# DRUG USE AND POLICY: A CROSS-DISCIPLINE DIALOGUE

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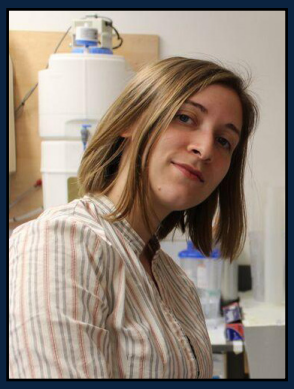
**DR. VERONICA MILLER**[2]: *I'm in the School of Public Health, and my perspective is on the regulation of new drug products. I teach a class on the Food and Drug Administration (FDA), drug development, and public health. My research program is concentrated in specific disease areas, in which we facilitate the drug development path.*

**DAVID SHOWALTER**[1]: *I'm a sixth-year PhD student in Sociology here at UC Berkeley. I use qualitative and ethnographic methods to study drug use and drug policy. In particular, I focus on opioid use and injection drug use. I come from a background of harm reduction work–for the past ten years, I've been involved in syringe exchange and overdose prevention programs. An important underlying principle to my research is helping people who use drugs live healthier and happier lives.*

**BREANNA FORD**[3]: *I am a fifth-year graduate student in Endocrinology, and most of my research is about molecular toxicology. I primarily look at pesticides and their harmful effects on humans. I also look at endogenous metabolites formed by pharmaceuticals and their direct interactions with the body.*



**DR. JOHANNES 'HAN' DE JONG**[4]: *I'm a postdoc in the Molecular and Cell Biology department. I study drugs as chemicals and how they affect the brain. Before that, I did my PhD in the Netherlands, where I studied sugar in the context of food addiction. I was also a member of a liberal political party called Democrats 66, which was the first party to legalize drugs in the Netherlands in the 1990s. I have also been involved in several harm reduction programs as a volunteer and an educator.*

**Research on both recreational and pharmaceutical drugs spans fields from neuroscience to sociology. This multidisciplinary approach informs regulatory drug policy and shapes the way drugs are perceived in society. *The Berkeley Scientific Journal* sat down with a diverse group of researchers (Fig. 1) to hear their insights into the mechanisms of drug addiction, challenges in drug regulation, and international attitudes toward drug rehabilitation.**

**BSJ**: What are the neurobiological mechanisms underlying addiction?

**JDJ**: The first phase in the development of addiction is called sensitization. Drugs affect the dopamine system in your brain, which reinforces behaviors that make you feel good. For instance, if you smoke cigarettes, you might not actually enjoy smoking, but the nicotine stimulates your brain to reinforce the behavior. That leads to the second phase, which is the conditioning phase. If you are trying to quit smoking and you see cigarettes on the table, then they are a salient cue for you to start smoking again. Over time, the drugs hijack the reward systems in your brain—both the dopamine system and the system that controls it break down. You cannot tell someone to stop being addicted—the very brain areas that they need to do that are destroyed.

**BSJ**: There is the historical example of veterans of the Vietnam War who used heroin while in Vietnam, but no longer sought it out when they got back to the United States. Could you elaborate on this phenomenon?

**JDJ**: This is a famous example, along with the example of Rat Park, which was a series of studies in the 1970s on drug addiction in rats.[5] The rats were exposed to a solution of morphine and would constantly drink it when in an isolated environment. However, when exposed to a more socially enriching environment, the rats would stop drinking the morphine. The same happened to heroin users who came back from Vietnam. Stressful environmental and social factors, combined with the effects of the chemical itself, caused the heroin addiction. After Vietnam, veterans came back to an environment where these social and psychological stressors no longer existed, so many people were suddenly not addicted anymore. However, there was a certain percentage of veterans who continued to be addicted to heroin despite having a family and being happy at home. We might conclude that these people were simply addicted to the chemical itself. Thus the biological, psychological, and social factors lead to addiction, but there's an ongoing debate about which factors are more influential.

**DS**: These examples are extreme cases, since most people who try heroin don't become addicted to it. There's a big gap between the number of people who have ever used heroin and the number of people who fit the criteria for heroin use disorder. There's so much more about what leads people to destructively use drugs beyond simply consuming the chemical. It's important to underline the difference between using a drug and being addicted to it.

**VM**: I wanted to ask a question from the perspective of someone who studies the regulation of pain medicine. Suppose someone breaks their leg while skiing. They get a prescription for pain relief medication, and two weeks later they become addicted to the medication. How do pain relief and addiction interact in the brain?

**JDJ**: The mu opioid receptor is the brain's natural pain-regulating system. That system is under tight control. Every pain medication that works on this system in some way down-regulates the mu opioid receptors. Over time, these interactions can change the system in a way that makes you addicted to the medication. Morphine has one of the strongest interactions with the mu opioid receptor. The trick is that morphine works in your body, but the blood-brain barrier prevents it from entering your brain. This makes morphine a good pain medication but not super addictive. On the other hand, heroin can sneak into the brain and become addictive. The holy grail of pain medication is to make a chemical that will only act in your body and not in your brain.

**DS**: Pain, whether physical or psychological, is at the root of why people use drugs. In a clinical setting, it's definitely true that widespread availability of prescription opioids is what got a lot of people hooked on the pills. However, about three quarters of people who are dependent on prescription opioids will say they first got them not from a doctor, but from a friend who got them from a doctor. We can't just cut people off from the pills, because the people who are prescribed the pills aren't the ones who are having problems using them. Instead, we need to think about how to prevent strong medications from getting into the hands of people who aren't able to use them in a safe way. The concern about addiction is sometimes misplaced when we just blame doctors or pharmaceutical companies.

**BSJ**: How does the FDA treat clinical and recreational drugs differently? Are there any instances of hypocrisy in the legislation?

**VM**: The FDA regulates medicines. These types of drugs include monoclonal antibodies, biologics, and vaccines; they all have a specific medicinal purpose. The drug packaging insert tells you what the drug is supposed to be used for and how it is supposed to be used. The FDA also has a regulatory oversight. They regulate what drugs come into the country, and they can go to the border and inspect shipments. Today, the FDA's efforts have expanded into social networks, as they examine websites that sell illicit drugs. The FDA has three primary roles: the first is to make sure we

have safe medicines to treat pain. The second is to make sure we have medicines to counteract addiction. The third is to oversee the import of drugs. Ultimately, the FDA looks at benefit and risk: what is the benefit that the drug provides, and what is the risk that the drug poses? The FDA cannot regulate clinical practice, because once a drug is approved, doctors have the discretion to prescribe drugs off-label, meaning in a way that is not indicated on the packaging insert. In a way, the FDA has its hands tied in directly interfering with the opioid epidemic besides encouraging the development of new drugs to treat addiction.

BF: I have a follow-up. The question addressed hypocrisy, but I'm not sure if hypocrisy is the most holistic term for what I think of as gaps in FDA oversight. To me, something that potentially falls into that category is that the FDA regulates food and pharmaceutical medications, but it doesn't regulate supplements and natural products that don't have a stated therapeutic value. Is it a problem that the FDA does not regulate these products?

VM: There are other agencies that regulate food, like the USDA. But the minute a supplement is claimed to have a medical benefit, it becomes a drug, and then the FDA can bar it from being sold as a drug. So I think that whole area is a wide open field, and much more could be done by the FDA.

BSJ: What obstacles posed by the FDA interfere with the process of drug research?

JDJ: A major issue is drug scheduling. In terms of addiction research, most addictive drugs are not Schedule I. I can easily do cocaine research because it's a Schedule II drug. It's the same for ketamine, a Schedule III drug that is frequently used for depression research. Meanwhile, marijuana is Schedule I, so nobody in the US can easily study it. For scientists, the bureaucratic process makes it difficult to conduct this research. MDMA, a methamphetamine, is another example. MDMA might have potential for treating PTSD, but it is very difficult to study because it is a Schedule I drug.

BF: Our lab does a lot of drug development research, and all of it is very pre-clinical—it will be years before our research interacts with the FDA. For most drug development research, the FDA does not have any direct interaction with researchers in the academic environment unless they are studying items that are analogs of known Schedule I substances or are part of the synthesis pathways of these substances.

BSJ: Besides drugs, pesticides are other chemicals that can be taken up by the human body. How do pesticides affect human health?

BF: We have this general belief that things that are natural must be good. This is reasonable in many ways. We eat food, which grows from the ground, and therefore we think things that grow from the ground must be okay, whereas things that are synthesized in a lab must be horrible for us. Pesticides are an example of this; we think of them as intentional, synthesized poisons, and

***Figure 1. Cross-discipline panel.*** *From left to right: Researchers David Showa a group of BSJ writers to share their insights on the role of drugs in modern*

therefore they must be bad. But if you think about pesticides as they relate to pharmaceuticals, there's a huge amount of overlap. Antibiotics and antifungals are really just pesticides that we use for a very specific purpose. This is where some of the ethical and psychological issues around what we think of as natural and unnatural come into play, and where the regulatory aspect becomes really important, because all of this is about managing risk and benefit. Is the risk of potential adverse effects of a pesticide, whether used in an agricultural or pharmaceutical way, worth the benefits it affords us both as individuals and as a group?

VM: Without getting too much into the endocrine system, most foreign things introduced to the body get metabolized by the liver. If the liver's enzymes have too much competition with these foreign elements, whether it's aspirin, Tylenol, ibuprofen, or pesticides sprayed on your apple, this interferes with other liver functions and drug metabolisms. It's all part of the same system.

BF: Exactly. The same can be said about the use of non-regulated drugs. They're all undergoing the same metabolism, and cross-interactions between illicit drugs and established pharmaceuticals are going to occur in your body. Understanding these interactions is incredibly important to maintaining human health.


*alter, Breanna Ford, Dr. Han de Jong, and Dr. Veronica Miller sat down with society.*

VM: A famous case of this is with St. John's wort, [a flowering plant with possible antidepressant activity]. It plays around with those liver enzymes and can seriously diminish concentrations of metabolites that you actually need. This is why a doctor will always ask a patient to list all of the drugs they are taking, even if the drugs are over-the-counter.

BSJ: What are some shortcomings of our current attitudes towards addiction rehabilitation, especially when it comes to illicit substances?

JDJ: What is generally true in the US is that people are high-minded and have strong principles. Whereas in Dutch culture, we are not proud at all.

VM: The Dutch are very pragmatic.

JDJ: Exactly! When I tell people in the US that I am Dutch, they immediately think about parties in Amsterdam. We did not legalize marijuana because we are all hippies. We legalized marijuana because Dutch policymakers, who are literally the most boring people in the world, looked at the data and worked out the best way to approach the problem. In the Netherlands, a country of 20 million people, there are 30 thousand heroin addicts. All of them are in treatment. The average age of the heroin addict increases by one year every year because the population is contained to the people in treatment. Additionally, no market exists for a heroin dealer, since heroin addicts are able to get the drug from clinics for free and use them in a safe space with a clean needle. All it takes is for us to step away from our principles. It might feel wrong that a certain percentage of your income tax supports heroin addicts. After all, they do not work, they receive money from the state, they get a free place to live, and they are allowed to take drugs. But it is important to take a step back and think pragmatically about what the future is going to look like if we implement these policies. That is what happened in the Netherlands. I think this is perhaps the major flaw in US policy: policies are based in principles and not in facts.

VM: It is a science, whether social or medical, of what works and what doesn't.

DS: Another thing is the assumption that if you use drugs, you have to go to treatment. Most people who quit using drugs don't go to treatment to do it. Instead, most people quit using drugs by basically aging out of it. Drugs are predominantly used by young people, those who do not have other things going on in their lives, or those who are seeking relief from something in their lives. But people grow up and get jobs, start families, fall in love, or find things that matter to them. These things fill the gaps that the drugs previously filled. As a result, these people no longer need drugs. There is also a lot of talk about the supply-side factor, such as overprescription. However, opioids were overprescribed in places that already had a large demand for drugs. These are usually places that have had substance abuse problems for decades. If we fix those root causes, there is going to be less of a demand for drugs. Therefore, I believe that the best treatment policy is ensuring that people have a good place to live, have a way to support themselves either through work or the welfare state, can form meaningful relationships, and aren't separated from their children or family members. If we achieve these things, the downstream consequence is that there will be fewer reasons for people to turn to drugs in the first place.

## IMAGE REFERENCES

1. David Showalter [Photograph]. Retrieved from https://sociology.berkeley.edu/graduate-student/david-showalter
2. Veronica Miller [Photograph]. Courtesy of Veronica Miller.
3. Breanna Ford [Photograph]. Retrieved from https://nst.berkeley.edu/users/breanna-ford
4. Johannes 'Han' de Jong. [Photograph]. Retrieved from https://www.lammellab.org/people/

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5. Alexander, B. K., Coambs, R. B., & Hadaway, P. F. (1978). The effect of housing and gender on morphine self-administration in rats. *Psychopharmacology, 58*(2), 175-179. doi: 10.1007/BF00426903