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>> From the JAMA Network, this is JAMA Internal Medicine author interviews, conversations with authors, exploring the latest clinical research, reviews and opinions featured in JAMA Internal Medicine.

>> Hello, and welcome to this author interview from the JAMA Network. This is Deanna Bellandi with JAMA Internal Medicine. The United States is grappling with an opioid epidemic. Two new studies published by JAMA Internal Medicine talk about the relationship between legal cannabis use and opioid prescriptions. Joining us to talk about all this are the study authors, Dr. Jason Hockenberry of the Emory University Rollins School of Public Health in Atlanta, and Dr. David Bradford of the University of Georgia in Athens, along with Dr. Kevin Hill of Harvard Medical School in Boston, who wrote an invited commentary. So welcome to you all.

>> Thank you.

>> Thank you.

>> Thanks for having me.

>> So Dr. Hill, let's start with you. Talk to us about the extent of what your editorial calls an opioid crisis in the United States and how the liberalization of marijuana might fit in.

>> Well, the United States is gripped right now by an opioid crisis. Each day, studies indicate that around 90 Americans die from opioid overdoses. And this crisis has been incredible reach. It affects everyone, every race, gender, age, different regions of our country. And as a result, a lot of stakeholders are looking at multi-pronged approaches to try to stem the tide of this crisis. And I think at this point, the data is building, along with strong anecdotal evidence that cannabis may play a role in this opioid crisis.

>> So given that context, Dr. Bradford and Dr. Hockenberry, I'm hoping you can tell us about your respective studies, which both looked at marijuana laws and opioid-prescribing patterns. Dr. Bradford, I want to start with you.

>> Sure, so I and my colleagues looked at prescribing for opiates in Medicare Part D, which, as you know, is probably one of the largest prescription payers in the United States. And we asked specifically what is the reaction in terms of dispensed opiates when states turn on active medical cannabis laws. That is either through a dispensary or through some home cultivation. And what we found were large, large responses. And that is, when, particularly when dispensaries were opened in states, we found something on the order of 14% reduction in the use of opiates in Medicare Part D. That was larger for dispensaries than for home cultivation, where it was only about 7%. And mostly focused on hydrocodone and morphine. But nonetheless, suggested that when you give people access, easy access to cannabis for the management of chronic pain, they actually do seem to shift away from opiates.

>> So Dr. Hockenberry, how about your work?

>> So similar to Dr. Bradford and his colleagues' works, Dr. Hefei Wen at the University of Kentucky and I looked at whether medical marijuana laws and adult use marijuana laws impacted prescribing in the Medicaid program. And what we looked at was not just the number of prescriptions or rate of prescribing in the population, but also the amount of spending. And generally what we find is in line with the same magnitudes that Dr. Bradford and colleagues found in Medicare that was slightly smaller in some cases. We do find that spending is also decreasing. And importantly, we find that the adult use marijuana laws, all of which were passed in states that had existing medical marijuana laws, seemed to be associated with a further reduction in opioid prescribing among Medicaid patients.

>> So now Dr. Hill, how does the science around cannabis these days square with policy?

>> Well, unfortunately, the policy is way out in front of the science. So there is a growing body of evidence, along with these two important new papers that suggest that, again, cannabis may play a role in the opioid crisis. There's strong pre-clinical research that shows common signaling pathways for both cannabinoids and opioids relative to tolerance, dependence, and addiction. And along with that, you have a lot of anecdotal evidence from patients saying that this can be a helpful way to perhaps reduce the amount of opioids they need. And I think that those pre-clinical results, the anecdotal evidence supports some important papers that have been published recently. So the Bachhuber paper in 2014, which was in JAMA Internal Medicine, showed that states that have medical cannabis laws had a 25% reduction in opioid overdose mortality. Another paper that came out in 2017, by Livingston et al., showed that legalization resulted in a decrease in opioid-related deaths in Colorado. So those papers are important. However, not all of the research goes along those lines. There was an important paper that came out by Oleson et al., in American Journal of Psychiatry in 2017, and that was a perspective study that suggested that cannabis use was associated with an increase in non-medical prescription opioid use and opioid use disorder. So there is some discrepancy in some of the research that we've seen at this point. But unfortunately, the states that have moved forward, we have 29 states in D.C. that have medical cannabis laws. We've got nine states in D.C. that have legalized recreational cannabis. Those states haven't paid as much attention to the science as they really should have.

>> Dr. Bradford and Dr. Hockenberry, what do your results suggest we should do?

>> I'll take a crack at that first. This is Dr. Bradford. You know, our results are suggesting that there are potential benefits from giving people access to cannabis for things like pain medication. And one of my co-authors and I had done some other work, looking more broadly in Medicare and in Medicaid as well, and find benefits in other disease categories, like anxiety and depression, and seizure disorders and things of the sort. So it does seem to us, based on our findings, that when you give people access to cannabis for clinical purposes, at least, they, along with their physicians, seem to react as if it's medicine. And, you know, as Dr. Hill pointed

out, cannabis is much safer, where there's a fairly narrow therapeutic window for opiates as the National Academy of Sciences, Engineering and Medicine said in their report in 2017, there's no evidence of any fatalities from cannabis. And indeed, if you think about cannabis compared to alcohol, cocaine, heroin and tobacco, it's got a much lower capture rate, as far as addiction goes. So I think we would suggest states and the federal government need to rationalize their policies towards allowing access to cannabis.

>> And this is Dr. Hockenberry. I largely agree with both of the other speakers on different dimensions here, in part because of what might happen because of adult use laws. Other studies that we're conducting, and one that's about to currently come out, suggests that adolescence and young adults change their attitudes around marijuana, both its legal and its health risks, when medical marijuana laws are passed. And with adult marijuana use laws on the books, there is a concern that the general equilibrium effects might eventually lead to more people using marijuana because of a perceived reduced harm or addiction potential. And we frankly just don't know what the long-term frequent use of marijuana does to the neurochemistry in the brain.

>> So Dr. Hill, how cautious do we need to be about treating one drug for another?

>> I think we have to be very cautious. But I think it's important to point out, when you look at important rigorously designed studies like these, to understand the difference between a patient who may have a prescription for opioids for chronic pain, and therefore, may get a medical cannabis certification and be able to reduce the amount of opioids they use, that's something that I think is encouraging in many ways, provided that the patient is working collaboratively with a physician that knows them, versus a different patient, a patient who is using elicit opioids, and meets the criteria for opioid use disorder. And so in those cases, when you have multiple medications, you have three FDA-approved medications that are very effective for opioid use disorder, I'd be cautious about using cannabis in this case as an exit strategy instead of the FDA-approved medications for opioid use disorder.

>> So let's wrap up with what needs to happen next, both in research and policy, and I'm hoping maybe you can all weigh in.

>> So this is Dr. Hockenberry. I'll take a first shot at this. You know, we've had medical marijuana laws now for something like 20 to 22 years. California was the first one in 1996. And we have very little long-term evidence on what the long-term physical and cognitive function impacts of marijuana use over that period have been. So I think studies need to start to understand what that looks like in the long run, given that there are some laws that created natural experiments towards increased use. And I think we need to continue to monitor how this is changing attitudes among young people about the relative risks of using marijuana vis-a-vis other substances.

>> One of the things that I've noticed in the literature that we've all done as researchers who have been starting this work is that we've looked where there is readily available low costs in

the case of our study free data, which is largely Medicare and Medicaid. One thing we need to do on the research side to understand the impact of broad access to cannabis, both medically and recreationally, is to look at other groups as well. Privately ensured individuals, for example. And I will also say that one of the hurdles that we have as a research community is that currently a lot of this is inferential in the sense that we see cannabis laws being turned on, we see dispensaries being opened, and we see prescriptions for opiates going down. We can't actually see the causal chain with prescriptions for opiates going down because use of cannabis has gone up. And that's largely because of the lack of retrospective data that were, of course, prospective, where it won't always be good, that links not only the clinical traditional medicine of prescription drugs and procedures, but also has cannabis use in it as well. So data sets like the Medical Expenditure Panel Survey, run by AHRQ, and other federally-managed broad data sets need to start asking questions about medical cannabis use.

>> I think papers like these are a call to action. More research is clearly needed to clarify the relationship between cannabis and opioids. As we said before, the policy is way, way ahead of the science. And so we need to pursue this type of research aggressively. And I think that the NIH should not be the only ones who are funding this type of research. There are many people who are profiting from cannabis at this point. States and businesses. And they should also have to fund some of this research. The research that everybody says that they want, we should actually do the research to have the answers as more and more people use cannabis in our country.

>> Well, thanks so much for talking to us about your work, Dr. Hill, Dr. Hockenberry, and Dr. Bradford.

>> Thank you.

>> Thank you.

>> Thank you.

>> This is Deanna Bellandi with JAMA Internal Medicine. For more author interviews, please visit us online at jamanetworkaudio.com. You can also subscribe to our podcast at Apple Podcasts and on Stitcher.

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