

New Challenges in Addiction Medicine: COVID-19 Infection in Patients with Alcohol and Substance Use Disorders – The Perfect Storm

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Funding sources: Intramural Research Programs of the National Institute of Drug Abuse (P.A.S., C.M., L.L.), National Institute on Alcohol Abuse and Alcoholism (L.L.) and National Institute on Neurological Disorders and Stroke (P. A. S.). The content of this article does not necessarily represent the official views of the funders.

Disclosures: all authors are U.S. government employees. Outside of his government work and employment, Dr. Leggio receives royalties from Rutledge for having served as Editor of a textbook and he receives a honorarium from the U.K Medical Council on Alcoholism for serving as Editor-in-Chief for Alcohol and Alcoholism

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Unfortunately for Mariners, the total amount of wave energy and storm does not rise linearly with wind speed, but to its fourth power. The seas generated by a 40-knot wind aren't twice as violent as those from a 20-knot wind, they are seventeen times as violent.

— Sebastian Junger, *The Perfect Storm: A True Story of Men Against the Sea*

The 2019 coronavirus disease (COVID-19) represents one of the worst acute pandemics of the last century. Among many ongoing efforts, it is important to identify categories of patients more susceptible to COVID-19 infection and its sequelae. Here, we aim to raise awareness of patients with alcohol and substance use disorders (ASUD). These disorders represent a dramatic public health crisis, which is taking a massive toll on individuals and society. As the *opioid epidemic* has shown us, responding to this crisis is challenging, since many factors (e.g. neurobiology of ASUD, availability and access to effective treatments, prevention strategies, socio-cultural context) need to be addressed simultaneously. With the current COVID-19 pandemic, tackling the ASUD crisis may result even more problematic, because, as in a *perfect storm*, a combination of elements concurs to worsen the already complex clinical conditions of ASUD patients. The consequences of this *storm* may spread long after the pandemic is resolved, and may affect a large proportion of the population, beyond individuals with current ASUD.

Individuals with ASUD present specific medical risk factors, making them more vulnerable to COVID-19 infections and its sequelae. Both alcohol and drugs of abuse dampen the immune system response (1), increasing the risk of respiratory infections and their complications. Moreover, patients with ASUD may be more prone to develop infection-related consequences, given the high rates of cardiovascular and pulmonary comorbidities linked to alcohol, opioids and

stimulants misuse. There are also reports of cerebral involvement by COVID-19 (2) that could have an impact on mental state and/or alcohol and substance use and it is conceivable that such direct interaction between virus and the abnormal brain in patients with ASUD may exacerbate both disorders. Furthermore, cannabis and nicotine consumption are linked to specific COVID-related risk factors and smoking is often associated with prolonged respiratory symptoms that may overlap with COVID-19 symptoms, leading to misdiagnosis and unnecessary hospital admissions. Disruption of illicit drug markets and liquor shop's closure may result in increased risk of withdrawal, which for alcohol in particular, may have life-threatening consequences, but may also induce patients to engage in higher-risk behaviors in order to alleviate withdrawal (e.g. drinking toxic products containing ethanol; violating quarantine to seek for drugs), which can further expose them to COVID-19 infection or other harms. People who inject drugs may suffer from low availability of sterile products, increasing risks of HIV and other infections (1).

The COVID-19 pandemic is also acting as a serious stressor, with millions of individuals experiencing fear, anxiety and social isolation over a prolonged period. Protracted exposure to stress has long been known to increase symptoms severity (e.g. craving, consumption) and risk of relapse in patients with ASUD. Furthermore, a positive association has been reported between exposure to stress during both adolescence and adulthood and vulnerability for ASUD (3). For example, higher use of alcohol and drugs has been found in survivors of traumatic events like Hurricane Katrina (see e.g. 4-5) and the September 11, 2001 terrorist attacks (see e.g. 6-7).

Chronic stress may trigger alcohol and drug use by inducing profound adaptations in circuits implicated in motivation, reward, behavioral and cognitive control. These alterations lead to impulsivity, poor decision-making, malaise and negative emotional states, and decreased ability to regulate stress, all factors contributing to increased risk for ASUDs. Importantly, dysfunctions

in these circuits are also observed as the consequence of prolonged exposure to alcohol and drugs, indicating that stress and addictive agents interact synergistically to drive and maintain compulsive alcohol and drug use. It is crucial to consider that stress-, alcohol- and drug-related alterations in the brain are all long-lasting, thus indicating that their effects persist even when the stressor passes and/or the individual reaches abstinence (8, 9). Specific examples of factors associated with stress and their consequences that contribute to ASUDs include, pain perception, social isolation, and access to appropriate treatments, as detailed next.

For example, chronic stress has a strong influence on pain sensitivity, with individuals experiencing either analgesia or hyperalgesia in response to different stressors (10,11). Increased pain perception, via exposure to chronic stress or in response to chronic alcohol and opioid exposure, may further promote ASUD (10,11).

Social isolation represents another important factor by which the COVID-19 outbreak will likely impact ASUDs-related outcomes. Prolonged exposure to social isolation, which can be considered itself a stressor, has been consistently linked with increased vulnerability to alcohol and drug use (12). Furthermore, there is evidence that the efficacy of several interventions for ASUD, including AA and NA, relies on providing social support to patients. As individuals are required to spend more time at their residence, a surge in at-home alcohol drinking and drug use may happen, especially among those individuals already at risk. Notable is also the increased risk of domestic harms, including domestic violence, related to substance use, especially alcohol.

Finally, we need to consider the challenges related to the availability and access to treatments for individuals with ASUD during the COVID-19 pandemic. These challenges are not new *per se*, in fact evidence-based treatments are often not provided to individuals with ASUD (13). This significant medical and public health issue is related to several and distinct, yet partially

overlapping, reasons which include current stigmas surrounding the misuse of alcohol and drugs, the lack of appropriate access to resources to combat addiction, the limited education and training on ASUD provided during medical schools, residencies and other clinical programs. All these issues may be further complicated during the COVID-19 pandemic. Subsequently, individuals suffering from ASUD may be even more marginalized in a phase where the urgency of addressing a serious and deadly pandemic may take priority over managing this chronic health condition. Patients with ASUD may fail to continue their usual treatment program or to initiate one, they may not have easy access to medications to curb craving and withdrawal, and may experience large unmet needs, because of services availability and financial barriers, but also as the consequence of stigmatization. Furthermore, patients may experience decreased availability of both social and health care resources even after the COVID-19 pandemic will resolve, as previously reported.

In this context, we should use any means available (see also NIAAA and NIDA websites). Online mutual support programs could be effective in helping individuals with ASUD (14). Online counseling and meetings with care providers can be very helpful when in person treatment options are not available. Clinicians can use telemedicine to evaluate withdrawal symptoms and associated risks, avoiding frequent emergency room (ER) visits. Telemedicine can and should also be implemented to provide behavioral treatments with proven efficacy in patients with ASUD (see e.g. 15) who are attempting to reduce or stop alcohol and/or drug misuse as well as for those individuals working to maintain recovery/abstinence. However, patients with ASUD often suffer of low social economic status and poor living conditions and patients living in shelters or who cannot bear the cost of electronic tools, may find difficult to access telemedicine or other online services.

If necessary, medications for alcohol and opioid use disorders and for smoking cessation may be prescribed remotely. Additional benefits from remote therapies include the application of targeted and effective personalized interventions reducing the frequency of in-person visits as well as prescription refills (e.g., depot buprenorphine as it offers the opportunity to limit treatment contacts to once a month). The amounts of take-home methadone may be increased, which is important because if patients need to get into long lines and crowded spaces for methadone, this can make difficult to comply with physical distancing recommendations. Harm reduction programs, including community-based programs offering naloxone distribution, should also be broadly implemented as part of the COVID-19 response.

Finally, it is also important to keep in mind that, in addition to the potential harmful role of the ongoing pandemic affecting individuals with current ASUD, the pandemic may play a critical role in promoting heavy alcohol drinking, misuse of drugs, increasing the risk of future development of ASUD. Indeed, stress and social isolation as well as unemployment and related financial burden may all represent critical risk factors for the general population to develop ASUD and/or other psychiatric disorders, which in turn may lead to ASUD.

In conclusion, ASUD patients face unique vulnerability factors during this dramatic global health crisis. Considering the current and long-term impact that the COVID-19 outbreak will have on individuals with ASUD, it is critical to ensure these patients continue to have access to available and appropriate treatments. Indeed, in the current unprecedented times, treatment services for patients suffering with ASUD should be enhanced and access be prioritized and maintained.

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