



Research on substance use disorders during the COVID-19 pandemic[☆]

Nora D. Volkow, Carlos Blanco^{*}

National Institute on Drug Abuse, 6001 Executive Boulevard, Bethesda, MD 20852, United States of America

ARTICLE INFO

Keywords

COVID-19
Health services research
Health disparities

ABSTRACT

The COVID-19 pandemic has triggered changes in the substance use disorder (SUD) treatment delivery system, in the availability of legal and illicit drugs, and in other social and economic factors. As such, these changes necessitate that the field re-evaluate research approaches to SUDs, including in epidemiology, clinical trials, health services, implementation and policy research, as well as basic and translational neuroscience.

COVID-19 has reduced researchers' access to target populations and made it difficult for them to obtain timely data to monitor changes in patterns of drug use and overdoses. These changes have increased researchers' interest in virtual technologies to expand and accelerate access to populations; increased modifications in the design, conduct, and analysis of clinical trials; and increased emphasis on implementation. Similarly, as researchers better understand the biology of COVID-19, they will better understand potential effects of COVID-19 on neurotransmitter receptors and signaling pathways, mechanisms underlying COVID-19 associated neurological and psychiatric sequelae, and interactions between COVID-19 treatments and psychoactive substances. The pandemic has also revealed the need for research that addresses health disparities.

Overall, the COVID-19 pandemic has challenged several aspects of current research on SUD. Responding to these challenges provides opportunities to develop robust research approaches that align with the goals of improving patient outcomes and public health and are resilient to the challenges of future crises.

1. Introduction

The COVID-19 pandemic has triggered changes in the treatment delivery system, in the availability of legal and illicit drugs, and in other social and economic factors that directly impact individuals suffering from a substance use disorder (SUD). As such, these changes necessitate a re-evaluation of research approaches to SUD (Luykx et al., 2020), including epidemiology, clinical trials, health services, and policy research, as well as basic and translational neuroscience.

2. Epidemiology

COVID-19 has exacerbated a barrier to research that already exists—access to target populations and difficulty obtaining timely data to monitor changes in patterns of drug use and overdoses. Those data are necessary to inform the efficient and equitable allocation of health resources, to track shifts in drug markets, and to identify vulnerable groups (Blanco, Compton, & Volkow, 2021). With the expansion of cell

phones and virtual technologies, increased access to the web across populations, the proliferation of wearables that can monitor patients' activities without physical contact (e.g., sleep and heart rate variability), and the ability to mail biological specimens, research has been afforded the opportunity to scale up alternative means of data collection on substance use and associated behaviors.

Information about the prevalence and geographic distribution of overdoses and opioid fatalities, which has been hard to obtain amid the COVID pandemic, could be improved through initiatives such as the Overdose Detection Mapping Application Program (ODMAP). ODMAP, developed by the Washington/Baltimore Drug Intensity Traffic Area (W/B HIDTA), provides near real-time suspected overdose surveillance data across jurisdictions by linking first responders and relevant record management systems (such as EMS, law enforcement, and health care data) to a mapping tool to track overdoses. Predictive analytic models to forecast future overdose mortality, using publicly available information and data from multicomponent overdose surveillance system, if sufficiently accurate, may also offer alternatives for faster data collection and

[☆] The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of the National Institute on Drug Abuse, the National Institutes of Health or any US government agency.

^{*} Corresponding author.

E-mail addresses: nvolkow@nida.nih.gov (N.D. Volkow), carlos.blanco2@nih.gov (C. Blanco).

<https://doi.org/10.1016/j.jsat.2021.108385>

Received 15 December 2020; Received in revised form 2 February 2021; Accepted 4 April 2021

Available online 8 April 2021

0740-5472/Published by Elsevier Inc.

policy response.

Similarly, school closings during COVID-19 have jeopardized the ability of those conducting Monitoring The Future (MTF; an annual national survey on drug use conducted in school classrooms) to collect data in person. COVID-19 will likely trigger a swift switch to web-based surveys, and researchers have already initiated studies to assess comparability of results using different data collection methods (Miech et al., 2020). Additionally, researchers need approaches to better cover hard-to-reach populations (e.g., incarcerated or homeless) or those without internet access, and data collection methods that are more timely and representative of the population and that combine multiple modalities.

3. Clinical trials

The shift toward telemedicine and patient's avoidance of hospitals and clinics to prevent infections has interfered with clinical trials recruitment, obtaining informed consent, and with patients' medical evaluations. Thus, researchers may need to modify procedures for clinical trials to increase feasibility and relevance to clinical practice as the pandemic evolves, such as allowing for informed consent through telehealth. Providers can also use telehealth to monitor adherence to treatment and improve retention. Studies that experienced interruptions or adaptations during the pandemic also face challenges to their analyses and interpretation, as treatment conditions might be very different from the original baseline and will continue to evolve, along with the pandemic. Researchers should develop and apply statistical techniques to address these challenges.

Also, as health resources and staff were diverted to deal with COVID-19, some of the structure and support that studies need might not be available, which might require simplifying face-to-face encounters and maximizing telehealth evaluations. Regional and national variations in the pandemic add another layer of complexity to multisite studies and studies will need to use statistical approaches that take into account those varying conditions to generate valid inferences.

4. Health services research

Shortly after the onset of the pandemic, several institutional review boards (IRBs) required that studies stop if they did not directly benefit participants. Several factors may have influenced those decisions, such as protecting research staff from being infected and complying with stay-at-home orders. However, because an ultimate goal of research is to improve patient outcomes and public health, these IRB decisions suggest the need to better align that goal with current research. These decisions reveal the need for improved collaboration between research and clinical practice, i.e., the development of learning health care systems and more broadly, greater focus on implementation (Blanco, Compton, & Volkow, 2021; Blanco, Wiley, et al., 2020). Although the need for implementation research is not unique to the challenges of the pandemic, the disruptions that COVID-19 has caused have further highlighted the need to develop systematic knowledge on how to adapt and scale up services to new settings, situations, and populations without compromising quality and the application of research into practice. A better alignment between patient goals and needs, and between research studies and implementation science can help to eliminate health care disparities.

Individuals with SUD and HIV or hepatitis C (HCV), who face the competing needs of their medical care, often face even greater stigma than those without these co-occurring conditions. As the pandemic has led to a reallocation of resources, individuals with SUD and co-occurring conditions may be disproportionately affected. As resources have become scarcer and practitioners have prioritized other needs, integration of care for SUD and general medical care may have slowed down. Studies on implementation and scalability of approaches that integrate general medical care with treatment for SUD represent an important research

opportunity. While integrative models are gaining ground in outpatient clinics (Blanco & Volkow, 2019), they have been understudied in inpatient settings, despite their potential to improve hospital outcomes, decrease costs, and increase patient satisfaction and linkage to outpatient treatment (McNeely et al., 2019; Schranz & Barocas, 2020).

The pandemic has disproportionately affected underserved minorities (Webb Hooper et al., 2020), increasing awareness of and the urgent need to eliminate racial and ethnic health disparities, including those among those with SUD (Khatri et al., 2021; Yang et al., 2020). To eliminate these disparities, policymakers and practitioners need to address the socioeconomic factors that increase this population's risk for worse outcomes, including improving access to quality education and health care. In the prevention and treatment of SUD practitioners should consider interventions that are adaptable for diverse populations, but that maintain their scalability. Interventions without sufficient flexibility may not be responsive to these populations' cultural sensitivities, while interventions that are difficult to adapt beyond a specific social or cultural group may not be sustainable. Policy-makers and treatment providers must address modifiable social determinants of health—such as access to education and housing, economic opportunities, and structural racism—to help to eliminate racial disparities in SUD treatment.

As with clinical trials, interpreting the findings of many health services studies will be challenging for scholars and practitioners. For example, in stepped wedged designs, the effect of the intervention may be hard to disentangle from the effects of changing conditions in the treatment system as the pandemic evolved. Interventions may have different effects if provided during a lockdown period than when vaccination rates increase and physical distance conditions change. Observational studies will face similar challenges, although if pre-COVID data exist, research could use the pandemic as an instrumental variable to compare the effects of interventions under different conditions (e.g., in-person versus virtual provision of care), such as virtual emergency systems for delivery of naloxone for overdose reversal as more people inject alone due to social distancing.

Research may be able to overcome limitations of traditional research approaches by using larger datasets (such as from EHR, from emergency medical services surveillance and emergency departments) and artificial intelligence to identify associations and uncover patterns and trends in prescriptions, SUD diagnoses or COVID diagnoses in those with SUD, and mortality from overdoses or from COVID-19 in individuals with SUD (Wang, Kaelber, et al., 2021). Simulations, which have been helpful in guiding strategies to contain COVID, also hold promise for evaluating different service provision approaches relevant to SUD due to their relatively low cost, and ability to efficiently examine a larger number of competing scenarios or estimate the effect of interventions in alternative settings (Hoertel et al., 2020; Horwitz et al., 2019).

5. Policy research

Although vaccine rollout and improved treatments are key to eliminating COVID-19, current approaches rely on policy interventions, such as physical distancing, use of face coverings, and limits on gathering size. The success of these approaches has led to calls for randomized trials of select interventions to support evidence-based policy. Research should examine the transportability of policies across countries, particularly their adaptation to low- and middle-income countries. COVID-19 forced temporary policy changes that now facilitate take home methadone medication, initiation of buprenorphine via telehealth, and approval for telehealth reimbursement, which have facilitated access to treatment among those with SUD. Some have called to maintain and possibly expand changes in state licensing for health care professionals, which could increase access to service, particularly in under-resourced areas (Mullangi et al., 2021). Research that evaluates the effects of these policies on quality of care and outcomes will help to guide how to optimize their benefit during and post-COVID. Treatment

providers and policy-makers should better document and overcome the digital divide that limits access to services to underserved populations by increasing access to broadband internet and other technologies (e.g., tablets), improving digital literacy, and adapting virtual therapeutics to the needs and preferences of the target populations (Eruchalu et al., 2021).

Policy-makers have also implemented policy changes directed at special populations, such as those directed at children and their return to school. Data do not yet exist on the effects of long periods of physical absence from schools and of limited social interactions on children's development and their patterns of drug use. Furthermore, research on universal approaches to substance use prevention, which often take place in school settings, has been hampered by major education shifts toward use of digital platforms for schooling. Further complicated matters, the populations at greater risk of substance use often have fewer resources and thus lower access to virtual delivery modalities (Marsch & Borodovsky, 2016).

Research has long recognized the need for new approaches to treatment and prevention for SUD in justice settings and the COVID pandemic has raised the urgency to address this need (Blanco, Wiley, et al., 2020). To reduce the risk of COVID infection among incarcerated individuals, many nonviolent offenders who were incarcerated for substance-related crimes were released into the community or if charged during the pandemic were not incarcerated. In parallel, the expansion of telehealth services into jails and prisons that occurred during the pandemic has enhanced the capacity to provide treatment for SUD and comorbid psychiatric disorders and co-occurring medical conditions. Access to new extended-release medications to treat opioid use disorders might also facilitate their use in incarcerated populations and research evaluating their effectiveness would help to accelerate implementation.

6. Ethical issues

Conducting research in the context of COVID-19 also raises ethical questions. For example, in the United States, regulations aimed at protecting individuals in correctional settings impose barriers to their participation in potentially beneficial research studies, such as studies involving vaccines or medication development, even though justice-involved individuals are at increased risk of COVID-19 infection (Persad et al., 2020; Wang, Zenilman, & Brinkley-Rubinstein, 2020). The ethics or equitable allocation of vaccines, access to testing or other scarce diagnostic or treatment resources are also under discussion and deserve careful ethics research to inform decisions regarding the current pandemic and any future crisis (Persad et al., 2020; Wang, Zenilman, & Brinkley-Rubinstein, 2020).

7. Basic and translational science

Emerging evidence suggests that individuals with SUD are at increased risk of being infected by COVID-19 and, once infected, have worse outcomes (Wang, Kaelber, et al., 2021). As researchers better understand the biology of COVID-19, opportunities for basic and translational research will arise, including understanding the potential effects of COVID-19 on neurotransmitter receptors and signaling pathways, mechanisms underlying COVID-19 associated neurological and psychiatric sequelae, and interactions between COVID-19 treatments and psychoactive substances. Understanding the effects of COVID-19 on brain development and the consequences from the stress associated with the pandemic and the shift of social interactions and learning from physical to virtual is important to inform new interventions.

8. Conclusion

The COVID-19 pandemic has challenged several aspects of current

research on SUD. Responding to these challenges provides opportunities to develop robust research approaches that are aligned with the goals of improving patient outcomes and public health and resilient to the challenges of future crises.

Declaration of competing interest

Drs. Blanco and Volkow report no conflicts of interest.

References

- Blanco, C., Compton, W. M., & Volkow, N. D. (2021). Opportunities for research on the treatment of substance use disorders in the context of COVID-19. *JAMA Psychiatry*, 78(4), 357–358. <https://doi.org/10.1001/jamapsychiatry.2020.3177>.
- Blanco, C., & Volkow, N. D. (2019). Management of opioid use disorder in the USA: Present status and future directions. *Lancet*, 393(10182), 1760–1772. [https://doi.org/10.1016/S0140-6736\(18\)33078-2](https://doi.org/10.1016/S0140-6736(18)33078-2).
- Blanco, C., Wiley, T. R. A., Lloyd, J. J., Lopez, M. F., & Volkow, N. D. (2020). America's opioid crisis: The need for an integrated public health approach. *Transl Psychiatry*, 10(1), 167. <https://doi.org/10.1038/s41398-020-0847-1>. 32522999.
- Eruchalu, C. N., Pichardo, M. S., Bharadwaj, M., Rodriguez, C. B., Rodriguez, J. A., Bergmark, R. W., ... Ortega, G. (2021, Jan 20). The expanding digital divide: Digital health access inequities during the COVID-19 pandemic in New York City. *J Urban Health*, 1–4. <https://doi.org/10.1007/s11524-020-00508-9> (Online ahead of print).
- Hoertel, N., Blachier, M., Blanco, C., Olsson, M., Massetti, M., Rico, M. S., ... Leleu, H. (2020). A stochastic agent-based model of the SARS-CoV-2 epidemic in France. *Nat Med*, 1417–1421. <https://doi.org/10.1038/s41591-020-1001-6> (Epub 2020 Jul 14).
- Horwitz, L. I., Kuznetsova, M., & Jones, S. A. (2019). Creating a learning health system through rapid-cycle, randomized testing. *N Engl J Med*, 381, 1175–1179. <https://doi.org/10.1056/NEJMs1900856>. 31532967.
- Khatri, U. G., Pizzicato, L. N., Viner, K., Bobyock, E., Sun, M., Meisel, Z. F., & South, E. C. (2021, Jan 4). Racial/ethnic disparities in unintentional fatal and nonfatal emergency medical services-attended opioid overdoses during the COVID-19 pandemic in Philadelphia. *JAMA New Open*, 4(1), Article e2034878. <https://doi.org/10.1001/jamanetworkopen.2020.34878>.
- Luyckx, J. J., Vinkers, C. H., & Tjebkink, J. K. (2020). Psychiatry in times of the coronavirus disease 2019 (COVID-19) pandemic: An imperative for psychiatrists to act now. *JAMA Psychiatry*. <https://doi.org/10.1001/jamapsychiatry.2020.1225>.
- Marsch, L. A., & Borodovsky, J. T. (2016). Technology-based interventions for preventing and treating substance use among youth. *Child and Adolescent Psychiatric Clinics of North America*, 25, 755–768. <https://doi.org/10.1016/j.chc.2016.06.005>. Epub 2016 Aug 3 27613350.
- McNeely, J., Troxel, A. B., Kunins, H. V., Shelley, D., Lee, J. D., Walley, A., Weinstein, Z. M., Billings, J., Davis, N. J., Marcello, R. K., Schackman, B. R., Barron, C., & Bergmann, L. (2019, Feb 19). Study protocol for a pragmatic trial of the Consult for Addiction Treatment and Care in Hospitals (CATCH) model for engaging patients in opioid use disorder treatment. *Addict Sci Clin Pract*, 14(1), 5. <https://doi.org/10.1186/s13722-019-0135-7>.
- Miech, R. A., Couper, M. P., Heeringa, S. G., & Patrick, M. E. (2020). The impact of survey mode on US national estimates of adolescent drug prevalence: Results from a randomized controlled study. *Addiction*. <https://doi.org/10.1111/add.15249>.
- Mullangi, S., Agrawal, M., & Schulman, K. (2021). The COVID-19 pandemic-an opportune time to update medical licensing. *JAMA Intern Med*, 181(3), 307–308. <https://doi.org/10.1001/jamainternmed.2020.8710>.
- Persad, G., Peek, M. E., & Emanuel, E. J. (2020). Fairly prioritizing groups for access to COVID-19 vaccines. *JAMA*. <https://doi.org/10.1001/jama.2020.18513> (online ahead of print, PMID: 32910182).
- Schranz, A., & Barocas, J. A. (2020 Sep). Infective endocarditis in persons who use drugs: Epidemiology, current management, and emerging treatments. *Infectious Disease Clinics of North America*, 34(3), 479–493. <https://doi.org/10.1016/j.idc.2020.06.004>.
- Wang, E. A., Zenilman, J., & Brinkley-Rubinstein, L. (2020). Ethical considerations for COVID-19 vaccine trials in correctional facilities. *JAMA*, 324, 1031–1032. <https://doi.org/10.1001/jama.2020.15589>. 32808972.
- Wang, Q. Q., Kaelber, D. C., Xu, R., & Volkow, N. D. (2021). COVID-19 risk and outcomes in patients with substance use disorders: Analyses from electronic health records in the United States. *Mol Psychiatry*, 26(1), 30–39. <https://doi.org/10.1038/s41380-020-00880-7>.
- Webb Hooper, M., Nápoles, A. M., & Pérez-Stable, E. J. (2020). COVID-19 and racial/ethnic disparities. *JAMA*, 323, 2466–2467. <https://doi.org/10.1001/jama.2020.8598>.
- Yang, J., Landrum, M. B., Zhou, L., & Busch, A. B. (2020 Nov-Dec). Disparities in outpatient visits for mental health and/or substance use disorders during the COVID surge and partial reopening in Massachusetts. *General Hospital Psychiatry*, 67, 100–106. <https://doi.org/10.1016/j.genhosppsych.2020.09.004>. Epub 2020 Oct 12 33091782.