem with the University of Pittsburgh Cancer Institute (UPCI), western Pennsylvania's only NCI-designed Comprehensive Cancer Center. As the academic and research partner, UPCI is nationally and internationally renowned for its translational, clinical, cancer control and population sciences research programs, thus providing a strong scientific base for the dissemination of knowledge and best practices to the community network of UPMC Cancer Centers.

UPMC Cancer Centers' integrated cancer care delivery network treats more than 36,000 new patients each year for hematologic and oncologic disorders. This translates to more than 285,000 patient visits annually. The working partnership with UPCI allows for the expedited implementation of new, more efficient ways of delivering cancer care by:

- Translating research discoveries to clinical therapeutic, early detection and prevention applications which are available at both the academic medical center and community satellite centers
- Providing cutting-edge treatments and technologies, including access to more than 150 clinical trials
- Developing and implementing clinical pathways for major types of cancer, to provide standardized approaches and best practices for care, to improve patient outcomes and efficiencies while decreasing operating costs
- Offering access to cancer control and ancillary support services such as symptom and side effect management, nutrition advice, family counseling, psychological care, stress management, close follow-up of cancer survivors, and cancer education resources

In addition to these activities in western Pennsylvania, UPCI is also playing a key role in implementation of the Pennsylvania Comprehensive Cancer Control Plan, that includes the establishment of the Coordinating Center for the Pennsylvania Cancer Control Consortium(PAC3) at UPCI, a statewide biorepository and clinical and tissue informatics network, as well as a statewide clinical trials network to facilitate the completion of innovative, investigator-initiated clinical trials originating in the academic cancer centers.

promoting partnerships between the NCI-designated Cancer Centers and the state health departments for maximal collaboration and utilization of the expertise and capabilities of the Cancer Centers in implementing the state cancer control plans.

- Provide funding by CDC for demonstration projects in some regions or states, particularly those led by NCI-designated Cancer Centers, for implementation of population-based cancer control efforts, especially those focused on cancer prevention and early detection of cancer.

  In states without an NCI-designated cancer center, a mechanism should be developed for some cancer centers, especially those in the same region of the country, to partner with academic medical centers and community hospitals, in order to play a significant role in dissemination. It is proposed that 10 such demonstration projects be implemented, each with an annual cost of $2.5 million.
- NCI-designated Cancer Centers, which generate most of the innovative early phase investigator-initiated clinical research studies, could disseminate these studies more widely by various mechanisms and processes.

  Supplements to NCI's Cancer Center grants (CCSGs) could be used to develop and implement infrastructure to effectively link together Cancer Centers in a region and to link those Centers with community hospitals, clinical oncologists, and primary care physicians for wider implementation of early phase studies on new treatments, early cancer detection, risk assessment, prevention, and improved survivorship.
- Support telemedicine approaches as important infrastructure for the Cancer Centers to effectively and conveniently communicate with other organizations and health care providers in the region, as well as to link the Cancer Centers with community hospitals, clinical oncologists, and primary care physicians.
- Support should be provided for developing a mechanism for Cancer Centers to effectively partner with state cancer registries to convert these registries from what are now mainly incidence registries, to outcomes registries.

  These converted registries would include detailed data on stage of disease, treatments administered, response to treatments, recurrence or development of metastatic disease, as well as deaths from cancer, development of a second primary cancer, side effects of therapy, and persistence of known environmental risk factors that may modify prognosis. It is estimated that such conversions would entail a one-time cost of $50 million, with maintenance then borne by the states and individual medical institutions.
- Supplements to CCSGs should be provided for use of state cancer registries and SEER data, coupled with GIS mapping, to identify areas and populations of disproportionate need for focusing outreach efforts.
- Leveraging of Federal support and leadership to obtain needed corporate and philanthropic support for effective dissemination of cancer control, including facilitation of close cooperation between Cancer Centers, community hospitals, and other health care providers in each region of the United States.
- Support for Cancer Centers, by CMS and private payers, to develop specific clinical pathways for best practices for treatment of patients at each stage of each type of cancer, and similarly for early detection approaches for the major types of cancer.
- Support, perhaps as supplements to CCSGs, for research studies of behavioral barriers to compliance by the relevant populations, with recommended best practices for cancer prevention, early detection, treatment, and improved survival, and ways to overcome the identified barriers.

  Defining and overcoming barriers to screening and early detection is a priority because after primary prevention, the greatest improvements in outcomes will be realized by identifying cancers early, when treatments are most effective.
- Support from CMS should be sought for demonstration projects, led by the Cancer Centers, to evaluate and demonstrate effectiveness of various dissemination efforts for maximal implementation of best practices in a region,

and for compliance with the recommended practices.
- Education of relevant populations about the importance of availing themselves of dissemination programs, and education of health care providers about the value and importance of promoting and utilizing the relevant dissemination programs for their patients.

Anticipated Outcomes and Potential Impact

The NCI-designated Cancer Centers can play a major role in education of various key groups about dissemination if the Centers are provided with needed support from the Federal and state governments and from philanthropic and business sources. This would support education programs for:

- Cancer patient populations about the importance of seeking out clinical oncologists and centers with cancer experts, about innovative clinical research programs, and utilization of best practices.
- General population and, most importantly, those at increased risk for cancer, about best practices for cancer prevention, risk assessment, and early detection of cancer.
- Health care providers about the value of clinical cancer research studies, best practices, and the technology needed for effective treatment, diagnosis, early detection, and prevention of cancer. Such educational programs could include various approaches for continuing medical and nursing education on best practices, including electronic tumor boards conducted by the NCI-designated Cancer Center.

It will be important not only to implement programs for dissemination beyond the Cancer Centers, but also to objectively evaluate the efficacy of the various efforts, e.g., the degrees of increased access to prevention, screening, clinical trials, and survivor services. Evaluation should also include monitoring the key outcomes in the regions served, e.g., cancer incidence, disease-free interval, morbidity, quality of life, and survival. National outcomes studies also should be planned and supported.

The economic benefits of dissemination can also be measured and support should be provided to NCI-designated Cancer Centers for this activity.

Together with the evaluation of the effects of the new program, there is a need for benchmarking to assess if quality of care is maintained and improved. This can be obtained through a national cancer data system working in connection with SEER and the National Cancer Data Base (NCDB).

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Appendix A

Selected positive phase III chemoprevention and dietary intervention trials funded by the National Cancer Institute and/or pharmaceutical industry

Site Trial Name	Reference	Trial Design	Major Result	Comments
Breast Cancer				
Breast Cancer Prevention Trial (BCPT)	Fisher et al. (1998)	13,388 women at intermediate to high risk; tamoxifen vs placebo for up to 5 years	50% reduction in the risk of invasive breast cancer	Equivalent effect of tamoxifen on DCIS; increased incidence of endometrial cancer and pulmonary embolism
Study of Raloxifene and Tamoxifen in Postmenopausal Women (STAR)	Wickerham et al. (2006)	19,747 women at intermediate to high risk; raloxifene versus tamoxifen for up to 5 years	Approximately 50% reduction in the risk of invasive breast cancer by both agents	Raloxifene was associated with a lower incidence of endometrial cancer, pulmonary embolism and deep vein thrombosis
Women's Interventional Nutrition Study (WINS)	Chlebowski et al. (2005)	2,437 women at high risk for developing second primary cancer (stage I and II breast cancer, within 1 yr of dx): low fat (<20% calories) vs standard diet	24% reduction in breast cancer recurrence risk associated with low fat diet	In contrast to low fat diet of up to 31% calories from fat at end of WHI trial, low fat diet in WINS was maintained
Cervix Cancer				
HPV-16 L1 virus-like–particle vaccine study	Koutsky et al. (2002)	2,392 women (age 16-23), HPV negative, randomized to placebo or vaccine	100% efficacy against HPV 16 infection	Trial led to recent FDA approval of Merck HPV 16/18 vaccine in June, 2006
Quadrivalent HPV 6, 11, 16, 18 vaccine study	Villa et al. (2005)	1,158 women (age 16-23), randomized to one of three vaccine preparations or placebo	90% efficacy (95% CI 71–97) against HPV-specific infection/ disease in the treated versus placebo groups	Trial led to recent FDA approval of Merck bivalent HPV 16/18 vaccine in June, 2006
Bivalent HPV 16/18 vaccine	Harper et al. (2004); Harper et al. (2006)	1,113 women (age 15–25), randomized to placebo or vaccine	95.1% efficacy (CI: 63.5–99.3) against persistent cervical infection with HPV-16/18 at close of study. significant vaccine efficacy against HPV-16 and HPV-18 endpoints at 4.5 year follow up: persistent infection: 6 month definition, 94.3 (CI: 63.2–99.9); 12 month definition, 100% (CI: 33.6–100)	GSK vaccine continues in development for future submission to FDA

Site Trial Name	Reference	Trial Design	Major Result	Comments
Colon Cancer				
Dartmouth Calcium Polyp Prevention Study	Baron et al. (1999)	930 polyp patients randomized to calcium carbonate versus placebo for 3+ years	Significant 19% reduction in risk of polyp recurrence at endpoint colonoscopy (adjusted risk ratio)	Significant 25% reduction in risk of the largest recurrent adenoma being > 5mm (unadjusted risk ratio)
Dartmouth Aspirin Polyp Prevention Study	Baron et al. (2003)	1121 polyp patients randomized to ASA 81 mg or 325 mg/day for 3+ years	Significant 19% reduction in polyp recurrence in 81 mg group	81 mg, but not 325 mg ASA dose effective; unadjusted risk ratio for advanced lesions 0.59 (CI: 0.38-0.92)
CALGB Aspirin Trial	Sandler et al. (2003)	635 patients with previous colorectal cancer randomized to 325 mg ASA or placebo	Signficant 35% reduced risk of new adenoma with ASA (CI: 0.46-0.91), adjusted relative risk	No significant difference in advanced adenomas
NCI/Pfizer Adenoma Prevention with Celecoxib Trial (APC)	Bertagnolli et al. (2006)	2,035 polyp patients randomized to 200 mg or 400 mg celecoxib BID or placebo	45% and 33% reduction in risk of polyp recurrence at 3-5 years, more pronounced in 400 mg group	Significant reduction in advanced adenoma ($p<0.0001$), but increased cardiovascular events, especially in 400 mg group
Pfizer American/ Israeli Celecoxib Polyp Prevention Trial (PreSAP)	Arbor et al. (2006)	1,561 polyp patients randomized to 400 mg QD or placebo for up to 5 years	36% reduction in risk of polyp recurrence at 3-5 years	Increased risk of cardiovascular events seen only in those with preexisting CV disease (1.3%)
Prostate Cancer				
Prostate Cancer Prevention Trial (PCPT)	Thompson et al. (2003)	18,882 men (age 55 or over) with normal DRE and PSA < 3 randomized to finasteride or placebo for 7 years	Significant 25% reduction in risk of biopsy-proven prostate cancer	Increase in sexual dysfunction ($p<0.001$) and increased incidence of advanced Gleason grade cancers associated with finasteride (6.4% vs 5.1% for placebo)
Skin Cancer				
Vitamin A Prevention Trial	Moon et al. (1997)	2,290 patients with evidence of moderate to severe actinic keratosis randomized to Vitamin A 25,000 IU/day for up to 5 yrs vs placebo	Significant 26% reduction in risk of squamous cell cancer of the skin	No effect of basal cell cancer risk; little or no Vitamin A toxicity
Nutritional Prevention Study with Selenium	Clark et al. (1996)	1,303 patients with resected non-melanoma skin cancers randomized to selenium 300 mcg QD vs placebo for up to 5 yrs	No effect on risk of developing new primary skin cancers	49% reduction in risk of prostate cancer as a secondary analysis (Duffield-Lillico, et al. 2003)

Executive Summary

With a risk of more than one in three of getting cancer over a lifetime, each of us is likely to experience cancer, or know someone who has survived cancer. Although some cancer survivors recover with a renewed sense of life and purpose, what has often not been recognized is the toll taken by both cancer and its treatment—on health, functioning, sense of security, and well-being. Long-lasting effects of treatment may be apparent shortly after its completion or arise years later. Personal relationships change and adaptations to routines and work may be needed. Importantly, the survivor's health care is forever altered.

The transition from active treatment to post-treatment care is critical to long-term health. If care is not planned and coordinated, cancer survivors are left without knowledge of their heightened risks and a follow-up plan of action. However, such a plan is essential so that routine follow-up visits become opportunities to promote a healthy lifestyle, check for cancer recurrence, and manage lasting effects of the cancer experience. The nature of these lasting effects and their long-term implications for survivors and their families is the subject of this report. There are now 10 million Americans alive with a personal history of cancer, all of whom are considered cancer survivors. Widespread adoption of cancer screening, successes in treating cancers, and the aging of the population will contribute to an even larger cohort of cancer survivors in the near future.

A committee was established at the Institute of Medicine (IOM) of the National Academies to examine the range of medical and psychosocial issues faced by cancer survivors and to make recommendations to improve their health care and quality of life. In effect, the committee took up the

task identified by Fitzhugh Mullan, a physician and cancer survivor, who in 1985 said, *"The challenge in overcoming cancer is not only to find therapies that will prevent or arrest the disease quickly, but also to map the middle ground of survivorship and minimize its medical and social hazards"* (Mullan, 1985). **This report focuses on survivors of adult cancer during the phase of care that follows primary treatment.** The committee recognized the importance of addressing unmet needs of the large and growing number of cancer survivors during this phase of care. Previous IOM reports addressed the needs of childhood cancer survivors (IOM, 2003) and issues concerning care at the end of life (IOM, 1997, 2001b).

The committee reviewed the consequences of cancer and its treatment and concluded that they are substantial. Although the population of cancer survivors is heterogeneous, with some having few late effects of their cancer and its treatment, others suffer permanent and disabling symptoms that impair normal functioning. Psychological distress, sexual dysfunction, infertility, impaired organ function, cosmetic changes, and limitations in mobility, communication, and cognition are among the problems faced by some cancer survivors. The good news is that there is much that can be done to avoid, ameliorate, or arrest these late effects of cancer. To ensure the best possible outcomes for cancer survivors, the committee aims in this report to:

1. Raise awareness of the medical, functional, and psychosocial consequences of cancer and its treatment.
2. Define quality health care for cancer survivors and identify strategies to achieve it.
3. Improve the quality of life of cancer survivors through policies to ensure their access to psychosocial services, fair employment practices, and health insurance.

The committee's findings and recommendations that follow are directed to cancer patients and their advocates, health care providers and their leadership, health insurers and plans, employers, research sponsors, and the public and their elected representatives.

RAISING AWARENESS OF CANCER SURVIVORSHIP

There are many ways to define cancer survivorship, but for the purpose of this report, it is a distinct phase of the cancer trajectory which has been relatively neglected in advocacy, education, clinical practice, and research. Quality cancer survivorship care involves the provision of four essential components of care within a delivery system that facilitates access to comprehensive and coordinated care (Box ES-1). Raising awareness of the medi-

BOX ES-1
Essential Components of Survivorship Care

1. **Prevention** of recurrent and new cancers, and of other late effects;
2. **Surveillance** for cancer spread, recurrence, or second cancers; assessment of medical and psychosocial late effects;
3. **Intervention** for consequences of cancer and its treatment, for example: medical problems such as lymphedema and sexual dysfunction; symptoms, including pain and fatigue; psychological distress experienced by cancer survivors and their caregivers; and concerns related to employment, insurance, and disability; and
4. **Coordination** between specialists and primary care providers to ensure that all of the survivor's health needs are met.

cal and psychosocial needs that may follow cancer treatment will help both survivors and their health care providers to ensure that appropriate assessments are completed and available interventions employed. The constellation of cancer's long-term and late effects varies by cancer type, treatment modality, and individual characteristics, but there are common patterns of symptoms and conditions that must be recognized so that health and well-being can be improved.

Recommendation 1: Health care providers, patient advocates, and other stakeholders should work to raise awareness of the needs of cancer survivors, establish cancer survivorship as a distinct phase of cancer care, and act to ensure the delivery of appropriate survivorship care.

Cancer patients and their advocates can call attention to their survivorship experiences and the need for change. The leadership of organizations representing physicians, nurses, and psychosocial care providers can collaborate to improve care. Third-party payors of health care and health plans can improve access to needed services through reimbursement policies and improvements in systems of care. Employers can ensure fair workplace policies and accommodations. Sponsors of research can improve the opportunities to increase what we know about survivorship and appropriate care. Congress and state legislatures can enact policies and ensure the support needed to improve survivorship care and quality of life.

PROVIDING A CARE PLAN FOR SURVIVORSHIP

The recognition of cancer survivorship as a distinct phase of the cancer trajectory is not enough. A strategy is needed for the ongoing clinical care of cancer survivors. There are many opportunities for improving the care of

cancer survivors—psychosocial distress can be assessed and support provided; cancer recurrences and second cancers may be caught early and treated; bothersome symptoms can be effectively managed; preventable conditions such as osteoporosis may be avoided; and potentially lethal late effects such as heart failure averted. Cancer survivors are often lost to systematic follow-up within our health care system and opportunities to effectively intervene are missed. Many people finish their primary treatment for cancer unaware of their heightened health risks and are ill-prepared to manage their future health care needs. Furthermore, recommended follow-up care is often not delivered and the psychosocial needs of cancer patients are often not addressed.

Recommendation 2: Patients completing primary treatment should be provided with a comprehensive care summary and follow-up plan that is clearly and effectively explained. This "Survivorship Care Plan" should be written by the principal provider(s) who coordinated oncology treatment. This service should be reimbursed by third-party payors of health care.

Such a care plan would summarize critical information needed for the survivor's long-term care:

- Cancer type, treatments received, and their potential consequences;
- Specific information about the timing and content of recommended follow-up;
- Recommendations regarding preventive practices and how to maintain health and well-being;
- Information on legal protections regarding employment and access to health insurance; and
- The availability of psychosocial services in the community.

These content areas, adapted from those recommended by the President's Cancer Panel (2004), are elaborated on in Chapter 3.

The content of the Survivorship Care Plan could be reviewed with a patient during a formal discharge consultation. Appropriate reimbursement would need to be provided, given the complexity and importance of the consultation. The member of the oncology treating team who would be responsible for this visit could vary depending on the exact course of treatment. The responsibility could be assigned either to the oncology specialist coordinating care or to the provider responsible for the last component of treatment. Oncology nurses could play a key role. The survivorship plan may help patients share in the responsibility for their health care. It could prompt survivors to raise questions with doctors and help ensure appropriate follow-up care.

Survivorship care plans have been recommended by the President's Cancer Panel and by the IOM committee, however, the implementation of such plans has not yet been formally evaluated. Despite the lack of evidence to support the use of survivorship care plans, the committee concluded that some elements of care simply make sense—that is, they have strong face validity and can reasonably be assumed to improve care unless and until evidence accumulates to the contrary. Having an agreed-upon care plan that outlines goals of care falls into this "common sense" area. Health services research should be undertaken to assess the impact and costs associated with survivorship care plans, and to evaluate their acceptance by both cancer survivors and health care providers.

DEVELOPING CLINICAL PRACTICE GUIDELINES FOR SURVIVORSHIP CARE

The Survivorship Care Plan would inform clinicians involved in the subsequent care of cancer survivors about treatment exposures and signs and symptoms of late effects, and, in some cases, would provide concrete steps to be taken. To carry out this plan, an organized set of clinical practice guidelines based on the best available evidence is needed to help ensure appropriate follow-up care. Some guidelines are available for certain aspects of survivorship care, but most are incomplete. Such guidelines would provide specific information on how to manage the complex issues facing survivors of adult cancers. Assessment tools and screening instruments for common late effects are also needed to help identify cancer survivors who have, or who are at high risk for, late effects and who may need extra surveillance or interventions.

Recommendation 3: Health care providers should use systematically developed evidence-based clinical practice guidelines, assessment tools, and screening instruments to help identify and manage late effects of cancer and its treatment. Existing guidelines should be refined and new evidence-based guidelines should be developed through public- and private-sector efforts.

Cancer survivors represent a very large at-risk population and without evidence-based clinical practice guidelines, health care providers will vary widely in their practices, leading to inefficiencies in care delivery (see Chapters 3 and 4). More than 60 percent of cancer survivors are aged 65 and older, so the Centers for Medicare and Medicaid Services (CMS) the administrators of the Medicare program, have a stake in developing clinical practice guidelines. The Agency for Healthcare Research and Quality (AHRQ) maintains a National Guideline Clearinghouse and supports Evidence-Based Practice Centers that review relevant literature on clinical, behavioral, or-

ganizational, and financial topics to produce evidence reports and technology assessments (AHRQ, 2001). Such reviews can form the foundation of evidence-based guidelines. Professional organizations (e.g., those representing oncology, primary care, nursing) also have a role to play in developing interdisciplinary guidelines. The guideline development process is a costly one, and public and private support is needed to improve and expedite the development process. Evaluations are needed of the impact of guidelines in the context of survivorship care.

DEFINING QUALITY HEALTH CARE FOR CANCER SURVIVORS

For certain types of cancer, some evidence-based measures of quality survivorship care exist. Survivors of breast cancer, for example, need to receive annual mammograms, survivors of prostate cancer need periodic testing with the prostate-specific antigen (PSA) test, and survivors of colon cancer require periodic colon examinations. Other measures could likely be developed with available evidence, for example, the need to monitor some individuals treated with certain chemotherapeutic agents for heart conditions and certain individuals treated by radiotherapy for thyroid conditions. In contrast to these disease-specific or treatment-specific measures, some evidence-based measures of quality apply broadly across all types of cancer. For example, routinely assessing cancer survivors for psychosocial distress is warranted because it often exists and effective interventions are available. Given the frequency of other common and treatable symptoms such as fatigue and sexual dysfunction, other measures of quality could likely be formulated with available evidence that would be broadly applicable to cancer survivors.

Recommendation 4: Quality of survivorship care measures should be developed through public/private partnerships and quality assurance programs implemented by health systems to monitor and improve the care that all survivors receive.

OVERCOMING DELIVERY SYSTEM CHALLENGES

The problems that cancer survivors face in getting comprehensive and coordinated care are common to those faced by others with chronic health conditions. Because cancer is a complex disease and its management involves the expertise of many specialists, often practicing in different settings, cancer illustrates well the "quality chasm" that exists within the U.S. health care system and the need for health insurance reforms and innovations in health care delivery. The committee endorses the conclusions and recommendations in the IOM report *Crossing the Quality Chasm* (IOM,

2001a). That report provided the rationale and a strategic direction for redesigning the health care delivery system. It concluded that fundamental reform of health care is needed to ensure that all Americans receive care that is safe, effective, patient centered, timely, efficient, and equitable. Needed is a health care environment that fosters and rewards improvement by (1) creating an infrastructure to support evidence-based practice, (2) facilitating the use of information technology, (3) aligning payment incentives, and (4) preparing the workforce to better serve patients in a world of expanding knowledge and rapid change.

Barriers facing cancer survivors and their providers in achieving quality survivorship care include (1) a fragmented and poorly coordinated cancer care system; (2) the absence of a locus of responsibility for follow-up care; (3) poor mechanisms for communication; (4) a lack of guidance on the specific tests, examinations, and advice that make up survivorship care; (5) inadequate reimbursement from insurers for some aspects of care; and (6) limited experience on the best way to deliver care.

Recommendation 5: The Centers for Medicare and Medicaid Services (CMS), National Cancer Institute (NCI), Agency for Healthcare Research and Quality (AHRQ), the Department of Veterans Affairs (VA), and other qualified organizations should support demonstration programs to test models of coordinated, interdisciplinary survivorship care in diverse communities and across systems of care.

Several promising models for delivering survivorship care are emerging, including:

1. A shared-care model in which specialists work collaboratively with primary care providers.
2. A nurse-led model in which nurses take responsibility for cancer-related follow-up care with oversight from physicians.
3. Specialized survivorship clinics in which multidisciplinary care is offered at one site.

There is limited evidence on which of these, or other delivery strategies, is feasible, cost-effective, or acceptable to survivors and clinicians (see Chapter 4). It is likely that different care models will be preferred and appropriate for different survivor groups and communities. Models for delivering survivorship care should address the fact that oncology specialists and primary care providers, facing an expanding population of cancer survivors, will become overburdened with follow-up care. The proposed demonstration programs could include assessments of methods to improve care with advanced information systems, such as electronic health records, virtual consultations, smart cards, and web-based approaches. CMS is the

primary payor of care for cancer survivors and should therefore have a strong interest in identifying cost-effective models of care.

SURVIVORSHIP AS A PUBLIC HEALTH CONCERN

The Centers for Disease Control and Prevention (CDC) and the Lance Armstrong Foundation have developed a public health approach to survivorship care that may assist communities in identifying and addressing the survivorship needs of individuals, their families, and their health care providers (CDC, 2004; CDC and LAF, 2004). Among the public health capacities that could be addressed are:

- Population-based surveillance systems for survivorship care and quality of life;
- Areawide community-based resource guides for survivors and health care providers;
- Service needs assessments;
- A clearinghouse for health care provider education and training opportunities;
- Provision of primary and secondary prevention services (e.g., smoking cessation, cancer screening); and
- Program evaluation and identification of best practices.

Health departments have had a long tradition of managing cancer registries, offering health education, and providing community-based health promotion and disease prevention activities. Interventions for common chronic public health problems such as heart disease and diabetes could well be germane to cancer survivors and their families. These public health approaches are early in their development. Resources are needed to evaluate the effectiveness of community-based services and comprehensive cancer control plans in improving the care and quality of life of cancer survivors.

Recommendation 6: Congress should support Centers for Disease Control and Prevention (CDC), other collaborating institutions, and the states in developing comprehensive cancer control plans that include consideration of survivorship care, and promoting the implementation, evaluation, and refinement of existing state cancer control plans.

IMPROVING HEALTH CARE PROFESSIONAL CAPACITY

Few oncology and primary care health professionals have formal education and training regarding cancer survivorship. With the growing ranks

of cancer survivors, it is likely that additional health personnel will be needed, particularly nurses with advanced oncology training. Online resources are increasingly available and appear to be an attractive means of reaching multiple provider audiences, but the effectiveness of this and other approaches needs to be assessed. Limited financial support has been available through public and private sectors for survivorship-related education and training.

Recommendation 7: The National Cancer Institute (NCI), professional associations, and voluntary organizations should expand and coordinate their efforts to provide educational opportunities to health care providers to equip them to address the health care and quality of life issues facing cancer survivors.

Efforts are needed to update undergraduate and graduate curricula for those in training and to provide continuing education for practicing providers of survivorship care. Continuing education is needed across many disciplines, but in order to ensure the provision of quality survivorship care, it is especially important to reach (1) medical oncologists, hematologists, urologists, surgeons, and radiation oncologists who initially treat cancer patients; (2) primary care physicians; (3) nurses; and (4) social workers and other providers of psychosocial services.

To augment the supply of nurses who could provide survivorship care, the committee recommends increasing the number of nursing schools that provide graduate training in oncology, providing incentives to nurses who seek certification in oncology, and supporting general efforts to ease the nursing shortage. To ensure access to psychosocial services, continuing education opportunities are needed for social workers and other mental health providers. In addition, efforts are needed to maintain social services in cancer programs. Detailed recommendations on professional education by health care specialty are outlined in Chapter 5.

ADDRESSING EMPLOYMENT-RELATED CONCERNS

Most cancer patients who are working require some kind of accommodation to work throughout treatment, and some experience difficulties at work after treatment. Estimates of the impact of cancer on employment vary. The majority of cancer survivors who worked before their diagnosis return to work following their treatment. However, as many as one in five individuals who work at the time of diagnosis have cancer-related limitations in ability to work 1 to 5 years later. Half of those with limitations are unable to work at all.

All survivors are at risk of experiencing subtle, although not necessarily blatant, employment discrimination. Federal laws enacted in the 1990s

have offered cancer survivors some protections from discriminatory practices such as firing or denial of benefits because of cancer. Such laws have clarified the responsibilities of employers to accommodate workers returning to work with health-related limitations. The most important of these laws, the Americans with Disabilities Act (ADA), continues to be interpreted by the courts. Although protections cover disabled cancer survivors, some survivors have not been fully protected from job loss and access to accommodations for cancer-related work limitations. Successful resolutions on the part of cancer survivors who have filed formal complaints against employers suggest that not all employers have yet fully complied with the law.

Recommendation 8: Employers, legal advocates, health care providers, sponsors of support services, and government agencies should act to eliminate discrimination and minimize adverse effects of cancer on employment, while supporting cancer survivors with short-term and long-term limitations in ability to work.

- Cancer providers, advocacy organizations, NCI, and other government agencies should continue to educate employers and the public about the successes achieved in cancer treatment, the improved prospects for survival, and the continuing productivity of most patients who are treated for cancer.
- Public and private sponsors of services to support cancer survivors and their families should finance programs offering education, counseling, support, legal advice, vocational rehabilitation, and referral for survivors who want to work.
- Providers who care for cancer survivors should become familiar with the employment rights that apply to survivors who want to work; make available information about employment rights and programs; and routinely ask patients who are cancer survivors if they have physical or mental health problems that are affecting their work
- Employers should implement programs to assist cancer survivors, for example, through short- and long-term disability insurance, return-to-work programs, accommodation of special needs, and employee assistance programs.
- Cancer survivors should tell their physicians when health problems are affecting them at work. Survivors should educate themselves about their employment rights and contact support organizations for assistance and referrals when needed.

Improving Access to Adequate and Affordable Health Insurance

The health insurance issues facing cancer survivors bring into sharp focus the gaps and limitations of health insurance in the United States. All Americans are at risk of becoming a cancer survivor and finding themselves without access to adequate and affordable health insurance. Cancer survivors, like other Americans with serious, chronic health conditions, face significant barriers to coverage because of their health status. In particular, access to individual health insurance may be denied to residents in many states if they have a history of cancer. Cancer survivors may also face surcharged premiums for coverage because of their cancer history, depending on where they live and the type of coverage they seek. The improvements in the care of cancer survivors envisioned by the committee can not be achieved without health insurance that is accessible, adequate, and affordable.

Health insurance provides protection from the very high costs of cancer care. Most cancer survivors have health insurance through the federal Medicare programs because they are aged 65 and older. Nevertheless, 11 percent of adult cancer survivors under the age of 65 are uninsured and, for these individuals, the costs of cancer care can be financially devastating. These younger uninsured cancer survivors report access to care problems due to concerns about cost—51 percent report delays in obtaining medical care; 44 percent report not getting needed care; and 31 percent report not getting needed prescription medicine. The financial problems posed by cancer loom larger, because even those with health insurance can have trouble paying for prescription drugs and other types of care.

The IOM Committee on the Consequences of Uninsurance, in its 2004 report, *Insuring America's Health*, recommended that the President and Congress develop a strategy to achieve universal insurance coverage and to establish a firm and explicit schedule to reach this goal by 2010 (IOM, 2004).

Recommendation 9: Federal and state policy makers should act to ensure that all cancer survivors have access to adequate and affordable health insurance. Insurers and payors of health care should recognize survivorship care as an essential part of cancer care and design benefits, payment policies, and reimbursement mechanisms to facilitate coverage for evidence-based aspects of care.

Cancer survivors need continuous access to health insurance that covers their health care needs. Policy makers should act to ensure that cancer survivors and others with serious chronic health conditions can obtain

health insurance that is adequate and affordable. For example, policy makers could provide federal support to improve state high-risk pools—through premium subsidies, lower cost-sharing options (e.g., lowering copayments and deductibles), expanded coverage for prescription drugs, and elimination of preexisting condition exclusion periods. This could help such programs better serve the needs of people with serious and chronic health conditions. Federal programs that guarantee availability of coverage (e.g., those provided under the Consolidated Omnibus Budget Reconciliation Act [COBRA] and the Health Insurance Portability and Accountability Act [HIPAA]) could also be expanded to include premium subsidies. Because federal legislation generally covers only federal programs such as Medicare and Medicaid, many health insurance reforms must also be addressed at the state level.

Policy makers can also improve other existing programs aimed at improving health insurance coverage of cancer survivors. In 2000, Congress established a new eligibility category option in Medicaid for uninsured women with breast and cervical cancer. However, only women screened through CDC-funded programs are eligible for this Medicaid coverage, and CDC-funded programs today reach fewer than 15 percent of the program-eligible population. Policy makers could strengthen and build on this program, first by ensuring that more eligible women with breast and cervical cancer are reached by it, and second by expanding Medicaid eligibility to include other cancer patients and survivors who have no other coverage options.

All health insurance in the United States, including Medicare, Medicaid, employer-sponsored group health plans, and individually purchased policies, should cover effective cancer survivorship care. National coverage standards should be promulgated and include interventions for which there is good evidence of effectiveness (e.g., certain post-treatment surveillance strategies, treatments for late effects, interventions for symptom management, rehabilitative services). Importantly, coverage standards should include the development of a post-treatment plan of survivorship care (see Recommendation 2). National coverage standards should evolve with the development of clinical guidelines and evidence-based research into the quality and effectiveness of care. Congress has already taken preliminary steps to assure adequacy of some cancer survivorship care. The Women's Health and Cancer Rights Act requires health insurance to cover reconstructive surgery, prostheses, and care for complications following mastectomy, including lymphedema. This model could be expanded to assure minimum federal standards for all cancer survivorship care under all health insurance.

Making Investments in Research

Within the past decade, a focus for federally sponsored research has been organized within NCI's Office of Cancer Survivorship. Findings from this first era of dedicated research have informed much of this report. A greater investment in research is needed to learn more about late effects and their management. Cancer treatments are constantly evolving, and consequently, what is known about today's cancer survivors may not be relevant to future patients. Newer therapies hold the promise of limiting the late effects of cancer, but mechanisms to monitor long-term effects need to be put in place. Also needed are studies to determine how best to detect and treat cancer recurrence, new primary cancers, and other late effects. Providers responsible for follow-up need to know which tests to use, how often to use them, and the relative costs and benefits of alternative surveillance strategies. Investments are needed in the science on which clinical decisions must be based.

Among the challenges to conducting survivorship research are the difficulties and costs associated with long-term follow-up, the complexities of accruing sufficient sample sizes through multi-institutional research endeavors, and emerging problems associated with compliance with privacy provisions of the HIPAA. Survivorship research is funded at relatively modest levels within both public and private sectors, especially as contrasted to levels of support for treatment-related research.

Recommendation 10: The National Cancer Institute (NCI), Centers for Disease Control and Prevention (CDC), Agency for Healthcare Reseach and Quality (AHRQ), Centers for Medicare and Medicaid Services (CMS), Department of Veterans Affairs (VA), private voluntary organizations such as the American Cancer Society (ACS), and private health insurers and plans should increase their support of survivorship research and expand mechanisms for its conduct. New research initiatives focused on cancer patient follow-up are urgently needed to guide effective survivorship care.

Research is especially needed to improve understanding of:

- Mechanisms of late effects experienced by cancer survivors and interventions to alleviate symptoms and improve function;
- The prevalence and risk of late effects;
- The cost-effectiveness of alternative models of survivorship care and community-based psychosocial services; and
- Interventions to improve the quality of life of cancer survivors, their families, and caregivers.

To conduct research in these priority areas, large study populations are needed that represent the diversity of cancer survivors in terms of their type of cancer and treatment as well as their sociodemographic and health care characteristics. Existing research mechanisms need to be fully utilized and in some cases enhanced to provide better opportunities for cancer survivorship research. For example:

- More long-term follow-up studies should be conducted of individuals enrolled in clinical trials through the NCI-sponsored Cooperative Groups;
- Additional survivorship special studies should be conducted through population-based cancer registries;
- National household and health care surveys should be analyzed to capture information on survivorship;
- Opportunities should be sought to link data from cancer registries to administrative databases;
- The follow-up period of ongoing cancer health services research studies should be extended to yield more information on long-term survivorship; and
- Investigators should be encouraged to use existing primary care and health services research networks to conduct cancer survivorship research.

In addition to harnessing these existing mechanisms, the committee recommends that federal (e.g., CMS, AHRQ, NCI) and private (ACS, health plans) research sponsors support a large new research initiative on cancer patient follow-up. Answers to the following basic questions about survivorship care are needed:

- How frequently should patients be evaluated following their primary cancer therapy?
- What tests should be included in the follow-up regimen?
- Who should provide follow-up care?

A call for such research was made in IOM's *Ensuring Quality Cancer Care* report (1999), but it has not yet been conducted. In some cases large clinical trials will be needed to answer these questions. The committee concluded that improvements in cancer survivors' care and quality of life depend on a much expanded research effort.

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Executive Summary

The end of cancer treatment is not the end of the cancer experience. As nearly 200 American and European cancer survivors, caregivers, health care providers, advocates, researchers, and others detailed in testimony provided to the President's Cancer Panel between May 2003 and January 2004, the end of treatment marks the beginning of a new phase of life: living *beyond* cancer. For the nearly ten million Americans now living with a cancer history, life after cancer means finding a new balance—one that celebrates the triumph and relief of completing treatment, recognizes changes or losses the disease has wrought, and assimilates revised perspectives, newfound strengths, and lingering uncertainties. Typically, few signposts exist to guide these highly personal journeys into a familiar but forever changed world.

Life after cancer treatment may hold diverse and often unexpected challenges. These challenges may be influenced by numerous factors, including the survivor's age at the time of diagnosis, the type and severity of both the cancer and its treatment, the duration of an individual's survival, financial and geographic access to needed follow-up care, employment and educational issues, information needs, and cultural, spiritual, literacy, and language differences. The impact of many of these factors, and the issues that arise from them, is magnified among many survivors from minority and other underserved populations.

Issues Affecting Cancer Survivors Across the Life Span

Both the testimony and additional data gathered suggested that several issues affect cancer survivors and their families regardless of whether the survivor was diagnosed as a child, an adolescent or young adult, in adulthood, or in older age:

- Many survivors leave treatment with neither adequate documentation of the care they received nor a written description of recommended follow-up care and resources for obtaining

"...being a cancer survivor is at the forefront of my self awareness. It enters into the conversations that I have with myself about what I want to do, how I want to spend money, how I want to spend time, my energy, all of that. Being a cancer survivor has added another dimension to my identity. I am a cancer survivor."

Mortimer Brown, 80, colorectal cancer survivor diagnosed age 75, Florida

"There is also an inefficient and sub-optimized patient data collection system and storage, where every doc holds on to their own records about the patient, and the patient holds on to nothing. And yet every doc has to keep in sync with all the other docs sharing the responsibility for the care of that patient."

Richard Migliori, physician and administrator, United Health Resources, Minnesota

"...I found out that I could possibly do *in vitro* fertilization with a surrogate mother....Well, there is a $10,000 payment that you have to plunk down right from the beginning...I am thinking, 'I have a PPO [preferred provider organization]. There is going to be no problem.'...Well, I was denied because I was not married and I was already on a form of birth control—[a hysterectomy]....I look back and I think of so many things that I could have done to preserve my chance of biologically having a child of my own and I cry...no one told me these things."

Tamika Felder, 28, cervical cancer survivor diagnosed age 25, Maryland

"...right now my health insurance is $950 a month...it continues to go up every three months. So at the time in my life when I should be saving for retirement it is kind of hard to do when you are having to pay $1,000 a month for health insurance."

Gloria Jean Moore, 51, Hodgkin's lymphoma and breast cancer survivor diagnosed ages 27 and 50, Texas

that care. The lack of a national electronic health record system is an impediment to continuity and quality of care for cancer survivors.

- Cancer survivors and their families need better information about existing laws and regulations that may protect their employment, insurance, and assets.
- Privacy provisions of the Health Insurance Portability and Accountability Act (HIPAA) are inhibiting needed research on survivor issues and blocking appropriate information sharing among providers and between providers and the patient's caregivers.
- Education about cancer, cancer treatment, and survivorship needs is inadequate. The general public, newly diagnosed patients and their caregivers, post-treatment survivors, and health care providers all have significant unmet information needs. Understanding of clinical trials also is limited among all of these groups.
- Many survivors, caregivers, and family members need, but are not receiving, psychosocial assistance and support, both during treatment and in the months and years that follow. Family caregivers increasingly are becoming medical care providers in the home, but are not receiving adequate training and ongoing support for this role.
- The risk of infertility associated with cancer treatment and opportunities for preserving reproductive capacity are not being conveyed fully to newly diagnosed cancer patients of reproductive age or to the parents of children diagnosed with cancer prior to selecting or initiating treatment. For many, access to available fertility preservation options is limited by cost.
- Existing insurance systems in the United States are a significant impediment to appropriate care for people with a cancer history. The link between employment and insurance particularly disadvantages cancer survivors, who risk losing both their employment and insurance during extensive treatment. Lower income, young adult, and near elderly survivors are particularly vulnerable to becoming uninsured. Coverage for psychosocial care and follow-up care is inadequate even under most comprehensive health plans or Medicare.

In addition, testimony provided to the Panel highlighted important nuances of these cross-cutting issues, as well as additional issues, that are distinct to survivors diagnosed at different ages.

Survivors Diagnosed as Children

Speakers identified five issues of special importance to survivors diagnosed before age 15:

- Survivors of cancer diagnosed in childhood may need special assistance to re-enter the classroom setting successfully and may require accommodations to learning difficulties resulting from their disease or its treatment. Parents of these survivors may need help advocating for their children in the school system.
- Some survivors of childhood cancers have social development and psychosocial issues that require attention years after treatment ends. These issues may include depression, social problems due to missing typical childhood experiences, and difficulty integrating the cancer experience as a part of the individual's life.
- Many survivors of childhood cancers are not being transitioned appropriately from pediatric care to adult health care settings and receive inadequate assistance in coordinating their follow-up care. Issues include inadequate transfer of information between pediatric oncologists and primary care providers, particularly if the child received treatment away from home, and lack of understanding among primary care providers of the follow-up care needs of childhood cancer survivors.
- Caregivers and siblings of children with cancer have longer-term psychosocial needs that are not being met. Both parents and siblings are vulnerable to post-traumatic stress disorder. Support groups and services available during the treatment period are far less available post-treatment, particularly when the patient was treated away from home.
- Continued research is needed on the long-term effects of cancer treatment on survivors of pediatric cancers. Limited follow-up of pediatric patients, even those treated on clinical trials, is a major barrier to better understanding late treatment effects experienced by this population. Specialized late effects clinics may prove useful for addressing this issue, but require further development and evaluation.

"...the younger a child is when he receives radiation, the more damage he receives...[Adam] was unable to get his high school diploma because he didn't pass the math portion of the competency test. He took that test ten times from the 9th grade to the 12th grade. He missed it by five points. He passed the English portion, and he passed the computer portion...The diploma issue has been hard for him as far as finding a job...It is very frustrating as a parent to see your child struggling and to see him want to be productive and he is not being given an opportunity."

Pam Cox, mother of Adam Cox, 20, brain tumor survivor diagnosed age 3, North Carolina

"It is clear from the last 20 years that these little incremental, piecemeal things, Federal and State legislation —we're not going to have major, effective, across-the-board health insurance reform until the public really demands it..."

Barbara Hoffman, attorney and advocate, New Jersey

"My concerns as a survivor have evolved the farther away I have gotten from treatment....During my treatment and for several years after...my primary concern was recurrence and, although I haven't had any, I would be lying if I say that I don't think about it all the time. [Now] I worry about secondary cancers...and problems due to my splenectomy... I am in premature menopause because of the high doses of chemotherapy I received, so I worry about osteoporosis, sexuality, cardiac problems, and yes, even wrinkles. I take hormone therapy but so little is known about young menopausal women that I can't help but be concerned."

Karen Dyer, 24, rhabdomyosarcoma survivor diagnosed age 15, New York

Survivors Diagnosed as Adolescents or Young Adults

In addition to concerns common to survivors of all ages, people diagnosed between the ages of 15 and 29 have other distinct needs:

- Adolescent and young adult cancer survivors—sometimes called the "orphaned cohort"—are a vastly understudied population. Because they often relocate to attend college or obtain employment, follow-up on this population has been particularly difficult.
- Diagnosis and treatment during this crucial developmental period often results in a range of psychosocial issues, including problems with depression, limited social skills, difficulty planning for the future and establishing independence, and coping with neurocognitive problems resulting from cancer treatment. Body image and fertility issues may be a significant impediment to developing intimate relationships.
- Similar to childhood cancer survivors, adolescents and young adults treated in the pediatric setting are not being transitioned effectively to care in the adult setting.
- Adolescent and young adult cancer survivors, particularly those with disabilities requiring accommodation, may find themselves at a disadvantage when competing for jobs, and may be starting adulthood burdened by significant treatment-related debt. In addition, once terminated from their parents' health insurance policies, they are highly likely to become uninsured and lose access to follow-up care.

Survivors Diagnosed as Adults

Survivors diagnosed between the ages of 30 and 59 face three additional issues that affect their care, livelihood, and quality of life:

- Limited recommendations exist to guide the follow-up care of people with adult-onset cancers due to a lack of research evidence on post-treatment needs of this population. Lack of recommendations limits insurance reimbursement for care recommended by survivors' physicians and presents a barrier to follow-up care.
- Cancer occurring during the prime and middle years of adulthood may seriously disrupt the survivor's ability to carry out family, social, and work-related responsibilities, which can damage self-esteem. In particular, many survivors of this age

are responsible for caring for children and aging parents at the same time they are battling their cancer or its after-effects. Recognition of and intervention for issues related to sexuality and intimacy is a largely unmet need.

- Many survivors diagnosed in adulthood face major income losses that endanger the security of their families, particularly if a spouse also must reduce work hours to care for the patient. These losses may be temporary or permanent. Adult survivors typically are unable to obtain or increase life or disability insurance, and may have difficulty securing mortgages or loans.

Survivors Diagnosed as Older Adults

Those diagnosed at age 60 or older comprise the majority of cancer survivors. In addition to issues relevant across the life span, five key issues were identified:

- Many survivors 60 and older still need and want to work. Job loss, forced retirement due to cancer, and resulting loss of health benefits prior to Medicare eligibility are of major concern. Out-of-pocket health care costs are a significant burden for those on fixed incomes.
- Many older people with cancer also have one or more other chronic medical conditions (comorbidities). Such illnesses continue to be a barrier to clinical trials participation by older survivors and to the best standard care for many who are treated in community settings. Comorbidities may mask signs of recurrence or late effects of cancer treatment, and suspicious symptoms may be attributed both by the survivor and medical personnel to age-related conditions.
- Because older survivors rarely have been included in research, little is known about late and long-term effects in this population. Providers may be unaware of cancer screening and other follow-up care needed by these survivors, and lack of Medicare reimbursement for preventive care has hampered efforts to gather information about them.
- Many older cancer survivors lack adequate social and caregiver support. Health care providers often assume that the patient has a support system; in fact, many—particularly older women—live alone far from family members or are cared for by an elderly spouse who may have illnesses, limited mobility, or short-term memory problems. For those who no longer drive, lack of transportation limits access to medical care or support services.

"I cannot lower my premium with [my] current insurance company because of my history of cancer and I cannot change to another insurance because of the same reason. I am not yet 65 years old and I am in the middle class, middle income household. And so I am not eligible for either Medicare or Medicaid. What can we do? Who do we turn to? I survived the cancer but I cannot pay for necessary treatment post-chemo. I feel like I am being punished for surviving cancer."

Boonsee Yu, 57, colon cancer survivor diagnosed age 53, New York

"I am currently being treated as an outpatient. This has enabled me to continue working, a necessity for me because I am a single parent. I am also having to deal with other family issues—an aunt with Alzheimer's and an 83-year-old mother. Many adult survivors are part of that "sandwich generation" caring for both their own children and helping their aging parents."

Debra Thaler-DeMers, 49, oncology nurse, Hodgkin's lymphoma and breast cancer survivor diagnosed ages 25 and 45, California

"[For impotence] they have a vacuum pump and they have a prosthesis that you can insert surgically. There is a lot of different things....I was trying to do injections into the penis and I used to say to my wife, 'Now, I am going to go in the bathroom and I am going to inject myself. If you get a headache you are in big trouble.'...Even though the mechanical part of it worked, the psychological, emotional part never worked."

Emanuel Hamelburg, 63, prostate cancer survivor diagnosed ages 47 and 51, Massachusetts

"...all of the times that I went for the various examinations...I always was alone....I remember sitting one day waiting for the dye to go through my system and I am looking at everybody coming and going....Everybody had somebody and there I sat. I couldn't help it. I wept. I had nobody but I managed to make it through."

Grace Butler, 67, colorectal cancer survivor diagnosed age 63, Texas

- Intimacy and body image issues remain an important, though often unaddressed need among older cancer survivors.

The testimony received at these and previous Panel meetings provides a critical dimension to the growing body of knowledge about cancer and the needs of cancer survivors. These extraordinarily candid survivor accounts of life during and after treatment convey the qualitative experiences that place quantitative information in the very human context in which it must be evaluated. Likewise, the daily experiences of health professionals who provide care to people with cancer, their families, and their caregivers are rich reservoirs of front-line information on the poorly charted journey each diagnosed person must make to live with and beyond cancer. It is with this understanding and in this spirit that the Panel has developed this report and recommendations for legislators, policy makers, the scientific and medical communities, employers, insurers, advocates, and others whose actions can so greatly affect the quality of life of people with cancer and their loved ones.

Recommendations

Issues Affecting Survivors Across the Life Span

Treatment and Follow-up Care Information

1a. Upon discharge from cancer treatment, including treatment of recurrences, every patient should be given a record of all care received and important disease characteristics. This should include, at a minimum:

- Diagnostic tests performed and results.
- Tumor characteristics (e.g., site(s), stage and grade, hormonal status, marker information).
- Dates of treatment initiation and completion.
- Surgery, chemotherapy, radiotherapy, transplant, hormonal therapy, gene or other therapies provided, including agents used, treatment regimen, total dosage, identifying number and title of clinical trials (if any), indicators of treatment response, and toxicities experienced during treatment.
- Psychosocial, nutritional, and other supportive services provided.
- Full contact information on treating institutions and key individual providers.

1b. Upon discharge from cancer treatment, every patient should receive a follow-up care plan incorporating available evidence-based standards of care. This should include, at a minimum:

- A description of recommended cancer screening and other periodic testing and examinations, and the schedule on which they should be performed.
- Information on possible late and long-term effects of treatment and symptoms of such effects.
- Information on possible signs of recurrence and second tumors.
- Information on the possible future need for psychosocial support.
- Specific recommendations for healthy behaviors (e.g., diet, exercise, sunscreen use, virus protection, smoking cessation).
- Referrals to specific follow-up care providers, support groups, and/or the patient's primary care provider.
- A listing of cancer-related resources and information (Internet-based sources and telephone listings for major cancer support organizations).

1c. The Department of Health and Human Services (DHHS) should establish a consortium of public and private institutional and community health care providers and payors, patient advocates, and technology experts to develop a blueprint for functional, content, format, and technology standards for creating a nationwide electronic health records system.

Legal and Regulatory Protections

2. Procedures should be established within diverse patient care settings to better inform patients/survivors and their caregivers about available legal and regulatory protections and resources.

HIPAA Privacy and Insurance Portability Provisions

3a. The Institute of Medicine should be commissioned to evaluate the impact of HIPAA provisions and provide guidance to legislators on amendments needed to make this law better serve the interests of cancer survivors and others.

3b. HIPAA privacy provisions inhibiting the ability to track and collect data for research on cancer survivors should be re-evaluated.

Cancer-related Education and Information

4a. National public education efforts sponsored by coalitions of public and private cancer information and professional organizations and the media (e.g., film, television, print and broadcast news) should be undertaken to:

- Raise awareness of survivor experiences and capabilities, and of the continuing growth of the cancer survivor population. These efforts should seek to enhance understanding of the post-treatment experiences of cancer survivors of various ages and their loved ones and the need for lifelong follow-up care.
- Provide accurate information and enhance community trust about participation in clinical trials and raise awareness of the importance of trials in developing new and better cancer treatments and other cancer-related interventions.

4b. Existing online resources, including those of the National Cancer Institute (NCI), that provide information on clinical trials and facilitate patient-trial matching should be improved to help patients more easily find trials for which they may be eligible and to simplify the enrollment process.

4c. A central online information resource on scientific evidence about late and long-term effects of cancer and its treatment should be developed and maintained by a consortium of interested constituencies (NCI, American Cancer Society, American Society of Clinical Oncology, and others). The NCI Physician Data Query database may provide a model for this effort.

- Using their existing networks, cancer awareness, education, and advocacy organizations should take a major role in helping to collect and disseminate (e.g., through newsletters, lay educators, workshops, other outreach efforts) late effects information as it becomes available.
- Individual cancer survivors should be able to contribute to this database information about their own experiences with late effects.

4d. The potential role of specialized long-term follow-up clinics or departments within or operated by medical or cancer centers should be evaluated for their benefit as a central education resource for cancer survivors. Ideally, such programs should provide the most current information to survivors and their families about late and long-term effects of cancer and cancer treatment and on complementary and preventive strategies (e.g., nutrition, exercise, sunscreen use, virus protection, stress reduction) to promote wellness.

4e. Education about possible late effects of cancer treatment and survivorship needs should be part of the core curricula for health care providers in training, and a part of continuing education for primary care physicians, oncologists, and non-physician health care providers.

Psychosocial and Support Needs

5a. All survivors should be counseled about common psychosocial effects of cancer and cancer treatment and provided specific referrals to available support groups and services.

5b. A caregiver plan should be developed and reviewed with a survivor's caregiver(s) at the outset of cancer treatment. It should include, at a minimum:

- An assessment of the survivor's social and support systems.
- A description of elements of patient care for which the caregiver will be responsible. Caregivers should be provided adequate

and, as needed, ongoing hands-on training to perform these tasks.

- Telephone contacts and written information related to caregiver tasks.
- Referral to caregiver support groups or organizations either in the caregiver's local area or to national and online support services.

5c. Providers should include psychosocial services routinely as a part of comprehensive cancer treatment and follow-up care and should be knowledgeable about local resources for such care for patients/survivors, caregivers, and family members. In particular:

- The transition from active treatment to social reintegration is crucial and should receive specific attention in survivors' care.
- Primary and other health care providers should monitor caregivers, children, and siblings of survivors for signs of psychological distress both during the survivor's treatment and in the post-treatment period.

Fertility

6a. All people of reproductive age who are diagnosed with cancer should be given complete culture- and literacy-sensitive information, both verbally and in writing, about options for preserving fertility and on possible effects of treatment on pregnancy or offspring before cancer therapy is selected or initiated.

6b. Parents of young children diagnosed with cancer must be given full culture- and literacy-sensitive information, both verbally and in writing, on the possible impact on fertility of treatment options prior to selecting and initiating treatment. If the patient is too young to understand this information at the time of treatment, parents should be urged to share this information with the survivor at the earliest possible time.

6c. Further research should be conducted to determine what fertility preservation options are possible for children and young adolescent cancer patients.

6d. Fertility preservation procedures and infertility treatment services should be covered by health insurance for cancer patients/survivors whose fertility will be or has been damaged by cancer treatment.

Health Insurance

7a. The Federal Government should revive efforts to implement comprehensive health care reform.

7b. Adequate reimbursement for prosthetics must be provided and it must be recognized that:

- Many prostheses must be replaced periodically.
- Access to prostheses is an integral part of psychosocial care for cancer.

7c. Coverage should be provided routinely for psychosocial services for which there is evidence of benefit both during treatment and post-treatment as needed.

7d. Public and private insurers should provide reimbursement for risk assessments, surveillance, and other follow-up care for cancer survivors, including care provided by appropriately trained non-physician personnel.

7e. Existing follow-up care clinic models should be evaluated and compared to ascertain their impact on survivor outcomes and their cost effectiveness.

Issues of Cancer Survivors Diagnosed as Children

School Re-entry

8a. Qualified providers in the treatment setting should train and assist parents to assume their crucial roles in helping the child with

cancer return to school and becoming an educator and advocate with individual teachers and the school system.

8b. Pediatric cancer centers should offer and promote teacher training as a part of their community outreach efforts to help ensure that the needs of pediatric cancer survivors returning to the classroom are met. Internet-based training modules also should be considered to extend the geographic reach of these training efforts. If possible, continuing education units (CEUs) should be provided to participating teachers.

8c. NCI and the Department of Education should explore collaborative opportunities to improve the classroom re-entry and reintegration of young people with cancer or other chronic or catastrophic illnesses (e.g., remote learning, teacher training).

Transition to Adult Care

9a. Centers that care for both children and adults with cancer should consider establishing a department or service specifically geared to provide for the needs of older children, adolescents, and young adults with cancer and to assist in their transition to adult care.

9b. As part of the process of transitioning survivors of childhood cancers into the adult care setting, information about young adult support groups, Internet sites, and other sources of information and support specific to this age group should be provided to survivors and their families. (See also Recommendations 1a and 1b.)

Psychosocial and Support Needs

10. Cancer care providers should inform families of cancer patients about supportive services, including special camps for families and siblings. (See also Recommendations 5a and 5c.)

Issues of Cancer Survivors Diagnosed as Adolescents or Young Adults

Surveillance and Research

11a. A working group comprised of representatives from public agencies and private organizations with established surveillance databases should be convened to determine what additional data collection, infrastructure, and related funding would be required to better capture treatment and survival data on adolescent and young adult cancer survivors.

11b. NCI and other cancer research sponsoring agencies should increase the priority of and funding for research on the issues of cancer survivors diagnosed as adolescents or young adults. Studies of biologic differences in cancer type and host factors, and of late effects of cancer and cancer treatment in this population should be emphasized to improve the knowledge base and inform the design of treatment, prevention, and quality of life interventions designed to benefit this population.

Psychosocial and Support Needs

12a. Family members, primary care providers, cancer specialists, and others who are close to or provide medical care to adolescent and young adult survivors should be made aware that depression, anxiety, or other psychosocial issues may affect the survivor long after treatment ends and should be instructed on how to intervene should the survivor experience such difficulties. (See also Recommendations 1b and 5a.)

12b. Adolescent and young adult survivors should be taught self-advocacy skills that may be needed to secure accommodations for learning differences resulting from cancer or its treatment. Physicians and other providers should act as advocates for survivors when necessary.

Issues of Cancer Survivors Diagnosed as Adults

Follow-up Care Recommendations

13. The American Society of Clinical Oncology, the American College of Surgeons, the American College of Radiology, and other major cancer clinician and research organizations should develop more complete recommendations to guide the post-treatment care of survivors of adult-onset cancers. These recommendations should be published and posted on a website and updated regularly to ensure that survivors, patient educators, providers, and insurers have access to them.

Issues of Cancer Survivors Diagnosed as Older Adults

Insurance

14. The Institute of Medicine or other independent body should undertake a periodic assessment of the impact of Medicare legislative changes on older cancer patients' access to care and other follow-up services.

Surveillance and Research

15. Public and privately sponsored research and surveillance on survivorship issues among people diagnosed with cancer in older adulthood should be increased significantly to address the information void on the needs of this population that will comprise an increasing percentage of people with cancer over the next several decades. (See also Recommendation 3b.)

Psychosocial and Support Needs

16. Health care providers must ascertain the strength of an older survivor's social and caregiver support system. This should be assessed at diagnosis, during treatment, and at intervals after treatment is completed. Oncology nurses, nurse practitioners, other advanced practice nurses, physician assistants, social workers, patient navigators, or other non-physician personnel may be best able to make these assessments and arrange assistance and services for survivors who lack adequate support.

17. Health care providers should not assume that older cancer survivors and their partners are uninterested in sexuality and intimacy. Survivors should be asked directly if they have concerns or are experiencing problems in this area and should receive appropriate referrals to address such issues.

Appendix D

Survivorship Activities at Cancer Centers

Due to the amount of information available, this appendix can be viewed at the following website:

www.cancer.gov/cancercenters/

Appendix E

Survivorship Activities at NCI Cancer Centers

Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Siteman Cancer Center Survivorship Activity					
Psychosocial Clinical Service					
	Medical care and counseling		X		
	Psychiatric and psychological services		X		
	Support groups for patients and family members		X		
	Nutritional counseling		X		
	Quality of life assessment and activities (institutional and NCI/NIH-funded clinical studies)	X	X		
Help Us Give Support (HUGS) program in breast cancer (Deshields Komen local funding)					
	Education and support activities for children related to breast cancer patients (Deshields Komen local funding)			X	X
	Support groups for children related to breast cancer patients (Deshields Komen local funding)			X	X
Young Women's Breast Cancer Program (Ivanovich Komen local funding)					
	Genetic counseling for young women (Ivanovich Komen local funding)		X	X	X
	Risk assessment for young women (Ivanovich Komen local funding)		X	X	X
Witness Program (Mathews Komen local funding)					
	Support groups for breast cancer patients/survivors (Mathews Komen local funding)				X
	Educational and support materials for breast cancer patients/survivors (Mathews Komen local funding)				X
	Relationships with local organizations, such as the Breakfast Club (Mathews Komen local funding)				X
Cancer Center Support Grant (CCSG) Shared Resources (Eberlein NCI P30)					
	Hereditary Cancer Core (Eberlein NCI P30)	X			
	Health Behavior and Outreach Core (Eberlein NCI P30)	X		X	X
Community Education and Screening Activities					
	Community education events (prevention, care, and survivorship) touching more than 28,000 people annually			X	X
	Screening activities across the spectrum of cancers			X	X
Clinical Support Services					
	Siteman Cancer Center at Barnes-Jewish Hospital - St. Peters: AWARE Program (guided imagery and relaxation); Conquer program (general support group); KIDScope (support group for children 4-13 whose parent or caregiver has cancer/adults meet at the some time to discuss parenting); Massage Therapy (offered weekly to patients and caregivers); DHHS/CDC skin cancer programs; and ACS programs (Look Good, Feel Better; Daffodil Days, ACS Days)		X	X	
	Siteman Cancer Center at Barnes-Jewish Hospital - West Co.		X	X	
	Bone Marrow Transplant		X	X	
Palliative Care Service					
	Routine medical follow-up and surveillance		X		
	Pain and symptom management		X		
	Medical management and counseling		X		
	Hospice management		X	X	

* Education may be student, patient or community education

Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Barnard Health and Cancer Information Center (BHCIC)					
	Print educational materials on cancer survivorship			X	
	Aduiovisual educational materials and kiosks on cancer survivorship			X	
	Information about websites related to cancer survivorship			X	
Program for the Elimination of Cancer Disparities (PECaD) Community Networks Program (Farria NCI U01)		X		X	X
	Research projects focused on reducing cancer-related disparities	X		X	X
	Educational programs focused on reducing cancer-related disparities			X	X
	Community (disease-oriented) action teams (community-based participatory research and education)	X		X	X
	Training programs for investigators and communities	X		X	X
Prevention and Control Research Program (Eberlein NCI P30)					
	Quality of life over time: DCIS vs early breast cancer (Jeffe NCI R01)	X			
	Geographic variation of breast cancer survival (Schootman NCI R01)	X			X
	Neighborhood effects on quality of life in breast cancer (Schootman NCI R01)	X			X
	Comorbidity prognostic impact in elderly cancer patients (Piccirillo NCI R01)	X			
	Centers of Excellence in Cancer Communications Research (CECCR) (Kreuter NCI P50)	X			X
	Minority pre-doctoral education to reduce disparities (Kreuter R25)	X			
	Health promotion and disease prevention research center (Brownson U48)	X		X	X
	Predictors of Relapse to Smoking in Lung Cancer (Walker NCI R01)	X			
	Mental Health History and Survival Among Breast Cancer Patients (Walker Longer Life Foundation funding)	X			
Translational and Clinical Research Program					
	Phase 2 Trial of Estradiol Therapy for Advanced Breast Cancer (Ellis NCI/Avon P30 supplement)	X			
	Impact of Neodadjuvant Chemotherapy With or Without Zometa on Occult Micrometastases and Bone Density in Women with Locally Advanced Breast Cancer (Aft Novartis and Pfizer funding)	X			
	Overcoming Barriers to Early Phase Clinical Trials: Coaching Promotion for Minority Recruitment (Fracasso NCI R21)	X			X
	Estimating the probability of death from prostate cancer or other competing risk factors (Yan Longer Life Foundation funding)	X			
Siteman Clinical Research Affiliates					
	Affiliates for clinical studies (two satellite/affiliate Siteman Cancer Centers, other study affiliates)	X			X
	Prevention and control affiliate (Columbia, MO)	X			X
	Member of Mayo Phase II Consortium (NCI funded)	X			X
	Member of Northwestern Phase II Chemoprevention Consortium (NCI funded)	X			X

* Education may be student, patient or community education

Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Abramson Cancer Center Survivorship Activities					
The Lance Armstrong Foundation Living Well After Cancer Program:					
	Consultative Programs:	x		x	TBA Penn Network Hospitals
	Breast Cancer Survivors				
	Lymphoma Survivors				
	BMT Survivors				
	Clinical Programs: (TBA Penn Network Hospitals)	x	x	x	TBA Penn Network Hospitals
	Testicular Cancer Survivors				
	Transition program-Young Adult Survivors of Childhood Cancers				
	(CHOP-PENN Model)				
The Abramson Cancer Center Patient and Family Services Program:					
	Psychosocial Counseling		x	x	
	Nutrition Counseling		x	x	
	Patient & Family Services		x	x	
	Genetic Risk Evaluation Program:				
	Breast Cancer	x	x	x	x
	Testicular Cancer	x	x	x	x
	Consultations:				
	Breast Ca Survivors				
	Lymphoma Survivors				
	BMT Survivors				
	Nutrition Counseling				
	Patient & Family Services				
	Psychosocial Counseling				
	Breast Cancer Genetic Risk Evaluation Program				
	Testicular Cancer Genetic Risk Evaluation Program				
	Databases:				
	Consultative Programs (Breast, Lymphoma, BMT)				
	Clinical Programs (Testicular, Young Adult)				
	Psychosocial Counseling				
	Breast Cancer Genetic Risk Evaluation Program				
	Testicular Cancer Genetic Risk Evaluation Program				
	Survivorship focused: Presentations (poster & podium), Consultations, Educational Programs, National working groups				
	ACC support groups for survivors of breast, prostate, head & neck, GI cancers & their families				

* Education may be student, patient or community education

Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Robert H. Lurie Comprehensive Cancer Center of Northwestern University					
	Cancer Survivors' Celebration and Walk				X
	Cancer Therapy Cutaneous Adverse Reaction Clinic	X	X		
	Community education programs			X	X
	EndLink			X	X
	EPEC-O Project			X	
	Fertility Preservation Program			X	
	Geriatric Oncology Consultation Services		X	X	X
	Health Learning Center Satellite			X	X
	Hospice/Palliative Medicine Program		X	X	X
	Lunchtime Lectures: Cancer Prevention/Control			X	X
	Lynn Sage Breast Cancer Symposium			X	X
	Lynn Sage Breast Cancer Town Hall Meeting			X	X
	Office of Special Population Initiatives			x	X
	Ovarian Cancer Survivor Course			X	X
	Patient Advisory Board			X	X
	Patient Navigator Program		X	X	X
	Patient Support Groups			X	X
	Psychosocial Oncology Program	X	X	X	X
	STAR (Survivors Taking Action and Responsibility)		X	X	X
	Survivors' Day with the Chicago White Sox				X
Norris Cotton Cancer Center Survivorship Activities					
	Community Outreach and Education				
	Cancer Help Line			X	X
	Cancer Support and Information Groups			X	X
	Patient and Family Libraries			X	X
	The Women's Health Resource Center			X	X
	Community Information and Education: Conferences, etc.			X	X
	Charting Your Course: Breast Cancer			X	X
	Programmatic Development at the State Level			X	
	American Cancer Society			X	
	Survivorship Research				
	Cancer Prevention and Risk Reduction				
	Chemoprevention Research	X			
	SunSafe	X		X	X
	Tobacco Control	X		X	
	Cervical Cancer Prevention	X	X		
	The Familial Cancer Program	X	X	X	
	Screening and Early Detection				
	Breast Imaging	X	X		
	The New Hampshire Mammography Network	X		X	
	The National Lung Screening Trial (NLST)	X	X		
	Interdisciplinary Prostate Cancer Risk Clinic	X	X		
	Primary Care Colon Cancer Screening Consortium	X			
	Quality of Life/Quality of Care				
	Psycho-Oncology	X	X	X	

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Clinical Care/Supportive Services for Cancer Survivors				
	Multidisciplinary Second Opinions		X	X	
	The Palliative Care Program	X	X	X	
	The Haelan Program of Complementary Therapies		X		
	Peer Mentorship		X		X
	Programs for Pediatric Cancer Survivors		X	X	
	The Center for Shared Decision Making	X	X	X	
	Chaplaincy Services		X		
	Rehabilitation		X		
	Case Management and Financial Planning Consultation		X	X	
M. D. Anderson Cancer Center Survivorship Program					
Follow-up/Surveillance					
	Life After Cancer Care (LACC) - Evaluates medical sequelae for survivors of any malignancy		X		
	Long-term Follow-up Clinics				
	Breast Survivorship Clinic		X	X	X
	Life After Cancer Care (LACC)		X		
	Melanoma		X		
	Pediatrics and the Children's Cancer Hospital (Childhood Cancer Survivors Study)		X		
	Prostate		X		
	Surveillance of Secondary Cancer				
	Cancer and Screening Prevention Clinic - surveillance of early cancer including 2nd malignancies	X			
	Melanoma and Skin Center - monitoring skin for changes in lesions		X		
	Prognostic risk characteristics for secondary primary cancers (Epidemiology research)	X			
Cancer/Treatment Effects					
	Fatigue				
	Fatigue Clinic - evaluates and treats cancer or cancer related fatigue	X			
	Fatigue and other symptoms in ovarian cancer patients (Behavioral Science research)				
	Co-morbidities				
	Chemotherapy Treatment Complications Clinic		X		
	General Internal Medicine Clinic - evaluates and treats survivors co-morbidities		X		
	Inpatient Service - survivors need acute mgt co-morbidity and symptoms		X		
	Blood sugar control to prevent steroid-induced hyperglycemia (Diabetes research)	X			
	Cognitive functioning				
	Behavior Interventions Clinic - addresses and remediate's cognitive dysfunction		X	X	
	Cognitive and vocational rehabilitation (Neuro-oncology)		X		

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Neuro-cognitive function hematological and testicular cancer (Cancer Medicine Research)	X			
	Pain Management and Palliative Care				
	Integrative Medicine Program				
	Complementary/Integrative Medicine Education Resources (CIMER) - website health information			X	
	Place...of wellness - complementary therapies to manage symptoms, relief stress & improve QOL		X		
	Research examining intervention programs to improve quality of life and clinical outcomes	X			
	Physical and Occupational Rehabilitation				
	Lymphedema		X		
	Treatment Effects				
	Cardiology - Post chemo CHF/cardiomyopathy (Cardiology Research)	X			
	GvHD - Late toxicities of GvHD (Pulmonary Research)	X			
	Neuropathy - defining mechanisms of chemotherapy induced peripheral neuropathy (Anes research)	X			
	Osteoporosis/Bone Disease				
	Bone Disease Program of Texas		X		
	Bisphosphonates relationship to osteonecrosis of the jaw (BDPT research)	X			
	Bone health among breast cancer survivors (Breast research)				
	Radiation and chemotherapy damage to the lung (Pulmonary research)	X			
	Pulmonary Rehabilitation to restore/enhance pulmonary function (Pulmonary)		X		
	Radiation - long term effects of radiation emphasis on pediatric patients (Radiation Physics research)	X			
	Fertility				
	Cancer related fertility - Parenthood after Cancer Conference (Research Behavioral Science)	X			
	Sexual dysfunction/early menopause				
	Sexual dysfunction research (Behavioral Science Research)	X			
Family/Caregiver Issues					
	Individual and family counseling (Social Work)		X		
	Psychiatric services (Behavioral Medicine)		X		
	Support groups (Social Work)		X		
	Breast Cancer Survivors, Physical Activity and Quality of Life (Behavioral Science research)	X			
	Predicting exercise among endometrial cancer survivors (Behavioral Science research)	X			
	Psychological & relationship functioning of lung patients & spouses (Behavioral Science Research)	X			
	Prostate cancer survivors (psychosocial status & physical activity) (Behavioral Science Research)	X			
	Weight gain prevention for breast cancer survivors (Behavioral Science Research)	X			

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Testicular cancer survivors quality of life and health behavior (Behavioral Science research)				
	Male breast cancer survivors (psychosocial status) (Cancer Medicine Research)	X			
	Quality of life and health behaviors (testicular, prostate and anal) (Cancer Medicine Research)	X			
	Providing cancer survivor services for follow-up and early detection (Caner Prevention research)	X			
	Exercise studies (Epidemiology Research)	X			
	Survivorship issues and rare cancers (Epidemiology)	X			
	Biology, anatomy and management grief in cancer survivors and caregivers (GI Med Onc research)	X			
	Psychosocial and neuro-cognitive aspects of pediatric cancer survivorship (Pediatrics research)	X			
	Quality of life (Neuro-oncology research)	X			
	Fear of recurrence or second malignancy (Symptom Research)	X			
Economic Effects					
	Short-term & long-term labor market performance among cancer survivors (Health Services research)	X			
	Retaining/returning to previous employment, vocational rehab, & insurability (Symptom Research)	X			
Health Disparities					
	Health Disparities Research - disparities in health care of minority groups	X			
	Asian Americans/Hepatitis and relationship hepatocellular cancer (research)	X			
Instrument Development					
	System assessment tools (Symptom Research)	X			
	Development of Chronic Graft Versus Host Disease Symptom Inventory) (Symptom Research)	X			
	World Health Organization Collaborating Center for Supportive Care (Symptom Research)	X			
Health Promotion					
	Screening and follow-up care - Cancer Screening Prevention Clinic		X		
	Risk factors/susceptibility- prognostic risk characteristics for second cancers (Epidemiology research)	X			
	Melanoma risk-reduction practices (Behavioral Science Research)	X			
	Tobacco cessation and control (Behavioral Science Research)	X			
Education					
	The Learning Center - 3 consumer health libraries			X	X
	Texas Medical Association - faculty work with TMA to develop programs for primary physicians to address needs of cancer survivors			X	X
Community Outreach					
	Anderson Network				
	Volunteer patient and survivor support group that shares information and support			X	X
	Living Fully with Cancer - annual patient/caregiver conference (in its 10th year)			X	X
	Young Breast Cancer Survivors workshop to take place in 2006			X	X

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Brain Tumor Conference for patients and family (biannual conference planned with National Brain Tumor)			X	X
	Gynecologic Awareness Month at Houston Astros			X	X
	Sprint for Life 5K (annual ovarian cancer fundraiser and community awareness event)			X	X
	Skin cancer screening (annual)			X	X
	Tobacco Outreach and Education Program (TOEP)				
Holden Comprehensive Cancer Center Iowa Survivorship Activities					
Clinical Components Adults					
Routine Follow-Up and Surveillance			x		
Pain and symptom management			x		
Emg. Housing Fund & Guest House			x		
Sexual Rehabilitation			x		
CAM Clinic			x		
Support Groups for pts & family			x	x	
Financial Counseling	Counseling		x		
Lymphedema Therapy			x		
Mindfulness Based Stress Reduction			x	x	
Nutrition therapy			x		
Speech, occupational, physical ther.			x		
Psychiatric & psychological services			x		
Palliative Care/Spiritual Support			x		
Coming Soon: ACS Hope Lodge			x		
Clinical Components-Pediatrics					
Routine Follow-up & Surveillance					
Room accomodations for parents			x		
Child development activities			x		
Procedure support			x		
Diversional activities			x		
Emotional support			x		
Support group-siblings			x		
Music Therapy			x		
New Do Head Covers			x		
Hospital teacher			x		
Sperm banking costs covered			x		
Amenities for parents					
Massage/spa for parents			x		
Breakfasts			x		
Vouchers: gas, food, hotels			x		
$500.00 per family for co-pays			x		
Ronald McDonald House			x		
Research Components					
Iowa Cancer Registry		x			
Cancer and Aging Program		x			
Quality of Life and Breast Cancer		x			
Healing Touch and Breast Cancer		x			
Quality of Life & Gynecologic Cancer		x			

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Neurobehavior Outcomes in Children		x			
Adverse Events After Childhood Cancer		x			
Education and Outreach Components					
IA Consortium Comp. Ca Control				x	x
Holden Cancer Information Service				x	x
NCI-CIS/ICCCC Partnership Position				x	x
Health for Your Lifetime				x	x
Cancer Survivor's Day					x
BM Transplant Reunion					x
Palliative Care Conference				x	
Prof. Psychosocial Oncology Conf.				x	
Scofield Adv. Oncology Nurse Conf.				x	
Holden Networks					
Iowa City Cancer Care			x		x
Outreach Services			x		x
Huntsman Cancer Center Survivorship Activity					
	Wellness/Survivorship Program		X	X	X
	Family Cancer Registries	X	X	X	X
	Pain Medicine and Palliative Care	X	X	X	X
	Social Work Services		X	X	X
	Department of Patient and Public Education		X	X	X
Hawaii Cancer Center Survivorship Activity					
Prevention and Control Program (current active projects only)					
	Quality of life in breast cancer survivors	x			
	CAM use in cancer survivors	x			
	Pilot writing progam	x			
	Quality of life in testicular cancer	x			
	Massage in cancer survivors and partners	x			
	Reflexology in cancer survivors	x			
	Internet-based health promotion for cancer survivors	x			
Epidemiology Program					
	SEER Registry	x			
	Mulitethnic Cohort	x			
	Colorectal Family Registry	x			
Clinical Trials Unit					
	Minority-Based Community Clinical Oncology Program	x	x	x	x
	Clinical Trials Update			x	x
Cancer Information Service		x		x	x
Community Networks					
	Imi Hale	x		x	x
	AANCART	x		x	x
Cancer Research Center of Hawaii					
	Cancer Research Day			x	x

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Fred Hutchinson Cancer Center Survivorship Activity					
	Transplant LTFU	X	X	X	X
	ACCESS	X	X	X	X
	Prostate Cancer Research	X	X	X	X
	Womens Wellness Center	X	X	X	X
	LIVESTRONG Survivorship Center of Excellence	X	X	X	X
	This incorporates the above programs and will add a survivorship program for all medical oncology patients				
Albert Einstein Cancer Center Survivorship Activity					
	Psychosocial Oncology Program		x	x	x
	Yoga-based Cancer Rehabilitation Pgm	x			
	Mind-Body Cancer Research Program	x			
	Quit Smoking Program	x	x	x	x
	Psychosocial Onc / QoL Volunteer Pgm			x	x
	H.O.P.E. Program		x	x	x
	Psychosocial Oncology Fellows Seminar	x		x	
	Psycho-oncology externship/internship		x	x	
Duke Cancer Center Survivorship Activity					
Prevention, Detection & Control Research Program		X			
	Physical Activity/Diet in Breast and Prostate Cancer Patients	X			
	RENEW: improving physical function in elderly	X			
	STRENGTH: Survivor Training for Enhancing Total Health	X			
	Preoperative exercise program for lung cancer patients	X			
	Value of cardiopulmonary exercise in breast/lung patients	X			
	Endurance training in early stage lung cancer patients	X			
	Endurance training in early stage breast cancer patients	X			
	Efficacy of caregiver-assisted copying skills training	X			
	Coping skills of African American cancer patients	X			
	Efficacy of partner-assisted emotional disclosure intervention	X			
	Efficacy of couple-based cognitive behavioral intervention	X			
	Studying communication in oncologist-patient encounters	X			
	Smoking relatives of lung cancer patients	X			
Clinical Intervention					
	Hereditary Cancer Clinic offers risk assessment for survivors		X		X
	Integrative Oncology Program focuses on care for survivors		X		
	Pathfinder, patient support program within a research project		X		
	Childhood Cancer Survivor Follow-up Program		X		
Patient Support and Education					
	Center for Cancer Survivorship			X	X
	Cancer Patient Support Program			X	X
	Cancer Patient Education Program			X	X
	Oncology Recreation Program			X	X
	Survivorship Patient Focus Group			X	
	Survivorship Advisory Council			X	

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Outreach					
	Power of Knowledge Seminar			X	X
	Melanoma Consortium			X	X
	Rainbow of Heroes - Pediatric Bone Marrow survivor event				X
	Cancer Survivors Day Celebration				X
	Cancer Information Service			X	X
	Cancer Center Notes newsletter			X	X
	cancer.dukehealth.org website			X	X
	Brain Tumor Action Week			X	X
	Gynecologic Seminar Series			X	X
Dana-Farber Cancer Institute Survivorship Activity					
Lance Armstrong Foundation Adult Survivorship Clinic		X	X		
David B Perini, Jr., Quality of Life Clinic for Childhood Cancer Survivors		X	X		
	Transitioning to Survivorship: What Every Parent Should Know	X	X	X	
	Health Lifestyles			X	
	Facing Forward for Childhood Cancer Survivors		X	X	
	Weekend Retreat for Childhood Cancer Survivors			X	X
Stop & Shop Family Pediatric Neuro-Oncology Outcomes Clinic		X	X		
Perini Family Survivors' Center					
	Living Proof: Celebrating Survivorship			X	X
	Survivorship Education Series (for patients)			X	
	Improving Life After Cancer Treatment (IMPACT) (for patients)			X	
	May 2006 Symposium (collaboration with Breast Oncology)				
	Nursing Education CEU Course (collaboration with Nursing ed)			X	
	Workshop for Psychosocial Oncology Researchers			X	
	Visiting Scholar Program	X		X	
	Survivorship Research Symposium (Oct. 2006)	X		X	
	Community Outreach Consortium	X	X	X	X
	A Group Educational Intervention for Female Hodgkin's Disease Survivors at Increased Risk for Breast Cancer	X			
	Calculation of cardiac valve irradiation in lymphoma patients treated with mantle radiation				
	Neuroendocrine Function in Survivors of Childhood Leukemia	X			
	Detection of microalbuminuria in survivors of childhood cancer: A pilot study.	X			
	Cardiac Screening in Survivors of Hodgkin's disease treated with mediastinal irradiation	X			
	Breast MRI Screening in Women Treated with Mediastinal Irradiation for Hodgkin's Disease	X			
Department of Care Coordination					
	Facing Forward After Breast Cancer Treatment		X	X	
	Stepping Stones			X	
	Young Survivors Support Group			X	

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Center for Community Based Research					
	Exploring the Healthcare Needs of Low Income Cancer Survivors	X			X
	A Web-based smoking cessation intervention for Cancer Survivors	X		X	X
	Proxy Information Agents Focus Groups	X			X
	Survivor Care after Cancer Survey	X			
	Coping After Breast Cancer	X			
Chicago Cancer Center Survivorship Activity					
Quality of Life Studies		X			
	Conflict of Interest Interview of Advanced Cancer Patients	X			
	Factors Related to and Influencing the Disclosure of Prognostic Information in the Advanced Cancer Setting	X			
	Improving Patient Understanding of EarlyPhase Clinical Trials	X			
	Quality of Life in Children Who Survived Neuroblastoma	X			
	Cognitve and Functional Outcomes of Cancer Treatment in Elderly Patients	X			
	Observational Cohort Study of Chemotherapy Decisions & Outcomes in Women Ages 55 or Older	X			
	A Study of Parental Disclosure of Genetic Test Results to Young Adolescents	X			
	Quality of Life in African American Cancer Survivors	X			
	Perceptions of Chemotherapy Between African Americans and Whites	X			
	Functional Impact of Breast Cancer Treatment in Older Women	X			
	Impact of Comorbidity and Functional Status on Outcome for Older Recipients of Allogeneic Transplant	X			
	Health Related Quality of Life for Hodgkin's Disease Survivors	X			
	Are the Elderly Capable of Informed Consent for Research Participation?	X			
	Comprehensive Geriatric Assessment to Examine Geriatric Domains in Older Prostate Cancer Patients	X			
Cancer Registry					
	The University of Chicago Cancer Research Center Clinical and Research Registry Protocol	X			
	Children's Oncology Group Registry	X			
	Cancer Registry Data Quality Subcommittee			X	
	Commission on Cancer - Cancer Liaison Committee				X
	Transplatation Registry Protocol	X			
Cancer Genetics					
	The Center for Clinical Cancer Genetics		X		
	University of Chicago Cancer Risk Clinic		X		
	Cancer Risk Assessment and Genetic Screening in Cancer Prone Families	X			
	Genetic Counseling and Testing				
	A Review of Preganancy Associated Breast Cancer at the University of Chicago Hospitals				
Patient and Family Services					
	University of Chicago Cancer Resouce Center			X	
	Facing the Mirror			X	
	Smoking Cessation		X		

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Massage Therapy		X		
	Look Good Feel Better		X		
	The Herbert T. Abelson Family Learning Center			X	
	Living a Healthy Life: How To Balance Good Eating, Exercise, Relaxation & Everything Else in Your Life				X
	Head and Neck Cancer Support Group			X	
	Lung Cancer Support Group			X	
	Family Nutrition Education Classes			X	
	University of Chicago Blood Bank		X		
	Crochet Classes for Cancer Survivors			X	
	Straight Talk for Teens		X	X	X
Departments					
	University of Chicago School of Social Service Administration	X		X	X
	Center for Interdiscipinary Health Diparities Research	X	X	X	X
Community Programs					
	Community Fitness				X
	Community Empowerment Forum				X
	University of Chicago Hospitals Office of Community Affairs			X	X
UNC Lineberger Cancer Center Survivorship Activities					
Behavioral Interventions					
	NC STRIDES	x			
	Managing uncertainty in prostate cancer	x			
	Managing uncertainty in breast cancer	x			
	Health eCommunities	x			
	Can Thrive	x			
	NC BEAUTY	x			
Epidemiological Studies					
	LIBCSP	x			
	Follow-up of African-American survivors				
	Head & neck cancer follow-up study				
	CanCORS	x			
Patient Family Resouce Center				x	x
Arizona Cancer Center Survivorship Activity					
Health Outcomes and Behavior					
	The Effect of Moderate Physical Activity on the Physical and Emotional Recovery of Patients with a History of Colon Cancer	x			
	Assessing the Needs of Long-term Breast Cancer Survivors	x			
	HR-QOL for colorectal cancer long-term survivors	x			
	Neurological Effects of Chemotherapy and Radiation Treatment: Colon Cancer	x			
	Green Tea Intervention for Weight Gain Prevention among Women with Breast Cancer				
	Women's Healthy Eating and Living (WHEL) Study	x			
	Longitudinal Effects of Intimate Partner Relationship Quality in Newly Diagnosed Breast Cancer Patients	x			
Psychosocial and Palliative Care					
	Routine medical follow-up and surveillance		x		

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
	Pain and symptom management	x	x	x	
	Sexual rehabilitation		x	x	
	Cognitive evaluation	x	x		
	Psychiatric and psychological services				x
	Support groups for patients and family members		x	x	x
	Speech, occupational and physical therapy			x	x
	Telephone counseling for breast cancer patients			x	x
	Nutritional counseling		x	x	x
	End-of-Life Care Curriculum	x		x	
Patient Education and Resource					
	Print and video educational material on cancer survivorship			x	x
	Monthly supportive care class for Patients and Survivors, family members		x	x	x
	Information about websites for cancer survivors			x	x
Community and Outreach Services					
	Sunstone Healing Center	x		x	x
	Referral to/from other cancer resources/centers (local and regional)			x	x
Vanderbilt-Ingram Cancer Center					
Health Outcomes and Behavior Program					
	Cognitive evaluation in pediatric oncology patients	x			
	Cognitive function in breast cancer survivors	x			
	Fatigue in cancer survivors	x			
Psychosocial and Palliative Care Program					
	Routine medical follow-up and surveillance		x		
	Pain and symptom management		x	x	
	Integrative Medicine		x		
	Cognitive evaluation		x		
	Psychiatric and psychological services	x	x		
	Support groups for patients and family members		x	x	
	Speech, occupational and physical therapy	x	x		
	Nutritional counseling	x	x		
Patient Education and Resource Center					
	Education and Community Outreach			x	
	Cancer Information Program (CT referrel service)	x	x	x	
	Print and audiovisual educational material on cancer survivorship			x	
	Full-time Patient Education Coordinator and Advocacy Manager			x	
	Survivorship Educational Programs			x	
	Wellness Community Cancer Survivor Program Grant			x	
	CancerHelp Touch Screen Monitor/Computer Education			x	
	Annual cancer survivor conference			x	
	Clinical Trials Mentor Program (pt advocacy)			x	
	Patient Navigation Conference			x	
Cancer Survivors Clinic (to be implemented Summer 2006)			x	x	
Minority Affairs Office					
	Southern Community Cohort Study	x		x	
	Educational programs focused on reducing cancer-related disparities		x	x	x

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Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
VICC Affiliate Network					
	Resource for conducting community-based studies	x	x		x
VICC Family Cancer Clinic					
	Family Risk Service				
Memorial Sloan Kettering Cancer Center					
Sexual Health Program		X	X	X	
Clinical Genetics		X	X		
Long-Term Follow-Up					
	Pediatrics	X	X	X	
	Young Adults	X	X	X	
	Adults	X	X	X	
BMT Program					
	Pediatrics	X	X		
	Adults	X	X		
Queens Cancer Center		X	X		X
Post-Treatment Resource Program			X		X
Integrative Medicine		X	X		
Counseling Center		X	X		
Smoking Cessation Program		X	X		
Physical Rehabilitation Program		X	X		
Behavioral Research		X			
Late Effects Research		X			
Patient Education Program					
	Patient Library			X	
	Survivorship Website			X	
	MSKCC Medical Library			X	
Jonsson Comprehensive Cancer Center UCLA					
Patients and Survivors CCSG Program					
	Breast, lung, CRC, Prostate	x			
	Pediatric young adult	x			
	Geriatrics	x			
Revlon Breast Center Breast CA			x		
	Follow-up Program				
Prostate Cancer IMPACT program					x
UCLA Family Cancer Registry		x	x		x
School of Medicine R-25 on Cancer Survivors				x	
Young adult survivors/ transition clinic		x	x		
Ted Mann Family Resource Center			x	x	x
Pediatric Pain Program		x	x	x	x
East-West Medicine Program			x		

LAF Center of Excellence		x			
Cancer Center	Survivorship Activity	Research	Clinical Care	Education *	Community Outreach
Moffitt Cancer Center Survivorship Activity					
Health Outcomes and Behavior Program					
	Fatigue in Breast Cancer Survivors	x			
	Cognitive Function in Prostate Cancer Survivors	x			
	Sexual Fuctioning in Cervical Cancer Survivors	x			
	Cognitive Function in BMT Survivors	x			
	Mindfulness Meditation for Breast Cancer Survivors	x	x		
	Exercise Training for Prostate Cancer Survivors	x	x		
	Barriers to Fertility Preservation in Cancer Patients	x			
Psychosocial and Palliative Care Program					
	Routine medical follow-up and surveillance		x		
	Pain and symptom management		x		
	Sexual rehabilitation		x		
	Cognitive evaluation		x		
	Psychiatric and psychological services		x		
	Support groups for patients and family members		x		
	Speech, occupational and physical therapy		x		
	Nutritional counseling		x		
Patient Education and Resource Center					
	Print and audiovisual educational material on cancer survivorship			x	
	Information about websites for cancer survivors			x	
Skillbuilding in Psychosocial and Palliative Care					
	Annual professional education conference			x	
Community and Outreach Services					
	Support group for Latina breast cancer survivors in Central Florida		x		x
Tampa Bay Community Cancer Network					
	Projects focused on reducing cancer-related disparities		x	x	x
Moffitt Affiliate Network					
	Resource for conducting community-based studies	x	x		x

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Shared Resources Survey

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Cell Biology, Immunology & Pathology Services	Antibody Development	UVA, RP, NW, NE, IA, MD, FH, CH, DF, AE, FC, PA, CO, WT, MI, DM, MSK	UVA, RP, FH, CH, DF, AE, FC, CO, WT, MI	Y: UVA, RP, NW, NE, IA, MD, CH, DF, FC, CO, WT, MI, DM, MSK N: JAX, FH, PA	Y: UVA, RP, NW, NE, IA, MD, CH, DF, FC, CO, WT, MI, DM N: FH, PA	Y: JHU, USC, JAX, FH, SJ, OH, WT, NM, DV, BI, DM N: RP, NW, IA, MD, CH, FC, PA, CO, MI
	Biologics Production – GMP	RP (GLP only), JHU, FH, CH, WU, PA, SJ, OH-cellular and viral, NY, COH, MSK	RP, JHU, FH, CH, WU, PA, COH	Y: RP, FH, CH, WU, NY, COH, MSK N: JHU, JAX, PA, SJ	Y: RP, FH, CH, WU, NY N: JHU, PA	Y: UVA, RP, WF, NE, IA, OH, WT, GT, NM, DM N: JHU, NW, JAX, MD, FH, CH, WU, PA, CO, NY, BI, COH
	Biologics Production – Research	RP, IA, FH, CH, PA, SJ, WT, COH, MI, DM, MSK	RP, PA, COH	Y: RP, IA, MI N: JAX, FH, CH, PA, SJ, WT, COH	Y: RP, IA, MI N: FH, PA, WT	Y: RP, NW, NE, OH, WT, GT N: JHU, JAX, IA, MD, FH, PA, CO, BI, MI
	Cell Analysis	RP, JHU, USC, NW, JAX, NE, IA, MD, FH, CH, WU, FC, CO, SJ, OH, SF, WT, GT, NY, VT, NM, DV, BI, COH, MI, OR, DM, IN, MSK	RP, JHU, USC, NW, IA, MD, FH, CH, WU, FC, CO, SF, WT, NY, VT, NM, DV, COH, MI, DM, IN	Y: RP, USC, NW, NE, IA, MD, CH, WU, FC, CO, SF, WT, NY, VT, NM, DV, MI, MSK N: JAX, FH, SJ, COH, OR, DM, IN	Y: RP, USC, NW , NE, IA, MD, CH, WU, FC, CO, SF, WT, VT, NM, DV, MI, IN N: JHU, FH, NY, OR, DM	Y: N: RP, JHU, USC, NW, JAX, IA, MD, FH, CH, WU, FC, CO, SF, WT, NY, VT, NM, DV, BI, MI, OR, DM, IN
	Cell Sorting	UVA, RP, JHU, USC, NW, JAX, WF, IA, MD, FH, CH, AE, WU, FC, PA, UT, CO, SJ, OH, SF, WT, SA, GT, NY, VT, NM, DV, BI, COH, MI, OR, DM, IN, MSK	UVA, RP, JHU, USC, NW, JAX, IA, MD, FH, CH, AE, WU, FC, PA, CO, SF, WT, GT, NY, NM, DV, BI, COH, MI, OR, DM, IN	Y: UVA, RP, JHU, USC, NW, IA, MD, CH, WU, FC, PA, UT, CO, SF, WT, SA, GT, NY, NM, DV, BI, MI, MSK N: JAX, WF, FH, AE, SJ, VT, COH, OR, DM, IN	Y: UVA, RP, JHU, USC, NW, JAX, IA, MD, CH, WU, FC, PA, CO, SF, WT, SA , GT, NM, DV, BI, MI, OR, IN N: WF, FH, AE, NY, VT, DM	Y: NE N: RP, JHU, USC, NW, JAX, WF, IA, MD, FH, CH, WU, FC, PA, CO, SF, WT, SA, GT, NY, VT, NM, DV, BI, MI, OR, DM, IN
	Cellular Immunoassays	RP, USC, JAX, MD, FH, CH, CO, SJ, DV, COH, MI, DM	RP, MD, CH, CO, COH, MI	Y: RP, USC, MD, CH, CO, MI, DM N: JAX, FH, SJ, COH	Y: RP, MD, CH, CO, MI, DM N: USC, FH	Y: NW, NE, IA, WU, WT, GT, NM N: RP, JHU, USC, JAX, FH, CH, CO, BI, MI, DM
	Cytokine Analysis	UVA, RP, USC, NW, JAX, MD, FH, CH, WU, PA, CO, DV, COH, MI, DM	RP, USC, NW, MD, FH, CH, COH, MI	Y: UVA, RP, USC, NW, MD, FH, CH, WU, CO, MI, DM N: JAX, PA, COH	Y: UVA, RP, USC, NW, MD, FH, CH, WU, CO, MI N: PA	Y: RP, NE, IA, WT, GT, NM N: JHU, USC, NW, JAX, FH, CH, PA, CO, BI, MI, DM
	ELISA	RP, NW, JAX, MD, FH, CH, PA, DV, MI, DM, MSK	RP, NW, MD, CH, DV, MI	Y: RP, NW , MD, CH, DV, MI, DM N: JAX, FH, PA	Y: RP, NW, MD, DV, MI N: FH	Y: RP, NE, IA, WU, WT, GT, NM N: JHU, NW, JAX, FH, CO, BI, MI, DM
	Hematopoetic Cell Production	MD, FH, CH, DF, WU, PA, CO, OH	MD, CH, DF, WU, OH	Y: CH, WU, OH N: JAX, MD, FH, DF, CO	Y: WU, CO, OH N: MD, FH, DF	Y: RP, NE, IA, WT, NM N: NW, JAX, FH, WU, CO, BI
	Hematopoetic Transplantation Analysis & Production	MD, FH, CH, DF, PA, CO, SJ, OH	MD, CH, DF, OH	Y: CH, OH N: JAX, MD, FH, DF, CO, SJ	Y: CO, OH N: MD, FH, DF	Y: RP, IA, NM N: NW, JAX, FH, CO, BI

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Cell Biology, Immunology & Pathology Services	Immuno-competent Cell Production	RP, MD, FH, CH, DF, WU, PA	RP, MD, CH, DF, WU, PA	Y: RP, CH, WU N: JAX, MD, FH, DF	Y: RP, WU N: MD, FH, DF	Y: RP, IA, WT, NM N: NW, JAX, FH, WU, CO, BI
	Immunohistochemistry	UVA, RP, USC, NW, JAX, NE, IV, MD, FH, CH, DF, AE, FC, PA, UT, CO, SJ, SF, GT, NY, NM, COH, MI, OR, DM, IN, MSK	RP, USC, NW, JAX, IV, MD, FH, CH, DF, AE, FC, SF, GT, NM, MI, OR	Y: UVA, RP, USC, NW, JAX, NE, IV, MD, CH, DF, AE, CO, SF, GT, NY, NM, OR N: FH, FC, SJ, COH, MI, DM, IN	Y: RP, USC, NW, JAX, NE, IV, MD, DF, AE, CO, GT, NM N: FH, FC, SF, NY, MI, OR, DM	Y: JHU, IA, OH N: RP, NW, JAX, IV, FH, FC, CO, SF, GT, NY, NM, BI, MI, OR, DM Maybe: USC
	Immunotyping	RP, USC, JAX, MD, FH, CO, SJ, NM, COH, DM, MSK	RP, JAX, NM	Y: RP, USC, NM N: JAX, MD, FH, CO, SJ, COH, DM	Y: RP, USC, CO, NM N: MD, FH, DM	Y: JHU, NE, IA N: RP, USC, NW, JAX, FH, CH, CO, NM, BI, DM
	MHC Tetramers	RP (purchased, service to strain, analyze), USC, JAX, MD, FH, PA, SJ, COH, DM, MSK	USC, FH	Y: RP, USC, MD, FH N: JAX, PA, SJ, COH, DM	Y: RP, USC, MD N: FH, PA, DM	Y: RP, JAX, NE, IA, FH, CH, OH, WT N: JHU, USC, NW, PA, CO, BI, DM
	Necropsy	RP, JAX*, MD, FH, AE, CO, SJ, DV, COH, MI	RP, JAX, DV, MI	Y: RP, JAX*, DV, MI N: MD, FH, CO, SJ, COH	Y: RP, JAX, CO, DV, MI N: MD, FH	Y: NE, IA, CH, WU, WT N: RP, JHU, NW, JAX, FH, CO, DV, BI, MI
	TCR Analysis	RP, MD, FH, WU, SJ	RP, WU	Y: RP, MD, WU N: JAX, SJ	Y: RP, MD, WU N:	Y: NE, IA , WT N: RP, JHU, NW, JAX, FH, CH, WU, CO, BI
	Veterinary Pathology	NW, JAX, IV-soon, MD, FH, AE, FC, CO, SJ, OH, GT, NY, DV, MI, OR, MSK	MD, FC, DV, MI	Y: MD, FC, NY, DV, MI, MSK N: NW, JAX, FH, CO, SJ, OR	Y: MD, FC, CO, DV, MI N: NW, FH, NY, OR	Y: RP, NE, IA, IV, CH, WU, WT, NM, BI, MI N: JHU, NW, JAX, FH, FC, CO, NY, DV, OR
Molecular & Imaging Services	Animal Imaging	UVA, RP, JHU, NW, JAX, WF, NE, IA, IV, MD, FH, CH, AE, WU, FC, PA, CO, SJ, OH, SF, GT, NY, NM, DV, BI, COH, MI, DM, IN, MSK	UVA, RP, WF, IA, IV, MD, WU, FC, PA, GT, NY, NM, DV, COH, MI, IN	Y: UVA, RP, JAX, WF, IA, IV, MD, WU, FC, CO, GT, NY, NM, DV, BI, MI, IN, MSK N: JHU, NW, NE, FH, PA, SJ, COH	Y: UVA, RP, JAX*, WF, IA, IV, MD, WU, FC, CO, GT, NM, DV, BI, MI, IN N: JHU, NW, NE, FH, PA, NY	Y: RP, IV, MI N: JHU, NW, JAX, WF, IA, FH, WU, FC, PA, CO, WT, GT, NY, NM, DV, BI, IN
	Bioinformatics Analysis	UVA, RP, JHU, NW, JAX, WF, NE, IV, MD, FH, CH, AE, WU, FC, PA, CO, SJ, OH, SF, WT, GT, HI, VT, NM, DV, BI, COH, MI, OR, DM, MSK	RP, JHU, NW, JAX, IV, MD, WU, FC, PA, WT, GT, VT, NM, DV, COH, MI, OR	Y: NW, JAX, NE, IV, WU, CO, WT, GT, NM, DV, COH, MI, OR, MSK N: RP, JHU, WF, MD, FH, FC, PA, SJ, SF, HI, VT	Y: NW, JAX, NE, IV, WU, FC, PA, CO, WT, GT, NM, MI, OR N: RP, JHU, WF, FH, SF, HI, VT, DV, COH	Y: IA, WU, WT, HI N: RP, JHU, NW, JAX, WF, IV, FH, FC, PA, CO, SF, VT, NM, DV, BI, MI, OR
	Cell Analysis	UVA, RP, JHU, JAX, NE, IA, MD, FH, CH, WU, FC, PA, UT, CO, SJ, OH, SF, WT, GT, NY, NM, DV, BI, MI, OR, PD, DM, IN, MSK	UVA, RP, JHU, IA, MD, FH, CH, WU, FC, CO, SF, WT, NY, NM, DV, MI, DM, IN	Y: UVA, RP, IA, MD, CH, WU, UT, CO, SF, WT, NY, NM, DV, MI N: JHU, JAX, NE, FH, FC, SJ, OR, DM, IN	Y: UVA, RP, IA, MD, CH, WU, FC, UT, CO, SF, WT, NM, DV, MI, IN N: JHU, JAX, NE, FH, NY, OR, DM	Y: WT N: RP, JHU, NW, JAX, IA, FH, CH, WU, FC, CO, SF, NY, NM, BI, MI, OR, DM, IN

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Molecular & Imaging Services	Cell Sorting	UVA, RP, JHU, JAX, WF, IA, MD, FH, CH, AE, WU, FC, PA, UT, CO, SJ, OH, SF, WT, GT, NY, NM, DV, BI, COH, MI, OR, PD, DM, IN, MSK	UVA, RP, JHU, JAX, IA, MD, FH, CH, AE, WU, FC, PA, CO, SF, WT, GT, NY, NM, BI, COH, MI, OR, DM, IN	Y: RP, JHU, IA, MD, CH, WU, PA, UT, CO, SF, WT, GT, NY, NM, MI N: JAX, WF, FH, FC, SJ, BI, COH, OR, DM, IN	Y: RP, JHU, JAX, IA, MD, CH, WU, FC, PA, UT, CO, SF, WT, GT, NM, MI, IN N: WF, FH, NY, OR, DM	Y: NE N: RP, JHU, NW, JAX, WF, IA, FH, CH, WU, FC, PA, CO, SF, WT, NY, NM, BI, MI, OR, DM, IN
	Confocal Microscopy	UVA, RP, JHU, USC, NW, JAX, WF, NE, IA, IV, MD, FH, CH, AE, FC, PA, UT, SJ, OH, SF, WT, SA, GT, VT, NM, BI, COH, MI, PD, DM, IN, MSK	UVA, RP, JHU, USC, NW, JAX, IA, IV, MD, FH, CH, AE, FC, UT, SF, WT, GT, VT, NM, BI, COH, MI, DM, IN	Y: UVA, RP, USC, NW, JAX, IA, MD, CH, FC, UT, SF, WT, GT, NM, BI, MI, MSK N: JHU, WF, NE, IV, FH, PA, CO, SJ, SA, VT, COH, DM, IN	Y: UVA, RP, USC, NW, JAX, IA, MD, CH, FC, UT, SF, WT, GT, NM , BI, MI, IN N: JHU, WF, NE, IV, FH, PA, SA, VT, DM	Y: WU, SA N: RP, JHU, USC, NW, JAX, WF, IA, IV, FH, CH, FC, PA, CO, SF, WT, VT, NM, BI, MI, DM, IN
	Deconvolution Microscopy	NW, JAX, IA, FH, CH, AE, FC, UT, SA, GT, NM, COH, MI, IN, MSK	CH, AE, FC, UT, NM, COH, MI, IN	Y: NW, JAX, CH, FC, UT, SA, NM, MI, MSK N: FH, CO, COH, IN	Y: NW, JAX, CH, FC, UT, SA, NM, MI, IN N: FH	Y: RP, MD, WU, WT N: JHU, NW, JAX, IA, FH, CH, FC, CO, SA, NM, BI, MI, IN
	DNA Sequencing	UVA, RP, USC, NW, JAX, WF, NE, IA, IV, MD, FH, CH, AE, WU, FC, PA, UT, CO, SJ, OH, SF, WT, GT, VT, NM, DV, BI, COH, MI, PD, DM, MSK	UVA, RP, USC, NW, JAX, IA, MD, FH, CH, AE, WU, FC, PA, CO, SF, WT, VT, NM, COH, MI, DM	Y: RP, USC, NW , JAX, WF, NE, IA, IV, MD, FH, CH, AE, WU, FC, PA, UT, CO, SF, WT, GT, VT, NM, BI, COH, MI, DM N: SJ	Y: UVA, RP, USC, NW, JAX, WF, NE, IA, MD, FH, CH, AE, WU, FC, PA, UT, CO, WT, GT, VT, NM, BI, MI, DM N:	Y: WU, SF, WT N: RP, JHU, USC, NW, JAX, WF, IA, FH, CH, FC, PA, CO, GT, VT, NM, BI, MI, DM
	Fluorescence Microscopy	UVA, RP, JHU, USC, NW, JAX, WF, NE, IA, IV, MD, FH, CH, DF, AE, FC, PA, UT, SJ, SF, WT, GT, VT, NM, DV, BI, COH, MI, PD, DM, IN, MSK	UVA, RP, JHU, USC, NW, IA, IV, MD, CH, DF, AE, FC, UT, WT, GT, VT, NM, COH, MI, IN	Y: RP, USC, NW, IA, MD, CH, DF, FC, UT, WT, GT, VT, NM, DV, MI, MSK N: JHU, JAX, WF, NE, IV, FH, PA, CO, SJ, COH, DM, IN	Y: RP, USC, NW, IA, MD, CH, DF, FC, UT, WT, GT, NM, MI, IN N: JHU, JAX, WF, NE, IV, FH, PA, VT, DM	Y: N: RP, JHU, USC, NW, JAX, WF, IA, IV, FH, CH, FC, PA, CO, SF, WT, VT, NM, BI, MI, DM, IN
	Gel and Blot Imaging	UVA, RP, JHU, NW, JAX, NE, IV, FH, AE, WU, GT, VT, NM, BI, MI, OR, PD, DM	UVA, RP, FH, AE, WU, VT, NM, MI	Y: UVA, RP, IV, FH, WU, NM, MI, DM N: JHU, NW, JAX, NE, CO, VT, OR	Y: UVA, RP, FH, WU, NM, MI, DM N: JHU, NW, JAX, NE, IV, VT, OR	Y: IA N: RP, JHU, NW, JAX, IV, MD, FH, CH, WT, VT, NM, BI, MI, OR, DM
	Genotyping (SNP and microsatellite)	UVA, RP, USC, NW, JAX, IV, MD, FH, CH, DF, AE, WU, FC, PA, UT, CO, SJ, SF, GT, HI, VT, NM, DV, COH, MI, OR, IN, MSK	UVA, RP, USC, JAX, IV, FH, CH, DF, WU, FC, PA, UT, CO, SF, GT, HI, NM, DV, COH, MI	Y: UVA, RP, NW, IV, MD, FH, CH, DF, WU, FC, PA, UT, CO, SF, GT, HI, NM, DV, COH, MI, OR, MSK N: USC, JAX, SJ, VT, IN	Y: UVA, RP, NW, JAX, IV, MD, FH, CH, DF, WU, FC, PA, UT, CO, GT, HI , NM , DV, MI , OR, IN N: USC, VT	Y: NE, IA, IV, FH, SF, WT N: RP, JHU, USC, NW, JAX, CH, WU, FC, PA, CO, HI, VT, NM, DV, BI, MI, OR, IN
	HPLC	UVA, RP, USC, JAX, IA, IV, MD, FH, CH, AE, FC, PA, SJ, GT, HI, NM, COH, MI, PD, MSK	UVA, RP, USC, IV, MD, FH, FC, HI, NM, COH, MI	Y: RP, USC, IV, MD, FC, HI, NM, COH, MI, MSK N: JAX, FH, CO, SJ	Y: RP, USC, IV, MD, FC, HI, NM , MI N: JAX, FH	Y: NE, WT N: RP, JHU, USC, NW, JAX, IA, IV, FH, WU, FC, CO, HI, NM, BI, MI
	Mass Spectrometry	UVA, RP, JHU, USC, WF, NE, IA, IV, MD, FH, CH, DF, AE, FC, PA, UT, CO, SJ, OH, WT, SA, GT, HI, NY, NM, BI, COH, MI, OR, PD, DM, IN, MSK	UVA, RP, JHU, USC, WF, IV, MD, FH, DF, AE, PA, UT, OH, WT, HI, NY, NM, COH, MI, OR, PD, IN	Y: UVA, RP, USC, WF, NE, IV, MD, FH, DF, AE, FC, UT, CO, OH, WT, SA, HI, NY, BI, COH, MI, PD, IN N: JHU, JAX, PA, SJ, NM, OR	Y: UVA, RP, USC, WF, NE, IV, MD, FH, DF, AE, FC, UT, OH, WT, SA, HI , NY, BI, MI, PD, IN N: JHU, PA, CO, NM, OR	Y: JAX , CO N: RP, JHU, USC, NW, WF, IA, IV, FH, FC, PA, WT, SA, HI, NY, NM, BI, MI, OR, IN

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Molecular & Imaging Services	Microarray	UVA, RP, JHU, NW, JAX, WF, NE, IA, IV, MD, FH, CH, AE, FC, PA, UT, CO, SJ, OH, SF, WT, SA, GT, NY, VT, NM, DV, BI, COH, MI, OR, PD, DM, MSK	UVA, RP, JHU, JAX, IA, IV, MD, FH, CH, AE, FC, PA, UT, OH, SF, WT, NM, DV, BI, COH, MI, OR	Y: UVA, RP, JHU, NW, JAX, NE, IA , IV, MD, FH, CH, AE, FC, PA, UT, CO, OH, SF, WT, SA , NY, NM, DV, BI, MI, OR, DM, MSK N: WF, SJ, VT, COH	Y: UVA, RP, JHU, NW, JAX, NE, IA, IV, MD, FH, CH, AE, FC, PA, UT, CO, OH, SF, WT, SA, NM, DV, BI, MI, OR, DM N: WF, NY, VT	Y: WU, WT, VT, DM N: RP, JHU, NW, JAX, WF, IA, IV, FH, CH, FC, PA, CO, SF, SA, NY, NM, DV, BI, MI, OR
	Peptide Synthesis	UVA, RP, JHU, USC, WF, MD, CH, AE, PA, UT, SJ, BI, COH, MSK	UVA, RP, MD, UT, COH	Y: UVA, RP, USC, WF, MD, UT, COH, MSK N: JAX, CO, SJ	Y: UVA, RP, USC, WF, MD, UT N: CO	Y: JAX, NE, IA, FH, WT, GT, NM N: RP, JHU, NW, WF, CO, BI Maybe: USC
	Protein Identification / characterization	UVA, RP, JHU, USC, JAX, WF, NE, IV, MD, FH, CH, DF, AE, PA, UT, CO, SJ, OH, SF, WT, GT, NY, BI, COH, MI, OR, IN, MSK	UVA, RP, JHU, IV, MD, FH, DF, PA, UT, OH, WT, NY, COH, MI, IN	Y: UVA, RP, USC, WF, NE, IV, MD, FH, DF, UT, OH, SF, WT, NY, COH, MI, IN, MSK N: JHU, JAX, PA, CO, SJ, OR	Y: UVA, RP, USC, WF, IV, MD, FH, DF, UT, OH, SF, WT, NY, MI, IN N: JHU, PA, CO, OR	Y: JAX, IA , CO, NM N: RP, JHU, NW, WF, IV, FH, PA, SF, WT, NY, BI, MI, OR, IN Maybe: USC
	Real-time PCR	UVA, RP, JHU, NW, JAX, NE, IA, IV, MD, FH, CH, AE, WU, FC, PA, UT, CO, OH, SF, WT, SA, GT, NY, VT, NM, DV, BI, COH, MI, DM, IN, MSK	UVA, RP, JAX, IA, MD, FH, CH, FC, UT, CO, OH, SF, NY, VT, NM, DV, COH, MI	Y: UVA, RP, NW, IA, MD, CH, FC, UT, OH, SF, WT, NY, NM, DV, MI, DM, MSK N: JHU, JAX, NE, IV, FH, WU, CO, SA, VT, COH, IN	Y: UVA, RP, NW, IA, MD, CH, WU, FC, UT, CO, OH, SF, WT, NM, DV, MI, DM, IN N: JHU, JAX, NE, IV, FH, SA, NY, VT	Y: N: RP, JHU, NW, JAX, IA, IV, FH, CH, WU, FC, CO, SF, WT, SA, NY, VT, NM, DV, BI, MI, DM, IN
	Scanning Electron Microscopy	UVA, RP, USC, JAX, WF, NE, IA, IV, MD, FH, CH, AE, FC, PA, UT, SJ, GT, VT, NM, COH, MI, MSK	UVA, RP, USC, JAX, WF, IA, MD, FH, AE, PA, VT, NM, COH, MI	Y: UVA, RP, USC, JAX , WF, NE, IA, MD, FH, AE, FC, PA, UT, GT, NM, COH, MI N: IV, CO, SJ, VT	Y: UVA, RP, USC, JAX, WF, IA, MD, FH, AE, FC, UT, GT, NM, MI N: NE, IV, PA, CO, VT	Y: USC, NW, MD, WU, WT N: RP, JHU, JAX, WF, IA, IV, FH, FC, PA, CO, VT, NM, BI, MI
	Transmission Electron Microscopy	UVA, RP, USC, NW, JAX, WF, IA, IV, MD, FH, CH, AE, FC, PA, UT, SJ, WT, GT, VT, NM, BI, COH, MI, MSK	UVA, RP, USC, JAX, WF, IA, MD, FH, CH, AE, FC, WT, VT, NM, COH, MI	Y: UVA, RP, USC, NW, JAX, WF, IA, MD, FH, CH, AE, FC, UT, WT, GT, NM, COH, MI N: IV, CO, SJ, VT	Y: UVA, RP, USC, NW, JAX, WF, IA, MD, FH, CH, AE, FC, UT, WT, GT, NM, MI N: IV, CO, VT	Y: MD, WU, WT N: RP, JHU, USC, NW, JAX, WF, IA, IV, FH, CH, FC, CO, VT, NM, BI, MI
Human Subject Study Services	Data Collection and Management	UVA, RP, JHU, USC, NW, WF, NE, IA, IV, MD, FH, CH, DF, AE, WU, FC, PA, UT, CO, SJ, GT, HI, NY, VT, NM, DV, COH, MI, OR, DM, IN	RP, USC, NW, IV, FH, WU, FC, UT, CO, VT, NM, DV, COH, MI, OR, IN	Y: NE, FH, WU, UT, CO, NM, DV, COH, MI N: UVA, RP, JHU, USC, NW, WF, IA, IV, MD, DF, FC, PA, SJ, HI, NY, VT, OR, IN	Y: NE, FH, WU, FC, UT, CO, HI, NM, DV, MI, IN N: UVA, RP, JHU, USC, NW, WF, IA, IV, MD, DF, PA, NY, VT, OR	Y: RP (excluding clinical research services), DV N: JHU, USC, NW, WF, IA, IV, FH, WU, FC, PA, CO, HI, NY, VT, NM, BI, MI, OR, IN
	Dietary Assessment	RP, FH, SJ, HI, MI	RP, FH, HI	Y: RP, FH, HI, MI N: CO, SJ	Y: RP, FH, HI, MI N: CO	Y: WF, NE, IA, FC N: RP, NW, MD, FH, CO, HI, BI, MI
	Exercise Studies	FH, MI	FH	Y: MI N: FH, CO	Y: MI N: FH, CO	Y: IA, FC N: NW, MD, FH, CO, BI, MI

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Human Subject Study Services	Feeding Studies	RP, FH	RP, FH	Y: N: RP, FH, CO	Y: N: RP, FH, CO	Y: IA, FC N: RP, NW, MD, FH, CO, BI
	Oncology Clinical Trials Support	UVA, RP, JHU, USC, NW, WF, NE, IA, IV, MD, FH, CH, DF, AE, WU, FC, PA, UT, CO, SJ, OH, SF, GT, HI, NY, VT, NM, DV, COH, MI, OR, DM, IN	RP, JHU, USC, NW, IV, MD, FH, CH, FC, UT, CO, GT, VT, NM, DV, COH, MI, OR, IN	Y: RP, USC, NE, WU, UT, GT, DV, COH, MI N: JHU, NW, IA, IV, MD, FH, CH, DF, FC, PA, SJ, SF, HI, NY, VT, NM, OR, IN	Y: RP, USC, NE, WU, FC, CO, GT, HI, DV, IN N: UVA, JHU, NW, IA, IV, MD, FH, CH, DF, PA, SF, NY, VT, NM, MI, OR	Y: DV N: RP, JHU, NW, IA, IV, FH, CH, WU, FC, PA, CO, SF, HI, NY, VT, NM, BI, MI, OR, IN
	Prevention Center – Research Clinic	RP, MD, FH, UT, CO, GT, NM, DV, MI	MD, UT, CO, NM, DV, MI	Y: UT, CO, DV, MI N: MD, FH, NM	Y: UT, CO, DV, MI N: RP, MD, FH, NM	Y: NE, IA N: RP, USC, NW, FH, CO, NM, DV, BI, MI
	Programming, Database Design and Development	RP, JHU, NW, IV, MD, FH, CH, AE, WU, FC, PA, UT, CO, SJ, SF, GT, NM, DV, COH, MI, IN	RP, NW, IV, MD, FH, WU, FC, PA, UT, GT, NM, DV, COH, MI	Y: FH, UT, GT, NM, DV, COH, MI N: RP, JHU, NW, IV, MD, WU, FC, PA, CO, SJ, IN	Y: FH, WU, FC, UT, GT, NM, DV, MI, IN N: RP, JHU, NW, IV, MD, PA, CO	Y: NE, IA, IV, MI N: RP, JHU, NW, FH, CH, WU, FC, PA, CO, NM, DV, BI, IN
	Technology & Scientific Project Management	RP, JHU, IV, MD, FH, CH, WU, UT, NM, MI	IV, MD, WU, UT, NM, MI	Y: WU, UT N: RP, JHU, IV, MD, FH, CH, CO, NM, MI	Y: WU, UT N: RP, JHU, IV, MD, FH, CH, CO, NM, MI	Y: IA N: RP, JHU, NW, IV, FH, CH, WU, CO, NM, BI, MI
	Telephone Interviewing	RP, JHU, IV, FH, CO, SJ, NM	RP, FH, CO, NM	Y: RP, FH, CO N: JHU, IV, SJ, NM, IN	Y: RP, FH, CO, IN N: JHU, IV, NM	Y: NE, IA, CH, FC, SF N: RP, JHU, NW, IV, MD, FH, CO, NM, BI, IN
	Tissue Procurement and Banking	UVA, RP, JHU, USC, NW, WF, NE, IA, IV, MD, CH, AE, WU, FC, UT, CO, SJ, OH, SF, GT, NY, VT, NM, DV, COH, MI, OR, IN, MSK	RP, USC, NW, IV, MD, CH, WU, FC, UT, CO, OH, SF, NM, DV, COH, MI, OR	Y: UVA, RP, USC, NE, IA, IV, CH, WU, UT, CO, OH, NY, NM, DV, MI, OR N: JHU, NW, WF, MD, FC, SJ, SF, VT, COH Maybe: IN	Y: RP, USC-limited space, NE, IA, IV, CH, WU, FC, UT, CO, OH, NM, DV, OR, IN N: UVA, JHU, NW, WF, MD, SF, NY, VT, MI	Y: UVA, WT, VT, DV, BI N: RP, JHU, USC, NW, WF, IA, IV, FH, WU, FC, CO, SF, NY, NM, MI, OR, IN
	Tracking Subjects	RP, JHU, USC, WF, IA, IV, MD, FH, DF, WU, UT, CO, SJ, GT, NY, NM, DV, COH, MI, DM	RP, IV, FH, DF, UT, CO, NM, COH, MI	Y: RP, IV, FH, UT, CO, DV, MI N: JHU, USC, WF, MD, DF, WU, SJ, NY, NM, COH, MI, IN	Y: RP, IV, FH, UT, CO, DV, IN N: JHU, USC, WF, MD, DF, WU, NY, NM, MI	Y: FC N: RP, JHU, USC, NW, WF, IA, IV, FH, WU, CO, NY, NM, DV, BI, MI, IN
Laboratory Support Services	Animal Imaging	UVA, RP, JHU, NW, JAX**, WF, NE, IA, MD, FH, CH, AE, WU, FC, PA, CO, SJ, OH, WT, NY, DV, BI, MI, DM, IN, MSK	UVA, RP, JAX, WF, IA, MD, WU, FC, PA, DV, MI, IN	Y: UVA, RP, JAX, WF, IA, MD, WU, FC, CO, OH, NY, DV, BI, MI, DM, IN N: JHU, NW, NE, FH, PA, SJ, WT	Y: UVA, JAX, WF, IA, MD, WU, FC, CO, OH, DV, BI, MI, DM, IN N: RP, JHU, NW, NE, FH, PA, WT, NY	Y: RP, MI N: UVA, JHU, NW, JAX, WF, IA, IV, FH, WU, FC, PA, CO, WT, NY, DV, BI, DM, IN
	Animal Husbandry and Veterinary Services	RP, JHU, NW, JAX, IV, MD, FH, CH, AE, FC, CO, SJ, OH, WT, VT, DV, BI, COH, MI, MSK	RP, JAX, IV, MD, FH, CH, FC, WT, DV, COH, MI	Y: RP, JAX , IV, CH, OH, WT, DV, MI N: JHU, NW, IA, MD, FH, FC, CO, SJ, VT, COH, IN	Y: RP, JAX, CH, CO, OH, WT, DV, MI N: JHU, NW, IA, IV, MD, FH, FC, VT, IN	Y: N: RP, NW, JAX, IA, IV, FH, CH, FC, CO, WT, VT, DV, BI, MI, IN

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Laboratory Support Services	Transgenic / Knockout Mice	UVA, RP, USC, NW, JAX, NE, IV, MD, FH, CH, AE, FC, PA, UT, CO, SJ, OH, WT, SA, NY, VT, DV, BI, COH, MI, OR, PD, DM, IN, MSK	RP, USC, JAX, IV, MD, CH, FC, PA, UT, WT, VT, DV, COH, MI, OR, PD, IN	Y: UVA, RP, USC, JAX, NE, IV, MD, CH, FC, UT, CO, OH, WT, SA, NY, DV, COH, MI, OR, PD, DM, IN, MSK N: NW, IA, FH, PA, SJ, VT	Y UVA, RP, USC, JAX, NE, MD, CH, FC, UT, CO, OH, WT, SA, DV, MI, PD, DM, IN N: NW, IA, IV, FH, PA, NY, VT, OR	Y: FH, VT, DM N: RP, USC, NW, JAX, IA, IV, CH, FC, PA, CO, WT, SA, NY, DV, BI, MI, OR, IN
	NOD / SCID Mice	RP, NW, JAX, MD, FH, CH, AE, FC, CO, SJ, OH, WT, BI, IN, MSK	RP, JAX, FC, IN	Y: RP, JAX, MD, CO, OH, WT N: NW, IA, FH, FC, SJ, IN	Y: RP, JAX, MD, CO, OH, WT, IN N: NW, IA, FH, FC	Y: IA, IV, FH, WT N: RP, NW, JAX, FC, CO, BI, IN
	Research Animal Technical Services	UVA, RP, JHU, NW, JAX, MD, FH, CH, AE, FC, UT, CO, SJ, WT, VT, DV, BI, MI, MSK	RP, JAX, MD, FH, FC, WT, DV, MI	Y: UVA, RP, JAX, UT, CO, WT, DV, MI, MSK N: JHU, NW, IA, MD, FH, FC, SJ, VT, IN	Y: RP, JAX , CO, WT, DV, MI N: JHU, NW, IA, MD, FH, FC, VT, IN	Y: IV N: RP, JHU, NW, JAX, IA, FH, FC, CO, WT, VT, DV, BI, MI, IN
	Tissue Culture Supplies	UVA, RP, USC, JAX, WF, IA, IV, MD, FH, AE, FC, PA, UT, CO, WT, OR, MSK (media)	RP, USC, IA, MD, FC, WT, OR	Y: RP, USC, IA, IV , PA, UT, CO N: JAX, WF, MD, FH, FC, WT, OR, IN	Y: RP, USC, IA, IV, FC, CO, IN N: JAX, WF, MD, FH, PA, WT, OR	Y: USC, IV N: RP, JHU, NW, JAX, WF, IA, FH, FC, PA, CO, WT, BI, OR, IN
Library, Computing and Graphic Services	Analytical Software	RP, JAX, FH, CH, AE, WU, FC, WT, VT, BI, MI, OR, MSK	RP, JAX, WU, FC, WT, MI, OR	Y: JAX, WU, WT, MI, OR N: RP, FH, CH, FC, CO, VT	Y: JAX, WU, FC, MI N: RP, FH, CH, WT, VT, OR	Y: WF, IA, MD, FH, OH, WT, VT, MI N: RP, NW, JAX, CH, WU, FC, CO, BI, OR
	Biostatistics	UVA, RP, USC, NW, JAX, WF, NE, IA, IV, MD, FH, CH, DF, AE, FC, UT, CO, SJ, OH, SF, WT, HI, VT, DV, COH, MI, OR, DM, IN, MSK	RP, USC, NW, JAX, WF, FH, CH, DF, FC, UT, CO, OH, HI, VT, DV, COH, MI, OR, DM	Y: UVA, JAX, NE , CH, UT, MI, OR N: RP, USC, NW, WF, IA, MD, FH, DF, FC, CO, SJ, SF, WT, HI, VT, DV, COH, DM, IN	Y: USC, JAX, NE, CH, FC, UT, HI, DV, MI, OR, IN N: RP, NW, WF, IA, MD, FH, DF, CO, SF, WT, VT, DM	Y: UVA, OH, WT, BI N: RP, USC, NW, JAX, WF, IA, FH, CH, FC, CO, SF, HI, VT, DV, MI, OR, DM, IN
	Computing Lab	RP, JAX, MD, FH, AE, FC, WT, BI, MI, MSK	RP, FH, FC, WT, MI	Y: RP, WT, MI N: JAX, MD, FH, FC, CO	Y: RP, FC, WT, MI N: JAX, MD, FH	Y: IA, OH N: RP, NW, JAX, FH, FC, CO, WT, BI, MI
	Graphic Design and Posters	RP, JAX, NE, MD, FH, DF, FC, SJ, BI, MI, MSK	RP, JAX, DF, FC, MI	Y: NE, FC, BI, MI N: RP, JAX, MD, FH, DF, CO, SJ, IN	Y: RP, FC, BI, MI, IN N: JAX, NE, MD, FH, DF	Y: IV, OH, WT N: RP, NW, JAX, IA, FH, FC, CO, BI, MI, IN
	High Performance Computing	RP, JAX, FH, AE, WU, FC, UT, SJ, WT, VT, BI, MI, MSK	RP, FH, WU, FC, UT, VT	Y: RP, UT, WT N: JAX, MD, FH, WU, FC, CO, SJ, VT, MI	Y: RP, JAX, WU, FC, WT N: FH, VT, MI	Y: JAX, IA, IV, MD, OH, WT, VT N: RP, NW, FH, WU, FC, CO, BI, MI
	Interlibrary Loan	RP, JAX, NE, MD, FH, CH, FC, UT, WT, BI, MSK	JAX, CH, FC, WT	Y: JAX, CH, FC, WT N: RP, NE, MD, CO	Y: JAX, CH, FC, WT N: RP, MD, FH	Y: JAX, IV, FH, OH, WT N: RP, NW, IA, CH, FC, CO, BI
	Online Databases & Journals	UVA, RP, JAX, NE, MD, FH, CH, FC, UT, SJ, WT, BI, COH, MSK	JAX, FH, CH, FC, BI	Y: JAX, CH, FC, WT N: RP, NE, MD, FH, CO, SJ, BI, COH	Y: JAX, MD, CH, FC, WT N: RP, FH	Y: RP, JAX, IV, OH N: NW, IA, FH, CH, FC, CO, WT, BI
	Photography and Digital Imaging	RP, USC, JAX, MD, FH, AE, FC, SJ, WT, BI, MI, MSK	RP, USC, FC, WT	Y: USC, FC, WT, MI N: RP, JAX, MD, FH, CO, SJ	Y: RP, USC, JAX, FC, WT, MI N: MD, FH	Y: IV, OH N: RP, USC, NW, JAX, IA, FH, FC, CO, WT, BI, MI

	Services	Which of these services do you currently provide?	Which of these are you particularly strong in?	Would you be willing to provide this service for a fee to other centers?	Do you have adequate capacity / could you expand to address expanded usage?	If these services were available from another cancer center, would you be a customer?
Library, Computing and Graphic Services	Programming, Database Design and Development	RP, NW, JAX, IV, MD, FH, CH, WU, FC, UT, WT, BI, MI, MSK	RP, NW, JAX, IV, FH, WU, FC, UT, WT, MI	Y: RP, FH, WU, UT, WT, MI N: NW, JAX, IV, MD, FC, CO	Y: RP, WU, FC, UT, WT, MI N: NW, JAX, IV, MD, FH	Y: RP, IA, IV, FH, OH, WT N: NW, JAX, WU, FC, CO, BI, MI
	Scientific Application Hosting	RP, JAX, MD, FH, FC, UT, WT, BI, MI	FC, UT, WT, MI	Y: RP, UT, WT, MI N: JAX, FH, FC, CO	Y: RP, FC, UT, WT, MI N: JAX, FH	Y: JAX, IV, MD, OH, WT N: RP, NW, IA, FH, FC, CO, BI, MI
	Slide Production	RP, JAX, MD, FH, BI, MSK	RP, JAX	Y: N: RP, JAX, MD, FH, CO	Y: RP N: JAX, MD, FH	Y: IV, WT N: RP, NW, JAX, IA, FH, CO, BI

*The Jackson Laboratory could more easily provide necropsy services (on mice only) for animals available from their production services—other animals would have to be shipped and possibly imported and bred depending on the specific research needs.

**The Jackson Laboratory could more easily provide imaging services (on mice only) for animals available from their production services—other animals would have to be imported and bred before the specific research service could be carried out.

Key	Cancer Center
UVA	University of Virginia
RP	Roswell Park
JHU	Johns Hopkins University
USC	University of Southern California
NW	Northwestern University
JAX	Jackson Laboratory
WF	Wake Forest University
NE	University of Nebraska
IA	University of Iowa
IV	University of California-Irvine
MD	MD Anderson Cancer Center
FH	Fred Hutchinson Cancer Research Center
CH	University of Chicago
DF	Dana Farber/Harvard Cancer Center
AE	Albert Einstein College of
WU	Washington University-St. Louis
FC	Fox Chase Cancer Center
PA	University of Pennsylvania
UT	University of Utah, Huntsman Cancer Center
CO	University of Colorado

Key	Cancer Center
SJ	St. Jude Children's Research Hospital
OH	Ohio State University
SF	University of California, San Francisco
WT	Wistar Institute
SA	Salk Institute
GT	Georgetown University
HI	University of Hawaii
NY	New York University
VT	Vermont Cancer Center
NM	University of New Mexico
DV	University of California, Davis
BI	Burnham Institute
COH	City of Hope National Medical Center
MI	University of Michigan
OR	Oregon Cancer Institute
PD	Perdue University Cancer Center
DM	Dartmouth: Norris Cotton Cancer Center
IN	Indiana University Cancer Center
MSK	Memorial Sloan Kettering Cancer Center

The Burnham Institute's Cancer Center in La Jolla, CA, has specialized expertise and high-end technologies that focuses on various aspects of chemical biology research and early-stage drug discovery. We currently have adequate capacity and/or could expand the following services to provide them for a fee to other Centers:

(1) Protein Expression for large-scale production and purification of multi-milligram quantities of recombinant protein in bacterial, yeast, insect and eukaryotic cell systems;

(2) Chemical Library Screening, which provides access to a ~200,000 compound library and fully integrated, robotic liquid handling systems for HT screening using either biochemical or cell-based assays;

(3) In silico Screening/Computational Modeling, which utilizes a dedicated Linux cluster, and applies docking algorithms for screening a virtual library of >1 million compounds for hits against protein targets when a high quality 3-dimensional structure is available;

(4) High-Throughput Microscopy, which houses several HT microscopes for cell-based screens using high-content imaging, along with supporting software for automated image analysis;

(5) NMR, which includes a 500 MHz instrument equipped with automatic sample changer for applying chemical compounds to protein targets, in addition to a 300 MHz instrument dedicated for chemical compound structure determination, and a 600 MHz instrument for protein structure determination, as well as supporting computer workstations and software for data analysis;

(6) X-ray Crystallography, which provides x-ray diffractometers and supporting computer workstations and software for determination of protein/chemical compound complexes at atomic resolution;

(7) Medicinal Chemistry, which performs contract-based synthesis and purification of analogs of compounds using medicinal chemistry approaches, including using structure-based methods for guiding medicinal chemistry efforts;

(8) Functional Genomics, which consists of HTS-formatted siRNA libraries.

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Notes

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