SPOTLIGHT ON **Immunotherapy**





ADVANCING THE FRONTIERS OF CANCER SCIENCE AND MEDICINE



American Association for Cancer Research®

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A Message from AACR

The last few decades have witnessed unprecedented progress against cancer. In the United States, overall cancer death rates are declining steadily since 1991, and an increasing number of individuals are living after a cancer diagnosis. This summary of the thirteenth edition of the American Association for Cancer Research® (AACR) Cancer Progress Report highlights the vital role of cancer research in saving lives. As emphasized in the report, federal investments in the National Institutes of Health (NIH) and the National Cancer Institute (NCI) have enabled researchers to decode the complexities of cancer and transform outcomes for patients. Despite major strides, cancer continues to pose a significant threat, as underscored by the estimated 609,820 lives that will be lost to cancer in 2023 in the United States. This number is predicted to increase considerably in the coming decades as the as the proportion of older adults in the U.S. population increases.

Thanks to bipartisan support in Congress for NIH, NCI, and other federal programs, we have the capability to deliver unprecedented advances routinely to patients with cancer. Medical research funding must continue to be a national priority in order to maintain the momentum against cancer. AACR urges Congress to support robust, sustained, and predictable annual growth of the NIH and NCI budgets, and to provide consistent and sufficient annual funding for the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). These actions will transform cancer care, increase survivorship, and bring lifesaving cures to the millions of people affected by cancer.

Cancer in 2023

Research: Driving Progress Against Cancers

Medical research is the foundation for progress against the collection of diseases we call cancer. Research is essential for cancer prevention, detection, survivorship, and improving the quality of life for patients with cancer, because it is the driving force behind every advance in public health, cancer screening, and cancer treatment. Decades of Congressional investments have spurred these advances through support for federal research and health programs. Research has given patients with cancer and their caregivers hope, and has led to more people living healthier and fuller lives after a cancer diagnosis. Thanks to this scientific progress, there are now more than 18 million cancer survivors in the United States.

Cancer: An Ongoing Public Health Challenge

Although incredible progress has been made against cancer, it remains a significant health challenge, in the United States and around the world. Research has identified complex and intersectional economic, cultural, behavioral, environmental, geographical, and other factors that place a disproportionately higher burden of cancer on medically underserved populations and contribute to ongoing disparities across the continuum of cancer care (see **Sidebar 1**, p. 3).



The medical research community is dedicated to achieving health equity and improving cancer outcomes for all people. Opportunities exist to increase representation from all communities in every aspect of cancer research and patient care.

Which U.S. Population Groups Experience Cancer Disparities?

According to the National Cancer Institute, cancer disparities are adverse differences in cancer such as the number of new cases and deaths, cancer-related health complications, quality of life after cancer treatment, financial burden, screening rates, and stage at diagnosis that are shouldered by certain population groups including:



Funding Cancer Research: A Vital Investment

Recent advances in cancer prevention, early detection, diagnosis, and treatment are a direct result of the cumulative efforts of researchers from across the spectrum of medical research. Most researchers in the U.S. medical community depend on federal funds to support their work and spur lifesaving innovations in cancer research. Investments in NIH and NCI help maintain the momentum of progress made against cancer by researchers, and it is imperative that Congress continue its bipartisan support of biomedical science. New lifesaving diagnostics and treatments for patients with cancer will continue to depend on sustained, robust, and predictable funding increases for NIH and NCI.



"Just ten years ago, we couldn't have imagined the victories we would be seeing in the cancer space today. I am confident that in another ten years, we'll be able to say the same."

THE HONORABLE MICHAEL T. MCCAUL, SR. U.S. Representative for Texas's 10th District



FIGURE 1



an individual's risk for developing cancer. By modifying behavior, individuals can eliminate or reduce many of these risks and thereby reduce their risk of developing

additional public health campaigns and policy initiatives can help further reduce the burden of cancers related to preventable cancer risk factors.

Support for medical research is needed not only to address the physical and psychological impacts of cancer, but also to reduce the immense personal and financial burdens that stem from a cancer diagnosis. With the high cost of cancer treatments resulting in 11% of patients needing to skip recommended treatments, reducing the burden of cost for patients must remain a priority.

Reducing the Risk of Cancer Development

Approximately 40 percent of cancer cases in the United States can be attributed to modifiable risk factors, including tobacco use, obesity, infections, and UV exposure (see Figure 1, p. 4).

Despite decades of decreasing tobacco use across populations, cigarette smoking remains the leading preventable cause of premature disease and death. The use of tobacco has a profound impact on cancer incidence and mortality, as it causes 18 types of cancer, results in 20 percent of all cancers diagnosed in the United States, and contributes to nearly 30 percent of cancer deaths each year (see Figure 2, p. 5).

Effective tobacco control policies enacted since the 1960s, including taxes, advertising restrictions, and minimum age limits, have greatly helped reduce smoking rates. Additional policies, such as banning all flavored tobacco products, reducing nicotine concentrations, and restricting online advertising, could further reduce tobacco use. Such policies are important because flavored tobacco products are addictive and detrimental to an individuals health, and because the predatory marketing strategies for these products specifically target racial and ethnic minorities, thus contributing to disparities (see Figure 3, p. 6). It is important that FDA quickly finalizes and implements a regulation to prohibit menthol cigarettes and flavored cigars, as well as proposes a limit on nicotine in tobacco products to further support tobacco cessation across all populations by making tobacco products less addictive.

Excess body weight increases risk for 15 different cancers. As obesity rates continue to increase, obesity is projected to overtake tobacco



"We must support our world-class researchers working tirelessly every day to find a breakthrough and save lives."

THE HONORABLE ROBERT P. CASEY, JR. **U.S. Senator Pennsylvania**





Smoking tobacco increases an individual's risk of developing not only lung cancer, but also 17 other types of cancer. No level of exposure to tobacco smoke is safe, including

use as the leading modifiable risk factor for cancer. Broad policies and programs to promote healthy nutrition and physical activity are important to reduce the growing impacts of obesity on cancer incidence.

Infections from Human Papilloma Virus (HPV) cause six types of cancer, including nearly all cases of cervical cancer. Widespread vaccination during adolescence, routine cervical cancer screening, and timely follow up care could potentially eliminate all cases of cervical cancer. However, only 57 percent of boys and 60 percent of girls who are eligible received the recommended HPV vaccinations in 2021. Additional policies to support HPV vaccination rates that reach the Healthy People 2030 goal of 80 percent in adolescents and increase access to screenings could eradicate cervical cancer.

Screening for Early Detection

Cancer screenings can determine whether a person has precancerous lesions or cancer before any symptoms of the disease appear. Routine cancer screenings help detect cancers earlier, increasing the success exposure to secondhand smoke. Use of smokeless tobacco (such as chewing tobacco and snuff) can cause oral, esophageal, and pancreatic cancer.

of treatment. At the population level, routine cancer screenings can reduce cancer burden and total health care spending. The decision of whether an individual should be screened for cancer is determined by several factors, including age; whether or not a person has a particular organ; smoking history; previous abnormal screenings; and personal and/or family history of cancer.

Currently, the U.S. Preventive Services Task Force (USPSTF) an independent, volunteer panel of national experts in disease prevention and evidence-based medicine—has screening guidelines for five types of cancer, four of which apply to individuals with an average risk of being diagnosed with breast, colorectal, prostate, or cervical cancer. Guidelines for lung cancer apply to people who smoke or have previously smoked, due to a higher risk of being diagnosed with the disease. By catching cancer at an earlier stage when it is easier to treat, and potentially curable, routine cancer screening can substantially decrease cancer mortality.

Unfortunately, many eligible individuals do not necessarily receive the recommended cancer screenings. Barriers, such as lack of access to health care facilities, gaps in health insurance,

How Flavored Tobacco Products Contribute to Disparities



Masks Harsh Taste



Cooling Effect of Menthol Hides Smoke Irritation



Menthol Increases Nicotine Receptors



Predatory Marketing



Youth More Likely to Try



Tobacco Smoke Causes 17 Types of Cancer Beyond Lung

The tobacco industry has used flavored products and predatory marketing practices, such as providing free samples of menthol cigarettes, to attract racial and ethnic minority communities to nicotine for decades. These aggressive campaigns were intentional business strategies to preserve market share as overall smoking rates dropped across the United States.

In 2023, close to 300,000 women in the United States will be diagnosed with invasive

breast cancer and over 13,000 people will be diagnosed with invasive cervical cancer. Reauthorization of the Screening for Communities to Receive Early and Equitable Needed Services for Cancer Act is crucial to continue to support the National Breast and Cervical Cancer Early Detection Program.

low health literacy, and miscommunication between patients and providers, contribute to low uptake of cancer screening. Furthermore, inequities in access to cancer screenings and followup testing if the initial test finds an abnormality are significant contributors to late-stage diagnoses among underinsured and uninsured patients. Stakeholders across the cancer care continuum are working together to educate the public and to increase access to cancer screening among the medically underserved populations. Some evidence-based interventions that have been effective to achieve this goal include comprehensive public health campaigns; increased access to health insurance; community outreach and engagement and culturally tailored interventions; reduced structural barriers; and improved patient– provider communication.

Advancing the Frontiers of Cancer Science and Medicine

Progress in cancer treatment results from decades of work by dedicated researchers from academia and industry, physician scientists, and regulators working together to understand basic cancer biology and translate this fundamental knowledge into novel therapies.

Clinical trials are vital to medical research and drug development because they determine whether new medical products are safe and effective compared to currently available options. Unfortunately, participation in cancer clinical trials remains very low. In the United States, only eight percent of adult patients and TABLE 1

Summary of Current Clinical Trial Practices and Recommended Changes

DRUG DEVELOPMENT TOPIC	CURRENT PRACTICES	RECOMMENDED PRACTICES
Trial Diversity	 Demographic data are analyzed after trials are completed 	 Build long-term partnerships with patient and community organizations Develop diversity strategies prospectively Address barriers to participation Support clinical research sites in historically underserved communities
Decentralized Trials	• Patients have frequent in-person visits to a large academic medical center	 Increase use of telehealth visits Enable remote consenting Utilize local health clinics and imaging Minimize unnecessary data collection
Accelerated Approval	 Relies on single-arm trials Confirmatory trials are initiated following Accelerated Approval 	 Increase use of randomized trials Either start confirmatory trial before submitting Accelerated Approval application, or continue existing trial
Dose Optimization	 Gradually increase dose until patients cannot tolerate the drug 	 Identify doses that elicit the intended biological effects Further study more than one dose following a dose- finding trial
Overall Survival Data	 Many trials do not collect or plan to analyze overall survival data Patients are followed for standardized time frames 	 Plan to collect and analyze overall survival data for every trial, even if it is exploratory Justify length of follow-up based on data For targeted therapies, prioritize recruitment of biomarker-positive patients

19.9 percent of pediatric and adolescent patients with cancer participate in clinical trials. Additionally, most clinical trials do not reflect the real-world diversity of patients with cancer. Chronic underrepresentation of racial and ethnic minorities, as well as patients from rural areas, in clinical trials leaves open questions about whether new therapies work as well for these patients as clinical trials may suggest. Numerous structural barriers prevent participation in trials, including strict eligibility criteria, transportation access and costs, dependent care responsibilities, and providers not inviting patients to participate. By issuing draft guidance, FDA has encouraged trial sponsors to improve diversity and increase decentralization in clinical trials to make participating in clinical research more accessible and improve the quality of data collected. Changes to clinical research recently proposed by FDA are summarized in **Table 1** (see p. 7).

Progress Across the Clinical Cancer Continuum

Discoveries from innovative cancer research are continually being transformed into lifesaving advances across the continuum of cancer care. Between August 1, 2022, and July 31, 2023, 14 new anticancer therapeutics and two new diagnostic imaging agents were approved by FDA. In addition,

Between August 1, 2022, and July 31, 2023, FDA approved:



New anticancer therapeutics that are now benefiting patients with various types of cancer



Previously approved anticancer therapeutics for treating new types of cancer

New imaging agents



FDA expanded the use of 12 previously approved anticancer therapeutics to treat new types of cancer.

These FDA approvals expand the treatment options available to patients with cancer across the "pillars of cancer treatment." These pillars include surgery, chemotherapy, radiotherapy, molecularly targeted therapy, and immunotherapy, which are often used in various combinations. Unfortunately, many patients do not

Disparities in Cancer Treatment

Research is constantly powering the development of new cancer treatments. However, medically underserved populations experience numerous barriers to quality cancer care and are less likely to receive recommended treatments. Examples of these disparities include:

29% less likely	Patients with non-small cell lung cancer living in neighborhoods with the lowest education or income levels were 29 percent less likely to receive immunotherapy compared to those living in the most educated or high-income areas.	
Significantly LONGER	Time between cancer diagnosis and the initiation of first treatment is significantly longer for Black patients (median = 16.5 days) compared to White patients (median = 9.5 days).	
The LONGEST	Median travel times to access cancer care are the longest for American Indian or Alaska Native children and adolescents and young adults (AYAs) compared to the overall population of children and AYA patients.	
38% more likely	Hispanic men with metastatic prostate cancer are 38 percent more likely to experience treatment delays compared to non-Hispanic White men.	
21% more likely	Patients from rural areas are 21 percent more likely to fail to undergo surgery for potentially removable non-small cell lung cancer compared to those from urban areas.	
26% less likely	Patients with breast cancer living in historically redlined areas are 26 percent less likely to receive surgery and they have poorer survival .	

receive or benefit from the recommended standard of care for their cancer. Gaps in equitable and affordable access to cancer treatment worsen survival rates and disproportionately affect population groups who have been historically underserved by the health care system (see **Sidebar 2**, p. 8).

While surgery and radiotherapy have been used to treat cancer for more than a century, technological advances are continually improving their safety and efficacy. The new ARPA-H Precision Surgical Interventions program, announced this year, aims to elevate cancer surgery to a new level by investing in cutting-edge surgical methods to improve the chances of removing every cancer cell and enhance the safety of removing tumors from difficult locations. Additionally, NIH-funded research on molecularly targeted therapies is identifying new ways to kill cancer cells with fewer negative impacts on healthy tissues.

Immunotherapies have led to particularly profound improvements in treating cancer over the past ten years, as has been highlighted in a special section of the report, Immunotherapy: Pushing the Frontiers of Cancer Medicine. This newest class of precision cancer therapy unleashes the immune system to eradicate cancer cells throughout the body; for some patients, this results in curing advanced disease that would have previously been untreatable. Like most novel cancer therapies, immunotherapies were initially approved to treat common cancers. Fortunately, there are increasing numbers of approvals for immunotherapies to treat rare forms of cancer, such as the case for **Isabella Fraser** (see p. 9) and **Alexis Browning** (see p. 9), who received atezolizumab to treat alveolar soft part sarcoma, an extremely rare and highly aggressive form of cancer that primarily affects adolescents and young adults.

Supporting Cancer Patients and Survivors

Each person diagnosed with cancer has a unique experience ranging from successful treatments and living cancer free to experiencing varying degrees of side effects and potential subsequent cancer diagnoses. Additionally, a cancer diagnosis impacts the lives of friends, families, and caregivers, necessitating an increased focus on building social support networks for those diagnosed with cancer.



"There is no way to advance science without people being willing to participate in research studies."

CINDY BROWN Age: 58 • California Diagnosis: Multiple myeloma **Treatment:** teclistamab-cqyv (Tecvayli)



"I have made it my mission to use my voice to advocate for and bring attention to the cause."

ALEXIS BROWNING Age: 28 • Kentucky Diagnosis: Stage IV alveolar soft part sarcoma (ASPS) Treatment: atezolizumab (Tecentriq)



"By focusing on these new treatments, research can provide the best that the future has to offer; I am hopeful."-*Emily Graton (Isabella's Mother)*

ISABELLA (BELLA) SNOW FRASER Age: 12 • Vermont Diagnosis: Stage IV alveolar soft part sarcoma (ASPS) Treatment: atezolizumab (Tecentriq)



"All cancer patients want to extend the time they have on this planet. And that is exactly what research is affording us."

JACLYN (JACKIE) VANRAAPHORST Age: 58 • Washington Diagnosis: Stage III ovarian cancer Treatment: mirvetuximab soravtansine-gynx (Elahere)



"We have lots of needs in this country, but saving people's lives is what's most important and we need to fund that."

LESA KIRKMAN Age: 61 • Florida Diagnosis: T1 high grade bladder cancer Treatment: nadofaragene firadenovec-vncg (Adstiladrin)



"I hope that robust funds will be allocated for future research to find ways to improve the treatments, to do more clinical trials, and to save more people."

BRIAN BECK Age: 59 • Tennessee Diagnosis: Stage IV colon cancer Treatment: tucatinib (Tukysa) and trastuzumab (Herceptin)



"Funding for cancer research is vital. Immunotherapy and CAR T-cell therapy would not have been options without research."

- Courtney Addison (Cayden's Mother)

CAYDEN ADDISON Age: 6 • Virginia Diagnosis: Acute lymphoblastic leukemia **Treatment:** CAR T-cell therapy



"I would tell Congress to fund cancer research, as if they were funding for their family members."

COLBERT ENGLISH Age: 61 • Pennsylvania Diagnosis: Prostate cancer Treatment: enzalutamide (Xtandi) and leuprolide (Lupron)

FIGURE 4

NCI Success Rates



Success rates at the National Cancer Institute (NCI), i.e., the percentage of grant applications that receive funding through NCI, have steadily declined over the past two decades for both targeted and untargeted research. Targeted research is the research for which an institute solicits grant applications

A cancer diagnosis can pose serious short and long-term physical, mental, and emotional health challenges for patients and their caregivers. Many compounding factors contribute to the challenges of survivorship, including age at diagnosis; access to immediate and follow-up care; financial instability; belonging to a medically underserved community; proximity to medical centers offering treatment options; management of daily tasks; and poor integration of palliative care. A multifaceted approach to treating cancer means ensuring survivors have the tools to address their needs. While in some circumstances resources can be readily available, coordination between these services can be challenging and stressful. Tools like telehealth serve as an incredible method for delivering survivorship care in areas where it might not have been readily available in the past. However, insurance reimbursement policies can make funding streams for these tools unsustainable and create additional stress for a patient or the caregiver. It is essential that federal health care policies, such as the frameworks established in

in a specific scientific area using Request for Applications (RFAs), and funds meritorious applications from a pool of dollar amount specifically set aside for that research area. Untargeted Research is the research that is not funded through grant solicitation in response to an RFA.

NCI's National Cancer Plan, provide both the patients and their support network with all the tools they may need to ensure optimal health and wellbeing.

Envisioning the Future of Cancer Science and Medicine

Decades of robust, sustained, and predictable federal funding of basic, clinical, and translational research has driven progress against cancer by deepening our understanding of the unique biological processes in cancer cells and the development of novel drugs that take advantage of these scientific insights.

As we look to the future, many researchers, including the **AACR President, 2023-2024, Philip D. Greenberg, MD, FAACR**, (see p. 10), are confident that we are on the cusp of a golden age in cancer science with so many promising ideas nearing clinical



Envisaging the Future of Cancer Research and Patient Care

"All of the advances in cancer research are coming together to make therapies increasingly precise so we can improve the quality of life of patients."

PHILIP D. GREENBERG, MD, FAACR AACR President, 2023-2024

FIGURE 5



NIH Funding: Continuing the Momentum of Robust Increases

The National Institutes of Health (NIH) appropriations from 2005 to 2022 have steadily closed the gap between appropriated funds and projected costs to conduct research, as illustrated by Biomedical Research and Development

use, such as cancer vaccines, targeting cancer cell metabolism, modulating the microbiome, and a steady identification and improvement of new drug targets. Additionally, cutting-edge technologies, such as liquid biopsies and artificial intelligence, have the potential to revolutionize how cancer is detected and monitored. With continued support for medical research from Congress, a new wave of innovation could achieve the goal of the reignited Cancer Moonshot to end cancer as we know it.

Advancing the Future of Cancer Research and Patient Care Through Adoption of Evidence-based Policies

Federal investments in scientific discoveries and initiatives at NIH, NCI, FDA, and CDC have been central to the steady declines in cancer incidence and mortality during the past three decades. The enormous excitement in cancer science and medicine has led to a surge in the number of grant applications from new career researchers, but NCI funding levels are struggling to keep pace with the tremendous interest and opportunities present in cancer science and medicine.

The grant application process is grueling and stressful, and is made even more frustrating when funding levels cannot keep up with the demand. Ensuring high success rates—the percentage of grant applications that receive funding—at NIH and NCI would enable new and early-stage investigators to pursue innovative Price Index (BRDPI), shown in blue. Continued bipartisan efforts are urgently needed to prevent stagnant funding and ensure a continued investment in lifesaving cancer research.

research projects, moving the dial on cancer progress even further (see **Figure 4**, p. 10). By meeting the NCI Director's Professional Judgement Budget level of \$9.988 billion in fiscal year (FY) 2024, Congress can enable NCI to increase the availability of research grants and accelerate the path to discoveries that will save lives. Achieving this level of funding would also help bolster the work laid out in NCI's National Cancer Plan and the Biden administration's reignited Cancer Moonshot, strengthening the fight against cancer.

Robust, sustained, and predictable annual budget increases for NIH and NCI are essential for maintaining the positive momentum that cancer researchers have gained against cancer (see **Figure 5**, p. 11). An ongoing Congressional commitment to support FDA would also ensure that anticancer therapies that reach the clinic are safe and effective, as well as provide FDA tools to address dangerous drug shortages. Additionally, federal support for CDC's cancer prevention and control programs helps bring lifesaving preventive services to those who need them the most, such as those who live in persistent-poverty areas, which have disproportionately high confluence of cancer risk factors. Federal investments are equally vital for diversifying the cancer research and care workforce, advancing regulatory science initiatives, and pursuing policies that improve cancer prevention, early detection, and control.

AACR Call to Action

AACR urges Congress to continue to support robust, sustained, and predictable funding growth for the federal medical research and health programs vital to the fight against cancer. We call on Congress to:

- Increase the FY 2024 base budgets of the NIH and NCI by at least \$3.465 billion and \$2.6 billion, respectively, for total funding levels of \$50.924 billion for NIH and \$9.988 billion for NCI.
- Provide \$1.7 billion in dedicated funding for Cancer Moonshot activities in FY 2024 across NCI, FDA, and CDC with the assurance that Moonshot funding will supplement rather than supplant NIH funding in FY 2024.
- Appropriate at least \$472.4 million
 in FY 2024 appropriations for the
 CDC Division of Cancer Prevention to
 support comprehensive cancer control,
 central cancer registries, and screening and
 awareness programs for specific cancers.
- Allocate \$50 million in funding for the Oncology Center of Excellence at FDA in FY 2024 to provide regulators with the capable staff and necessary tools to conduct expedited review of cancer-related medical products.

By following through these recommendations, Congress will help accelerate the rate of discovery, solidify our competitive edge in advancing science, and create a vital pathway for young scientists to contribute to future advances in cancer research. Ultimately, this will improve our nation's health, including the lives of the millions of individuals who have been touched by cancer.

For your free copy of the full report, go to CancerProgressReport.org or scan the QR code to download a copy today



AACR Mission

To prevent and cure all cancers through research, education, communication, collaboration, science policy and advocacy, and funding for cancer research.

Through its programs and services, the AACR fosters cutting edge research in cancer and related sciences; accelerates the dissemination of new research findings among scientists, clinicians, patient advocates, and others dedicated to preventing and curing all cancers; promotes science education and training; and advances the understanding of cancer etiology, prevention, detection, diagnosis, regulatory science, and treatment throughout the world.

As the leading scientific organization dedicated to the conquest of all cancers and to the core values of diversity, equity, and inclusion, the AACR works to eliminate cancer health disparities through scientific and policy initiatives, and to eradicate racism and racial inequality in cancer research. The AACR is deeply committed to realizing the bold vision of health equity for all populations.



615 Chestnut Street, 17th Floor, Philadelphia, PA 19106-4404 215-440-9300 • AACR.org



FINDING CURES TOGETHER