

Dr. Brenda Curtis and Dr. Lorenzo Leggio

Behind the Mask

January 2023

Brenda Curtis, Ph.D., Ms.P.H., Investigator in the Translational Addiction Medicine Branch, Chief in the Technology and Translational Research Unit, NIDA

Lorenzo Leggio, M.D., Ph.D., Clinical Director and Deputy Scientific Director, NIDA; Chief, Translational Addiction Medicine Branch, NIDA IRP; Chief, Clinical Psychoneuroendocrinology and Neuropsychopharmacology Section, NIDA/NIAAA

Note: Drs. Curtis and Leggio provided written responses about their COVID-19 work and experiences in January of 2023.

GB: Dr. Leggio, will you discuss some of your initial concerns for those with alcohol and substance use disorders in the early days of the pandemic and some of your recommendations for how to best meet their needs in COVID times that you describe in a 2020 *American Journal of Psychiatry* editorial? Where are we today? What are your main concerns?

LL: When we wrote that 2020 *American Journal of Psychiatry* editorial, we were at the beginning of the pandemic and in the middle of the lockdown. With that article, we wanted to increase awareness on a few clinical and public health concerns. First, patients with alcohol and substance use disorders often present with altered immune system and higher risk of infection, making them more vulnerable to COVID-19 infections and its sequelae. Second, it was clear that the COVID-19 pandemic, in addition to its medical consequences, was also a gigantic source of stress for everyone. Stress, fear, and anxiety are all significant risk factors that may contribute to the development and maintenance of alcohol and substance use disorders and for those in recovery, they represent important risk factors for recurrence. A third important point we made in that editorial was the significant concern that the lockdown and the pandemic in general could prevent patients to have access to addiction treatments. Accessing evidence-based treatments and providing care to patients with alcohol and substance use disorders was already a challenge even before the pandemic and our concern was that the COVID-19 pandemic was making that even worse.

GB: Dr. Curtis, will you speak about survey that you were a part of compiling and distributing that looked at the connection between loneliness and daily alcohol consumption during the COVID-19 pandemic including how you and your team went about recruiting participants, how you defined and measured loneliness, and how you went about analyzing the results? Will you speak about your findings including the interesting report that when people were feeling more depressed that drank less that day?

BC: We noticed some conflicting findings regarding the relationship between loneliness and alcohol consumption and realized that this may have been due to the disaggregation of between-person vs. within-person changes. Essentially, a person's average overall loneliness when compared to others may have a different effect on alcohol consumption than when the individual person is feeling lonelier than usual. More, the association between loneliness and alcohol consumption during widespread social isolation was unknown. To examine the effects on fluctuations on both within- and between- person loneliness and alcohol consumption, we designed a pilot study with 78 participants recruited online via Facebook to measure these fluctuations using daily ecological momentary assessments administered for 30 days.

At baseline we collected information on their household relationships and social distancing practices. The daily assessments measured loneliness by asking participants to rate their subjective feeling of loneliness, rating their satisfaction with their social support for the day, and tallying the number of face-to-face conversations each day. We then asked them to report their alcohol consumption for that day.

Our findings for between-person effects were consistent with our hypothesis that people who felt lonelier on average consumed more alcohol. However, within-person loneliness was marginally significant in the opposite direction of our hypothesis, meaning that individuals tended to consume less alcohol when they were feeling lonelier than usual. We think this could be due to the individual's preference for drinking in social situations, and this was supported by our exploratory analysis, where we found that those with more face-to-face conversations tended to consume less alcohol when they were feeling lonelier than usual.

GB: You were part of a similar study that delved deeper into the connection between loneliness and substance misuse tracking the daily number of alcoholic drinks, cannabis use, and non-cannabis drug use from October 2020-May 2021 in 2, 648 adults in the United States. Will you speak about the analysis of the data and some of your conclusions?

BC: Based on emerging data showing an increase in substance use during the pandemic, we wanted to leverage our pilot study design and expand our research to explore alcohol use as well as other substances and their association with subjective loneliness. This project aimed to elucidate associations between loneliness and daily substance use with intensive longitudinal data collected through a large daily diary study.

Again, we felt it was important to evaluate both the between- and within-person effects of loneliness on alcohol and substance use during the major social isolation period within the COVID-19 pandemic. We recruited a national sample of participants online using Qualtrics® Panel Services, and at baseline we collected information about participants' housing, employment, and COVID-19 impact measures. We also administered 25 psychological and behavioral assessment scales.

During the study we administered daily ecological momentary assessments, once a day surveys, that asked about loneliness in the ways described in the pilot study above (subjective rating of loneliness,

satisfaction with social support, and number of face-to-face conversations). We also asked participants to calculate their alcohol consumption, cannabis consumption, and consumption of other substances. Finally, we used data from the Oxford COVID-19 Government Response Tracker to create a daily score of the participant's degree of COVID restrictions for the participant's location.

To analyze the data, we used multilevel models to evaluate the within- and between-person effects of loneliness on daily number of alcoholic drinks, cannabis, and noncannabis drug use and examined the data descriptively to identify any seasonal effects (such as increased consumption during the holiday seasons).

The significant results from our analysis suggest that during the COVID-19 Pandemic, when social distancing guidelines were in place across the United States, adults drank more on days when they felt a particularly high or particularly low degree of loneliness beyond their individual average. Furthermore, feeling lonelier than usual was also a significant risk factor for noncannabis drug use. When looking at the linear effect of within-person loneliness, our findings replicated those in our pilot study. However, exploratory analysis revealed that when individuals consumed more alcohol when they felt "much more lonely than usual" or "much less lonely than usual," which may suggest that only severe changes in subjective loneliness supports an increased consumption of alcohol.

In contrast to our pilot study, there was no significant relationship between people's average loneliness levels and their daily alcohol use, an unexpected finding given the significant positive association we found in our pilot study and correlational analyses of baseline loneliness and alcohol measures. One possible explanation for the different within- and between-person effects of loneliness is that the context of individuals' alcohol use is a key factor, such as a preference to drink alone or drink in social settings. Thus, feeling lonely is a risk factor for those who drink alcohol alone, but people who report drinking in social settings may be less likely to drink when feeling lonely.

We did not find any significant relationship between increased loneliness and increased cannabis use. This may have been due to the average age of our population, which included more middle-age and older adults. Prior research suggests that whereas younger people use cannabis to relieve boredom, middle-aged and older adults are more likely to use cannabis to help with sleeping or to treat medical conditions (Haug et al., 2017).

The effect of loneliness on noncannabis use was more consistent with prior literature. There was a significant effect regarding within-person loneliness and increased use of noncannabis substances. Our results indicate that feeling "lonelier than usual" is a significant risk factor for noncannabis drug use. The finding that more severe lockdown restrictions were positively associated with noncannabis drug use also highlights how social restrictions have heightened risk of individuals with SUDs.

GB: Dr. Curtis, another study you were a part of examined women's substance abuse and mental health during the fall of 2020. Will you discuss some of the factors that made women particularly compelling to study?

BC: We felt it important to focus on women's wellbeing because women were experiencing greater unemployment and increased stress from childcare responsibilities than men during the COVID-19 pandemic. Moreover, COVID-19 restricted women's access to resources for intimate partner violence (IPV) while it also escalated their risk for IPV victimization. It is important to note, however, that this population of women was limited to cisgender women.

GB: Will you discuss the creation of this survey including the types of questions asked and the findings?

BC: A number of previously validated questionnaires were used to assess mental health, substance use, and other non-COVID specific measures. To assess the severity of the impact of COVID-19 on daily life, the question "How much does COVID-19 (coronavirus) impact your day-to-day life" was used (Harkness Behar-Zusman, & Safren, 2020). This item was scaled from 1 (Not at all) to 5 (Extremely). Other questions were asked regarding the specific impact of COVID-19, such as experiences of financial loss. A three-item scale was developed to measure anxiety specific to COVID-19. The scale included the following items: "During the past month, how often have you thought about your chances (or risks) of getting COVID-19?" "During the past month, how often have thoughts about your chances (or risks) of getting COVID-19 affected your mood?" and "During the past month, how often have thoughts about your chances (or risks) of getting COVID-19 affected your ability to perform daily activities?" All items were scaled from 1 (Not at all) to 4 (A lot). The average of these questions was used as the COVID-19 anxiety score for each individual ($\alpha = .76$). Location-based policy measures in response to COVID-19 were downloaded from the Oxford COVID-19 government response tracker (Hale et al., 2021). A lockdown index score was calculated by summing the closure policy indicators (e.g., school closures, restrictions of public gatherings). IPV was also assessed by adapting screener questionnaires from Heron, Thompson, Jackson, and Kaslow (2003) and Feldhaus, Koziol-McLain, Amsbury, Lowenstein, and Abbott (1997).

There was a significant positive relationship between the COVID-19 anxiety measure and mental health measures, including depression, anxiety, and perceived stress. Self-efficacy, loneliness, and intolerance of uncertainty were also related to COVID-19 anxiety. More, those with high-risk alcohol use scored higher in depression and anxiety than those with low-risk alcohol use.

GB: Will you comment on the strong correlation between domestic violence and coping with substances?

BC: With regards to IPV, approximately 30% of women surveyed stated that their IPV problems had gotten worse since the pandemic started, and about 17% said that they have increased their drug or alcohol use to cope with their relationship problems.

GB: What actionable items do you hope will come from this research including potential further studies on larger, more diverse populations?

BC: The large number of women experiencing mental health problems indicates a clear need for mental health services. As a response to the pandemic, many providers have offered more digital options for accessing medical services (frequently termed “telehealth”). Digital provision could expand access safely while helping overcome common barriers, such as distance and lack of reliable transportation. Based on findings from this study and others, we recommend that IPV should be included as part of mental health screening. Providing digital mental health screenings to patients and connecting them to treatment resources could be beneficial. Decoupling health insurance and employment could ensure continued access to health care, including mental health care, for those who have lost their jobs during the pandemic. In addition, given that our findings support previous commentaries suggesting increased risk for IPV victimization during the pandemic, we suggest increased use of screening tools for IPV in spaces that primarily serve women, such as obstetrics/gynecology clinics, in order to identify women in need of support.

GB: Dr. Curtis, what was your role in the study that explored COVID-related victimization, racial bias and employment and housing disruption Increase mental health risk among U.S. Asian, Black and Latinx adults?

BC: As the Principal Investigator on this study, I worked with the team on study conceptualization, methodology design, funding acquisition, and manuscript preparation. Based on recent trends of increased substance use among BIPOC during the pandemic in combination with historically inadequate substance use disorder (SUD) treatment and negative SUD outcomes, we wanted to examine the relationship and impacts between this newly increased substance use in combination with increasing trends in pre-existing health and socio-economic disparities, employment and housing disruptions, coronavirus victimization distress, and perceived societal racial bias among Asian, Black, Hispanic/Latino, and non-Hispanic White adults during the COVID-19 pandemic.

GB: Dr. Curtis, how did you become involved in the study that looked at the spread of misinformation about COVID by bots, and what were each of your roles?

BC: By March of 2021, there were over 115 million documented cases of COVID-19 and 2.5 million deaths worldwide. The United States accounted for almost 25% of all cases, more than any other country. At the same time, almost 75% Americans reported using an online news source for COVID-19 information, with almost 50% of those reporting that the online source was social media. More, preliminary research was showing that there was an acceleration of misinformation spreading online through social media platforms. Such misinformation could have real impacts on people’s access or willingness to seek

medical treatment or engage in effective preventative measures. Because of our experience analyzing the characteristics of tweets in our prior work, we felt we could effectively contribute to this examination.

GB: Was there a reason you focused on Twitter vs. other social media platforms?

BC: Twitter has generally had its pulse on the current issues in our society and is often a source utilized by journalists and referenced by newspapers. Further, most research involving bots and their online behavior has been with Twitter data. For this project, we were able to use a publicly available Bot Repository, which has been identifying and documenting Twitter bots for several years. This allowed us to identify bots and collect their tweets to analyze them for misinformation.

GB: Will you speak briefly about your process?

BC: Using a program that can collect tweets by particular users, we were able to collect over 3 million tweets posted by almost 4,000 bot accounts. We then searched for tweets that used COVID-19-related language.

GB: What were some of your findings?

BC: We found that over 50% of the bots were actively tweeting about COVID-19, corroborating the findings from other studies. Previous findings by other researchers noted that misinformation about COVID-19 was more likely to come from non-human accounts, and that those tweets contained a number of conspiracy theories, such as QAnon, in addition to retweeting links from partisan news sites, with headlines that often-featured content about the virus being created in a lab or being a biological weapon.

GB: Misinformation has been a problem for a while. What did you find particularly interesting, shocking, or revealing from this study?

BC: The potential for real-world impacts on people's health and safety. Examples of these real-world consequences include shortages of hydroxychloroquine (a drug that is crucial for treating lupus and malaria) due to increased demand from people who believed it would protect them from COVID-19. Moreover, belief in conspiracy theories about COVID-19 is associated with a decreased likelihood of engaging in protective measures such as frequent handwashing and social distancing, suggesting that

misinformation may even contribute to the severity of the pandemic. In addition, exposure to misinformation has been negatively correlated with intention to take a COVID-19 vaccine.

GB: Some of the trajectories for substance use were climbing even before SARS-CoV-2. How much can be attributed to the effects of the pandemic?

LL: The pandemic has played a key role in the additional climbing of alcohol and substance use worldwide. And indeed, its effects go beyond addiction and include mental and other medical issues at large (let's think about how many people missed their regular screenings for cancer, they missed their regular checks with their PCP, etc.). Let's use alcohol use disorder as an example. Unhealthy alcohol use is a leading cause of mortality and morbidity, with alarming increasing numbers even before the pandemic. Recent data from NIAAA indicate that the number of deaths involving alcohol increased between 2019 and 2020 (the first year of the COVID-19 pandemic) from 78 927 to 99 017 (relative change, 25.5%); the age-adjusted rate also increased from 27.3 to 34.4 per 100 000 (relative change, 25.9%).

GB: What are your concerns about those with substance use disorders whose issues will last longer than the pandemic? How can the US and other countries prepare for these scenarios?

LL: As mentioned before, in addition to the potential harmful role of the pandemic affecting individuals with current alcohol and substance use disorders, the pandemic may play a critical role in promoting heavy alcohol drinking, misuse of drugs, hence increasing the risk of future development of alcohol and substance use disorders. Indeed, stress as well as unemployment and related financial burden may all represent critical risk factors for the general population to develop alcohol and substance use disorders and/or other psychiatric disorders, which in turn may lead to alcohol and substance use disorders.

The best we can do to prepare for these scenarios is to fortify screenings and early interventions, including among adolescents. We need to identify soon individuals at risk of developing alcohol and substance use disorders and individuals who have developed initial, mild alcohol and substance use disorders, and we need to provide interventions right away that may prevent the development of these serious medical disorders.

GB: Dr. Leggio, will you speak about your participation in a longitudinal study that looked at the risk of burn-out and stress working on a COVID team?

LL: My role in that study was minor, yet I was thrilled to collaborate with that team in Rome (Italy). The main goal was to conduct a pilot study describing the risk of burnout and stress among physicians working in a COVID team during the initial phase of the pandemic in 2020. The main take-home message

was that, as specialty doctors were deployed to work in the COVID teams, they were at higher risk of burnout and stress, compared to those who were already working in internal medicine unit (so, already trained and used to manage complex clinical cases).

GB: Have you all contributed or plan to contribute to other COVID-19 initiatives at NIH or outside of NIH?

LL: Within NIH, and specifically at the NIDA IRP, I was part of our return to physical workspace committee that led the development of SOPs aimed at helping our staff to return to work on-site. In parallel, as one of the physicians in the program, I also contributed to the development of SOPs aimed at organizing the re-opening of our clinical operations, after the several months during which most of the clinical research was on hold.

GB:-What personal challenges and opportunities has the pandemic presented for you?

LL: On a personal note, I had a couple of challenges but to be honest, nothing compared to many other people whose lives and families were much more affected from the COVID-19 pandemic. One challenge was that my family is from and lives in Italy and you may remember that Italy was the first European country that was seriously hit by the COVID-19. So, living in the US and unable to travel there, and seeing many friends and colleagues struggling was quite concerning, especially the inability to help them more. Thankfully, my family remained safe during those challenging times. The other challenge was that while we had to put my NIH clinical research operations on hold and my entire team and I moved the full remote work, on the other side, my wife was working as an internal medicine resident in a community hospital and obviously not only couldn't she work remotely, but also her workload increased significantly. I was very worried for her while of course I was very proud of her and the fact that she helped so many patients during those quite challenging times.

Publications:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8499726/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8776461/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8139392/>

<https://pubmed.ncbi.nlm.nih.gov/32660296/>

<https://onlinelibrary.wiley.com/doi/10.1111/acer.14889>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9349236/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8239751/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8585986/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8646498/>

<https://pubmed.ncbi.nlm.nih.gov/37097736/>

<https://pubmed.ncbi.nlm.nih.gov/37033081/>

<https://pubmed.ncbi.nlm.nih.gov/37033081/>