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Revising our attitudes towards agonist medications and their diversion in a time of pandemic[☆]



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ABSTRACT

The COVID-19 pandemic led government regulators to relax prescribing rules for buprenorphine and methadone, the agonist medications that effectively treat opioid use disorder, allowing for take home supplies of up to 28 days. These changes prioritized the availability of these medications over concerns about their misuse and diversion, and they provided a means for overdose prophylaxis during the highly uncertain conditions of the pandemic. In considering how to capitalize on this shift, research should determine the extent to which increased diversion has occurred as a result, and what the consequences may have been. The shifts also set the stage to consider if methadone can be safely prescribed in primary care settings, and if the monthly injectable formulation of buprenorphine is a suitable alternative to increased supplies of sublingual strips if concerns about diversion persist. The disruptions of the pandemic have caused a surge in overdose deaths, so carefully considering the prophylactic potential of agonist medications, in addition to their role as a treatment, may help us address this mortality crisis.

1. Introduction: judgment in a time of crisis

After showing signs of leveling off in recent years, fatal opioid overdoses in the United States appear to have surged to record levels with the onset of the COVID-19 pandemic (Katz, Goodnough, & Sanger-Katz, 2020). The causes of the surge are myriad, and it occurred despite efforts to forestall it by the federal agency that regulates addiction treatment. The pandemic required a series of rapid judgments by the Substance Abuse and Human Services Administration (SAMHSA) about how to maintain adherence and retention in opioid use disorder (OUD) treatment under challenging circumstances. The decisions SAMHSA made allowed providers to emphasize two ideas. The first was that agonist medications for opioid use disorder (MOUDs) are an indispensable part of treatment for OUD. The second was that fears of MOUD diversion and misuse were not as important as ensuring access to treatment, retention in it, and the ability of these medicines to prevent overdoses.

Evidence supports these concepts. Retention in agonist MOUD treatment has been found to substantially lower all-cause and overdose mortality (Sordo et al., 2017), and a recent study concluded that the consumption of even diverted buprenorphine is associated with a reduction in reported overdoses (Carlson, Daniulaityte, Silverstein, Nahhas, & Martins, 2020). Although the pandemic presents a research

environment that makes it difficult to discern the effects of greatly reduced concerns about diversion, it presents us with an opportunity to maintain these critical changes, evaluate them when the pandemic has run its course, and consider expanding their scope (Davis & Samuels, 2020).

2. Agonist medications as the critical part of OUD treatment

There has long been a tension between the view that agonist medications are one component of a comprehensive OUD treatment program that aims at tapering and eventual opioid abstinence, and the view that they are the central part of treatment long term for OUD, with counseling and wraparound services as beneficial but not indispensable supplements (Friedmann & Schwartz, 2012). SAMHSA's response to the pandemic addressed this tension by giving providers the opportunity to make MOUDs the principal focus of treatment like never before: stable patients could be prescribed 28 days of take-home methadone or buprenorphine between appointments, the latter of which could be prescribed to patients inducted into treatment by phone (Substance Abuse and Mental Health Services Administration, 2020). The goal was to limit the spread of COVID-19 by minimizing visits to opioid treatment programs (OTPs) and other facilities. Other aspects of treatment could be satisfied by the emerging practice of telemedicine, which has not

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been conclusively evaluated in addiction treatment settings.¹ The result is that OUD treatment during the pandemic could consist of dispensing monthly supplies of agonist MOUDs as its primary feature, with studies suggesting that the majority of patients will remain illicit opioid abstinent and avoid overdose for weeks even without additional interventions (Sigmon et al., 2016).

3. A de-emphasis on safeguards against misuse and diversion

The perceived risks of diversion for both patients and providers are one of the principal reasons physicians decline to prescribe agonist medications, or increase the number of patients they treat for OUD using them (Andraka-Christou & Capone, 2018; Wakeman & Barnett, 2018). The regulatory reforms of the pandemic may give us a reason to reconsider this outlook, reduce our concerns about diversion, and put more MOUDs into the community of people with OUD even if we cannot fully control who consumes them. The alternative is a circular dilemma: diversion of agonist MOUDs often results from a lack of lawful access to these medicines (Carroll, Rich, & Green, 2018), but concerns about facilitating diversion provide disincentives for lawfully dispensing enough buprenorphine to meet this need in the first place (Cooper et al., 2020). Providing 28-day supplies of agonist MOUDs with few or no additional controls signals the government's shift in priorities, albeit owing to an unrelated virus. Regulators do not accurately know the rate at which MOUDs were diverted before the pandemic, or if relaxed rules have increased it, but they certainly have not had a prohibitive effect on the ability to divert these medicines. Presumably, larger take-home supplies with refills via telemedicine make doing so easier.

The pandemic has therefore set the stage for studying if the diversion of partial agonists produces collateral benefits. The illicit use of buprenorphine can be associated with an increased willingness to use prescribed buprenorphine as a part of formal treatment (Kenney, Anderson, Bailey, & Stein, 2018), so relaxed diversion controls and reduced enforcement of drug possession laws may actually increase the number of people amenable to MOUD treatment. Despite these reforms, the confounding effects of COVID-19 mean we can't be certain of what's working or not at this point. Research shows that increases in unemployment are associated with increased illicit drug use (Nagelhout et al., 2017), and the pandemic is ushering in a pronounced recession (Goodman, 2020). There is reporting that the pandemic's disruption of a reliable illicit drug supply combined with people's sense of desperation and despair are contributing to the increase in overdose witnessed across the nation (Katz et al., 2020; Wan & Long, 2020).

4. MOUDs as overdose prevention

For people with OUD, these fatalities provide a compelling motive to increase the consumption of less risky agonist substitutes for fentanyl, which dominates the black market for opioids. The amended prescribing practices that provide weeks of these MOUDs to patients without verifying daily adherence imply that at least some of them will be diverted, so we should consider if partial agonist MOUDs can serve as overdose prophylaxis for people with OUD even if they are consumed illicitly. Research supports this idea, finding that diverted buprenorphine consumed even intermittently by PWUD is associated with a reduced frequency of overdose (Carlson et al., 2020). When the pandemic wanes, it would be beneficial to specifically examine this outcome and see if it can be replicated by further studies.

One new danger is that with 28 days between visits to their providers, patients who significantly divert their supplies will have to wait longer for a refill, increasing their risk of acute withdrawal, relapse, and

overdose. Yet diverted medication still provides the benefits of withdrawal management and overdose prophylaxis to the person with OUD who ultimately consumes it, so it can still yield benefits at the population level. Some executive policymakers have felt comfortable acting on this premise: a handful of jurisdictions refuse to arrest or prosecute people for possessing diverted buprenorphine on the grounds that even illicit consumption can help save lives (del Pozo, Krasner, & George, 2020).

5. Methadone: the remaining frontier

There is another aspect of MOUD-based treatment that the pandemic's reforms may pave the way for considering. It is the ability to prescribe methadone in primary care settings as well as conventional SAMHSA-certified OTPs. Doing would be predicated on a utilitarian calculus that any resulting risks of misuse and diversion, although much more serious than those of buprenorphine, are outweighed by the convenience and appeal of primary care dispensing. In place of daily supervised dispensing in a clinic, primary care settings allow patients to take home methadone and self-administer it, reducing the burdens of frequent travel to a clinic. In cities such as Baltimore, OTPs are already sending people home with more methadone than ever before (Prudente, 2020), and this sets the stage for conducting trials with an eye towards further reform. The experiences of Australia, Britain and Canada of prescribing methadone in less-regulated primary care settings suggest that while doing so has its hazards, it produces positive results "if assessed through the lens of overall mortality" (Samet, Botticelli, & Bharel, 2018). Prescribing this way rather than solely from OTPs would not only increase the availability of OUD treatment, it would reduce frequent—often daily—visits to a place that many people in treatment find demoralizing and that reinforces self-stigma (Rawson, Rieckmann, Cousins, McCann, & Pearce, 2019), possibly improving outcomes.

6. The implied potential of extended release buprenorphine

SAMSHA's statement deregulating buprenorphine applies to the medicine's sublingual strips, but the result is to provide patients with a quantity of them that lasts as long as a single dose of the medicine's extended release formulation, which has been available as a treatment since 2017. If diversion remains a regulatory concern for providers after the pandemic has run its course, a single shot of it releases a steady dose of buprenorphine into the patient's bloodstream from a diversion-proof subcutaneous depot for up to a month, albeit at a much greater cost. If the pandemic confirms that extended supplies of sublingual buprenorphine are found to be effective and desirable for patients, the depot likewise simplifies adherence and promotes retention by reducing the need for visits to pharmacies and physicians (Tompkins, Neale, & Strang, 2019). If normative concerns about MOUD diversion persist, then extended supplies of sublingual buprenorphine should be supplemented by expanded access to its depot formulation for patients who feel it would be an effective course of treatment.

7. The post-pandemic future

Illicit drug use and addiction treatment are social phenomena, and COVID-19 has profoundly altered the social ecologies in which they take place. It is critical to rapidly survey practitioners and patients to see how they have responded to these changes in treatment, but it is equally important to catalog the corresponding changes to law and policy that brought them about, possibly using the framework of legal epidemiology (del Pozo, Beletsky, & Rich, 2020). The challenge will be to determine which observations point to generalizable outcomes, and which are artifacts of the pandemic (Becker & Fiellin, 2020). This would allow us to consider a future approach to OUD treatment where patients receive buprenorphine once a month in either a sublingual or extended release formulation, methadone dispensed from a wider array of

¹ Such evaluations would not only examine how suitable telemedicine is for addiction treatment, but compare the effectiveness of audio/video sessions with ones that were audio only, e.g., conducted by telephone.

locations at safe but extended intervals, and both as the result of evidence-based practice rather than the emergency measures of a crisis. This vision of treatment is one that many patients and practitioners have sought for some time, but it was the sudden threat of viral infection that made a thoughtful but rapid transition to this approach possible.

CRedit authorship contribution statement

Brandon del Pozo: Conceptualization, Writing - original draft, Writing - review & editing. **Josiah D. Rich:** Conceptualization, Writing - review & editing.

Declaration of competing interest

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