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# Opioid Use Disorder and COVID-19: Biological Plausibility for Worsened Outcomes

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## Abstract

**Background:** Alarms have been raised that COVID-19 may disproportionately affect certain populations with substance use disorders, particularly Opioid Use Disorder (OUD), however warnings have largely focused on social risks such as reduced availability of services.

**Objectives:** This commentary highlights three plausible biological mechanisms for potentially worsened outcomes in patients with OUD who contract COVID-19.

**Results:** Opioid-related respiratory depression may amplify risks of hypoxemia from COVID-19 viral pneumonia. Complex opioid immune modulation may impact host response to COVID-19, though the effect direction and clinical significance are unclear. Drug-drug interactions may affect individuals with OUD who are co-administered medications for OUD and medications for COVID-19, particularly due to cardiac adverse effects.

**Conclusions/Importance:** There are plausible biological mechanisms for potentially worsened outcomes in patients with OUD who contract COVID-19; these mechanisms require further study, and should be considered in individuals with OUD.

### Keywords

Opioid Use Disorder; OUD; COVID; coronavirus; risk factors

As the Coronavirus disease 2019 (COVID-19) pandemic continues globally, there is ongoing concern it could disproportionately affect some populations with substance use disorders. Several authors have sounded the alarm about risks for increased transmission in this group, particularly given homelessness and incarceration are more common in substance users (Malta et al., 2019; Akiyama et al., 2020; Yamamoto, Needleman, & Gelberg 2019; Tsai & Wilson, 2020). Additional attention has been drawn to the risks of reduced services availability, such as medication for OUD (Volkow, 2020). Beyond these social risks, we

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wish to highlight three plausible biological mechanisms for potentially worsened outcomes in patients with OUD who contract COVID-19: respiratory toxicity, immune mechanisms, and drug-drug interactions.

COVID-19 principally targets the lungs, so the virus may pose an especially serious threat to those with respiratory toxicity from opioids (respiratory depression, naloxone failures) or polysubstance use (vaping, marijuana, crack cocaine, etc). Opioid use may result in respiratory depression with resultant hypoxemia; within 6 months of opioid initiation, risks of respiratory depression range 1.9–83.4%, depending on group risk (Babu, Brent, & Juurlink 2019). COVID-19 causes hypoxemia secondary to viral pneumonia, and in one large New York City case series, prevalence of hypoxemia on hospitalization was 20.4% (Richardson et al., 2020). Although unstudied, risks of opioid-related respiratory depression are likely amplified in the setting of concomitant hypoxemia from viral pneumonia, and therefore patients using opioids who get COVID-19 may have increased risk of adverse respiratory outcomes.

Opioid users may have additional vulnerability to COVID-19 from opioid suppression of immune function. The pathogenesis and host immune response to this virus is under active investigation, but involves both adaptive and innate immunity (Ye et al., 2020). For the related SARS virus, a mouse model suggested inadequate T cell responses may promote lung injury (Zhao, Zhao, & Perlman 2010). Opioid drugs are linked to numerous immunosuppressive consequences such as inhibited cytokine secretion and leukocyte recruitment, with detrimental effects on macrophages, neutrophils, dendritic cells, natural killer cells, mast cells, and B and T cell lymphocytes (Roy et al., 2011; Vallejo, de Leon-Casasola, & Benyamin 2004). COVID-19 can cause a viral cytokine storm, an uncontrolled host immune response thought to exacerbate viral disease progression and organ injury (Ye et al., 2020). Several immune-modulators are being trialed, with benefits currently unclear. It is unknown whether drugs with specific immunosuppressive mechanisms may have benefit while others cause harm, and it is unknown if immunosuppressive drugs impact disease progression or risk of initial infection. Based on opioid-induced immunosuppression, it is plausible that opioids potentially increase risk of COVID-19 infection and/or progression.

Numerous drugs are being administered as potential COVID-19 treatments while efficacy studies are underway. These include antibiotic and antiviral drugs, anticoagulants, and immunosuppressants. Some treatments may increase the risk of adverse cardiovascular events secondary to baseline QTc prolongation or drug-drug interactions, especially dysrhythmia (Juurlink, 2020; Giudicessi et al., 2020). This is particularly crucial in patients taking medications for OUD, as methadone can significantly prolong QTc and increase dysrhythmia risk (Alinejad et al., 2015).

There is an urgent need for research to better characterize the role that respiratory toxicity, immune mechanisms, and drug-drug interactions play in worsening outcomes for individuals with OUD infected with COVID-19.

## References


Akiyama MJ, Spaulding AC, & Rich JD (2020). Flattening the curve for incarcerated populations-Covid-19 in jails and prisons. The New England Journal of Medicine, 382(22), 2075–2077. 10.1056/NEJMp2005687 [PubMed: 32240582]

Alinejad S, Kazemi T, Zamani N, Hoffman RS, & Mehrpour O (2015). A systematic review of the cardiotoxicity of methadone. EXCLI Journal, 14, 577–600. 10.17179/excli2015-553 [PubMed: 26869865]

Babu KM, Brent J, & Juurlink DN (2019). Prevention of opioid overdose. The New England Journal of Medicine, 380(23), 2246–2255. 10.1056/NEJMra1807054 [PubMed: 31167053]

Giudicessi JR, Noseworthy PA, Friedman PA, & Ackerman MJ (2020). Urgent guidance for navigating and circumventing the QTc-prolonging and torsadogenic potential of possible pharmacotherapies for Coronavirus Disease 19 (COVID-19. Mayo Clinic Proceedings, 95(6), 1213–1221. 10.1016/j.mayocp.2020.03.024 [PubMed: 32359771]

Juurlink DN (2020). Safety considerations with chloroquine, hydroxychloroquine and azithromycin in the management of SARS-CoV-2 infection. Cmaj : Canadian Medical Association Journal = Journal de L'association Medicale Canadienne, 192(17), E450–E453. 10.1503/cmaj.200528

Malta M, Varatharajan T, Russell C, Pang M, Bonato S, & Fischer B (2019). Opioid-related treatment, interventions, and outcomes among incarcerated persons: A systematic review. PLOS Medicine, 16(12), e1003002. 10.1371/journal.pmed.1003002 [PubMed: 31891578]

Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, … Zanos TP (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA, 323(20), 2052. 10.1001/jama.2020.6775 [PubMed: 32320003]

Roy S, Ninkovic J, Banerjee S, Charboneau RG, Das S, Dutta R, Kirchner VA, Koodie L, Ma J, Meng J, & Barke RA (2011). Opioid drug abuse and modulation of immune function: Consequences in the susceptibility to opportunistic infections. Journal of Neuroimmune Pharmacology: The Official Journal of the Society on NeuroImmune Pharmacology>, 6(4), 442–465. 10.1007/s11481-011-9292-5 [PubMed: 21789507]

Tsai J, & Wilson M (2020). COVID-19: A potential public health problem for homeless populations. The Lancet. Public Health, 5(4), e186–e187. 10.1016/S2468-2667(20)30053-0 [PubMed: 32171054]

Vallejo R, de Leon-Casasola O, & Benyamin R (2004). Opioid therapy and immunosuppression: A review. American Journal of Therapeutics, 11(5), 354–365. 10.1097/01.mjt.0000132250.95650.85 [PubMed: 15356431]

Volkow ND (2020). Collision of the COVID-19 and addiction epidemics. Annals of Internal Medicine, M20–1212. 10.7326/M20-1212

Yamamoto A, Needleman J, & Gelberg L (2019). Association between homelessness and opioid overdose and opioid-related hospital admissions/emergency department visits. Social Science & Medicine, 242, 112585. [PubMed: 31634808]

Ye Q, Wang B, & Mao J (2020). The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. Journal of Infection, 80(6), 607–613.

Zhao J, Zhao J, & Perlman S (2010). T cell responses are required for protection from clinical disease and for virus clearance in severe acute respiratory syndrome coronavirus-infected mice. Journal of Virology, 84(18), 9318–9325. 10.1128/JVI.01049-10 [PubMed: 20610717]