

COBRE on Opioid and Overdose: A Collaborative Research-Based Center Addressing the Crises in Rhode Island and Beyond

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ABSTRACT

Overdose deaths across the country have spiked since the onset of the COVID-19 pandemic. It is crucial now, more than ever, to address the continuing and worsening, complex and dynamic opioid and overdose epidemics. In 2018, The Center of Biomedical Research Excellence (COBRE) on Opioids and Overdose, based at Rhode Island Hospital, launched with three major goals: 1) establish a center of scientific excellence on opioids and overdose; 2) train the next generation of scientists to become independent investigators and address the opioid and overdose crises; and 3) contribute to the scientific progress and solutions to combat these epidemics. To date, we have made substantial progress. While the opioid and overdose crises continue to evolve, the COBRE on Opioid and Overdose and its team of investigators are well poised to address the daunting task of understanding and meaningfully addressing these deadly epidemics, with the ultimate goal of saving lives.

KEYWORDS: opioid, overdose, fentanyl, prison, jail

INTRODUCTION

Preliminary data from 2020 suggests that there has been a 30% increase in overdose deaths in Rhode Island. Despite a gradual decline in overdose deaths over the prior four years, 2020 marks, by far, the worst year yet.^{1,2} This alarming trend is not unique to Rhode Island. Overdose deaths across the country have spiked since the onset of the COVID-19 pandemic.³ The horror of the pandemic has diverted attention away from the worsening overdose crisis, which was the leading cause of accidental death nationally before the pandemic. It is crucial now, more than ever, to address the continuing and worsening opioid and overdose epidemics. One thing is quite clear – the opioid and overdose epidemics are very complex and dynamic and demand extensive attention to address them effectively.

A majority of the overdose deaths in the country are opioid-related.⁵ The current opioid epidemic in the United States started in the mid-1990s when pharmaceutical companies began heavily marketing their opioid medications to physicians eager for pain management solutions.⁶ The first wave of the opioid crisis in the United States was defined by

physicians over-prescribing opioids and was marked with a steady increase in overdose deaths.⁷ By 2010, the prescription opioid crisis had evolved into an illicit heroin epidemic as opioid dependence became more common, resulting in higher demand for a more consistent pill supply than was affordable or accessible.⁸ The impact of increased demand for heroin has most recently led to increased production of more powerful synthetic opioids, notably fentanyl and its related analogs. Illicit fentanyl and synthetic compounds are between 50 and 100 times more potent than heroin and have a more rapid onset of action, making them far more deadly for people without adequate tolerance or unintentionally consuming fentanyl,⁹ for example, when it contaminated cocaine. In 2018, over 70% of Rhode Island's 308 overdose deaths involved fentanyl.⁵ Further, with increases in fentanyl presence in the illicit drug supply and increases in polysubstance use in Rhode Island, there has also been a recent surge in overdoses involving stimulants (e.g., cocaine and methamphetamine) alone and together with opioids,⁵ underscoring the need for interdisciplinary research and programming to address the opioid and overdose epidemics.

THE COBRE ON OPIOIDS AND OVERDOSE

In 2018, The Center of Biomedical Research Excellence (COBRE) on Opioids and Overdose launched with three major goals: 1) establish a center of scientific excellence on opioids and overdose; 2) train the next generation of scientists to become independent investigators and address the opioid and overdose crises; and 3) contribute to the scientific progress and solutions to combat these epidemics. To date, we have made progress on all three fronts.

The COBRE on Opioids and Overdose, based at Rhode Island Hospital (RIH), is the first center of its kind to address the opioid and overdose epidemics collaboratively. The center is funded with a five-year, Phase 1 grant from the National Institute of General Medical Sciences (NIGMS) and is currently in its third year (P20GM125507). The COBRE is an innovative, multidisciplinary research center that brings together dedicated investigators and utilizes a comprehensive approach to understand and develop solutions to the opioid and overdose crises. There is a tremendous need, especially considering the COVID-19 pandemic, for a greater scientific understanding of the mechanisms underpinning opioid use disorder and overdose and developing effective interventions to address them.

Structures and Cores

The COBRE’s director Josiah Rich, MD, MPH, and deputy director Traci C. Green, PhD, MSc, are both expert advisors to the Governor’s Overdose Prevention and Intervention Task Force with over 40 years of combined research experience on people with opioid use disorder and other substance use disorders. Over the past two years, they have spearheaded the Center’s mission to bring together experts from across the state to provide mentorship to junior investigators committed to addressing the opioid epidemic that is devastating Rhode Island. The COBRE’s External Advisory Committee, NIGMS, and RIH have provided an open and encouraging environment that has allowed the Center to fund new, creative and innovative ways to address the epidemic by partnering with local organizations such as the Rhode Island Communities for Addiction Recovery Efforts (RICARES), the Rhode Island School of Design (RISD) and the Providence/Boston Center for AIDS Research (CFAR).

Within short order, the COBRE on Opioids and Overdose has proven to be extraordinarily successful. Since its inception in 2018, it has supported over 35 Investigators,

9 Pilot Projects, 4 Research Projects, and 3 Research ‘Cores’ (see **Table 1**). Additionally, 40 publications have received COBRE support, 21 of which have been published by COBRE Junior Investigators, Pilot Project Awardees, and COBRE Graduates; 22 scientific presentations have been given, and 16 applications have been submitted for funding outside the COBRE funding mechanism. Additionally, two Research Project Leaders have graduated from the COBRE and received independent funding. The COBRE on Opioids and Overdose has worked exceptionally hard to establish a presence in Rhode Island and beyond through cutting-edge research and innovative projects showcased on the COBRE website, along with a successful 2020, week-long, virtual symposium jointly hosted with the University of Nebraska’s Rural Drug Addiction Research COBRE Center and the West Virginia Clinical and Translational Science Institute with over 400 attendees. Social media posts and YouTube channel platforms are further leveraged to amplify the COBRE reach and elevate the contributions to science and community through short, engaging videos.

Table 1. COBRE on Opioids and Overdose Research Projects and Pilot Projects

Research Project	Neonatal Abstinence Syndrome (NAS): Fetus to First Years	Adam Czynski, DO	9/1/18–present
Research Project	CoMBAT Opioid Use Disorder: A Pilot RCT of a Combined Medication and Behavioral Activation Treatment for People Living with Opioid use Disorder	Jaclyn White Hughto, PhD, MPH	5/1/19–present
Research Project (proposed)	Estimating the Causal Effects of Residential Eviction on Substance Use Treatment Outcomes	William C. Goedel, PhD	3/1/21–present
Pilot Project	Unintentional Fatal Opioid Overdose in Women: Toxicologic and Pharmacologic Sex Differences in Cause of Death	Rachel S. Wightman, MD	11/1/20–present
Pilot Project	Evaluation of a Nonopioid Recovery Pathway After Percutaneous Nephrolithotomy	David Sobel, MD	12/1/20–present
Pilot Project	Trauma and Stressor-Related Disorders Among Layperson Opioid Overdose Responders	Brendan Jacka, PhD	12/1/20–present
Pilot Project	Buprenorphine with Additional Rx Exposure (B-WARE)	Steven Kogut, PhD	12/1/20–present
Pilot Project	Development of a Text Message Delivered Intervention to Promote Engagement in Medication Assisted Treatment among the Criminal Justice-Involved Population	Kirsten Langdon, PhD	4/1/20–present
Pilot Project	Co-Occurrence of Post-traumatic Stress Disorder and Opioid Use Outcomes among Community Individuals	Nicole Weiss, PhD	12/1/19–present
Mini-Pilot Project	Factors Associated with Establishment of Emergency Department-Initiated Buprenorphine Induction for Opioid Use Disorder in Rural New England.	Noah Rosenberg, MD	1/16/20–1/15/21
Graduate–Research Project	Informed Opioid Prescribing for Acute Musculoskeletal Pain After Motor Vehicle Collision: A Support Tool for Assessing Risks and Benefits of Analgesic Medications Before Prescribing (STAAMP).	Francesca Beaudoin, PhD, MD	9/1/18- 2/28/20
Graduate–Research Project	Contingency Management in Combination with MAT for Opioid Use Disorder	Sara Becker, PhD	9/1/18–11/14/18
Former Pilot Project Awardee	Use of Non-opioid and Non-drug Treatments for Chronic Pain: Trends and Relationship with Opioid Prescribing and Outcomes in the Rhode Island All Payer Claims Database	Patience Moyo, PhD	1/1/19–12/31/20
Former Pilot Project Awardee	Monitoring Newborn Sleep to Improve Treatment and Outcomes from Opioid Exposure	Amy Salisbury, PhD	3/1/20–7/1/20

Administrative Core

The COBRE is led by an Administrative Core with an oversight structure and has three scientific Cores to support Rhode Island-based investigators. This Administrative Core, responsible for the general management of the COBRE, oversees three committees (Executive Committee, Internal Advisory Committee, and External Advisory Committee) that provide integral feedback on the center's progress and ensure the program is meeting the guidelines and missions of NIH, NIGMS, RIH, and the COBRE. The Executive Committee plays an essential role in monitoring the COBRE's Research Cores' productivity and finances and facilitates additional mentorship for the Research and Pilot Project Leaders. The Internal Advisory Committee provides feedback specifically on COBRE projects' development and provides mentorship to junior investigators. Lastly, the External Advisory Committee conducts an annual evaluation on the progress of the Project Leaders, the mentorship program's effectiveness, and the usefulness of the Core services. The External Advisory Committee's Year 2 annual evaluation was overwhelmingly positive and stated that they "were highly impressed with the progress the investigators are making and how successful they have been in publishing and writing grants." In addition to overseeing these feedback-providing committees, the Administrative Core also leads several working groups, including the Medication for Opioid Use Disorder in Corrections Working Group. This working group is in the process of developing a comprehensive website that streamlines up-to-date data on medication for opioid use disorder in correctional settings nationally (see The Prison Opioid Project on www.opioidcobre.org). In addition to the Administrative Core, the three research 'Cores' collaborate closely and play an essential role in supporting Rhode Island-based investigators with services that assist them in refining research methods, increase their network of collaborators, assist with grant and manuscript development and provide additional resources as needed.

Data and Research Methods (DRM) Core

The Data and Research Methods (DRM) Core, led by Dr. Brandon Marshall at Brown University's School of Public Health, assists COBRE Project Leaders and Pilot Project Investigators with methodological, analytic, and data-related support. This Core has focused on supporting junior investigators and pilot applicants during the past two years by providing workshops on innovative research methods. The DRM Core has done a remarkable job supporting junior investigators by reviewing and assisting in analytical plans revisions. Additionally, the DRM Core has also organized and hosted a series of talks focused on innovative research and methods, as well as co-sponsored a Community Overdose Data Workshop with the Brown School of Public Health that focused on using novel analytic methods, such as

machine learning and predictive analytics, to better implement interventions to prevent fatal overdoses. Notably, the DRM Core has provided analytic support for the publication of seven new manuscripts published in prestigious journals, including *The Lancet* and *Addiction*.

Special Populations (SP) Core

The Special Populations (SP) Core, led by Drs. Curt Beckwith and Tim Flanigan located at The Miriam Hospital, supports investigators and researchers in addressing practical challenges posed when conducting opioid and overdose research with vulnerable and underserved populations. This Core supports the COBRE's mission by building an infrastructure to recruit and retain vulnerable individuals as participants in research studies, build capacity in the ethical conduct of research, and promote research among populations most impacted by opioids and overdose. The SP Core has provided mentorship on research protocol design, study development, institutional review board applications, and study recruitment materials. The SP Core also works to develop training modules (seminars, webinars, and course curriculum) to promote clinical and translational research among populations most impacted by opioids and overdose. Notably, the SP Core recently created a multi-disciplinary continuing education harm reduction module targeting community health providers.

The SP Core has successfully established a Community Advisory Board (CAB). The CAB was developed and expanded by reaching out to community partners to identify individuals interested in bettering overdose-related research. Through these efforts, the CAB successfully recruited 42 members throughout the five initial meetings. Members of the CAB include people who are in recovery from opioid use disorder; people living with HIV; people who are homeless; people with a history of incarceration; people who use drugs; people with a history of sex work; recovery and harm reduction advocates; and people of diverse gender identities, races and ethnicities, sexual orientation, and ages. The CAB diversity is essential to the Core's work to support investigators in researching vulnerable populations. The CAB is committed to ensuring low-barrier access to the meetings and partners with recovery and harm reduction specialists to determine meeting locations. Additionally, transportation and meals are provided at every meeting. The CAB meetings have addressed a spectrum of concerns and community needs, from initial discussions around the role of CABs in supporting research to reviewing intervention content to providing feedback to Junior Investigators on their methods such as recruitment and reimbursement. A discussion-based CAB meeting about stigma and discrimination, facilitated by a community member, helped the SP Core identify the need for further research and developed a call for pilot programs specifically focused on the impact of stigma on recovery.

Translational and Transformative Research (T2) Core

The Translational and Transformative Research (T2) Core led by Drs. Traci C. Green and Susan Ramsey is dedicated to providing expert support in translating innovative findings to transform the care of addiction and overdose. The urgency of the opioid crisis in our state calls for innovative research and interventions and necessitates rapid dissemination of said research. The goal of the T2 Core is to establish a hub of translational and transformative resources to support junior investigators as they bridge research from theory and bench to bedside, from bedside to neighborhood, and from the community to policy change, to transform the care of opioid use disorder and the prevention of overdose. Due to the challenges posed by COVID-19, the T2 Core met with investigators. It helped them revise their protocols to maximize productivity, minimize study delays, and continue to pursue the aims of the studies. Additionally, the COBRE recently partnered with RIH to establish a buprenorphine hotline that can be used to access low barrier buprenorphine during the pandemic. To increase the hotline's reach, the T2 Core assisted in the development and distribution of materials regarding the hotline in the community. In addition, T2 Core members have engaged in community outreach activities to increase hotline traffic, including placing phone calls to patients who have been recently seen in local emergency departments for an opioid-related cause.

In fall 2019, the T2 Core hosted a successful Hackathon event. Teams of community members, students, and professionals were charged with developing innovative “hacks” or solutions to combat the opioid epidemic. The participants were encouraged to collaborate to address one or more topics: a community strategy for opioid overdose, healthcare solutions to opioid overdose, or policy solutions to opioid overdose. The three winning teams created high impact projects that continue to garner community and professional development opportunities (see YouTube Channel on www.opioidcobre.org). As a result of the hackathon, these projects received COBRE funding and became feasibility projects under the COBRE to further develop their innovations.

The COBRE on Opioids and Overdoses is not only committed to mentorship and collaboration among its investigators, but it also has been dedicated to institutional and organizational partnerships. In September 2019, the COBRE on Opioids and Overdose and the Rural Drug Addiction Research (RDAR) COBRE at the University of Nebraska – Lincoln began small efforts to collaborate to increase access to research around substance use and addiction science more broadly. This started with brief phone calls between center PIs and administrators, a site visit and quickly expanded to a fully realized partnership as synergies emerged across almost all programming areas. Our early goal of sharing more information across centers has grown into a valuable collaboration that includes hosting joint seminars, events, workshops, training, and conference symposiums. We built

on the existing resources and expertise that each of our COBRES provides to further increase our efficiencies and capacities at both institutions. This successful collaboration with the RDAR COBRE has piloted efforts to grow our successful COBRE collaboration with other substance use focused centers across the US in the coming years.

CONCLUSION

Although Rhode Island is the smallest state, it has been disproportionately impacted by the opioid and overdose crises. However, it has made a substantial impact. In 2017, the state government initiated the Governor Raimondo's Overdose Prevention and Intervention Task Force. Three COBRE Leaders serve as the Task Force's Expert Advisors. Additionally, the Rhode Island Department of Corrections initiated the first-ever statewide comprehensive program for medication for opioid use disorder in a correctional setting. This program has led the charge to provide people who are incarcerated access to the gold-standard treatment for opioid use disorder in a correctional setting. While the opioid and overdose crises continue to evolve, the COBRE on Opioid and Overdose and its team of investigators are well poised to address the daunting task of understanding and meaningfully to address these deadly epidemics to save lives.

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Disclaimer

The views expressed herein are those of the authors and do not necessarily reflect those of the funders, or Rhode Island Hospital, Brown University or The Miriam Hospital.

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