

Aaron Van Dorn ([00:07](#)):

Welcome to AJP Audio for June, 2023. I'm Aaron Van Dorn. Dr. Mark Olfson, a professor of psychiatry, medicine and law and professor of epidemiology at Columbia University, joins us this month to discuss an article looking at the relationship between opioid prescriptions and suicide rates in the United States. Afterwards, American Journal of Psychiatry editor-in-chief, Dr. Ned Kalin, will join us to discuss the June issue, which focuses on issues surrounding substance use disorders.

([00:30](#)):

Dr. Olfson, past research has shown that removing access to lethal suicide methods, such as removing firearms or installing suicide barriers on bridges, are associated with substantial declines in suicide deaths. Your study looks at the association between opioid prescribing patterns and suicide risk in commuting areas across the US. What did you find?

Dr. Mark Olfson ([00:46](#)):

Well, we found that regions of the US with the greatest declines in people filling opioid prescriptions also tended to have the greatest decreases in suicide deaths. This finding suggests that restraining opioid prescribing helped to lower risks of suicide death.

Aaron Van Dorn ([01:01](#)):

Why did you choose to look at opioid prescribing patterns and suicide risk via individual geographic areas?

Dr. Mark Olfson ([01:06](#)):

So to understand why we looked at individual geographic areas, let me first back up and describe our primary research objective. There's controversy over whether mental health effects of policies to reduce opioid prescribing. And so while you can imagine that fewer opioid prescriptions in a region might reduce the local risks of overdose deaths including suicide, it's also true that when some people who are receiving opioids are tapered, they can become desperate, and if their pain becomes worse, you can also imagine that there are countervailing concerns that policies to reduce opioid prescribing might increase, rather than decrease, risks of suicide in some circumstances.

([01:44](#)):

So one way to inform this debate is to look at the experiences of geographic regions with different trends in opioid prescribing. That's what we did by breaking the United States into approximately 900 different regions and then studying changes in opioid prescribing in relation to changes in suicide within those regions. In effect, using each region as its own control.

Aaron Van Dorn ([02:07](#)):

Can you describe the five opioid prescription measures that you looked at?

Dr. Mark Olfson ([02:10](#)):

So we looked at five different measures of opioid prescription. One is we looked at the opioid prescriptions on a per capita basis, and this is the measure that the CDC uses to evaluate the volume of opioid prescribing. We also looked at the percentage of individuals within a region who receive at least one opioid prescription, percentage who receive high dose prescribing, the percentage that receive long-term prescriptions, and those that have three or more prescribers in the course of a year.

Aaron Van Dorn ([02:40](#)):

And what did you find with those measures?

Dr. Mark Olfson ([02:41](#)):

So the main thing that we found is that there was a direct relationship between changes in opioid prescribing and changes in risk of suicide death, and we found that that change was robust, in the sense that we could pick it up with the various measures of opioid prescribing. So the two tend to move together; areas that experience the greatest increase or decrease in opioid prescribing also tend to experience the same corresponding increase or decrease in suicide risk.

Aaron Van Dorn ([03:09](#)):

While opioid prescriptions across all five of the measures of your study looked at, they're declined during the period you were studying 2009 to 2017, the rate of suicide increased during the same period. But your analysis indicated that absent that decrease in opioid prescription rates, the rate of suicide would've actually increased an additional 3% over that period. How did you reach that conclusion?

Dr. Mark Olfson ([03:27](#)):

Well, I agree it's somewhat counterintuitive, so let me break it down. The main model estimated that there was a positive correlation between change in regional opiate prescribing and risk of suicide. This means that opioid prescribing and suicide risk both tended to move in the same direction. Applying this finding with the nation allows us to estimate the counterfactual situation. Had opioid prescribing stayed constant rather than decline during the study of 2009 to 2017? Had that occurred, we estimate that the national suicide rate would've risen even faster than it did. In other words, the policies that reigned in opioid prescribing appeared to have slowed the national growth in the number of suicide deaths.

Aaron Van Dorn ([04:09](#)):

You also found that in the two youngest age cohorts you looked at, three of the regional opioid prescribing measures and unintentional opioid related death had significant negative associations. What can we take from that?

Dr. Mark Olfson ([04:19](#)):

Some younger adults with opioid dependence who live in regions with falling opioid prescribing may have become more likely, as the availability of prescription opioids diminished, to turn to heroin, other illicit opioids that compose even greater risks of overdose. And so for them, lower regional opioid prescribing may have paradoxically driven greater overdose risks. And I might add that the dangers of overdose may be especially great in areas with high concentration of fentanyl contamination of the illicit opioid supply.

Aaron Van Dorn ([04:52](#)):

Were the rates that you found in changes in opioid risk consistent across the US or was there regional variation?

Dr. Mark Olfson ([04:57](#)):

Oh, there's substantial regional variation. During the course of the study period, rates of opioid deaths spread out across the country, basically moving from east to west, there are areas out western United States that were spared opioid related deaths early on during the study period.

Aaron Van Dorn ([05:15](#)):

What were the limitations of your study?

Dr. Mark Olfson ([05:17](#)):

Well, perhaps most importantly, this study assumes that opioid prescribing was the only thing related to suicide risks that was changing differentially across these study regions during the study period. And of course, many other aspects of the environment during this period were changing, including firearm regulations, socioeconomic conditions, access to mental healthcare and so forth. We also couldn't measure illicitly obtained opioids. In addition, some overdose events may be misclassified in their death certificates, with respect to intent.

Aaron Van Dorn ([05:49](#)):

Do your results have immediate clinical implications either for opioid prescription considerations or for those working on suicide prevention initiatives?

Dr. Mark Olfson ([05:55](#)):

Well, the findings reinforce the importance of judicious opioid prescribing and safe disposal of unused opioids, especially to patients who have a mental health history, maybe an increased risk of suicidal behavior. More broadly, the findings provide an example of how sometimes health policies, in this case, policies to restrain opioid prescribing, can have welcomed unintended consequences.

Aaron Van Dorn ([06:20](#)):

What's next for your research?

Dr. Mark Olfson ([06:21](#)):

Recently, I have become interested in and haven't started studying whether, and to what extent, healthcare workers who often have ready access to opioids and other controlled substances may, themselves, be at increased risk for drug overdose deaths and what measures might be taken to reduce those risks.

Aaron Van Dorn ([06:36](#)):

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

Dr. Mark Olfson ([06:39](#)):

Well, thank you very much for your questions this morning.

Aaron Van Dorn ([06:42](#)):

Up next, Dr. Ned Kalin. Dr. Kalin, welcome back to AJP Audio for June, 2023.

Dr. Ned Kalin ([06:46](#)):

Thank you. It's great to be back.

Aaron Van Dorn ([06:48](#)):

The June issue of the journal takes a close look at substance use disorders and related conditions. Earlier I spoke with Dr. Mark Olfson on opioid prescribing rates by commuting regions in the United States and suicide rates. What can you tell us about the paper and how it fits into the issue?

Dr. Ned Kalin ([07:00](#)):

Well, this entire issue is dedicated to focusing on substance use disorders with a focus on opioids, and also, there's a really interesting paper on craving, which is, sets the stage for the underpinnings for addictive disorders. The particular paper that you've brought up is really interesting because this looks at the relation between prescribed opiates and suicide deaths.

[\(07:23\)](#):

But what's really important about this paper is that the analyses are done at a regional level throughout the United States. But basically, what this shows is that as doctors and healthcare providers have attempted to decrease the number of opioid prescriptions, that there is a concomitant decrease in deaths related to opioid overdose in general. But again, what's really important about this is that it's done at the regional level, so at these different, what are considered commuting zones, which are thought of as being related to travel work areas and also the counties that constitute these commuting zones, that when one commuting zone would go down, that within that commuting zone, then we would see a reduction also, not only the prescriptions of opioids, but in the overall suicides that related to opioids. And then if there was a case where it went up in another commuting zone, then it would follow that, as well.

[\(08:16\)](#):

So overall, the opioid prescribing was down during this period of time, which was from 2009 to 2017, there was a concomitant reduction in deaths related to opioid suicide related suicides.

Aaron Van Dorn ([08:29](#)):

Up next, we have a paper from Vickers-Smith and colleagues looking at racial and ethnic bias in the diagnosis of alcohol use disorder in veterans.

Dr. Ned Kalin ([08:36](#)):

This is an important paper because it really uncovers biases within our healthcare system. This particular paper was focused on the veteran's system, the VA system, and used data from the Million Veteran Program, which is a very large program attempting to sample over a million veterans from the standpoint of phenotypic and genotypic data. And in this particular study, the investigators used data from over 700,000 veterans. And what they basically did was compared the self-report of alcohol use with the diagnostic information that was in the VA medical chart in relation to alcohol use disorder, and they were particularly interested in focused on disparities between individuals of color and white veterans. And this is related to the fact that there are more alcohol use disorder diagnoses and individuals of color within the VA than there are in white veterans.

[\(09:30\)](#):

And what, basically, the researchers found was that the disparity in the alcohol disorder diagnosis is related to self-report of alcohol use, but in a way that is inconsistent across black and white individuals and Hispanic individuals. So for the same amount of self-reported alcohol use between black individuals

and white individuals, there was a greater likelihood of a black individual getting a diagnosis of alcohol use disorder, and this was also the case for Hispanic veterans.

[\(10:04\)](#):

And just to give you an example of this, at the highest levels of reported drinking where the differences were the most levels where it's considered to be unhealthy alcohol use and above, white male veterans were about one third less likely than black male veterans to receive a diagnosis of alcohol use disorder, even though in both cases they reported the same amount of unhealthy alcohol use. So importantly, it uncovers this bias, and now, with the uncovering this bias, hopefully actions will be taken to mitigate this disparity.

Aaron Van Dorn [\(10:34\)](#):

Next, there's a fascinating paper for Rognli and colleagues looking at the risk of transitioning from substance use induced psychosis to schizophrenia spectrum disorder and bipolar disorder in a cohort of individuals in Norway.

Dr. Ned Kalin [\(10:44\)](#):

So this is also an interesting paper because clinically, we've known that when individuals have psychotic symptoms that are related to substances, that sometimes they go on to have more chronic illnesses or will develop more chronic illnesses like schizophrenia or bipolar disorder. This study, which is done in a large Norwegian cohort, it's a Norwegian patient registry, looked at individuals from 2010 to 2015 that had a diagnosis of a substance induced psychosis and then followed them longitudinally, or looked at the data longitudinally, to see what percent of those individuals went on to develop either a schizophrenia spectrum disorder or bipolar disorder.

[\(11:23\)](#):

They identified over 3000 individuals that had a diagnosis of substance induced psychosis during that time period; roughly 14% had alcohol-induced psychosis, roughly 18% had a cannabis induced psychosis, 22% amphetamine induced psychosis, around 30 to 38 to 40% had psychotic symptoms related to multiple substance induced symptoms. Of these individuals, of the 3,100 individuals, roughly 600 of them went on to develop a diagnosis of schizophrenia spectrum disorder. Out of those individuals, about 100 of them who had a substance abuse psychosis went on to develop bipolar disorder. So more common to develop schizophrenia spectrum disorder than bipolar disorder.

[\(12:09\)](#):

And when the, in relation to schizophrenia spectrum disorder, the cumulative six year risk for developing schizophrenia spectrum disorder after an episode of substance induced psychosis was around 27%, and the greatest risk was associated with cannabis induced psychosis, with roughly a 36% conversion rate. Roughly a third of individuals that have substance induced psychosis, at least in this study, went on to develop more serious psychiatric problems, either more commonly, schizophrenia spectrum disorder, or also bipolar disorder.

Aaron Van Dorn [\(12:44\)](#):

Finally, We have a paper from Garrison and colleagues looking at craving as a target for trans-diagnostic modeling and looking at substance use disorders. What did they find?

Dr. Ned Kalin [\(12:51\)](#):

So I mentioned earlier that craving and understanding craving is really critical when we think about maladaptive use of substances or maladaptive behaviors that are associated with repetitive drives. For example, eating behaviors or gambling behaviors, all of those things can become addictive, and when we think about the addictive process, we think of craving. Now, craving is a very common experience, which has been we all experience it, but again, when it is excessive and when that supports maladaptive behaviors, then it becomes a problem. And craving is particularly prominent in substance use disorders during periods of abstinence or withdrawal or not having the access to the substance that one has been using.

[\(13:38\)](#):

So this particular sample that was studied was a sample that ranged from individuals that had some substance use problems to normal individuals. It was a widespread of individuals, roughly 274 people that were studied with MRI to look at the bold response to a variety of different situations that would induce craving. A number of the types of paradigms that were used were related to personalized guided imagery scripts designed to activate a competitive processes associated with one's favorite food or drug, for example. There were paradigms that were related to stressors, and other paradigms were neutral or relaxing.

[\(14:18\)](#):

The imaging data was analyzed with machine learning techniques to try to develop a brain network that is predictive of individual differences in subjective responses of craving in these different situations that were used in the scanner. And the investigators were able to use machine learning to come up with a network in the brain which involved various regions, including the default mode network, which appeared to provide the most robust contributions to the prediction. And so once defining the so-called craving network in the brain, they then tested in another sample whether this would predict individual differences in craving using a bit of a different paradigm, which was actually a paradigm in which individuals required to fast before and after a 10 hour fast on their craving ratings. This previously derived brain network was predictive of individual differences in cravings.

[\(15:10\)](#):

So this now begins to give us an idea of the network that underlies craving, which is critical both adaptively and maladaptively, when we think about substance use disorders, and it also begins to shed some light on not only the regions that may be involved in the brain, but a method that may be somewhat predictive of craving in a way that could be useful as we move forward with personalized diagnoses and using more sophisticated tools like imaging, perhaps, to be part of our overall workup for patients.

Aaron Van Dorn [\(15:42\)](#):

Dr. Kalin, thank you once again for joining us.

Dr. Ned Kalin [\(15:44\)](#):

You're welcome. It's a pleasure.

Aaron Van Dorn [\(15:46\)](#):

That's all for this month's AJP Audio, but be sure to check out our other podcasts from the APA. You can check out Finding Our Voice Psychiatric Services, From Pages to Practice, Psychiatry Unbound and others, all@psychiatryonline.org/podcasts or wherever you get podcasts.

[\(16:00\)](#):

AJP Audio – Dr. Mark Olfson – June 2023

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