

ALCOHOL AND SUBSTANCE USE DISORDERS RESEARCH PROGRAM



Vision: Improve the clinical outcomes of alcohol, opioid, and other substance use disorders

Mission: To explore integrated approaches to address alcohol and substance use disorders, and reduce the number of opioid and other substance use-related deaths, through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols and enhanced quality of life for Service Members, Veterans, and the American public

PROGRAM HISTORY

The problem of alcohol and substance use disorders (ASUD) is a growing concern among the general public, as well as military personnel and Veterans alike, even more so if accompanied by Post-Traumatic Stress Disorder (PTSD). In 2013, the Institute of Medicine (now the National Academy of Medicine) reported in “Substance Use Disorders in the U.S. Armed Forces”¹ that the increasing medical burden imposed on the Military Health System by excessive alcohol use elicited their recommendation that the Department of Defense (DOD) assume leadership to ensure the consistency and quality of treatment services available to those with ASUD, given the burden of ASUD in the military. The peer-reviewed Alcohol and Substance Use Disorders Research Program (ASUDRP) did not receive an appropriation in fiscal year 2020 (FY20), but continued to manage open awards. In FY21, \$4 million (M) was appropriated to the ASUDRP as Congress recognized the ongoing threat posed to Warfighters and the general public by the opioid epidemic (those who may develop an opioid dependency following an injury generally struggle with addiction). Service Members who have family members that struggle with addiction often are not positioned to dedicate themselves entirely to the required military mission. The Committee encouraged the Assistant Secretary of Defense (Health Affairs) to prioritize congressionally directed medical research on substance use disorders aimed at reducing the

overall number of opioid-related overdose deaths. The ASUDRP has established a network of multidisciplinary, translational research teams with the explicit goal of accelerating the delivery of new or improved treatments for ASUD; as a result, the ASUDRP has distributed a total of \$52.1M to relevant research. The FY22 Congressional appropriation was \$4M.

PROGRAM GOAL

The program’s goal is to explore integrated approaches to address ASUD, especially comorbid ASUD with PTSD and other psychological disorders and reduce the number of opioid and other substance use-related deaths through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols and enhanced quality of life for Service Members, Veterans, and the American public.

RESEARCH STRATEGY

The overall strategy of the ASUDRP supports the following Research Aims:

- **Aim 1 – Discover:** Test new chemical entities and repurpose existing medications in preclinical and non-clinical models of ASUD with comorbid PTSD and other psychological disorders.
- **Aim 2 – Phase 1 First-in-Human Safety:** Conduct clinical trials of potential medications that include assessment of medical safety and doses for potential efficacy in subjects with ASUD and comorbid PTSD and other psychological disorders.
- **Aim 3 – Phase 2 Efficacy:** Conduct multiple-site clinical trials to test the preliminary efficacy and safety of potential medications or medication combinations in humans with ASUD and comorbid PTSD and other psychological disorders, as well as to explore precision medicine tools for matching patients to these medications.

This approach should accelerate the translation of contemporary basic science knowledge into enhanced clinical pharmacological treatment protocols for ASUD, including a regulatory strategy for Food and Drug Administration (FDA) compliance.

“I can’t believe I get to be involved in this amazing work to help develop new medications or treatments that could actually significantly improve the lives of Veterans struggling with addiction.”

SPC Robert Elder, (U.S. Army, retired), Veterans Engagement Board, FY21 Programmatic Panel Member



¹ Committee on Prevention, Diagnosis, Treatment, and Management of Substance Use Disorders in the U.S. Armed Forces; Board on the Health of Select Populations; Institute of Medicine. 2013. Substance Use Disorders in the U.S. Armed Forces: 2, Understanding Substance Use Disorders in the Military (O’Brien CP, Oster M, and Morden E, Eds.). National Academies Press, Washington, DC. <https://www.ncbi.nlm.nih.gov/books/NBK207276/>



Exploring integrated approaches to identify pharmacotherapeutics for ASUD, especially comorbid ASUD with PTSD and other psychological disorders



Scope of the Opioid Use Problem

Deaths from drug overdoses soared to **>100,000** in 2021

The death toll jumped **up 15%** from 2020, >80,000 deaths associated with opioid use¹

Veterans with PTSD appear to be susceptible to developing opioid use disorder.²

PTSD sufferers may self-medicate with opioids, which can manifest as opioid use disorder.³

¹ <https://www.washingtonpost.com/health/2022/05/11/drug-overdose-deaths-cdc-numbers/>
² Shiner B et al., 2017.
³ Bremner JD et al., 1996.

Impact of PTSD and Co-Existing Alcohol Use Disorder (AUD)

The comorbidity between PTSD and AUD are higher in Veterans than civilians.⁴

Those with PTSD and co-existing AUD exhibit greater severity of symptoms.⁵



Veterans with both PTSD and AUD exhibit more persistent, severe, and treatment-resistant symptoms and are at much higher risk for suicide than Veterans who have either disorder alone.⁶

⁴ Roberts et al., 2015.
⁵ Jacobsen et al., 2001; Norman et al, 2012.
⁶ McCarthy and Petrakis, 2010.

Areas of Emphasis

- Improved formulations to treat ASUD with comorbid substance use
- Improved formulations to treat ASUD with comorbid PTSD and other psychological disorders
- Stronger, longer-duration formulations to counteract opioid (including fentanyl analogs) overdose
- New formulations and/or combinations of existing medications to improve treatment compliance, prevent relapse, and reduce risk of misuse
- Novel medications and immunotherapies to treat substance and/or ASUD
- New medication targets for the treatment of substance and/or ASUD

Measuring Success



Conduct studies of new medications to treat ASUDs

- **32** funded institutions/46 projects
- **52** published papers
- **1** patent application
- **7** FDA-approved, currently active Investigational New Drug applications
- **35** projects focused on AUD or SUD



Special emphasis on comorbidities of TBI and PTSD in populations of Service Members and Veterans

- **2** clinical trials on active-duty populations (Fort Gordon and Point Loma)
- **15** clinical trials at VA Medical Centers



Use a translational approach to understand the complex interaction of ASUDs with the military stress comorbidities of PTSD and TBI

- **8** active pharmaceutical collaborators
- **2** compounds transitioned to the pharmaceutical industry for further development
- **1** compound being studied by both PASA* and NIAAA**
- **23** preclinical and **22** clinical projects

* Pharmacotherapies for Alcohol and Substance Use Disorder Alliance
 ** National Institute on Alcohol Abuse and Alcoholism

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