U.S. Department of Health and Human Services
National Institutes of Health
Office of AIDS Research

Office of AIDS Research Advisory Council
Fifty-Ninth Meeting
February 24, 2022

Virtual
https://videocast.nih.gov/watch=44363

Meeting Minutes

Council Members Present: Dr. Blanton S. Tolbert (Chair), Dr. Tabia H. Akintobi, Dr. Margaret L. Brandeau, Dr. Tricia H. Burdo, Dr. Kathleen L. Collins, Dr. Heidi M. Crane, Ms. Lynda M. Dee, Dr. Shruti H. Mehta, Dr. Veronica Miller, Dr. Ricardo A. Rivero, Dr. Jonah B. Sacha, Dr. Kimberly K. Scarsi, Dr. Bruce R. Schackman, Dr. John W. Sleasman

***Ex Officio* Members Present:** COL Julie A. Ake, Dr. Victoria J. Davey, Dr. Rohan Hazra, RADM Jonathan Mermin; Dr. Maureen M. Goodenow; Dr. Carl Dieffenbach

Advisory Council Representatives Present: Dr. Francis Ali-Osman, Dr. Carlos del Rio, Dr. Monica Gandhi, Dr. Marguerita Lightfoot, Dr. Robert Yarchoan

Office of AIDS Research Leadership Present: RADL Timothy H. Holtz, Deputy Director; CAPT Mary T. Glenshaw, OARAC Designated Federal Official and Supervisory Senior Science Advisor; Dr. J. Rafael Gorospe, Medical Officer

Invited Speakers and Guests Present: Ms. Leia Butler, Dr. Nahida Chakhtoura, Dr. Joshua Denny, Dr. Jennifer Kates, Dr. Alice K. Pau

Welcome and Introductions

Blanton S. Tolbert, Ph.D., OAR Advisory Council Chairperson and Professor, Case Western Reserve University
CAPT Mary Glenshaw, Ph.D., M.P.H., OAR, National Institutes of Health

Dr. Blanton S. Tolbert welcomed participants to the fifty-ninth meeting of the National Institutes of Health (NIH) Office of AIDS Research Advisory Council (OARAC) meeting. A quorum was present. Meeting materials provided to Council members included the agenda, a conflict-of-interest form, and minutes from the fifty-eighth OARAC meeting, held on October 28, 2021.

A motion to accept the minutes of the fifty-eighth OARAC meeting was approved unanimously.

Dr. Tolbert reviewed the fifty-ninth meeting agenda, noting the inclusion of time for public comments.

Report from the NIH Office of AIDS Research Director
Maureen M. Goodenow, Ph.D., OAR, NIH

Dr. Maureen M. Goodenow welcomed attendees and congratulated Dr. Tolbert on his new appointments as Vice Dean for Diversity, Equity, and Inclusive Excellence at Case Western Reserve University School of Medicine and as the first Associate Director for Diversity, Equity, and Inclusion at Case Comprehensive Cancer Center.

Dr. Goodenow reported information according to four key NIH OAR functions: to convene, catalyze, coordinate, and communicate NIH HIV research.

Convene
Dr. Goodenow thanked five OARAC outgoing members: Drs. Tricia Burdo, Kimberly Scarsi, Bruce Schackman, and Babafemi Taiwo and Ms. Lynda Dee. She thanked Dr. Carlos del Rio for his continued service as National Advisory Council on Drug Abuse (NACDA) Advisory Council Representative and noted that clearance of a new NACDA representative is pending. Dr. Goodenow formally welcomed and introduced Dr. Shruti Mehta as a new voting member of OARAC and Dr. Marguerita Lightfoot as the new Advisory Council Representative from the National Advisory Mental Health Council. She informed attendees that the next OARAC meeting, scheduled for June 23, 2022, will be virtual.

Dr. Lawrence Tabak currently is serving as acting NIH director and Dr. Tara Schwetz is serving as acting principal deputy director. Dr. Alondra Nelson has been named the acting director of the White House Office of Science and Technology Policy; former NIH director Dr. Francis Collins has been named the acting science advisor to the president and acting co-chair of the President's Council of Advisors on Science and Technology.

The *National HIV/AIDS Strategy for the United States 2022–2025* (NHAS) was released on World AIDS Day 2021, December 1. The OAR led the NIH observance of World AIDS Day with the theme of "The Role of Research in the National HIV/AIDS Strategy." The program highlighted the contributions of groundbreaking HIV research funded by the NIH to the updated NHAS. The NHAS provides the roadmap to accelerate efforts to end the HIV epidemic in the United States by 2030. It reflects the president's commitment to reenergize and strengthen a whole-of-society response to the epidemic while supporting people with HIV and reducing HIV-associated morbidity and mortality. The NIH World AIDS Day program featured remarks from Congresswoman Barbara Lee, the founder and co-chair of the Congressional HIV/AIDS Caucus, and Mr. Harold Phillips, whose leadership at the Office of National AIDS Policy was critical to updating the NHAS. Dr. Wafaa El-Sadr of Columbia University moderated a panel discussion with a diverse group representing early-stage investigators (ESIs), academia and research representatives, community engagement leaders, and industry partners. The event had more than double the number of live viewers as the 2020 event; additional information is available on the OAR website.

OAR represented the NIH at a number of conferences with extramural investigators, community members, and advocates. At the 25th Annual National Centers for AIDS Research (CFAR) Meeting, at which Dr. Goodenow provided an overview of NIH's role in the *Ending the HIV Epidemic in the U.S.* (EHE) initiative, updates on OAR's outreach activities, and an outline of efforts to diversify and increase the early-career HIV investigator workforce. OAR and the NIH Office of Research on Women's Health coordinated presentations at the Inter-CFAR Women and HIV Virtual Symposium to highlight the effect of the COVID-19 pandemic on existing gaps in representation and compensation of women in research positions, the decrease in racial and

gender diversity among faculty as seniority increases, and the need to improve participation of women and minorities in HIV research. The symposium emphasized strategies to support a diverse and gender-balanced next generation of HIV investigators, an initiative already in motion at OAR. Dr. Goodenow participated in the U.S. Conference on HIV/AIDS (USCHA) Town Hall on Aging and HIV; OAR moderated a virtual listening session in conjunction with USCHA, during which panelists highlighted the importance of combating stigma to improve HIV testing within marginalized communities and the need for community inclusion along the research and information dissemination pipeline. At the 18th Annual National African American MSM Leadership Conference on Health Disparities and Social Justice in January 2022, Dr. Goodenow reviewed the recent advances from NIH-supported HIV research in the context of African American men who have sex with men, initiatives to support early-career HIV investigators, and details about OAR's response to COVID-19.

At the federal level, OAR continues to work with interagency colleagues, primarily on NHAS- and EHE-related activities, through recent and ongoing engagements including NIH representation on the President's Advisory Council on HIV/AIDS, the federal EHE Operational Leadership Team, and the NHAS Implementation Working Group. OAR conducts outreach to agency leadership, such as recent separate and joint engagements with the Centers for Disease Control and Prevention (CDC) Division of HIV Prevention and the Health Resources and Services Administration HIV/AIDS Bureau. These engagements featured discussions of interagency collaborations on EHE and cross-agency opportunities in community engagement, NHAS implementation, and implementation research. OAR met with Mr. Jin Park, director of the President's Emergency Plan for AIDS Relief (PEPFAR) Office within the U.S. Department of Health and Human Services Office of Global Affairs, to discuss NIH HIV research priorities related to PEPFAR's focus on implementation and opportunities for expanded NIH-PEPFAR collaborations.

Catalyze

Dr. Goodenow highlighted HIV investigators who presented two significant clinical reports at the 2022 Virtual Conference on Retroviruses and Opportunistic Infections (CROI). The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1107 protocol team reported the first case of a woman with HIV remission following a stem cell transplant for treatment of acute myelogenous leukemia. The source of the stem cells was banked umbilical cord blood homozygous for the CCR5Δ32 genetic mutation and haploidentical peripheral blood stem cells from a relative. The study participant, a U.S. woman, discontinued antiretroviral therapy (ART) 37 months post-transplant. Except for transient trace levels of HIV DNA detected at 14 weeks, no HIV has been detected for 14 months.

Through the National Cancer Institute (NCI) AIDS Malignancy Consortium, new data from the ANal Cancer High-grade squamous intraepithelial lesions (HSIL) Outcomes Research (ANCHOR) trial were presented at CROI. ANCHOR shows for the first time that anal cancer can be prevented even in high-risk populations, such as people with HIV, who often have precancerous lesions that can be difficult to treat. Because of the high success rate of the treatment, the clinical trial was halted early.

OAR staff attended U.S. Military HIV Research Program meetings focused on acute HIV science and HIV vaccine science on February 10 and 11. The Acute HIV Science meeting included sessions on clinical updates, events during acute HIV infection, and viral rebound. The Vaccine Science meeting sessions covered cohort studies, clinical vaccine trials, preclinical studies, virologic and immunologic analyses, and future directions. Panelist feedback encouraged researchers to include more women in HIV remission studies, develop animal

model studies to address research needs to follow up human studies and for new research directions, and continue coordinating among research agencies to strengthen the framework for future clinical and translational efforts. Panelists underscored the importance of developing novel adjuvant and mRNA vaccine platforms.

HIV and aging is a key focus area for the NIH HIV research agenda. OAR partnered with the National Institute on Aging to expand research on HIV and aging through 1-year administrative supplements recently announced through a joint Notice of Special Interest. These supplements are intended to accelerate new knowledge related to the science of HIV and aging and expand the pool of researchers working in the HIV and aging intersectional space. OAR is co-sponsoring an NIH Intramural NeuroHIV Research Workshop in March, which will describe ongoing studies within the intramural program and provide an opportunity to present results and outline future directions for the program. Dr. Holtz will deliver the introductory presentation highlighting NIH's investment in NeuroHIV. Funding levels for research related to the pathogenesis and treatment of HIV-related neurological disease in fiscal year (FY) 2021 were almost 7 percent higher than FY 2017 and 11.7 percent higher than FY 2019.

OAR staff have two articles in press with the *American Journal of Public Health* as part of a special issue on intersectional stigma. One is a paper on recent efforts to improve HIV-related intersectional stigma and discrimination research, coauthored by Drs. Goodenow and Dianne Rausch (director of the Division of AIDS Research within the National Institute of Mental Health [NIMH]). The second article focuses on U.S. government health agencies' efforts to address HIV-related intersectional stigma, co-authored by several OAR staff members and several federal partners. These papers are a precursor to an NIH OAR and NIMH satellite session on intersectional stigma at the International AIDS Society 2022 conference (AIDS 2022) in July. A third paper authored by OAR staff, titled "The Role of NIH in the Ending the HIV Epidemic in the U.S. Initiative: Research Improving Practice," now is in press for publication in a *Journal of Acquired Immune Deficiency Syndromes* special issue on EHE.

Coordinate

In response to feedback from engagements with ESIs, OAR launched new web-based content that centralizes grant opportunities and provides key information and resources for early career investigators. OAR will update the page on an ongoing basis in collaboration with the NIH AIDS Executive Committee (NAEC) to ensure that the information reflects all opportunities across the NIH. Dr. Goodenow encouraged OARAC members to review the information and provide feedback. OAR has a series of activities planned for HIV ESIs to stimulate scientific exchange, networking, and collaboration among the next generation of HIV investigators, mentors, and NIH program staff. These plans include a 1-day workshop in late April that will include NIH Institute, Center, and Office (ICO) presentations on each ICO's HIV program and research priorities; a presentation by the Center for Scientific Review (CSR) about the NIH review process; a mock grant peer review; and opportunities for questions, answers, and discussion.

A key OAR activity involves enhanced information dissemination efforts to promote the policies and processes that guide the NIH HIV research enterprise. The initiative engages NIH, federal, and community partners to enhance understanding of the NIH HIV research agenda, NIH HIV research priorities, and key OAR functions. Immediate outputs of information dissemination include new fact sheets posted on the OAR website (e.g. a new high-level fact sheet about OAR available in the About OAR section); ongoing monthly engagement with the NAEC; and updated materials from the OARAC orientation session. Dr. Goodenow thanked those who participated

in the recent OARAC orientation and encouraged those who could not attend to do so next February (the Handbook was included in OARAC members' meeting materials).

OAR virtual listening sessions from September 2020 through July 2021 contained consistent themes influenced by the COVID-19 pandemic and the resurgent social justice movement: 1) the importance of addressing the impact of COVID-19 on HIV research; 2) redressing inequities in the HIV research enterprise, expanding and diversifying the HIV research workforce; 3) enhancing the relationships between academic and community partners; and 4) addressing challenges specific to ESIs. Many of OAR's priority activities have been developed as a direct result of input from the listening sessions. OAR has responded to community input by expanding support of early-career HIV investigators, increasing focus on HIV and aging, and conducting information dissemination activities. Many challenges conveyed to OAR during these listening sessions are complex, intersectional, and require OAR partnerships with other government agencies for discussion and resolution. Listening sessions in 2022 will include meeting with the partners in Texas, Puerto Rico, and American Indian/Alaska Native communities, organizations and agencies.

The OAR website is updated frequently with items of interest to partners. Since the last OARAC meeting, OAR has posted blog entries highlighting NIH OAR participation at USCHA, the role of research in the NHAS, NIH OAR efforts related to enhanced support of the next generation of HIV researchers, and the February 7 observance of National Black HIV/AIDS Awareness Day. Dr. Tabak distributed his message on Black History Month earlier in February and announced that the NIH is in the process of developing its first Diversity, Equity, Inclusion, and Accessibility (DEIA) Strategic Plan. Dr. Goodenow concluded her remarks by noting the deaths of several important members of the HIV community—Archbishop Desmond Tutu and Drs. Zena Stein, Luc Montagnier, and Paul Farmer.

Discussion Highlights

OARAC members discussed whether enough programs support ESIs in HIV research and enroll underrepresented minorities in clinical trials. A report, Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups (2022) , from the National Academies of Sciences, Engineering, and Medicine presents specific recommendations for improving representation of minorities and women in clinical trials. Participating in clinical research is an important component of health equity; OARAC should consider this issue with a broader lens than HIV research and identify ways to make changes across the health spectrum. Researchers need to work harder to intentionally enroll segments of the population that are not well represented in trials. Enrollment strategies should be changed for different subgroups and different geographies; continued guidance and support from NIH OAR and other entities will reinforce those suggestions. Additionally, conversations about underrepresented populations must include discussion of long-acting therapeutics and pre-exposure prophylaxis (PrEP) and include people who inject drugs as one of the underrepresented populations. Adolescents and young adults represent another group that has been under-enrolled in treatment trials.

OARAC members noted that disentangling the enrollment of underrepresented groups from community engagement is critical. Community engagement requires building relationships—investigators must understand the importance of establishing and maintaining trustworthiness and the degree to which that trust can be maintained when enrolling participants for studies. The need to increase representation in clinical trials should be linked to the need for workforce

development, pathway programs, and community engagement efforts. These overlaps should be understood, as should methods for leveraging these efforts to achieve the desired outcomes.

Dr. Goodenow pointed out that former NIH director Dr. Francis Collins worked diligently during the development of the COVID-19 vaccines to increase the diversity of trial participants, but much work remains. A 2017 article by Dr. Collins about ESIs focused the NIH to set goals for improving it, which have been surpassed. Dr. Goodenow cautioned that the overall increase in ESIs is not reflected to the same extent among HIV researchers, thus OAR has made HIV ESI support a priority.

All of Us **Research Program**

Joshua Denny, M.D., M.S., Chief Executive Officer, All of Us Research Program, NIH

Dr. Joshua Denny outlined the *All of Us* Research Program, which aims to accelerate health research and medical breakthroughs, enabling health research and care for all members of society. The program has three components: (1) nurturing partnerships for decades to attain at least 1 million participants who reflect the diversity of the United States; (2) delivering one of the largest, richest biomedical data sets that is broadly accessible and secure; and (3) catalyzing an ecosystem of communities, researchers, and funders who make *All of Us* an indispensable part of health research.

The program was launched publicly in May 2018; more than 460,000 people have consented to participate, with 321,000 completing the initial enrollment steps. Electronic health records (EHRs) from 277,000 people and 342,000 biosamples have been collected. All in-person recruitment activities were paused because of the COVID-19 pandemic, but these efforts are being restarted and increased. Additionally, more contactless approaches to recruit patients and collect biospecimens have been implemented. Participants have been enrolled in all U.S. states and territories; more than 80 percent of participants are from populations underrepresented in biomedical research (including age, race or ethnicity, sex assigned at birth, educational attainment, sexual orientation, gender identity, income, or geography). Data collected from *All of Us* participants include consent and EHRs, participant surveys—including a social determinants of health survey that includes physical measures, biosamples, data from mobile and wearable technologies, etc.

One of the core values of *All of Us* is returning genomic results to participants, who often ranked genomic results as one of their highest priorities. The program currently returns non-health genetic traits and ancestry to participants; 66,000 participants have viewed these results. Return of health-related genetic traits, including hereditary disease risk and a “Medicine and Your DNA” measure, will launch in mid-2022. Participants can choose the results they want to receive. Hereditary disease risk results will be validated in clinical validation laboratories and returned through genetic counselors. *All of Us* will offer confirmatory clinical genetic testing.

Dr. Denny outlined the tiers of access available. The program has many data providers; data are gathered into the raw data repository, where they are curated to harmonize them, add privacy, and apply quality assurance measures. Data then are sorted into access tiers based on level of privacy. Individual biospecimen and participant data are the most private, followed by the controlled tier, which includes genomics, real dates, and clinical narrative data, but no obvious personally identifying information. Both these tiers will become available for research in the future. The registered tier, available now on the Researcher Workbench, includes survey

responses, EHRs, physical measurements, and shifted dates. The public tier, available now on the Data Browser, includes summary statistics and aggregate counts.

Data currently available include 267,600 physical measurements, 214,200 EHRs, 11,600 Fitbit records, and 329,000 surveys. The EHR and Fitbit data include historical information, allowing longitudinal and trend analysis. Although only adults have been enrolled in *All of Us* to date, pediatric data from 20,000 participants are available through EHRs. Genomic data, including 100,000 whole genomes and 160,000 arrays with diversity similar to the rest of the data set, will be available in the spring.

The public Data Browser allows users to explore summary statistics of participant data, including EHR data, survey responses, and physical measurements. Dr. Denny showed an example of HIV-related information that can be accessed with the data browser, including a diagnosis of HIV for about 4,300 people in EHRs. In this tier, HIV information is presented under "condition" and "laboratory information," as well as aggregated codes. The Researcher Workbench is a registered tier (i.e., a researcher can apply for access and begin using the data almost immediately). Access operates under a passport model, so separate institutional review board approval is not needed to begin a new study. Currently, access is limited to people representing U.S. nonprofit institutions, which sign master agreements that allow anyone representing that institution to begin conducting research in less than 2 hours. Web-based components can be used to build a cohort for a study. HIV-related information at this tier includes diagnoses, as well as medications and the number of participants using each medication. The Researcher Workbench was launched in May 2020 and now has 1,400 researchers using it for 1,100 projects. At least 27 publications have used *All of Us* data. More than 280 institutions are registered, more than 26 percent of which are historically Black colleges and universities, Hispanic-serving institutions, or other minority-serving nonprofits.

Dr. Denny reviewed a case study from a genome-wide association study (GWAS) of type 2 diabetes in a preproduction test data set. A user first would build a cohort by selecting diabetes conditions, then build a data set on which to conduct an analysis using demographics for cases and controls. With the *All of Us* tools, a user can progress from creation of the cohort of more than 10 million variants and 5,000 participants to GWAS results in less than 30 minutes and at a cost of less than $30.

Dr. Denny concluded his remarks by describing five *All of Us* program goals to be completed by the end of 2026:

- Enroll 1 million diverse participants, including children.
- Generate genome sequences, health, survey, and environmental data.
- Launch ancillary studies
- Enroll 10,000 researchers using the data productively.
- Return value to participants, including genomics and EHRs.

Discussion Highlights

OARAC members commended the impact and importance of the *All of Us* project, as well as the diversity of participants the project has included to date.

When asked whether existing cohorts can be integrated into the *All of Us* platform, Dr. Denny explained that the program will build up infrastructure over time to include existing cohorts. Presently, the focus is on new recruitment of participants without specific diseases to ensure that results are not biased. Although some researchers are disinclined to share their cohort

data, the *All of Us* technology could be applied to other efforts. Dr. Rohan Hazra pointed out that appropriate comparison groups often are not available for pediatric cohorts, so *All of Us* could serve as the comparison group after children are added.

Dr. Denny explained that the diversity represented in the cohort is gathered in many ways, beginning with engagement with a diverse set of community partners. Health care provider organizations conduct significant outreach, usually with outreach staff. Materials are tested frequently to ensure they are appropriate for diverse populations.

When asked about how to consider the uncertain nature of genomics as an emerging field, Dr. Denny explained that the most common feedback from participants is a desire for more genomics information. He pointed out that some genomic tests perform better than others, so the program returns information very conservatively. *All of Us* will be providing additional recommendations for ways to use genomics information to guide participants, but many elements of the genomics return process require more development. Ideally, the program will review the data set each year and contact people when additional information about connections between variants and risk is discovered. He agreed that explaining to people how new results may arise would be challenging.

Dr. Denny clarified the process by which researchers are approved quickly, emphasizing that *All of Us* was always intended to be one of the most accessible data sets, particularly because any barriers would be more detrimental to researchers from underrepresented minority groups. Participating institutions sign a master agreement that grants access to anyone from that institution, most commonly through use of an institutional email, in exchange for accepting the risk of someone who uses the data set inappropriately. Each institutional user completes a brief training. As users create their workspaces, they answer questions, some of which trigger reviews by *All of Us* staff. Because the database is public and cloud-based, it can be audited; Dr. Denny added that transparency ensures that *All of Us* staff can conduct such checks quickly.

Dr. Denny explained that the cohort has been used for a wide variety of projects. Disease-based research is most common, particularly for cancers, as well as diabetes. Some researchers have used the virtual pediatrics set, while others have examined very specific information, such as data on eye diseases.

When asked how *All of Us* communicates with researchers about the representativeness of the population, Dr. Denny clarified that the cohort is not representative—for example, Arizona is the state from which the most participants have been recruited, but not the most populous state. The program works to make that message clear, but users could have this assumption. At this time, *All of Us* does not provide weighting for surveys. Dr. Denny noted that a number of users are conducting studies that compare *All of Us* data to population-based rates, such as disease risk. *All of Us* hopes to create a platform that other researchers can use to develop those kinds of uses. OARAC members pointed out that disease-specific researchers might be less attuned to social science methods; other data, for example, would be more representative of the HIV population. Dr. Denny noted that some comparisons can be used regardless of representation; for example, body mass index (BMI) at a certain age in the pediatric data could be compared to adult BMI.

Dr. Denny noted that presently, program staff are building a way to track publications based on the *All of Us* data. Researchers send their publications and staff monitor the literature, but some publications likely have been missed.

UNITE Update

Leia Butler, J.D., Program Manager, UNITE Initiative, NIH

Ms. Leia Butler explained that the NIH UNITE Initiative was created in response to the disparate COVID-19 mortality among minorities, the murder of George Floyd, and the killing of Asian women in 2020 and 2021. These events clarified the ongoing reality of racial and ethnic injustice in the United States and the responsibility of everyone to address it. The NIH developed a shared commitment to address structural racism in the biomedical research enterprise.

UNITE is composed of five committees with specific goals: (1) understanding stakeholder experiences through listening and learning; (2) new research on health disparities, minority health, and health equity; (3) improving the NIH culture and structure for equity, inclusion, and excellence; (4) transparency, communication, and accountability with internal and external stakeholders; and (5) the extramural research ecosystem and changing policy, culture, and structure to promote workforce diversity. UNITE's three focus areas are health disparities, minority health, and health equity research; the external workforce; and the internal workforce. Under the NIH Common Fund, $58 million has been committed to the initiative, with 11 awards announced for two funding opportunity announcements (FOAs) related to DEIA.

For the internal workforce, the UNITE team developed executive performance requirements, including racial and ethnic equity plans (REEPs) as a component of the DEIA performance metric. REEPs are designed to show accountability and flexibility; executives can customize the plans according to each IC's structure and culture. Progress must be reported with long- and short-term measures; this progress should be analyzed and shared with other ICs to promote learning. Ms. Butler noted that investment of the necessary resources is critical. The plans began in November and are underway; NIH ICs now are developing their plans, which must be completed by April 1 for May implementation. Ms. Butler displayed photos from a project to expand the color palette of art in NIH buildings to better represent NIH staff and recognize the inclusive workforce.

Regarding the external workforce, Ms. Butler highlighted the success of the Distinguished Scholars Program, which builds on the Stadtman and Lasker investigator programs to create a self-reinforcing community of principal investigators (PIs) devoted to diversity and inclusion. Another program, the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program, aims to create cultures of inclusive excellence using a faculty cohort model for hiring, multi-level mentoring, and professional development.

Anticipated future opportunities to increase career opportunities for underrepresented groups include expanding the Science Education Partnership Award (SEPA) program to include the entire NIH, strengthening diversity and mentoring language in parent training grants and fellowship FOAs, increasing the use of diversity supplements for small business innovation research and small business technology transfer awards, and incorporating the Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative Plan for Enhancing Diverse Perspectives into NIH research FOAs.

Anticipated future opportunities to promote extramural institutional culture change in support of inclusivity and equity include the launch of: (1) a program to fund excellence in DEIA investigator grants; (2) a program to provide support for institutions to conduct objective climate assessments and critical self-studies, then developing action plans based on the results; and (3) a prize for institutional innovation and advancement in DEIA. To build and sustain research capacity at minority-serving institutions (MSIs), anticipated future opportunities include

developing an S10 instrumentation grant program for MSIs, developing targeted institutional training grants, expanding the Sponsored Programs Administration Development grants program, developing an entrepreneurial training program, and organizing a yearly meeting between NIH leadership and MSI leaders. Planned activities to identify and change NIH processes and policies contributing to inequities in extramural funding include developing and launching a training program for scientific review offices and program officers to reduce implicit bias and enhance equity and inclusivity of NIH interactions with the extramural community, developing guidance to help ICs enhance the diversity of PIs funded in their research portfolios, and improving the review criteria descriptions to decrease possible sources of bias.

An NIH request for information (RFI) on how to advance DEIA and health disparities research was open March 1 through April 23, 2021, and received 1,100 responses, most of them from academia. Three preliminary findings emerged from the responses: (1) the need for actions beyond words, (2) the importance of enhancing programs and activities, and (3) the caveat that no “easy button” is available. Ms. Butler noted that a small number of respondents commented that they perceived no issues with racism or DEIA at the NIH or in the broader biomedical community. Next steps are to continue to conduct analyses within the RFI tool, analyze and synthesize the findings for a full report, and triangulate the findings with other data.

Discussion Highlights

When asked about repeat analysis of the paper on underrepresentation of women in the scientific workforce published by Dr. Donna Ginther 10 years ago, Ms. Butler explained that an update is pending; results are anticipated shortly.

In response to a question about improving diversity among scientific review officers, Ms. Butler agreed that this issue is a matter of concern and noted that the Anti-Racism Steering Committee, an offshoot of the UNITE Initiative, is investigating this area.

When asked for examples of situations in which the parent language of an FOA was strengthened to improve diversity, Ms. Butler pointed to SEPA, which provides resources to underrepresented minority groups in pre-K through 12th grade. SEPA information is intended to pique younger students’ interests and increase their exposure to clinical research as a career path. Ms. Butler added that diversity cannot be increased overnight, so expanding the pipeline is critical for ensuring a more diverse future.

HIV and COVID-19

OAR HIV and COVID-19 Taskforce Readout

Jennifer Kates, Ph.D., Senior Vice President and Director of Global Health & HIV Policy, Kaiser Family Foundation

Dr. Jennifer Kates reported on the January 27 meeting of the HIV and COVID-19 OAR Taskforce that was established in the second quarter of 2020. The group’s charge is to provide input to OAR on focus areas and action plans in the HIV and COVID-19 space and foster bilateral discussions between OAR and its partners on shared scientific, programmatic, and operational interests relevant to HIV and COVID-19. The taskforce includes eight OARAC members, 10 NIH program staff members—including NAEC representatives—one invited stakeholder, and four OAR staff members. The purpose of the January meeting was to assess, document, and understand the continued impact of the COVID-19 pandemic on HIV research, including ongoing challenges, positive impacts and lessons learned, and solutions and

mitigation approaches for HIV research recovery. Points of discussion included the impact of the pandemic on HIV research progress, publications, and grant submissions; the impact on training and ESIs; requests for funding extensions and supplemental funding; recruitment and retention of participants in clinical studies; lessons learned and positive impacts that can be applied to HIV research; and potential solutions and mitigation approaches to ongoing challenges.

CSR provided information on HIV study sections to gauge the impact on grant submissions. In four of the six study sections, the number of grant submissions did not change. However, grant submissions decreased in the HIV Coinfections and HIV-Associated Cancers study section and in the HIV Immunopathogenesis and Vaccine Development study section. The taskforce heard a presentation from the Office of Research Infrastructure Programs on the effects of the pandemic on nonhuman primate (NHP) research. NHP availability for HIV/AIDS research was affected by a ban on animal importations, the diversion of NHPs to COVID-19 research, infrastructure project delays because of increased construction costs, delays in breeding. Even where NHP availability was sufficient, supply chain shortages reduced the availability of personal protective equipment (PPE) and other supplies. Staffing challenges—including shortages, the “all hands-on deck” approach that forced many HIV/AIDS researchers to pivot to COVID-19 research, and the increased need for PPE and monitoring of staff for infection—affected NHP research, as well. In particular ESIs, experienced delays in research project completion and career advancement.

The taskforce identified several ongoing challenges for HIV research. The effects of the COVID-19 pandemic on institutions and investigators were disproportionate—junior investigators and institutions with limited resources experienced greater impacts. Delayed research likely will remain behind schedule. The increased clinical time of investigators in response to the COVID-19 pandemic makes translating work back to HIV research challenging. Reduced HIV testing and difficulty recruiting certain populations, such as older participants, affected study protocols and recruitment. Impacts on funding and extension requests were discussed—although the NIH released numerous emergency funding opportunities early in the pandemic, research has returned to more traditional investigator-initiated submission routes. Extension requests and supplemental funding requests are varying as investigators gauge the impacts on their research and their research recovery needs.

The taskforce identified some positive aspects associated with the COVID-19 pandemic. Focus increased on integrated and more collaborative, interdisciplinary science, which had a positive effect on career prospects and increased collaborations among disciplines. Telehealth and virtual platforms advanced, increasing diversity in recruitment, flexibility, and opportunities for consultations. Diagnostics and self-testing advanced, which increased accessibility and convenience and spurred the development of innovative diagnostic platforms, which could be applicable to the HIV and broadly to sexually transmitted infection fields. The research approaches and strategies developed in response to COVID-19 now are being applied to HIV and other research areas.

Interim Guidance for COVID-19 and Persons with HIV

Alice K. Pau, Pharm.D., Staff Scientist/Clinical Pharmacist, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Dr. Alice Pau explained that the five HIV clinical guidelines panels collaborated to develop Guidance for COVID-19 and People with HIV, which was initially published in March 2020. This guidance explained that whether people with HIV were at a higher risk of complications associated with COVID-19 was unknown, but many people with HIV have comorbidities that

could put them at risk of serious disease. The guidance emphasized that people with HIV should be treated the same as other patients for clinical management and medical triage and provided recommendations for managing treatment of people with HIV during lockdown: using telehealth instead of in-person visits whenever possible; reducing laboratory monitoring in stable patients; ensuring an adequate supply of antiretroviral (ARV) medication, drugs for opportunistic infections, and other medications; avoiding regimen changes unless absolutely necessary and until close monitoring is possible; and advising patients on when to seek in-person medical visits. The guidance emphasized that people with HIV hospitalized for COVID-19 should be managed the same as other patients with COVID-19. These patients should continue ART and opportunistic infection medications. ARV substitution should be avoided; an HIV specialist should be consulted before making any ARV changes. The guidance emphasized the need to assess for drug interactions and overlapping toxicities and provided resources for crushing pills when taking oral tablets is not possible. Additionally, the guidance encouraged enrolling people with HIV into clinical trials for COVID-19 treatment and prevention.

Dr. Pau reviewed key additions to the guidance since March 2020. Recent data suggest that people with HIV, especially those with low CD4 counts or the presence of viremia, are more likely to have complications related to COVID-19, including hospitalization, mechanical ventilation, and death. The COVID-19 vaccine is recommended for all people with HIV, in line with guidelines from the Advisory Committee on Immunization Practices (ACIP). Monoclonal antibodies, such as tixagevimab plus cilgavimab (Evusheld)—which received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) for use in individuals at high risk for severe COVID-19 outcomes, including those with advanced HIV—are recommended for SARS-CoV-2 prophylaxis. Two forms of SARS-CoV-2 post-exposure prophylaxis received EUA, but distribution of these treatments has been halted because they are ineffective against the Omicron variant. The guidance points out that a number of antiviral drugs, anti–SARS-CoV-2 monoclonal antibodies, and immunomodulators have been approved or granted EUA for use in patients with COVID-19. The Guidelines Panels continue to stress that people with HIV should receive treatment for COVID-19 when indicated. Ritonavir-boosted nirmatrelvir (Paxlovid) is a new oral antiviral therapy for nonhospitalized patients; the guidance recommends that people with HIV who receive a regimen that includes ritonavir or cobicistat should continue their ART without dosage modification.

Dr. Pau outlined key information for children with HIV. All children, including those with HIV, can be infected with SARS-CoV-2 and develop COVID-19, but data are very limited on the course of COVID-19 illness in children with HIV. Multisystem inflammatory syndrome in children is a severe but rare manifestation of SARS-CoV-2 infection in children. Vaccines are available for children 5 years and older; the guidance includes links to CDC and FDA websites for the most up-to-date information on vaccines for children. The guidance includes key considerations related to pregnancy, HIV, and COVID-19 addressing the increased risks of severe illness and death in pregnant versus non-pregnant individuals with COVID-19 and the higher risks of complications, adverse pregnancy outcomes, and mortality in pregnant people with COVID-19. The guidance notes emerging data about an increased risk for stillbirth in pregnant people with COVID-19, with a stronger association when the Delta variant was predominant versus the pre-Delta variant period. Transmission of SARS-CoV-2 from mother to infant appears to be very uncommon; neonatal infection appears to occur postnatally in most cases. No updates were included about pregnancy or maternal outcomes for persons with COVID-19 and HIV because data remain limited. The guidance strongly recommends the COVID-19 vaccine for pregnant and lactating individuals, as well as those planning pregnancy.

OARAC Members Roundtable Discussion

OARAC members engaged in a roundtable discussion on the effects of the COVID-19 pandemic on HIV research. Dr. Kates pointed out that the taskforce did not discuss how to prevent the abrupt end of funding for some researchers. OARAC members noted that the lockdowns had particularly strong effects on junior investigators, especially those involved in clinical studies, and suggested that OARAC identify ways to mitigate these effects, such as cost extensions or targeted funding streams for particularly vulnerable investigators. Senior investigators who pivoted were affected, as well—many now have two full portfolios of HIV and COVID-19 research, in addition to supporting junior investigators, so burnout is a concern. The pandemic has had disproportionate effects on those conducting face-to-face research. Although new tools are available, such as telehealth, populations that cannot access these tools have been disproportionately lost to follow-up and might never return. Dr. Mehta commented that everything requires more time and resources than before.

Dr. Tolbert described the challenge of hiring for entry-level positions and the notable exit of people who are choosing other types of work, emphasizing the need to pay attention to how these trends relate to the salary and feasibility of the work. Dr. del Rio added that the exhaustion and frustration of many researchers may affect the future of HIV research. This situation requires those in the field to rethink many aspects of the response to this pandemic and how future threats will be addressed in a way that is sustainable for researchers.

COL Julie Ake pointed out that hiring issues are present beyond the entry level, especially regarding individuals with significant experience and expertise in development of infectious disease products, who are very sought after by industry. Retaining individuals in academic or government settings is challenging because these settings cannot compete with the salaries offered by industry. COL Ake suggested that lifestyle advantages, rather than salaries, could be an incentive for retaining individuals in academia or government settings. Dr. Jonah Sacha agreed that the effects of the pandemic have been felt at all levels of the research enterprise—many of his best and brightest researchers have moved to other positions, particularly in industry, where they may feel more financially supported. He pointed out that NIH R01 support has not increased in many years, which makes conducting these studies increasingly difficult, especially when NHPs are needed for long periods. Ms. Dee noted the need to consider the cost and value of cure research conducted with NHPs and the need to include chronically ill people in trials.

Many trainees who are transitioning from the postdoctoral level to faculty face challenges under normal circumstances, and during the early stages of the COVID-19 pandemic, clinician trainees were pulled into the clinic and had difficulty protecting their research time. Extensions to K awards was suggested as a consideration. Additionally, graduate students supported by training grants have been affected given the difficulty of conducting in-person training during the pandemic, particularly when they need to be shown something at very close range, such as under a microscope. Dr. Kathleen Collins emphasized the need to accept that training will take longer when it occurs during a pandemic.

Dr. Schackman pointed out that funding limitations on grants has not changed in many years, but the cost of personnel has increased. Although the NIH intends to award as many grants as possible, enough funding to support the work is necessary, so reevaluating the limits might be appropriate at this time. The amount of preliminary work expected of K awardees has increased, making it difficult for promising trainees to achieve even prior to the COVID-19 pandemic. Dr. Schackman noted that some barriers to accessing treatment and prevention have been

removed during the pandemic and would be worth studying—how long those barriers remain removed will vary, but if any barriers return, the reasons should be understood.

Dr. Scarsi commented that although she was granted an R01 extension easily to compensate for the supply chain delays, the extension applies only to the original budget, despite the increased time now required to support her staff. Strategies other than extension are needed. Many institutions have extended the promotion and tenure period, but colleagues have reported that such extensions require sustaining the same high workload over a longer period of time. Dr. Scarsi emphasized that now is the time to consider what aspects of this process should be prioritized. Dr. Tolbert pointed out that women and underrepresented minority faculty have experienced disproportionate pressures as a result of the COVID-19 pandemic.

When asked whether the Guidelines Panels discussed boosters for immunocompromised populations, specifically those with HIV, Dr. Pau reported that vaccine recommendations come from ACIP, not the Guidelines Panels. However, the Panels are developing a section on immunocompromised people and are defining which groups are considered under this heading. The Panels are considering such measures as CD4 count and viremia and are trying not to overstep their bounds. The Panels have encouraged ACIP and the CDC to make changes in the past; Dr. Pau explained that CDC representatives serve on the Panels and have taken advice from the community on many occasions, including advice on medical triage early in the pandemic.

RADM Jonathan Mermin reported that the CDC experienced disruptions similar to those of other groups, including research delays, but was able to adapt administrative procedures to streamline the research process. The CDC was inspired to address some identified gaps, such as diagnostics, more rapidly because of COVID-19 limitations. The development and rapid approval of vaccines followed a similar path. RADM Mermin encouraged OARAC to think about areas where science is on the cusp of success and how to provide an extra “push” because of what was learned in the COVID-19 pandemic.

Attendees discussed the positive outcomes from the pandemic, including the importance of investment in clinical trials infrastructure. International infrastructure was identified as being very important as well, particularly South African, Brazilian, and some East African sites. COL Ake pointed out that although initial trials occurred in the United States, international sites increasingly were used for other types of vaccines. She noted that the COVID-19 Prevention Network (CoVPN) presently is conducting a study in South Africa asking questions pertinent to people with HIV. In the clinical trial infrastructure, new partnerships have been formed and networks have been expanded; researchers’ capacity to conduct large trials has increased. COL Ake commented that although an HIV vaccine trial might be very different, those in the field have learned what clinical trial infrastructure can be accessed if needed, what early partnerships with industry can accomplish, and the importance leveraging government funding.

Dr. Tolbert commented that a highlight of the taskforce’s discussions was the importance of working across disciplines and conducting team science as a result of the COVID-19 pandemic; he suggested incorporating cross-disciplinary interactions into training programs as a component of increasing the diversity of individuals engaging in HIV science.

Ms. Dee emphasized the importance of engaging the community to develop creative ideas for recruitment, retention, and sustainability in trials, noting that the community perspective on logistical situations often is helpful for investigators.

Regarding the positive effects of the pandemic, Dr. Heidi Crane noted the benefits of telehealth, such as communicating more frequently with patients. The data collection and interventions that can occur via telehealth for research do not replace in-person visits but serve as an additional support system and increase generalizability. Dr. Schackman commented that the challenge is translating creativity in the research context into sustainability outside research—many insurance providers have not adjusted to telehealth, so some providers have a financial incentive to return to old methods.

HIV Clinical Guidelines Working Groups of OARAC Working Group Updates

Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission

Nahida Chakhtoura, M.D., Ms.G.H., Medical Officer/Physician, Eunice Kennedy Shriver *National Institute of Child Health and Human Development (NICHD), NIH*

Dr. Nahida Chakhtoura reported on updates to the Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States that were published in December. First, the names of the Panel and title of the Guidelines were changed to incorporate gender-inclusive language; gender-inclusive content was added in selected sections and in a new section under Special Populations. Guidance for preconception care has been changed to pre-pregnancy care, in alignment with updates from the American College of Obstetricians and Gynecologists. Changes were made to facilitate access to key information, such as a reorganization of the HIV PrEP section to focus initially on clinical management of PrEP and the integration of content from the section on stopping ARV drugs during pregnancy into other sections. The Panel added a recommendation that all pregnant people and people who are trying to conceive receive the COVID-19 vaccination.

The Panel reviewed recent data and updated situation-specific recommendations about the use of ARV drugs. Dolutegravir continues to be listed as a *Preferred* ARV for use during pregnancy and when trying to conceive. Based on reassuring data from the most recent analysis of data about neural tube defects from Botswana, the Panel has removed most bulleted recommendations with dolutegravir-specific cautions. With added data about use and safety in pregnancy, tenofovir alafenamide is now listed as a *Preferred* nucleoside reverse transcriptase inhibitor for persons with HIV-1 and has been added as a *Recommended* option for those with HIV-2. Oral cabotegravir and the new long-acting injectable regimen of cabotegravir and rilpivirine have been classified as *Not Recommended* for initiation of ART during pregnancy and as *Insufficient Data* for persons who are trying to conceive or who become pregnant while on this regimen; the Panel recommends changing to a *Preferred* or *Alternative* ARV regimen.

The Panel updated selected recommendations about ARV regimens. Dolutegravir-based ARV regimens now are the only *Preferred* regimens for pregnant people with acute HIV; ritonavir-boosted darunavir regimens are classified as an *Alternative* option. Although the oral two-drug ARV regimens are classified as *Insufficient Data* for use during pregnancy, the component drugs are recommended for use. The Panel now recommends that pregnant persons who present to care on these regimens and have successfully maintained viral suppression can continue these two-drug regimens with more frequent viral load monitoring. The Panel continues to strongly recommend patient counseling and support for informed decision-making about the use of all ARV drugs during pregnancy or when trying to conceive and has updated the ARV Counseling Guide.

The Monitoring During Pregnancy section and the ARV Recommendations Overview were updated to address the risk for weight gain and obesity that may be present with the use of tenofovir alafenamide and/or integrase inhibitors during pregnancy and postpartum. A recommendation was added to clarify that hepatitis B virus/HIV coinfection and/or hepatitis C virus/HIV coinfection is not an independent indication for cesarean delivery. A new section was added, titled "Perinatal HIV Prevention for Transgender and Gender-Diverse People Assigned Female Sex at Birth." The Panel has determined that in most cases, extrapolating recommendations based on data in presumed cisgender women to all people assigned female sex at birth, including transgender and gender-diverse people, is appropriate, with modification when indicated, such as for drug interactions with gender-affirming hormones. Additional recommendations and content address the unique and varied needs of transgender and gender-diverse people during pregnancy or when trying to conceive.

Table 9, Antiretroviral Drug Dosing Recommendations for Newborns, has been updated to include abacavir dosing recommendations for infants and nevirapine dosing for infants 32 to 34 weeks gestation at birth, but abacavir is not recommended for presumptive HIV therapy. For people with HIV who decide to breastfeed, guidance about ARV prophylaxis for breastfeeding infants has been updated to address the provision of infant prophylaxis beyond the recommended time period of 4 weeks in an infant of a parent receiving ART with viral suppression, which is controversial. Appendix B, Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy, has been updated to incorporate new data and newly approved drugs.

Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV, and Antiretroviral Agents in Adults and Adolescents Living with HIV

Alice K. Pau, Pharm.D., Staff Scientist/Clinical Pharmacist, National Institute of Allergy and Infectious Diseases, NIH

Dr. Pau outlined updates to the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. The Panel includes representatives from several other organizations, including the CDC, HIV Medicine Association, and Infectious Diseases Society of America. Analytics show that use of the Opportunistic Infection Guidelines remains strong and even increased slightly over the past year, which justifies their continued existence. As in many other years, the section on *Pneumocystis* pneumonia was the most viewed opportunistic infection section. Dr. Pau noted that 22 new members have been added to this Panel and some leadership positions changed; in particular, the Panel wanted to emphasize diversity in its new members and roles. One major recent update is the recommendation for latent tuberculosis infection. The treatment now recommends two weekly regimens, isoniazid-rifapentine (3HP) and isoniazid-rifampin (3HR), over isoniazid (INH) and has designated daily isoniazid-rifapentine (1HP) as an alternative regimen. Information about drug interactions has been noted.

Some significant changes have been made to the section on immunizations. The Panel has tried to reduce the amount of information about the COVID-19 vaccine in the Guidelines because the guidance changes so frequently. The Guidelines recommend that all people with HIV receive the COVID-19 immunization regardless of CD4 count and refer users to the CDC recommendations for additional information. Information on immunizations for pneumococcus and zoster aligns with recommendations from the CDC and ACIP, respectively. A number of updates to other sections are in progress, including the sections on hepatitis B and C, toxoplasmosis, progressive multifocal leukoencephalopathy, syphilis, and bacterial enterics.

Dr. Pau then presented updates to the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, which she noted have been updated less frequently because of COVID-19. Fewer advances or approvals have occurred in the field; additionally, the majority of panel members now care for both COVID-19 patients and HIV patients.

One major update is a change to the levels at which individuals with acute HIV should be retested. Previous Guidelines suggested that individuals with suspected acute HIV, but a viral load less than 10,000 copies/mL could represent a false positive result. They recommended a repeat test to confirm the findings. With more sensitive HIV RNA tests, false positives at such high levels are very unlikely; the threshold was reduced to less than 3,000 copies/mL, which aligns with CDC guidelines for HIV testing and diagnosis. The recommendations for testing and ART initiation for individuals found to be HIV positive while on PrEP were updated, as well.

The other major update relates to the discontinuation or interruption of ART and guidance on actions to take if patients have an unexpected inability to take oral solid medications. The Panel has provided recommendations for steps to take if long-acting injectable ARV drugs need to be delayed or stopped. Finally, the Guidelines discuss stopping ART during analytic treatment interruptions (ATIs), with particular focus on the need for close monitoring to inform patients about the risks of viral rebound, including disease progression and the risk of HIV transmission to others.

Discussion Highlights

OARAC members emphasized the continued importance of the Guidelines, including for the increasing number of immunosuppressed patients. Dr. Pau confirmed that the Panels are working on including guidance on the use of long-acting agents.

When asked about ATIs, Dr. Pau explained that the Panel has made some general recommendations and is reviewing individual study designs to determine what guidance is needed. Some ATIs may have been halted because of the pandemic. OARAC members suggested working with the community to compensate for pauses in trials caused by the pandemic. OARAC members noted that ATIs now are used in hepatitis B cure research, demonstrating how lessons from HIV research are translated.

In response to a question about capturing information on the use of the Guidelines for purposes other than care of people with HIV, Dr. Pau explained that the usage data cannot collect this information and surveys may not accrue a representative group of responses. However, further assessment of usage could provide evidence-based approaches for other groups and justify the investment in HIV research.

Updates from the NIH Advisory Council Representatives

AIDS Research Advisory Committee (ARAC)

Monica Gandhi, M.D., M.P.H., Professor of Medicine and Associate Chief, Division of HIV, Infectious Diseases, School of Medicine, University of California, San Francisco (UCSF); Global Medicine Director, UCSF-Gladstone Center for AIDS Research; Medical Director, "Ward 86" HIV Clinic, San Francisco General Hospital

Dr. Monica Gandhi provided updates from the most recent NIAID Council meeting and noted NIH's contribution to the development of the COVID-19 mRNA vaccines. NIAID's budget has increased 4.5 percent since the last allocation. ARAC members discussed ESIs, noting that the

established PI R01 payline at NIAID is at the 10th percentile and new PIs are at the 14th percentile. The K award cutoff is 20 percent, so ARAC members discussed how to support ESIs with an increased payline for K awards.

Regarding emergency supplemental funding in response to the COVID-19 pandemic, Dr. Gandhi noted implementation gaps that need to be addressed in HIV, including testing, treatment, retention in care, viral suppression, prevention and harm reduction services, food and housing security, and human rights, including stigma and discrimination reduction. She highlighted research on the failure to achieve virologic suppression with hard-to-reach populations, including 65 percent of adults and 59 percent of children studied. Additional work is needed, including expanding the use of long-acting therapies.

ARAC members discussed recent EHE awards. Dr. Gandhi noted that the FDA has approved the first injectable PrEP treatment, long-acting cabotegravir. Another research advance is NIAID's investment in coronavirus research since the COVID-19 pandemic began, including substantial investment in pan-coronavirus and pan-variant vaccine research. Dr. Gandhi noted the new NIH Policy for Data Management and Sharing, which is necessary to enable the validation of research results. The NIH policy will become effective on January 25, 2023.

National Advisory Council on Drug Abuse (NACDA)

Carlos del Rio, M.D., Executive Associate Dean, Emory University School of Medicine & Grady Health System, Distinguished Professor, Department of Medicine, Division of Infectious Diseases, Hubert Professor and Chair, Department of Global Health, Rollins School of Public Health, Emory University School of Medicine

Dr. del Rio provided updates from NACDA on racial equity and inclusion. COVID-19 has had a disproportionate effect on minorities, particularly related to mortality. The HIV pandemic similarly has been a pandemic of racial and ethnic minorities and health inequities, both in the United States and globally. New HIV diagnoses in the United States mostly occur among Black and African American people and Hispanic people. The lifetime risk of HIV diagnosis is highest among Black men and women compared to other racial and ethnic populations.

Dr. del Rio pointed out that HIV remains a pandemic of Black and brown people globally—the vast majority of people with HIV are people of color. African Americans and Hispanic populations already have the highest rates of chronic health conditions in the United States, which has contributed to a disproportionate burden of severe COVID-19 disease and death among minorities. Racism has been recognized as a social determinant of health, with many contributing aspects. Dr. del Rio emphasized the need to focus on health disparities and racism as social determinants of health to end both the HIV and COVID-19 epidemics.

Dr. del Rio added that NIH awards have continued to be given mostly to white researchers, so the National Institute on Drug Abuse (NIDA) has developed four program announcements specifically designed to build the next generation of minority investigators, which is a necessary component to addressing social determinants of health.

National Advisory Mental Health Council (NAMHC)

Marguerita Lightfoot, Ph.D., Associate Dean for Research at the Oregon Health & Science University and Portland State University School of Public Health

Dr. Marguerita Lightfoot provided an update from NIMH. The NIMH Division of AIDS Research supports research to reduce the incidence of HIV worldwide and decrease the burden of living

with HIV/AIDS. Primary areas that inform that work are behavioral science, clinical neuroscience, and mental health. Several recent workshops brought together leading experts in the neuroHIV field to identify and analyze common data elements from HIV-associated central nervous system (CNS) disease studies. Instead of a purely clinical approach, the workshops involved integrating elements of underlying psychopathology with currently available measures. Such meetings encourage the researchers to use creative approaches that integrate multidimensional data and tools to identify biotypes or clusters based on psychopathology and advance the understanding of the basic and clinical neuroscience of HIV-associated CNS complications.

Dr. Lightfoot pointed out that the concept for this meeting was based on a recent paradigm shift to integrate psychiatry more fully with the neurosciences. Adapting this idea to neuroHIV allows a better understanding of the biotypes associated with factors of neuropsychiatry that can lead to the development of precision medicine.

The meeting included discussion of new initiatives, which Dr. Lightfoot noted had very good response and represented cutting-edge science with a number of innovative approaches, technologies, and models. Funding decisions are in progress. Two other current initiatives are Deciphering Immune-CNS Interactions in People Living with HIV on Antiretroviral Therapy and Advancing Communication Strategies to Support Future HIV Vaccine Use.

A new concept focuses on expanding collaborative implementation science to support the EHE national plan. Although highly efficacious strategies to prevent and treat HIV exist, inequities persist in who can access these strategies. Social and structural determinants of health are increasingly recognized as root causes of these HIV inequities and must be addressed urgently. EHE was launched in 2019 and aims to reduce new HIV infections by 90 percent by 2030. The EHE effort will be critical to the NIH mission of broadening health equity. Some proven structural interventions have not been adapted or scaled up; other new interventions need to be developed. The overall goal of the new concept is to encourage collaborative implementation research to develop and test HIV interventions that target social and structural determinants of health while simultaneously testing strategies to facilitate their uptake and adaptation. Expected outcomes include new data regarding the effectiveness of HIV interventions targeting social and structural determinants of health and their implementation, a generalizable knowledge base, collaboration across several ICs, and encouragement of research from investigators at historically Black colleges and universities and other MSIs. Dr. Lightfoot noted that this initiative is intended to be an NIH-wide effort that will demonstrate a collective dedication to addressing HIV health inequities.

National Cancer Advisory Board

Robert Yarchoan, M.D., AIDS Coordinator, Director, Office of HIV and AIDS Malignancy; Chief, HIV and AIDS Malignancy Branch; Senior Investigator, NCI, NIH

Dr. Robert Yarchoan shared preliminary results from the ANCHOR study, which was conducted by the AIDS Malignancy Consortium. Screening for and treating cervical intraepithelial neoplasia, called cervical HSIL, is effective at preventing cervical cancer, but effectiveness had not been shown for anal cancer. Anal HSILs often are large, missed on examination, difficult to treat, and frequently recurring. Currently, no national screening programs are available to identify anal cancer or anal HSIL in at-risk populations. Formal national guidelines recommending anal screening and treatment of HSIL do not exist either. A trial to determine whether treatment of anal HSIL prevents anal cancer has been needed before widespread screening would be adopted.

The rate of anal cancer has been increasing; MSM and people with HIV have higher incidences than other populations. The ANCHOR study aims included determining the effectiveness of screening for and treating anal HSIL to reduce the incidence of anal cancer in HIV-positive men and women and creating a bank of blood, anal swabs, and tissue specimens to support correlative science studies of molecular pathogenesis and biomarkers of progression to anal cancer. Other goals include measuring the effects of screening for and treating HSIL on quality of life and evaluating the safety of treatments for HSIL. ANCHOR was a multicenter study conducted at a variety of sites around the United States.

The study was powered to detect the difference between 50 out of 100,000 patient years in the treatment arm and 200 out of 100,000 patient years in the active monitoring arm at the two-sided 0.05 significance level with a power of 0.90. The study used an event-driven analysis and a primary outcome of time to cancer. The projected number of participants was 2,529 per arm—a total of 5,058—to detect 31 anal cancers. The study was randomized 1:1 and stratified by study site, CD4 count, and lesion size. The arms were a treatment arm using one of several modalities and an active monitoring arm.

Between September 24, 2014, and August 5, 2021, 10,723 patients were screened; 52.2 percent of these had biopsy-proven anal HSIL. Those with anal HSIL comprised 53.3 percent of men screened, 45.8 percent of women, and 62.5 percent of transgender individuals. Seventeen individuals were diagnosed with anal cancer. In total, 4,446 patients older than 35 were entered and randomized 1:1 between treatment and active monitoring. The Data and Safety Monitoring Board was notified when 32 cancers were diagnosed; the final analysis was based on 30 cases. Nine participants were diagnosed with invasive anal cancer in the treatment arm and 21 in the active monitoring arm. With a median follow-up of 25.8 months, the study showed a 57 percent reduction in anal cancer. Cancer incidence in the treatment arm was 173 per 100,000 patient years of follow-up compared with 402 per 100,000 patient years in the active monitoring arm. Overall, the time to confirmed cancer cases was much greater in the active monitoring arm than the treatment arm.

The study showed that treatment of anal HSIL is effective in reducing the incidence of anal cancer. Dr. Yarchoan noted that these data should be included in an overall assessment for inclusion of screening for and treating anal HSIL as a standard of care. Biomarkers for HSIL progression or regression are needed, as are optimized screening algorithms for HSIL and a large scale-up of high-resolution anoscopy training programs. These results can be extrapolated to other groups at high risk of anal cancer.

NAEC

J. Rafael Gorospe, M.D., Ph.D., Medical Officer, Senior Science Advisor, OAR, NIH

Dr. J. Rafael Gorospe reviewed concepts and FOAs related to HIV cleared by IC advisory councils and published since the previous OARAC meeting. Between September 2021 and February 2022, 12 HIV-related concepts were cleared by the advisory councils of NIAID; NICHD; NIMH; and the National Heart, Lung, and Blood Institute (NHLBI); comprising four new concepts and eight reissues. Nine FOAs have been published since the previous meeting through the NCI, NHLBI, NIAID, NICHD, NIDA, NIMH, and the National Institute of Dental and Craniofacial Research.

Discussion Highlights

When asked about concerns that NIH's new data-storage requirements will increase workloads disproportionately, particularly for investigators with fewer resources, Dr. Gandhi planned to return that concern to ARAC.

Dr. Lightfoot clarified that the collaborative implementation program is a concept, adding that not all concepts result in a request for applications (RFA). She planned to inform OARAC if the concept becomes an RFA and to suggest collaboration with *All of Us* to the NAMHC.

Public Comment

CAPT Mary Glenshaw, Ph.D., M.P.H., OAR, NIH

CAPT Glenshaw confirmed that no public comments had been received.

Closing Remarks and Adjournment

RADM Timothy Holtz, M.D., M.P.H., FACP, FACPM, OAR, NIH
Blanton Tolbert, Ph.D., OARAC Chairperson, Professor, Case Western Reserve University

RADM Holtz thanked the Council members and speakers on behalf of Dr. Goodenow and reminded them that these remarks all were part of the public record.

Dr. Tolbert added his thanks, reminded attendees that the June meeting will be virtual, and adjourned the meeting at 4:34 p.m. EST.

Certification

I hereby certify that, to the best of my knowledge, the foregoing summary minutes are accurate and complete.

Blanton Tolbert Digitally signed by Blanton Tolbert
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Blanton Tolbert, Ph.D.
Chair, OARAC

07/07/2022
Date

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CAPT Mary Glenshaw, Ph.D., M.P.H.
Executive Secretary, OARAC

07/07/2022
Date