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## Medication treatment for opioid use disorder in the age of COVID-19: Can new regulations modify the opioid cascade?

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### ARTICLE INFO

#### Keywords:

COVID-19  
Opioid cascade  
Methadone  
Buprenorphine  
Opioid use disorder  
Medication treatment for opioid use disorder  
Regulations  
Telemedicine  
Low-threshold buprenorphine  
Barriers to implementation  
Disparities

### ABSTRACT

The temporary loosening of regulations governing methadone and buprenorphine treatment for opioid use disorder (OUD) in the U.S., instituted to prevent the spread of COVID-19, has created an opportunity to explore the effectiveness of new models of care for people with OUD. The opioid cascade describes the current status of the treatment system, where only a fraction of people with OUD initiate effective medication treatment for OUD (MOUD), and of those only a fraction is retained in treatment. Regulatory changes—such as availability of larger take-home supplies of methadone and buprenorphine initiated via telemedicine (e.g., no initial in person visit; telemedicine buprenorphine permitted across state lines)—could modify the cascade, by reducing the burden and increasing the attractiveness, availability, and feasibility of MOUD both for people with OUD and for providers. We review examples of more liberal MOUD regimens, including the implementation of buprenorphine in France in the 1990s, primary care-based methadone in Canada, and low-threshold buprenorphine models. Research is needed to document whether new models implemented in the U.S. in the wake of COVID-19 are successful, and whether safety concerns, such as diversion and misuse, emerge. We discuss barriers to implementation, including racial and ethnic health disparities, and lack of knowledge and reluctance among potential providers of MOUD. We suggest that the urgency and public spiritedness of the response to COVID-19 be harnessed to make gains on the opioid cascade, inspiring prescribers, health systems, and communities to embrace the delivery of MOUD to meet the needs of an increasingly vulnerable population.

The public health response to the COVID-19 epidemic has been imperfect, but nonetheless within a matter of weeks during Spring of 2020 the American public adopted social distancing and infection control practices, while the health system battled to cope with the severe cases. This succeeded in “flattening the curve” of cases and deaths from COVID-19 (The Editorial Board, 2020). COVID-19 is also colliding with the epidemic of opioid use disorder (OUD) with its own curve of overdose deaths yet to be flattened (N.D. Volkow, 2020a). People with OUD are likely at increased risk for COVID-19 (American Medical Association, 2020; Wang, Kaelber, Xu, & Volkow, 2020). Economic and health disparities increase risk for both health threats. People with active OUD may not have the means or environment conducive to social-physical distancing, and they are less likely to access effective care.

Research has conceptualized the barriers of engagement and

retention in effective care for OUD as an “opioid cascade” (Williams, Nunes, Bisaga, Levin, & Olfson, 2019). Modeled after the HIV cascade, the opioid cascade describes the problem that among all people affected with OUD, only a fraction engage in effective medication treatment for OUD (MOUD), i.e. maintenance treatment with methadone, buprenorphine, or naltrexone, and of those only a fraction remain in treatment long enough to achieve stable remission and protection against death from overdose. Data from the National Survey on Drug Use and Health in 2019 estimate that only 19% of adults with OUD received medication treatment (Center for Behavioral Health Statistics and Quality, 2020). Further, even in clinical trials, where concerted efforts are made to retain patients on medication, rates of retention on buprenorphine or extended-release injection naltrexone for 6 months are in the 40% range (Hser et al., 2014; Lee et al., 2018), while in studies of insurance claims

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data, reflective of community-based practice, dropout rates are even higher (Larochelle et al., 2018; Morgan, Schackman, Weinstein, Walley, & Linas, 2019; Wakeman et al., 2020). Barriers to engagement and retention on MOUD include stigma (N.D. Volkow, 2020a, 2020b), lack of availability of treatment, and lack of attractiveness of the treatments to patients. For example, many communities lack any services offering MOUD (Grimm, 2020), many physicians who perform the requisite training and obtain the “X-waiver” to prescribe buprenorphine never begin to prescribe (Hutchinson, Catlin, Andrilla, Baldwin, & Rosenblatt, 2014). Regulations can render MOUD burdensome for patients and clinicians, including requirements for in-person visits and counseling for buprenorphine, and requirements for daily clinical attendance for directly observed dosing of methadone with restrictions on which methadone patients can be allowed “take-home” doses and hence fewer clinic visits.

In response to COVID-19, the loosening of the regulations governing MOUD is a possible silver lining and has the potential to engage more people with OUD in treatment, modifying the cascade effect at key junctures of engagement in MOUD and retention on MOUD. Faced with the urgent need to prevent the spread of COVID-19 within the vulnerable population with OUD, and the clinicians and staff who care for them, SAMHSA, DEA (Drug Enforcement Administration), and state regulators moved swiftly to encourage telemedicine and lower barriers to treatment. They have loosened restrictions on take-home doses of methadone, buprenorphine can be initiated and maintained via telemedicine without in person visits, and telemedicine is permitted across state lines. These changes have the potential to reduce the burden of and increase the attractiveness, availability, and feasibility of MOUD both for people with OUD and for providers. Will this increase the proportion of people with OUD engaged in care, stabilized on MOUD? And will it be safe?

Concerns that weigh against loosening regulations on MOUD include diversion of prescribed opioids onto the black market and potential harms of misuse of prescribed medications. Methadone, a potent full opioid agonist, is dangerous if misused due to risk of overdose. Risk of overdose increases during initiation of methadone treatment if the dose is escalated too quickly or methadone is combined with other drugs (Baxter et al., 2013). Buprenorphine, a partial agonist, carries less risk of overdose, but can still be dangerous particularly if combined with other sedating drugs (Schuman-Olivier et al., 2013). Frequent in-person visits and counseling may improve adherence and outcome, as dropout from treatment is associated with poor outcomes.

Some evidence already exists that implementation of MOUD under more flexible regulations can be safe and effective. In response to an epidemic of opioid overdose deaths in France in the 1990s, the country introduced buprenorphine with low barriers to entry. General physicians could prescribe it, and pharmacies engaged in supervising dosing. The number of people with OUD treated with buprenorphine rose substantially and opioid overdose deaths declined (Auriacombe, Fatséas, Dubernet, Daulouède, & Tignol, 2004), and the reduced risk of death has been directly linked to being in treatment with buprenorphine (Dupouy et al., 2017).

So-called low-threshold buprenorphine models have shown promise. Examples include initiating buprenorphine at emergency departments (D’Onofrio et al., 2015; Fox & Nelson, 2019), and an on-demand outpatient model where buprenorphine is dispensed in a tamper-proof dosing device after a brief clinical screening, circumventing waiting lists for care (Sigmon et al., 2016).

In Canada, methadone maintenance became available through primary care practitioners starting in the 1990s, attracting a large number of patients into methadone treatment. Some have raised concerns about high-volume prescribers (Kurdyak, Jacob, Zaheer, & Fischer, 2018), and what seem like high rates of methadone treatment per capita in certain regions. Other evidence suggests reductions in mortality overall associated with the availability of low-threshold methadone (Nolan et al., 2015).

The abrupt relaxation of regulations surrounding MOUD in the U.S.

represents a natural experiment on a large scale. Research should evaluate the impacts on quality and availability of care. Relevant questions include: Among patients already enrolled in maintenance treatment with buprenorphine or methadone, what is the impact of remote telemedicine-based counseling, reduced pickup schedules, and reduced requirements for urine testing on the outcomes of retention in treatment, substance use, and risk of overdose and other complications? Will buprenorphine available by telemedicine and less restrictive methadone regimens attract more people with OUD into treatment and lead to more sustained engagement with good outcomes and safety (Samuels et al., 2020; Weintraub, Greenblatt, Chang, Himelhoch, & Welsh, 2018)? Will more providers join the field, increasing the availability of MOUD? Are there patient-treatment matching factors to distinguish patients who do well with flexible and remote treatment models, versus those needing a traditional structured approach? We need observational or comparative effectiveness studies to examine these questions.

Lack of access to treatment is partly a function of geography. Many regions of the U.S., particularly rural areas, have no methadone maintenance available, and few if any buprenorphine prescribers (Grimm, 2020). Many residential treatment programs, and jails or prisons, similarly lack prescribers to initiate MOUD prior to discharge, an important imperative given the elevated risk of overdose death after release from controlled settings (Binswanger et al., 2007; Ravndal & Amundsen, 2010). Telemedicine has the potential to reach across such barriers.

The COVID-19 pandemic is disproportionately affecting African Americans and Latinos, particularly underserved individuals in these communities who use drugs. African American and Latinx people who use drugs face a greater number of challenges in accessing and remaining in drug treatment than white populations due to chronic health disparities and fewer personal and community resources. With the new treatment regulations, special attention needs to be paid to African American and Latinx drug users and economic inequities, such as a lack of computer or telephone technology to be able to access telemedicine, homelessness, unemployment, and inadequate public transportation in suburban and rural counties. Providers and policy-makers must consider the unique needs of underserved populations in the context of their communities (N.D. Volkow, 2020b). Disparities in the opioid cascade will continue to widen, if these health disparities are not addressed.

Reluctance and lack of knowledge among providers is another important barrier that research should address. Surveys of primary care physicians in the U.S. (Hutchinson et al., 2014; Quest, Merrill, Roll, Saxon, & Rosenblatt, 2012) and Canada (Livingston, Adams, Jordan, MacMillan, & Hering, 2018) reveal similar concerns that discourage provision of MOUD: lack of familiarity with the patient population, concerns about severity of illness and the time required to manage patients’ multiple needs, lack of behavioral health backup, lack of expert consultation for complicated cases often with psychiatric comorbidities. The SAMHSA-funded provider clinical support system (PCSSnow.org.) and the state targeted response-technical assistance (opioidresponse-network.org) initiatives seek to help educate and expand the numbers of MOUD providers. Inadequate funding for MOUD treatment is a related barrier that clinicians have voiced (Quest et al., 2012). Successful community-level programs to expand MOUD, such as the Vermont hub and spoke system (Brooklyn & Sigmon, 2017), involved substantial government funding. Like Ryan White Act funding for HIV, policy-makers should consider expanded funding to combat the opioid epidemic.

Can the urgency and public spiritedness of the response to COVID-19, along with the changes in regulations governing methadone and buprenorphine treatment, be harnessed to make dramatic gains on the opioid cascade? We hope the COVID-19 pandemic can be an opportunity to inspire more physicians and other prescribers, policy-makers, health systems, and communities to embrace the treatment of OUD with medications, finding creative solutions to make MOUD attractive and

available and meet the needs of an increasingly vulnerable population.

### CRediT authorship contribution statement

Edward V. Nunes: Conceptualization, Writing - Original Draft, Writing - Review & Editing.

Frances R. Levin: Conceptualization, Writing - Review & Editing.

Muredach P. Reilly: Conceptualization, Writing, Writing - Review & Editing.

Nabila El-Bassel: Conceptualization, Writing - Review & Editing.

### Declaration of competing interest

Dr. Nunes served as unpaid consultant to Alkermes, Braeburn-Camurus and Pear Therapeutics and has received in-kind medication for studies from Reckitt/Indivior, Alkermes, and a therapeutic application from Pear Therapeutics for a study. Dr. Levin receives grant support from NIDA, SAMHSA and US World Meds as well as a consultant for Major League Baseball. She was an unpaid member of a Scientific Advisory Board for Alkermes, Novartis and US World Meds but did not personally receive any compensation in the form of cash payments (honoraria/consulting fees) or food/beverage (she declined food/beverages in each circumstance) nor receive compensation in the form of travel reimbursement (honoraria/consulting fees). Dr. Reilly and Dr. El-Bassel have no conflicts to declare.

### Acknowledgements

The authors thank Elizabeth Costello for her assistance preparing this manuscript.

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