

Event Background

On Thursday, December 21, 2017, the Irving Institute for Clinical and Translational Research, Columbia University's Clinical and Translational Science Award (CTSA) Program hub, hosted a brainstorm session about the opioid crisis. Experts were convened from across Columbia University (CU), New York-Presbyterian Hospital (NYP), New York State Psychiatric Institute (NYSPI), and Northern Manhattan community organizations. Columbia University experts represented the spectrum of opioid and pain research ranging from the mechanisms of pain to community interventions, implementation research, and education for pain and opioid addiction. The brainstorm was held from 11:30am – 2:00pm and featured a pre-meeting lunch (11:30am-12:00pm), an introduction and overview (12:00 – 12:05pm), brief talks from six experts (12:05 – 12:35pm), four individual breakout group sessions (12:40 – 1:30pm), a discussion session integrating all breakout groups (1:30 – 1:50pm), and a closing summary (1:50 – 2:00pm). The following document is a summary of the brainstorm session.

Introduction and Overview

The brainstorm session began with a brief introduction from Dr. Muredach Reilly, the Director of the Irving Institute and Principal Investigator of Columbia's CTSA Program hub. Dr. Reilly addressed the urgency of the opioid epidemic and discussed the rationale behind the Irving Institute hosting the brainstorm session. During the most recent CTSA Program meeting held on October 26, 2017 in Washington, D.C., the Director of NCATS, Dr. Chris Austin, spoke of future plans to use the CTSA network to address the opioid public health emergency. Specifically, Dr. Austin was approached by Dr. Nora Volkow, Director of the National Institute on Drug Abuse (NIDA) to collaborate with her institute and to leverage the CTSA network for broad NIH opioid research initiatives. Although the details of the NCATS-CTSA and NIDA collaboration are still in development, the Irving Institute decided to convene a group experts from CU, NYP, NYSPI and community organizations to discuss current research projects, brainstorm ideas for local and national collaborations, and develop a more connected network able to quickly respond to future opportunities within the CTSA Program network and potential NCATS/NIDA initiatives.

Short Talks

Following the Introduction and Overview, there were six short presentations by diverse experts from across CU and NYP. The speakers were asked to present current research and implementation activities in their domain of expertise, challenges and opportunities in their field, discuss potential local and collaborative projects at CU, NYP, and NYSPI, and also touch upon potential regional and national collaborations with other institutions and the national CTSA Program network. Each speaker was chosen with the intention of spotlighting their specialties and the work they're doing or could potentially be done as we work towards interdisciplinary initiatives to overcome the opioid epidemic.

Talk 1 – James Peacock, MD

New York-Presbyterian Hospital Initiatives

The first speaker, Dr. James Peacock, Assistant Professor of Medicine-Cardiology at Columbia University Medical Center (CUMC), Assistant Chief Medical Officer at NYP, and Project Lead for the NYP Opioid Use Disorders Workgroup, presented the NYP dashboard that was developed in collaboration with CU and Cornell University. The dashboard is designed to assist clinicians and researchers in analyzing opioid prescribing patterns and to better determine patients at high-risk for developing an opioid addiction. NYP is also rolling out educational efforts for prescribers and high risk patients as well as engaging with community physicians to improve patient care for addiction.

Talk 2 – Frances R. Levin, MD

Opioid addiction treatment

From the Department of Psychiatry and NYSPI, Dr. Frances Levin, Kennedy-Leavy Professor of Psychiatry and Chief of the Division on Substance Use Disorders, spoke on current opioid research projects and opportunities. This Division in

Psychiatry is leading national and international researchers in opioid overdose and treatment interventions. They are currently working on supporting clinical trials, improving naltrexone inductions, and assessing how well evidence-based interventions are implemented nationally.

Talk 3 – Deborah Hasin, PhD

Epidemiology

The following speaker was Dr. Deborah Hasin, Professor of Epidemiology in Psychiatry and Director of the Substance Dependence Research Group (SDRG). The SDRG conducts national and regional studies on clinical epidemiology of drug and alcohol problems, which includes time trends of drug related issues, the relationship of marijuana laws to substance abuse problems, and technological enhancements of brief interventions to reduce drug and alcohol use. This group is currently performs several NIDA and National Institute on Alcohol Abuse and Alcoholism (NIAAA)-funded projects examining state medical marijuana laws and the relationship to measures of addiction to prescription opioids and opioid use in chronic pain patients.

Talk 4 – Suzanne Bakken, RN, PhD, FAAN, FACMI

Community and informatics

The fourth speaker, Dr. Suzanne Bakken, Alumni Professor of the School of Nursing and Professor of Biomedical Informatics, and Co-Director of the Health Analytics Center at the Data Science Institute, specializes in symptom management, informatics, data science, and community engagement. She touched upon tools and data that can be used for opioid-related projects such as the Observational Health Data Sciences and Informatics (OHDSI) and the Electronic Medical Records and Genomics (eMERGe). From a data sciences perspective, Dr. Bakken highlighted the many opportunities and challenges in trying to reach multiple targets and audiences – from institutional structures, policies, and systems all the way to the individuals affected by the opioid crisis.

Talk 5 – Joachim Scholz, MD

Mechanisms of pain

Dr. Joachim Scholz, Assistant Professor of Anesthesiology and Pharmacology, discussed his research on chronic pain, a hot topic in regards to opioids. His preclinical research includes mechanisms of neuropathic pain, the transition from acute to chronic pain, and highlights the opportunities in better understanding pain mechanisms and novel therapeutic strategies for pain.

Talk 6 – Elizabeth M. C. Hillman, PhD

Biomedical engineering

The final speaker, Dr. Elizabeth M. C. Hillman, Professor of Biomedical Engineering and Radiology, and a Principal Investigator at the Zuckerman Mind Brain Behavior Institute, specializes in optical imaging techniques. Her lab uses these techniques to image brain function and to explore the relationship between neural activity and blood flow in the awake mouse brain. After being involved in a recent NIH workshop, she realized they were many places where engineering approaches could be used to help address the opioid crisis. After listing several NIH funding opportunities that involve new devices and mechanisms for pain research, Dr. Hillman went on to describe student design projects in her own classrooms and across the School of Engineering and to highlight their process and strategies that they employed through their Columbia Design Challenge held at the Morningside campus in October 2017 for engaging students and expert stakeholders from across campus and beyond. These design projects included alternatives for pain relief rather than systemic opioids.

Individual Breakout Group Sessions and Discussion

Following the brief talks, attendees were instructed to divide into four groups focusing on various aspects of the opioid crisis. Guests were encouraged to select a breakout group of choice prior to the meeting. Those who did not select a

breakout group were instructed to divide equally among the four groups. Each breakout session was assigned a group facilitator and co-facilitator who were responsible for leading the discussion and summarizing the top ideas for future local and national collaborations. After the individual breakout group sessions, each group developed a one-slide summary of the top ideas which the group facilitator then presented to the larger brainstorm session group. The following is a summary of each breakout group's top ideas and discussion points.

Breakout Group 1 – Improving Prescribing and Pain Management

The “Improving Prescribing and Pain Management” breakout group was led by **Guohua Li, MD, DrPH**, Mieczyslaw Finster Professor of Anesthesiology and Professor of Epidemiology. Co-facilitating the group was **Rudina Odeh-Ramadan, PharmD**, Vice President for Research Administration, Clinical Trials Office. The group discussed several topics including educational efforts for prescribers and patients and research on alternative pain treatments. Top ideas included:

Facilitate the review and implementation of the Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids for chronic pain. There are many opportunities for collaboration in implementing the CDC guidelines and to educate clinical prescribers and patients. The CTSA Program network could be leveraged to develop training modules to improve prescription practice. Partnerships with community-based organizations can be formed to better reach out to community physicians. Improvements can also be made to better identify patients at risk for proper pain management, and to ensure and evaluate compliance with the guidelines.

Integrate training into existing frameworks and requirements. Online training modules for opioids can be integrated into existing physician training requirements.

Buprenorphine pilot trial. A potential trial on the use of buprenorphine as primary analgesic for select indications could be an area for possible collaboration.

Increase cannabis research. More research is needed to determine when and how cannabis can be used instead of opioids for treatment of neuropathic pain.

Breakout Group 2 – Improving Addiction Treatment

The “Improving Addiction Treatment” group was led by **Sandra D. Comer, PhD**, Professor of Neurobiology (in Psychiatry) at CUMC. Co-facilitating the group was **Nasir Naqvi, MD, PhD**, Assistant Professor of Clinical Psychiatry, Psychiatry Substance Abuse at NYP. The group discussed two ways to approach the improvement of addiction treatment: 1) Improving therapies in opioid addiction; and 2) Improving resources and strategies for treatment. The top ideas included:

Increase fentanyl research. More basic research is needed on fentanyl. The current medicine-assisted treatments (MAT) for fentanyl are ineffective or work at a lower efficacy. More research is needed to address this low response rate in the current MAT as well as overall physiological effects of the opioid.

Improve Naloxone usage and effectiveness. Research is necessary in administering higher doses of Naloxone. Organic chemistry could be used to create a better naloxone or alternative medication. Naloxone is short acting, so perhaps a longer acting substance.

Improve access to treatment resources. More resources are needed in large hospitals (such as NYP). Adapting MAT to non-Substance Use Disorder (SUD) specialty settings is crucial to our goal of improving overall treatment, as well as pushing for treatment-matching protocols. Systemic biases against treatment centers stand as obstacles for

implementation of these goals. We need to assess and strategize a way to overcome these barriers at local and national policy levels. Apart from more treatment centers available, there is also a lack of insurance coverage for long-term MATs even in the majority of cases where long-term therapies are needed. Transitioning patients to different available therapies based on their insurance requirements becomes an obstacle to their treatment plan.

Studies could be designed to measure respiratory distress via implantable devices, which, triggered by opioids, would quickly alert EMTs. This would increase treatment capacity, as first responders would not need to rely on a person's communicable response. Furthermore, automated External Defibrillator (AED) are available in many places, perhaps combining approach with Naloxone could be more effective to expanding its availability.

Breakout Group 3 – Improving Engagement of Community Resources

The “Improving Engagement of Community Resources” group was led **Isaac Kastenbaum, MPA**, Director of Population Health at NYP, and co-facilitated by **Ana Abraido-Lanza, PhD**, Professor of Sociomedical Sciences at the Mailman School of Public Health, CUMC. The discussion included ideas for targeting patients outside of hospital settings, including models for patient outreach and treatment and for population-based approaches to better understand the opioid crisis and to prevent further opioid addiction. The socio-political aspects of the epidemic were also discussed. Top ideas included:

Develop a local task force to engage community providers - independent community physicians. Doing so can help target patients outside of the network of Columbia and NYP-affiliated providers. Providers in the community see significantly more patients than Columbia and NYP providers. These providers can be targeted as partners in research on the opioid crisis and for training related to prescribing behavior. Another venue would be urgent care settings.

Reproduce the HIV care cascade for opioid addictions. The HIV care cascade model could be adapted for opioid addiction. It is a vetted and well-researched model that wouldn't require “reinventing the wheel”.

Analyze existing data sources. Existing data sets can be leveraged to conduct area-based analyses (e.g. compare New York City to other regions, etc.). Examples include analyzes of existing data on opioid prescriptions (e.g., by type of health care provider), sales, and overdose deaths by sociodemographic characteristics of various communities and areas.

Socio-Political research and action. Work with the New York City Mayor's office, including Dr. Mary Bassett, Commissioner of the NYC Department of Health and Mental Hygiene to develop effective city-wide approaches to treat and to prevent further spread of the epidemic. Support research and other activities to examine the role of the pharmaceutical industry in creating the problem. Understand the politics and policies that gave rise to the opioid crisis, which put some communities at increased risk for addiction. It is also important to understand the social factors (e.g., poverty, limited opportunity structures) underlying the problem currently, and that serve to perpetuate it. Using a socioecological framework will help to frame and understand the opioid epidemic from a more macro level, rather than simply from the level of the individual.

Determine specific strategies for treatment and engagement. The group discussed the importance of promoting harm reduction strategies (e.g., needle exchange and other programs) to address the crisis. In addition, there is a need for multi-level intervention projects to treat and prevent opioid addiction, including community-based participatory research to develop appropriate models and programs. These approaches should be implemented by considering the specific needs and circumstances of particular types of clients (e.g., chronic pain sufferers versus others).

Breakout Group 4 – Facilitating Bench to Bedside Discoveries and Translation

The “Facilitating Bench to Bedside Discoveries and Translation” breakout group was led by Jonathan A. Javitch, MD, PhD, Lieber Professor of Experimental Therapeutics in Psychiatry, and Professor of Pharmacology in Center for Molecular Recognition and in Physiology and Cellular Biophysics. Co-facilitating the group was Joel Lavine, MD, PhD, Professor of Pediatrics. The group discussed various topics ranging from developing a working group to continue their discussions to larger initiatives such as establishing core facilities and resources at Columbia to facilitate basic science research and animal studies. Top ideas included:

Develop a working group. The breakout group identified the development of a working group for prioritization of ideas, initiatives, and programs as the top strategy that could be implemented within the next year.

Develop a roadmap for how to move a compound from synthesis to a certain point in an academic medical center. It is very difficult to bridge the gap from discovery to first in human studies. This often requires financial resources only available through pharmaceutical companies, and companies are reluctant to work with opioids and other drugs that have the potential to be abused. Obtaining INDs to meet FDA requirements are also a barrier as the abuse potential needs to be completed if the product is going to market. A landscape analysis of what resources are currently available at CUMC would also be beneficial to this effort. The Irving Institute’s Translational Therapeutic Resource and Biomarkers Core Laboratory are resources that can support such efforts but more resources are needed because such commercialization steps and services are very costly and typically provided by clinical research organizations (CRO).

Establish core facilities and infrastructure for animal studies. There is a lack of core facilities for behavioral testing for pain, collecting data for PK information, pain measures, efficacy models, etc. This core facility could include preliminary toxicology, PK studies. In addition there is difficulty in constructing self-administration models for opioid abuse and to predict behavior. Non-human primates are better animal models than rodents, but are expensive and less accessible to investigators. Further development and research in imaging biomarkers for pain is also needed.

Build a shareable workforce. There are staffing issues for basic science/pre-clinical studies. The expense of doing PK could be lessened by building and leveraging workforce capacity and intellectual capital at Columbia.

Summary Discussion and Closing

The brainstorm session was summarized and closed by Harold Pincus, MD, Professor of Psychiatry in Health Policy & Management, Vice Chair of Psychiatry, and Co-Director of the Irving Institute. He indicated that this meeting was just a start and that the Irving Institute will follow up on this very successful initial effort in a number of ways. Dr. Pincus highlighted meaningful opportunities to leverage Columbia’s substantial resources and strengths, which include:

- The presence of national leaders representing a broad spectrum of areas of relevant expertise (across all schools and campuses)
- The ability to build on a range of highly relevant currently funded projects
- The presence of extensive databases and data networks (and a Data Science Institute to support use of these networks)
- Engagement in strong clinical networks – especially with NYP
- Strong community linkages
- Effective connections to national and state networks to implement research and impact policy

These strengths provide fertile ground to expand productive collaborations targeted toward the mission of combatting the opioid epidemic. Important opportunities were identified in areas related to: improving prescribing, reducing deaths from opioid overdose, enhancing addiction treatment, engaging community connections, applying bench to bedside strategies to develop novel therapeutics, and developing and applying innovative technologies.

Dr. Pincus suggested a series of next steps (“Six C’s”) to build on the enthusiasm and productive interactions generated by the efficiently and effectively run session. These include:

- Collect and integrate ideas from brainstorming event and other inputs
- Communicate internally throughout Columbia, NYP, CBOs, NYC, NYS, and nationally including providing feedback to NCATS and other stakeholders
- Convene a larger symposium; maybe smaller follow-up meetings for certain areas
- Continue to expand opportunities for collaborations and discussion including working groups
- Consider augmenting Irving Institute pilot programs
- Carry on developing additional ideas