

# Professional Judgment Budget Proposal for Fiscal Year 2025

#### - TABLE OF CONTENTS -

#### DIRECTOR'S MESSAGE & PROFESSIONAL JUDGMENT BUDGET PROPOSAL

<b>«</b>	Director's Message	.2
«	NCI Professional Judgment Budget Proposal	.4

#### **RESEARCH PORTFOLIO**

« NCI Research Portfolio: Driving Discovery to End Cancer as We Know It......8

#### **HIGHLIGHTED SCIENTIFIC OPPORTUNITIES**

<b>«</b>	Improving Patients' Lives through Symptom Science	13
«	Revolutionizing Cancer Clinical Trials	14
<b>«</b>	Clarifying the Impact of the Environment on Cancer Risk	15
<b>«</b>	Harnessing the Power of Cancer Data	<b>16</b>
<b>«</b>	Unraveling the Complexity of Cancer Metastasis	17

#### **STORIES OF CANCER RESEARCH**

<b>«</b>	Enrolling in a Clinical Trial in Rural America	. 18
«	Engaging Primary Care Providers in Cancer Survivorship Care	20



## **DIRECTOR'S MESSAGE**

Cancer is one of the greatest health challenges we face. It remains the number two killer in the United States, with nearly two million new cases of cancer diagnosed each year. Today, there are more than 18 million cancer survivors, and as each family affected by cancer knows, the disease often touches every aspect of a patient's life. For so many people with cancer, that means treatments that can be as toxic as the disease. Many others have limited treatment options or face significant societal barriers to care.

Yet the future holds great potential for preventing cancer or changing the meaning of a cancer diagnosis for an individual, their family, and their community. President Biden has set forth ambitious goals to end cancer as we know it for all people through the Cancer Moonshot<sup>SM</sup>. By aiming to decrease the overall cancer death rate at least 50% by 2047 and improving cancer care for everyone, that vision is within reach.

To succeed, we must accelerate progress for the most common cancers and confront those for which significant headway remains elusive, such as pancreatic cancer, glioblastoma, and certain childhood cancers. Moreover, we must eliminate inequities that contribute to worse outcomes for certain populations, especially Black Americans, people living in rural communities, and others who have not benefited from the progress made against cancer.

This year, in partnership with organizations across the cancer community, NCI released a National Cancer Plan as a framework to accelerate progress. This rallying cry for action challenges everyone to find new strategies that leverage existing solutions to reach all people, while investing in research to identify, develop, and implement new approaches to prevent, detect, and treat cancer early, and turn all cancers into treatable diseases.

NCI employs an important strategy to make it easier for people to participate in cancer research: bringing clinical trials to where people live through the NCI Community Oncology Research Program (NCORP). Kellie's story, featured in this Fiscal Year 2025 Professional Judgment Budget Proposal, is emblematic of this strategy. Kellie, who was diagnosed with stage III non-small cell lung cancer, lives in a small town, hours away from major cancer centers. Thanks to NCORP, she receives treatment and contributes to research through a clinical trial close to home, without the hardship of long-distance travel. When cancer research has the resources to eliminate obstacles that hinder people's participation, we can find solutions that work for all who need them.

NCI, the largest funder of cancer research in the world, is the engine that drives progress. Institutions across the cancer research community—such as the 72 NCI-Designated Cancer Centers, 2,200 National Clinical Trials Network sites, and 46 NCORP network sites with more than 1,000 practices nationwide—depend on NCI's support to unlock basic biological understanding of cancer, turn that knowledge into potential new approaches against cancer, and test whether these approaches work for all populations.

Through major investments in data infrastructure, NCI enables researchers across the country to access critical data and technology they need to find answers. These valuable resources include the

Cancer Research Data Commons, Childhood Cancer Data Initiative, and human tumor atlases. NCI training programs, in turn, produce a pipeline of researchers that contributes diverse talent to institutions nationwide, allowing us to meet the promise of all opportunities and discover lifesaving advances.

To seize today's opportunities, we need to fully power the cancer research enterprise. This Fiscal Year 2025 Professional Judgment Budget Proposal outlines the investments required to make bold progress by taking full advantage of the incredible body of knowledge and scientific resources we have available to us. This foundation, built on years of sustained support, allows for the pursuit of basic science to provide the comprehensive biological understanding we still need for many cancers. It is also the basis for research programs that turn knowledge gained into answers that help many more people overcome cancer's devasting challenges.

By funding cancer research as described in this proposal, we can capitalize on critical scientific opportunities, continue to lessen the impact of the past two decades of inflation that have eroded the purchasing power of NCI's budget by a staggering \$1.1 billion, and ensure that all people can benefit from our advances.

This proposal highlights five scientific opportunities that stand out as catalysts for progress:

- improving patients' lives through symptom science to better understand how to deliver optimal care and decrease the harsh effects of treatment
- revolutionizing cancer clinical trials to more rapidly identify effective approaches for all cancer types and all people
- clarifying the impact of the environment on cancer risk, which is critical to finding ways to reduce the threat of cancers caused by environmental exposures
- harnessing the power of cancer data from every laboratory experiment, clinical trial, and patient experience to enable us to find answers that have long eluded us
- unraveling the complexity of cancer metastasis in the body, a process responsible for most cancer deaths, so we can find ways to stop it

NCI's support for cancer research has led to many important breakthroughs for patients. The **progress** made against lung cancer, the leading cause of cancer death in the United States, is an excellent example. NCI-supported research played a vital role in developing targeted therapies responsible for the recent twofold decline in deaths from non-small cell lung cancer, the most common type of lung cancer.

Through basic science and immunology studies, NCI also laid the foundation for the development of immune checkpoint inhibitors to enhance the body's immune response against cancer. Several of these inhibitors are now approved for treating lung cancer and have substantially improved outcomes for many people with non-small cell lung cancer.

In addition, NCI supported the development of an exciting new type of targeted therapy that was approved by the Food and Drug Administration in 2021. This advance shows great promise for treating cancers resistant to other therapies, including lung cancer and other challenging diseases such as pancreatic cancer. Expanding these investments will lead to more new treatments and offer hope to many more people still at risk of having time with their loved ones cut tragically short.

For the sake of all those whose lives are affected by cancer, we must seize upon the considerable scientific opportunities before us and break down barriers to cancer prevention and care. To achieve this, we need strong and sustained investments in cancer research to illuminate a path forward and ensure that no one facing cancer is left behind.



### Dr. Monica Bertagnolli

Director National Cancer Institute

# **NCI PROFESSIONAL JUDGMENT BUDGET PROPOSAL**

Robust and sustained increases in funding for cancer research are needed to meet the Cancer Moonshot<sup>™</sup> goal of reducing cancer death rates by 50% over the next 25 years. Age-adjusted cancer death rates in the United States have declined about 2% per year since 2015, but this progress is not fast enough. We must accelerate the decline in cancer death rates to reach the 50% goal by 2047.

This Professional Judgment Budget Proposal presents NCI's assessment of the funding needed in fiscal year 2025 (FY25) to support readily obtainable research opportunities and accelerate progress to benefit all people with cancer and those at risk. In addition to supporting new avenues of discovery, funding for cancer research must also keep pace with increasing research costs, including the costs of training the next generation of cancer researchers and clinicians, and the costs of supporting critical research infrastructure.

### NCI FISCAL YEAR 2025 (FY25) PROFESSIONAL JUDGMENT BUDGET PROPOSAL

Prior (FY24) Professional Judgment Budget Proposal	\$9,988*	
Proposed Budget Increase for FY25	\$1,478	<ul> <li>\$518 Cancer Biology Research</li> <li>\$161 Cancer Prevention Research</li> <li>\$240 Cancer Detection &amp; Diagnosis Research</li> <li>\$338 Cancer Treatment Research</li> <li>\$111 Public Health &amp; Cancer Control Research</li> <li>\$110 Training &amp; Infrastructure</li> </ul>
FY25 TOTAL	\$11,466	

(DOLLARS IN MILLIONS)

\*This proposal includes \$1,581 million for the Cancer Moonshot and \$50 million for the 6th year of the Childhood Cancer Data Initiative.

# How the cost of conducting cancer research affects the pace of progress

NCI is the largest funder of cancer research in the world, supporting research project grants, training programs, and infrastructure that lead to an in-depth understanding of cancer and innovative prevention, screening, and treatment strategies. However, the increasing cost of research and clinical trials has significantly eroded NCI's ability to fund research by reducing the buying power of NCI's budget. In fact, based on the Biomedical Research and Development Price Index (BRDPI), NCI has 13% less buying power than it did 20 years ago. That 13% reduction translates to a budget that can fund \$1.1 billion less research in 2023 than it did in 2003.

**Biomedical Research and Development Price Index (BRDPI)**: A projection that indicates how much the National Institutes of Health (NIH) budget must increase to maintain purchasing power. The BRDPI was developed and is updated annually by the Department of Commerce's Bureau of Economic Analysis, under an interagency agreement with NIH.

### NCI'S RESEARCH BUYING POWER IS \$1.1 BILLION LESS THAN 20 YEARS AGO



\*Biomedical Research and Development Price Index

<sup>†</sup>Actual Annual Budget excludes funds from the American Recovery & Reinvestment Act and 21st Century Cures Act

This budget deficit affects NCI's ability to fully fund its research portfolio at a time when new opportunities in cancer research have led to a tremendous surge in research project grant applications to NCI. In recent years, R01 grant applications to NCI have accounted for almost one-fifth of all R01 applications received by NIH. Moreover, the growth of NCI R01 applications over the last 10 years is almost 3 times that of the rest of NIH combined. This burst of interest in cancer research, coupled with increasing biomedical research costs, has outstripped NCI's ability to fund these new opportunities. As a result, it is difficult for NCI to optimally support cancer research, train future researchers, and expand and maintain research infrastructure.

Despite reduced buying power, recent budget increases have allowed NCI to increase the nation's investment in investigator-initiated research and fund more R01 applications. In FY23, NCI received a nearly 6% budget increase that supported investments across the institute's portfolio, including a one percentile increase in the R01 payline—that is, the percentile cutoff point of peer reviewed R01 applications that NCI intends to fund in a given fiscal year—to the 12th percentile. This increase will fund 100 additional R01 and early-stage investigator awards.

Making those commitments to new grants in addition to multiyear funding commitments for grants, research and development contracts, and infrastructure has significant, long-term budget implications. So, despite the budget increase from a supportive Congress, NCI still faced difficult choices: having to balance the increased investment in R01 grants with other demands for investment, including clinical trials, training programs, and research infrastructure.

For example, to increase the number of new investigator-initiated R01 grants, NCI reduced the budgets of continuing noncompeting grants—that is, years 2 through 5 of a typical 5-year grant. These reductions affected investigators who must alter their research plans while managing the increasing costs of conducting research in this era of higher inflation. This slows cancer research progress and its benefits to all people. Also, there remain significant numbers of meritorious applications that NCI cannot fund. This means that we are missing opportunities that could translate into advances for people with cancer and those at risk for the disease.

# Increasing investments in training, infrastructure, and investigator-initiated research

Investigators conducting RO1 and other NCI-funded research projects don't do so alone or in a vacuum. They depend on, among other things, graduate students and postdoctoral fellows supported by NCI training programs, research infrastructure that exists at NCI-Designated Cancer Centers, and NCIsupported resources such as biospecimen repositories and cancer data commons. These critical parts of the cancer research enterprise require funding on top of investigator-initiated, grant-supported research.

The funding requested in this FY25 Professional Judgment Budget Proposal would allow NCI to make needed investments in training the next generation of diverse cancer researchers and supporting key infrastructure, such as:

- the K99/R00 Pathway to Independence Award supporting researchers through completion of mentored training and transition to independent investigators
- the Early Investigator Advancement Program helping scientists from diverse backgrounds progress to independent investigators
- the NCI-Designated Cancer Centers Program treating people with cancer, facilitating laboratory and clinical research, and training researchers and health care professionals at 72 centers in communities across the United States
- NCI's clinical trials networks enabling people to participate in research studies at over 2,500 academic and community sites across the United States
- the Surveillance, Epidemiology, and End Results (SEER) Program providing information on cancer statistics to inform research and programs to reduce the cancer burden
- the Cancer Research Data Commons, a cloud-based data science infrastructure, providing secure access to large, comprehensive, and expanding collections of cancer data

Today's investments in basic cancer research establish the foundation for tomorrow's breakthroughs, and NCI's portfolio must continue to grow through annual inflation-adjusted increases if we are to succeed in the goal to end cancer as we know it for all people. This FY25 Professional Judgment Budget Proposal would allow NCI to raise the R01 payline to the 15th percentile, and to capitalize on scientific opportunities to prevent, detect, and treat cancer, while growing and diversifying the cancer research workforce. This budget would also support a heightened level of research grant support with necessary investments in research infrastructure that keep pace with inflation and drive the National Cancer Program to deliver on the goals of the National Cancer Plan.

### The Cancer Moonshot beyond the 21st Century Cures Act

This NCI FY25 Professional Judgment Budget Proposal includes a little over \$2 billion to support the ambitious but attainable goals of the next phase of the Cancer Moonshot, which will benefit patients through improved and equitable cancer prevention, screening, and treatment. This request will allow NCI to make new investments in several key areas, including cancer clinical trials and data infrastructure, while building on the success of the 21st Century Cures Act funding.

Cancer Moonshot research initiatives, supported by \$1.8 billion of 21st Century Cures Act funding over a 7-year period ending in FY23, are delivering important insights into the mechanisms that drive cancer. This includes addressing cancer disparities, identifying evidence-based strategies for health care delivery, and developing new approaches to prevent, screen, diagnose, and treat cancer. For example, Cancer Moonshot–supported networks enabled numerous improvements in cell-based therapies for solid tumors, including engineering targets for chimeric antigen receptor T-cell therapy against pediatric brain tumors.

To reach the new Cancer Moonshot goal of a 50% reduction in age-adjusted cancer death rates by 2047, we must sustain the progress enabled by the 21st Century Cures Act and invest more broadly to discover, develop, test, and deliver new approaches for cancer prevention, detection, and treatment. With the funds in this FY25 Professional Judgment Budget Proposal, this next phase of the Cancer Moonshot will:

- · modernize cancer clinical trials to increase accrual and completion rates
- · translate discoveries into innovative cancer prevention and treatment approaches
- · transform cancer screening and diagnosis practices to save more lives
- · ensure rapid dissemination of standards of care to all people equitably
- expand and enhance the diversity of the cancer research workforce

These areas are interconnected and must be simultaneously supported along with NCI's existing investments in cancer research, through our base appropriation.

This FY25 Professional Judgment Budget Proposal will help NCI to fully leverage the scientific opportunities before us, to maximize research advances for the American people, and to end cancer as we know it.

## NCI RESEARCH PORTFOLIO: DRIVING DISCOVERY TO END CANCER AS WE KNOW IT

NCI enables advances against cancer by investing in a broad portfolio of research, supporting the cancer research workforce, and sustaining the infrastructure that enables cutting-edge research to succeed. All these components are essential to lead progress against cancer and accomplish the goals of the National Cancer Plan.

NCI's support of basic, translational, and clinical research is helping patients by driving discovery to improve cancer risk assessment, prevention, detection, diagnosis, treatment, and survivorship. Sustained and robust support for NCI's work is needed to realize the long-term vision of ending cancer as we know it.

# **CANCER RESEARCH CONTINUUM**



## Providing hope: The power of cancer biology research

Virtually every new cancer diagnostic, therapeutic, or preventive measure begins with a basic science research question. Through decades of carefully planned experiments in laboratories around the world, researchers generate knowledge about cancer. It's these investments in cancer biology research that

support the groundwork needed to discover and advance lifesaving cancer interventions. Continued support is required to build on these findings.

NCI is the largest funder of the basic research that is critical for making sustained progress against cancer. Cancer survivors and those at risk of developing the disease rely on the innovative approaches that cancer biology research delivers. Cancer survivors and those at risk of developing the disease rely on the innovative approaches that cancer biology research delivers. For example, through cancer biology research, NCI-supported researchers have:

- identified rare antitumor immune cells that may one day help advance personalized cancer immunotherapies for patients whose cancers do not respond to standard treatments
- revealed unique genetic patterns in tumors from people with lung cancer who never smoked
- uncovered vulnerabilities in potentially lethal brain tumors that are notoriously difficult to treat
- discovered early molecular changes and immune suppression in precancerous lesions that could help identify people at risk of developing lung cancer

Discoveries like these open the door to new treatment options where few or none currently exist and provide hope that one day all cancers will be treatable.

Read more about NCI's related research areas, including cancer biology research, cancer genomics research, and research on causes of cancer.

## Reducing the burden: The potential of cancer prevention

While overall cancer mortality continues to decrease, researchers estimate that more than half of cancer deaths are preventable. More research investments are needed to learn how to implement, improve, and build on current prevention strategies and intercept cancer more effectively by improving treatment of precancerous lesions.

The knowledge gained from cancer prevention research can be used to refine guidelines and implement targeted measures to reduce the incidence of cancer. Researchers have identified several preventable factors in cancer development, such as certain health behaviors, exposure to cancer-causing agents, and social determinants of health. However, there is still much more to learn about how changes in these risk factors influence cancer risk. The knowledge gained from cancer prevention research can be used to refine guidelines and implement targeted measures to reduce the incidence of cancer.

For example, NCI-funded researchers are developing

experimental vaccines and other medicines to prevent cancers caused by underlying diseases. This research has enabled progress in several areas. NCI-supported studies have:

- tested vaccines to prevent or delay the onset of hereditary cancers, such as those seen with Lynch syndrome, a condition marked by an 80% chance of developing colon cancer and a significant chance of developing endometrial cancer
- found that one dose of human papillomavirus (HPV) vaccine is effective in protecting young girls and boys against infections that can cause cervical, anal, and head and neck cancers—reducing the vaccine doses needed and allowing more people to be vaccinated worldwide
- discovered a druggable protein target to prevent nonalcoholic steatohepatitis, the biggest contributor to the recent rise in liver cancer cases

Through rigorous scientific studies, researchers can assess the impact of cancer prevention strategies, identify areas for improvement, and develop more efficient and accessible intervention approaches to reduce the burden of cancer.

Read more about NCI's related research areas, including cancer prevention research.

# Intervening early: The urgency of cancer detection and diagnosis research

Imagine if fewer people suffered and died from cancer because we detected and diagnosed the disease or its precursors at the earliest possible stage.

Accurately identifying cancer—and precancerous lesions—and assessing its severity is the primary goal of cancer detection and diagnosis research. Early detection can save lives. An imprecise approach, however, can lead to overdiagnosis, overtreatment, and unnecessary physical, psychological, and financial harm.

Investing in cancer detection and diagnosis research can help develop more sensitive, accurate, and costeffective methods that support targeted cancer therapies and precision medicine. It will also help establish the impact that screening could have on survival rates for more cancer types and clarify any negative outcomes from multi-cancer screening tests currently under investigation.

With recent advances in NCI-funded detection and diagnosis technology, scientists have capitalized on novel opportunities. For example, NCI-supported researchers have:

- developed a blood test that in most people can accurately detect liver cancer, the third leading cause of cancer death worldwide, even in early stages of the disease
- developed new artificial intelligence tools to help radiologists improve prostate cancer diagnoses for tumors that are difficult to find during biopsy
- combined a specialized form of microscopy imaging with a type of artificial intelligence known as deep learning to expedite brain tumor diagnosis during surgery

Cancer detection and diagnosis research is primed with these emerging technologies. Carefully assessing their impact on cancer outcomes will limit risk and ensure benefit from these new screening and detection methods.

Read more about NCI's related research areas, including cancer screening and early detection research and cancer diagnosis research.

# Innovating treatment: The need for more effective and less toxic cancer therapies

For more than 50 years, NCI has played a vital role in the development of more effective and less toxic therapeutic options for patients with cancer. Despite the steady progress in improving treatments, some forms of cancer still lack effective therapies, many cancers eventually develop resistance to treatment, and not all people have equal access to cutting-edge treatments. Adding to these challenges, patients with cancer often experience severe

Investments in treatment research today will inspire and sustain the safe and effective cures of tomorrow.

side effects from the disease and its treatment, which for childhood cancer survivors can impact their quality of life for decades.

These challenges can be overcome. Investments in treatment research today will inspire and sustain the safe and effective cures of tomorrow. For example, NCI-supported researchers have:

- developed the first approved drug to treat chronic graft-versus-host disease, a complication of bone marrow transplants in which the donated immune cells attack the recipient's body, leading to painful and debilitating symptoms
- designed a novel type of drug to treat glioblastoma, a highly lethal brain cancer that often develops resistance to current therapies, without harming normal brain cells
- conducted clinical research that led to the approval of the first new treatment in over 20 years for Kaposi sarcoma, a form of cancer that mostly affects those who are immunocompromised
- completed the OlympiA clinical trial, which led to the approval of a new drug that improves overall survival in people with high-risk *BRCA*-mutant breast cancer

More research is needed to ensure that all patients with cancer have safe and effective therapies and the highest possible quality of life.

Read more about NCI's related research areas, including cancer treatment research and research on childhood cancers.

# Improving public health: The role of cancer control and health care delivery research

Each year, cancer has a significant impact on public health, affecting the nation's economy and the quality of life for millions of people in the United States. NCI invests in studies to identify population-wide trends in cancer and to improve the delivery of cancer interventions.

More research is needed to design interventions that improve cancer prevention, screening, treatment, and survivorship outcomes and to address why certain racial, ethnic, and rural populations suffer disproportionately from some cancers. This research can inform policies that reduce cancer-causing exposures, ensure greater compliance with health recommendations, minimize misinformation, and address gaps in the health care system when cancer survivors transition from oncology care to primary care.

Investing in cancer control and implementation research will ensure that all people benefit equally from advances in cancer research.

Additional investments in cancer control and implementation research will improve the lives of cancer survivors and the general population, while ensuring that all population groups benefit equally from advances in cancer research. For example, NCI-supported researchers have:

- revealed that physical activity before and during treatment for breast cancer reduces "chemo brain," a treatment-related cognitive impairment that affects up to 75% of people with breast cancer who receive chemotherapy
- developed an effective intervention to increase breast, cervical, and colorectal cancer screenings in women who live in rural locations
- completed simulation studies showing that a joint lung cancer screening and smoking cessation intervention would drastically reduce deaths from lung cancer

Researchers are working hard to understand population-level impacts on cancer control and to design and test interventions along the cancer continuum that can address disparities and ensure good health for all people.

Read more about NCI's related research areas, including public health research and cancer and cancer health disparities research.

# Strengthening the research enterprise: The need for a robust cancer research workforce and infrastructure

An extensive research infrastructure and a stable, diverse workforce are the backbone of the entire cancer research enterprise, and NCI provides a level and scope of infrastructure and training that cannot be matched by other organizations. Investing in these critical needs is of the greatest importance in leading progress against cancer.

All cancer research requires a robust workforce and infrastructure. This includes cancer centers where clinical trials can test new approaches to prevent and treat cancer, facilities that develop and manufacture novel technologies and medicines, electronic databases to support large amounts of biomedical data, and programs and initiatives to train a diverse workforce that drives cancer research forward. These elements need continued investments to remain strong and to capitalize on new opportunities. For example, NCI investments have:

- funded and continue to support the NCI Cancer Research Data Commons, a cloud-based infrastructure that provides secure access to a large, comprehensive, and expanding collection of cancer research data
- delivered research reagents to more than 150 laboratories worldwide as part of the NCI-funded RAS Initiative
- launched the Cancer Moonshot Scholars and Early Investigator Advancement Program to grow and diversify the cancer research workforce
- supported over 1,400 extramural training awards in the most recent fiscal year, 41% to predoctoral researchers and 59% to postdoctoral researchers and those in early stages of research independence

Investing in the NCI-supported cancer research workforce and infrastructure ensures that all research areas supported by the NCI budget produce the highest quality research in the most effective way possible.

Read more about NCI's cancer research infrastructure and the Center for Cancer Training.

## HIGHLIGHTED SCIENTIFIC OPPORTUNITIES IN CANCER RESEARCH

NCI continually pursues new and emerging scientific opportunities that, with further investment, would catalyze progress in cancer research. With more knowledge than ever before, researchers have many opportunities to make research advances faster, expand clinical trial access to more people, and clarify the many influences on cancer risk and patient outcomes.

Read about five areas of opportunity for fiscal year 2025 and how sustained investments in each area would support the goals and strategies of the National Cancer Plan.

## Improving Patients' Lives through Symptom Science

More people with cancer are living longer after their diagnosis, which marks the beginning of cancer survivorship. With more than 18 million cancer survivors in the United States, delivering optimal cancer care must include a focus on mitigating the immediate and long-term effects of cancer and its treatment, including the development of second cancers. We must also understand how co-occurring health conditions—such as high blood pressure, diabetes, and other chronic illnesses-contribute to cancer outcomes. Investments in symptom science, a field of research to identify individuals at risk for developing treatment-related symptoms and limit the occurrence and severity of those symptoms, are critical for allowing cancer survivors to maintain productive and vibrant lives.

Reaching the goals of symptom science is not easy. Every patient is unique in their genetic makeup, health status, and lived experiences. Some cancer treatments have severe or difficult-to-treat side effects—such as cardiotoxicity, neurotoxicity, and pain—that can interrupt or delay treatment. And novel therapies will create new challenges that must be addressed. Therefore, research on how to monitor, prevent, and reduce these cancer-related



complications is critical, especially in young cancer survivors who may live decades after their cancer diagnosis.

Sustained investments in symptom science research and innovative long-term care of cancer survivors will enhance treatment delivery, limit long-term side effects, and have a positive impact on millions living with cancer now and in the future.

# **Revolutionizing Cancer Clinical Trials**

Clinical trials are essential for achieving progress against cancer. They help provide the evidence that informs health care providers on the best approaches for preventing, diagnosing, and treating cancer, and on how to manage cancer-related symptoms. As part of ongoing work to modernize clinical trials, NCI is working to increase clinical trial accrual, maximize the diversity of participants, and expand clinical trial infrastructure into communities that are medically underserved or underrepresented.

More work is needed to revolutionize clinical trials. This includes designing flexible or pragmatic trials that save on cost and time, incorporating artificial intelligence technologies to accelerate progress, and re-examining clinical trial inclusion criteria to make participation easier for patients.

With additional investments, NCI can build on the lessons learned from clinical trials conducted during the COVID-19 pandemic (such as using telemedicine) and harness the full capabilities of the extramural clinical research community and the NIH Clinical Center to expand access to clinical trials. As clinical trials become more decentralized, investments are needed to study novel strategies to harmonize data across the myriad of clinical studies and incorporate real world avidence whi



clinical studies and incorporate real-world evidence, while always safeguarding patient privacy.

One of the National Cancer Plan strategies for developing effective treatments includes moving promising new treatments from discovery to clinical trials more quickly and ensuring equitable access to all treatments. Another National Cancer Plan strategy is to develop new methods to detect cancers early, especially ones that don't yet have effective screening tests. As new screening strategies emerge, clinical trials can help bring these lifesaving methods into routine practice sconer. These strategies rely on continued investment in NCI clinical trials programs to enable their successful modernization and growth.

# Clarifying the Impact of the Environment on Cancer Risk

Environmental exposures, including the air we breathe, the food we eat, and the places we live and work, can have a large impact on cancer development, progression, and survivorship. However, precisely how such environmental exposures alter the trajectory of cancer is difficult to capture and varies dramatically between people and from one location to the next. We need to focus on accurately measuring environmental exposures; understanding how our bodies respond to our physical environments, social influences, and economic circumstances; and learning how environmental exposures affect cancer outcomes.

NCI supports research on environmental impacts along the entire cancer continuum. This spans studies on cellular changes after toxic exposures to research on why some communities are disproportionately impacted by environmental factors associated with cancer risk. For example, NCI-supported research is looking at the impact of climate change on cancer rates, cancer care delivery, cancer-related behaviors, and health equity.

More investments are needed to harmonize and integrate measurable information about



environment-related cancer risk with information about tumor biology, such as from The Cancer Genome Atlas and the Human Tumor Atlas Network. This work could help identify people who are more susceptible to specific exposures and inform cancer prevention and treatment strategies.

Such investments in environmental risk research are critical to supporting the National Cancer Plan goals of preventing cancer and eliminating inequities. Over decades, NCI has built a foundation to effectively conduct this type of research.

# Harnessing the Power of Cancer Data

Imagine a cloud-based platform that automatically manages the ever-increasing amount of cancerrelated data and is accessible to the entire cancer community, from computational biologists to laboratory scientists to clinicians and patients. Building an interconnected Cancer Research Data Ecosystem to collect, integrate, and share data from a broad range of sources is critical to maximizing the utility of data from every laboratory experiment, every clinical trial, and every patient experience.

The NCI-supported Cancer Research Data Commons; Surveillance, Epidemiology, and End Results (SEER) Program; and Childhood Cancer Data Initiative are fundamental components of the data ecosystem. Many NCI programs, such as the Human Tumor Atlas Network and Cancer Systems Biology Consortium, are already poised to incorporate data collected through these efforts into a better understanding of cancer. NCI also supports research to advance artificial intelligence and machine learning methods to analyze cancer data, while bringing together diverse perspectives to ensure robust and ethical use of artificial intelligence for cancer research.



However, a cloud-based platform that could integrate

these distinct types of data into one virtual ecosystem does not yet exist. We also require better tools that allow the broad scientific and clinical community to use these data in a way that preserves data security and patient confidentiality.

With such an ecosystem, the cancer research community could more efficiently and effectively harness the power of data. For the patient, this means more accurate predictions about cancer risks and, for those with cancer, responses to treatment. For the researcher, this means the ability to mine cancer-related data to uncover innovative approaches for early detection and treatment to reduce the burden of cancer for patients and their families.

# Unraveling the Complexity of Cancer Metastasis

The spread of cancer cells from the primary tumor to other sites in the body, a process called metastasis, is responsible for most cancer deaths. Decades of cancer biology research have led to a basic awareness of how metastasis happens. However, a deeper understanding is needed to prevent and treat this often-devastating progression of the disease. NCIsupported research—driven in part by the Metastasis Research Network—is diving into the complex mechanisms underlying the metastatic process, including its early triggers, the adaptation to new environments, the influences from surrounding tissues and immune cells, and the development of drug resistance.

Historically, metastasis has been considered a problem in the later stages of cancer, but recent research has revealed that cancer can begin spreading at the very early stages, before a primary tumor is even detectable. As a consequence, individual colonies of cancer cells, some of which may have treatment-hindering traits that are distinct from the primary tumor, can remain hidden for months, years, or even decades. Why some metastatic cells lie dormant in the body—escaping immune surveillance before emerging and growing into overt metastatic disease—is a key unanswered question.



Sustained investment in metastasis research to answer these persistent questions is essential for meeting the National Cancer Plan goal to develop effective treatments for people with metastatic cancer. NCI investments to date have led to innovative technologies that can now reveal metastases, circulating tumor cells, and tumor genomics at never-before-seen resolution. These technologies, combined with a large body of knowledge about cancer biology and advanced computational modeling, offer more opportunities than ever to unravel the complexities of the cancer metastasis process.

## **STORIES OF CANCER RESEARCH**

## Enrolling in a Clinical Trial in Rural America

In the Piedmont hills of western South Carolina, surrounded by peach and apple orchards, lies a small town with fewer than 700 residents. Kellie is one of those residents. She has two young daughters and works as a massage therapist and dental hygienist. In her spare time, she's in her garden or fishing at a nearby pond. She's strong in faith and considers these activities "my God time."

While giving a massage to a client in 2021, Kellie felt an acute pain in her right shoulder. She ignored it, thinking it was a strained muscle. Over the next year, the pain became stronger. When she started coughing up blood in the summer of 2022, she took action and had a chest x-ray. What it showed concerned her doctors, who ordered additional imaging scans. The scans revealed a single spiculated mass (a lump of tissue with spikes on the surface) in the lung, with enlarged lymph nodes nearby.

Kellie was diagnosed with stage III non-small cell lung cancer (NSCLC). Her diagnosis came 2 weeks after her brother informed her that he'd been diagnosed with the same cancer. Both had been smokers, although Kellie quit 17 years earlier, after their father died of esophageal cancer.



Kellie's lung cancer is treated at the hospital close to her home. The NCI Community Oncology Research Program helps cancer patients in their local communities.

Credit: Photo courtesy of Kellie

There are several types of NSCLC, which account for nearly nine out of every 10 lung cancer diagnoses. Some people

with early-stage NSCLC can have surgery to remove their tumors, followed by chemotherapy. For Kellie, surgery was not an option, as her mass had spread too far.

### Enrolling in an NCORP clinical trial

Her doctors wanted her to start the standard therapy immediately: chemoradiation followed later by an immunotherapy called durvalumab (Imfinzi). They also offered her the opportunity to participate in a clinical trial that is testing the effect of giving durvalumab during and after chemoradiation.

The trial is offered through the NCI Community Oncology Research Program (NCORP), a national network that brings cancer clinical trials and care delivery studies to people in their own communities. This means that Kellie can participate in the clinical trial without having to travel far from home to receive treatment at a major cancer center. Kellie jumped at the opportunity, enrolled, and learned she was randomly assigned to the experimental arm.

Once a month, Kellie drives 20 minutes from her house to the local hospital for lab tests. While waiting for those results, she meets with her oncologist. With satisfactory blood work, she receives consecutive infusions of chemotherapy and durvalumab. Her time at the hospital starts at 8:30 a.m., and she is typically done by noon.

Kellie is thrilled that she can receive her treatment so close to home and participate in helping others. Without NCORP, she would have had to travel hundreds of miles to Charlotte, NC, or Atlanta, GA.

### Looking forward as a cancer survivor

So far, the treatment is shrinking the tumor, and her side effects have been limited to a cough and some fatigue. She will continue to get the treatment through November.

"If someone can benefit, then I'm happy to participate. And if I can benefit," she mused, "then all the better."

Kellie is looking forward to finishing treatment and traveling. She hopes to cover the US East Coast from Maine down.

Keith Dee, Ph.D., research coordinator for the Upstate Carolina NCORP that offers the clinical trial in Kellie's area, is pleased with her progress on durvalumab. He notes the convenience that NCORP offers to Kellie and many more Americans.

"NCORP brings national trials to many who don't live in a big city," Dr. Dee said. "Through this program, people in rural areas can drive 10 to 40 minutes, instead of traveling hundreds of miles and incurring expenses associated with overnight stays at hotels to receive the same treatment." In his eyes, this makes NCORP a resounding success.

## Engaging Primary Care Providers in Cancer Survivorship Care

On any given weekend, Erin Hahn, Ph.D., M.P.H., might be found tending native plants like sage, salvia, and mallow in her garden, with her husband and three rescue dogs nearby. During the week, this penchant for cultivating spills into her work as a researcher at the Kaiser Permanente Southern California Department of Research and Evaluation to improve care for cancer survivors.

Erin studies cancer care delivery with a focus on cancer survivorship, a phase that people enter after receiving a cancer diagnosis and a research area that she believes needs nurturing. "Cancer care is uniquely complex. Cancer survivorship," she noted, "is a distinct phase of care and needs to be attended to."

There are concerns that the current oncology workforce may be insufficient to care for the rapidly growing population of survivors, with more than 18 million cancer survivors living in the United States today. This population is only expected to grow as innovations in treatment allow cancer patients to live longer past diagnosis. Erin points to cancer surveillance and primary prevention procedures—such as mammograms, colonoscopies, vaccines, lipid profile testing, and cardiovascular risk management—as underused tools in the care of cancer survivors.



With her first R01 grant, a Cancer Moonshot award, Erin is testing whether specialized training in cancer survivorship care for primary care physicians improves outcomes for cancer survivors.

Credit: Photo courtesy of Erin Hahn

### First independent RO1: A Cancer Moonshot award

In 2019, Erin applied for her first NCI R01 grant and received it in 2020. The R01 grant is considered the "gold standard" for independent investigators working to answer specific research questions. Erin's grant was funded through the Cancer Moonshot<sup>SM</sup> on the topic of optimizing and managing cancer survivor care. "When I saw that topic, it was right up my alley," she said. "I knew I had to apply."

Through her grant, she is studying novel models of care for cancer survivors in a large health system. Health system–based research provides evidence that, when applied, can make care more affordable, effective, equitable, accessible, patient-centered, and safer. Erin hopes her research will answer the question: Will primary care cancer survivorship clinics, staffed by primary care physicians trained in cancer survivorship care (such as cancer surveillance and managing late effects of treatment), help optimize care for cancer survivors?

For the study, Erin is leveraging the relationship that the Department of Research and Evaluation in Southern California has with the Kaiser Permanente health system. In Southern California, Kaiser Permanente provides care to 7 million members. This gives Erin unique access to several thousand earlystage breast and colorectal cancer survivors across the Kaiser Permanente Southern California system. Having access to such a large group of patients is a boon for Erin's research, and ultimately, she hopes to learn if the primary care survivorship clinics are effective and can be scaled up nationally across large health systems like Kaiser Permanente, which has about 12.7 million members in the United States.

Prior to receiving the R01, Erin focused on several areas of implementation science that helped coalesce her approach to research on cancer survivorship care in a large health care system. While working on her master of public health degree, she was strongly influenced by a mentor who taught her that research influences policy, and that health care research can be an effective way to get evidence into practice. Erin went on to receive an NCI predoctoral (R25) award, followed by a Kaiser Permanente postdoctoral fellowship in delivery system science with a focus on cancer care.

### Collaborating on cancer care and prevention

Shortly after receiving her first R01, Erin applied for and received two more NCI awards. As with her first grant, she brings her health systems perspective to these projects. For her second NCI award, Erin is collaborating with four other principal investigators on a program project grant (P01) surveying the care given to adolescent and young adult cancer survivors with the intent to learn about their care experience and where interventions to improve care delivery are needed.

Her third NCI award is an R01 grant on which she is a co-principal investigator. This research compares several strategies across 60 Kaiser Permanente pediatric practices to help increase uptake of the human papillomavirus (HPV) vaccine, which can prevent cervical and several other HPV-related cancers, among youths ages 9 to 12.

Erin's efforts to improve health care for cancer survivors and advance cancer prevention are central to NCI's goal of improving the experience of people living with and after cancer and the institute's mission to advance scientific knowledge to help all people live longer, healthier lives.

"Health system–based research is critical," Erin said. "Figuring out how to do research within such systems in a way that positively affects our patients' lives is really important. The kind of work I do, the kind of strategies I use, the tools I develop," she reflected, "they are very purposefully designed for dissemination. For cancer care, there are a lot of points where we can intervene and improve."