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In this Issue

Letter from the Editor

Our first article in this issue is a review of Post-Acute Sequelae of COVID-19 by Jen Alexander-Brett, Hara Levy, Indu Ayappa, Leslie Spikes and Navneet Dhillon.

The article provides a description of our current understanding of the myriad ways in which COVID-19 infections may evolve into "Long COVID", the spectrum of pulmonary and extra-pulmonary manifestations, and our emerging understanding of how best to manage and treat this very large and growing group of patients. The article provides a detailed description of opportunities for research support in this area coming from both the NIH and Biden Administration. There also is a link to a website listing information about specific sites providing care for these patients across the country.

In a subsequent article, Indu Ayappa and colleagues provide an opinion piece on sleep-related research. In particular, they have identified 4 potential gaps in the broad array of research directions listed in the recent National Institutes of Health Sleep Research Plan.

These potential gaps, as outlined in Dr. Ayappa's article, include the need to develop longitudinal cohort studies of patients with sleep disorders and the need to focus more efforts on research related to identifying the impact of sleep disordered breathing on patient-reported outcomes, including in patients with common respiratory diseases such as COPD, asthma, and interstitial lung diseases. The authors suggest that these issues should be of high interest to all ATS members, and I agree.

In another article, Dr. Mark Klein and I have provided a brief update on the Veterans Health Administration's relatively new Lung Precision Oncology Program. Despite that name, much of the activity in this new program relates to research and care related to early detection of lung cancer through lung cancer screening. The program started in November 2020 with 18 newly funded sites across the VA. It now has grown to 99 funded VA sites, in part because of a large contribution to expand lung cancer screening from President Biden's Cancer Moonshot Program. The article describes some of the research topics being undertaken in the program related to lung cancer screening. It also lists some sessions at the May ATS International Conference that are of related interest.

Also in this issue, Valerie Adelson, Associate Director, Government Relations, for the ATS, has provided an excellent description of the reignited Cancer Moonshot and its specific goals and programs as well as some information about important new appointments coming from the Biden administration.

Sincerely,

James K. Brown MD
Chair, Research Advocacy Committee

Post-Acute Sequelae of COVID-19 and Funding Opportunities

Jen Alexander-Brett MD PhD, Hara Levy MD, Indu Ayappa PhD, Leslie Spikes MD and Navneet K. Dhillon PhD

Now approaching 3 years since the first reported cases of SARS-CoV2, we reflect on the tremendous worldwide impact of this viral pandemic. Multiple waves of infection swept the globe, driven by novel variants, with cases rising sharply and peaking each time higher than before. However, the international scientific community met the pandemic with a groundswell effort to develop diagnostic assays, treatments for acute illness and, ultimately, highly effective vaccines with unprecedented speed.

In accordance with these clinical milestones, there was an explosion of research activity aimed at understanding the pathophysiology behind this novel and highly contagious virus and the basis for the morbidity and mortality of COVID-19 illness. We quickly learned the virus enters cells primarily via ACE2 receptors, abundant on pulmonary alveolar type II and endothelial cells, making the respiratory tract the site of viral replication. Hyperinflammation, cytokine storm, acute lung injury and the resulting hypoxemic respiratory failure were early prominent features of severe illness. Autopsy findings from fatal cases of COVID-19 also revealed widespread pulmonary alveolar capillary micro-thrombosis, occlusion and neovascularization. Large-vessel venous thromboembolism was a variable pathologic feature, and this is widely acknowledged as a significant complication of severe COVID-19 infection that can occur even in the presence of prophylactic or therapeutic anticoagulation. Pulmonary parenchymal and vascular endothelial damage, along with negative inotropic, pro-thrombotic, and pro-fibrotic effects of cytokine storm, combine to increase pulmonary artery pressures with resultant RV dysfunction.

At this stage of the pandemic, we now recognize that COVID-19 is a multisystem disease with potential for long-term post-infectious sequelae. Up to 10-30% of patients experience a variety of residual symptoms that can last months or more following acute illness. Generally, these patients can be divided into two main categories: those that had initial moderate-severe acute infection that required hospitalization with radiographic COVID pneumonia and those that had initial mild disease and may not have had any radiologic or pulmonary function abnormalities during acute illness. The most common chronic respiratory-related symptoms include persistent dyspnea, ongoing chest pain, fatigue, palpitations, brain fog, sleep disturbance and exertional intolerance. Upper respiratory symptoms such as anosmia or dysgeusia are common during acute SARS-CoV2 infection, with a substantial number of patients experiencing persistent disorders of taste and smell post-infection. These complications are commonly known as 'long COVID' syndrome, or more formally, post-acute sequelae of COVID-19 (PASC), currently defined as persistent symptoms after SARS-CoV2 infection beyond 12 weeks regardless of acute disease severity. Risk factors may include female gender, more than 5 symptoms during the first week of illness, obesity, advanced age and a history of asthma or other comorbidities. Health disparities have also contributed to a disproportionate burden of PASC among minority populations.

Longitudinal studies are revealing the spectrum of chronic pulmonary diseases that develop following acute COVID-19 illness. Persistent ground-glass infiltrates, evidence of fibrotic changes and decreased DLCO are the most common abnormalities observed in the survivors of COVID-19 infection in the months following hospitalization. These could be explained by non-resolving endothelial injury or chronic hyperinflammation that lead to permanent pulmonary vascular remodeling and parenchymal fibrosis. Management of these persistent physiologic and radiologic abnormalities is yet to be defined, but some have attempted prolonged treatment with corticosteroids and multiple antifibrotic agents are being investigated as potential therapies. These patients are furthermore at increased risk for pulmonary vascular disease in the long-term, developing pulmonary hypertension by a variety of mechanisms including by autoimmune effects and/or endothelial injury (group I PAH), persistent myocardial involvement (group II), an ongoing parenchymal lung fibrosis (group III) or venous thromboembolism (group IV).

Fatigue, poor sleep and sleep disruption are common PASC symptoms and overlap with multiple sleep disorders. The detrimental impact of poor sleep on cognition, especially in the domains of attention and processing speed is known, and may be related to the symptom of brain fog. Evaluation of existing sleep disorders (prior history of insomnia, poor sleep hygiene and obstructive sleep apnea), through

validated questionnaires and/or objective assessment of sleep quantity and quality may help explain symptoms, guide therapy and help understand the mechanisms of PASC. In addition, because the defining symptoms of PASC are similar to myalgic encephalomyelitis/chronic fatigue syndrome (fatigue, unrefreshing sleep, cognitive disturbances) examination of sleep and circadian abnormalities in subjects with PASC is likely to provide clues to the sites of injury and guide therapy. PASC patients also have dysfunctional breathing during exercise, suggesting a respiratory control dysfunction of neurological origin. Evaluation and treatment plans for patients with brain fog post COVID-19 should include screening for sleep disorders, sleep quality as well as anxiety and depression. Some data suggest that these sleep disorders may improve with time, but whether sleep quality returns to baseline in PASC has yet to be evaluated.

The clinical course of COVID-19 generally seems to be milder in children, but a proportion do develop hyperinflammatory disease manifest as multi-inflammatory syndrome in children (MIS-C) or PASC syndromes following mild or severe illness similar to adults. While PASC in adults was identified early in the pandemic, data on prolonged symptoms in children are scarce. Furthermore, as COVID-19 vaccine efficacy trials are extended to include younger children, there is a need to characterize the response to SARS-CoV-2 infection in relation to disease severity to identify those as risk for PASC and/or inform risk mitigation. Controversy remains as to whether severity in pediatric patients is associated with a hyperinflammatory cytokine storm or failure of the host protective immunity that results in unrestrained viral dissemination. To that end, there is need for a concerted effort to evaluate pediatric patients, as their symptoms may or may not evolve after SARS-CoV-2 infection, and distinct responses to SARS-CoV-2 could explain at least some of the variability in COVID-19 disease severity in children. The rapid spread, high morbidity and mortality and inability to identify those at risk for PASC have highlighted the urgent need for understanding viral dynamics and host response in order to facilitate strategies for antiviral treatment, vaccination, and epidemiological control in pediatric populations.

In evaluating patients with PASC, the subset with long-term term symptoms after mild infection can be frustrating to both patients and physicians. In many cases their objective testing, including pulmonary function testing, radiologic imaging, and echocardiograms are largely unrevealing. There have been some algorithms suggested for further diagnostic testing, including cardiopulmonary exercise testing and cardiac MRI, but thus far diagnostic utility of these studies is unclear. Therefore, a comprehensive approach should be taken including the involvement of multiple subspecialists. In response to the high demand for specialized PASC care, a growing number of post-COVID care clinics (PCCCs) have been established, and as of early 2022, a total of 66 clinics had been established through hospitals and health systems in the US.

Given the increasing prevalence of PASC and anticipated high demand for PCCC services in the future, it is paramount to focus research efforts toward understanding the pathophysiologic basis of PASC,

discovering new effective treatments and establishing the best practices of care. Toward that effort, the NIH launched a trans-NIH PASC Initiative with the goal to improve understanding of recovery from SARS-CoV-2 infection and how to prevent and treat PASC. In February 2021, the NIH announced research opportunities in support of the Researching COVID to Enhance Recovery (RECOVER) initiative OTA-21-015; these included A) clinical science, data resource as biorepository cores and B) recovery cohort studies. This was followed in May 2021 by additional announcements focused on C) mobile health platforms and D) data repositories. Additional areas of special interest (NOSI) include host resilience as a determinant of heterogeneous outcomes in ARDS/ALI (NOT-HL-20-814); effects of smoking/vaping on COVID-19 outcomes (NOT-DA-21-011); mechanisms of COVID-19 associated coagulopathy (NOT-HL-23-003); and investigations of pediatric COVID-19 and respiratory viral co-infection (NOT-HL-22-004). Additional R01 opportunities are available through NHLBI to investigate HIV-related comorbidities and clinical trial administrative supplements are available through the Office of Research on Women's Health to study gender influences on COVID illness.

In April 2022, the Biden Administration announced the White House's plan to direct federal resources through the HHS to support patients with PASC (Long COVID). The four-part plan included: 1) Expanding PASC clinics run by the Veterans Affairs Department; 2) Investing $20M through AHRQ to establish healthcare system PASC "Centers of Excellence"; 3) Strengthening coverage for PASC care through Medicaid/Medicare/Insurance marketplace; 4) Accelerating research by directing more support to the NIH RECOVER Initiative. As part of this effort, the National Research Action Plan on Long-COVID was developed in order to summarize the current state of PASC research and to create a government-wide national research agenda on prevention, diagnosis, treatment and services. The Administration plans to accelerate enrollment of 40,000 patients into the RECOVER cohort and requested an additional $25M in funding to support research into the characteristics, risk factors, mechanism of disease and impacts of PASC.

A list of PCCC clinics can be found here: https://www.beckershospitalreview.com/patient-safety-outcomes/13-hospitals-health-systems-that-have-launched-post-covid-19-clinics.html

More information about NIH funding opportunities can be found at: https://www.nhlbi.nih.gov/coronavirus/nhlbi-covid-19-guidance-researchers

Research Priorities in Sleep for ATS Members

Indu Ayappa PhD, Reena Mehra MD, Susheel Patil MD PhD, Robert Owens MD, Mihaela Teodorescu MD, Atul Malhotra MD, and Sanjay R. Patel MD

The NIH Sleep Research Plan has proposed a broad array of research priorities. Given the relatively short, anticipated completion time for the plan (5 years), it seems appropriate early on to identify gaps which we feel should be filled soon to ensure the effective advancement of the field. Herein, based on the state of the field, we identify several of what we call Critical Opportunities which deserve attention and are not prioritized in the NIH Sleep Research Plan. They also relate to areas that should be of interest to ATS members. These area are: 1) to develop longitudinal cohorts of patients with sleep disorders, 2) to focus on patient reported outcomes and quality of life measures, 3) to underscore the importance of investigation of sleep and pulmonary overlap syndromes, inclusive of overlap hypoxia, and 4) to further develop, diversify, and sustain a scientific workforce to support the mission of the National Center for Sleep Disorders Research (NCSDR). Below, we describe in greater detail each of these Critical Opportunities.

Establish Longitudinal Cohort Studies of Patients with Sleep Disorders:
A fundamental understanding of the trajectories leading to sleep-disordered breathing, commencing early in life, is critical to providing multi-faceted insights on human health and disease. Multicenter longitudinal cohorts across the age spectrum of patients with sleep-disordered breathing are needed to understand several important aspects of the problem. These aspects include the natural history of sleep and breathing disorders, the natural history and progression of sleep-disordered breathing, the occasional recurrence or exacerbation during key life stages (e.g., pregnancy or menopause), the risk of adverse health consequences, and the impact of various treatment modalities. A wealth of literature now demonstrates that there is substantial difference in community-based cohorts identified based on use of screening sleep studies and those which include patients presenting first for clinical care. While significant investments in screening cohorts have been made by NIH, investment in clinical cohorts has not kept pace. The uncoordinated and unlinked care path for patients with sleep-disordered breathing between medical professionals, durable medical equipment (DME) providers, dentists, and other providers, as well as the importance of patient-reported outcomes, makes use of "real world" clinical data extracted from EHRs inadequate and further highlights the importance of investment in research cohorts of diseased patients.

Focus on Impact of Sleep-Disordered Breathing on Patient Reported Outcomes:
As evidenced by the recent draft Agency for Healthcare Research and Quality (AHRQ) report on the benefit of CPAP therapy in OSA, there has been a systematic under-valuation of patient reported outcomes. This under-valuation comes despite the fact that these symptoms are the primary reason patients seek treatment and their improvement is an important mechanism through which OSA treatment can improve well-being. There has been too little research invested in optimizing measurement and collection of patient reported outcomes, such as sleepiness and chronic fatigue, snoring, restorative sleep, sleep disruption, nocturia, morning headaches, concentration/attention deficits and brain fog. These are the key reasons patients present to clinics and their improvement (or not) is the most important outcome to the 1 billion patients suffering from these disorders worldwide. These symptoms also relate to public health concerns, such as work productivity and drowsiness while driving. There is an imperative for investigations on how sleep disordered breathing impacts these patient-reported outcomes. Because of the extraordinarily large numbers of patients impacted and the associated cost of treatments, it is critical to understand the mechanisms underlying the heterogeneity of symptom profiles and responses to different treatments. This area has become more apparent given that post-acute sequelae of COVID-19 (PASC), and the associated fatigue and sleep difficulties, have become so common.

Examine Overlap of Pulmonary Disease with Sleep Disordered Breathing
Although compelling retrospective data and evidence from smaller studies suggest that the co-occurence of pulmonary disease (e.g., chronic obstructive pulmonary disease, asthma, pulmonary hypertension and interstitial lung disease) with sleep disordered breathing may confer worse health outcomes and increased mortality, there are no definitive cohort studies or trials that confirm these suggestions. Furthermore, there is no firm understanding of how co-morbid sleep-disordered breathing may impact pulmonary disease outcomes and responses to standard therapies. The impact of "overlap hypoxia", i.e., intermittent hypoxia superimposed on sustained hypoxia-- remains poorly understood, as are the effects of other features of sleep disordered breathing, such as work of breathing and sleep fragmentation. In addition, understanding the biologic basis of sleep related hypoventilation and central sleep apnea disorders, and their association with patient reported and objective health outcomes, is a critical knowledge gap.

Further develop, diversify, and sustain a scientific workforce to support the mission of the NCSDR:
Mechanisms that sustain and retain junior and established investigators in sleep medicine should be prioritized to maintain a highly skilled workforce. System-wide latitude to all NIH fellows and grantees should be provided to accommodate delays in research due to COVID. These accommodations should be extended to both clinical and basic scientists, particularly to women and underrepresented minorities. Particular attention should be given to attracting and retaining under-represented physician scientists in the sleep field, because of the severely limited physician-scientist pipeline overall. The extent to which existing NIH structures and grant reviewing

processes, specific to sleep, limit the development and diversification of the sleep scientific workforce needs to be evaluated. For example, greater investment in population health research, particularly in research directed to studying disparities in access and care of sleep disorders, may better align NIH funding with interests and values of under-represented physician scientists.

Update on Veterans Health Administration's New Program for Lung Cancer Research and Care

By James K. Brown MD and Mark A. Klein MD

In November 2020, the Veterans Health Administration embarked on an ambitious endeavor to enhance research and care related to lung cancer among the 6 million Veterans within the VA's 1255 health care facilities. The new program, called the Lung Precision Oncology Program (LPOP), has two focuses. These are, first, early detection of lung cancer through use of lung cancer screening and, second, precision oncology and participation in cutting-edge treatment trials for those with more advanced stage disease.

The timing was appropriate for the initiation of this new program. Publication of the National Lung Cancer Screening Trial (1) had demonstrated for the first time the beneficial effects of lung cancer screening, using annual low-dose chest CT scans (LDCTs), on lung cancer-related mortality in a high-risk population. However, other subsequent smaller European studies showed less clear cut results, thus casting doubt on NLST's reproducibility. But the quite recent publication of the European NELSON trial (2) settled the matter. In a large study with over 15,000 high-risk participants randomly assigned to LDCT screening or no screening and followed for a 10-year period, screening reduced lung cancer-associated mortality by 24% in men and by 33% in women. Another recent landmark study (3) demonstrated that recent improvements in survival of those with advanced-stage non-small cell lung cancer survival may well have correlated with availability of novel treatments for those with tumors expressing targetable mutations, such as *EGFR* and *ALK*, as well as immune-based therapies. Within the VA, this new focus on lung cancer is highly appropriate in that some 900,000 Veterans are at high-risk risk of getting lung cancer, as defined by United States Preventative Services Task Force criteria using age and cigarette smoking history. Each year, 400,000 Veterans receive care in the VA for lung cancer, 43,000 new Veterans are diagnosed with lung cancer, and 5,000 die from it.

Administration and Leadership:
The general approach used by the VA in LPOP has been to designate so-called "Hub" sites in the VA around the country which serve as centers of excellence in these areas of lung cancer care and research. In most of these sites, a pulmonary physician is the co-PI in charge of lung cancer screening and a thoracic oncologist serves as co-PI in charge of precision oncology and treatment trials. Associated with each Hub site are several "Spoke" sites that are smaller regional VA hospitals providing care to more rurally based Veterans. LPOP is led by an Executive Steering Committee and co-chaired by VHA's Chief Research and Development Officer Rachel B. Ramoni, D.M.D, Sc.D., and by Michael Kelley, M.D., National Program Director for Oncology in the VA. Dr. Kenute Myrie, Senior Portfolio Manager, Office of Research and Development, provides important administrative leadership of the program. The work of the program is facilitated by the Cooperative Studies Program Coordinating Center at the West Haven VA.

To serve as facilitators of lung cancer screening programs within LPOP, three were chosen at the beginning of the program: Chris Slatore (Portland VA), Renda Weiner (Boston VA), and Jim Brown (San Francisco VA). Shortly after the beginning of LPOP, Chris Slatore was appointed Chief Consultant, Lung Cancer Screening, and Director of a new VA National Center for Lung Cancer Screening. Among its many contributions, leaders of this new center have overseen the development and management of a Lung Cancer Screening Platform (LCSP), a registry and database that allows an individual site in LPOP to keep track of screening activity in its own site as well as across the VA. LCSP is a suite of clinically useful decision support tools embedded in the VA's electronic health record. It assists staff in identifying eligible patients, enrolling them in local screening programs, tracking Veterans with screening-detected nodules to ensure appropriate follow up, and displaying important program data and metrics to ensure quality screening and continuous improvement.

Dramatic Growth of the Program:
In November 2020, at the time of the program's beginning, 18 Hub sites were funded, along with a few affiliated Spoke sites. But shortly after LPOP's initiation, the number of sites in the program began to grow with encouragement and support from LPOP's Executive Steering Committee. Also, in recent months, President Biden's Cancer Moonshot Initiative provided a large award to support further expansion of lung cancer screening in LPOP such that totally different sites in the VA within LPOP now has reached 99. As a consequence of this growth, the number of Veterans screened for lung cancer in LPOP has increased from 59,921 at the beginning of the program to 111,880 at present. To accommodate the increased needs for clinical oversight and scientific support, a number of Workgroups and Sub-workgroups have been created, including related to Lung Cancer Screening for early detection and to Treatment and Therapeutics for those with advanced stage disease. The research-related activities in these Workgroups are described briefly below.

Lung Cancer Screening-Related Workgroups:
The general goal of the projects in these workgroups has been to find practical ways to improve efficiency, efficacy, and equity of lung cancer screening across the VA. The workgroups, their chairs, and a brief description of some of the research projects under development within them are as follows:

(i) **Pre-Screening Workgroup** (chair: Renda Wiener): optimizing treatment of tobacco dependence in the context of screening; improved assessment of life expectancy and co-morbidities to improve patient selection in screening; evaluating deployment-related military and occupational exposures in patient selection for screening; engaging provider and Veteran peers in efforts to enhance recruitment into screening programs; use of risk prediction models to implement patient selection for screening.

(ii) **Radiology Workgroup** (chair: Bob Sherrier): use of teleradiology to assist in managing radiologist workload.

(iii) **Radiomics/Artificial Intelligence Sub-Workgroup** (chair: Anant Mantabhushi): providing a core facility for radiomics and artificial intelligence-related research in LPOP.

(iv) **Outcomes Workgroup** (chair: Jim Brown)

- **Sub-Workgroup 1** (chair: Nichole Tanner): evaluation of an intervention to increase adherence in screening programs; evaluating current practices for communicating results of LDCT scans to patients; using interstitial lung disease (ILD)-associated incidental abnormalities on screening CT's to intervene early in ILD management.
- **Sub-Workgroup 2** (chair: Charles Atwood): evaluating the efficacy of PET/CT scans to guide selection of biopsy sites for high-risk findings in screening.
- **Sub-Workgroup 3** (chair: Scott Shofer): use of a quantitative radiomics assessment of emphysema on initial LDCT scans for risk stratification in screening; evaluation of outcomes by pre-screening health status for Veterans with early-stage lung cancer; evaluating current and best practices for evaluation and management of screen-detected ground-glass opacities; comparing community care-based versus VA-based thoracic surgery for screening-detected lung cancer in Veterans; establishing a VA-wide registry for invasive procedures used in screening programs.

Trials and Treatment Scientific Workgroup (chairs: Mark Klein, Shadia Jalal, Jimmy Ruiz): The missions of TTSW within LPOP are to: 1) promote investigator-initiated studies to evaluate lung cancer precision oncology-based treatment in Veterans and 2) identify clinical trials that may be an especially good fit for them. One of the strengths of LPOP is the emerging ability to work as a national enterprise and, in so doing, take advantage of the economy of scale. Thus, after some initial iterations in the formation of the workgroup, TTSW has been meeting monthly to achieve these goals in a collaborative fashion. A

unique aspect of the approaches to research, taken by LPOP and the VA Office of Research and Development, has been the ability to take advantage of public/private partnerships where the VA may provide funding (via competitive grant review) for study operations in partnership with industry where a study drug is provided by a company. In the last year, one such VA investigator-initiated phase 2 trial was funded, and several other similar concepts have been reviewed. These study concepts are in various stages of design and peer review. Separately, TTSW has engaged with several industry partners over the last year, and numerous partnerships between VA and industry are burgeoning. A unique aspect is that the TTSW will engage with industry partners in a centralized and VA-based fashion to more efficiently open studies that are scientifically robust and consider the unique challenges that Veterans with lung cancer may face. LPOP is of large enough scale that multiple studies, with similar eligibility criteria and testing treatments with similar mechanisms of action, may be accommodated at the same time to enhance the study opportunities for Veterans. At this time, a handful of industry-based studies are moving through this process with a large number of others soon to be vetted in a similar fashion.

What's Ahead?
Since LPOP's beginning, virtual 2-hour meetings have been held every month. The first face-to-face meeting was in Ann Arbor, Michigan, in September 2022. Strong consideration is being given to having the next LPOP face-to-face meeting on Saturday, May 20, 2023, in Washington DC, in conjunction with the American Thoracic Society's International Conference there.

Two important sessions at the upcoming ATS International Conference in May are as follows. Both are closely related to the VA's LPOP and will take place on Monday, May 22, 2023:

9:15 AM: Session 372: REIGNITING THE CANCER MOONSHOT: ATS = MISSION CONTROL FOR LUNG CANCER
Chairs: Nichole Tanner, Renda Wiener, and M. Patricia Rivera

Topics/Speakers:

"Introduction to the 2022 Reignition of the Cancer Moonshot".
Steven Lieberman, Deputy Under Secretary for Health, U.S. Department of Veterans Affairs, Washington DC

"Reducing Disparities Across the Lung Cancer Continuum: Expanding Use of Proven Early Detection Strategies."
Melinda C. Aldrich, MPH, PhD, Vanderbilt University Medical Center, Nashville

"Lung Cancer Screening: Harnessing the VA Enterprise to Expand Proven Early Detection Strategies."
Christopher Slatore, MD, Portland VA Medical Center, Portland, Oregon.

Tobacco control and treatment: a major key to cancer prevention.
Anne Melzer, MD, Minneapolis VA Health System, Minneapolis, MN.

"Precision Oncology for lung cancer: developing new enabling cancer technologies. "
Patrick Nana-Sinkam, MD, Virginia Commonwealth University, Richmond, VA.

12 NOON: Session L13: GENOMICS ANALYSES FROM MILLION VETERAN PROGRAM IMPROVE LUNG CANCER DETECTION AND CARE
Chair: James K. Brown

Topics/Speakers:

 "Update on the Million Veteran Program".
Sumitra Muralidhar PhD, Director, Million Veteran Program, Office of Research and Development, Veterans Health Administration, Washington DC

"Genome-wide Association Study of Lung Cancer in MVP".
Saiju Pyarajan PhD, Director, VA Center for Data and Computational Sciences, VA Healthcare Systems, Boston, Massachusetts.

"Incorporation of Health Care, Genetic and Imaging Data for Lung Cancer Risk Prediction and Precision Lung Cancer Screening".
Samuel Aguayo MD, Associate Staff for Research, Phoenix VA Health Care System, Phoenix, Arizona.

"Predictive Model for Lung Cancer Treatment with Immune Checkpoint Inhibitors".
Michael Green, MD, PhD. Director, Center for Tumor Radiobiology and Immunotherapy in Cancer, VA Ann Arbor Healthcare System, Ann Arbor, Michigan.

References:

1. The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.
2. HJ de Koning et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. N Engl J Med 2020;382:593-513.
3. N Howlander et al. The effect of advances in lung-cancer treatment on population mortality. N Engl J Med 2020;383:640-649.

Cancer Moonshot Progress and Other Initiatives

By Valerie Adelson

Since the initial launch of the federal Cancer Moonshot in 2016, cancer patients, advocates, researchers, and clinicians have made measurable progress toward three ambitious goals: to accelerate scientific discovery in cancer, foster greater collaboration, and improve the sharing of cancer data. In February 2022, President Biden announced a reignition of the Cancer Moonshot, highlighting new, additional goals: reduce the cancer death rate by half within 25 years and improve the lives of people with cancer and cancer survivors.

To address cancer on multiple fronts across the federal government, President Biden convened a Cancer Cabinet, bringing together myriad departments, agencies, and White House components, including the Departments of Health and Human Services, Veterans Affairs, Defense, Energy, Agriculture, Environmental Protection Agency, Office of Science and Technology Policy, Domestic Policy Council, Office of the First Lady, Office of the Vice President, and many others.

On Monday, September 12, 2022, President Biden spoke at the Kennedy Presidential Library in Boston, outlining the progress and new initiatives as part of the federal Cancer Moonshot. September 12, 2022 was the 60th anniversary of President Kennedy's delivering his moonshot address announcing the goal of "landing a man on the moon and returning him safely to the earth" before the end of the 1960's, a goal which was successfully achieved in 1969.

President Biden described the Cancer Cabinet's progress towards delivering game-changing cancer detection technologies and supporting talented researchers from across the United States, including:

National Cancer Institute Vanguard Study on Multi-Cancer Detection

A new four-year pilot study by the National Cancer Institute has been launched on effective blood tests for multi-cancer detection, providing the opportunity for additional, less-invasive tools for early detection. The study will enroll 24,000 people ages 45 to 70 years to lay the groundwork for a large, randomized controlled trial that will enroll 225,000 subjects.

The Vanguard study will be conducted through the NCI Cancer Screening Research Network, a new network of organizations to include health care systems, practice-based networks, academic institutions, and consortia of researchers. Members of existing clinical trial networks such as NCI's National Clinical Trials Network and the NCI Community Oncology Research Program

may also participate. Funding opportunities to develop the CSRN and the Vanguard study were released in late 2022, and NCI will begin recruiting volunteers for the study in 2024.

Cancer Moonshot Scholars Program

Advancing health equity is a top priority for President Biden and Department of Health and Human Services Secretary Xavier Becerra. The Cancer Moonshot Scholars Program is an early-career grant program with a focus on developing a cancer research workforce that is representative of the U.S. population. The program aims to improve the diversity of the applicant pool for NCI R01 grant funding. The program will provide grants to early-stage investigators from underrepresented minorities to support the next generation of diverse, world-class scientists and health innovators.

The National Cancer Institute intends to fund at least 45 early-stage investigators in initial rounds beginning in 2023, with project periods of up to 5 years, investing approximately $135 million.

Telehealth Centers of Excellence

The National Cancer Institute's Telehealth Research Centers of Excellence (TRACE) Initiative will fund multiple centers which will study the role of telehealth in cancer prevention, screening, diagnosis, treatment, survivorship, and equity of access and outcomes.

NCI is investing $23 million in the program over 5 years (2022-2027) to four academic research institutions. Each center will focus on an overarching cancer-focused telehealth research theme that will frame their studies and will work with local clinical practices in their areas to support the studies. The centers are:

- Making Telehealth Delivery of Cancer Care at Home Effective and Safe (MATCHES) – Memorial Sloan Kettering Cancer Center
- Scalable TELehealth Cancer CARe (STELLAR) Research Center – Northwestern University at Chicago
- Telehealth Research and Innovation for Veterans with Cancer (THRIVE) Research Center – New York University and Grossman School of Medicine
- University of Pennsylvania Telehealth Research Center of Excellence (Penn TRACE) – University of Pennsylvania

Other New Actions and Appointments

President Biden announced several new actions and appointments that his Administration is taking to advance the Cancer Moonshot. The president signed an Executive Order to launch a National Biotechnology and Biomanufacturing Initiative. This initiative is intended to grow the strength and diversity of domestic biomanufacturing capacity, expand market opportunities for bio-based products through federal programs,

drive research and development across all relevant agencies, streamline and harmonize appropriate regulation, and prioritize investments in applied biosafety research in biosecurity to reduce risk throughout research and development lifecycles.

President Biden appointed longtime biologist and former government scientist Dr. Renee Wegrzyn as the first director of the nascent Advanced Research Projects Agency for Health. The president officially launched the agency in March, 2022, with $1 billion in initial funding allotted by Congress, but the search for its inaugural director took months.

Dr. Wegrzyn previously worked at Boston-based Ginkgo Bioworks, a company focused on biological engineering, but she also has prior experience in two government agencies that inspired the creation of ARPA-H, that is the Defense Advanced Research Projects Agency and Intelligence Advanced Research Projects Activity.

"I am deeply honored to have the opportunity to shape ARPA-H's ambitious mission and foster a vision and approach that will improve health outcomes for the American people, including President Biden's Cancer Moonshot," Dr. Wegrzyn said in a statement referring to the president's goal of ending cancer deaths and curbing new cases.

Dr. Wegrzyn did not need Senate confirmation for her role. However, she will nonetheless likely face Congressional scrutiny about the need for a new health agency, which could replicate efforts at the National Institutes of Health.

Dr. Wegrzyn received her Ph.D. in applied biology from Georgia Tech. She has served on the scientific advisory boards for the National Academies of Science Board on Army Research and Development, Revive and Restore, Air Force Research Labs, the Nuclear Threat Initiative, and the Innovative Genomics Institute.

In addition, on October 3, 2022, Monica M. Bertagnolli, MD, took office as the 16th director and first woman director of the National Cancer Institute. She succeeds Norman E. Sharpless, MD, who stepped down as director in April 2022. Douglas R. Lowy, MD, had been NCI's acting directing since April 30, 2022.

Dr. Bertagnolli joins NCI from Harvard Medical School, where she served as the Richard E. Wilson Professor of Surgery in the field of surgical oncology at Brigham and Women's Hospital in Boston. She was also a surgeon at Brigham and Women's Hospital and a member of the Gastrointestinal Cancer Treatment and Sarcoma Centers at Dana-Farber Cancer Institute in Boston.

Her experience as a physician-scientist inspired Dr. Bertagnolli to become an advocate for increasing the diversity of patients in clinical trials. She has championed and advanced patient-focused programs in rural and remote communities. ●