

**U.S. Department of Health and Human Services
National Institutes of Health**

**Minutes of the Tenth Joint Meeting of the
National Advisory Council on Alcohol Abuse and Alcoholism,
National Advisory Council on Drug Abuse, and
National Cancer Advisory Board**

**May 11, 2022
NIH Webcast**

Members of the National Advisory Council on Alcohol Abuse and Alcoholism (NIAAA), National Advisory Council on Drug Abuse (NIDA), and the National Cancer Advisory Board of the National Cancer Institute (NCI) convened for their tenth joint meeting on May 11, 2022, online via Webex and NIH Webcast. Chaired by Nora Volkow, M.D., Director of NIDA, and George F. Koob, Ph.D., Director of NIAAA, this open session convened at 11:00 a.m.

National Advisory Council on Alcohol Abuse and Alcoholism Members Present:

Nancy Barnett, Ph. D.
Jill B. Becker, Ph.D.
Andrew MacGregor Cameron, M.D., Ph.D.
Christopher S. Carpenter, Ph.D.
Christina Chambers, Ph.D.
H. Westley Clark, M.D., J.D.
Constance M. Horgan, Sc.D.
Rhonda Jones-Webb, Ph.D.
Beth Kane-Davidson, LCADC, LCPC
Charles H. Lang, Ph.D.
Mary E. Larimer, Ph.D.
Laura E. Nagy, Ph.D.
Laura Elena O'Dell, Ph.D.
Scott J. Russo, Ph.D.
Katie Witkiewitz, Ph.D.

National Advisory Council on Drug Abuse (NACDA) Members Present:

Charles Chavkin, Ph.D.
Anna Rose Childress, Ph.D.
Dennis Deer
Lakshmi A. Devi, Ph.D.
Amit Etkin, M.D., Ph.D.
Shelley F. Greenfield, M.D.
Paul J. Kenny, Ph.D.
Jessica Hulsey Nickel
Travis N. Rieder, Ph.D.
Rajita Sinha, Ph.D.
Melissa L. Walls, Ph.D.
Sharon L. Walsh, Ph.D.

National Cancer Advisory Board Members Present:

John D. Carpten, Ph.D., Chair
Lawrence O. Gostin, J.D.
Howard J. Fingert, M.D., F.A.C.P.
Amy B. Heimberger, M.D.
Karen M. Winkfield, M.D., Ph.D.

Chairs: George F. Koob, Ph.D., and Nora Volkow, M.D.

National Institute of Alcohol Abuse and Alcoholism (NIAAA) Director: George F. Koob, Ph.D.

National Institute on Drug Abuse (NIDA) Director: Nora D. Volkow, M.D.

National Cancer Institute/Division of Cancer Control and Population Sciences (NCI/DCCPS) Director: William Klein, Ph.D., on behalf of Katrina Goddard, Ph.D.

NIAAA Deputy Director: Patricia Powell, Ph.D.

NIDA Deputy Director: Wilson Compton, M.P.E., M.D.

NIAAA, Director, Office of Extramural Activities: Abraham P. Bautista, Ph.D.

NIDA, Director, Division of Extramural Research: Susan B. Weiss, Ph.D.

NCI, Director, Division of Extramural Activities: Paulette S. Gray, Ph.D.

NIDA Senior Staff: Gaya Dowling, Ph.D.; Katia Howlett, Ph.D.; Troy Zarccone, Ph.D.

NIAAA Senior Staff: M. Katherine Jung, Ph.D.; Raye Litten, Ph.D.; David Lovinger, Ph.D.; Antonio Noronha, Ph.D.; and Bridget Williams-Simmons, Ph.D.

NCI Senior Staff: William Klein, Ph.D.

Additional Participants

Approximately 200 observers joined the meeting, including representatives of constituent groups, liaison organizations, and members of the general public.

Call to Order and Introductions

Susan Weiss, Ph.D., Director of Extramural Research, NIDA, and Executive Secretary of the National Advisory Council on Drug Abuse (NACDA), called to order the tenth meeting of the National Advisory Councils of NIAAA, NIDA, and NCI in open session at 11:00 a.m. on Wednesday, May 11, 2022. Dr. Weiss was representing NIDA Director Nora Volkow, M.D., who was testifying at the NIH appropriation hearings before Congress. Dr. Weiss welcomed participants and shared the following land acknowledgement: “We acknowledge that the NIH exists on the traditional lands of the Piscataway and Anacostan people, past and present. We honor the land itself and the people who have stewarded it with gratitude.”

NIDA Director's Presentation

In a pre-recorded presentation, Dr. Volkow began by reviewing data from the 2021 Monitoring the Future (MTF) study to shed light on the impact of the COVID-19 pandemic on drug use, especially among young people. Looking at the trend between 2020 and 2021, use of most substances—including alcohol, marijuana, and vaped nicotine—declined significantly among 8th, 10th, and 12th graders. This may be explained by the social isolation resulting from imposed lockdowns, as substance use among teens is linked to social interaction and peer pressure. Data from the 2022 survey will provide new data showing what happens to substance use rates now that teens are back in school.

HEALthy Brain and Child Development. Dr. Volkow introduced a new initiative, the HEALthy Brain and Child Development (HBCD) Project, a longitudinal observational study to understand neurodevelopment from birth to age 9-10 involving 7500 infants. Knowledge of brain trajectories will contribute to understanding how children may be affected by exposure to substances (e.g., opioids, alcohol, tobacco, cannabis), stressors, trauma, and other environmental conditions, including those that promote resilience. HBCD follows on the success of the Adolescent Brain and Cognitive Development (ABCD) Study. The HBCD Study was initiated after a two-year planning phase. For the full study, sites were funded in September, 2021. HBCD is enhancing recruitment for infants who have been exposed to opioids and/or alcohol, tobacco, and cannabis in utero, in order to provide an accurate assessment of the actual harms of consuming these substances on development and how that may vary by social environment. In addition to neuroimaging and behavioral/cognitive assessments, substance exposures, risk and protective factors will be assessed. Biospecimens will be collected for analysis of substance exposure, genomic factors and epigenetic changes. Wearable sensors will also collect information on heart rate, sleep, and activity.

Overdose Deaths. Drug overdose deaths continued to increase in 2021. Close to 107,000 individuals died from overdoses that year, an almost 16 percent rise from what was already the highest numbers of overdose deaths previously recorded (a 30 percent increase in 2020 from 2019). The drugs associated with the overdose deaths are diversifying. Deaths from heroin have reduced by 30.6 percent and deaths from prescription opioids have declined slightly. Increased deaths from methadone have not occurred, despite concerns that they might do so. But there has been a significant increase in overdoses from synthetic opioids, particularly illicit fentanyl (24.4 percent), cocaine (19.8 percent) and other psycho-stimulants, mostly methamphetamines (36 percent). In three-quarters of the cocaine overdoses and half of the methamphetamine ones, the drug had been mixed with illicit fentanyl or fentanyl-related substances. It is believed that approximately 15 percent of these overdoses also involved alcohol.

The demographics of those affected by the overdose crisis have changed dramatically. Initially, it was White Americans who were most likely to be prescribed opioids which is where the overdose crisis first emerged. The pattern of use among Native Americans was parallel to that of Whites, although higher. In 2015-2016 when illicit fentanyl began emerging as a contaminant of other drugs, a rise in overdose deaths among underrepresented minorities began to occur. Today, the sharpest risk for overdose deaths is among Black Americans. The contamination of cocaine with illicit fentanyl is a major contributing factor to this phenomenon. Native Americans/American Indians also show an increasing risk, which may reflect, in part, the contamination of methamphetamine. The overdose death rate per 100,000 for some underrepresented groups—41.9 percent for Native Americans/Americans Indians and 35.4 percent for African Americans, compared to 32.8 percent for White Americans—highlights important health disparities and the need for targeted prevention strategies to address them.

Dr. Volkow also presented data on fentanyl and non-fentanyl involved overdose deaths among teenagers 15-29 years old. In 2019, there began a steep increase in drug overdoses in this age group, which was surprising given their low use of heroin according to the MTF. Their very dramatic increase in overdose deaths may be attributable to the contamination of the illicit prescription pill market, including stimulants, benzodiazepines and opioid pain pills, etc. Teens can easily order illicit medications through the Internet. Monitoring of law enforcement seizures of illicit pills between 2018-2021 revealed that fentanyl-containing pills have increased more than thirty-fold.

To address the overdose crisis, multiple approaches are needed. Pain treatments and the treatment of opioid use disorder (OUD) are both crucial, but insufficient. Treatment of other substance use disorders (SUDs) must be deployed because of the high risk of contamination of other drugs; the overdose treatments must be diversified since those that are currently effective for opioids may not work on these drug combinations. It is also evident that prevention efforts must be launched, including a focus on early initiation or experimentation to educate teens about the risks of illicitly manufactured prescription drugs; and enhancement of screening and brief treatment interventions for subclinical SUD to prevent escalation of drug taking. Significantly better data are needed, including timely reporting of fatal and non-fatal overdoses. Recognition and strategies to address social determinants of health (SDoH) are crucial to reduce the risk of individuals experimenting with drugs and transitioning into addiction. Further, once an individual is addicted, SDoH are crucial in determining his or her best path to recovery.

Discussion. Howard Fingert, M.D., asked if there are any data available on regional/state differences in substance use that might be informative about regional or state health practices. He also asked about methods to measure the impact of SDoH and their impact. Wilson Compton, M.D., responded that regional data of overdose deaths can be broken down to the county level; however, because of the smaller number of cases per county, it is difficult to do a good analysis at that level. Regional data has, however, allowed for the identification of regional hot spots such as Appalachia; or tracking of the movement of fentanyl from the East Coast and Mid-West to the West. NIDA is partnering with the NIH Office of Behavioral and Social Sciences Research, and with NIAAA and NCI to examine SDoH. It has been difficult to merge Census data or other SDoH datasets with NIH's large-scale surveys in the addiction field. Dr. Weiss added that the ABCD study offers the opportunity to look at SDoH, prevention, and trajectories of substance use in a large cohort of adolescents followed prospectively. That's one way to start addressing the question from the prevention side. Dr. Compton added that the impact of SDoH will also be considered in the All of Us cohort study in the future. Travis Rieder, Ph.D., inquired about harm reduction strategies for overdoses from stimulants, noting the success of Narcan for reversing opioid overdoses. Dr. Compton replied that naloxone can still be helpful with stimulant overdoses because of drug combinations. NIDA's medications development program is exploring treatments for overdoses when only stimulants are involved. For example, monoclonal antibodies might work fast enough to address a methamphetamine overdose. But it's unlikely such a medication would become widely available to communities; distribution would most likely be restricted to providers. Thus, it may not serve as a harm reduction approach. NIDA is open to suggestions on this issue. Dr. Rieder asked: What do we tell our communities? Dr. Weiss commented that NIDA is making medication development a priority for both stimulant and opioid overdoses, as well as defining what an overdose with stimulants looks like, e.g., it could be a cardiac toxic event, seizures, etc. H. Westley Clark, M.D., J.D., commented that there are not many behavioral strategies that work well with stimulants. One that does is incentive-based contingency management. He asked why there was an administrative lag in removing restrictions on its use. He also encouraged NIAAA and NIDA to conduct more research on demand for stimulants. Dr. Compton responded that NIDA partners with multiple groups within the Department of Health and

Human Services (HHS) to address contingency management strategies and hopes the barriers to its use will be removed soon.

NIAAA Director's Presentation

Dr. Koob focused his presentation on closing the alcohol treatment gap for alcohol use disorder (AUD). The pandemic has exacerbated alcohol-related problems in the United States. Too few people who need help get it. Therefore, NIAAA is undertaking multiple efforts to close the treatment gap, including advancing medications, screening and brief interventions, developing new resources, and addressing recovery, telehealth, stigma, and diversity.

Scope of the Problem. The U.S. Centers for Disease Control and Prevention (CDC) reports that over 140,000 people die each year due to alcohol-related causes. During the first year of the pandemic (2020), death certificates listing alcohol increased 25.5 percent from 78,927 in 2019 to 99,017 in 2020. Alcohol was listed in 1 in 6 (16 percent) of drug overdose deaths in 2019 and 2020. Alcohol-related traffic fatalities increased by 14 percent to 11,654 in 2020 – the highest since 2008.

Alcohol misuse correlates with poor mental health. It often precedes diagnoses of mental health conditions. Alcohol is commonly used in an effort to cope with mental health-related symptoms; however, in the end, it makes the prognoses worse. Similarly, mental health conditions complicate treatment for AUD. The COVID-19 pandemic contributed to a global decline in mental health. For example, the World Health Organization estimates there has been a 28 percent increase in cases of major depressive disorder (MDD) and a 26 percent increase in cases of anxiety disorders (AD). In the United States, the pandemic worsened already declining mental health, including increases in “deaths of despair” and other indicators of declining mental health prior to the pandemic, as well as increases in anxiety and depression for people of all ages, but particularly adolescents and young adults. More people reported being in treatment (counseling/medications) for mental health-related conditions, but the treatment gap also grew (i.e., more people needed treatment but did not receive it).

Given the links between poor mental health and alcohol misuse, one might expect an increase in drinking to cope during the COVID pandemic. In fact, studies suggest around 1 in 4 people (23 percent) began drinking more during the pandemic while 1 in 4 (23 percent) drank less. Drinking to cope was a common reason for increasing consumption. A longitudinal NIAAA-funded study found that, compared to right before the pandemic, people were 48 percent more likely to indicate they drank to forget their worries early in the pandemic. Further, the odds of drinking to cope were far higher when respondents also reported symptoms of depression and anxiety. For example, 29 percent of respondents in one survey reported drinking more and the odds of increasing alcohol use were higher for those with symptoms of anxiety or depression. Such findings are concerning given that drinking to cope increases the likelihood of developing AUD and related harms.

In addition to an increase alcohol-related deaths during the pandemic, there has also been a simultaneous rise in other alcohol-related harms. This is documented by increases in: the percentage of emergency department visits that involve acute excessive alcohol consumption, the incidence of alcohol withdrawal in hospitalized patients, deaths from alcohol-associated liver diseases, and hospitalizations for alcohol-related hepatitis (AH) between 2019 and 2020 – particularly for women and people under age 40. In addition, there has been a 14 percent increase in alcohol-impaired driving fatalities.

Closing the Treatment Gap: The treatment gap refers to the difference between the number of people who need alcohol treatment and the number who receive it. At present, there are effective evidence-

based behavioral treatments for AUD such as cognitive behavioral therapy (CBT) and motivational interviewing (MI). In addition, there are three FDA-approved medications for treatment of AUD: disulfiram (Antabuse), naltrexone (Vivitrol, ReVia), and acamprosate (Campral). Despite these effective treatments, fewer than 10 percent of people with AUD receive any treatment. Therefore, NIAAA has established the following goals to close the treatment gap: (1) develop and refine behavioral treatments, (2) identify novel pharmacotherapy targets and support medications development, (3) explore alternative clinical trial endpoints, (4) define AUD recovery, (5) integrate prevention, early detection, intervention, and treatment into routine health care, and (6) disseminate NIAAA's Health Professional's Core Resource on Alcohol (HPCR).

SBIRT. Integrating alcohol screening, brief intervention, and referral to treatment (SBIRT) into routine health care is an important strategy for achieving these goals. One study based on the National Survey on Drug Use and Health (NSDUH) data revealed that 81.4 percent of people with AUD saw a clinician in the past year. Of these, 69.9 percent were asked at least one question about their alcohol consumption, most likely on an intake form (screening). Among people who were screened, 11.6 percent were offered advice/information (brief intervention) but only 5.1 percent were advised about treatment options or other resources (referral to treatment). People with severe AUD were more likely to receive advice (23 percent) and/or referral (12.5 percent), but the numbers are still far too low. Importantly, screening for alcohol misuse can also help clinicians spot other health-related issues. For example, adults who binge drink are more likely than drinkers who do not binge to report past-year suicidal ideation (6.3 percent vs 3.8 percent), episodes of major depression (9.2 percent vs 6.5 percent), and prescription pain medication misuse (6.2 percent vs 2.7 percent).

Resources. NIAAA's resources for the public and health professionals to help close the treatment gap include "Rethinking Drinking," a website and print publication for a general audience to help individuals assess their drinking habits and find ways to make a change and the "NIAAA Alcohol Treatment Navigator," an online resource to help people understand treatment options and locate nearby treatment, including telehealth options. The newest resource, launched on May 10, 2022, is "The Healthcare Professional's Core Resource on Alcohol," an educational tool that includes modules on presentation in primary care, diagnostic criteria, addressing stigma, medication interactions, and more. The Core consists of 14 interconnected articles covering the basics of what every healthcare professional needs to know about alcohol. The Core articles provide user-friendly, practical overviews of foundational knowledge for understanding alcohol-related problems (4 articles), clinical impacts of alcohol (4 articles), strategies for prevention and treatment of alcohol problems (5 articles), and how to "put it all together" to promote practice change (1 article). Free continuing education credit--0.75 to 1 credit hour for each of 14 articles (10.75 credit hours total)—is offered for physicians, physician assistants, nurses, pharmacists, and clinical psychologists.

NIAAA Research Definition of Recovery. Little is known about what sustains longer-term recovery. To enhance health, NIAAA is expanding its focus on longer-term recovery. NIAAA has defined recovery from alcohol use disorder (AUD) based on qualitative feedback from key recovery stakeholders (e.g., researchers, clinicians, and recovery specialists). Recovery is viewed as both a process of behavioral change and an outcome that incorporates time periods for two key components: remission from the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 AUD and cessation from heavy drinking (a non-abstinent recovery outcome). The NIAAA definition of recovery also emphasizes the importance of biopsychosocial functioning and quality of life in enhancing recovery outcomes.

Telehealth. The COVID-19 pandemic caused a rapid expansion in the use of telehealth. Evidence suggests telehealth can be effective for addressing alcohol misuse and can reach people who might not otherwise get support. NIAAA supports a variety of telehealth projects (pre-pandemic and pandemic related). These projects include SBIRT with clinicians by phone or video chat and CBT with a clinician or self-guided. Additional project includes telehealth to address post-traumatic stress disorder and alcohol use following sexual assault; and video-conferencing-based MI for alcohol misuse and medication adherence in patients living with HIV. The NIAAA Treatment Navigator links to effective telehealth options. NIAAA anticipates a larger role for telehealth for alcohol prevention, treatment, and recovery going forward.

Words Matter. The stigma associated with alcohol-related conditions can be alleviated by consistent use of non-pejorative, non-stigmatizing language to describe these concerns and the people who are affected by them. Some words that are commonly used in society, such as “alcoholic” and “alcohol abuse,” are stigmatizing. Instead, NIAAA recommends using alcohol use disorder instead of *alcohol abuse*, *alcohol dependence*, and *alcoholism*. In addition, alcohol misuse instead of *alcohol abuse is preferred* when referring broadly to drinking in a manner that could cause harm. The term *alcoholic* is replaced by person with alcohol-related problems, and *recovering alcoholic* with person in recovery. And finally *alcoholic liver disease* is now replaced by alcohol-associated liver disease.

Addressing Diversity and Improving Health Disparities. NIAAA fully supports and is committed to the NIH UNITE initiative, a coordinated effort to address structural racism and promote racial equity and inclusion at NIH and within the larger biomedical research enterprise. The Institute is also focusing on three primary areas in addressing diversity: improving the NIAAA workplace and culture, increasing diversity and equity in the NIAAA scientific and administrative workforce, and enhancing the NIAAA scientific research portfolio. Health services research is an example of an area in which NIAAA is supporting projects to address health disparities. One project in this area is assessing the effectiveness of a culturally adapted, personalized feedback intervention among Latinx individuals with alcohol misuse and anxiety within community-based health clinics. Another study is exploring the impact of various combinations of follow-up engagement after alcohol-related hospitalization and assessing alcohol-related outcomes across racial and ethnic groups, including analysis of social determinants of health. A third study is examining barriers to AUD care by surveying Medicaid health plan policies related to delivery and management of AUD treatment and their relationship with access to and outcomes of care for racial/ethnic minorities, women, and rural Americans.

Discussion. Dr. Clark asked about strategies to address substance misuse that are appropriate for homeless populations. Patricia Powell, Ph.D. commented that NIAAA had supported a homelessness and AUD treatment project several years ago. This demonstrated that stabilizing an individual’s housing situation first was effective in addressing AUD and individuals did not have to be abstinent initially. Abstinence can be a requirement for a homeless person to gain access to housing. Dr. Koob commented that NIAAA supports research on community reinforcement approaches to ensure people have a home and a job to support recovery, and conveyed that NIAAA should consider these approaches more extensively. Dr. Compton agreed, noting that NIDA has some research in the area of homelessness, including research on individuals with HIV who have SUDs and chronic healthcare conditions that has demonstrated promising findings. Dr. Klein reported that NCI has supported research on tobacco use among homeless individuals and ways to address tobacco cessation. Dr. Lakshmi Devi asked if NIAAA is considering workshops at conferences to let researchers and healthcare professionals to know about the Healthcare Professional’s Core Resource on Alcohol. Dr. Koob replied that NIAAA is planning to engage multiple associations and organizations to get the word out. He also noted that NIAAA is

planning to convert the Core into a medical school curriculum. Dr. Greenfield, agreed with Dr. Devi that dissemination of the Core is important. She suggested letting state boards across multiple specialties know about its existence. Given that comorbidities, especially for depression and alcohol among women, exist, she suggested grant announcements to examine co-occurring mental health conditions and AUD. Dr. Greenfield also noted the powerful alcohol advertising campaigns that target women, as well as the multiple beverages marketed to them. Advertising can be a driver of behavior change for both alcohol and tobacco. Finally, she suggested that another “elephant in the room” is the healthcare system that fails to provide incentives to clinicians to conduct case identifications and interventions. Dr. Koob stated that he was writing all these ideas down. He also noted that he, Dr. Volkow and Thomas McLellan, Ph.D., Treatment Research Institute, are considering the concept of “pre-addiction,” with a goal of intervening and treating individuals with low to moderate SUD rather than waiting for them to advance to a severe disorder. More information on this topic will be forthcoming in the future. Dr. Clark piggybacked on Dr. Greenfield’s comments, reminding Dr. Koob about the importance of community health centers and the Health Resources and Services Administration (HRSA)’s primary care services. He recommended including counselors because they are the first line of defense. Dr. Koob asked Council members to send their suggestions for dissemination to him. Charles Chavkin, Ph.D., asked Dr. Koob to explain more about pre-addiction and the defining features that move an individual from mild to severe. Dr. Koob responded that he and Drs. Volkow and McLellan are working on a paper for *Lancet Psychiatry* on the topic. Without going into details, meeting at least two DSM-5 criteria might be sufficient for an intervention to take place. Dr. Greenfield commented this would be a first step in encouraging healthcare providers to start a conversation with patients about substance use.

CRAN-related NCI Activities and Priorities

William Klein, Ph.D., Associate Director, NCI Behavioral Research Program in the Division of Cancer Control and Population Sciences (DCCPS), reported that Katrina Goddard, Ph.D., is the new DCCPS Division Director, replacing Robert Croyle, Ph.D., who retired. NCI is currently awaiting the appointment of a new Director, who is a presidential appointee.

Tobacco Control Research and Impact. The Tobacco Control Research Branch is one of DCCPS’ largest branches in terms of funding and staff because tobacco is the leading cause of preventable death. With more than \$54 million in direct funding, its portfolio consists of over 100 grants. Almost half of these grants focus on interventions for cessation, primarily for adults, while approximately 30 percent address tobacco policy. Cigarettes have been the type of tobacco most often addressed, although grants addressing multiple types of tobacco are steadily increasing. About three-quarters of all grants are focused on a priority population, including youth/young adults; low-income; and locale-specific populations. The focus on youth/young adults is largely on prevention; efforts (both pharmaceutical and behavioral) directed toward cessation with this audience have been less successful than those for adults. More work on youth cessation is needed.

Cessation. A major priority of the Branch is enhancing the capacity of the NCI cancer centers to address tobacco cessation with cancer patients. With funding from the Cancer MoonshotSM, 52 cancer centers were funded via supplements to their P30 Cancer Center Support grants for 1-3 years each. Funded centers are expected to take a population-based approach and commit to sustaining the program. In a population-based approach, tobacco use status is assessed and documented for every cancer center patient, cessation treatment is delivered to every patient who uses tobacco (motivational treatments for those not willing to make a quit attempt), and a tobacco user registry is created and used via electronic health record. In June 2022, the NCI Tobacco Control Monograph series is expected to publish its 23rd monograph, “Treating Smoking in Cancer Patients: An Essential Component in Cancer Care,” to provide

cancer care clinicians with the latest knowledge concerning smoking cessation treatment among their patients and scientists with descriptions of research gaps to be filled. Dr. Klein noted that cancer survivorship is increasing dramatically, so that prevention efforts targeting the survivor community are important.

NCI's Smokefree.gov Initiative (SFGI) offers a suite of free web- and mobile-based smoking cessation resources that provide positive, evidence-based information and support to people who use tobacco and want to quit. Smokefree.gov resources reach approximately 7-8 million people per year. NCI maintains active partnerships with several Federal agencies, including CDC, the Food and Drug Administration (FDA), Indian Health Service, and the US Department of Veteran's Affairs.

NCI Research Impacts on Policy: Monograph 9 ("Cigars: Health Effects and Trends") in the NCI Tobacco Control Monographs series provided evidence used for FDA's proposed rule on flavors in cigars. NCI funding laid the groundwork for the Navaho Nation's Air is Life Act of 2021, the first comprehensive ban on commercial tobacco products on American Indian tribal lands. Finally, NCI-funded research helped build the science base for FDA's proposed rules prohibiting menthol cigarettes and flavored cigars (April 28, 2022).

Alcohol Research Initiatives. Alcohol's link to cancer has not garnered the attention that it should. Alcohol has been linked to seven types of cancer, including breast and colorectal cancer – two of the leading causes of cancer death. Alcohol ranks highly on the list of modifiable risk factors for cancer, comparable in attributable risk to UV radiation and physical inactivity.

NCI has been considering how to approach the role of alcohol in cancer. To date, it has published two articles in leading scientific journals, as well as convened a meeting on Alcohol and Cancer: Identifying Evidence Gaps and Research Challenges Across the Cancer Spectrum (December 8-10, 2020). It has also conducted a series of webinars, including "Communication Approaches for Increasing Awareness of the Link Between Alcohol and Cancer" (2022); "Alcohol as a Target for Cancer Prevention and Control: Research Challenges" (2020); and "Alcohol and Cancer in the United States" (2018). Dr. Klein noted that the profile for alcohol's role in cancer is different from that of tobacco, e.g., tobacco use more prevalent among lower socioeconomic groups, whereas alcohol use is more prevalent among higher socioeconomic populations. These patterns prompt differences in communication strategies and how to think about the role of alcohol in research and policy.

Cannabis Research Initiatives. Cannabis is a new area for NCI. Cannabis may be viewed as a predictive risk factor for tobacco use that leads to cancer and/or as a palliative treatment for cancer patients. In December 2020, NCI convened a "Cannabis, Cannabinoids, and Cancer Research Symposium" to provide guidance on how NCI might approach this problem space. To date, NCI has provided supplements to selected cancer centers located in states with different types of legal status for the drug (e.g., legal for recreational or medical use) to address questions such as: How and why are cancer patients currently using cannabis (mode, dosage, frequency, and product)? What are the potential benefits and harms of cannabis use among cancer patients associated with cancer and its treatments, comorbidities; other medications?

American Indian/Alaska Native (AI/AN)-Specific Initiatives. "Intervention Research to Improve Native American Health" (IRINAH) was initiated by NCI in 2011, and is now led by NIDA (starting in 2021). The program has 15 ICs participating in an FOA seeking applications for R01/R21 grants. Funded grantees have monthly meetings to maintain a network of researchers. NIH staff are currently updating a

portfolio analysis of related projects. NCI's portfolio from this FOA includes three R01s, such as two focusing on colorectal cancer screening and prevention, one on lung cancer screening, and one R21 focusing on smoking cessation.

NCI is also supporting dissemination of a colorectal cancer screening program across American Indian communities in the Southern Plains and Southwest United States using Cancer MoonshotSM supplement awards to three NCI designated cancer centers (beginning in 2018). This is a parallel effort to NCI's Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS) program. Its long-term goals are to enhance health equity through the reduction of colorectal disparities in morbidity, mortality, stage-at-diagnosis, and increased survival among American Indians.

Funding. NCI's cancer centers are a great resource to address major research priorities in ways that leverage funding. Most NCI funding is dedicated to investigator-initiated research. NCI provides supplements to its cancer centers to address pressing questions, such as those described above for tobacco cessation and cannabis use.

Dr. Klein highlighted selected current and past FOAs related to tobacco, alcohol, and cannabis. Current FOAs include: Notice of Special Interest (NOSI): Basic Mechanisms of Cannabis and Cannabinoid Action in Cancer (NOT-CA-22-085); Notice of Special Interest (NOSI): Administrative Supplements for Examining Patterns of Tobacco and Cannabis Use (NOT-CA-22-070); Notice of Special Interest (NOSI): Public Policy Effects on Alcohol-, Cannabis-, Tobacco-, and Other Drug-Related Behaviors and Outcomes (NOT-AA-21-028); Integrative Research on Polysubstance Abuse and Disorder (PAR-20-035); and Notice of Special Interest (NOSI): Alcohol and Cancer Control (NOT-CA-20-034).

Data Collection. Dr. Klein described two major data collection initiatives sponsored by NCI. The first is the Health Information National Trends Survey that includes variables such as the public's alcohol risk perceptions, tobacco use and tobacco product risk perceptions, and e-cigarette use and electronic nicotine delivery systems (ENDS) risk perceptions. The survey has been conducted annually or biannually since 2003, and all datasets are publicly available at hints.cancer.gov. The second data collection initiative is the Tobacco Use Supplement to the Current Population Survey (TUS-CPS) that contains variables on tobacco use, e-cigarette use, and tobacco and marijuana co-use (for the 2022-2023 questionnaire). It can be linked to the Tobacco Longitudinal Mortality Study (TLMS) to allow research that explores long-term patterns of tobacco product use and associated morbidity/mortality (1+ million records, 1993-2019).

Discussion. Rajita Sinha, Ph.D., commented on the role of traumatic stress on the brain's ability to manage emotions and substance use. She stated that it will be important in terms of prevention and early intervention to recognize the relationship between traumatic events (such as a school shooting) and cancer risk. Dr. Klein replied that there has been significant focus over the past 40-50 years on single exposures to carcinogens, e.g., environmental exposures, but less emphasis on stress. Some recent research has identified a relationship between stress and cancer. Stress is not a great predictor of cancer initiation, but it can accelerate growth of primary and secondary tumors. Further, stress can lead to alcohol use and other behaviors that influence cancer risk. Dr. Sinha noted that traumatic stress has an impact on the next generation by influencing behavior patterns and health choices. She recommended broadening the narrative about primary and secondary interventions by recognizing biological and social signs and symptoms in order to intervene earlier. Dr. Klein reflected that the effects of the pandemic (e.g., increased alcohol use, increased obesity) will play out in cancer risk 20 years into the future.

Karen Winkfield, M.D., Ph.D., inquired about the cannabis research supplements for the comprehensive cancer centers. She noted that the centers are located in demographically diverse areas, but their staffs are often not diverse. She asked how the supplements are being leveraged to require inclusive behaviors. Dr. Klein commented that the supplements are targeted to the cancer centers, but that NCI is working to diffuse these efforts outside the designated cancer centers. He also noted that diversity is a funding requirement for the centers who need to bring in more diverse staff. However, he conceded that Dr. Winkfield is correct that the center staff tend to occupy higher socioeconomic status (SES) than do patients and that this has an impact on treatment.

Rhonda Jones-Webb, Ph.D., asked if NCI is looking at the relationship between cancer pain and alcohol use. Dr. Klein responded that NCI is very interested in pain management and inequities in how pain is managed. He said more research is needed on the relationship between pain and alcohol use, noting that some physicians recommend drinking to alleviate pain but that may raise the patient's risk for secondary cancers. Laura O'Dell, Ph.D., inquired about vaping versus combustible tobacco use. Dr. Klein said that cigarette use is declining, while vaping rates have increased. However, there is a concern about data gathered from teens during the pandemic, as the adolescents were completing questionnaires while at home with their parents which could have raised social desirability concerns.

Adolescent Brain and Cognitive Development (ABCD) Study Update

Dr. Weiss introduced Gaya Dowling, Ph.D., Director of the ABCD study, who updated Council members on the status of the study. Dr. Dowling's co-presenters were Elizabeth Hoffman, Ph.D., and Kim LeBlanc, Ph.D., who summarized recently published research based on ABCD data.

Retention and COVID-19 Impacts. The ABCD study defines all participants as retained unless they deliberately withdraw from the study. By that definition, 98.1 percent of the ABCD cohort has been retained. The program monitors participant demographics to ensure that the cohort remains diverse, as it has.

The pandemic shut down site operations for a period, resulting in a lag in completing follow-up visits. Currently, about 70 percent of two-year follow-up visits have been completed. In Year 3, 79 percent of visits were completed remotely and thus some neuroimaging and biospecimen collection for this period are missing. By Year 4, over one-half (55 percent) of visits were hybrid, with the neuroimaging and biospecimen collections completed in person and the remainder of the data collected remotely. Thus, the pandemic introduced unexpected variability into the study and ABCD investigators are examining questions such as: What is the impact of hybrid assessments on data quality? Is there differential participation in hybrid vs. in-person visits by race/ethnicity, SES? Does this impact data completeness?

ABCD Justice, Equity, Diversity, and Inclusion (JEDI) Progress. The JEDI component of the ABCD study has focused on ensuring diversity-sensitive assessment measures, diversity in ABCD staff, and responsible use of ABCD diversity data. There is currently a search for an Associate Director for Justice, Equity, Diversity, and Inclusion at the ABCD Coordinating Center and efforts to broaden Steering Committee membership. To ensure diversity-sensitive methods, wording of questionnaires and scripts has been changed to be more inclusive and training in culturally-sensitive hair collection has been provided to sites. To increase diversity in the scientific workforce, ABCD launched a Scientific Training in Addiction Research Techniques (START) pilot program for historically underrepresented/underserved scholars to increase access to the rich ABCD dataset by providing hands-on instruction and mentorship. Finally, a paper titled “Responsible Use of Open-Access Developmental Data: The Adolescent Brain Cognitive Development (ABCD) Study” was published in *Psychological Sciences* (May 27, 2021).

COVID-19 Data Collection. In 2020, the ABCD study began sending questionnaires (between May 2020 and May 2021) to all participants to survey pandemic-relevant issues such as family situation, schooling, mental health, substance use, screen time, and COVID-19 experience, among others. The study also correlated the questionnaire data with variations in community impact of COVID using existing datasets such as COVID prevalence relative to population density, timing of implementation of state/local policies, social distancing based on cell phone movement, and changes in unemployment. It also collected pre- and post-pandemic data on activity, sleep, heart rate using FitBit among a subset of ABCD participants. This effort resulted in a number of publications. A key finding was that alcohol use decreased during the pandemic, while nicotine use increased. Investigators are currently examining this data using longer timeframes.

The ABCD Study is also now part of NIH’s new Researching COVID to Enhance Recovery (RECOVER) study of “long COVID.” The aims of the pediatric study arm are threefold. 1) To characterize the incidence, prevalence, and long-term sequelae, including clinical and biological features, severity, and distinct sub-phenotypes, following SARS-CoV-2 infection. 2) To characterize the clinical course and recovery of acute and post-acute sequelae over time and determine associated risk factors for long COVID among SARS-CoV-2 infected individuals compared to uninfected individuals. 3) To define the pathophysiology and biologic mechanisms of post-acute sequelae, including direct and indirect causal effects of SARS-CoV-2 infection, and potential modifiers (e.g., sex, age and race/ethnicity).

With better characterized infection status, i.e., COVID antibody results and the Long COVID symptom survey, the ABCD Study has the potential to address the prevalence of infection and long COVID in adolescents, and within different communities and subgroups as well as pre-infection risk and resilience factors that modify the ‘infection-related’ outcomes. It will also be able to isolate infection effects vs pre-pandemic and general pandemic impacts, describe in-depth brain, cognitive, and mental health phenotyping, and identify long-term outcomes given that ABCD will follow this cohort for another six years.

Data Sharing and Use. Curated ABCD data are released annually via the NIMH Data Archive. The 2021 Data Release 4.0 is now available. It includes two years of neuroimaging data. Listed below are two Requests for Application (RFAs) and two Program Announcements issued that can be used to support secondary analysis of ABCD data.

- Accelerating the Pace of Drug Abuse Research Using Existing Data (R01 Clinical Trial Optional) (RFA-DA-22-037)

- Accelerating the Pace of Drug Abuse Research Using Existing Data (R01 Clinical Trial Optional) (RFA-DA-22-038)
- Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R01 Clinical Trial Not Allowed) (PAR-22-137)
- Accelerating the Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R21-Clinical Trial Not Allowed) (PAR-22-138).

As of December 2021, 73 NIH-funded grants have leveraged ABCD data and, as of May 22, 2022, 342 scientific papers using ABCD data have been published.

Recent Findings. Dr. Hoffman summarized two recent articles using ABCD data. The first, “Reproducible Brain-wide Association Studies Require Thousands of Individuals” (Marek et al. [2022], *Nature*) sought to highlight the shortcomings of small sample sizes in neuroimaging studies that may contribute to replication failures in Brain Wide Association Studies (BWAS) linking individual variability in brain to variation in behavior. It used neuroimages from 50,000 individuals from the ABCD Study, UK Biobank, and Human Connectome Study to examine associations between the brain (cortical thickness; resting state functional connectivity) and behavioral phenotypes (cognitive ability; psychopathology). The investigators reported less variability in effect sizes with increasing sample size in univariate BWAS; stronger multivariate out-of-sample associations compared to univariate; and greater concordance between in-sample and out-of-sample replicates with larger sample sizes. Thus, they concluded that large sample sizes are needed for accurate estimation of effects in BWAS. The article generated considerable discussion within the scientific community with some believing it indicated that the value of neuroimaging studies with small sample sizes was being denigrated. However, the authors are clear that their analysis was specific to BWAS studies and do not extend to all neuroimaging studies.

Li et al., evaluated whether predictive models using machine learning that are widely used in population neuroscience and precision medicine can generalize to non-white populations. (“Cross-ethnicity/race Generalization Failure of Behavioral Prediction from Resting-state Functional Connectivity” (Li et al. [2022], *Science Advances*). They investigated algorithmic fairness using data from the Human Connectome Project and the ABCD Study. They matched African American (AA) and white Americans (WA) on demographics and behavioral performance and compared prediction accuracy between WA and AA, when models were trained on the entire sample. This mimics the dominant approach currently taken in the field. In general, given equivalent actual scores on a particular measure, prediction errors in AAs were larger than in WAs. For example, cognition (picture vocabulary, working memory, matrix reasoning, crystallized cognition) was more poorly predicted in AA than WA. To attempt to obtain a more valid predictive model, training was performed separately on WA and AA using data from ABCD. For the model trained on AA, 8 of 36 measures showed greater prediction accuracy for AA than WA but 19 of 36 measures still showed greater prediction accuracy for WA than AA. In contrast, for the model trained only on WA, there was greater prediction accuracy in AA compared to WA for only two measures. Thus, training the model specifically on AA increased prediction accuracy but not completely. Li et al. investigated algorithmic fairness in predictive models of behavioral phenotypes from resting-state functional connectivity and found that given equivalent actual scores, the prediction data do not generalize across populations. Training the models specifically on data from African American participants resulted in greater prediction accuracy for African American participants compared to when the models were trained on data from white participants. That said, even for models trained on data from African American participants, many of the measures still showed greater prediction accuracy for white American than African American participants. It is not clear what else is causing the generalization failure, but what is clear is that the difference in prediction performance between the two groups was at

least partly related to the dominance of white Americans in the datasets, and racial/ethnic data composition is important for the fairness of prediction results. More data from underrepresented groups are critically needed. This is related to the broad framework in Simmons et al. (Responsible Use of Open-Access Development Data: The Adolescent Brain Cognitive Development (ABCD) Study *Psychological Science* 32:866-870) that provides guidelines on responsible data use, analysis and interpretation. They emphasize the responsibility that researchers have to enhance accuracy in measurement and interpretation. Toward that aim, researchers should carefully consider the role of contextual factors, heterogeneity, and individual experience when approaching research questions.

Dr. LeBlanc summarized “Brain Charts for the Human Lifespan” (R. A. I. Bethlehem et al. [2022] *Nature*). She explained that growth charts have long existed for bodies, but no reference standards currently exist for brain development. Traditionally, the challenge has been that neuroimaging data is highly sensitive to variation in scanner platforms and sequences, data quality control, pre-processing and statistical analysis. However, large scale datasets (like ABCD) and recent advances in neuroimaging and statistics have now made brain development charts possible. In this study, investigators used 123,984 MRI scans, across more than 100 primary studies, from 101,457 human participants between 115 days post-conception to 100 years of age, fitting Generalized Additive Models for Location, Scale and Shape (GAMLSS) to structural MRI data from control subjects for total cortical grey matter volume (GMV), total white matter volume (WMV), total subcortical grey matter volume (sGMV) and total ventricular cerebrospinal fluid volume. They found that primary sensory regions reached peak volume earliest and showed faster post-peak declines and that fronto-temporal association cortical areas peaked later and showed slower post-peak declines. This spatial pattern recapitulated a gradient from sensory-to-association cortex that has been previously associated with multiple aspects of brain structure and function. The study serves as proof of principle for defining normative trajectories of sex-stratified, age-related change in multiple MRI-derived phenotypes across the lifespan and for quantifying neuroanatomical atypicality of brain scans collected across multiple clinical disorders. It should be noted, however, that the dataset is biased towards European and North American populations and European ancestry groups, as well as higher SES individuals. Fetal, neonatal and mid-adulthood (30–40 years of age) groups were under-represented. Finally, brain charts are not immediately suitable for clinical use or quantitative diagnosis. However, this study shows that building normative charts to benchmark individual differences in brain structure is achievable at global scale and over the entire life-course.

Discussion. For the benefit of those unfamiliar with neuroimaging, Dr. Sinha pointed out that very large samples are needed because they are measuring very dynamic changes that occur during development in response to social and environmental factors. However, single-site studies should not be dismissed because they are often controlling for a number of factors that cannot be done in multi-site studies. Thus, there are trade-offs in how studies are conducted. The study that Dr. Hoffman reported on recorded accurate and replicable brain associations that are informing clinical outcomes and prevention and treatment development. Secondly, she also emphasized that resting state functional connectivity is only one aspect and that was what was shown. There is a growing literature indicating that resting state does not predict behavior in a validated way with sensitivity compared to task-based states. Finally, gray matter volume is only one aspect, and it can change with only a four-day intervention. It is problematic that neuroimaging is discussed as a single static measure. It will not be helpful to the field if oversimplified messages, such as the one surrounding the given study, are disseminated. Dr. Dowling concurred, noting multiple discussions among ABCD investigators on this topic. Investigator Nico Dosenbach, Ph.D., is planning to write a commentary on exactly this issue. Dr. Sinha added that other dynamic changes occurring between ages 5-7 are not being captured because the ABCD study does not

capture this age range. She also stressed the importance of examining factors such as stress, poverty, etc. She asked how the ABCD study will account for these factors. Dr. Dowling acknowledged the point. The paper in *Psychological Sciences* that she mentioned in her presentation highlights all the data that ABCD collects, including poverty, discrimination, environmental factors, etc., that should be incorporated into models to understand racial/ethnic differences in particular, as well as the developmental context, acknowledging that changes in the environment can change developmental trajectories. Researchers are often leaving out variables in order to make the analysis more manageable. However, in doing so, they are losing the richness of the data. ABCD has the potential to elucidate the factors impacting development more fully because the data exists. Anna Rose Childress, Ph.D., echoed Dr. Sinha's comments. She noted, however, that it is extraordinary to observe what ABCD has been able to capture, even in the pandemic. It is difficult, however, to convey all the subtlety and nuance in the data. She asked where the field can find good writers to frame the content of papers in such a way that oversimplified headlines do not produce a reaction that all brain data or all ABCD data is not good. Dr. Dowling replied that while the open science model is wonderful, it comes with pitfalls. ABCD is leaving it up to the scientific community to evaluate its research. That said, the study is considering publishing some reviews of papers that have emerged to present the findings in a way that allow people to have a clear "take home" message.

Amit Etkin M.D., Ph.D., offered a different perspective on the issue of sample size in neuroimaging studies. He believes that smaller studies can provide a big impact. From a funding agency perspective, all BWAS are about effect size, retest reliability, and power; they affirm what researchers should already know. The problem with small studies is publications of under-powered studies conducted by trainees in order to gain needed publication credits. NIH should be addressing how to review trainees' funding requests and journal editors should not be publishing under-powered studies that have not been replicated. Dr. Hoffman interjected the need to be careful about messaging study findings, including identification of where large samples are needed and understanding that there are areas where a smaller sample is fine. Dr. Dowling reiterated that ABCD investigators cannot provide granular details in such a large study. Smaller studies can go into more depth in certain areas. Dr. Amit responded that he is not saying that small studies are not valid, simply emphasizing that they need to be replicated. As a funding agency, NIH needs to look at trainee grants and ask: Will this proposal meet the bar in five years? Can their work be replicated? Dr. Childress commented that, from a trainee perspective, the idea that a study cannot get published unless there are thousands of subjects is daunting, especially in the face of funding and other challenges that may deter them from a research career. She said it was important for these young investigators to understand that with some distinctions in the kinds of paradigms used and replicability, small studies can take them far in their research.

Solutions to End Suicide and Prevent Substance Use Disorder (SUD) in Alaska: Building Multi-Level Strengths and Protective Factors within Alaska Native Communities and Cultures to Reduce Risks

Dr. Koob introduced Stacy M. Rasmus, Ph.D., Director, Center for Alaska Native Health Research, University of Alaska Fairbanks, who reported on intervention approaches to prevent suicide and SUDs based on cultural processes and systems among Yup'ik people located in western Alaska. Her goal was to shift the paradigm and narrative about health disparities by focusing on community strengths and assets rather than community or individual deficits.

The Setting. Alaska is a geographically large state with a very diverse indigenous population of over 180,000 people belonging to 228 Federally recognized tribes. In the Central Yup'ik region, which is the size of Nebraska, 58 villages are served by the Yukon Kuskokwim Health Corporation in Bethel, the

region's hub community; one village is 350 miles away and only accessible by air. Mental health services in the region are limited. Suicide is the leading cause of death at 212 suicides/100,000 people, compared to a national average of 13 suicides/100,000 people. The highest suicide rate was among Alaska Native males ages 20-29. Of those tested, over one-half (54 percent) of Alaska Native suicide decedents were positive for alcohol. Alcohol use is high in the region, although most villages ban importation and sale of alcohol and vote to be 'dry' under the AK local option law. The opioid overdose rate increased by 68 percent between 2020 and 2021; fentanyl was a factor in 60 percent of those deaths.

Dr. Rasmus attributed these serious health issues in the region to the transition from living a traditional lifestyle where protective factors were in place, noting that alcohol and other drugs were not part of Indigenous cultures in Alaska and suicide among young people was unheard of in the memories of today's elders. She described an intervention approach that began 20 years ago when tribal elders approached University of Alaska providers/researchers with their concerns: In 1967-1977, suicide rates doubled in the area and did so again 1977-1987. They have remained very high since then. The elders identified young people's disconnection from their traditional way of life as the driving force behind mental health and substance use disorders in the community.

Qungasvik. Dr. Rasmus explained "Qasgiq means to encircle, and in coming together around our youth in the ways of our ancestors, we are strengthening our collective spirit in an effort to cast suicide out from our communities, forever". It is also a term that denotes a traditional way of life/a communal house. It is also a verb that describes traditional ways of coming together. The researchers developed an indigenous theory of change based on the Qasgiq model (Communal Home) model. It delineates community strengths (tribes, churches, families, etc.). These include inputs that are protective factors at the community, individual, and family levels and outputs/strategies such as protective factors, activities, and workgroups, and multi-level outcomes at the community, family, and individual levels such as reasons for life and reasons for sobriety. The theory requires communities to change first, followed by engaging families and youth in activities using Qungasvik (Tools for Life). The researchers measure protective factors identified by the elders, as well as community outcomes.

The 18-module Qungasvik Toolbox (available online) supports local people to develop a multi-level, strengths-based and indigenous protective factors model that moves prevention upstream to work with all young people (12-18 yrs) and the whole community. It also engages culture as prevention in a process of Indigenous intervention science, provides indigenous young people with protective cultural experiences as a hedge against risk, and, most importantly, empowers Yup'ik indigenous knowledge and re-centers communities around traditional structures and systems of care.

Youth activities have included fishing, hunting, harpooning, gathering wood for elders, tool building, and preparing traditional Yup'ik foods. These activities are out on the land, reflecting the tribes' land-based way of life. They function as rites of passage in which young people recognize that they are providers for their families and communities. These activities build protective factors. For example, *Maliqianeq* (seal hunt) promotes *Ellangneq* (awareness), self-efficacy, and communal mastery. Dr. Rasmus provided examples of successful Qungasvik projects in various villages within the region.

Outcomes. Since the program started 20 years ago, meaningful changes have been observed. Strengths of the program include delivery of specific protective factors as the function of each Qungasvik intervention activity. Other strengths include the central role of measurement development in outcomes assessment with culturally distinct groups, tests of Qungasvik protective factors model as an Indigenous theory of change, and the feasibility of implementing Qungasvik interventions in rural Yup'ik

Alaska Native communities. Additional strengths include comparative effectiveness using dose effects, mechanisms of change in protection from alcohol misuse based on findings from mediation analysis, and ongoing prevention trials of community level intervention.

The ongoing research measures ultimate variables, including reasons for sobriety (alcohol protective factors), reasons for life (suicide protective factors), attitudes about alcohol use, and a sobriety timeline follow back. Intermediate variables include individual protective factors (e.g., communal mastery, becoming a role model), family protective factors (family relationship), and community protective factors (e.g., connections with elders, social connectedness).

A comparative effectiveness study across two villages found that the higher the Qungasvik dose, the stronger the outcomes, especially among younger males.

Summary. In conclusion, Dr. Rasmus provided the following summary of this research: Qungasvik is a strengths-based, community-level intervention grounded in a multi-level theory of protection and an Indigenous theory of change and implementation. Qungasvik can be feasibly implemented in the remote, arctic, rural Yupik Alaska Native community context to produce dose related measurable effects. Higher intensity intervention produces enhanced protection in contrast to lower intensity intervention. Effects are strongest among youth with lower levels of protection at baseline, and among males, particularly those under age 15.

Discussion. Dr. Koob asked if some of the core principles developed in this program could be generalized to other indigenous communities across the United States as well as to minority populations. Dr. Rasmus responded that every community has Qasgiq as a cultural way of working together. The protective factors in Yup'ik culture are universal and will build protections for all young people. The program has already been applied within Alaska to a different Alaska Native community. Evidence-based practices from White communities are transferred into AI/AN communities, so a transfer in the opposite direction should work just as well. It's about the process of the intervention more than the target audience. Dr. Weiss commented that the book *Dreamland: A True Tale of America's Opiate Epidemic* by Sam Quinones makes a similar point to Dr. Rasmus' presentation about the dissolution of community leading to the opioid crisis. Without restructuring, there will be no progress. Dr. Rasmus commented that her team has recently received funding from the U.S. Department of Defense to translate their intervention into the military community in Alaska where there has been a cluster of suicide among young soldiers. The military culture shares similarities with the tribal one.

Melissa Walls, Ph.D., asked for more details about the measurement of community factors and how those translate to the individual, particularly in light of NIH's interest in measures to assess structural racism. Dr. Rasmus described multiple strategies for examining community factors and their impact on youth, including asking youth about how safe they feel, how connected they are to the elders, their attendance at tribal council meetings, and available opportunities for employment, help, and support. They also do a social network analysis and use a protective community factors scale with adults, asking them to assess how healthy and functional they perceive their communities to be, what spiritual practices they use, etc. They have found that there is a lower rate of suicide in communities where adults report greater community cohesion.

Dr. Sinha inquired about the availability of the intervention manual, who delivers the interventions, and whether specific, vulnerable young people were targeted. Dr. Rasmus shared the link to the online Qungasvik manual that describes the intervention process which takes 2-3 years to implement. It is a

community-delivered intervention. The University hires two coordinators in each location, one male and one female, who are knowledgeable about the culture and respected in the community. These coordinators bring the community together in a formal Yup'ik process. The community identifies the activities to implement based on a seasonal calendar. The coordinators identify experts to be instructors in specific activities. Dr. Becker noted that the suicide rate is higher among males than among females. She asked if different strategies are implemented for boys and for girls. Dr. Rasmus responded that the suicide success rate is higher among males, but suicide attempts are higher among young women. The approach used in this project is a universal prevention strategy for all young people, primarily those 12-18-years-old. There is tailoring around young males who are taught to be powerful men and providers. Traditional gender roles are an important part of the culture's teaching. Young men's roles have changes more dramatically than young women's have over time.

Round Table Discussion

Dr. Chambers commented that she is intrigued by ABCD's diversity initiative and its START program as a base for developing guidelines for placing data in context. She asked if START could provide an avenue for developing such guidelines. Dr. Dowling responded that while the START investigators considered the contextual use of data, the real challenge is getting the scientific community at large engaged in these discussions. The push for open data has to go hand-in-hand with consideration of its responsible use. Dr. Chambers suggested this could be made a requirement for the use of the open dataset. Dr. Dowling replied that the ABCD investigators have been talking about requiring training in how to analyze the data ethically and responsibly before someone can access the datasets. Dr. Hoffman commented that this should be an NIH-wide requirement. There are agreements in place for getting access to data but there is a need to develop a training module that people must pass before using data. With big datasets, all levels of researchers are likely to use data in ways that are not contextually informed. Dr. Dowling said that a system is also needed for adjudicating misuse of data and ABCD is trying to learn from others' efforts to do this. Dr. Chambers commented that this needs to be done in a way that does not antagonize people. She also noted that while most diverse researchers are likely to be junior, there is a real need for more diverse senior researchers who could be the biggest leaders of a change in approach.

Dr. Fingert, referring to Dr. Etkin's earlier comments about under-powered studies, emphasized the role of program officers who are highly empowered, especially under the second Moonshot that will bypass the Board of Scientific Advisors (BSA). He asked if the program officers are really trained in the relevant issues so that they can guide applicants appropriately. Dr. Weiss responded that there is no simple answer to his question because there are multiple ways for projects to obtain funding and program officers are highly empowered in a limited number of cases. With NIH's new requirements around data access and sharing, it becomes increasingly important that people use the data responsibly and in context. The ABCD experience has raised the possibility that people can misuse data in ways that can be harmful. This is bringing the need for training before use of public data to the forefront. Dr. Gray noted that all ICs have structures in place to ensure that program officers follow guidelines for interacting with the scientific community. There is no initiative released within NCI that would bypass the BSA. Dr. Klein concurred, stating that some of the initiatives in NCI's Behavioral Research Program are funded by the Moonshot, but all have gone through the BSA. Dr. Fingert said that it was his understanding that programs funded under the second Moonshot would not be reviewed by BSA. Dr. Gray clarified that the second Moonshot is a Presidential initiative, but projects must still be reviewed by NCI's BSA. Dr. Klein noted that although the new Moonshot is a Presidential initiative with specific priorities, NCI staff will be the ones developing the program that will have to go through traditional review processes. Dr. Gray said that all concept initiatives must be approved by the BSA. When the grants are approved, second level

peer review is conducted by the National Cancer Advisory Board (NCAB). However, with a Presidential initiative, immediate discussion is by the NCAB.

Dr. Walls raised the issue of changing the way that NIH and the advisory process approaches decisions such that equity remains front and center. She stated that inequities continue to increase. If science continues to be conducted the way it always has been, nothing will change. She called the culturally responsive approach described by Dr. Rasmus as a game-changer and called for radical thinking about this issue, suggesting that taxpayer funds should go directly to the communities involved. Dr. Koob responded that he can only speak on behalf of NIAAA which has identified equity as a primary theme in its new strategic plan and which is working diligently to address diversity and equity. There are multiple initiatives within NIH addressing health inequities and disparities; each IC is developing its own plan. He believes change is coming to the scientific enterprise. Dr. Compton noted that Dr. Volkow started NIDA's social equity initiative in 2020. NIH's efforts have three major components: 1) focus internally with each IC addressing its own workplace issue; 2) promote workforce diversity to overcome the lack of diversity among principal investigators, especially low numbers of Black and AI/AN investigators; and 3) conduct health disparities research, e.g., the COVID Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) initiative to bring COVID testing to underserved communities. He believes there is increasing visibility of entrenched inequities at NIH. Dr. Weiss commented that there's been a big shift in how NIH is looking at chronic disorders, especially about the role of SDoH. These factors are being incorporated into NIDA's funding opportunities. It may not be happening quickly enough, but NIH is trying to address health inequities. Dr. Compton added that Dr. Volkow has asked staff who make funding recommendations to support less resourced institutions, e.g., Historically Black Colleges and Universities (HBCU), in NIDA's funding plans to reduce inequities in the distribution of funding. Dr. Greenfield commented that she liked the ideas for shared responsibility to increase diversity and inclusion, such as including diversity statements in biosketches or asking about the diversity of a laboratory. She recommended increasing opportunities for mentors across multiple institutions to share their experiences. She also noted that there is a false dichotomy in the belief that an intervention can be tailored to a specific community but not scaled up. For example, an RFA could require a consortium of different communities to adapt the culturally responsive model described by Dr. Rasmus. Dr. Winkfield commented on the need to ensure that reviewers with expertise in community-engaged research are on review panels. She also noted the challenges to conducting research within minority-serving institutions and recommended that NIH fund partnerships between them and academic research institutions. Dr. Chambers noted the success of the Sex as a Biological Variable (SABV) and reproducibility policies in changing research; adding a diversity requirement to applications would help move the field toward greater workforce diversity.

Adjournment

Dr. Koob adjourned the meeting at 3:03 p.m.

CERTIFICATION

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

For NIAAA:

/s/

George Koob, Ph.D.
Director
National Institute on Alcohol Abuse and
Alcoholism
and
Chairperson
National Advisory Council on Alcohol Abuse and
Alcoholism

/s/

Abraham P. Bautista, Ph.D.
Executive Secretary
National Advisory Council on Alcohol Abuse and
Alcoholism
National Institute on Alcohol Abuse and
Alcoholism

For NIDA:

/s/

Nora Volkow, M.D.
Director
National Institute on Drug Abuse
and
Chairperson
National Advisory Council on Drug Abuse

/s/

Susan Weiss, Ph.D.
Executive Secretary
National Advisory Council on Alcohol Abuse
National Institute on Drug Abuse

For NCI:

/s/

John D. Carpten, Ph.D.
Chair
National Cancer Advisory Board
National Cancer Institute

/s/

Paulette S. Gray, Ph.D.
Executive Secretary
National Cancer Advisory Board
National Cancer Institute