

2019 NIH Institute Director's Session

December 8, 2019

Orlando, Florida

National Institute on Alcohol Abuse and Alcoholism (NIAAA):

1. What is the one thing you would like for people to know about alcohol?

The effects of alcohol are far more pervasive than people realize. Alcohol is associated with over 200 diseases and injury-related health conditions, including alcohol use disorder (AUD) and other mental health disorders. While any amount of alcohol can increase the risk for injuries and certain conditions, it is important for people of legal drinking age who do choose to drink to stay within the [U.S. Dietary Guidelines for alcohol consumption](#). Some individuals such as those under the age of 21 and pregnant women should avoid alcohol completely. It is important for the general public to be aware of these risks.

2. What areas of alcohol research are ripe for expansion if funding wasn't a limitation?

There are many areas and some that come to mind are:

- Medications development for AUD – Currently, only 3 FDA-approved medications are available for AUD. The heterogeneous nature of AUD drives the need for a broader range of pharmacotherapy options.
- Medications development for alcohol-associated liver disease (ALD) - Nearly half of U.S. liver disease deaths are attributable to alcohol misuse, and ALD is the most common alcohol-related cause of death as well as the leading cause of liver transplantation due to chronic liver disease. There are no FDA-approved treatments for ALD and current treatments often have limited efficacy and numerous side effects.
- Integrated treatment for AUD and ALD co-morbidity – Research suggests that an integrated treatment approach can result in improved health outcomes, including reduced relapse and mortality.
- Treatment for AUD and other co-morbidities - AUD frequently co-occurs with other chronic health conditions such as PTSD and HIV. Both AUD and PTSD are linked to dysregulation of the brain's stress systems and understanding the neurobiological mechanisms that underlie resilience or vulnerability to stress has the potential to inform new treatment approaches AUD-PTSD co-morbidity. Regarding HIV, recent research shows that integrating AUD treatment in the context of HIV care can improve measures of HIV-related disease.

- The relationship between alcohol misuse and aging – Older adults tend to be more sensitive to alcohol’s effects, and are more likely to experience health conditions exacerbated by alcohol misuse as well as alcohol-medication interactions. Recent evidence also indicates that alcohol misuse among older adults is increasing.
- The relationship between alcohol misuse and women’s health – Studies show that women start to have alcohol-related problems such as blackouts, liver inflammation and certain cancers more quickly and at lower drinking levels than men. Also, a growing body of evidence indicates that drinking, binge drinking, and AUD among women are increasing.
- The relationship between alcohol misuse and pain – A significant number of people in chronic pain report using alcohol to relieve their pain, and many people with AUD report experiencing chronic pain. Understanding the effects of alcohol on pain, and vice versa, could improve treatment outcomes for both conditions.
- The relationship between alcohol misuse and sleep dysregulation - A major impediment in the recovery from AUD is persistent sleep problems during abstinence. Understanding the mechanisms that underlie the relationship between alcohol and sleep could reveal novel targets to prevent relapse and sustain recovery.
- Mechanisms that contribute to individual differences in sensitivity to alcohol, the development of tolerance, and progression to AUD – Excessive alcohol use increases vulnerability to AUD and is linked to alcohol tolerance and social/cultural factors. Understanding the mechanisms that underlie alcohol sensitivity and tolerance could reveal new prevention and treatment targets.
- Development of miniaturized technologies for accurate, real-time monitoring of blood alcohol levels - A discreet, wearable alcohol biosensor device could aid researchers, clinicians, and therapists by providing more accurate data about a person’s alcohol consumption as well as assist members of the public who are concerned with their personal drinking or who are in treatment for alcohol use disorder, enabling them to use a discreet device without stigma.

3. What research training opportunities are available for scientists from underrepresented groups?

The cultivation of a diverse and trained biomedical workforce is instrumental for continued advancement in the field of alcohol research. Below are training opportunities and training support programs for scientists from underrepresented groups:

[Research Supplements to Promote Diversity in Health-Related Research](#) (Diversity Supplements). Administrative supplement awarded to an existing parent grant. Funding is provided for salary support, research supplies, and travel. The program supports individuals at the high school, undergraduate, predoctoral (graduate), postdoctoral, and investigator levels. *NIAAA Staff Contact: Jenica Patterson, Ph.D., Jenica.Patterson@nih.gov*

Ruth L. Kirschstein Predoctoral Individual National Research Service Award (NRSA) Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research (F31). Mentored research training opportunity for up to 5 years of support toward a research doctoral degree (Ph.D., D.Sc.). Provides annual stipend, funds for tuition/fees, research supplies, equipment, travel and other related research items. *NIAAA Staff Contact:* Judith Arroyo, PhD, jarroyo@mail.nih.gov

NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00). This program aims to encourage and retain outstanding graduate students who are from diverse backgrounds underrepresented in neuroscience research. This two-phase award will facilitate completion of the doctoral dissertation and transition students to strong neuroscience positions. *NIAAA Staff Contact:* Ivana Grakalic, Ph.D., igrakalic@mail.nih.gov

Ruth L. Kirschstein Undergraduate NRSA Institutional Research Training Grants (T34). Currently the National Institute of General Medical Sciences (NIGMS) is the only NIH Institute that supports the T32 mechanism. This program aims to prepare high-achieving, underrepresented students for doctoral programs in biomedical research fields.

BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity (K99/R00) - The BRAIN Initiative K99/R00 award is intended for individuals from diverse backgrounds (including nationally underrepresented groups) who are working in research areas supported by the BRAIN Initiative, who have no more than five years of postdoctoral research experience, and who require at least 12 months of mentored research training and career development (K99 phase) before transitioning to the independent research (R00) phase of the program. *NIAAA Staff Contacts:* Changhai Cui, Ph.D. Changhai.Cui@nih.gov and Ivana Grakalic, Ph.D. igrakalic@mail.nih.gov

Providing Research Education Experiences to Enhance Diversity in the Next Generation of Substance Abuse and Addiction Scientists (R25) - The overarching goals of the NIH R25 program are to: (1) complement and/or enhance the training of a workforce to meet the nation's biomedical, behavioral and clinical research needs; (2) encourage individuals from diverse backgrounds, including those from groups underrepresented in the biomedical and behavioral sciences, to pursue further studies or careers in research; (3) help recruit individuals with specific specialty or disciplinary backgrounds to research careers in biomedical, behavioral and clinical sciences; and (4) foster a better understanding of biomedical, behavioral and clinical research and its implications. *NIAAA Staff Contact:* Laura Kwako laura.kwako@nih.gov

[NIH Blueprint Program for Enhancing Neuroscience Diversity through Undergraduate Research Education Experiences \(BP-ENDURE\)](#) (R25)– The over-arching goal of this R25 program is to support educational activities that encourage individuals from diverse backgrounds, including those from groups underrepresented in the biomedical and behavioral sciences, to pursue further studies or careers in research. *NIAAA Staff Contact: NIAAA Staff Contact: Laura Kwako* laura.kwako@nih.gov

- 4. There is a disturbing trend in scientific and lay publications to refer to suicide, opioid and alcohol use related deaths as “deaths of despair”, eroding the understanding that they are due to brain disorders and moving psychiatric conditions closer to “social determinants of health” domains. Are there trends in the portfolio showing studies focused on despair in this context?**

In 2015, economists Case and Deaton reported that mortality in mid-life was increasing for some groups as a result of drug overdoses, alcohol-associated liver disease, and suicides. They referred to these deaths as “deaths of despair”. Alcohol plays prominent roles in deaths of despair, contributing to at least 15% of drug overdoses, 26% of suicides and 50% of liver disease deaths. While such deaths are particularly prominent among non-Hispanic whites aged 45-54 with less than a high school education who live in geographic areas hit by economic decline, recent reports suggest that measures of despair (e.g., depressive symptoms and suicidal ideation) and deaths due to a wide variety of causes, including alcohol misuse, are increasing among people in mid-life across racial and ethnic groups.

AUD emerges from alterations in brain circuitry and manifests in a cycle of bingeing to intoxication, experiencing withdrawal and negative affect, and being preoccupied with drinking again. Understanding the environmental contingencies that influence whether someone develops AUD does not change the underlying biological basis of the disease. Instead, such research is vital for informing the development of effective prevention and treatment strategies.

National Institute on Drug Abuse (NIDA):

Topic: Drug use increase in US?

Q: What is the role of social media in drug usage increase?

A: The relationship between social media use and changes in drug use is an active area of study. In adolescents, who use social media heavily, most forms of drug use have declined in recent years, or else held steady (e.g., marijuana); any causal relationships between drug use patterns and social media use, if there are any, remain unclear. Future research, including the ABCD study, will help answer such questions.

- Advertising and social media focused on e-cigs can influence youth use and provide unique exposure to tobacco advertising ([Pierce, 2018](#) and [Camenga, 2018](#)).

- As youth vaping increased, so too did JUUL sales, leading to a 40% share of the e-cigarette market. This was accompanied by a variety of innovative, engaging and wide-reaching campaigns on social media conducted by JUUL and its affiliated marketers ([Huang, 2018](#)).
- NIDA is funding research aimed at understanding the impact of e-cigarette/vaping advertising and other policies on patterns of ENDS and tobacco use ([5R01DA039968-04](#)).

Topic: Societal effect of increased cannabis use.

Q: Regular cannabis use has an impact on volition and productivity, reduced motivation in young adults that may interfere with long-term planning. Are long-term consequences well-understood? Will there be a warning (similar to tobacco products) to warn about the risks of cannabis use (including increased risk of psychosis) on the legally sold cannabis products?

A: The long-term consequences of cannabis use are still not well-understood; longitudinal studies, for instance on the relationship between cannabis use and IQ, show conflicting results, and have been based on use patterns and dosages that are different from what exists currently. The hope is that studies like ABCD will shed needed light on this question in the future.

Topic: Child/adolescent models in preclinical research.

Q: Much of the illnesses we study (addiction and mental health, so NIAAA, NIDA, NIMH funded studies) originate in children and adolescents. ABCD and HBCD studies are starting to add to the wealth of human data on the topic. But the majority of the basic science work funded by the agencies focus on using adult models. Are there any plans to change the emphasis on animal/preclinical research to focus on younger subjects?

A: Adolescent animal models have been used in NIH-funded addiction research for decades, especially in research on the developmental impacts of alcohol (e.g., binge drinking) and nicotine, but also other drugs. Preclinical animal research related to developmental impacts of substances will ordinarily use age-appropriate animal models.

Topic: Vaping mortality.

Q: In the media, vaping mortality has been attributed to using THC oils in devices. Is use of oil the cause of fatal lung injury or are there other factors?

A: The CDC continues to study the illnesses and deaths attributed to vaping of (mostly) THC products. At present (1/29/20), vitamin E acetate in a few THC vape products has been found to be closely associated with the illnesses, but other ingredients in vape oils are still being investigated.

Topic: CBD (Cannabidiol).

Q: Role of CBD in opioid and marijuana treatment (prospects)

A: NIH supported \$19 million on CBD research in FY 2018, including research on therapeutic potential of CBD for pain, inflammation, digestive disorders, HIV, SUD, and PTSD. Each NIH institute studies CBD as a therapy as relevant to their individual missions—for NIDA, this means

CBD as a potential treatment for substance use disorders. While there are preliminary results that warrant further investigation into CBD as a therapeutic for SUDs, there is not currently enough evidence to know whether it is effective.

Topic: CBD & Research.

Q: Are there plans for NIDA’s Drug Supply Program to provide CBD to researchers?

A: NIDA’s Drug Supply Program currently does include CBD in its catalogue of drugs available to researchers.

Topic: Addiction in the US.

Q: What can we do as scientists to get more involved in policy making during this opioid crisis?

A: Scientific societies have offices devoted to influencing policy on behalf of their members, so working through the professional societies you belong to is one effective way to have an impact on policy. Conducting and publishing high-quality scientific studies that can inform policy is the most critical role that scientists play.

Topic: Rehabs?

Q: How can we develop evidence-based criteria for drug and alcohol REHAB programs?

A: NIDA is funding research to develop and rigorously test the effects of strategies to improve opioid treatment quality measures, both on changes in the measures themselves and on patient outcomes. NIDA is also working with the Centers for Medicare and Medicaid Services (CMS) to fund research relevant to the development of quality metrics.

Topic: Comorbidity research

Q: The divide between mental and substance (and alcohol use) disorders has a long history, but epidemiological data clearly shows they are most often comorbid (e.g. nearly 60% of patients with lifetime MDD have a substance use disorder). How might research to study “dually diagnosed” patients be fostered.

A: NIDA supports a portfolio of research studying comorbidities between SUD and other mental illness and collaborates with the National Institute of Mental Health on such issues. NIDA studies how SUD and other mental illnesses can be risk factors for one another, and how they influence the progression and presentation of one another, as well as strategies for treatment. One barrier that often hinders both effective treatment and rigorous research on such individuals is that SUD treatment is isolated from other parts of the health care system. Such individuals may end up in care for severe mental illness or in the criminal justice system, where SUD may go undetected and untreated, may be given lower priority, or may simply require expertise and personnel that a program does not have. The more we can make strategic alliances for research across these boundaries, the better—several flagship projects within the HEAL initiative, such as the Justice Communities Opioid Innovation Network and the HEALing Communities Study are designed to make precisely such alliances.

Topic: Funding.

Q: What's the current pay line @ NIDA? Trends?

A: Success rates are a better indicator than paylines of the percentage of applications we are funding for each activity code. A success rate is roughly the number of applications funded by an institute divided by the number of peer reviewed applications referred to it (excluding resubmissions that occur in the same fiscal year—each application is counted only once). To find success rate data, go to: https://report.nih.gov/success_rates/Success_ByIC.cfm

Topic: HEAL.

Q: How many awards do you anticipate making for the HBCD development initiative in Phase II?

A: There are currently 29 HBCD grants funded in Phase I. During Phase II, the NIH anticipates making awards for a Coordinating Center, a Data & Informatics Center as well as several research sites that depend on the level of available funding and information we will learn from the ongoing planning phase.

Topic: HEAL.

Q: Is another congressional distribution expected (in addition to the original d/B)?

A: It is Congress' prerogative to decide how much money to appropriate to this issue. So far, Congress has provided similar amounts of dedicated appropriations for FY18, FY19, and FY20.

Topic: Exploratory grants for new ideas.

Q: Why is the R21 mechanism not used by all the institutes for basic pre-clinical work? (NIMH—bring back!)

A: NIDA accepts investigator-initiated exploratory/developmental projects (R21) for all program areas supported by the Institute. NIDA uses the R21 mechanism to provide support for projects in the early stages of developing or testing innovative ideas in any area relevant to the mission of the Institute. Since this mechanism is intended to enable an investigator to receive support for the early and conceptual stages of an innovative research question or approach, preliminary data specific to the proposed project are not expected. Novel scientific ideas, model systems, tools, agents, targets and technologies that have the potential to advance research in substantial ways and relevant to the mission of NIDA are appropriate for this mechanism. Long-term projects or projects designed to establish knowledge in a well-established area should not use the R21 mechanism.

Topic: Minority F32 Postdoctoral Training Grant.

Q: As a female Hispanic scientist working to become an independent researcher, training in pain and addiction models, what are currently available opportunities?

A: There are several opportunities available to support your advancement to becoming an independent investigator. Opportunities can be found here: <https://researchtraining.nih.gov/>.

Veterans Affairs (VA):

1. Are investigators outside of USA eligible for these awards and grants?

VA is an intramural funding program with eligibility requirements for awardees. Key among those requirements is that the recipient of VA funding must be employed at a VA medical center, as either a clinician or a non-clinician. This means that individuals living outside the US cannot receive VA awards.

2. For University researchers for those with a university appointment how can we access funding support for VA relevant research? I have been conducting research on combat PTSD and TBI in a VA university affiliate for several years. How is it possible for researchers like me to access VA funding support (eg, Merit) to conduct VA relevant research?

You should connect with the local Va's Research & Development office at your nearest VA Medical Center. Approximately 100 VA medical centers across the country, and which are affiliated with universities, are able to support research across the country. Location/contact information is available on the medical center's website.

3. The vision and emphasis on modernizing VA research infrastructure at the leadership level sometimes does not translate to the local facilities. Are there initiatives aimed at relieving this bottleneck?

We in the office of Research & Development recently initiated "Listening Tours" to visit VAMCs and hear about local issues. We are currently preparing a report of the issues brought to our attention during recent visits to 27 programs. We are also receptive to hearing about additional concerns. These should be submitted to VHABLRD-CSR@va.gov

4. Will data from the Million Veterans be shared to the wider community?

While the program is making moves to increase access to MVP data (by increasing computational capacity and assessing the regulatory landscape), there is no *current* mechanism for new research studies to access MVP data, beyond the currently approved 30+ VA studies that already have access. MVP is working on creating a Data Commons where much of this information will be available to the research community through an approval process. Additionally, summary statistics and metadata of MVP research results will be available through the NIH's dbGaP database. We suggest everyone stay tuned while the details of future access become available.

National Institute of Mental Health (NIMH):

1. How/when will NIMH settle on specific wording to describe rodent behaviors?

While it is not in the purview of NIMH to dictate how rodent behaviors are described in the literature, we have set out specific guidelines for the use of animal neurobehavioral approaches in grant applications.¹ In general, we urge researchers to use experimental designs that define and test hypotheses, and caution against approaches that rely on validity of animal models of psychiatric disease. For more, see also my Director's Message on the topic.²

2. How representative are mouse models of psychiatric disease? Are we going too far with the mouse?

As per above, the NIMH recognizes that mouse models are not representative of the full complexity of psychiatric disease. However, there are numerous neurobiological questions that can be addressed in mouse models that have relevance for the understanding of psychiatric disease, and we continue to support this work.

3. What are the...funding initiatives to strengthen and diversify the physician-scientist workforce?

All our training programs, including those dedicated to physician-scientists such as the R25 residency research training programs, emphasize and support diversity in the workforce. For information about specific programs, visit our training webpage.³ We have also recently joined the Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program, an NIH-Wide effort to support diversity that combines K99/R00 awards for members of underrepresented groups with a UE5 cohort-based mentoring program.⁴

4. How do you evaluate/decide on the proper balance...in your portfolio? Related: Who is funding clinical research that will have an immediate impact in the clinic?

To maximize our public health impact, NIMH maintains a diverse portfolio of short-, medium-, and long-term investments. Our portfolio is informed primarily by the quality of the science in the applications we receive, and secondarily by consideration of diversity across a range of areas, including disease topic, population, investigator, and timeframe. Combined, these factors

¹ <https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-053.html>

² <https://www.nimh.nih.gov/about/director/messages/2019/a-hypothesis-based-approach-the-use-of-animals-in-mental-health-research.shtml>

³ <https://www.nimh.nih.gov/funding/training/index.shtml>

⁴ <https://www.nigms.nih.gov/training/careerdev/Pages/MOSAIC.aspx>

determine our portfolio balance. Currently, approximately 40% of our grant dollars are spent in intervention development and services research. Within this area, NIMH is funding a great deal of clinical research with immediate impact; areas of high priority include serious mental illness and suicide prevention. For additional information on portfolio balance at NIMH, see my Director's Message on the topic.⁵

5. What are the plans for adding a schizophrenia program to the Accelerating Medicines Partnership (AMP)?

AMP is an umbrella program run by the Foundation for the NIH (FNIH) that has projects in a number of areas, including Alzheimer's and Parkinson's diseases, autoimmune diseases, Diabetes, and more. FNIH is partnering with NIMH and other groups to organize a series of workshops on a potential Schizophrenia AMP.

6. When will there be funding announcements for non-human primate research in brain circuits and/or CRISPR-CAS editing?

NIMH is currently reviewing applications for an RFA in this area and will consider reissuing this RFA if necessary.⁶ We also encourage investigator-initiated grants in the area. The BRAIN Initiative also funds resource and technology development for studying circuits in non-human primates. More information on BRAIN Initiative RFAs can be found on their website.⁷

7. What content is most important in Letters of Intent, and how are LOIs used?

The content and use of LOIs differ depending on the purpose. I would urge investigators to discuss with the relevant program staff to get specific answers in advance.

⁵ <https://www.nimh.nih.gov/about/director/messages/2018/nimhs-portfolio-balance-quality-science-comes-first.shtml>

⁶ <https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-20-320.html>

⁷ <https://braininitiative.nih.gov/>