Abstinence Among Alcohol Use Disorder Patients During the COVID-19 Pandemic: Insights From Spain

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Background: Patients with alcohol use disorder (AUD) are likely to suffer disproportionate harms related to the COVID-19 pandemic and related policy measures. While many surveys have been conducted, most are focused on drinking changes in the general population and validation with biological markers is lacking.

Method: We performed a retrospective cohort study among patients with AUD attending a urine drug screening program. With mixed-effects logistic regression models, we assessed the probability of screening positive for ethyl glucuronide according to patients’ main clinical characteristics and time of analysis (either prior to or after a lockdown was implemented in Spain).

Results: A total of 362 patients provided 2,040 urine samples (1,295 prior to lockdown, 745 during lockdown). The mean age of participants was 52.0 years (SD 12.6), and 69.2% were men. Of the 43% of patients tested for other drugs 22% screened positive. After adjusting for all covariates, the odds of screening positive for ethyl glucuronide during lockdown almost doubled (OR = 1.99, 95% CI 1.20 to 3.33, p = 0.008). Other significant covariates included testing positive for other drugs (OR = 10.79, 95% CI 4.60 to 26.97) and length of treatment (OR = 0.59, 95% CI 0.47 to 0.74).

Conclusions: Our data support an association between the lockdown due to COVID-19 and increased alcohol use in patients with AUD. Thus, addiction healthcare systems could face significant challenges ahead. In light of these findings, it is essential to evaluate prospectively how patients with AUD are affected by the pandemic and how health systems respond to their needs.

Key Words: Alcohol, Alcohol Use Disorder, Abstinence, Relapse, COVID-19.
population who were exposed to SARS showed an increase in drinking among previous alcohol users (Lau et al., 2005).

In line with this, preliminary evidence for the current COVID-19 pandemic points to a link between distress and increases in alcohol use in multiple countries (Georgiadou et al., 2020; Manthey et al., 2020a; Stanton et al., 2020; Wardell et al., 2020). Reports have described that perceived stress related to the pandemic was associated with increases in alcohol consumption in the general population (Rodriguez, Litt and Stewart, 2020) and in those who reported a history of heavy drinking (Manthey et al., 2020a). Survey findings suggest that the likelihood of increasing alcohol use during the pandemic increases with drinking levels, with high-risk drinkers being most vulnerable to drinking more often and drinking greater quantities during the first half of 2020 (Chodkiewicz et al., 2020; Manthey et al., 2020a).

Regarding this growing body of evidence, 2 main concerns are identified. First, there is a shortage of studies among heavy drinking persons or clinical populations—that is, among patients diagnosed with alcohol use disorders (AUD). While population-level changes during this worldwide pandemic are of public interest, the alcohol-attributable societal burden is heavily concentrated among people with AUD (Mohapatra et al., 2010). Moreover, with these increases in drinking levels, people with AUD worsen their state of health during the pandemic and further increase their risk of a severe COVID-19 course (Testino, 2020).

Second, the vast majority of the COVID-19-related literature is based on self-reports. While these are a standard practice in alcohol research, self-report measures for alcohol perform worse for heavy drinking persons and have several pitfalls for clinical populations (de Beaurepaire et al., 2007; Livingston and Callinan, 2015; Sommers et al., 2000; Zemore, 2012). Therefore, they should be complemented with the addition of other measures, such as wastewater analyses (Bade et al., 2020) or, for individual-level assessments, using biological markers for alcohol use (Barrio et al., 2016; Wurst et al., 2015).

As experts have recommended, alcohol consumption should continuously be monitored in order to understand the impact of COVID-19 upon drinking patterns (Clay and Parker, 2020; Rehm et al., 2020; Wright et al., 2021). In this paper, we aim to assess the changes in alcohol consumption and abstinence rates among patients with AUD attending an outpatient facility in Barcelona, Spain, covering a population area with 400,000 residents, as assessed by changes in the overall number of positive screens prior to and during lockdown. It is worth noting that the lockdown in Spain was one of the strictest in the world, with citizens only being allowed to leave their homes to buy food and other very basic needs (excluding, e.g., any possibility for outdoor physical activity).

### MATERIALS AND METHODS

#### Study Design and Subjects

We performed a retrospective cohort study. Data gathering was conducted via a review of electronic medical records. Patients included in the study had all been diagnosed with AUD and were attending an Addictions Unit outpatient service at a tertiary hospital in Barcelona, Spain. All included patients had to provide at least 1 urine specimen during the study time.

#### Procedure

Ethics approval was obtained from the local Institutional Review Board. Urine samples were collected from patients attending the outpatient service of the Addictive Behaviors Unit, where routine urine screening is an established procedure for monitoring abstinence and relapse prevention. Patients are routinely encouraged to provide frequent urine samples to allow for closer monitoring. As part of routine care, a nurse meets with the patients briefly and collects the samples prior to its analysis. Additionally, if patients regularly receive periodic psychiatric consultations as part of their care. Alcohol intake is assessed by screening for ethyl glucuronide in the urine sample, using immunoassay techniques (using Thermo Scientific equipment). The results of the assessments are made available to the patient, the nurse, and the psychiatrist responsible for the patient. As a positive urine screen is widely known to predict a higher likelihood of abandoning treatment (Barrio et al., 2017), patients are encouraged to keep attending the program irrespective of their results. In fact, it has been argued that sensitive assessments—such as those provided by ethyl glucuronide—allow for a more honest and deeper collaboration between patients and professionals (Barrio, Wurst and Gual, 2018). As such, positive screens are framed as an opportunity for clinicians to discuss difficulties in achieving abstinence with their patients.

For analysis purposes, 2 timeframes were defined. The first one was for a prelockdown period, specifically from January 31, 2020 to March 13, 2020—ending 1 day before the implementation of the lockdown. Lockdown was considered to last from March 14, 2020 to June 30, 2020 and represents the final timeframe for our analysis. It is important to note that attending medical appointments was allowed during the lockdown period, so the assessment routine in the 2 timeframes can be considered to be the same. The observation period was defined by the need to include a similar number of patients in both periods in order to have the sample sizes roughly balanced.

#### Measures

For each participating subject, we collected the following variables: age, sex, ethyl glucuronide (EtG) screening result as a binary outcome (positive or negative), treatment length (as assessed using the date of first urine screening in the patient’s medical record), the presence or absence of other drugs found in the urine sample (which was used as a proxy for addictive comorbidities).

#### Statistical Analyses

First, we performed descriptive analyses to assess variations of the probability of receiving a positive screening result across all patients visiting the clinic, based on the sex and age of the patient, their length of treatment, as well as other drug test results. To test whether the probability of a positive test result differed between the periods prior to and during lockdown, we performed mixed-effects logistic regression models, which allowed us to include random intercepts for each patient and estimate the probability of test results based on individual patient characteristics, as well as a dummy-coded lockdown variable. We included every urine screening test
result for all patients visiting the clinic during the 2 observation periods included in the models. Thus, patients visiting the clinic prior to but not during the lockdown were included in the analyses, which allowed us to adjust for differences in patient characteristics prior to and during lockdown.

Consecutive models were built, adding 1 variable of interest after another, and candidate models were compared using likelihood ratio tests. All analyses were performed in R version 4.0.2, and the mixed-effects regression models were performed using the lme4 package (R Core Team, 2020). We performed likelihood ratio tests to compare candidate models by comparing twice the difference in log-likelihoods to a chi-square distribution. The original data and R code detailing the analyses are published in the figshare repository (Manthey, 2020b; Manthey and Barrio, 2020c).

RESULTS

Globally, during our study period a total of \( N = 362 \) patients provided \( N = 2040 \) urine samples (\( N = 1295 \) prior to lockdown, \( N = 745 \) during lockdown). The mean age of participants was 52.0 years (SD 12.6), and 69.2% were men. Of all patients, 43% were tested for other drugs and 22% screened positive for any other drug.

Table 1 shows key characteristics for patients visiting the clinic prior to the lockdown, prior to and during lockdown, and those occurring only during the lockdown period. With the exception of the number of visits (\( p < 0.001 \)), ANOVA and chi-square tests indicated no differences between the 3 groups for the examined variables (all \( p > 0.05 \)).

In Figure 1, the number of total visits and the proportion of visits where there was a positive test for alcohol identified are presented. The figure illustrates that upon commencement of the lockdown, very few patients visited the center for a number of weeks. In the 28 days before the lockdown, there were \( N = 827 \) visits to the clinic, compared to \( N = 87 \) in the 28 days following the lockdown. The proportion of visits which resulted in a positive alcohol test did not differ between those 2 periods (before lockdown: 19.4%, during lockdown: 17.4%; Chi\(^2\) = 1.04, \( p = 0.308 \)).

Results from descriptive analyses of potentially confounding variables suggested that the likelihood of testing positive did not vary between the sexes (probability across all visits by females: 18.8%; probability across all visits by males: 18.6%), across tests for other drugs (probability across all visits without a test: 18.1%; probability across all visits with a test: 19.6%), but did vary across age and length of treatment (with the probability of screening positive decreasing with length of treatment and increasing with age; see Figures S1 and S2) and the result of the testing for other drug(s) (probability across all visits with negative other drug test: 16.1%; probability across all visits with positive other drug test: 31.3%). On average, 1302.7 days had passed since patients began their treatment at the clinic; however, treatment length differed across sex (females: 1666.4 days; males: 1143.9 days) and age (18 to 39 years: 874.6 days; 40 to 59 years: 1481.8 days; 60 + years: 1202.8 days). Given the skewed distribution of sample characteristics recorded before and after lockdown, all possibly confounding variables were considered in the regression models.

In 6 subsequent models, all possibly relevant confounding variables were entered (see Table 2). The 6th model included all relevant variables and provided a best model fit according to AIC criteria and log likelihood. In likelihood ratio tests, this model showed improved fit over the other 5 models (all \( p < 0.001 \); for detailed results, see Supporting information).

Only in this model—which accounting for differences between patients with regards to sex, age, other drug tests and their results—did the odds for being tested positively for alcohol double during the lockdown period compared to the 6-week comparison period prelockdown (OR = 1.99, \( p = 0.008 \)). There was also a strong negative association with treatment length, with a 1% increase in treatment length being associated with a 40% reduction in testing positive for alcohol at any given visit. Lastly, patients testing positive for any other drug had a more than 10-fold chance for testing positive for alcohol.

DISCUSSION

While we are still in the midst of the COVID-19 pandemic, some of its short-term consequences can already be elucidated. In this study, we found that the odds of screening positive for alcohol in patients with AUD following outpatient care doubled during the 14-week period after the lockdown was implemented in Spain. Our findings thus corroborate the elevated risk of relapse among patients with AUD during the first wave of the COVID-19 pandemic (Kim et al., 2020).

Interestingly, one of the most significant covariates found in this study was the presence of other drugs in the urine, with higher positive test results being recorded after lockdown. Comorbid drug use is a well-established risk factor for relapse in AUD. What remains to be elucidated is whether a higher rate of positive drug tests is the result of increased
drug use during lockdown. Survey findings tend to present mixed results on that matter (EMCDDA, 2020; Rolland et al., 2020), while respective evidence among populations with AUD are not known to the authors.

Due to the nature of our data, we were not able to examine the underlying drivers for the increased relapse risk. A number of risk factors for relapse are well established, including but not limited to individual (e.g., medication adherence, comorbidity), social (e.g., support and activities), and environmental factors (e.g., presence of alcohol cues) (Carvalho et al., 2019; Sliedrecht et al., 2019). During the pandemic, it can be reasonably expected that more than one of these factors has changed for the worse, increasing the risk for relapse among patients with AUD. For instance, relevant increases in the levels of mental health distress were found for the general population in the UK (Pierce et al., 2020). If patients

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**Table 2. Results From Multilevel Logistic Regression Models**

|                          | Model 1          | Model 2          | Model 3          | Model 4          | Model 5          | Model 6          |
|--------------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Treatment length (centered and logarithmized) | 0.63*** (0.51 to 0.77) | 0.61*** (0.48 to 0.74) | 0.60*** (0.48 to 0.74) | 0.60*** (0.48 to 0.74) | 0.60*** (0.48 to 0.74) | 0.59*** (0.47 to 0.74) |
| Lockdown (ref: before)   |                  |                  |                  |                  |                  |                  |
| Sex (ref: male)          | 1.49 (0.47 to 4.78) | 1.48 (0.47 to 4.78) | 1.54 (0.49 to 5.01) | 1.46 (0.46 to 4.74) |                      |                  |
| Age group 18 to 39 years |                  |                  |                  |                  |                  | 1.37 (0.29 to 6.78) |
| Age group 40 to 59 years |                  |                  |                  |                  |                  | 1.57 (0.33 to 8.10) |
| Age group 60+ years      |                  |                  |                  |                  |                  | 1.66 (0.34 to 8.72) |
| Tested for other drug    |                  |                  |                  |                  |                  |                  |
| Tested positive for other drug | 1.59 (0.29 to 9.22) | 1.56 (0.29 to 9.22) | 2.03 (0.34 to 12.88) | 2.27 (0.38 to 14.81) | 0.53 (0.21 to 1.34) |
| Constant                 | 0.03** (0.01 to 0.06) | 0.02** (0.01 to 0.05) | 0.02** (0.01 to 0.05) | 0.02** (0.003 to 0.07) | 0.01** (0.002 to 0.06) | 0.01** (0.001 to 0.05) |
| Observations             | 2,040            | 2,040            | 2,040            | 2,040            | 2,040            | 2,040            |
| Log Likelihood           | −649.4           | −647.8           | −647.6           | −647.5           | −647.1           | −631.0           |
| Akaike Inf. Crit.        | 1,304.8          | 1,303.7          | 1,305.2          | 1,308.9          | 1,310.0          | 1,280.0          |
| Bayesian Inf. Crit.      | 1,321.7          | 1,326.16         | 1,333.3          | 1,348.3          | 1,355.0          | 1,330.6          |
| Likelihood ratio test    | 36.84**          | 33.68**          | 33.21**          | 32.92**          | 32.05**          |                  |

Presented are odds ratios (95% confidence intervals) from multilevel logistic regression analyses, including a random intercept for each patient. *p < 0.01; **p < 0.001.

*aReported are chi-square from likelihood ratio tests, comparing each model with Model 6.*
with AUD experience enhanced levels of distressors, they may be more likely to consider alcohol use as an option to help them cope. It should be further noted that during the lockdown alcohol was widely available in supermarkets and other essential stores that were kept open. Thus, patients with AUD had alcohol use as one readily available activity, while social support or other activities were less available. The fact that alcohol in Spain is among the cheapest in the whole EU (Palle, 2020; The WHO Regional Office for Europe, 2020) may have further increased the risk of relapse for people with AUD during the pandemic.

Taken together, our findings bear important implications for the near future. First, addiction healthcare systems could be facing relevant challenges ahead (López-Pelayo et al., 2020). More frequent and severe withdrawals as well as increased alcoholic liver disease have already been reported in the literature due to the pandemic (Da, Im and Schiano, 2020; Narasimha et al., 2020). Given the expected economic crises, another key challenge is resource allocation, where SUD services must compete with elective surgery and other procedures that have been put on hold during the pandemic. In addition, as has been seen throughout the history of addiction treatment, SUD services will probably have to battle against stigma (Volkow, 2020). Different solutions could help addiction services face these impending challenges. For example, telemedicine and digital solutions have shown favorable results for the reduction of alcohol use and other related outcomes, such as a reduction in depressive symptoms, increased satisfaction, and, also importantly, reduced costs (Kruse et al., 2020). Other relevant interventions could include home hospitalizations, and consultation-liaison addiction services provided in general hospitals with an emphasis on integrated addiction care.

Several limitations must be considered when interpreting the findings of this study. Most importantly, its retrospective and observational design precludes the establishment of causality links. It should also be noted that data gathering was performed through electronic health records, and therefore many relevant mediator variables such as perceived distress could not be incorporated into the statistical models. Also worth noting is that the short-term nature of this study should be complemented in the future by long-term studies assessing the links between COVID-19 and addiction behaviors.

CONCLUSIONS

More time and more studies will be required to fully understand and evaluate the impact of COVID-19 upon patients with addictive disorders. The short-term evidence provided by this study suggests that the distress hypothesis could play a significant role in the effects of COVID-19 pandemic upon patients with AUD, with increases in consumption already observed. Treatment length and comorbid drug use seem to be relevant variables related to these increases. It remains essential to prospectively evaluate how this population evolves and how health systems respond to their growing needs.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Fig S1. Probability of visit with a positive alcohol test, depending on length of treatment (logarithmized).

Fig S2. Probability of visit with a positive alcohol test, depending on patient age.