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Technology-assisted methadone take-home dosing for dispensing methadone to persons with opioid use disorder during the Covid-19 pandemic

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ABSTRACT

Introduction: Covid-19 confers substantial risk for the >400,000 patients who receive methadone for the treatment of opioid use disorder (OUD) and methods for safely dispensing large quantities of methadone to patients are lacking.

Methods: This study evaluated the MedMinder “Jon”, an electronic and cellular-enabled pillbox that provides real-time monitoring to remotely manage take-home doses of methadone using a 12-week, within-subject, Phase II (NCT03254043) trial. We transitioned all participants from liquid to tablet methadone one week prior to randomization. Participants completed both treatment-as-usual and electronic pillbox conditions before choosing a condition in a final “choice phase”. We assessed feasibility, satisfaction, and safety outcomes during the exit interview.

Results: Overall, we randomized 25 participants, 24 (96.0%) completed >1 study session, and 21 (84.0%) completed the exit interview. We dispensed 167.92 g (1,974 doses) of methadone. Participants would use the pillbox again (86.3%) and recommend it to others (95.4%). Overall, 52.4% selected the pillbox in the choice condition and those who did not cited issues related to study requirements. Less than 1% of pillbox alerts were for medication being consumed outside the dosing window and we observed no evidence of actual or attempted methadone diversion.

Discussion: We were able to adequately manage patients who would not otherwise qualify for large quantities of take-home methadone when we dispensed methadone tablets via a secure pillbox. The integration of a commercially available pillbox into routine clinic operations increases opportunity for dispensing medication. Our data support remote monitoring of methadone take-home doses and may inform clinic practices related to Covid-19.

1. Introduction

Approximately 400,000 people in the United States receive treatment with methadone for opioid use disorder (OUD) annually (Abuse, 2017) and a global pandemic of coronavirus disease 19 (referred to as “Covid-19”) is currently disrupting routine methadone treatment practices (Becker & Fiellin, 2020; Henry et al., 2020). The virus that causes Covid-19, SARS-Cov2, is highly contagious and produces substantial and often unpredictable health consequences. SARS-Cov2 appears to be readily spread through exposure to airborne droplets and the current predominant recommendation for avoiding exposure to SARS-Cov2 is to stay home and practice social distancing.

SARS-Cov2 poses many unique problems for persons receiving methadone for the treatment of OUD. To effectively social distance, individuals are advised to shelter-in-place (most often home) as much as possible and to actively avoid small public spaces that may have more than 5–10 people. In contrast to these recommendations, methadone treatment clinics generally have >100 patients who attend the clinic daily or near daily during the same restricted time window (e.g., 6 am–2 pm) for methadone dosing. Missing a dose results in significant consequences, such as developing an acute opioid withdrawal syndrome and risk of opioid relapse, so clinics have had to quickly reorganize their operations to adhere to social distancing guidelines. In addition, patients receiving methadone have a greater prevalence of medical

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comorbidities that are associated with developing a severe course of Covid-19 (Guan et al., 2020; Sweeney et al., 2019; Volkow, 2020), further emphasizing their need to social distance. Evidence is already emerging that supports the unique vulnerability of these patients (Dubey et al., 2020), and there are calls for changes in regulations related to methadone dispensing to reduce their exposure risk (Dunlop et al., 2020; Green et al., 2020) and prevent what is being referred to as a potential fourth wave of the opioid epidemic (McCann Pineo & Schwartz, 2020).

One previous randomized trial has suggested that an electronic medical dispensing device can be used to effectively manage buprenorphine dosing in a sample of patients undergoing interim treatment for OUD (Sigmon et al., 2016). However, the significant differences that exist with buprenorphine regulation compared to methadone have slowed the adoption of this technology for use with methadone. Whereas buprenorphine is a tablet or filmstrip that can be legally dispensed to a patient in multi-day increments for unsupervised home consumption after a single primary care visit, federal opioid treatment standards (42 CFR § 8.12) stipulate that methadone that is administered for the treatment of OUD must be dispensed in opiate treatment programs (OTPs), usually with frequent clinic in-person dispensing and typically in liquid form.

We designed the current study to evaluate the feasibility and acceptability of an electronic and secure pillbox to deliver split-doses of methadone to persons receiving methadone who also had persistent pain. We initiated the study prior to the Covid-19 pandemic and concluded the study at the onset of the pandemic. The purpose of this study was to evaluate whether this electronic pillbox could be used to deliver methadone doses at home to pave the way for subsequent trials of methadone split-dosing versus standard daily dosing schedules for OTP patients experiencing persistent pain. The emergence of Covid-19 and its global impacts and implications on social behavior and health care delivery revealed new and important implications for this study. The data presented in this paper are the *a priori* identified primary outcome data for this trial, which are well-positioned now to contribute meaningfully to how methadone clinics may respond to the current Covid-19 pandemic.

2. Methods

2.1. Study design

Between March 2018 and March 2020, persons maintained on methadone self-referred or were referred by their counselors to complete a 13-week, within-subject, Phase II (NCT03254043) trial consisting of two randomly assigned 4-week treatment-as-usual and electronic pillbox phases and a final 4-week “choice phase” determined by the participant. Eligible participants were ≥ 18 years old, had been receiving methadone for ≥ 90 days, and received the same dose strength for ≥ 30 days, had previously received ≥ 1 take-home dose, and reported current chronic pain that averaged ≥ 5 over the past 24 h on the Brief Pain Inventory. We excluded participants who were pregnant, had a serious medical or psychiatric illness that was expected to interfere with study participation, were planning to end methadone treatment within 13 weeks, were not receiving 10–100 mg of methadone, or were being treated for pain. We integrated methadone dispensing into routine clinic operations. We transitioned all participants from liquid to tablet methadone for one week before randomly assigning them to phase order, and they remained on tablet methadone for the entire 13-week study period.

2.2. Randomization to phase order

Following a 1-week transition to a tablet form of methadone, we randomized participants within each sex group (using a random number generator) to phase order (pillbox to treatment-as-usual or treatment-as-usual to pillbox). At the end of the second phase, we asked all participants to choose their preferred condition for the final 4-week period.

2.3. Medminder “Jon” pillbox

During the pillbox phase, we assigned participants to a “Jon” pillbox (MedMinder, Inc.), an autonomous cellular-enabled box with 28 individually programmed and remotely activated cells that provide visual and audible alerts when medication is available and sends real-time notices to staff when deviations in dosing (e.g., missed doses, attempts to open a locked medication cell) occur. The Medminder “Jon” pillbox is a commercially available product that helps to promote adherence to medications and reduce problems related to noncompliance and/or challenges with polypharmacy. This study was the first that evaluated its use for managing methadone for the treatment of OUD.

Each cell in the “Jon” pillbox locks independently to secure a medication cup that can be filled with several tablets/capsules. Each cell is remotely unlocked automatically for a brief period, at a time that the patient and staff member predetermine, to allow the patient to remove the medication cup and consume his or her medication. Staff members are able to remotely reprogram the time at which cells are unlocked to accommodate unexpected changes in patient schedules. The pillbox records all instances when the medication cup is removed (e.g., medication dispensing, participant consumption) and replaced in real-time, and sends a series of real-time alerts to predetermined staff members when any activity (expected or unexpected) is registered.

Staff received real-time alerts from the pillbox via phone and email. We designated alerts into categories that signified patient-related events (e.g., nursing’s removal/return of the medication cup during the dispensing process, patient’s removal/return of the medication cup, or patient’s failure to return/remove the medication cup) or nonpatient/medication events. Nonpatient/medication events included notifications that the box had been registered/deregistered to patients, staff confirmations of changes in assigned dosing periods, notifications of low batteries on the box, temporary loss/reconnection of wireless connection to the server, and standard weekly reports. Staff contacted participants promptly in response to any unexpected patient-related events (e.g., failure to take medication at predetermined time).

2.4. Study sessions

Since this study was an initial proof-of-concept study, we required participants to follow their routine methadone take-home schedule, with the exception that we reassigned participants who were receiving more than 7 take-home doses to a weekly pick-up schedule. We required all participants to transport the Jon pillbox with them to every scheduled clinic visit. We also required participants to adhere to the program’s routine call-back schedule, a process that required them to call a dedicated phone line each day to learn whether they had been randomly selected to return their take-home doses to the clinic (in this case their box) for inspection. By virtue of being in this study, we assigned all participants to return for take-home inspection within 3 days of receiving their first take-home dispensing and thereafter we returned them to their standard call-back schedule. At a minimum of once weekly, research staff inspected the box for evidence of damage or other changes that might signify attempts at forcing locked cells open. In preparation for the subsequent trial, we also shifted all participants to a split-dose methadone schedule wherein they received 50% of their original methadone dose in the morning and we issued them a 50% dose via the pillbox for afternoon consumption. As a result, participants had a range of 1–13 take-home doses dispensed to them each day, depending on their existing take-home schedule.

Participants completed a series of questionnaires on a weekly basis. We examined changes in opioid withdrawal, and administered a global assessment of functioning and the Brief Pain Inventory. Participants completed more thorough pain ratings at the end of each phase in support of the subsequently planned study. The current study excludes data on pain ratings and outcomes, which we present in a separate report. Participants also completed an exit interview once, at the end of

the choice phase (week 13). The exit interview contained the a priori primary outcomes for this evaluation, which was participant-perceived feasibility and satisfaction with the pillbox, including their willingness to use the pillbox again and to recommend it to others. We assessed safety and fidelity of medication dosing by determining the number of automated pillbox alerts related to deviations in predetermined medication cup removals. Final choice phase also served as a primary outcome for evidence of patient acceptability.

3. Results

We present a summary of participant demographics and outcome data in Table 1. We randomized twenty-five participants, 24 (96.0%) completed ≥ 1 study session, and 21 (84.0%) completed the exit interview. Overall, we dispensed 167.92 g, comprising 1974 doses of methadone, via the pillbox. We recorded a total of 8222 events, 2852 (34.6%) of which were patient-related. As Table 1 shows, we classified 2683 (94.0% of patient-related events) as events associated with routine methadone care, which consisted of the removal and return of the medication cup by nursing staff during the medication dispensing process. We identified only 169 (5.9%) of patient-related events as nonroutine events that prompted staff follow-up. These events included removal of a medication cup registered to be empty (3.1% of nonroutine events), a medication cup not being returned to the cell (1.4%), failure to remove the medication cup as scheduled (0.9%), and medication cup being removed at an unscheduled time (0.5%). Staff inspections of the pillboxes did not result in any observable evidence of damage or other changes to the pillbox that would suggest attempts to force a locked cell to open. Few participants (13.0%) reported problems with the tablet formulation of methadone and the majority of participants indicated that they would use the pillbox again (86.3%) and would recommend it to others (95.4%). Approximately half (52.4%) of participants selected the pillbox in the choice condition and those who did not primarily cited issues related to frequent transporting of the box to the clinic for study requirements.

4. Discussion

We designed the current study to evaluate the use of an electronic pillbox to deliver split-dose methadone to OTP patients who had moderate and persistent pain. We initiated data collection prior to but concluded at the onset of the Covid-19 pandemic. The main findings of the study are highly relevant to OTP health care delivery, particularly methadone take-home dosing practices. The vast majority of participants reported liking the pillbox (86.3%) and willingness to recommend it to others (95.4%); however, only 52.4% of patients actually selected the pillbox during the choice phase. Our discussions with the participants indicated this discrepancy was most likely due to the study requirements that the box be transported with the participant to each of their routine visits. Since this was an initial proof-of-concept study it seemed premature to deviate from a routine care schedule without evidence that the pillbox would maintain fidelity in dosing. However, these data now suggest that there is value in using the pillbox to shift away from routine visit schedules, consistent with the new needs related to care that Covid-19 has presented.

These findings build on prior technology-assisted buprenorphine dispensing (Sigmon et al., 2016) and provide evidence that patients who exhibited several characteristics that generally signified lower stability in treatment or greater risk of opioid relapse (e.g., elevated pain, recent illicit drug use) and may not have historically qualified for large quantities of take-home methadone under standard clinic procedures were adequately maintained in treatment when methadone tablets were dispensed via a secure pillbox. This is important; though federal regulations aimed at preventing diversion of methadone take-home doses have remained unchanged for many years, the onset of Covid-19 led to abrupt loosening of restrictions. Whereas, patients historically needed to

Table 1
Participant details and study outcomes.

Demographic information	(N = 25)
Age (mean yrs SD)	33.0 (10.7)
Male (%)	42.3
Race (%)	
Caucasian	56
African American	44
Married (%)	61.5
Unemployed/disability (%)	57.7
Drug and treatment history	
Daily methadone dose in mg (mean, SD) ^a	84.9 (15.1)
Injection drug history (%)	57.6
First time in treatment (%)	23.1
Number previous treatments (mean, SD)	4.1 (3.2)
Experienced problems with tablet form of methadone (%) ^c	13.0
Pillbox outcomes (N/%) ^d	
Selected pillbox intervention (N = 11)	
Liked having more take-home doses	6/11; 54.5%
Liked having a secure box available to store take-home doses at home	8/11, 72.7%
Liked for "other" reasons ^b	4/11, 36.4%
Willing to use pill box to manage routine methadone take-homes	11/11, 100%
Would recommend pill box to other patients for management of routine take-homes	11/11, 100%
Experienced problems with pillbox during study	9/11, 81.8%
Selected treatment as usual (N = 10)	
Box was too big, bulky, heavy, or otherwise cumbersome	7/10, 70%
Did not like having to bring the pillbox to the clinic every time	6/10, 60%
Storing the pillbox at home was a hassle	4/10, 40%
Disliked for "other" reasons ^b	5/10, 50%
Willing to use pill box to manage routine methadone take-homes	7/10, 70%
Would recommend pill box to other patients for management of routine take-homes	9/10, 90%
Experienced problems with pillbox during study	5/10, 50%
Patient events recorded ^e	2852
Events associated with routine medication dispensing	2683, 94.0%
Medication cup returned to unit ^f	1359, 45.0%
Medication cup removed from unit	1324, 43.8%
Non-routine events ^g	169, 5.6%
Empty medication cup taken out	89, 3.1%
Medication cup not returned to compartment	40, 1.4%
Failure to take out medications cup on schedule	27, 0.9%
Medication cup taken out at the wrong time	13, 0.5%

^a Persons with methadone dose >100 mg/day were excluded.

^b Participants who endorsed "other" were able to write in additional reasons.

^c Problems (n = 3) were explained in an open-ended question and were a) did not like taste, b) upset stomach, c) constipation.

^d Percentages calculated as a function of number participants per choice condition Data were collected during the exit interview that occurred at the end of the final choice phase.

^e Percentages calculated as a function of total patient events.

^f Extra alerts related to medication cup returns are related to challenges early in the study in accurate placement of cups within the cells. This issue was quickly recognized and easily resolved.

^g It is possible for some events to be related to staff box examinations and/or medication dispensing.

demonstrate stability in treatment, wait ≥ 90 days to receive more than one dose of methadone for take-home consumption, and be in treatment continuously for 2 years before they could receive a 28-day supply of take-home doses, the Substance Abuse and Mental Health Services Administration (SAMHSA) released guidance in March 2020 that allowed OTPs to dispense up to 2 weeks of medication to patients who were not necessarily stable in treatment and up to 28 days of medication to patients who were stable in treatment (SAMHSA, 2020). These changes were made to help OTPs limit patient exposure and support stay-at-home orders but were implemented abruptly and with little

available guidance or research regarding best practices for dispensing large quantities of medication to patients who may not have previously qualified. The current study provides initial evidence that this can be feasibly done using an electronic pillbox, though the rigorous monitoring system used during this study may have impacted outcomes, so it is important to assess performance directly in response to the revised SAMHSA guidelines.

Thus, while this study was initiated prior to the Covid-19 pandemic, these data may provide valuable information to clinic providers who are seeking alternatives to conventional methods for managing methadone dispensing during this crisis. Dispensing methadone via tablet formulation in a secure pillbox can be considered for patients who are at greatest risk of acquiring or progressing to the severe form of Covid-19, or who otherwise need to comply with stay-at-home orders. That this medication pillbox was integrated into the routine clinic operations as an alternate approach to standard take-home dispensing practices, and that the box is a commercially available product that meets HIPAA and other regulations increases the possibility for this method to be easily disseminated.

More broadly, dispensing take-home doses in tablet form in an electronic pillbox that continuously reports medication adherence data to the OTP extends the critical monitoring that is usually performed in the OTP setting (in-person dosing) to the patient's home environment, independent of patient self-reports. This represents a major paradigm shift for how methadone is used to treat OUD in general and opens up new opportunities for improved clinical management and treatment satisfaction. Such a change could increase treatment satisfaction for patients and providers, improve patient retention in treatment, and increase the number of patients receiving treatment with methadone.

These results also have important implications outside of Covid-19. There is a significant OUD treatment gap in the United States and the majority of efforts to expand treatment have focused on buprenorphine-related innovations (Jones et al., 2015). However, emerging data suggest that an increasing number of patients who are seeking treatment for OUD have been using heroin that has been adulterated with high levels of fentanyl (Ochalek et al., 2019), and accumulating evidence suggests that recent fentanyl exposure makes induction onto buprenorphine extremely difficult (Antoine et al., 2020), likely because illicit fentanyl exposure takes up to 2 weeks to be fully excreted (Huhn et al., 2020). The net result is a growing number of reports that buprenorphine may not provide adequate withdrawal suppression for these patients (Gryczynski et al., 2019; Silverstein et al., 2019). Therefore, the field must begin to expand patient access to methadone treatment, yet the restrictive regulations imposed on OTPs makes this very challenging and decreases the likelihood that innovations in treatment delivery can happen as quickly as may be needed. Remote management of methadone take-home doses may provide a method for expanding methadone access that can more quickly help to address this growing OUD treatment gap.

This study has several strengths, most notably the integration of this approach into the routine clinical operations of the clinic, which supports its dissemination and scaling across clinics. The study also has important limitations. One of these limitations is its small sample size, which is somewhat mitigated by the within-subject design. The positive response that participants had to the pillbox suggest that the pillbox might be well-accepted across other OTP patients. The requirement that participants transport the box with them to every visit proved to be a source of frustration to some, however, and may have unduly impacted our primary outcome (e.g., choice of final phase). These methods were appropriate for a first proof-of-concept evaluation but indicate the need for additional research to innovate and expand upon this model to assess its value for changing the manner through which methadone take-home dosing is monitored. In addition, two of the study eligibility criteria may have implications for dissemination and scaling of this approach. First, we limited the study to persons with methadone doses <100 mg. This cautious approach was necessary because this was an initial proof-of-

concept study and we had concerns that diverted product could pose a significant public health risk. Second, the study sought to evaluate the feasibility of this medication dispensing approach in persons who were both receiving methadone and reporting persistent pain, as a precursor to a larger study that would more specifically target that population. Both of these inclusion criteria may have resulted in the enrollment of a unique subgroup with OUD and the impact this may have on efforts to scale up this approach is unknown. Finally, while this proof-of-concept study was not prospectively designed to improve take-home dosing in the context of the Covid-19 pandemic, the focus on feasibility, satisfaction, and safety of an electronic pillbox can be generalized to the current context to provide clinics with additional options to consider for modifying their routine care practices in the current environment.

Overall, these data support further exploration of an electronic pillbox to manage take-home doses of tablet methadone in persons being maintained on methadone for the treatment of OUD. These data can be used to inform clinic practices during the Covid-19 crisis as well and could serve as a foundation for examining methadone expansion outside of OTP settings to address capacity issues resulting from the ongoing fentanyl epidemic.

CRediT authorship contribution statement

KED and RKB conceptualized and received funding for the study. All study authors contributed to data collection, analyses, project supervision and management, and writing the manuscript (original and revision).

Declaration of competing interest

This project was supported by a grant funded by the National Institute on Drug Abuse (NIDA) grant R34DA042926 (PI Dunn). The authors report no relevant conflicts of interest and have no conflicts related to the box described in this study. KED has consulted for Grunenthal, Inc. and Canopy Corporation, and has participated as an advisory board member for a Canopy-Beckley Therapeutics study. KBS serves on the Board of Directors of the American Association for the Treatment of Opioid Dependence. RKB was Director of the Addiction Treatment Services methadone clinic during the period in which this study was conducted. The study team also thanks Kori Kindbom, Michael Sklar, Rachel Burns, Jennifer Mucha, and James Blucher for their work on the study.

References

- Abuse, S. (2017). *Mental Health Services Administration, 2017. National Survey of Substance Abuse Treatment Services (N-SSATS): 2015. Data on substance abuse treatment facilities. BHSIS series S-88, HHS publication no. (SMA) 17-5031. Substance Abuse and Mental Health Services Administration.*
- Antoine, D., Huhn, A. S., Strain, E. C., Turner, G., Jardot, J., Hammond, A. S., & Dunn, K. E. (2020). Method for successfully inducing individuals who use illicit fentanyl onto buprenorphine/naloxone. *The American Journal on Addictions*. <https://doi.org/10.1111/ajad.13069> (Advance online publication. doi:10.1111/ajad.13069).
- Becker, W. C., & Fiellin, D. A. (2020). When epidemics collide: Coronavirus disease 2019 (COVID-19) and the opioid crisis. *Annals of Internal Medicine*, *M20-1210*. <https://doi.org/10.7326/M20-1210> (Advance online publication).
- Dubey, M. J., Ghosh, R., Chatterjee, S., Biswas, P., Chatterjee, S., & Dubey, S. (2020). COVID-19 and addiction. *Diabetes & Metabolic Syndrome*, *14*(5), 817–823. <https://doi.org/10.1016/j.dsx.2020.06.008> (Advance online publication).
- Dunlop, A., Lokuge, B., Masters, D., Sequeira, M., Saul, P., Dunlop, G., Ryan, J., Hall, M., Ezzard, N., Haber, P., Lintzeris, N., & Maher, L. (2020). Challenges in maintaining treatment services for people who use drugs during the COVID-19 pandemic. *Harm Reduction Journal*, *17*(1), 26. <https://doi.org/10.1186/s12954-020-00370-7>.
- Green, T. C., Bratberg, J., & Finnell, D. S. (2020). Opioid use disorder and the COVID 19 pandemic: A call to sustain regulatory easements and further expand access to treatment. *Substance Abuse*, *41*(2), 147–149. <https://doi.org/10.1080/08897077.2020.1752351>.
- Gryczynski, J., Nichols, H., Schwartz, R. P., Mitchell, S. G., Hill, P., & Wireman, K. (2019). Fentanyl exposure and preferences among individuals starting treatment for opioid use disorder. *Drug and Alcohol Dependence*, *204*, 107515.

- Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... Du, B. (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine*, *382*, 1708–1720.
- Henry, B. F., Mandavia, A. D., Paschen-Wolff, M. M., Hunt, T., Humensky, J. L., Wu, E., ... El-Bassel, N. (2020). COVID-19, mental health, and opioid use disorder: Old and new public health crises intertwine. *Psychological Trauma Theory Research Practice and Policy*. <https://doi.org/10.1037/tra0000660> (Advance online publication. doi: 10.1037/tra0000660).
- Huhn, A. S., Hobelmann, J. G., Oyler, G. A., & Strain, E. C. (2020). Protracted renal clearance of fentanyl in persons with opioid use disorder. *Drug and Alcohol Dependence*, *214*, 108147. <https://doi.org/10.1016/j.drugalcdep.2020.108147>. Epub 2020 Jul 2 32650192.
- Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015). National and state treatment need and capacity for opioid agonist medication-assisted treatment. *American Journal of Public Health*, *105*(8), e55–e63. <https://doi.org/10.2105/AJPH.2015.302664>.
- McCann Pineo, M., & Schwartz, R. M. (2020). Commentary on the coronavirus pandemic: Anticipating a fourth wave in the opioid epidemic. *Psychological Trauma Theory Research Practice and Policy*. <https://doi.org/10.1037/tra0000622> (Advance online publication. doi:10.1037/tra0000622).
- Ochalek, T. A., Parker, M. A., Higgins, S. T., & Sigmon, S. C. (2019). Fentanyl exposure among patients seeking opioid treatment. *Journal of Substance Abuse Treatment*, *96*, 23–25.
- Sigmon, S. C., Ochalek, T. A., Meyer, A. C., Hruska, B., Heil, S. H., Badger, G. J., ... Higgins, S. T. (2016). Interim buprenorphine vs. waiting list for opioid dependence. *New England Journal of Medicine*, *375*(25), 2504–2505.
- Silverstein, S. M., Daniulaityte, R., Martins, S. S., Miller, S. C., & Carlson, R. G. (2019). “Everything is not right anymore”: Buprenorphine experiences in an era of illicit fentanyl. *International Journal of Drug Policy*, *74*, 76–83.
- Substance Abuse and Mental Health Services Administration (SAMHSA). (2020). Opioid treatment program guidance. Retrieved from <https://www.samhsa.gov/coronavirus>. (Accessed 8 May 2020).
- Sweeney, M. M., Antoine, D. G., Nanda, L., Geniaux, H., Lofwall, M. R., Lofwall, M. R., ... Umbricht, A. (2019). Increases in body mass index and cardiovascular risk factors during methadone maintenance treatment. *Journal of Opioid Management*, *15*(5), 368.
- Volkow, N. D. (2020). Collision of the COVID-19 and addiction epidemics. *Annals of Internal Medicine*. <https://doi.org/10.7326/M20-1212>.