DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
17th VIRTUAL NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
31 August 2022

Virtual Meeting
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
31 August 2022

The National Cancer Advisory Board (NCAB) convened for its 17th virtual regular meeting on 31 August 2022. The meeting was open to the public on Wednesday, 31 August 2022, from 1:16 p.m. to 4:00 p.m., and closed to the public from 4:10 p.m. to 4:35 p.m. The NCAB Chair, Dr. John D. Carpten, Professor and Chair, Department of Translational Genomics, Royce and Mary Trotter Chair in Cancer Research, Keck School of Medicine, University of Southern California, presided during both the open and closed sessions.

NCAB Members

Dr. John D. Carpten (Chair)
Dr. Francis Ali-Osman
Dr. Nilofer S. Azad
Dr. Anna D. Barker
Dr. Luis Alberto Diaz, Jr. (absent)
Dr. Howard J. Fingert
Dr. Christopher R. Friese
Mr. Lawrence O. Gostin (absent)
Dr. Andrea A. Hayes (absent)
Dr. Amy B. Heimberger
Dr. Scott W. Hiebert (absent)
Dr. Nikan Khatibi (absent)
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Margaret R. Spitz
Dr. Susan Thomas Vadaparampil
Dr. Ashani T. Weeraratna
Dr. Karen M. Winkfield

President's Cancer Panel

Dr. John P. Williams (Chair) (absent)
Mr. Robert A. Ingram (absent)
Dr. Edith P. Mitchell

Alternate Ex Officio NCAB Members

Dr. Michael A. Babich, CPSC
Dr. Gwen W. Collman, NIEHS
Dr. Joseph R. Graber, DOE
Dr. Michael Kelley, VA
Dr. Richard Pazdur, FDA (absent)
Dr. Tara A. Schwetz, NIH (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Douglas R. Lowy, Acting Director, National Cancer Institute
Dr. Oliver Bogler, Director, Center for Cancer Training
Dr. Philip E. Castle, Director, Division of Cancer Prevention
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
Dr. Katrina A.B. Goddard, Director, Division of Cancer Control and Population Sciences
Dr. Satish Gopal, Director, Center for Global Health
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the NCI Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies McConville, Acting Director, Office of Scientific Operations, NCI at Frederick
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program
Dr. Diane Palmieri, Acting Director, Center for Research Strategy
Dr. Henry Rodriguez, Director, Office of Cancer Clinical Proteomics Research
Mr. Jeffrey Shilling, Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Biomedical Informatics and Information Technology
Ms. Donna Siegle, Executive Officer and Deputy Director for Management, Office of the Director
Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development
Dr. Sanya A. Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

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WEDNESDAY, 31 AUGUST 2022

I. CALL TO ORDER AND OPENING REMARKS—DR. JOHN D. CARPTEN

Dr. John D. Carpten called to order the 17th virtual National Cancer Advisory Board (NCAB) meeting. He welcomed members of the Board, *ex officio* members, President's Cancer Panel (PCP, or Panel) members, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Carpten reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to accept the minutes of the 14–15 June 2022 Joint Meeting of the Board of Scientific Advisors (BSA) and the NCAB was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. JOHN D. CARPTEN

Dr. Carpten called Board members' attention to the future meeting dates listed on the agenda.

III. NCI ACTING DIRECTOR'S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Acting Director, NCI, welcomed NCAB members and attendees to the 17th virtual meeting. He titled his report "Ending Cancer As We Know It—For All" and provided an update on NCI announcements, cancer research highlights, the Cancer Moonshot℠, addressing health disparities in NCI clinical trials, and Frederick National Laboratory for Cancer Research (FNLCR) programs.

NCI Announcements. Dr. Lowy announced that the White House has named Dr. Monica Bertagnolli, Richard E. Wilson Professor of Surgery, Harvard Medical School, and a surgeon at Brigham and Women's Hospital, to become the new NCI Director. Dr. Bertagnolli is an outstanding physician–scientist and surgical oncologist. Because it is unclear how long the vetting process will take, it is not exactly known when she will be appointed. The NCI is looking forward to Dr. Bertagnolli assuming this leadership role. She will be the first woman to serve as NCI Director.

The NCI plans to publish the *Annual Plan and Budget Proposal for Fiscal Year 2024* in September 2022. The Annual Plan (also called Bypass Budget) always is released one year ahead of the federal budget and this year highlights four areas of scientific opportunities: multi-cancer detection tests, undruggable targets, cell therapy, and persistent poverty. The NCI anticipates that the fiscal year (FY) 2023 enacted appropriations will continue the trend of being more than the President's budget proposal. Dr. Lowy noted that Ms. M.K. Holohan, Director, Office of Government and Congressional Relations (OGCR), NCI, will provide further details on the NCI FY 2023 budget later in the meeting.

Cancer Research Highlights. Dr. Lowy highlighted that the NCI Intramural Research Program (IRP), Division of Cancer Epidemiology and Genetics (DCEG), investigators reported on all-cause mortality, including cancer and the association with physical activity in the 24 August 2022 issue of the *JAMA Network Open*. The study enrolled adults ages 59 to 82, with an average age of 70, evaluated different types of physical activity, and had a 10-year follow-up. The results showed that mortality rates were independent of the type of physical activity, but were dependent on the metabolic equivalent of task (MET) measurement. This measure is more precise than the number of minutes. For example, walking at 20 minutes per mile or 3 miles per hour equals three METs. A substantial decrease occurred in the all-cause mortality rate in comparison with aged-matched individuals who did not exercise.

Findings from the international clinical trial, KEYNOTE-355, were published recently in the 21 July 2022 issue of the *New England Journal of Medicine*. The study evaluated a combination of standard chemotherapy plus pembrolizumab in women with advanced triple-negative breast cancer, who had higher levels of programmed death ligand 1. The data show a survival benefit after approximately 3.5 years of treatment.

In June 2022, the NCI released *Tobacco Control Monograph 23,* which focuses on smoking cessation in cancer patients. This report highlights compelling evidence that if patients are current smokers and develop cancer, their outcome as a group will be improved if they stop smoking. The NCI-Designated Cancer Centers (Cancer Centers) through the Cancer Center Cessation Initiative (C3I) have been striving to better understand this level of care. The goal is to ensure that this C3I practice is disseminated broadly to patients who are treated outside of the major Cancer Centers. Dr. Lowy remarked that the message is that it is never too late to quit smoking and that quitting has clear benefits regardless of cancer type.

Dr. Lowy called attention to the NCI–American Cancer Society (ACS) joint report on cancer treatment and survivorship statistics published in the 23 June 2022 issue of the *Cancer Journal for Clinicians*. The authors explained that with mortality rates decreasing, survival rates are increasing such that the number of cancer survivors in the United States continues to increase. More than 5 percent of the total population of the United States are cancer survivors, totaling 18 million people; and more than two-thirds are over age 65. Although this is significant progress to be celebrated, the NCI and the ACS are seeking to further improve these statistics.

Cancer Moonshot℠ Update. Dr. Lowy reported that the Cancer Cabinet, established during in the reignited Cancer Moonshot announcement, convened on 13 July 2022 at the White House. First Lady Dr. Jill Biden presided, and representatives from across the government attended. Several priority actions of the Cancer Cabinet were discussed, including bringing cutting-edge research through the pipeline to patients and communities. Dr. Lowy commented that even advances that reduce mortality rates by 50 percent or more will not end cancer as we know it if the field does not change the outlook for people who have cancer. During the July meeting, a *White House Fact Sheet* was released and announced President Joseph R. Biden's intent to appoint three new PCP members: Dr. Mitchell Berger, University of California, San Francisco; Dr. Carol L. Brown, Memorial Sloan Kettering Cancer Center; and Dr. Elizabeth M. Jaffee, Sidney Kimmel Comprehensive Cancer Center, Skip Viragh Pancreatic Cancer Center, and Johns Hopkins University. Dr. Lowy acknowledged and expressed appreciation to the current Panel: Dr. John Williams, Chair; Mr. Robert Ingram; and Dr. Edith Mitchell. He noted the recent Panel's report on bridging the cancer screening gap, which aligns with the priority actions of the Cancer Cabinet.

In support of the next phase of the Cancer Moonshot, the NCI has issued requests for applications for implementing three new programs: Cancer Moonshot Scholars, Telehealth Research Centers of Excellence (TRACE), and multi-cancer detection. The first cohort of Scholars is anticipated to be announced in 2023. The NCI issued the first TRACE awards to four academic institutions in August 2022. The multi-cancer detection effort has been widely endorsed and is underway.

Addressing Health Disparities in Clinical Trials. Dr. Lowy noted that the NCI has a long-term commitment to increasing enrollment of underrepresented groups in NCI clinical trials. He acknowledged Dr. Worta McCaskill-Stevens, Chief, Community Oncology and Prevention Trials Research Group, Division of Cancer Prevention (DCP), and her team, which has led this effort within the NCI Community Oncology Research Program (NCORP). Minority accruals in NCI's National Clinical Trials Network (NCTN) increased from 14 percent during the effort's initial 3-year period (1999–2001) to 25 percent during the most recent 3-year period (2017–2019). The majority of the increase in enrollment has been in Black/African American and Hispanic populations. Minority enrollment data collected during the pandemic from 2020 and 2021 are pending. An important component of the reignited Cancer Moonshot

also is to increase enrollment of underrepresented groups in NCI clinical trials. The goal is to mimic at-risk populations for the specific cancer studied, emphasizing a need for greater investment (e.g., community engagement) and more diversity among health care providers. The NCI is in the process of taking steps to ensure that this becomes a reality. The NCI Equity and Inclusion Program will host the NCI Summit on Increasing Diversity, Equity and Inclusion in Cancer Clinical Trials on 16 November 2022. The aim is to identify and discuss the implementation of best practices for increasing inclusion and equity in NCI cancer clinical trials.

FNLCR Programs and Activities. Monkeypox treatments are available, but they have not been subjected to rigorous efficacy trials in humans. Dr. Lowy explained that the FNLCR is supporting the National Institute of Allergy and Infectious Diseases (NIAID) in working with the Democratic Republic of the Congo (DRC) to combat an outbreak of monkeypox strain-1. This strain causes more serious disease than strain-3 (i.e., West African strain), which has been spreading in the United States. The expectation is that the monkeypox virus treatment clinical trial in the DRC to evaluate the safety and efficacy of tecovirimat in patients with the disease will provide the demonstrated efficacy that will be generalizable across virus strains.

Dr. Lowy remarked that the importance of training and diversity and equity extends to NCI-Frederick and the FNLCR. Several academic collaborations and partnerships, including those with Historically Black Colleges and Universities (e.g., Howard University), have been established in recent years. He explained that Dr. Ethan Dmitrovsky, Laboratory Director, FNLCR, President, Leidos Biomedical Research, Inc., (Leidos Biomed), has led these efforts. Activities include hosting seminars for graduate students and underrepresented groups. Additional partnerships are underway.

Members were informed that the U.S. Department of Health and Human Services (HHS) Secretary Xavier Becerra, HHS Region 3 Director, Dr. Ala Stanford, and Senators Ben Cardin (D-Maryland) and Chris Van Hollen (D-Maryland) and Rep. David Trone (D-Maryland) visited the FNLCR on 22 July 2022. Dr. Melinda G. Hollingshead, Chief, Biological Testing Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis (DCTD), NCI, who manages the Patient-Derived Models Repository (PDMR), provided a hands-on demonstration of generating patient-derived xenografts (PDXs) from cancer patients' tumors. The delegation was thoroughly engaged, and NIH Performing the Duties of the Director Dr. Lawrence A. Tabak also attended. This visit provided a forum to highlight to Congress the opportunities the NCI envisions for cancer research. Dr. Lowy highlighted that the PDMR currently has 600 PDX models, with the goal of developing 1,000 in total. These models will be readily available to the cancer research community for designing new interventions for treating cancer.

Questions and Answers

NCAB Chair Dr. Carpten commented on the role of the PDX Development and Trial Centers Research Network (PDXNet) in increasing diversity in cancer model systems. He noted the expansion of PDXNet to include Minority PDX Development and Trial Centers and that 60 percent of models will be obtained from underrepresented minority patients. This will allow better understanding of cancer in the broader context.

In response to a question from NCAB Chair Dr. Carpten about the operation of FNLCR, the funding, and its relationship with the NCI, Dr. Lowy explained that FNLCR is a government resource and contract laboratory. The amount of money spent to support FNLCR varies each year; two-thirds of the funding comes from the NCI and one-third from the NIAID. During the COVID-19 pandemic, the NCI took a leading role in SARS-CoV-2 serology, and the FNLCR transitioned some of its activities to this effort and served as a test center for the U.S. Food and Drug Administration (FDA) for informing emergency use authorizations. Cancer research activities include managing the NCI RAS (an oncogene

mutated in 30 percent of cancers) Initiative and related resources, supporting the NCI Molecular Analysis for Therapy Choice (NCI-MATCH) trial, and assisting with the NCI Experimental Therapeutics (NExT) program.

Dr. Anna D. Barker, Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California, asked about the FY 2023 paylines, expectations of a decrease in the number of investigator-initiated grant (e.g., R01) applications the NCI receives, and success rates. Dr. Lowy replied that paylines are a high priority for the NCI and noted the progressively increasing investments in the Research Project Grant (RPG) pool compared with the percentage of the overall NCI budget. The large increase in R01 applications during the past years has plateaued, but the number of awards have not kept pace with the number of applications received. Dr. Norman E. Sharpless, then NCI Director, developed the idea of implementing a 15th percentile payline by 2025. Paylines increased from the 8th to the 11th percentile in a short period of time. The NCI needed to pause in FY 2022 but remains hopeful about resuming efforts toward the "15 by 25" goal, which will depend on support from Congress.

NCAB Chair Dr. Carpten inquired on the paylines for early-stage investigators (ESIs). Dr. Lowy pointed out that the NCI will continue to provide ESIs a 5 percentile enhancement compared with established investigators. The number of awards provided to ESIs in FY 2021 exceeded those of the previous three to four years.

Dr. Electra D. Paskett, Marion N. Rowley Professor of Cancer Research, Director, Division of Cancer Prevention and Control, Department of Internal Medicine, College of Medicine, The Ohio State University, appreciates enrolling underrepresented populations in NCI clinical trials as a priority of the next phase of the Cancer Moonshot. She commented on the need to consider the recruitment of minority populations where the question is relevant and important for that population and to set accrual goals to reach sufficient statistical power to answer that question for that research group, similar to the model used by the Alliance for Clinical Trials in Oncology and the Guiding Endocrine Therapy Success through Empowerment and Technology (commonly called GET SET) Study.

Dr. Howard J. Fingert, Consultant, asked about the predicted directions emanating from the Cancer Immune Monitoring and Analysis Centers (CIMAC) and the immuno-oncology biomarkers that are being published, as well as the validation work that is ongoing to advance immunotherapy clinical trial accrual goals. Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research, and Director, DCTD, NCI, explained that the most important, immediate result of the CIMAC is establishment of the assay development program. This program obtains samples from patients who have been accrued to trials already. Progress on new precision medicine activities will be provided at a future meeting. One such activity is the immunoMATCH (or iMATCH) trial, in which patients are screened for a standardized set of immunological biomarkers prior to entering the trial, with the aim of developing prospective biomarkers.

IV. LEGISLATIVE REPORT—MS. M.K. HOLOHAN

Ms. Holohan reported on FY 2023 appropriations, pending legislation to monitor, the congressional calendar, and midterm elections. She called attention to the detailed legislative report in the Board meeting book. Ms. Holohan reminded the Members of the process through which NCI receives its appropriation. The process begins with the release of President's budget proposal, which for FY 2023 occurred in late March 2022. In the second step, Congress convenes hearings and begins preparing spending bills. In step three, the appropriations committees conference, conduct bipartisan negotiations, and finalize the spending bills to be enacted in the summer. Ideally, appropriations are received before the start of the fiscal year. In the past 26 years, this has happened twice for the NIH, in 1996 and in 2018. In 2018, the FY 2019 bill was paired with the defense bill, sparing the NIH from the longest government shutdown in history. The fiscal year ends in less than 1 month, and Congress is preparing for a continuing

resolution (CR), but a government shutdown is not anticipated. It is unlikely that the appropriations process will be completed before the November elections. Although it could carry over into the next Congress, retiring congressional members who are senior appropriators will be motivated to complete appropriations before the end of the current Congress.

The NIH FY 2023 appropriation hearings and budget proposals were held in May 2022, i.e., in the House and the Senate on 11 and 17 May, respectfully. Dr. Lowy testified at these hearings. The FY 2022 omnibus was completed weeks before these hearings, and bipartisan support from Congress enabled a $353 million (M) increase for the NCI. The FY 2023 appropriations are pending; the major threshold issue is defense versus non-defense funding levels, followed by immigration, border security, and abortion policy issues. The House passed its bill out of committee and proposed a $466 M increase for the NCI. The Senate's draft bill proposed a $290 M increase.

Ms. Holohan noted that the Advanced Research Projects Agency for Health (ARPA-H) is still in its early stages of development. NIH Acting Principal Deputy Director Dr. Tara A. Schwetz presented a comprehensive report of ARPA-H to the NIH Advisory Committee to the Director at its June 2022 meeting. The FY 2022 omnibus included $1 billion (B) in funding for ARPA-H, which can be spent over 3 years and was distributed in April. In addition, HHS Secretary Becerra was authorized to temporarily transfer ARPA-H into the NIH and has done so. Authorizing legislation for ARPA-H is pending and disagreement exists within the scientific community. Larger debate is occurring about where ARPA-H should reside, within or independently outside the NIH. Three bills have been proposed: two in the House and one in the Senate. Representative Anna Eshoo (D-California), Chair, Health Subcommittee of the House Committee on Energy and Commerce, introduced a bill to establish ARPA-H within HHS, but not the NIH. Senator Patty Murray (D-Washington), Chair, Senate Committee on Health Education, Labor and Pensions, and Senator Richard Burr (R-North Carolina) introduced a bill that would allow ARPA-H to be established within the NIH, but prohibits it from being geographically located in the Washington, D.C., area and the hiring of anyone who had been employed by NIH within the prior 3 years. In May 2022, HHS Secretary Becerra appointed Dr. Adam Russell as ARPA-H Acting Deputy Director.

In August 2022, the Biden-Harris Administration and congressional Democrats advanced two major pieces of legislation along party line votes. The Creating Helpful Incentives to Produce Semiconductors (CHIPS) and Science Act (previously called Endless Frontiers Act) was enacted on 11 August 2022, will invest $52 billion in U.S. production of semiconductor chips, and authorizes a 5-year $81 B increase in funding for the National Science Foundation. The Inflation Reduction Act was enacted on 16 August 2022 and advances some key domestic priorities, including health care, clean energy, and taxes. Must-pass legislation includes expiring authorizations for FDA User Fee Reauthorization, Small Business Innovation Research/Small Business Technology Transfer program, and the National Defense Authorization Act. Other pending legislation the NCI is monitoring includes the Pandemic Preparedness and ARPA-H authorizations, telehealth continuation and expansion, and clinical trials access and inclusion.

Ms. Holohan noted that the congressional calendar always is subject to change. Some legislators will return on 6 September 2022, with 3 weeks to pass a CR to avoid a government shutdown and to address the must-pass legislation. Both chambers will be in session for 11 days prior to the November midterm elections. All members of the House are up for reelection, as is one-third of the Senate. Approximately 90 nominations for the Administration are pending. Historically, the President's party loses seats in the midterms, with two exceptions since 1946: President Bill Clinton's second term and President George W. Bush's first term. Ms. Holohan also noted that voter turnout was higher for the 2018 elections than for most recent midterms. She remarked that it is difficult to forecast voter turnout in 2022.

Questions and Answers

In response to a question from NCAB Chair Dr. Carpten about the budget for the next phase of the Cancer Moonshot, Ms. Holohan pointed out that that appropriators can fund new projects in regular appropriations, set-asides, or mandatory funding.

Dr. Christopher R. Friese, Elizabeth Tone Hosmer Professor of Nursing, Director, Center for Improving Patient and Population Sciences, Associate Director for Cancer Control and Population Sciences, University of Michigan Rogel Cancer Center, University of Michigan, expressed concern that additional COVID-19 relief packages have stalled. Surges in cases will hinder the cancer community in enrolling patients in clinical trials. He asked whether there had been an evaluation of the connection between the COVID-19 relief funds and the impact on cancer care delivery. Ms. Holohan was not aware if that connection had been evaluated across diseases. She explained that the NCI had received $306 M in COVID-19 funding to work on SARS-CoV-2 serology and noted the rapid adjustments made to clinical trials to continue programs and access for patients.

V. HUMAN PAPILLOMAVIRUS (HPV) EPIDEMIOLOGY PREDICTS COST-EFFECTIVE CERVICAL SCREENING—DR. MARK SCHIFFMAN

Dr. Mark Schiffman, Senior Investigator, Clinical Genetics Branch, DCEG, discussed how epidemiologic understanding of HPV and cervical carcinogenesis can guide cost-effective screening strategies. He acknowledged Dr. Nicole Gastineau Campos, Senior Research Scientist, Center for Health Decision Science, Harvard T.H. Chan School of Public Health, who has been supporting this effort. Dr. Schiffman explained that the field understands more about cervical cancer and HPV than any of the other major cancers and has a unique opportunity to identify the causal agent and how to block it. He focused his presentation on low-resource settings where cervical cancer burden is highest, reviewed some key principles, and provided an example of one possible strategy being examined.

Disparities in cervical cancer mortality are increasing and are specific to settings, not countries. In 2018, the World Health Organization issued a Call to Action for the elimination of cervical cancer. In that context, the NCI realized that the path to such an end would be uneven depending on the starting point. Millions of women beyond the target age for HPV vaccination have never been screened for cervical cancer, regardless the income level. Ages 30–49 represent the best screening years to identify precancerous lesions and prevent cancer. The majority of mortality from cervical cancer has been observed in low- and middle-income countries. Some resources are available, but whether they will be allocated to HPV vaccine and screening programs is unclear. To address this issue, the NCI IRP has built a framework for a cost-effectiveness analysis of screening. This framework consists of three components, all of which are ongoing: developing a natural history model, estimating the impact of selected prevention strategies, and performing health decision modeling analysis to compare strategies.

Over the past 40 years, the NCI IRP has been broadening the scope of cervical HPV epidemiology to inform a natural history model and has made presentations to the NCAB at each implementation. The first area of emphasis that started in the 1970s was ideology and pathogenesis to investigate the cause and causal pathway of the disease. The main research partners included clinicians, pathologists, cytologists, and molecular biologists. Dr. Schiffman remarked that the established HPV and cervical cancer causal pathway is one of the best understood natural histories of any major cancer. In this pathway, from a normal cervix to the first exposure leading to minor abnormal tissue changes, the infection of 13 different HPV types is involved in the progression to precancer and then cancer followed by death if not successfully treated. Because of this research, the specific causative HPVs are known, have been well characterized, and can be measured accurately. The second area of emphasis was prevention models to conduct cohort studies, vaccine trials, and screening tests in the 1990s and 2000s. The main research partners included immunologists, virologists, and DNA diagnosticians. The third area

of emphasis was clinical epidemiology and included studies of risk estimation, artificial intelligence guidelines, prevention strategies, and cost-effectiveness analysis, which is the focus of today's presentation. Guidelines groups, optical engineers, and artificial intelligence health-decision scientists comprise the research partners.

The preventive measures (i.e., interventions) implemented based on the established HPV and cervical cancer causal pathway have included vaccination to eliminate the first exposure and screening to identify precancer. Several methods have been validated, and the main focus now is on strategies. Dr. Schiffman explained that despite these advances, which have been recognized since 2005, efforts are ongoing to deliver these interventions to the people who need them most. In fact, the decline in cervical cancer in the United States has been stagnant and mortality in high-risk areas worldwide continues to increase. The NCI is evaluating ways to make these interventions simple and cost effective. The emphasis always has been on absolute risk, and the HPV epidemiology field has derived questions to help identify those at high risk in a screening population. HPV screening reassures people who are at risk for developing cervical cancer and test negative and alerts those who test positive. A triage test can reveal precancers among people who are HPV positive within a screening population and identify people in need treatment.

Dr. Schiffman noted that it is well understood that accuracy equals efficacy. Older technologies need repetition to overcome an error, but a highly accurate test performed less often is preferable. This principle is true in high-resource settings for efficiency and minimal morbidity and in low-resource settings for affordability and sustainability. Within the microscopic approximation of a causal pathway for cervical cancer, the traditional terms of clinical assessment (e.g., cervical intra-epithelial neoplasia) are useful for communicating about the abnormal changes, but are proxies for the real molecular processes that are at the center of carcinogenesis. In a visual approximation of the cervix to determine a causal pathway, pathologists are challenged to know the difference between infection and precancer.

Dr. Schiffman described a consortium-based study of a prevention strategy designed to be cost effective in low-resource settings, i.e., the Cancer Moonshot–supported Human Papillomavirus and Automated Visual Evaluation (PAVE). He informed members that the aim is to accelerate HPV-based therapies in the United States and internationally. To date, PAVE includes 10 international partners. After being delayed by COVID-19, screening to validate this prevention strategy is soon to begin. The goal is to achieve accurate screening in resource-limited settings by matching cervical cancer risk with equal management of that risk. The first step is to screen where the disease is most prevalent and the 5-year average death rate from cervical cancer is high. Following that, the next step is to identify individuals who are at risk using a self-swab technique (i.e., self-sampling). He noted that the sample, which has been shown to have the same sensitivity as a clinician sample, is analyzed using a low-cost high-risk HPV test developed in the DCEG. Samples that test positive are triaged to groups based on risk-informed HPV genotyping. The appearance of precancer or cancer is evaluated using the machine learning/deep learning–based automated visual evaluation (AVE) method, which Dr. Schiffman and his team have been working on and refining for several years. The results are confirmed in the HPV-AVE Strategy for Screen-Triage-Treat study underway in the PAVE consortium. Biopsies are performed, results are validated, and individuals are treated.

Dr. Schiffman remarked on how direct measurement of translational probabilities, by leveraging deep learning, adapting to different image collection devices, and creating a dedicated device, results in increased trustworthiness for health decisions. He concluded by highlighting some take-home messages for implementing a cost-effective screening program in low-resource settings: (1) follow HPV natural history and cervical carcinogenesis accurately, (2) screen at appropriate ages in high-risk geographical regions where prior screening has been limited, (3) use HPV tests on self-collected specimens, and (4) let HPV type guide risk estimation. He remarked that accurate risk estimation is achievable, but more work is needed to improve affordability and sustainability.

Questions and Answers

In response to a question from NCAB Chair Dr. Carpten about whether this model will make a noticeable change or can be implemented in regions of high cervical cancer rates persist and large gaps in awareness of the disease remain (e.g., Mississippi Delta), Dr. Schiffman noted that the NCI, through its Health Communication and Informatics Research Branch, has been able to communicate in low-resource settings how HPV science and artificial intelligence can predict cervical cancer risk and has been working to better understand what information people need to decide on screening.

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor Emeritus of Neurosurgery, Duke University Medical Center, suggested exploring mechanisms within the cervical HPV epidemiology project to work with governments at the state, local, or international levels in low-resource settings to ensure that individuals found to be at high risk for cervical cancer or who have tested positive for HPV are provided options for interventions and treatments.

Dr. Margaret R. Spitz, Professor Emeritus, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, asked whether this approach had been considered with oropharyngeal cancers, which also have been associated with HPV infection. Dr. Schiffman noted that researchers have reported no pre-cancerous state well-identified for the oropharynx. Finding a surrogate endpoint precursor would be a major step of a screening effort.

NCAB Chair Dr. Carpten suggested investigating other noninvasive approaches (e.g., microbiome) for detecting precancerous lesions.

Dr. Karen M. Winkfield, Executive Director, Meharry-Vanderbilt Alliance, Ingram Professor of Cancer Research, Vanderbilt-Ingram Cancer Research, Professor of Radiation Oncology, Vanderbilt University School of Medicine, commented that cervical cancer is one that can be prevented and cured. She noted the NCI's National Outreach Network (NON) and Community Health Educators (CHE) program as resources to leverage for health education and suggested providing such resources in traditionally underserved communities in the United States.

Dr. Susan Thomas Vadaparampil, Associate Center Director, Community Outreach, Engagement, and Equity, Professor, Department of Health Outcomes and Behavior, Moffitt Cancer Center, noted Federally Qualified Health Centers and community clinics being funded to provide health education and outreach in low-resource settings, globally. She suggested advancing such efforts in underserved areas in the United States.

Dr. Paskett suggested reviewing the overall trends in timely follow-up and treatment of abnormalities found during cervical cancer screening in the United States. She highlighted a multilevel approach to implementation that includes improving HPV vaccination rates and access and addressing cultural sensitivities.

VI. ONGOING AND NEW BUSINESS—DR. JOHN D. CARPTEN

NCAB *ad hoc* Subcommittee on Experimental Therapeutics. Dr. Amy B. Heimberger, Jean Malnati Miller Professor of Brain Tumor Research, Vice Chair for Research, Department of Neurosurgery, Northwestern University Feinberg School of Medicine, and Chair of the NCAB *ad hoc* Subcommittee on Experimental Therapeutics, presented the report of the 31 August 2022 meeting. During the meeting, the Subcommittee was presented an update on activities related to cellular therapies for solid tumors by Dr. Rose Aurigemma, Associate Director, Developmental Therapeutics Program, DCTD, NCI,

and Subcommittee Executive Secretary. The initiative resulted in three companion funding opportunity announcements for the Cancer Adoptive Cell Therapy Network (Can-ACT).

The Subcommittee also discussed the need for increased training in the area of translational research, even for established investigators. Dr. Oliver Bogler, Director, Center for Cancer Training, NCI, presented information regarding the Interagency Oncology Taskforce Fellowship, which provides training in research and research-related regulatory policies and regulations. Additionally, the Subcommittee was reminded that the NCI supports extramural cancer training at multiple career stages through a variety of funding mechanisms, although these grants often do not encompass the translational research continuum. The Methods in Clinical Cancer Research Workshop, which is held annually to educate and train ESIs on best practices related to clinical design, also was highlighted. The Subcommittee discussed specific challenges associated with translational research, including the need for increased workforce diversity, institutional support for intellectual property needs, understanding of industry processes, institutional infrastructure to support good laboratory practices, and understanding of legal- and business-related aspects of research. Dr. Heimberger explained that the Subcommittee proposed a centralized, comprehensive NCI curriculum to provide investigators the necessary research, regulatory, and legal expertise to perform accelerated translational research. The curriculum could incorporate real-world experiences into regulatory training.

Questions and Answers

Dr. Fingert noted other initiatives that have focused on optimizing translational research from academia into commercialization, including the European Strengthening Training of Academia in Regulatory Science initiative and the FDA's Project Catalyst. He added that international collaborations could provide opportunities for harmonization.

Motion. A motion to accept the report of the 31 August 2022 NCAB *ad hoc* Subcommittee on Experimental Therapeutics meeting was approved unanimously.

NCAB Subcommittee on Planning and Budget. Dr. Barker, Chair of the NCAB Subcommittee on Planning and Budget, presented the report of the 31 August 2022 meeting. Dr. Barker reminded the Board that the number of NCI grant applications has increased substantially in recent years, and the NCI paylines have been affected. The importance of supporting ESIs was emphasized. NCI appropriations for FY 2022 totaled $6.9 B, of which $6.7 B is base appropriations. NCI's base appropriations include funds for the initial Cancer Moonshot, which is in its final year of funding. Overall, paylines have been sustained at the level of the previous year. The Subcommittee discussed the challenges of raising paylines; commitments beyond the initial year of funding must be considered.

An update on the FY 2023 budget, including current developments and trends, was presented by Mr. Patrick McGarey, Associate Director for Finance and Legislation, and the Subcommittee Executive Secretary. Mr. McGarey informed members that the House and the Senate have been considering the NIH and NCI budgets for FY 2023. The proposed NCI budget for FY 2023 includes increases of 6.7 and 4.2 percent by the House and Senate, respectively. The House and Senate have proposed $2.75 B and $1.0 B, respectively, for ARPA-H in FY 2023. The Senate proposed that ARPA-H be housed within the NIH, and the House proposed that ARPA-H be housed within HHS, but not within the NIH. Additionally, the NCI has submitted several ideas regarding the next phase of the Cancer Moonshot. The initial Cancer Moonshot focused on accelerating cancer research in specific areas, and the reignited Cancer Moonshot will enable a greater emphasis on delivering care more quickly and effectively.

The Subcommittee discussed the Sergeant First Class Heath Robinson Honoring Our Promise to Address Comprehensive Toxics (PACT) Act 2022, which is broadly relevant to the field of cancer research. It was noted that the NCI is interested in leveraging resources among federal agencies. The

Subcommittee also discussed the importance of multi-cancer detection and standards of care, noting a paradigm shift within the field of cancer research. Additionally, they noted the importance of using mortality endpoints in clinical trials. Additionally, it was noted that the NCI and NIH manage resources to assess the allocation of funds among different areas of cancer.

Questions and Answers

NCAB Chair Dr. Carpten commented on the importance of planning for future funding models, such as the reignited Cancer Moonshot. Dr. Barker explained that this topic is under consideration. She noted that the next phase of the Cancer Moonshot likely will be more focused on patients and delivery of care, especially for minority and other underserved populations.

In response to a question from NCAB Chair Dr. Carpten about how the recompete for FNLCR will affect future NCI budgets, Dr. Lowy clarified that the recompete is an open competition, and the current contractor may apply. A transition period will occur, but personnel turnover will be limited. Ongoing work will continue, and a high maximum dollar amount is in place within the budget.

Motion. A motion to accept the report of the 31 August 2022 NCAB Planning and Budget Subcommittee meeting was approved unanimously.

Future Agenda Items. The NCAB members were asked to forward suggestions for potential future agenda items to Drs. Carpten and Gray. During the meeting, Members requested a report on the status of ARPA-H from Acting Deputy Director Russell or his staff; an update from the Subcommittee on Cancer Centers on Medicaid coverage among the NCI-Designated Cancer Centers; a report on the trajectory of the number of ESI proposal submissions and grants funded over the past 5–10 years; and a presentation on the current status and plans for immunotherapeutic biomarkers among NCI intramural investigators.

VII. ADJOURNMENT OF OPEN SESSION—DR. JOHN D. CARPTEN

Dr. Carpten adjourned the open session. Only Board members and designated NCI staff remained for the closed session.

VIII. CLOSED SESSION—DR. JOHN D. CARPTEN

"This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c)(4), 552b(c)(6), Title 5 U.S. code, and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2)."

There was a review of grants and a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

The Board was informed that a comprehensive listing of all grant applications to be included in the **en bloc** vote was in the Special Actions package. Those grant applications, as well as those announced during the closed session, could be considered for funding by the Institute.

The NCAB **en bloc** motion to concur with IRG recommendations was unanimously approved. During the closed session, a total of 2,035 NCI applications were reviewed, requesting direct cost support of $782,829,814 and three FDA applications requesting direct cost support of $850,184.

IX. ADJOURNMENT—DR. JOHN D. CARPTEN

Dr. Carpten thanked all the Board members, as well as the visitors and observers, for attending.

There being no further business, the 17th virtual meeting of the NCAB was adjourned at 4:35 p.m. on Wednesday, 31 August 2022.

Date	John D. Carpten, Ph.D., Chair, NCAB
Date	Paulette S. Gray, Ph.D., Executive Secretary