Ruth Adewuya, MD (host):

Hello, you are listening to Stanford Medcast, Stanford CME's podcast where we bring you insights from the world's leading physicians and scientists. This podcast is available on Apple Podcasts, Amazon Music, Spotify, Google Podcast, and Stitcher. I am your host, Dr. Ruth Adewuya. Welcome to season four of Stanford Medcast. This episode is part of our opioid mini series, and in this episode I will be talking to Dr. Keith Humphreys. Dr. Humphreys is a professor of psychiatry and behavioral sciences at Stanford University. His research focuses on addiction disorders and translating science into public policy. He received his bachelor's from Michigan State University and his master's in PhD in psychology from the University of Illinois.

Dr. Humphreys has extensive experience in public policy formation, having testified before the US House and Senate Committees and in numerous state legislatures. He served on the White House Commission on Drug-Free Communities during the Bush administration and a senior policy advisor in the White House office of National Drug Control Policy under President Obama. He co-founded and co-directs the Stanford Network on Addiction Policy, which aims to improve public policies related to addictive substances by bringing together scientists and policymakers. Dr. Humphreys, thank you so much for chatting with me today.

Keith Humphreys, PhD (guest speaker):

Very happy to speak with you.

Ruth Adewuya, MD (host):

Today we are talking about the opioid crisis from the lens of policy and guidelines. What role do guidelines and regulations play in shaping safe opioid prescribing practices?

Keith Humphreys, PhD (guest speaker):

I think it's important to think about this in terms of how we got here. So we had from the late nineties to about 2010 or so, a very large increase in prescribing in the United States, about 400% per capita increase. Sometimes that was appropriate prescribing. We have terrible problems with untreated pain and sometimes opioids are the right thing for that. But we also know that there was a lot of prescribing that was not appropriate. We're aware of one in every eight people who had a twisted ankle was walking out of an ER with a bottle of pills, for example. And there were many cases like that, and those pills were often diverted. People got addicted to them, sometimes they sold them. And that's where we got into a situation where we needed to take a hard look at how do we prescribe these very important and useful medications in a way that relieves pain but does not put either the patient or those around them at risk.

And that's what guidelines are for. And then but let me talk a little also about regulations. So we're all subject to regulations. Our hospitals, in clinics in which we work, also all professions are regulated. And that's another area where there's been a lot of work to try to make sure that professionals and healthcare organizations are acting in the interest of their patients not being over influenced by the pharmaceutical industry. Of course, we need a pharmaceutical industry, but we also need to make independent judgements in the best interest of patients. And there's been some improvements in that regard as well. That is why I think prescribing, the United States, is actually far more careful than it was 10, 15 years ago.

Ruth Adewuya, MD (host):

It's encouraging to hear that there have been some changes in how guidelines and regulations are being implemented. This addiction crisis has also prompted various federal, state, and even local policy initiatives. Which specific policy measures have shown the most promise in combating the crisis and reducing opioid related harm?

Keith Humphreys, PhD (guest speaker):

Where we are right now is that most of the harm is coming not from prescription opioids, but from illicit markets. So drugs people will have heard of, they're being traded on the street like fentanyl or heroin, and there have been some very productive things done to reduce the scale of that problem. So there's rescue medications. Naloxone is the one that people would know the best, and that is an opioid antagonist. And so what that does is when a person has taken an opioid and they're in overdose because opioids do suppress breathing, it essentially knocks that molecule out of the new receptor lock and quickly restores them so the respiration starts. So the federal government has spent an enormous amount of money to get naloxone out there through communities, through doctors. For example in the Veterans Administration now, it's quite common when prescribing a high dose opioid to also give the person co-prescription of naloxone.

That's something that's worked pretty well. There's a substantial amount of money that has come to improve the quality of treatment, and that comes about both in terms of the grants that the federal government gives to states to provide treatment, but also through better enforcement by the federal government of what are called parity regulations. And those are things that insurers like the Blue Cross/Blue Shield and so on have to follow to make sure that if your plan says you are covered for care of addiction, that in fact you actually are covered.

Ruth Adewuya, MD (host):

You touched on the existing program that the federal government has making naloxone more readily available and putting it out there and that it is something that the federal government has invested so much money and time making sure that it is accessible. I think it's also important to recognize that the opiate crisis has affected diverse communities very differently. And so from your perspective, how can policymakers design and implement equitable interventions and address the unique opioid addiction crisis in a way that is relevant to each community?

Keith Humphreys, PhD (guest speaker):

We in the Lancet Commission spent a lot of time digging into this data. In the early years of the epidemic, the addiction and overdoses were very heavily affecting whites. So in places like where I'm from, West Virginia, Kentucky, Ohio, western Pennsylvania, and that was true for over a decade. But as the supply of the drugs has shifted and as more of it has moved into illicit markets, we've seen a really tragic surging of deaths among African-Americans. In the last five years, the fastest growth has been among African-Americans, and that would be people who, for example, may have gotten exposed to fentanyl in cocaine that they didn't know it was there. Or maybe there were people who were actually stable on using heroin for a long time, but fentanyl's just so much stronger, their bodies couldn't handle it. So a lot of older African-Americans have passed away. A group that gets forgotten all the time, but I don't want to forget is the indigenous populations. Native communities throughout that whole period have suffered enormously.

So when whites were the group suffering the most, native communities were actually just about the same level, and now they're just about the same level as Black Americans. So that's been a tragic story that's gotten almost no attention at all, and I don't feel we've done right by those communities. So I

couldn't answer the question, how do we do right by them because I think we've just failed on that sense. And how do you handle all of these differences equitably? You need to have a lot of different voices at the table. You can't have just one region or people of one race or one background. Second, we have to be realistic about just the geographical differences in life where we all live. So just as an example, we talked a little about naloxone. It's utterly different strategy to distribute and use naloxone in the Tenderloin neighborhood of San Francisco versus King County, California where the average person lives two hours from the hospital. And you're not going to just stumble upon somebody passed out from an opiate overdose because people live way far apart in distant community and that strategy won't work.

And another one is we have, thank goodness, we have treatments like methadone maintenance, FDA-approved very effective, but you got to visit these clinics day-after- day. And that's doable if you live in an urban area, it's pretty hard if you live in a rural area. And that's partly why there's been changes to telehealth rules so that we can deal with that inequity. The other point to remember is that racial groups differ in which insurance that they have. So we have higher rates of uninsurance among African-Americans than we do among whites. That means that you have to strengthen the public insurance programs, the people who don't have private insurance rely upon if you want to have an equitable response. And I've been really glad to see, for example, expansions in Medicaid benefit in a lot of different states for substance use disorder.

I've also been really glad to see that we're also expanding that for people who've been incarcerated, which is a big source of inequity. So California is the first state ever that is going to turn Medicaid back on before people leave incarceration so that we can stop losing so many lives. The transition out of prison is a very, very dangerous time for people. You wouldn't think that, you would think your prison isn't really dangerous. Well, it can be, but even more so if you've been using opioids, you go into prison, they're hard to get in prison, your tolerance goes away and you come out and you use your normal dose and it takes your life. It happens all the time. So the expansion of Medicaid into the correctional system, which has never been done before in the United States, that will go a long way for the most vulnerable groups. And because of course there's huge racial disparities in prison that also is a good force for equity.

Ruth Adewuya, MD (host):

One of the things that is quite apparent is the interconnectedness of all of these issues. You've talked about how access to care impacts, how policies are rolled out, insurance impacts this. The prison system impacts access to care, which makes the crisis even harder to deal with and to create solutions for it because it's almost like you have to move all of these levers for it to be sustainable change. We talked about some of the policy initiatives and how some of them focus on restricting access to prescription opioids while others emphasize expanding access to addiction treatment and harm reduction services. And I can imagine that finding that balance can be challenging between those approaches. What are your thoughts on how we can strike a balance between these approaches to achieve that comprehensive solution?

Keith Humphreys, PhD (guest speaker):

One of the things we worked very hard on in the opioid commission is to never say that there was something bad about opioids. And a lot of times people frame it that way, "These evil drugs, why don't we get rid of them? Why do we even have such a horrible drug like fentanyl?" Well, I can tell you I had a surgery this year. I got my anesthesia, I certainly got fentanyl. So will most people who get surgery in the United States, it's a terrific drug when it's in the hands of someone who knows what they're doing and

cares about you and is there to help you. And that's true of all opioids. And so we have to avoid the natural tendency to want to demonize and instead think, okay, there's times where we absolutely have to expand access to opioids. Buprenorphine is an opioid, methadone is an opioid, but they're also FDA-approved because they really help people stop using heroin, stop injecting fentanyl.

Those are really good things. At the same time, we want to say there's other areas where we have to restrict them. I mentioned the fact that we had an awful lot of opioids being given for things like headache in adolescents or a twisted ankle or people prescribing for legitimate things, but just prescribing too much and stopping that makes everybody safer. And that dual message can be hard to get across and certainly it can get very contentious. There's times where we've restricted too much and times where we've prescribed too much. And many people have horrible experiences on either one of those policies and we'll get very upset when you talk either about restricting or about expanding. But we have to do both things depending on the purpose because opiates aren't good or bad, it's a matter of how they're used.

Ruth Adewuya, MD (host):

I truly appreciate that context that you provided because we can easily become very narrow minded and have a very narrow lens when looking at an issue or problem. And we should allow for the nuances and the complexities of issues because either extreme is not good. Too much access and the lack of access either way, it's impacting patients, it's impacting their clinical care. And I think this leads to the concept of prescription drug monitoring programs, which has been widely adopted to really focus on that idea of restricting access. And I believe the idea was that it would help monitor opioid prescribing and prevent that clinician hopping that patients might do. What have you seen as the impact of these drug programs on reducing opioid over prescribing and the diversion of prescription drugs?

Keith Humphreys, PhD (guest speaker):

Prescription monitoring programs have a couple different purposes. One is one you mentioned, is to catch the person who has 10 doctors and 30 prescriptions and essentially just running a business. They're selling drugs in the healthcare system providing them. Also has another purpose, which is to stop doctors from accidentally harming patients. So let's say if someone comes in, "I've injured my back." And the doctor thinks I'm going to give Keith Vicodin, and then looks up and say, "Oh, Keith's in therapy for anxiety disorder with a psychiatrist in the community and he's on high dose benzodiazepines." So that means those two drugs together can be risky, I may think differently about Keith's prescribing. So those two things, it's protection and then also reducing inappropriate kinds of use. And I'd have to say that it's been a mixed bag depending on how it's done. All states have a prescription drug monitoring program.

They really vary in their quality. They're hard to use, and the doctors are always busy. They're still relying on facts, we'll get back to you in a month. And what they really need to be is instantaneous electronic answers immediately while you do clinical care. The second thing is that like jury duty, you need to have a lot of people willing to do it for it to have high quality. And in some states, actually probably the majority of states, you're not required as a prescriber either to enroll or to check. And so if that's the case, then let's say I look up and all I can see when Keith comes in is if he happen to see the 5% of very conscientious doctors, then I know what Keith's been doing, but otherwise I really have no idea and it's just a waste of my time to check the system and then that kind of cynicism breeds on its own.

States where it's mattered and where we see it's mattered and where you have really good data, like in Medicare, is when you're required to enroll and to check. So when Medicare adopted that, then things like just the emergency room for opioid overdose dropped. So that's the type it needs to be. And now I

can hear all my physician friends saying, "Ah, that takes time. That's really pain." They're right. And my answer to that is they should be paid for it. Just like you get paid when you do due diligence on any other procedure, that's part of your work. Yeah, they should be compensated. The cost of the systems should not have to be borne by them. The cost of typing in patient names should not have to be borne by them. That's a perfectly reasonable request that I think policymakers should honor.

Ruth Adewuya, MD (host):

So I guess we still have work to do there.

Keith Humphreys, PhD (guest speaker):

Yes.

Ruth Adewuya, MD (host):

One of the things that you mentioned earlier in our conversation had to do with prisons and prison reform and access. We know that criminal justice reform has gained attention as a way to address the opioid crisis, reduce rates for drug related offenses. How can these diversion programs and drug courts play a role in providing treatment rather than punishment?

Keith Humphreys, PhD (guest speaker):

One of the things we recommended in the opioid commission was preventive strategy, which is it is so dangerous for somebody who is addicted to opioids to go into a jail cell for even a week that we should not put people in jail cells. Because they possess illicit opioids or because they have a needle or something like that, paraphernalia loss. So just stop doing that and try anything we can to have non-carceral approaches to addiction, to possession of drugs. That is better than anything we could do inside the walls because people go through withdrawal, it's dangerous, it's unpleasant, and then they're out with low tolerance, then it can have high overdose. Now obviously we have to do something because they may be addicted to opioids and then they assault somebody and steal their wallet, and there's a victim there saying, "I expect some justice." And it's understandable, people want that.

So then in those cases, we have to remember that one of the historical purposes of corrections was rehabilitation, which we've forgotten in the United States. Yes, it's about punishment. Yes, it's about protecting the public, but it's also supposed to be about rehabilitation. So we also say every single correctional facility should have addiction care available for every person who wants it, including the FDA-approved medications. And we've actually made some significant progress in that direction in California, I'm pleased to say. And some really great people in our legislature have pushed for that. Also, for people on parole after leaving prison, people on probation, that is all very good. But there are regions of the country where people don't really believe fundamentally that people who are addicted deserve rehabilitation or deserve care or they're despairing.

They think, "Yeah, I'd like to, but you know how" quote/unquote "these people are, they're just going to go out and use again. So why should we waste our hard earned tax dollars on taking care of them?" So that's a hard hill to climb. You have to really go state-by-state because it is states and not the federal government that run our prison system for the most part, and make that argument over again. I know this because I've done it in lots of states and sometimes it's worked and sometimes it's sad to say it hasn't.

Ruth Adewuya, MD (host):

The stigma component to addiction and this idea of how we don't look at it as a public health issue as we would if somebody said they had cancer. We would feel empathy. "What can we do to support you? Let's try and find the best cancer care. And there's all of these resources that we have around cancer care," as we should versus it seems like looking at someone with an addiction problem, "That's a you problem and you put yourself into that. So you need to figure that out and not be a drain on society." How can we shift that mindset as a society and do you think that in some way public policy or the lack of policy action can enhance that idea or perpetuate that idea of stigma surrounding addiction?

Keith Humphreys, PhD (guest speaker):

That's a great question and it's interesting. You're absolutely right, And we have compassion to cancer, even when cancer was caused by an addiction, all of a sudden then we become compassionate when it was carcinogenic alcohol or tobacco, but not while the person is addicted in the first place. I have a feeling this has something to do with the fact that addiction is a health problem and it is also a public safety problem. So in addiction, people do things like drive their cars in crazy ways and injure people. When you're under the influence of multiple drugs are linked to aggression, violent incidents or also just people are not as attentive to taking care of the people they love when they're is an addiction. So many people have had experience of my mom, my dad was addicted, my husband, my wife, and they're hurt and they're angry, which is understandable, and that can come out in these ways.

So I honor that and not tell people that you're hardhearted or stupid if you feel negative feelings towards addiction, and [inaudible 00:19:28], "Tell me where you got to that place." And often you find there's a narrative of pain, and if you honor that, then suddenly it's the person's compassion can open up. But not if they feel what you're saying is people who are addicted matter and you don't. What happened to you doesn't matter. That's a really long-term conversation that takes a lot of trust to build. But I think that underlies a lot of this argumentation and I think we'll have that, some negative feelings are going to be there because of that, because there'll always be some harm about it. It isn't important to say that there are very pragmatic reasons to provide addiction treatment. So there are other motives that I've had work, honestly, working with policymakers, where I say, "You're entitled to feel whatever you feel towards people who are addicted.

But let me just tell you a truth that if you care for the population, if you provide treatment, there will be less crime in your community. There will be fewer people in jail at a much lower cost. So even if they make you really mad as people, I'm just telling you, if you would like safer communities and you would like lower taxes, then it is actually the sensible pragmatic thing to do." And there are people would be moved by that who can't ever really feel a lot of love for addicted people, but they can see, okay, but that life would be better that way, wouldn't it? And that's okay. I don't need everything to be done from the highest of motives. World gets better. I'm for it.

Ruth Adewuya, MD (host):

I want to talk about prescription drug disposal and take back programs because I think at the beginning of the conversation you had mentioned the growing way that people are getting access to this is now through the illicit drug market. And I imagine that maybe some of that market might be coming from the incorrect disposal of prescription drugs. And so they seem like they are an essential part of preventing opioid diversion and misuse. What policies are in place or do you think can be implemented to promote safe and responsible disposal of unused prescription opioids?

Keith Humphreys, PhD (guest speaker):

Billions of pills are left over each year even from appropriate prescriptions and they just accrue in American medicine cabinets. And that's not good because if you're an adult, maybe you have some teenagers who are curious and they'd like to try or have a party or take them to school or share them with their friends or that kind of thing. Or someone who is addicted, might be over at your house for dinner and say, "Could I use the bathroom?" And go through and clean you out. All these kinds of things. Or people could sell them again. So it's good to soak up as much of that as we can. And historically it was hard because if you went back to your doctor and said, "Hey, doc, my broken wrist wasn't that bad. I still have half of these pills left here. Take them." The doctor wasn't allowed to take them.

It was a crime. So there's been changes in the law that there are now places that you can dispose of them. Pharmacies can operate disposal services where you have a secure safe and you just pop them down in there and then no questions asked. And then the pharmacy has a routine where they dispose of things that basically incarcerate the pills. Take up on that has been poor. GAO did an analysis of it, but 2% of pharmacies are actually doing this probably because there's cost to it and probably because a lot of us aren't incentivized either. So one of the things we called upon in the commission as an example was the experience of bottle recycling. When I was a kid, I used to go out and gather as a lot of my friends did, discarded pop bottles, beer bottles because you could get 5 cents for each one.

And that was originally done to incentivize. Well now, we just do this like we've been trained. So when we leave the cafeteria, it's okay, my compost goes here and my recycles go there. We don't have to have the incentive, but it's been brought into the culture, but it didn't start that way. And we suggest there should be an incentive to get the public to just think of this as a normal thing. You recycle your extra pills like you recycle the box they came in. And a way to do that would be to have the pharmaceutical companies pay for it, but really as side effect of their industry. And you could think of it as like an environmental hazard and they're obligated to clean it up. So you could say if your pharma's going to have a deal with whatever, the three biggest pharmacy chains, that you bring back your pills and you throw them in there, you get a coupon for five bucks of something you want in that pharmacy.

And just do that until we all get used to that idea of picking up my new prescription. I'm throwing away the extras to the old one, and that would be a way to do it. There's also some countries where you can mail them back, which is another model. There's some risks there about security of the mail, but not huge ones. And then the last way is there are some products, they're like charcoal bags where you can put pills in and then pour some water and that makes them inert and then you can just throw them away safely. That's another possible strategy we could use.

Ruth Adewuya, MD (host):

I was really pleased to hear that there are several options that we can consider. When you started responding to that question. I was quickly in my mind's eye just looking at my own bathroom cabinet. I'm like, oh yeah, I do have from the last time I had this procedure and that procedure. And yeah, it's literally just sitting there. I don't feel right throwing it away in the trash, feels like that's not the appropriate place. But at the same time it's just sitting there.

Keith Humphreys, PhD (guest speaker):

I had colleague and she said, "We don't have any of those." She goes, "Well, we have one because of my husband's ankle. Oh wait, no, we have two because I, actually I think we have, no actually there should be four. Okay, I'm going to do something." She had just had children. I said like, okay, now you want to start thinking about this kind of stuff. Wouldn't it be great if we all go to the pharmacy for something? If you could just pick them up and just boom, done out of your hair and they take care of everything for you.

Ruth Adewuya, MD (host):

Yeah. It sounds like it would be a natural place to do that because we would frequent that place if we needed another one or just like recycling places are readily available, I suppose that could be something to consider. Now I have an action item from this to find the closest place that does that and actually make that happen and clear out my medicine cabinet. As we wrap up our conversation, in light of this ever-evolving nature of the opioid crisis, what role do you think ongoing research plays in informing evidence-based policy decisions and adopting initiatives to meet emerging challenges?

Keith Humphreys, PhD (guest speaker):

That is a great question. Actually brings me to probably one of my biggest frustrations about this epidemic, and this is what it is. So last time I testified in Congress, I held up my cell phone and I said, Covid did not even exist two years ago. Yet right now on my phone, I could call up how many people died of Covid in each of your states and it would tell me the answer. Yet we've had addiction forever and if I want to tell you how many people died of opioid overdose in your state, the best I could say is get back to me in six months. And that does partly come out of stigma, but just like this is not an important problem. So we don't have these really fundamental questions answered because we have not invested in them. Like how many people in the United States use heroin?

How many are addicted to it? How many use fentanyl? How many people are using diverted pills? Our measures of all that are really awful and they're slow. It's like that joke about the restaurant, the food is terrible, but at least the portions are large. So our measures are rotten, but at least it takes us a long time to get them out there. So we really need investment on that side, and there are some exciting things happening and you can do some remarkable things with just the wastewater, which we learned with Covid. We monitored sewer pipes and we were able to tell communities have this much Covid, that much, Covid. That technology is very well developed for drugs. So instead of what we do now, which is we had a Fluor of fentanyl outbreak in San Francisco, it was early this year, we found out about it when we had a lot of dead bodies.

We could have found out about it really promptly if we'd had wastewater and then told people, there's fluor fentanyl in San Francisco drug supply. I'm working with some really bright people here at Stanford, lead by Russ Altman. We're also using the internet. People discuss drugs on Reddit, they discuss them on Twitter, they discuss them on Instagram. Scraping all those sites and pulling together real time things of like where are the overdose hotspots based on what people are talking about? Where are the new drug outbreaks of the drugs we don't understand? Where are their treatment shortages, all that. So we really need a lot of that innovative epidemiology like we got with Covid so quickly, where we've been at this for 25 years, we haven't done it. We definitely need that. Then there's also just better understanding of the human brain, which neuroscience certainly including at Stanford has made so many great leaps on in terms of we actually know where opioids bind in the brain.

We know the various pathways in the brain that they activate. It would be wonderful to be able to separate those pathways which has been done in animals. So what I mean by that is when you take an opioid, you're basically doing three things. You get some euphoria, which is why people use them. You get analgesia, that's why they're so useful in medicine. And then you get respiratory suppression and suppression of other biological functions like digestion. Well, there's some studies in animals showing with a tweaking the molecule, you can activate one without the others, and boy would that be great for a pain doctor to be able to say, "I've got you a different kind of opioid that will relieve the pain," but there's no chance that it will kill your patient with an overdose. And they won't get this huge dopamine spike of pleasure so they won't be tempted to take it five times as often as you tell them to take it.

That's an example of a scientific breakthrough would be fantastic. You could also use breakthroughs on the medication front. It's good. We have some very nice medications. They're not very many though. They don't work for everybody. And more development on that front. Maybe using pathways different than the opioid pathways, which is what most of them rely on right now. And there's some treating work of that sort going on, for example, through maybe the cannabinoid system or other systems in the brain that could possibly perturb the course of opioid use disorder. That's a place where it's very important. And then the last place, people don't think about this because we're mostly health people, but we could learn a lot more about how to intelligently use law enforcement. For example, in open air drug markets. We know a lot from the war on drugs of all the damage that law enforcement can do. What can it do well?

There are public safety threats around this. There are multiple shootings in the city in the last couple of weeks but evidence matters there too. You can figure out things like what strategies could police pursue? Is it gun removal? Is it focused deterrent strategies? Is it prevention? Is it community partnerships? But that kind of thing, which we tend in public health not to think about that much is really important to try to within law enforcement, public safety officials learn everything we can so that police make the problem less serious rather than doing things that actually can make it worse.

Ruth Adewuya, MD (host):

Thank you for taking the time to chat with me today and to share your incredible insights on this topic. So grateful to learn from you and for the work that you're doing in this space.

Keith Humphreys, PhD (guest speaker):

I really enjoyed the conversation.

Ruth Adewuya, MD (host):

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