Aaron Van Dorn (00:07):

Welcome to AJP Audio for September 2023. I'm Aaron Van Dorn.

(00:10):

Today on the podcast I spoke with Dr. Antony Chum, Canada Research Chair of Population Health Data Science in the York University School of Kinesiology and Health Science in Toronto. Dr. Chum and colleagues investigated disparities in suicide related behavior between people of different sexual orientations and genders of large population in the Province of Ontario.

(00:28):

Afterwards, we'll check back in with APJ Editor-in-Chief, Dr. Ned Kalin, on the rest of the September issue of the American Journal of Psychiatry.

(00:34):

Dr. Chum, your study investigated the disparities in suicide related behaviors across sexual orientations by gender in a large cohort of individuals in Ontario. Previous research into suicide related behavior among sexual minority individuals has shown that gay and lesbian and bisexual individuals are at greater risk of suicide related behavior than heterosexual individuals, but your study finds that much of the prior existing data and research into this area is lacking. Can you tell us about that?

Antony Chum (00:56):

Absolutely. Previous research has indicated that sexual minority individuals such as gay, lesbian and bisexual individuals face increased risk of suicide related behaviors, or SRB, compared to heterosexuals. However, our study aimed to address the gaps and limitations in the prior research.

(01:16):

So many existing studies relied on self-reported data or small sample size or convenience samples or cross-sectional design. One of the issues, for example, with selection bias, is the fact that previous studies has relied on survey-based research. So with the survey, those who have died by suicide or are too sick as a result of self-harm behaviors can't respond to a survey. Or convenience sampling, which is based on the community-based surveys, aren't really representative of the larger population.

(01:49):

These limitations have been addressed in our study. Our study sought to overcome these limitations using a large population-based cohort in Canada, linking it to health administrative databases to obtain the clinical outcomes that we're looking at. This approach allowed us to provide more robust and representative estimates of disparities in suicide related behaviors across sexual orientations.

Aaron Van Dorn (02:14):

What did you find in your research?

Antony Chum (02:16):

Our study found that sexual minority individuals, specifically gay and lesbian and bisexual individuals, were at significantly higher risk of suicide related behaviors compared to heterosexual individuals. So the crude incidents rates per a hundred thousand person years were 224 in heterosexual individuals, but we found that it was 665 in gay and lesbian individuals, and 5,912 in bisexual individuals.

(02:47):

So after adjusting for a number of factors like socioeconomic status, marital status, et cetera, we found that bisexual individuals were three times more likely to experience suicide related behaviors, and gay and lesbian individuals were about two times more likely compared to heterosexual individuals. And these findings were robust after we controlled for a number of confounders.

Aaron Van Dorn (03:11):

You mentioned that your data was pulled from health administration data sets from the Province of Ontario. Can you tell us something about the data that you drew from and how you hope to use it to correct some of the gaps you observed in previous research in this area?

Antony Chum (03:21):

Yeah. Our study drew from multiple cross-sectional cycles of the Canadian Community Health Survey, and we linked that to the health administrative database in Ontario. So this administrative database includes the discharge abstract database, which contains all the hospitalizations, Ontario Mental Health Reporting Systems for any psychiatric inpatient and outpatient encounters. We have National Ambulatory Care Reporting System, or NACRS, which reports all the Emergency Department visits. We have OHIP, which is Ontario Health Insurance Plan, which contains physician billing and physician diagnosis. And then ORGD, which are all the mortality records.

(04:00):

So by linking all of this data to our population-based surveys, what we wanted to do was overcome the limitations in the previous research to provide a more comprehensive and population wide view of all acute care visits, hospitalizations and mortality related to suicide related behaviors. So this approach allowed us to capture both fatal and non-fatal suicide related behavior events and obtain more accurate estimates, reducing survivorship bias and also social desirability bias that's inherent in the surveys and self-reported data.

Aaron Van Dorn (04:34):

Your study was aiming to correct some of the limitations in previous research, but what were the limitations for your study?

Antony Chum (04:40):

We do have unmeasured confounders. We were not through the health administrative database. Even though we have longitudinal health records and health status, we don't have longitudinal employment status. So at the time of the survey, we might know these things at the time that they took the population-based survey, but in the longitudinal follow-up, we were not able to get the longitudinal employment status, housing status and income. The health administration database also excludes people who move out of the province. The sample was not large enough to examine fatal events alone. Our sample didn't include people who indicated that they were non-binary gender. And other sexual orientations, like asexual or queer, were not asked about on the survey.

(05:27):

Another important dimension actually is that sexual orientation is complex. So you've got attraction, behavior and identity. And our question focused more on how people identify. So whether they identify gay, lesbian, bisexual, but it didn't capture attraction and behaviors. That's an important aspect of sexual orientation that could have been missed.

Aaron Van Dorn (05:50):

Your study looked at longitudinal data over a long period of time, including a period that had a huge number of changes in the social status of LGB people in North America. Did your study take into account the changes and the fact that the data from earlier in the period might be skewed in a way of how people chose to identify themselves versus later on in this dataset when the socialist mores had changed some?

Antony Chum (06:11):

Yeah. The way that we did this study is there's certain things that we can control and certain things we can't. We did try to do a sensitivity analysis using the earlier parts of the data versus the later parts of the data, and the results were consistent.

(06:27):

The other thing that we do is that even though people are interviewed at one point in time, we look at their entire life history as much as we can. So the time that they took their survey, let's say, was in the middle of the study period; we look backwards and we also look forward. People who come out later, for example, we're still able to use that information by going back in time by looking at their health records previously.

(06:54):

Now, one thing to note is that more people are able to identify as LGB; lesbian, gay, and bisexuals, because of change in societal pressures, things like that. That's why I say one of our limitations is it's based on sexual orientation identity rather than behaviors and attraction. So if we were to redo this study, being able to capture people's behaviors and attraction, it's likely the results might look a little bit different.

(07:22):

In fact, there's studies out there now saying that when behaviors and attraction and identity does not align, often people call that branched sexuality. So for someone who might identify as heterosexual, but who is a man who is having sex with other men and are attracted to other men, that's a kind of branched sexuality that might have unique risk factors over and above those who identify as a gay man.

(07:48):

So further research, I think, is needed to understand these kinds of cases.

Aaron Van Dorn (07:55):

Are there immediate clinical implications for your study?

Antony Chum (07:57):

Yeah. The findings highlight the need for increased education and awareness among mental health professionals about the elevated risk of suicide related behaviors engaged by sexual and lesbian individuals. Many health professionals should be equipped with more knowledge to identify and address the unique risk factors and discrimination faced by sexual minorities.

(08:20):

These factors can range from individual level to societal level. At the individual level, we have things like bullying at school, discrimination in the workplace, being targeted for LGB on social media, social

isolation or rejection from family members. But at the societal level, it's also really important to look at some of these recent changes.

(08:43):

In the US, for example, such as the anti-drug bans, forcing students to come out to their parents. There's laws around that. There's also laws that ban the use of any words related to LGBTQ+ in schools. In fact, the human rights campaign recently declared a national state of emergency for LGBTQ+ Americans. More than 75 anti-LGBTQ+ bills have been signed into law just this year alone, which more than doubled last year's numbers, which is previously the worst year on record.

(09:17):

So by understanding the whole spectrum of risk factors from individual to societal, clinicians can provide more support and interventions and treatments for individuals at risk of suicide related behavior. Implementing educational initiatives that educate mental health professionals about these risk factors might help to reduce incidents of SRBs in sexual minority populations.

Aaron Van Dorn (09:46):

What's next for your research?

Antony Chum (09:47):

There might be ethnic differences in suicide related behaviors in lesbian, gay, and bisexual groups. Even though there are many health and social services that are targeted at LGBTQ+ individuals in Canada, many of them don't consider cultural diversity. For example, PFLAG, which is parents and friends of lesbians and gays, traditionally have offered resources to help teens and youths and even adults come out and work with families and parents. But some of these resources aren't available to say East Asian and Chinese LGBTQ+ youth and their parents. What we want to do with this research is to understand some of these ethnic differences within LGBTQ+ groups.

(10:32):

Another project that recently was funded from our lab, we are looking at self-harm in trans and non-binary individuals. So understanding the impact of policies on gender-affirming care on suicidality and self-harm behaviors in transgender population. So we are partnering with EGAL Canada and other community organizations to talk to trans folks about how they're experiencing in getting gender-affirming care or not being able to get this care affected their wellbeing and self-harm ideation and behaviors. We also have quantitative components which tracks laws banning gender-affirming care or introducing them in different regions to understand its impact on suicide related behaviors in trans and non-binary folks.

Aaron Van Dorn (11:18):

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

Antony Chum (11:20):

Thank you so much for your time.

Aaron Van Dorn (11:22):

Up next, Dr. Ned Kalin.

(11:23):

Dr. Kalin, welcome back to AJP Audio for September 2023.

Dr. Ned Kalin (11:26):

Thank you, Aaron. It's good to be here.

Aaron Van Dorn (11:28):

This month I spoke with Dr. Antony Chum regarding suicide related behaviors across sexual orientations. Let's begin there.

Dr. Ned Kalin (11:34):

Aaron, this is an interesting and important paper that gets at an increased risk for suicide and suicidal behaviors in individuals that belong to sexual minorities. What's really important about this is not only identifying the increased risk but also recognizing the increased stress that these individuals face, mostly related to discrimination and destigmatization and other factors that are marginalizing in our society for these individuals.

(12:09):

What the researchers did here was to conduct a study in Canada where they selected over a hundred thousand individuals randomly. They looked at their medical records and other data, and looked at how many individuals engaged in fatal and non-fatal self-harm related behavior, how many suicides were committed, and they followed the data for these individuals over on average about 11 years.

(12:38):

What they found was that out of this 120,000 or so individuals that about 3,000 or 3,100 actually engaged in at least one suicide act, and there were 164 people that actually killed themselves tragically. Importantly, the main finding is that individuals that belonged to sexual minorities had this marked increased risk for these behaviors, and more specifically, what they found was is that compared to heterosexual individuals, the risk to engage in suicide related behavior increased about twofold for gay or lesbian individuals and about threefold for bisexual individuals.

(13:16):

This is important information. It's new data, and it's clinically relevant from the standpoint of thinking about additional risk factors for suicide related behaviors in the patients that we see. And also at a societal level, emphasizes the importance of the field being active in relation to sexual minority individuals from the standpoint of the additional stress they face, and making sure that we do everything we can to reduce the bias and stigmatization that these people have faced. It's resulted in their marginalization.

Aaron Van Dorn (13:51):

Turning to the rest of the issue, we have two reviews. What can you tell us about them?

Dr. Ned Kalin (13:55):

Along the lines of discrimination and marginalization, we have a paper that is a review that is first authored by Dr. Alik Widge from the University of Minnesota. It also has other members of the American Psychiatric Association Council Research as co-authors. This paper is specifically directed at looking at basically barriers for individuals that come from minoritized groups to have academic careers in psychiatry.

(14:27):

It's an important piece because it really highlights the impact of structural racism in relation to the development of research careers in psychiatry, but more broadly is applicable to psychiatry in general and also, I would say, medicine in general. This paper not only identifies factors related to structural racism that have over the years contributed to this issue and the barriers but also make some suggestions about how to overcome some of these barriers to enhance the diversity among psychiatric researchers and to produce the effects of structural racism.

(15:06):

The overview by Dr. Justin Russell and Dr. Ryan Herringa, both from the University of Wisconsin, is an overview on childhood post-traumatic stress disorder. It's really worth reading. It gets into the mechanisms that may be associated with childhood PTSD. It gets into issues about how PTSD in children may be different than those in adults, and it gets into thinking about treatment issues as well.

Aaron Van Dorn (15:34):

Up next, we have two studies looking at the efficacy of the same drug, zuranolone. First up is a phase three trial by Deligiannidis and colleagues looking at the treatment of depression in postpartum women. What did they find?

Dr. Ned Kalin (15:44):

These two papers their definitely complimentary. The first paper is looking at a double-blind placebo controlled trial for postpartum depression, and the second paper is a double-blind placebo controlled trial for major depression, not postpartum depression.

(16:05):

The first paper on postpartum depression looks at a group of 98 women with postpartum depression who received zuranolone 15 milligrams a day for two weeks, and an additional 98 women with postpartum depression that received placebo. The point here is that these individuals were treated for just two weeks, and they all had postpartum depression. They could be on other medications if they were on them for a period of time, other antidepressant medications.

(16:35):

The findings were really quite interesting and replicated work that had been done previously. In this particular study that we're talking about now, the dose of zuranolone was 50 milligrams per day. The earlier study was 30 milligrams per day.

(16:50):

I should also mention that zuranolone is a synthetic compound that is very much related to allopregnanolone, which is what we call a neurosteroid. Allopregnanolone levels sometimes decrease in the blood after giving birth. It's a metabolite of progesterone, one of the sex steroids. And as we've discussed in the past, these drugs are related to brexanolone, which has been approved by the FDA to be administered IV for the treatment of postpartum depression. So now the idea is the development of orally active neurosteroid drugs that are related to brexanolone or allopregnanolone and testing their efficacy.

(17:32):

Coming back to this particular study, what the researchers found was that after 14 days of administration of 50 milligrams per day, that there was significant reductions in depressive symptoms at three days, 28 days, and 45 days, which is as far out as they study the individuals.

(17:47):

What they also found, and this is important, was that there was a significant effect at 45 days between these zuranolone treated patients and the control patients, or placebo patients, from the standpoint of remission rates. 44% of the zuranolone patients were in remission compared to 29% of the placebo group.

(18:07):

I should also mention that there were reductions in anxiety, which is not surprising because this drug works by modulating GABA receptor function. And not only were there reductions in anxiety, but also there were some side effects that you might associate with this type of mechanism, including tiredness, dizziness, and some sleepiness. However, generally well tolerated.

(18:29):

So really nice study. This study was a study that contributed to the data that was used by the FDA for the recent approval of zuranolone for the treatment of postpartum depression.

(18:41):

The next paper, which is related as I mentioned by Clayton and co-authors, basically is the same design but now looks at major depression, not postpartum depression. And it should be pointed out also that these are patients that were not treatment-resistant patients.

(18:57):

In this particular study, similar findings; reductions in depression scores were seen at a number of the time points. But what's different in this study from the standpoint of outcomes is that the remission rates between zuranolone and the placebo groups were not significantly different at 45 days. They differed for some reason at day three, but not at the other assessment days. So not as convincing from the standpoint of the strength of the effect, but certainly the effects were in the same direction and the same kinds of side effects as well, and also reductions in comorbid anxiety.

(19:32):

So all in all, these two papers contribute to the database for this new mechanism acting drug, a derivative or a synthetic derivative related to allopregnanolone and zuranolone with a recent approval by the FDA for the treatment of postpartum, but not for major depression.

Aaron Van Dorn (19:53):

Finally, we have a paper from Kumar and colleagues looking at subcortical brain alterations in genomic copy number variants. What did they find?

Dr. Ned Kalin (19:59):

This is another example of how we can take a gene-first approach to trying to understand psychiatric symptoms and psychiatric illnesses as well as the underlying brain alterations that may be related to those symptoms. So it sort of helps us think about how we can go from a genetic alteration to perhaps a brain alteration, to symptoms, to illness.

(20:27):

What these investigators did is they used a fairly large sample to look at what we call copy number variants. We've talked about these before. Copy number variants are relatively large components of a gene where there's a duplication of a sequence or a deletion of a sequence. Many copy number variants have been associated with neuropsychiatric illnesses or neuropsychiatric symptoms.

(20:53):

Perhaps one of the best studied and well-known is what is called the 22q11.2 deletion. Individuals that have this are at a marker risk to develop schizophrenia-like symptoms. They can also develop autism-like traits.

(21:09):

What this particular study did was to look at individuals across this group of 675 individuals that had these copy number variants. The authors focused on 11 depletion or duplication copy number of variants that are known to be associated with neuropsychiatric illnesses. What the question was was what did the brain alterations look like in these individuals? Did these different copy number variants have different patterns of brain alterations at a structural level, or in fact, was there overlap and did they have some similarities?

(21:45):

The reason this is interesting is because even though we can identify these genetic defects and link them to symptoms, the symptoms can be different in different individuals... we call that pleiotropy... of the way the gene is expressed, and also there can be shared symptoms across different genetic variants. So the question here now is at the brain level, are the brain changes distinct in relation to these distinct genetic alterations, or are they shared, or is there some combination of both?

(22:18):

What the researchers found I think is important. They found that there are some distinct brain alterations, and there are many shared brain alterations across these types of genetic alterations.

(22:30):

They also found that the genetic alterations or copy number variants that are most likely associated with psychiatric illness had the greatest number of brain changes from a standpoint of structure. Also, there was considerable overlap between a number of these copy number variant individuals. Suggesting that there's both shared and distinct components that are related to the brain alterations that may be underlying or at least associated with the symptoms that we see when individuals with these genetic alterations present with psychiatric symptoms.

(23:05):

In addition to this giving us insight into these specific genetic alterations as they relate to brain and also to behavior and symptoms, really this idea supports again, the genetics-first approach... Put that in quotes; genetics-first... linking genes to pathways in the brain, pathways to symptoms, and ultimately, the idea would be that this would help us develop new treatments as well.

Aaron Van Dorn (23:31):

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

Dr. Ned Kalin (23:34):

Oh, it's my pleasure. Have a good day.

Aaron Van Dorn (23:36):

You too.

(23:37):

That's all for this month's AJP Audio, but be sure to check out the other podcasts published by the APA.

(23:41):

This month on Psychiatric Services From Pages to Practice, Dr. Henry Chung joins Dr. Dixon and Dr. Berezin to discuss the differences between the collaborative care model and the co-location model and the impact on Medicaid cost and utilization for the treatment of patients with depression. That and much more can be found at psychiatryonline.org/podcast, or wherever you get podcasts.

Speaker 4 (24:00):

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