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

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

May 3, 2017
Rockville, Maryland

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 fifth joint meeting on May 3, 2017, in Rockville, Maryland. Chaired by Dr. George Koob, Director of NIAAA, and Dr. Nora Volkow, Director of NIDA, this open session convened at 9:03 a.m.

National Advisory Council on Alcohol Abuse and Alcoholism Members Present:

Carmen E. Albizu-Garcia, M.D.
Louis E. Baxter, Sr., M.D
Daniel J. Calac, M.D.
Carlo C. DiClemente, Ph.D.
Tom Donaldson
Alex M. Dopico, M.D., Ph.D.
James H. Eberwine, Ph.D.
Paul J. Kenny, Ph.D. (by telephone)
Joe L. Martinez, Ph.D.
Adolf Pfefferbaum, M.D.
Arun J. Sanyal, M.D.
Vijay H. Shah, M.D.
Rajita Sinha, Ph.D.
Susan M. Smith, Ph.D.
Constance M. Weisner, D.R.P.H.

National Advisory Council on Drug Abuse Members Present:

Judith D. Auerbach, Ph.D.
Julie A. Blendy, Ph.D.
John Carnevale, Ph.D.
Linda Chang, M.D.
H. Westley Clark, M.D.
Arthur T. Dean
Karl Deisseroth, M.D., Ph.D. (by telephone)
Marie Gallo Dyak
Kenneth P. Mackie, M.D.
Lisa A. Marsch, Ph.D.
Edward V. Nunes, M.D.
Robert G. Rancourt, J.D.

Eric M. Verdin, M.D.

National Cancer Advisory Board Members Present

Francis Ali-Osman, D. Sc.
Scott W. Hiebert, Ph.D.
Electra D. Paskett, Ph.D.
Margaret R. Spitz, M.D. (by telephone)

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

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

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

Acting 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 R.B. Weiss, Ph.D.

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

NIDA Senior Staff: Carlos Blanco, M.D., Ph.D.; Gaya Dowling, Ph.D; Ivan Montoya, M.D.; Jack Stein, Ph.D.; Mark Swieter, Ph.D.; Rita Valentino, Ph.D.; Katia Delrahim-Howlett, Ph.D.

NIAAA Senior Staff: Vicki Buckley, M.B.A.; Ralph Hingson, D. Sc.; Robert Huebner, Ph.D.; Kathy Jung, Ph.D.; Raye Litten, Ph.D.; Antonio Noronha, Ph.D.

NCI Senior Staff: Michele Bloch, M.D., Ph.D.; Mark Parascandola, Ph.D.

Additional Participants

Seventy-one (71) observers joined the meeting, including representatives of constituent groups, liaison organizations, and members of the public.

Call to Order and Introductions

Dr. George Koob called to order the fifth joint meeting of the National Advisory Councils of NIAAA, NIDA, and NCI in open session at 9:05 a.m. on Wednesday, May 3, 2017. Council members and Institute leaders introduced themselves.

NIAAA Director's Presentation

Alcohol's Impact: Dr. Koob reviewed the cost and scope of alcohol-related problems in the United States, noting that 14 percent of people age 18+ met the criteria for alcohol use disorder (AUD) in the Diagnostic and Statistical Manual of the American Psychiatric Association Fifth Edition (DSM-5) in the past year, with approximately 88,000 people dying annually from alcohol-related causes. About half of all liver disease in the U.S. is attributable to alcohol misuse. There has been an increase in the intensity of underage binge drinking and hospitalizations in last 10 years. Less than 10 percent of people with AUD get any treatment. There are three medications approved by the Food and Drug Administration (FDA) for AUD.

NIAAA Overview: NIAAA supports research to study how alcohol affects health and well-being at various stages of life, from fetus to seniors, with research on neurobiology, metabolism, genetics, epigenetics, epidemiology, and health services. NIAAA's new Strategic Plan for 2017-2021 establishes the following strategic priorities for the Institute: Identify mechanisms of alcohol action, alcohol-related pathology, and recovery; improve diagnosis and tracking of alcohol misuse, AUD, and alcohol-related consequences; develop and improve strategies to prevent alcohol misuse, AUD, and alcohol-related consequences; develop and improve treatments for alcohol misuse, AUD, co-occurring conditions, and alcohol-related consequences; and enhance the public health impact of NIAAA-supported research.

Surgeon General's Report: NIAAA, along with NIDA, played a key role in the development of *Facing Addiction: The Surgeon General's Report on Alcohol, Drugs, and Health*, the first one addressing alcohol and other substance misuse, and substance use disorders (SUDs).

HBO Documentary on Risky Drinking: Produced in conjunction with NIAAA and featuring NIAAA experts, this HBO documentary has been described as a" no-holds-barred" look at AUD through the intimate stories of four people who's drinking dramatically affects their relationships. Initially airing on December 19, 2016, it aims to provoke conversation about how to identify risky drinking and to suggest alternatives to a one-size-fits-all approach for treating it. NIAAA will be showing it at the Research Society of America and American Psychiatric Association meetings this year.

Wearable Alcohol Biosensor Challenge: NIAAA completed its first Challenge in 2016 for a wearable alcohol biosensor. The winning prototype was submitted by BACtrack, a company known for designing and selling portable breath alcohol testers for consumer use. Their entry, the BACtrack Skyn, is worn on the wrist and detects alcohol in perspiration. It offers continuous, non-invasive blood alcohol concentration (BAC) monitoring, storing the data to a smartphone via Bluetooth. A second Challenge is now open (12/10/16 - 5/15/17) to design a wearable sensor using technologies that detect alcohol non-invasively in blood or interstitial fluid.

NCANDA Initial Findings: The National Consortium on Alcohol and Neurodevelopment in Adolescence **(**NCANDA) is a cross-sectional longitudinal study with approximately 900 subjects supported by the Division of Neuroscience and Behavior, NIAAA. Data are beginning to come in from the study. One finding, for example, is that those at risk for binge alcohol use, at risk alcohol use, or marijuana use tend to stay up late at night, and express a preference for sleeping in in the morning. This may prove to be a sensitive measure of vulnerability to future alcohol use. Another key finding: 117 youth in the "exceeds drinking" group had attenuated connectivity between the emotion network seed of the amygdala and default-mode network regions of the posterior cingulate cortex/precuneus, relative to a subgroup of 117 no/low drinking youth matched to the drinkers in age, sex, education, ethnicity, and ratio of scanner manufacturer. Information from NCANDA is providing new insights into the effects of alcohol on

development and provide key new information of use for the Adolescent Brain Cognitive Development (ABCD) study

CollegeAIM: The College Alcohol Intervention Matrix (CollegeAIM) is an evidence-based decision guide and interactive website to help schools address harmful and underage student drinking. It rates nearly 60 individuals- and environmental-level interventions based on factors such as cost, effectiveness, and ease of implementation. NIAAA is holding regional workshops to introduce CollegeAIM to institutional officials.

Addiction Neuroclinical Assessment Paradigm: The National Institute of Mental Health's Research Domain Criterion (RDoC) has stimulated thinking within NIAAA and NIDA about measures that might be used to help diagnose addiction, in addition to the current ratings used in the DSM-5. These include incentive salience, negative emotionality and stress, and executive function.

Medications Development: NIAAA has a small but active medications development program. The Division of Medications Development was established to coordinate efforts to identify, screen, and evaluate compounds for treating AUD. Components of the program include human laboratory screening studies to bridge the gap between preclinical and clinical trials; a Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) program to bridge the "valley of death" between basic and clinical research by facilitating studies leading to the development of an Investigational New Drug (IND) application to the Food and Drug Administration (FDA); and an NIAAA Clinical Investigations Group (NCIG) to streamline AUD medications development by conducting "fast success/fast fail" Phase II clinical trials with 18 month turn-around time. NCIG launched a clinical trial of gabapentin in June 2015. NIAAA's intramural program also conducts clinical studies on novel compounds with AUD treatment potential, and NIAAA disseminates information about treatment options, including medications, to health professionals and the public.

Novel AUD Targets by Stage of the Addiction Cycle: NIAAA has done significant work on the neurobiology of addiction, which could lead to future medications. NIAAA has had one successful clinical trial of vasopressin 1B antagonist, which effectively ameliorated and reduced heavy drinking in a double-blind placebo-controlled clinical trial. Unfortunately, there is currently no pharmaceutical company interested in developing it.

NIAAA Treatment Navigator: To assist people in finding AUD treatment, NIAAA is developing the NIAAA Alcohol Treatment Navigator. The Navigator is a one-of-a kind resource that outlines the features of evidence-based AUD treatment; describes the varied routes to recovery; and provides tools for locating the most qualified treatment specialists.

Recovery Factors: Dr. Koob shared findings from a paper published in the *American Journal of Psychiatry* (168:2; February 2011) by K. Rando, K.L. Hong, A. Bhagwagar, C.S. Li, K. Bergquist, J. Guarnaccia and R. Sinha, showing that those with smaller prefrontal cortex volumes in an MRI scan are less likely to recover from alcohol use disorders. This reinforces findings that the frontal cortex has a critical role in the vulnerability for developing an alcohol used disorder

Alcohol Policy Information System (APIS): NIAAA is participating in a database that tracks and facilitates research on alcohol-related policies at the state and federal levels**.** The database has recently been expanded to include recreational marijuana policies.

New Efforts to Promote a Stronger and More Stable Biomedical Research Workforce

**PLEASE NOTE that the GSI policy process is ongoing and iterative; the summary statement below does not reflect the most current information on the GSI plan. For the most up-to-date information on the GSI plan, please visit *https://grants.nih.gov/ngri.htm*.

Lawrence Tabak, D.D.S., Ph.D., Principal Deputy Director of NIH and Deputy Ethics Counselor, presented a new NIH strategy to maximize the impact of its research investment while also developing and sustaining the most qualified biomedical research workforce possible. He began by sharing a number of observations about the state of U.S. biomedical research from articles published in biomedical journals to NIH's own research. He noted that institutions expect that investigators will submit multiple applications each year; many institutions expect two R01s as the "minimum" level of support and incentivize faculty to obtain as many grants as possible. The system is characterized by hyper-competition: There are many more applicants, but the number of awardees is stable. In a Point of View article (eLife 2015; 4:e09305), Judith Kimble and colleagues reported that a workshop they conducted at the University of Wisconsin in Madison identified two core problems that the U.S. biomedical research community faces: 1) too many researchers vying for too few dollars; and 2) too many postdocs competing for too few faculty positions. An analysis of the age of NIH-funded investigators reveals that only those older than 60 increased as a percentage of funded investigators between 1990 and 2015. This is not merely a reflection of Baby Boom demographics; multiple analyses indicate established Principal Investigators (PIs) are outcompeting other groups. Over the same period, there has been a sharp decline in the percentage of funded investigators between the ages of 46-60; those younger than 46 were also in decline until NIH instituted early career investigator (ESI) guidelines. Currently 10 percent of investigators receive 40 percent of all NIH research dollars, and 20 percent receive over half (56 percent). The concentration of resources among the most senior investigators challenges NIH's ability to maintain a future biomedical research workforce.

NIH conducted a bibliometric analysis of over 71,000 PIs to examine whether the skewed distribution of resources yields optimal productivity. The study revealed that incremental research output according to the extent of grant support begins to diminish after an investigator receives the equivalent of two R01 grants per year. These findings are consistent with published studies on the issue. While well-funded investigators are very productive, NIH must determine if it will get a greater return by giving a third or fourth grant to someone or by awarding a grant to a highly promising investigator who would otherwise have no resources.

Thus, NIH is grappling with these questions: How can the agency increase the number of early-career funded scientists? How can NIH stabilize the career trajectories of scientists? How can it maximize the impact of its research funding? NIH considered several approaches recommended by the research community, including consistent recommendations from published articles such as the Kimble et al. paper cited above, from the Federation of American Societies for Experimental Biology (FASEB), and from comments in response to a 2015 Request for Information on "Optimizing Funding Policies and Other Strategies to Improve the Impact and Sustainability of Biomedical Research." Capping the number of NIH grants or amount of funds a PI can have were among the most common suggestions by both individual and institutional respondents.

NIH is committed to normalizing funding patterns across all career stages. It will carefully track funding patterns of scientists across all career stages, and Institutes and Centers (ICs) will continue to make full

use of all current approaches to "bend the curve" including: adherence to the Early Stage Investigator (ESI) policy; expanding R01 investigator initiated-research at the 'expense' of Institute-solicited Funding Opportunity Announcements (FOAs); prioritizing R56 Bridge Awards for ESIs to increase R01 resubmission success rates; and targeting R35 awards for mid-career "Emerging Investigators." None of the current approaches addresses directly the issue of diminishing returns in the labs of highly funded investigators, most of whom are supported by two or more ICs. Therefore, NIH will institute a new trans-NIH policy that resets expectations for the support provided to any single investigator, beginning with applications being submitted in the fall of 2017.

The new policy will use a Grant Support Index (GSI) as a measure of a PI's grant support. The GSI will be a modified grant count to estimate the "bandwidth" of principal investigators. It will not be simply a measure of dollars, in recognition of the fact that some science is more expensive to conduct. The GSI will be benchmarked to an R01 award (7 points), with R03 and R21 grants receiving fewer points and R35, P50, and U54 (PI) awards receiving more. NIH will strive to reset expectations for the support provided to any single investigator by monitoring levels of PI "bandwidth" using the GSI. In general, the agency will limit the "bandwidth" of any single PI to a GSI of 21 (roughly equivalent to three R01s). Investigators above a GSI of 21 will be required to present a plan with any new or competing application that mitigates any increase to their GSI. A rigorous "exceptions" process can be initiated by IC directors, considering, the unique research requirements of an IC, the success of the IC to normalize funding patterns among all career stages, and the need to maximize productivity of grant resources. Final decisions will be made by the NIH Director's Office

NIH is encouraging input into how to implement this plan for extramural funding. An analogous program will also be put into place for the NIH Intramural program. NIH also recognizes that each home institution has a different policy, e.g., receiving two R01s or four R01s before the investigator can get tenure. Thus, there needs to be conversations that reset expectations everywhere; this has to be a partnership between NIH and universities.

Discussion: Alex Dopico, M.D., Ph.D., asked how NIH would apply metrics to those with relative involvement, e.g., Multiple Principal Investigators (MPIs), co-PIs, etc. Dr. Tabak asked for guidance on the number of points to be assigned. Dr. Dopico responded that PI partnerships often consist of one senior researcher and one who is junior; they can't be held equal. Dr. Tabak replied that one of the two generally spends more time on the project; NIH considered pegging the number of points to effort, but that metric is flawed. Arun Sanyal, M.D., observed that there must be a mechanism to bring new people into the leadership without cutting the head off the successful investigator. Dr. Tabak agreed, but asked how many multi-center clinical trials can one person do, plus other studies? Clinical trials may require more bandwidth than an R01, but those are issues that NIH needs to parse through via feedback from the research community and internal conversations. He acknowledged that leadership of a major center requires particular skills and asked how NIH could incentivize senior investigators to bring along the next generation of research leaders. James Eberwine, Ph.D., stated that the proposed policy represents a fundamental change in the way science is conducted in the United States and around the world; he expressed concern that it would limit the creativity of those who may be poised to make major contributions in science, noting that many studies have established that biologists are most productive in their 40s and 50s. He also asked two questions. The first addressed the role of the scientific review process, while the second concerned how bandwidth would be calculated for those with outside funding, in addition to NIH funding. Dr. Tabak responded that young investigators make up six percent of all investigators; NIH believes that over time, it can free up enough funds to support about 1600 new awards that will go to people under 45 and at the peak of their creativity. Dr. Eberwine countered that

he believes those who have received six grants can still be creative because each application represents a new idea. Dr. Tabak argued that the data say otherwise. Dr. Eberwine asked if the data show that the redistribution of 1600 grants will result in more creativity. Dr. Tabak responded that NIH doesn't know, but needs to do the experiment to find out. Concerning Dr. Eberwine's other questions, the proposed plan doesn't involve study sections because the decisions will be made by staff, not by study sections. The calculation of bandwidth will take into account only NIH funds; there is a question if NIH can legally consider other funding sources. Dr. Weisner observed that there will be a need to educate study sections. Dr. Sinha noted that the proposed plan represents a major shift in NIH policy. She stated that all senior investigators are trying to develop younger investigators by attaching them to big center laboratories and providing support. She shared two concerns: 1) team science will be issue to wrestle with; and 2) what downstream effects will this policy have on the very group that is trying to support young investigators? Dr. Tabak responded that NIH appreciates the need for young people to get early training under a senior research mentor. However, current efforts are not working, since those 45 and younger are failing at obtaining their first independent funding, and it's not because their applications are inferior. Mid-career investigators are also challenged because most funding is going to the most senior investigators. New approaches are needed.

Edward Nunes, M.D., observed that NIH has de-emphasized the K award, which was one way to bring younger investigators along. He also noted that the PI of a T32 training program can't draw any salary from the T32. He encouraged NIH to look at incentives for senior investigators to support younger investigators. Dr. Tabak reported that NIH has had discussions about how many points a T32 PI should get. He said that K awards are very valuable, but sometimes they're just holding patterns; the current system is not letting people become independent investigators. Dr. Nunes suggested that if senior researchers could get their salaries paid (e.g., bring back the K05), they would have less pressure to get their own R01s. Dr. Tabak asked if the group thought that senior individuals at their home institutions would begin to pivot to more mentorship roles if appropriate support were given to free up resources to support that role. The consensus was that some institutions would, some would not. Electra Paskett, Ph.D., observed that the major problem is that funding levels are falling and universities are squeezing their faculty members, who may lack tenure and must provide full funding to cover their salaries, in addition to mentoring younger investigators. She predicted many senior investigators will retire in response to these pressures, and no one will be available to mentor younger scientists. Dr. Tabak argued that the issue is not funding; NIH pumped $10 million in additional research funding into the system from the American Recovery and Reinvestment Act of 2009 (ARRA). It all went to the senior people. Awards remain flat, but NIH has more and more applicants because the ecosystem demands there be more trainees. There needs to be a meeting of the minds between the research institutions and NIH, and faculty are caught in the middle.

Louis Baxter, M.D., noted that most of the analysis and recommendations have centered on R01s. He asked how NIH would handle other funding mechanisms, such as P01 awards. Dr. Tabak responded that they may count for more points than an R01, but NIH needs to consider this further. For example, should the top leader be scored a 10-12 or should she or he be assigned an 8 because of being in a leadership role and each sub-project leader be assigned a 6? Dr. Baxter recommended that NIH bring back the R29 mechanism for younger investigators. With respect to senior investigators, he observed that they play a critical role that younger people can't. Therefore, it's important to incentivize senior researchers, i.e., if a young investigator wins a grant, his or her mentor receives some salary support. Dr. Tabak said NIH did away with the R29 and its predecessor, the R23, because it determined that people were receiving just enough money to fail. Susan Smith, Ph.D., reported on another finding from the University of Wisconsin-Madison workshop based on her experience in that group: The emphasis on

training people to become PIs. She suggested there needs to be more emphasis on supporting technicians and scientists in the labs. This means thinking about the funding models differently. Dr. Tabak stated that universities sometimes have a problem with what NIH calls staff scientists and universities call research associates because they don't want to view them as permanent employees. Judith Auerbach, Ph.D., asked if NIH also looked at how mentees are getting credit on the authorship of papers as one measure of mentorship. Dr. Tabak replied that NIH could examine that question. But, he argued, the most important metric is getting grant support.

Dr. Volkow thanked Dr. Tabak for his presentation and candid discussion. Dr. Tabak thanked the Council members for their feedback, which NIH will synthesize and take into account as the new funding plan moves forward.

NIDA Director's Report

Nora Volkow, M.D. focused her presentation on the challenges facing NIDA. Two issues are currently very relevant: marijuana use and the opioid crisis.

NIDA Leadership Changes: Rita Valentino, Ph.D., is now the Director of the Division of Neuroscience and Behavior. Phil Skolnick, Ph.D., formerly Director of the Division of Therapeutics and Medical Consequences, is now working in the pharmaceutical industry; Ivan Montoya, M.D., is currently the Acting Director. A search for a new director will be undertaken when the federal hiring freeze is lifted.

2016 Monitoring the Future Study: The key findings are that tobacco, alcohol, and other drug use among teens continued to decline between 2015 and 2016. This was true for all substances and for all grades, with the exception of marijuana in 12th graders, which remained stable. This decline continues a trend reported over the past five years. In contrast, among 18-25 year olds marijuana use is increasing as is binge drinking, which may mean that young adults are consuming more alcohol than in previous years. The reasons for the declines in drug use by secondary school students are unclear. However, the use of technology and social media may be factors. Interactions via social media rather than face-to-face may be protective, since drug use is likely to be a group activity in which peer pressure plays a role. However, the use of videogames may also be a concern--these are much more powerful than those available 25 years ago, and may even be addictive. Some teens may play them compulsively to the extent that they don't sleep. In the fall of 2017, NIDA will convene a small group of innovative thinkers from academia and industry at a workshop on Social Media, Mobile Technology, and Youth Risk Behaviors to discuss opportunities and methodological challenges in studying how youth behavior is affected by social media engagement.

ABCD Update: The ABCD Study will have its inaugural raw data release (https://data-archive.nimh.nih.gov/abcd) shortly. The release contains unprocessed neuroimaging data from 2000 participants, aged 9-10 years old, as well as basic participant demographics (age, sex), including: High-resolution structural data (3D T1 - and T2-weighted scans); Advanced diffusion MRI (multiple b-values and directions); Resting State fMRI; and Task fMRI (Monetary Incentive Delay, Stop-Signal, and Emotional N-Back), along with raw E-Prime task files.

Opioid Crisis: Opioid prescriptions fell by over 15 percent from 2010-2015 after an aggressive campaign, but opioid fatalities are still increasing. Last year, the Centers for Disease Control and Prevention (CDC) reported more than 33,000 deaths from opioids. As prescription opioids have become more restricted, their cost on the black market is going up. Heroin from Mexico is taking up the slack. Over three-

quarters (75-80 percent) of new heroin users are transitioning from prescription opioids (however, only 4-6% of prescription opioid user transition to heroin), and there is now a steep increase in heroin-related deaths. Illicit synthetic opioids also pose an emerging threat. These include fentanyl-laced heroin and prescription drugs, as well as other synthetic opioids, such as carfentanil. Fentanyl is 100 times more potent than morphine. Carfentanil is ~10,000 times more potent than morphine. These drugs have raised major challenges for first responders because 1) they can breathe it in themselves; and 2) a user's overdose is difficult to reverse because the drug stiffens the lungs quickly. NIH can help address these challenges by conducting more implementation research, preferably in partnership with the Substance Abuse and Mental Health Services Administration (SAMHSA); and working to improve treatments and practice, including physician training about chronic pain management. Also needed is the pharmaceutical companies' interest in developing effective medications for substance use disorders and pain. Currently, there are three medications for opioid use disorder: Methadone, buprenorphine, and Vivitrol. No medications exist to treat cocaine or marijuana misuse, nor to reverse fentanyl overdoses.

The Case for a Public-Private Partnership to End the Opioid Crisis: NIH Director Francis Collins, M.D., Ph.D. sought to accelerate the development of medications to treat opioids by presenting the idea of a public-private partnership at a meeting with 20 pharmaceutical companies. He received a positive response, and therefore three Cutting Edge Science meetings are planned to address the Opioid Crisis. The first, on June 5, 2017, will seek to stimulate innovative directions in preventing and treating opioid use disorders and overdoses. The second, on June 16, 2017, has as its goal to expedite development of medications to treat chronic pain with little or no potential for misuse or addiction. The third, on July 7, 2017, will address the neurobiological mechanisms of pain to accelerate the development of novel pain treatments.

Collaborative Research on Addiction at NIH (CRAN): RFA-CA-008/009: Using Social Media to Understand and Address Substance Abuse and Addiction is a CRAN initiative that began in June 2015 with a grantee introduction webinar, followed a year later by a grantee meeting. Findings were presented at a 2016 Society for Prevention Research panel. To date, there have three R21 awards completed in 2016, and eight R01 awards in the last year, resulting in 34 papers to date.

NCI Monograph 21: The Economics of Tobacco and Tobacco Control

Michele Bloch, M.D., Ph.D., and Mark Parascandola, Ph.D., NCI, presented the key findings from a new NCI Tobacco Control Monograph, *The Economics of Tobacco and Tobacco Control* (https://cancercontrol.cancer.gov/brp/tcrb/monographs/21/) Dr. Bloch explained there are three key reasons to study the economics of tobacco: 1) Economic issues are a key influence on tobacco use behaviors; 2) Decision makers want information on the cost of tobacco use and cost effectiveness of tobacco control interventions; and 3) The tobacco industry often uses economic arguments that are not grounded in science to promote their products.

The monograph takes a global approach because tobacco is a key modifiable risk factor for cancer everywhere in the world. The World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) is the agency's first treaty, a little over 10 years old, and has had a dramatic impact on tobacco control. The NIH International Tobacco and Heath Research and Capacity Building Program (TOBAC), funded by the Fogarty International Center, NCI, and NIDA, is working in multiple countries around the world.

The NCI Tobacco Control Monograph Series consists of 21 volumes to date on a tremendous diversity of topics. Monograph 21 was developed by NCI in collaboration with WHO, and includes contributions from more than 60 leaders in the field; it was peer-reviewed by more than 70 scientific experts. It confirms that "evidence-based tobacco control interventions make sense from an economic as well as a public health standpoint."

Dr. Parascandola reviewed the nine major conclusions from the report:

1. The global health and economic burden of tobacco use is enormous and is increasingly borne by low and/or middle-income countries (LMICs).
2. Failures in the markets for tobacco products provide an economic rationale for governments to intervene in these markets.
3. Effective policy and programmatic interventions are available to reduce the demand for tobacco products and the death, disease, and economic costs that result from their use, but these interventions are underutilized.
4. Policies and programs that work to reduce the demand for tobacco products are highly cost-effective.
5. Control of illicit trade in tobacco products, now the subject of its own international treaty, is the key supply-side policy to reduce tobacco use and its health and economic consequences.
6. The market power of tobacco companies has increased in recent years, creating new challenges for tobacco control efforts.
7. Tobacco control does not harm economies.
8. Tobacco control reduces the disproportionate burden that tobacco use imposes on the poor.
9. Progress is now being made in controlling the global tobacco epidemic, but concerted efforts will be required to ensure that progress is maintained or accelerated.

While progress is being made in reducing tobacco use, in some areas progress has been limited. For example, cigarette prices have increased steadily in most high-income countries, but have not changed as much in middle and low-income countries; as a result, cigarettes have become more affordable in these nations. Additionally, for key tobacco control interventions the cost per healthy life-year gained is lower in the low-income countries compared with the higher income countries; thus, cost should not be a barrier to implementing tobacco control interventions.

One of the most effective strategies that has emerged, e.g., in Australia and the United Kingdom, is standardized cigarette packaging with graphic warning labels, standardized color schemes, and no branding beyond the name of the cigarette brand in plain text. Evidence from Australia suggests that plain packaging is contributing to an accelerating decline in tobacco use.

In conclusion, the findings reveal that the science is clear, but that tobacco control policies are under-utilized. The time for action is now. In those countries where the tobacco epidemic has yet to mature, there is a particularly unique opportunity to intervene earlier to see an earlier reduction in tobacco use and tobacco-related disease. NIH research has contributed to the field, and there is an ongoing need for continued research. The monograph includes several research recommendations and NCI looks forward to working with the research community on tobacco control issues.

Meyerhoff Scholar Program at UMBC

Dr. Koob invited Michael Summers, Ph.D., to provide an overview of the University of Maryland, Baltimore County (UMBC)'s Meyerhoff Scholar Program (MSP), an undergraduate initiative that seeks to increase diversity among future leaders in science, engineering, and related fields. Dr. Summers began his presentation by reviewing African American Education in the U.S.: African Americans represent 12 percent of enrolled college students; 8.7 percent of bachelor degrees; and 2.6 percent of science and

engineering Ph.D. degrees. He noted that the United States is moving toward becoming a minority majority population by 2050, with Hispanic and African Americans comprising the largest minority groups within the country.

The goal of the MSP is to encourage students to stay in science. The College Board reports that equal numbers of minority and Caucasian freshmen aspire to science, technology, engineering, or math (STEM) degrees. Yet few are retained through the Ph.D. level. Low expectations, exacerbated by recent negative news about biomedical research career trajectories, discourage many.
UMBC itself has undergone a radical climate change since 1987, when African American students protested the racist attitudes of the STEM faculty. By 2012, under the leadership of President Freeman Hrabowski III, Ph.D., it had become the top origin school of black M.D.-Ph.D.s and the top white school origin of black Ph.D.s.

The MSP opened with 19 African American males in 1989. A year later, the program opened to African American female students. In 1996, it was opened to all students. Currently, there are 271 funded students out of 300 total; two-thirds (67 percent) are URMs. Just over one-half (54 percent) are male. The Program has produced impressive results. One hundred and ninety-four graduates have earned Ph.D. awards from institutions such as Harvard, Stanford, and Duke. Of these, 77 percent were URM students. Forty-one have earned M.D.-Ph.D. awards; of these, 85 percent were earned by URMs. Currently, another 164 Meyerhoff alumni are enrolled in Ph.D. programs and 39 in M.D.-Ph.D. programs across the country.

The key elements of the program contributing to its success are attracting well prepared, high achievers; providing early intrusive support, with high expectations; emphasizing group approaches to learning; providing early immersion in research; and conducting regular evaluations. The outcome metrics used in the Program's evaluation include retention; academic performance; institutional impact; graduate placement; and graduate program completion. The results to date include 900 graduates out of 1300 participants since 1989; 92 percent of the graduates received STEM degrees and 65 percent matriculated to graduate school. Since 1996, Meyerhoff alumni include 136 African American Ph.Ds., 35 African American M.D.-Ph.D.s; 186 African American STEM Master's; and 162 African American students enrolled in graduate school. On average, the Program has produced about 15 African American Ph.D.s per year.

In 2012, the MSP received 2100 nominations and 500 applications, of whom 80 percent are in-state, 50 percent are male, and 57 percent are URMs. The Program has had a broad effect at UMBC:
African American science and engineering grade point averages (GPAs) at graduation match those of Caucasians; 450 African American science & engineering majors enrolled at the university in 2005 (only 140 are Meyerhoffs); and there were 75 African American science and engineering graduates in 2005 (including 35 Meyerhoffs). Those who declined the program graduated with similar GPAs, but were half as likely to graduate with STEM degrees and six times less likely to pursue STEM graduate degrees.
Funded by an NIH-Minority Biomedical Research Support (MBRS) Initiative to Maximize Student Development (IMSD) grant, the Meyerhoff Fellows Program focuses on promoting cultural diversity in the biomedical sciences at the graduate level. It includes the following components: Outreach via a Summer Research Program for Undergraduates (non-UMBC); a 10-week Summer Bridge program for first-year students including a research rotation, a technical writing or problem solving course, and social activities; monthly meetings; seminars by mentors and guest speakers, especially by established underrepresented scientists; an annual weekend retreat; student travel to scientific meetings to present thesis research results; and counselors to provide consultation, assistance, and support. The IMSD

initiative produced 68 Ph.D.s from 2005-2015 (with 28 advancing to candidacy); there were six URM Ph.D.s between 1987-1997. There are 102 URMs currently enrolled. The program has achieved an 84 percent retention rate since its inception. The long-term impact of UMBC's efforts includes 49 URM STEM faculty members, including 20 in tenure track positions and 29 adjunct appointments.

To determine if the Meyerhoff Scholar Program could be replicated in larger institutions with different histories but like-minded leadership, an initiative funded by the Howard Hughes Medical Institute was launched to establish similar programs at the University of North Carolina-Chapel Hill and Penn State University. Results indicate that both campuses are exceeding early UMBC MSP outcomes and achieving present-day MSP outcomes. Further, clear, palpable change has occurred on both campuses. Major long-term financial commitments, program expansion, new hires, and institutionalization of the programs are all positive signs of significant climate change.

In conclusion, Dr. Summers reiterated the following key points. For undergraduate training, there are large numbers of URMs interested in STEM, but few are retained. MSP may be considered "cherry picking" the best and brightest, but too many cherries go unpicked. High achievers will succeed without support, but they are less likely to pursue STEM Ph.D.s. For graduate training, URM Ph.D. applicants are growing steadily, but continued outreach is critical. Key decisions (e.g., recruitment, guidance, candidacy, etc.) are made by the faculty. Therefore, faculty (not administrators) can lead the development of Ph.D. inclusion efforts. Finally, Meyerhoff-like outcomes can immediately be achieved at large, predominantly majority research universities with like-minded administrative and faculty leadership if facilitated by inter-institutional partnerships.

Discussion: Dr. Sinha inquired about the size of the initial investment in MSP. Dr. Summers explained that Bob and Jane Meyerhoff donated $500,000, which covered tuition, housing, and other costs for the first cohort of students. All other administrative and programmatic activities were initially covered by UMBC staff and faculty with other responsibilities. Eventually, resources were identified to hire dedicated staff to work full-time with the students (currently about 330 enrolled Meyerhoff Scholars). Dr. Sinha asked how UMBC recruited UNC and Penn State. Dr. Summers responded that they both approached UMBC, which approached Hughes. Hughes said they could afford to support only one of the universities. Penn State agreed to implement the program on its own. Hughes then decided it wanted to be involved with both institutions, and invested about $300,000 in each. Penn State has committed more than $2M annually, a number that is growing, and they pay all student costs (similar to UMBC in the early years). Penn State has made their program a key element in their Capital Campaign. UNC has also made major long-term institutional commitments, but does not provide full support. UMBC also no longer covers all student costs, and parents are willing to pay because of the value of the program.

Adolescent Brain and Cognitive Development (ABCD)

Dr. Volkow introduced Dr. Gaya Dowling, Director of the Adolescent Brain and Cognitive Development (ABCD) study, to provide an update on the initiative. Dr. Dowling reported that collaboration has grown over the past year from eight ICs to now include the NIH Office on Women's Health; the National Institute of Justice, which is interested in delinquency and victimization; and CDC's Division of Adolescent and School Health, which helped provide entrée to schools and has a particular interest in sexual and gender minority health.

A year ago, the study was preparing to launch a pilot study of the baseline protocol, which addressed physical health, brain imaging, biospecimens, mental health, neurocognition, culture and environment,

and substance use. At nine hours, the length of the protocol turned out to be even longer than expected. Therefore, significant work occurred after the pilot to reduce the time commitment. Some items were dropped until the one-year follow-up. The baseline protocol for the youth is now 6-7 hours.

Enrollment began in September 2016 at 21 sites across the country. There were some changes to the number and location of sites, e.g., the University of Hawaii site moved to University of Maryland, Baltimore. The University of Wisconsin-Milwaukee and the Medical College of South Carolina were also added. Sites did not all start study activities at the same time, and there is currently a need to ramp up recruitment to meet the study's goals. The Data Analysis and Informatics Center has developed a program to monitor performance at all sites in real time. The study is not at target yet. Some sites are exceeding their enrollment targets; some of the newer sites have very steep slopes. The monitoring program allows administrators to identify who is having recruitment challenges, e.g., the compensation some sites were offering was lower than other sites, and implement solutions.

As of April 30, 2017, ABCD sites have recruited 2302 participants. The sites are currently taking all those willing to participate; they are not yet trying to balance enrollments for desired targets. For example, the target for African American participants is 13 percent; African American enrollment is currently at 7 percent. The 24 percent target for Hispanics has been met. The goal is to have half the participants at high risk of substance use; a screener has been developed for this purpose. Screening suggests that 43 percent of participants are at high risk. However, study researchers are not yet sure how accurate the screener is. Examining the socio-economic status of enrollees to date, they are relatively well off in terms of income and education. Study administrators are analyzing enrollment demographics with researchers at the University of Michigan and comparing it with the demographics of the local catchment areas and participating schools.

In addition to monitoring enrollment, they are also monitoring data quality such as completeness of non-imaging and imaging data and number of minutes of motion-free resting state imaging data. The imaging protocol takes over 90 minutes to complete four scans; there is some drop-off in the completeness as participants move through the imaging protocol. Motion can be a big issue during the scanning for children. The protocol calls for four 5-minute resting blocks, which is difficult for 9- and 10-year-olds. To date, about three-quarters (76 percent) could meet the desired 11.5-12 minutes of motion-free resting state data.

The first release of data will consist of raw imaging data with minimal demographic information. It will be available in the NIMH Data Archive at https://data-archive.nimh.nih.gov/#abcd-anchor.
ABCD is planning research symposia at upcoming meetings to disseminate information about the study. These include the May 2017 meeting of the American Psychiatric Association; the August 2017 meeting of the American Psychological Association, and the December 2017 meeting of the American College of Neuropsychopharmacology (submitted). The consortium is also working toward developing a special issue of *Developmental Cognitive Neuroscience* that will outline all aspects of the protocol. The goal is to have that issue come out in conjunction with the first annual curated data release in December that will include all of the imaging data, all of the questionnaires, and all of the neurocognitive data.

Discussion: Dr. Volkow praised the project for its speed of implementation. Marie Gallo Dyak asked if the screener used the Adverse Childhood Experiences instrument and if the study plans to track people's movement from place to place, which may be an adverse event in their lives. Dr. Dowling responded that this instrument is not included in the screener although stressful life events are being measured. She asked a NIDA colleague, Kevin P. Conway, Ph.D., to describe how the high risk screener was

developed. He explained that the researchers analyzed a series of longitudinal epidemiological studies that examine the predictive relationship between a host of potential risk factors and the outcomes of interest, which is early substance use as well as substance use problems. They then reduced the research to the set of variables that most predicted the outcomes. The resulting best fit was essentially parental smoking, or family smoking, as well as a few externalizing symptoms. The addition of other variables did not markedly change the predictive ability of the risk factors. Dr. Dowling interjected that the researchers are looking at other issues in the baseline assessment to see if they should be included. She also said the study can track children if they move within a site's catchment area or from the area of one site to another, but do not yet have an established protocol for following study participants who move outside the area of any ABCD site.

Presentation of the 2017 NIAAA/NIDA Lifetime Science Award

Dr. Volkow announced the recipient of the first-ever NIAAA/NIDA Lifetime Science Award was A. Thomas McLellan, Ph.D. The award is a symbol of the ongoing partnership between NIAAA and NIDA. Dr. Volkow said that what Dr. McLellan has done for the substance abuse field has been transformative, citing three broad contributions: 1) his capacity to look at a complex problem, identify the main structure in a simple way, and then convey it in such a manner that it can change clinical practice; 2) his creation of a roadmap to clarify the different stages of substance use disorders (SUD) and where to put resources; and 3) his recognition that the field needs a "consumer report" to identify evidence-based treatment, and the program he launched to achieve that. Dr. Koob identified some highlights of Dr. McLellan's career, including development of the Addiction Severity Index, establishment of the Treatment Research Institute in Philadelphia, and his tenure as the deputy "drug czar" at the Office of National Drug Control Policy (ONDCP). Council members gave Dr. McLellan a standing ovation as Drs. Volkow and Koob presented the award.

Dr. McLellan shared his experiences in the challenges of translating addiction research into clinical practice, using the introduction of a Screening and Brief Intervention (SBI) in a modern medical center as an example. If properly implemented, SBI could have a real impact on health care because alcohol and drug use—even at levels below "addiction"-- can lead to misdiagnoses, poor adherence to prescribed care, interference with commonly prescribed medications, greater amounts of physician time, unnecessary medical testing, poor outcomes, and increased costs, particularly in the management of chronic illness.

The chief executive office of the health care system in question wanted to implement SBI because it was required by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO). The administrator of the cancer center agreed to serve as the pilot site. At the first meeting with the cancer center staff, Dr. McLellan gave an impassioned presentation, ready to discuss procedures; the physicians in the group had no questions but later sent an email to the dean, complaining that "trolling for addicts is not part of our mission." At a second meeting with cancer center staff, Dr. McLellan came armed with research indicating that alcohol is a significant predictor of susceptibility to breast cancer; that alcohol at any dose accelerates tumor growth; and that a brief intervention reduces alcohol use among non-dependent drinkers. The physicians agreed to review the research. At the third meeting, it was clear that the staff were surprised but convinced by the research. However, they expressed new concerns about the fit and clinical value of the SBI in the work setting, raising issues about training and time, workflow, what exactly they should say and do, how patients might react, and insisting that the intervention must be part of the Electronic Health Record (EHR). Fortunately, the individual who managed the health system's EHR was a 20-year veteran of Alcoholics Anonymous (AA) and agreed to develop the

application. Early results of the pilot revealed no patient complaints, no intrusion into workflow/routine, and no alcoholism (although six percent of patients drank above the threshold). Further, the cancer center received the Continuous Quality Improvement (CQI) prize from the hospital. By the fourth meeting, the cancer center staff was on board. However, they worried about how to prepare for the five percent of patients who may need substance abuse treatment. The chair of the psychiatry department was unwilling to provide outpatient or office-based care for cancer center referrals because the only "money maker" was residential care. In the end, the solution created by Dr. McLellan was for referrals to go to a community provider affiliated with a local (competing) university medical center. More recent results indicate there are still no patient complaints, still no "alcoholism" detected, and still no outpatient care for substance abuse disorder at this medical center. In 2016, SBI was turned into a CQI standard measure for breast cancer, and SBI is part of cancer care at three regional cancer training centers.

This story illustrates how little the fine points of science matter in terms of translation to clinical practice. Instead, the "fit" of an intervention is critical, and adaptation may be necessary. To successfully translate research into practice, the translator must "speaks several languages," understanding both the research and clinical cultures that need to be addressed if research findings are to be integrated into practice. Most researchers don't do this well. There is a need for industry and business (e.g., health insurance) involvement to institutionalize the change in practice. The goal is to learn how to apply research findings to do the greatest good.

Dr. Volkow recognized Charles O'Keeffe of the Friends of NIDA who said Dr. McLellan is one of the most respected leaders in the field and thanked him for his contributions.

The meeting broke for lunch at 12:44 p.m. and resumed at 1:19 p.m.

Facing Addiction: Surgeon's General's Report on Reducing Misuse and Addiction

Dr. McLellan, Senior Scientific Editor, provided an overview of the new Surgeon General's report on Alcohol, Drugs, and Health. He began by defining terms, as they are used in the Report: Use is defined as any use of any substance, driven by market forces (cost, availability). Misuse (rather than "abuse") is use that can harm self or others, driven by consequences. Addiction is compulsive use, driven by progressive brain changes. These distinctions are important for policy makers to help them understand addiction-related issues. The majority of people in the United States use substances, not at all or infrequently. Forty-one million meet the criteria for use or misuse, while 20.8 million meet the criteria for a substance use disorder. Only 2.2 million or about 10 percent receive any type of treatment for their substance use disorder. This is the lowest level of treatment of any major disease. The annual cost of substance misuse is over $440 billion in crime, health, and lost productivity.

The major sections of the *Report* include an introduction by Dr. McLellan; neurobiology by Drs. Koob and Volkow; prevention by Dr. Catalano; treatment by Dr. Clark; Recovery by Dr. Humphreys; and health care systems by Dr. Weisner. The report concludes with a vision and recommendations.

The premise of the *Surgeon General's Report* is that society has misunderstood addiction and institutionalized inappropriate solutions. Science indicates addiction is a public health problem that can be reduced with the right tools. This has already been demonstrated successfully with tobacco control. The 1964 Surgeon General's report on smoking started the cascade of legislation and demand for

smoke-free environment that has resulted in a 64 percent reduction in tobacco use over the past fifty years.

A coordinated strategy to reduce substance misuse and substance use disorders includes prevention efforts directed at families and communities for those just starting to use. Mainstream health care, which has largely ignored substance use, can contribute by instituting screening, brief interventions, and disease management and monitoring. Specialty treatment programs, based on a continuing care model, address the needs of those who are addicted.

Prevention: To prevent substance misuse and addiction, risk factors should be reduced and protective factors enhanced through policies and programs. Adolescence is the most critical risk period. Some risk factors predict many problems (e.g., dropping out, pregnancy, etc.) and reducing the risk for any problem reduces the risks for many problems. Effective prevention policies include increasing the price of alcohol and reducing its availability. Higher prices or taxes can reduce drinking by 30 percent, as documented in 112 studies. Policies that reduce alcohol outlets have been shown to decrease drinking by 20 percent, a finding established in 21 longitudinal studies. State policies to privatize alcohol sales, however, increase the sales by 40 percent. One of the most serious consequences of alcohol misuse is death on the highways. Between 1990 and 2010, alcohol-related driving fatalities have decreased by 64 percent, as a result of state policies raising the legal drinking age to 21.

Prevention programs are most effective in community-based settings. They include coordinating continuous delivery of community prevention services and supporting each community group (e.g., parents, schools) to learn appropriate evidence-based practices. Consolidated results from community prevention studies comparing prevention to control communities found that among 12th graders, there was 31 percent less substance use in prevention communities, 39 percent less truancy, 25 percent less delinquency, and 16 percent fewer substance use-related deaths. There was also less pregnancy, school violence, and suicide.

Treatment: Treatment, targeting those in the misuse and addiction segments, is typically specialty care rather than primary care. Historically, addiction has been treated as a character disorder or equated with physical dependence; there has been a belief that only those who have suffered addiction can treat it. The new science, in contrast, focuses on diagnosis, brain imaging, and genetics. The DSM-5 criteria for substance use disorders focus on diminished self-control. Diminished self-control is caused by incremental, substance-induced change observed in gene expression; stress response systems; and brain circuits controlling motivation, inhibition, and reward sensitivity. These changes endure long after drug cessation. Technology now allows scientists to observe changes in the brain that occur during substance use and recovery. Currently, treatment options and insurance are based on an acute model of care, rather than a chronic one that takes into account the actual length of recovery in the brain. Addiction treatment goals are like those of other chronic illnesses, including reducing key symptom severity, improving general health and function, and requiring mastery of self-management skills. The treatment approach is the same, i.e., a personalized care plan.

In summary, substance misuse is a public health problem that is hurting and killing young people. Prevention policies and programs can work if they are delivered throughout the “at risk” period (ages 12 – 25). Substance misuse and disorders are prevalent but ignored in all healthcare settings. This is hurting healthcare by reducing the quality, effectiveness and safety of all healthcare delivery. SUD education must be required in medical, nursing and pharmacy schools. Addiction is an acquired brain illness. Continued misuse damages brain circuits, ultimately leading to diminished control. Those with family

histories of SUD or mental illnesses are most vulnerable. Addiction can be effectively treated with continuing care and monitoring. Everyone, including specialty health care and the insurance industry, have to "get in the game" to successfully address this public health issue.

Adjournment

The meeting adjourned at 2:02 p.m.

CERTIFICATION

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

For NIAAA:

/s/
George F. 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/
Francis Ali-Osman, D.Sc.
Acting Chair
National Cancer Advisory Board
National Cancer Institute

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