Aaron van Dorn (00:07):

Welcome to AJP Audio for February 2024. I'm Aaron van Dorn. This month on the podcast, I spoke with Dr. Ofir Livne, a psychiatrist and assistant professor of clinical psychiatry at Columbia University in New York. Dr. Livne and colleagues have a paper in the February issue of AJP, looking at the trends in the prevalence of cannabis use disorder among US Veterans with and without psychiatric disorders.

Aaron van Dorn (00:27):

American Journal of Psychiatry Editor-in-Chief, Dr. Ned Kalin, will join us afterwards, to discuss the rest of the February issue, which takes a look at other issues surrounding cannabis and opiate use disorders. Stick around.

Aaron van Dorn (00:37):

Dr. Livne, your study found that cannabis use disorder rates have more than doubled during the period of your study, which looked at Veteran's Health Administration patients between 2005 to 2014, and 2016 to 2019. What can you tell us about the results? And why did you look at the two different time periods?

Dr. Ofir Livne (00:51):

Thank you. Yeah. In a previous study that we did, and these are all NH funded projects and IDA funded projects. In a previous study focusing on cannabis use disorders, or CUD, in the use of veteran population, we indeed found that between 2005 and 2019, prevalences of diagnoses of cannabis use disorders, which is basically the DSM-5 nomenclature for cannabis addiction, the prevalences have increased substantially among veterans receiving care in the Veteran's Health Administration, or the VHA.

Dr. Ofir Livne (01:26):

This was a finding that generally correlated with the general population and other patient populations. In that paper, we showed that this increase was consistent in all age groups. For example, in 2005, the prevalence of CUD in veterans under 35 was 1.7%, and that increased to nearly 5% by 2019. In terms of sex, the prevalence of CUD was consistently higher among men. But interestingly, in the more recent years, the prevalence increased more rapidly among women compared to men. In terms of race, Black patients have a consistently higher prevalence of CUD than any other racial or ethnic group.

Dr. Ofir Livne (02:06):

To answer your question about those two different time periods, the two different time periods are purely due to a technical issue. The codes in electronic health records in the VA changed from ICV-9 to ICV-10 around 2015. We couldn't perform a full trend analyses including all of those years.

Dr. Ofir Livne (02:26):

If I may take another minute, I'll just say that these increases that we found in CUD, there are various possible explanations for these increases. Among these are the decreasing perception of cannabis as a risky substance. Changing laws, of course. Increasing cannabis potency. Stressors relating to growing socioeconomic inequality. And use of cannabis to treat pain and various psychiatric disorders, which has become increasingly common nowadays.

Dr. Ofir Livne ([02:55](#)):

These findings are part of a growing body of literature, and I think that clinicians, policy makers and the public, of course, should be aware of these increases in addictions to cannabis. We know that CUD is associated with significant morbidity and mortality. This clearly has many, many individual and public health ramifications.

Aaron van Dorn ([03:16](#)):

The legal status of cannabis in the United States is extremely complex. It remains illegal at the Federal level, while an increasing number of states have legalized for personal or medical use. Indeed, a scientific FDA panel recently suggested rescheduling. How did the status impact your attempt to study cannabis use disorder and does it affect your analysis?

Dr. Ofir Livne ([03:33](#)):

This is a very interesting question, which many substance use researchers are intrigued by. We didn't directly examine the effect of legislation of the increasing rates of CUD in the different groups and different populations that we examined, but we did do this in another study. The question are increasing recreational and medical cannabis laws in the US effecting the prevalence of cannabis use disorder, that's an interesting question. The data on the effect of medical and recreational laws on cannabis use is pretty consistent. We're seeing that legislation is causing an increase in use in the US. But there's less data on the role that laws play in the increase in CUD, cannabis use disorder, in the population.

Dr. Ofir Livne ([04:21](#)):

In that study that we did, again using VA data, we showed significant but small effect sizes for medical and recreational legalization. Our analysis showed that medical legislation accounts for a bit less than 5% of the increases in the prevalence of CUD that we observed. And that recreational legislation counts for nearly 10% of the overall increases in CUD among US Veterans.

Dr. Ofir Livne ([04:47](#)):

This basically means that, although legislation contributed to increasing CUD rates, the role of laws in these increase may not have played a very significant role. There's definitely more research needed in this area. I'll mentioned, maybe in a bit, what future research we [inaudible 00:05:05] for this.

Aaron van Dorn ([05:06](#)):

Studies have pointed to association between cannabis use disorder and psychiatric disorders. The relationships here are extremely complicated. But what can you tell us about how cannabis and other substance use disorders interact with other psychiatric disorders?

Dr. Ofir Livne ([05:17](#)):

The recent paper we published in the American Journal of Psychiatry basically touches on this subject. There are many studies that point to associations between cannabis use, and CUD, and psychiatric disorders. There are several ethological models that makes the mechanisms that underlie these, indeed, complex relationships.

Dr. Ofir Livne ([05:39](#)):

One model is the shared vulnerabilities model. An example for this would be people who have genetic predisposition to both substance use disorders and to psychiatric disorders. Another ethological model is the secondary psychiatric illness model, where a substance use disorder precipitates psychiatric illnesses. Of course, the secondary substance use disorder models, which pose that psychiatric disorders increase individuals' vulnerability to develop an SUD, or substance use disorder. This model, of course, includes the self-treatment model, which is particularly relevant to cannabis. People today use cannabis more and more because they believe in the health benefits of cannabis and are self-treating for various health and mental health conditions.

Dr. Ofir Livne (06:23):

One important question that we asked in our recently published study was from which populations are we seeing that the prevalence of CUD is more rapidly increasing? We observed greater increases in prevalence of cannabis use disorder diagnoses in veterans with, compared to without, psychiatric disorders. These disproportionate increases in CUD were greatest in veterans ages 35 or less, between 2005 and 2014, and in those ages 65 years and older, in the more recent time periods, 2016 and 2019.

Dr. Ofir Livne (07:01):

I will say that, among patients with psychiatric disorders, the greatest increases in cannabis use disorder prevalences were observed in those with, I would say, the more major psychopathologies. Specifically, bipolar and psychotic spectrum disorders.

Aaron van Dorn (07:17):

Are there immediate clinical implications for your research in this population?

Dr. Ofir Livne (07:20):

I think our research is another confirmation that a group we need to really closely look at and monitor is a group of people who have a psychiatric disorder, all the way from depression and anxiety to schizophrenia, and that are also using cannabis. These are people who are likely much more vulnerable to develop an addiction, and that we need to target in terms of our preventative and therapeutic interventions.

Dr. Ofir Livne (07:44):

What our study also shows, on the macro level, is the trend itself. Addiction's increasing at a much higher rate in these groups. That's not necessarily going to change, because people are likely going to continue self-medicating and actually increase the risk of developing disorder.

Aaron van Dorn (08:00):

What were the limitations of your study?

Dr. Ofir Livne (08:02):

We had several limitations as part of this study. First thing to remember is that this was an analysis of VA patient records, or Veteran's Affairs patient records. VA veteran patients are largely white, middle-aged males with high rates of medical disorders. Our findings may not be necessarily generalizable to non-VA veterans. Also, to women or to the general population. I will mention, however, that our trend results are largely consistent with other general population findings.

Dr. Ofir Livne ([08:35](#)):

Another limitation of our study, and generally of any study that uses electronic health records, is that diagnoses were based on ICD patient encounter codes. These were entered by VA providers, rather than on actual research assessments. We're expecting some degree of provider error here.

Dr. Ofir Livne ([08:54](#)):

Another limitation is that some psychiatric disorders were not included in our analysis. For example, ADHD. And probably one of the more important limitations to note is that our models did not account for temporality. Meaning, we don't necessarily know if the psychiatric disorder preceded the cannabis use disorder, or vice versa. Here, we basically did a trend analysis so that was not a question being asked, but we need more longitudinal data to answer questions that might shed light on various ethological models that I mentioned earlier.

Dr. Ofir Livne ([09:25](#)):

I will mention one last limitation. We didn't have data on measures of cannabis use, such as frequency, route of administration, or motives for use. It would be nice if we did have that, because we could factor those measures into the observed trends. That's definitely something to look for in the future.

Aaron van Dorn ([09:42](#)):

What's next for your research?

Dr. Ofir Livne ([09:44](#)):

We have several additional studies currently underway. The one question that seems rather intuitive, based on the study that I mentioned that was recently published in the American Journal of Psychiatry, is if people substitute their use of psychiatric medications, for example antidepressants, with cannabis. There is some evidence for this, but not based on large scale data. That is definitely at least one interesting direction that we're heading in.

Aaron van Dorn ([10:09](#)):

Dr. Livne, thank you for taking the time to speak with us today.

Dr. Ofir Livne ([10:11](#)):

Thank you very much.

Aaron van Dorn ([10:12](#)):

Up next, Dr. Ned Kalin.

Aaron van Dorn ([10:13](#)):

Dr. Kalin, welcome back to AJP Audio.

Dr. Ned Kalin ([10:15](#)):

Thank you. It's a pleasure to be here.

Aaron van Dorn ([10:17](#)):

The February issue of AJP takes a close look at the developments in the treatment and understanding of opioid and cannabis use disorders.

Aaron van Dorn ([10:23](#)):

Earlier in this episode, I spoke with Dr. Ofir Livne, about trends in cannabis use disorder among a large cohort of US Veterans. Let's start there.

Dr. Ned Kalin ([10:30](#)):

This is an interesting paper and one of among a number of papers in this issue that are dedicated to understanding more about opiate use disorder and cannabis use. This is a study that was done in VA patients, basically from 2005 to 2019, looking at records from patients treated at all VA facilities across the United States. And really, asking the question, what is the prevalence of cannabis use and cannabis use disorder, and is it different in psychiatric patients, as compared to patients that don't have psychiatric disorders.

Dr. Ned Kalin ([11:06](#)):

What the researchers found was that it, indeed, is greater in psychiatric patients as compared to those that do not have psychiatric diagnoses. For example, when looking at the 2019 data, roughly 4.7% of psychiatric patients also had a diagnosis of cannabis use disorder, compared to only .4% of patients who did not have a psychiatric diagnosis.

Dr. Ned Kalin ([11:32](#)):

The authors also point out that, over this period of time of study, from 2005 to 2019, there's an increase in cannabis use disorder in general in this population, in the VA population, going from something like .85% to 1.92%. And also, not surprisingly, I guess, an increase in psychiatric disorders overall, running from 19% to 29%. But the bottom line is that, along with these increases, there's a disproportionate prevalence in psychiatric patients, highlighting the importance for clinicians to be aware of cannabis use disorder as a comorbid diagnosis. What the authors also found was that the diagnoses that were most likely to be affected with also having cannabis use disorder were patients that had bipolar disorder and psychotic spectrum disorders.

Aaron van Dorn ([12:25](#)):

Up next, Gustafson and colleagues look at the use of a mobile in the treatment of opioid use disorder. What did they find?

Dr. Ned Kalin ([12:30](#)):

This is an interesting study, attempting to use a mobile app, a cell phone app basically, as an adjunct of treatment for a treatment of patients in the outpatient clinic that are being treated for opiate use disorder. In this particular study, the app that was used was called A-CHESS, which stands for comprehensive health enhancement support system. This has been demonstrated to be useful in a variety of other illnesses, including an alcohol use disorder.

Dr. Ned Kalin ([12:59](#)):

The question that was asked by the investigators in the 414 patients that were studied was that, in addition to the treatment as usual with medications, which could be either buprenorphine, naltrexone

or methadone, or some combination. Would adding this mobile app further enhance treatment? What the study design was that half the participants got treatment as usual, but also received this app. They were treated for 16 months, and then were followed for up to 24 months.

Dr. Ned Kalin ([13:28](#)):

What the findings revealed was that, somewhat surprisingly, that the addition of this app was not helpful and did not have significant effects from the standpoint of abstinence in these patients that were being treated for opioid disorder, as assessed by drug screens. There were some positive effects of adding the app, and those were seen in individuals that did not have withdrawal symptoms when they were being treated. In those individuals, they did show increased abstinence. It's hard to understand why that occurred in that subset. Overall, there was also a decrease in visits to the emergency room and urgent care in the group that got the mobile app.

Dr. Ned Kalin ([14:07](#)):

Mixed results. Not as positive as the authors hoped, from the standpoint of having a main effect, increasing abstinence. But some effects. The other thing that was noted is that, by the Editorialist, Dr. Thomas McLellan, was that the adherence to this app was quite high. Which also, he basically said was a positive indicator of using this type of an app. So more research needs to be done. Some positive effects, but not the major effects that researchers set out to determine.

Aaron van Dorn ([14:37](#)):

Garland and colleagues investigated the impact of mindfulness training in conjunction with longterm opioid therapy for chronic pain. What can you tell us about that?

Dr. Ned Kalin ([14:44](#)):

This is a similar kind of study. It's also an individuals that are using opiates for pain control. This was in a VA sample. It was study of 230 individuals that had chronic pain and were using opiates for at least three months. The pain could not be due to cancer. The patients were either randomized to receive eight group therapy sessions, teaching them how to do mindfulness types of interventions, so a mindfulness oriented recovery enhancement program. The comparison was group therapy with supportive therapy.

Dr. Ned Kalin ([15:19](#)):

This did have quite positive effects. The mindfulness intervention demonstrated that there were significantly greater decreases in pain related measures in that group, and also in opioid dosing. As an example, the group that received the mindfulness intervention had a 20% decrease in opiate doses, whereas the supportive group therapy had about a 4% decrease in opiate dose over time. Also, the group that received the mindfulness training had greater reductions in anhedonia and greater increase of positive affect, decreases in craving. I should point that this is a population that had a high level of comorbidity with depression and PTSD.

Aaron van Dorn ([16:01](#)):

Cannabis use is common among people who also use heroin. Wilson and colleagues looked at a longitudinal cohort of heroin users in Australia to investigation the relationship between usage.

Dr. Ned Kalin ([16:10](#)):

This is a study, as you mentioned, that was done in Australia. It was a study done in individuals that were treated for heroin dependence, and then were followed up to 20 years with repeated assessments. The major question in this paper that was addressed was what is the co-usage of cannabis in these individuals that have a history of heroin abuse disorder and then were treated for heroin abuse or overuse.

Dr. Ned Kalin ([16:38](#)):

Not surprisingly, there was a lot of co-usage of cannabis in this group, especially when the group started out. At the beginning of the study, roughly 40% of the participants also reported using cannabis. Over the course of 18 to 20 years, the treatment itself was effective, as roughly six to 10 percent of the participants self-reported using heroin 18 to 20 years later. There was a reduction also in cannabis use. Roughly 20% of individuals self-reported that they were still using cannabis at that time.

Dr. Ned Kalin ([17:10](#)):

One of the interesting questions that the authors pursued was whether or not there were relations within an individual, between using heroin and cannabis. With the idea that one might substitute for the other, or that one might lead to the use of the other over time. They did analyses that allowed them to look at time relationships within an individual, as to whether the use of cannabis at one point predicted the use of heroin at another, or vice versa. They really didn't find any indication for this.

Dr. Ned Kalin ([17:40](#)):

Overall, I would say that this study demonstrates, not surprisingly, that individuals that have a history of heroin use also have a history of cannabis use. And that over time, they seem to be somewhat related but they're not really predictive of each other and don't really portend anything about whether or not one is going to predict a greater usage of the other.

Aaron van Dorn ([18:01](#)):

Finally, Huang and colleagues looked at cortico striatal engagement during drug cue reactivity studies.

Dr. Ned Kalin ([18:06](#)):

This is an imaging study, trying to get an understanding of the neuro-circuitry that is involved with craving in patients that use heroin and who also had opiate use disorder. It was done in a relatively small sample. It was done with 32 patients that met criteria for opioid use disorder. They were currently being treated an inpatient facilities with either methadone or buprenorphine. 21 individuals served as a control group or a comparison group. The patients were put in the MRI scanner and were engaged in tasks that involved looking at pictures that reminded them of the usage of heroin, cues that would trigger that. Drug related cues, but also cues related to food, and cues that were also associated with neutral conditions. They were also asked, in the scanner, to attempt to down regulate the salience of the drug related cues when they saw them. When they saw food related cues, they were also asked, in a separate task, to try to increase the positive value or the savor the food cues.

Dr. Ned Kalin ([19:12](#)):

What they did, then, is that they looked at the brain responses to these three different conditions and then tried to understand how this relates to individual differences in subjective levels of craving that these individuals had as they were being treated for their opioid use disorder. The bottom line is what they found is is that regions of the brain that have to do with reward were overactive in individuals with

opioid use disorder when they saw the drug related cues. One of the regions that revealed this finding was the nucleus accumbens, which is well known to be associated with reward and positive reinforcement.

Dr. Ned Kalin ([19:50](#)):

The authors also found that the opposite effects in the substance abuse individuals as compared to the controls. They saw more activation to drug related cues in the individuals that had substance use disorders, or opioid use disorders, and more activation to the food related cues, especially during the savoring condition, in the control individuals.

Dr. Ned Kalin ([20:14](#)):

Interestingly, when they looked at individual differences in subjective craving, they found that activation in regions of the ventral medial prefrontal cortex were positively with individual [inaudible 00:20:26] of drug craving. This is an interesting study. It's in a relatively small group of individuals. It begins to get at the differences in brain reactivity related to drug related cues and cues that are also positive, like food, which are not drug related, how that differentiates control individuals from individuals suffering from substance use disorders, in this case opioid use disorder. And also, begins to get at a brain region, under certain conditions, that when it's active, is predictive of individual differences in cravings.

Dr. Ned Kalin ([20:59](#)):

This has some interesting implications when thinking about treatment. We have a really nice editorial by Dr. Kent Barrage, from the University of Michigan, who's an expert in this area, who further discusses how different neuro models of craving and substance use disorder are related to these findings.

Aaron van Dorn ([21:16](#)):

Dr. Kalin, thank you for helping us put this issue into context.

Dr. Ned Kalin ([21:18](#)):

Oh, you're welcome. It's a pleasure.

Aaron van Dorn ([21:19](#)):

That's all for this month's AJP Audio, but be sure to check out our other podcasts presented by APA, including Psychiatric Services From Patients to Practice, Psychiatry Unbound with Dr. Laura Roberts, and the Medical Mind Podcast. All of that and more is available at psychiatryonline.org/podcasts, or wherever you get podcasts.

Aaron van Dorn ([21:37](#)):

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