Dr. Ivan Montoya
Oral History
November 27, 2023

Richie: Thanks for taking the time to meet with us. I'm Jason Richie, a volunteer at the Office of NIH History and Stetten Museum. I am interviewing Dr. Ivan Montoya, who is the Acting Director at the Division of Therapeutics and Medical Consequences [at the National Institute on Drug Abuse (NIDA)]. Today is November 27, 2023. I was really intrigued to hear about your background and how you shifted from psychiatry to working at the NIH [National Institutes of Health]. I am really curious where you grew up in Colombia and what your early formative years were like?

Montoya: I was born in Medellin, Colombia, and I went to medical school at the University of Antioquia in the same city. After I graduated from medical school, I began to work at a substance abuse clinic, treating many patients with substance use disorder, because as you probably know, cocaine is widely produced and exported and used in Colombia. I saw the need to treat many, many patients with the disorder, and I became very interested in the field. I decided to pursue a residency in psychiatry with the goal of becoming an addiction psychiatrist. But at that time, there was no specialty on addiction psychiatry in Colombia, and I was very interested also in research. I applied for a Fulbright scholarship (called the Humphrey fellowship) to come to the US to study. I came to the Johns Hopkins School of Public Health in Baltimore to broaden my knowledge about research and also substance abuse. I was very lucky to work with an excellent group of substance abuse researchers at Johns Hopkins. Then, as part of the fellowship, I was accepted for what used to be called a professional affiliation, like an internship, at the intramural research program of NIDA [National Institute on Drug Abuse] at the Johns Hopkins campus. That was a great opportunity for me to learn more about research and more about substance abuse treatment research.

When I finished my Fulbright scholarship, I was offered a postdoctoral fellowship in Baltimore, where I stayed for five years conducting mostly treatment research with an excellent group of mentors. Then, after the postdoc, I went back to Colombia to work at the University of Antioquia and start a program of research on substance abuse research, which didn't exist, so I started that program. A couple of years later, I was offered the possibility of coming back to the US to the Pan American Health Organization, which is part of the World Health Organization, to set up some international programs in Latin America. Being there, I was approached by the American Psychiatric Association to direct what is called the Practice Research Network. [The Practice Research Network] is a network of psychiatrists throughout the country to conduct research to clinical practice. I was very interested in learning more about psychiatry practice, but especially addiction psychiatry practice in the US. Actually being there, I was offered a position back at NIDA to start what is called a Clinical Trials Network, to help as a medical officer to start with this network, which is a network that still exists; this is 20 years ago. There's a very large network of universities and community treatment programs to do dissemination research, real-world type of clinical research. Then after that, I became the Deputy Director of the Division of Therapeutics.

That is what I've been doing for the past 10 years, I've been the Deputy Director of the Division, and I've been, for about four out of those 10 years, the Acting Director of the division. That is the position that I have right

now, which is in the Division of Therapeutics and Medical Consequences. The mission is to support research, looking at advancing the treatment of all substance use disorders, and all kinds of treatments. That includes medications, biologics like vaccines and monoclonal antibodies, and also behavioral therapies, devices, digital therapeutics, and the medical consequences of drug abuse, like HIV [and] hepatitis C. It's a pretty broad portfolio of research.

Richie: I imagine.

Montoya: In about 2019, with the HEAL [Helping to End Addiction Long-term] initiative the portfolio of, especially medications, but in general the portfolio of treatment for opioid use disorders grew exponentially because of the new funds available, that were coming from the HEAL initiative, which is the reason why you are interested in talking with me, right?

Richie: Yes. I was also curious about when you were at the American Psychiatric Association [APA] since you were there for I believe, two or three years; how did that change your view of research, having been in the association world, and then leaving that to go back to NIDA?

Montoya: What I learned at the American Psychiatric Association was mostly about how psychiatrists treat general psychiatric disorders and specifically how they treat substance use disorders; for example, what kind of medications do they use. What is the best approach? What is their knowledge about the different treatments for substance abuse? It was really eye opening to do that research because essentially there is a gap between science and implementation of science, and that's why they became very interested in the dissemination of research to try to bridge that gap, trying to make sure that what we find in research is really translated into actual better treatments for patients. That, I think, was the main lesson that I learned from my experience at the APA.

Richie: I'm sure from the time you were there to your time to now with HEAL, you've seen stigma really be addressed more and more, especially in the workplace.

Montoya: Absolutely, yes. Stigma is a big issue in substance abuse research because not only [do the] patients have stigma, but also clinicians have suffered from certain stigma. It was interesting. What I learned from the Practice Research Network was the certain different distinctions that psychiatrists make between the general circuit like bipolar disorders, schizophrenia, and addiction psychiatry. Sometimes addiction psychiatry is seen like the Cinderella of psychiatry. Some psychiatrists don't like to deal with substance use disorder, basically. General psychiatry is like, “Oh, I don’t want to deal with addicts.” So patients with substance use disorders, they are rejected everywhere. They suffer a lot of stigma.

Richie: We have gradually seen stigma decrease here in the US, albeit have you seen stigma decrease in Latin America?

Montoya: I haven't practiced in Colombia in a long time. That was 20 or 25 years ago, when I used to see patients in Colombia. I don't see patients anymore. In Colombia, yes, there was a lot of stigma, but as you know,

there was also the issue of drug trafficking—the combination of Narco terrorism, trafficking—so it was very complicated. What I have seen here in this country, especially in the last, I would say, five, three to five years, is a real concerted effort to fight the stigma associated with substance abuse. I think one of the main contributions of the HEAL initiative is the effort in trying to fight the stigma of opioid use disorder. Stigma is part of the risk factors associated with opioid overdose. Sometimes people are afraid of talking about it or are afraid of going to the doctor where they hide their opioid use disorder, and then they don't know the options available to better manage their opioid dependence.

Richie: I know some people can see Naloxone [Narcan] as more of a symptom than a solution. How does this compare to some of the longer-term efforts you're working on like vaccines and other treatments?

Montoya: In the substance use disorders field, there are multiple clinical manifestations of the disorders. One of them is opioid overdose. Luckily for opioid overdose we have two antidotes. We have Narcan, which is naloxone. Then we also have Nalmefene. Then commercial name is OPVEE; that's the most recently approved by the FDA. Those are specifically to treat overdose. As you know, substance use disorders are chronic diseases, and they require long-term treatment. For long-term treatment, there are other approaches and can be with buprenorphine or methadone. Or for relapse prevention and people who have been detoxified, the FDA approved the naltrexone. Naltrexone is also an opioid antagonist. Similar to Naloxone, Nalmefene is used for relapse prevention, to prevent relapses of opioids. It's two different approaches. It's like if you have an infectious disease, you take something for the pain, you take something for the sore throat or the nasal congestion, you take something for the fever. Here, you take Naloxone or Nalmefene for an overdose. For the actual treatment of the disorder, we have buprenorphine, methadone, or naltrexone.

Richie: Right, and now you have the removal of the X-waiver, which I understand should help increase prescribing?

Montoya: That's specifically for buprenorphine.

Richie: How is your work or your funding of vaccines part of your overall goal at the DTMC as well as NIDA?

Montoya: My division is funding the research with biologics. I've mentioned before that includes vaccines, monoclonal antibodies, enzymes, and oils that are considered large molecules. One of the projects that my division is supporting is the development of this anti-opioid vaccine that Dr. [Marco] Pravetoni and Dr. Sandra Comer are developing, and that is the first anti-opioid vaccine that has been tested in humans. So, for the first time.

Richie: In clinical trials?

Montoya: In clinical trials, correct. We are very involved in that research. That research is being supported by cooperative agreements. Cooperative agreements are a special funding mechanism of NIH. It's different from the from regular grants because in the cooperative agreement there's much more involvement of NIH staff in the research. So basically, NIH staff is embedded in the project almost as a co-investigator and provide

significant feedback to the investigators. The vaccine that Pravetoni and Comer are developing is through a cooperative agreement in which my division is very intimately involved in the development.

Richie: Of course, that's a very interesting development, especially as we have talked about addiction as a chronic disease. What else do you see on the horizon that you are working on in your efforts?

Montoya: Well, we have a pretty robust portfolio of medications that are in the pipeline for substance use disorders. What I see very promising is actually a monoclonal antibody to help with fentanyl overdose. It started also as the first monoclonal antibody that is being tested in humans for opioid overdose. That is something that is really very promising. There are also older, promising approaches, like for example, there is a molecule that's based on the chemical structure. It works to prevent the axis of growth to the brain.

Richie: It acts like a block?

Montoya: It's a molecule that has a C shape [makes C shape with hands]. What it does is that it captures fentanyl, for example, or methamphetamine, and prevents the axis of the drug to the brain. That is something that we're very excited about, that approach. Right now, the clinical trials are going to start very soon with that new approach. There are many, also, what we call new formulations of approved medications—for example, long-acting formulations of naltrexone, of nalmephene, of buprenorphine, of methadone so patients don't have to take a medication every day. They can take it like once every month or every three months or every six months. That is also a very promising approach. Many new molecules that are being investigated, new targets and different targets. It's pretty robust, the portfolio research.

Richie: That's great. That's very interesting. I know there's been so many developments especially with the data ecosystem as well. I was also going to ask, how is NIDA involved with a larger Clinical Trials Stewardship Initiative. Is NIDA part of the multi-agency approach or multi department approach?

Montoya: I know that the Clinical Trials stewardship Initiative within NIH is multiple institutes actually, with all the institutes. NIDA, of course, is actually involved in that initiative because we have multiple clinical trials. I think NIDA is probably one of the institutes with more clinical trials; we have many studies, many projects that are being tested in humans. We have a pretty low bar and a pretty big footprint in terms of the clinical trials at NIH. We are supporting and participating in the Clinical Trials Stewardship Initiative.

Richie: Okay, great. Let me take one more step back in terms of research. I understand you're also focusing on xylazine or Tranq? From what I understand that's more of a sedative so it's not responsive to Naloxone? Is that something that you're focusing on right now as well?

Montoya: No, no, we are focusing on it right now because it is a public health emergency that we have. As you probably know, a lot of the fentanyl is already contaminated with xylazine. Xylazine has a very different mechanism of action than fentanyl. Fentanyl is an opioid agonist and has effects similar to morphine and produces very severe respiratory depression, and many people died as a result of overdose with fentanyl. Xylazine has a different mechanism. It is an alpha two agonist. It's similar to other alpha two antagonists. Now,

the problem is that the combination of psilocybin and fentanyl produces some effects that patients find desirable, and they use that combination, but also many times patients don't know that their fentanyl is being contaminated with Xylazine. The problem is that Xylazine can produce very severe side effects including very graphic skin lesions, almost like burning, in the skin. So right now there's no antidote for humans. Xylazine is approved for veterinary use to anesthetize big animals for surgery or things like that. For animal use, there is an antidote that has been used by veterinarians for a long time. That is not approved for humans. There's no antidote for humans and Xyalazine, and one of the areas that we are really focusing and putting a lot of emphasis [on], given the public health emergency, is developing antidotes or evaluating if the antidote that is already approved for veterinary use can be used in humans. We don't know that. Right now, there is no antidote approved. There's a huge need for that.

Richie: Right. That's a clinical gap.

Montoya: Exactly.

Richie: Okay. I know we're running a bit on time. So let me focus a bit more on your day-to-day efforts at NIDA. I was also curious, how did your team work during the pandemic? How were you impacted by that, not only from a research perspective, but more on a day-to-day?

Montoya: Well, the research was significantly affected by the pandemic because especially clinical trials had to stop recruiting patients. Many of those clinical trials were delayed, and/or they couldn't complete the samples size that were expected. Also, some animal studies had to be delayed because some of the animal labs had to be closed. In terms of our staff, my staff in my division, we basically very quickly adapted to the remote work. Interestingly, we'd be even more productive than where we were before. Right now, most of my staff in my division are working remotely. Because there's no need to go to an office, we are very, very efficient and maintain doing the work that we do because right now, we can Zoom and Teams—all the platforms that we can use to communicate with people. We don't need to go to any place for meetings so we can meet with investigators and learn about their research or participate, as I said, as co-investigators in the projects, basically, at any time. That has been very beneficial for our program. The pandemic was terrible, but in a way, it was very good that we were able to make that transition and there was a very smooth transition to remote work.

Richie: I know different departments have adapted differently. It's nice to hear about yours. That's actually a really good question. How many people do you have in your department?

Montoya: I have 30 people in my department.

Richie: They range from research to administrative?

Montoya: Yes, we have chemists, toxicologists, pharmacologists, internists, psychiatrists, general practitioners, behavior pharmacologists. It is very multidisciplinary.

Richie: Then in your role, especially when you were Acting Director, how closely do you interact with Dr. [Rebecca] Baker [Director of the NIH Helping End Addiction Long-term Initiative] and Dr. [Nora] Volkow [Director of NIDA]?

Montoya: With Dr. Baker, I used to interact a lot because one of the components of the HEAL initiative was the development of novel therapeutics, but I don't know if you know that the HEAL office was reorganized. Rebecca Baker is not the director of HEAL anymore. There's no NIH/OD office anymore. All the responsibilities were transferred to either NINDS, the Neurological Disorders Institute, or to NIDA. Right now, we are learning to operate the HEAL iniative within NIDA. We are in the process of implementing that, and I haven't had any interactions with Rebecca since October when HEAL was transferred.

Richie: A fairly new change then to come under the NIDA umbrella?

Montoya: Correct. Dr. Volkow and I interact on an almost daily basis, [I have a] very close interaction with her. She's the institute director and she is very involved in the HEAL initiative and also very bold, specifically in my program, or she's very interested in it; it's one of her highest priorities. And in terms of developing new treatments for substance use disorders.

Richie: What have you enjoyed the most about your time at the NIH and at NIDA?

Montoya: Well, I enjoy the ability to influence the field on a very large scale. By being able to manage the research and administer the funds that we have through an age of healing, we were able to shape the field and advance the science in drug abuse. And for me, it’s being at the cutting edge of research and being able to meet that current cutting edge and make sure that the field advances and progresses for the benefit of patients, in benefit of public health. And for me, it's very exciting also that NIDA is the institution that supports most of the research in the world on substance use disorders, and probably 90% or 95% of the research on treatment for substance use disorders. For me to be in this position is like being a world leader and having that role in the treatment of substance use disorders.

Richie: Right and I imagine it must be so rewarding to see so many of these clinical trials move forward and see that real-time progress?

Montoya: Yes, that's the most exciting part of the job.

Richie: What advice would you give to those who wish to pursue a career in research, particularly in substance use disorder, focusing on addiction issues, if they wanted to follow in your footsteps?

Montoya: One piece of advice: patience. It’s very rewarding, but it takes a long time to get that reward because treatments take a long time to be evaluated and be approved by the FDA, in not only time but also resources and money. It's very expensive. It is some work that requires passion for it; you have to have a pretty high level of tolerance to push through frustration, because we have tried many experiences with multiple treatments,

and there are really very few that really have shown efficacy or have become approved by the FDA. It is important to be very patient in tolerating frustration.

Richie: I think sometimes it can be hard to balance that when you see the acute need that's out there as well.

Montoya: Sometimes we get very impatient. For example, with Xylazine, we see that big public health emergency, but we need to do the research; we can’t go ahead and treat the patients with a drug that has not been tested in humans. We have to do the research in order to be able to make sure that any new treatment is not only efficacious, but it's also safe, that is safe to administer it to people.

Richie: Then my last question is, is there anything that you would like to share with us about your experiences? Or your time at NIDA?

Montoya : Well, I think you covered most of the areas I know.

Richie: Well, it's been so fascinating to learn about your work. I'm looking forward to following you in the future.

Montoya: Thank you.