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Is Methadone Safe for Patients With Opioid Use Disorder and Coronavirus Disease 2019 Infection?

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has led to not only increase in substance misuse, substance use disorder, and risk of overdose but also lack of access to treatment services. Due to lack of knowledge of the course and impact of COVID-19 and outcomes of it's interactions with existing treatments, the Substance Misuse Service Team initiated a safety improvement project to review the safety of opioid substitution treatment, particularly the safety of methadone. This preliminary retrospective cross-sectional audit of safety improvement intiative underscores the importance of providing treatment services to those with opioid use disorders and that methadone is safe among this population with a high burden of comorbidity, most of which leads to negative outcomes from COVID-19. The outcomes show that patients who have COVID-19 should continue with opioid substitution treatment with methadone. Although treatment with methadone is safe, symptomatic patients should be monitored. In addition, patients who take methadone at home should be educated on the risk of overdose due to, and adverse outcomes from, COVID-19 infection. Patients should monitor themselves using pulse oximeter for any signs of hypoxia.

Keywords: Buprenorphine, COVID-19, Methadone, Opioid Use Disorder

INTRODUCTION

The global impact of coronavirus disease 2019 (COVID-19) pandemic is unprecedented, causing disproportionate deaths and social suffering to the world populations. In particular, COVID-19-related restrictions have led to an increase in use of drugs and alcohol, increased prices, access to impure drugs, switching to other substances, increased use of new drugs, and decreased use of others (Dubey et al., 2020; Enns et al., 2020; Farhoudian et al., 2020; MacKinnon et al., 2020; Reta et al., 2021; Wardell et al., 2020). In addition, because of reduced trafficking of drugs, the purity of drugs has reduced, which has led to an increase in the amount bought and used by people with substance use disorders (SUDs) United Nations Office on Drugs and Crime, 2020). Furthermore, with the speculated dip in supply of heroin and synthetic cannabinoid and the restricted movement of suppliers causing intermittent supply, drug users are also likely to buy drugs in large quantities. This could increase drug-related deaths and overdose (Dubey et al., 2020; Enns et al., 2020; MacKinnon et al., 2020; Torun & Coşkunol, 2020; Wardell et al., 2020). The pandemic is currently associated with an increase in SUDs (Dubey et al., 2020; Enns et al., 2020; MacKinnon et al., 2020).

The COVID-19 pandemic led to changes in the provision of drug and alcohol services in the community. Because of lockdown and physical "social" distancing, the level of contact between patients and drug services reduced drastically on short notice. Evidence shows that lockdown led to reduced access to treatment services including harm reduction and psychosocial interventions (Croxford et al., 2021; Dubey et al., 2020; Enns et al., 2020; MacKinnon et al., 2020; Reta et al., 2021; Wardell et al., 2020). In addition, pharmacies have been encouraged to reduce close contact with patients, with many switched from daily supervised consumption to large quantities of take-home medications. In some countries, the COVID-19 pandemic led to initiation of virtual platforms for clinical encounters and writing of longer scripts (Mackinnon et al., 2020). Because of the way that restrictions were rushed through, there was not enough time to prepare patients through adequate risk assessment and care planning for the transition. This has undoubtedly led to ineffective monitoring of patients, with evidence suggesting that social distancing and strict lockdown measures could lead to increase in opioid overdoses and fatalities because of lack of observers who could administer

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naloxone (Volkow, 2020) or call for medical emergency response. In addition, because of a high demand in acute care and lack of walk-in services, people with SUDs are less likely to access urgent treatment, which is an important component in mitigating the effects of drug overdoses and intoxications. Moreover, it is not known whether the combination of therapeutic opioids with COVID-19 infection could lead to worse outcomes. Unfortunately, there is a lack of coroner's data on drug overdose fatalities from the United Kingdom, although evidence from Canada indicates an increase in overdose deaths (Mackinnon et al., 2020).

It remains unclear whether pharmacological effects of drugs of abuse, such as opioid-induced respiratory depression, could increase risk for adverse outcomes from COVID-19 infections (Wang et al., 2021). This evidence would be important as COVID-19 infection can lead to a silent hypoxia, a significant low level of oxygen experienced without the usual sign of shortness of breath (Luks & Swenson, 2020). Hypothetically, if such a patient is given therapeutic opioid such as methadone as usual, they could develop respiratory depression, rapidly deteriorate, and have adverse outcomes from COVID-19. Opioid substitution treatment (OST)-related respiratory depression could cause hypoxemia in patients with COVID-19, which could in turn lead to cardiac, pulmonary, and neurological complications (Zibbell et al., 2019) or even overdose death. Although the effect direction and clinical significance remain unclear, it is also possible that opioid immune modulation might have an influence on the COVID-19 outcomes (Schimmel & Manini, 2020).

Currently, there is lack of evidence on the effect of therapeutic opioids on the patients with COVID-19 as well as whether it does influence outcomes among patients with COVID-19 infections. Although emerging evidence show that medications used to treat opioid use disorders (OUDs) like methadone, buprenorphine, and naltrexone did not have an effect on SUD patients' risk for COVID-19, especially those with a recent SUD diagnosis (Wang et al., 2021), cautions have been suggested regarding the interactions between medications used in the treatment of opioid addiction and those used in the treatment of COVID-19 (Mansuri et al., 2020). More importantly, there is a lack of evidence on how those on OST with a COVID-19 diagnosis would fare on treatment and whether these medications, methadone and buprenorphine, could increase deterioration of patients with COVID-19. There is evidence that medications for SUDs like methadone even at low doses have the potential to cause prolongation of the QT interval and development of ventricular tachycardia (Behzadi et al., 2018). Hypothetically, combination of these adverse reactions with COVID-19 symptoms could lead to adverse outcomes.

CAN TREATMENT WITH OST CAUSE ADVERSE OUTCOMES FOR PATIENTS WITH COVID-19?

There is an interface between COVID-19 and opioid withdrawal symptoms. COVID-19 signs and symptoms fall into four major categories of systemic, respiratory, gastrointestinal, and cardiovascular (Struyf et al., 2020). The most common of these signs and symptoms are cough, sore throat, fever, myalgia or arthralgia, fatigue, and headache (Struyf et al., 2020). In addition, loss of taste, shortness of breath or difficulty breathing, chills, muscle or body aches, fatigue, congestion or runny nose, nausea or vomiting, hypoxia, and diarrhea have also been reported (Lapointe-Shaw et al., 2020a, 2020b; Menni et al., 2020). These symptoms such as nausea, vomiting, congestion or runny nose, muscle or body aches, fatigue, and hot and cold flushes are similar to opioid withdrawal symptoms after cessation of opiate intake. This complicates not only the diagnosis of opioid withdrawals but also the safe initiation and continuation of opioid substitution treatment with either methadone or buprenorphine among those who could be infected with COVID-19. Moreover, when treatment has been initiated, the similarity of opioid withdrawal and COVID-19 symptoms complicates the review of treatment as a patient who is having COVID-19 symptoms could be misdiagnosed as either having opioid withdrawal symptoms, intoxicated, or sedated. Currently, there is no research evidence on the complexity of treatment of those with comorbid COVID-19 infection and OUDs. Furthermore, the similarities among symptoms increase the risk of missing diagnosis of COVID-19 as the patient and clinical staff might focus on opioid withdrawal symptoms.

Despite the evidence indicating the vulnerability of people with substance misuse disorders to COVID-19 as well as outcomes from infection, there is lack of evidence so far to confirm this. One study that described clinical characteristics, related factors, and clinical outcomes of COVID-19 in people with SUDs admitted to a public referral hospital found that a small number of people with SUDs were admitted with COVID-19 pneumonia and that the patients with SUDs admitted were over 50 years old, diagnosed with alcohol use disorder, and had a high prevalence of comorbidities (Vallecillo et al., 2021). In another study, there was an association among overdose, COVID-19 infection, and mortality (Allen et al., 2021). Although there is evidence that those with substance misuse disorders are at risk of poor outcomes from COVID-19 infection, little is currently known about the relationship among SUDs, treatment with methadone or buprenorphine, and COVID-19 severity.

Because of lack of evidence on the effect of OST on COVID-19 outcomes, the Substance Misuse Service carried out a safety evaluation audit. The current Substance Misuse Service's clinical protocol indicates that prisoners who are within 5 days of induction into treatment have access to 2–5 days of review clinic where withdrawal signs and symptoms as well as assessment for signs of sedation and intoxication are reviewed before administration medication. The attention is focused on oxygen saturation level and pulse rate. A patient presenting with a suboptimal level of these would require a medical review before medication is administered.

The COVID-19 pandemic and having prisoners who either have symptoms of COVID-19 or have tested positive for COVID-19 led to concern around safety because of potential risk of adverse outcomes for patients. The national UK

guidelines stipulated that any person who either tested positive for or reported symptoms of COVID-19 had to self-isolate for 10 days was implemented in the prison setting (National Audit Office, 2020). As result, patients who either had a positive test or had reported signs and symptoms of COVID-19, and any close contact, were isolated for 10 days (NHS England, 2021). Because of unknown outcome for a combination of OST and COVID-19, the Substance Misuse Service reviewed the treatment protocol with the aim of enhancing safety and clinical outcomes for the patients.

After a team discussion, the substance misuse service developed a protocol to guide the monitoring of deterioration of patients who were COVID-19 positive, reported symptoms, or were a close contact so as to forestall the effect of methadone or buprenorphine because of concurrent experience of signs and symptoms and COVID-19 as well as opioid withdrawal and potential impact of opioids on patients with COVID-19. The protocol developed was discussed by the Substance Misuse Service Team. In addition, a training was provided to all the members of nursing team using the Health Services Journal's Covid Early Warning System's training resources on the use of pulse oximetry (https://training.hsj.co.uk/covid-early-warning-system-saves-lives). The protocol indicated that before the administration of medication to patients who were in isolation, the nurse would assess for alertness, mobility, and acute breathlessness as patients walk toward the cell door, the patients would then sit on a chair, and the nurse would ask and assess for any symptoms as well as assess for pulse and oxygen saturation levels using a finger oximeter. We defined hypoxia as an oxygen saturation below 94% in the absence (or below 88% in the presence) of CO_2 retaining chronic lung disease (O'Driscoll et al., 2017). Low and high pulses were defined as a pulse lower or higher than a normal resting heart rate of 60–100 beats per minute, respectively. However, according to new early warning system, the normal pulse rate is between 51 and 90 beats per minute (Royal College of Physicians London, 2017). A patient with suboptimal levels of oxygen saturation and pulse would not be medicated but escalated appropriately as per the new early warning system protocol (Royal College of Physicians London, 2017), which provides prognostic information including risk of transfer to hospital (Royal College of Physicians London, 2017; Sbiti-Rohr et al., 2016). The UK and World Health Organization guidelines recommend that pulse oximetry be used in the assessment and monitoring of deterioration of high-risk patients with suspected or confirmed COVID-19 infection who are at risk of seriously being unwell (National Institute for Health and Care Excellence, 2020; NHS England, 2020; World Health Organization, 2021). In addition, available evidence indicates that pulse oximeters can detect silent hypoxia associated with acute COVID-19 at home when used appropriately (Greenhalgh et al., 2021).

AIM

We conducted a retrospective audit of patients tested for COVID-19 who were receiving opioid substitution treatment, to evaluate the outcomes of an intervention that the Substance Misuse Service put in place to manage and monitor the safety of OST among prisoners with SUDs. We aimed at evaluating the safety of methadone and buprenorphine among patients positive for COVID-19 and whether these medications could be a risk factor in adverse outcomes among these patients. In addition, we also evaluated whether patients with SUDs are at risk of deterioration from COVID-19 infection.

ETHICAL CONSIDERATIONS

The Substance Misuse Service is an NHS service provided by Oxleas NHS Foundation Trust as part of Public Health England's commissioned service, and all the data obtained were for the purposes of auditing safety and quality of care. We did not require a formal ethical approval to collect data for quality of care improvement. The approval was granted by Oxleas NHS Foundation Trust as part of efforts aimed at improving quality and safety of care.

METHOD

Setting

A service evaluation audit was carried out in a Substance Misuse Service provided by Oxleas NHS Foundation Trust within HMP Thameside. HMP Thameside is a male remand prison in South London that receives on an average 90 prisoners a month with substance misuse disorders requiring treatment. Currently, the substance misuse service, being mainly a clinical intervention service, focuses on the care of prisoners diagnosed with opiate and alcohol addictions.

Data Collection

Mass COVID-19 testing was introduced in the prison after the second wave of COVID-19 pandemic. The prisoners were tested on Day 1 and Day 5 of arrival into prison. In addition, a prisoner within Wings were randomly subjected to mass testing to forestall the mass spread of COVID-19. In addition, prisoners who reported symptoms of COVID-19 were screened. The prisoners who reported any symptoms associated with COVID-19 or tested positive for COVID-19 were subject to isolation in their cells for 10 days with any preexisting cellmate.

This was a retrospective case–control audit of SystmOne, an electronic medical record system, to identify patients who tested positive for COVID-19 between January and February 2021. A positive COVID-19 test was generally defined as patient with a positive result on reverse transcriptase polymerase chain reaction assays of nasopharyngeal swab specimens. The samples were analyzed at the pathology laboratory of a local hospital.

We were interested on the following outcomes: COVID-19 positive, patients on methadone or buprenorphine, and adverse outcomes (assessed by overdose, intoxication, sedation, review of medication, and hospital transfer because of deterioration). Deterioration of medical condition was measured by low pulse and desaturation. The diagnosis of patients was classified using the International Classification of Diseases - 10 codes (ICD, 2019). In addition to patients' demographic identifiers, we recorded comorbid medical and psychiatric conditions, the types of illicit drugs taken, prescribed medications,

accommodation types, status of treatment in the community, and injecting status.

Study Population

The study population consisted of patients who were recently diagnosed with substance misuse disorder (ICD, 2019), were on opioid substitution treatment with either methadone or buprenorphine, tested positive for COVID-19, and had been in isolation for at least 10 days.

Results

We identified 23 patients who met inclusion criteria. Nine patients were excluded because they did not complete the full 10 days of isolation period in prison because of early release. Table 1 below shows the characteristics of the patients. The mean age of patients was 40 years, with a range of 20–54 years and an *SD* of 8.55. Most of the patients were White, and 56% were homeless. All the patients were polydrug users. This was confirmed through urine drug screen at initial screening at the First Night Reception Clinic. Even the eight patients (35%) who were on the OST in the community used illicit drugs on top. All patients had a history of smoking tobacco in the community.

Many patients (68%) had an additional diagnosis of mental illness. On the other hand, only 30% had an additional physical illness diagnosis, with respiratory conditions accounting for 9%. Because of comorbid conditions, 68% of patients were on additional psychiatric medications, and two patients with chronic obstructive pulmonary disease were on inhalers.

When prisoners are admitted into prison, they are often started on a low dose of methadone sugar-free oral solution 1 mg/1 ml, 10 mg, and buprenorphine sublingual tablet, 4 mg, with a slow titration up as per the national clinical guidelines (Independent Expert Working Group, 2017). Because of this, 39% ($n = 9$) of patients were on titration, with most ($n = 8$) on methadone, and only one patient was on buprenorphine.

On injecting status, 22% ($n = 5$) were currently injecting, whereas 26% ($n = 6$) had a previous history of injecting drugs. Twelve patients denied having a history of injecting drugs.

During isolation, all patients were physically observed and examined using pulse oximeter, paying attention to pulse and oxygen saturation before administration of morning medication. In addition, all patients were asked whether they had any symptoms. The mean and *SD* for pulse were 76.64 beats per minute and 10.65, respectively. In addition, the mean and *SD* for oxygen saturation were 97.9% and 1.16, respectively.

The reasons for patients being put in isolation were varied. Three (13%) prisoners were isolated directly from reception as they had presented with information from police custody that they had reported symptoms or had recently tested positive for COVID-19. Their COVID-19 status was additionally confirmed through a prison healthcare screening process. Four (17%) patients tested positive through the initial screening at reception, seven (30%) tested positive after testing at Day 5 of being in custody, one patient (4.3%) was screened after reporting of symptoms (sore throat and headache) associated with COVID-19, one had shared a cell with a symptomatic cellmate, and seven (30%) patients tested positive after mass testing on the Wing. Only two patients reported one COVID-19-associated symptom of fever.

DISCUSSION

The efficacy of pulse oximeter to detect silent hypoxia and desaturation among patients with COVID-19 is shown in this study. It is known that patients with COVID-19 are at risk of having silent hypoxia without exhibiting symptoms of respiratory distress like low oxygen saturation and low pulse (Greenhalgh et al., 2021; Luks & Swenson, 2020; NHS England, 2020; Quaresima & Ferrari, 2020). Because of this, the NHS England proposed to roll out the provision of pulse oximeters in the community for patients diagnosed with COVID-19 so that they could monitor themselves to reduce the risk of serious deterioration and prevent death (NHS England, 2020). This scheme was also to be expanded across prisons in England to improve on outcomes for patients with COVID-19 in custody. Regular blood oxygen monitoring could provide advance warning of hypoxia and an early indicator of whether a patient with COVID-19 may require hospitalization or could be continued to be cared for in the prison. In fact, the use of pulse oximeters to monitor acute pulmonary problems has been studied and showed to be feasible for monitoring deterioration and progress of patients (Bonnevie et al., 2019; Shah et al., 2017). In our sample, none of the patients had suboptimal pulse and oxygen saturation levels.

The main aim of this audit was to confirm the safety of OST with methadone and buprenorphine in the treatment of substance misuse disorders. We measured the safety of medications based on outcomes such as overdose, intoxication, sedation, review of medication, and hospital transfer because of deterioration in health. The results indicate that none of the patients deteriorated. Our results show that methadone and buprenorphine are safe among patients positive for COVID-19 and that the medications on their own did not lead to adverse outcomes among patients with COVID-19. The results also show that OST patients are not at an increased risk of deterioration from COVID-19 infection.

Although it might appear that the sample was composed mainly of healthy populations with little or no comorbid conditions associated with adverse outcomes from COVID-19, we were aware of the underdiagnosis and lack of engagement with health services among this cohort (Peat et al., 2016). In addition, the sampled patients had a history of smoking crack cocaine, heroin, and tobacco, commonly associated with respiratory and cardiovascular diseases (Buster et al., 2002; Kleerup et al., 2002; Mehta et al., 2020; Vidyasankar et al., 2015). Generally, evidence indicates that patients with SUDs have a significantly high prevalence of comorbidities such as chronic lung, liver, kidney, and cardiovascular diseases; metabolic disorders; compromised immune systems; and psychiatric conditions compared with patients without SUDs (Gupta et al., 2021; Leece et al., 2015; Mallet et al., 2021; Melamed et al., 2020; Volkow, 2020; Wei & Shah, 2020;

TABLE 1 Characteristics and Behaviors of Patients

		%	*n*	Mean	*SD*
Total Number of Patients			**23**		
Reasons for isolation	On arrival with information	13	3		
	Reception testing	17.4	4		
	5-Day testing	30	7		
	Symptomatic	4.3	1		
	Symptomatic cellmate	4.3	1		
	Mass testing	30	7		
Age				40	8.55
Ethnicity	White	69	16		
	Asian	13	3		
	Black	9	2		
	Mixed	9	2		
Type of accommodation	NFA	56	13		
	Fixed address	44	10		
Polydrug use		100	23		
Type of drugs used	Heroin	95.7	22		
	Crack	56.5	13		
	Cocaine	30	7		
	Alcohol	13	3		
	Benzodiazepines	13	3		
	Cannabis	17.4	4		
	Tobacco	100	23		
Injecting status	Not injecting	52	12		
	Previously injected	26	6		
	Currently injecting	22	5		
OST in the community		35	8		
Previously on OST		100	23		
Current OST medication	Methadone	87	20		
	Buprenorphine	13	3		
Physical illness diagnosis	Epilepsy	4.35	1		
	DVT	4.35	1		
	COPD	8.6	2		
	Lymphedema	4.35	1		
	Cellulitis	4.35	1		
	Chronic leg ulcer	8.6	2		
Mental illness diagnosis	Paranoid schizophrenia	17.4	4		
	Depression	47.8	11		
	Psychosis	4.35	1		
	EUPD	8.6	2		

(continues)

TABLE 1 Characteristics and Behaviors of Patients, Continued					
		%	*n*	Mean	*SD*
Total Number of Patients			**23**		
Psychotropic medication	Olanzapine	8.6	2		
	Sertraline	17.4	4		
	Mirtazapine	26	6		
	Risperidone	4.35	1		
	Quetiapine	8.6	2		
	Aripiprazole	4.35	1		
Physical health medication	Salbutamol inhaler	4.35	1		
	Spiromax	4.35	1		
Symptoms reported	Sore throat	4.35	1		
	Fever	8.9	2		
	Headache	4.35	1		
Physical examinations/observations	Pulse			76.64 bpm	10.65
	Oxygen saturation			97.90%	1.16
OST medication	Methadone		20	36 mg/ml	11.58
	Buprenorphine		3	6.66 mg	1.89

COPD = chronic obstructive pulmonary disease; DVT = deep vein thrombosis; EUPD = emotionally unstable personality disorder; NFA = No Fixed Abode; OST = opioid substitution treatment.

Wang et al., 2021; Zhao et al., 2018). These conditions are known risk factors for severe illness, hospitalizations, and mortality among those infected with COVID-19. In addition, the misuse of drugs such as crack cocaine and heroin, by having an effect on the cardiovascular and respiratory systems, compromises their inherent functions (Barsky et al., 1998; Frishman et al., 2003; Ghuran & Nolan, 2000; Kleerup et al., 2002; Meisels & Loke, 1993; Nightingale et al., 2020; Tashkin et al., 1992; Vidyasankar et al., 2015). Because of this, people with substance misuse disorders who have high rates of physical health conditions, both diagnosed and undiagnosed, are more likely to have adverse outcomes when infected with COVID-19 in comparison with the general populations (Jemberie et al., 2020; Leece et al., 2015; Wang et al., 2021; Wei & Shah, 2020; Wurcel et al., 2015). People who smoke crack cocaine and heroin have been shown to have quicker disease progression and reduced lung capacity (Nightingale et al., 2020). Furthermore, many patients with SUDs who were positive for COVID-19 were classified as "No Fixed Abode," which is likely accountable for the notably higher diagnosis of COVID-19 on entry to the prison. Despite the above evidence, our patients did not suffer adversely with COVID-19.

A retrospective case–control study of electronic health records found that COVID-19 patients with SUDs had significantly worse outcomes measured by death and hospitalization compared with other patients with COVID-19 (Wang et al., 2021). Regardless of the type of addiction, this study also found that prevalence of known risk factors for COVID-19 among patients with OUDs was not higher than that among patients with other types of SUDs (Wang et al., 2021). Currently, there is a lack of studies on the interactions between COVID-19 and substance misuse disorders (Wei & Shah, 2020), as well as the outcome for people with substance misuse disorders who are infected with COVID-19. In addition, there is very little evidence on the differential effects of substances such as opioids, cocaine, cannabis, alcohol, and benzodiazepines on the susceptibility to COVID-19 infection and to adverse outcomes (Volkow, 2020).

Although methadone appears to be safe, this was largely a closely monitored population that did not have access to additional illicit drugs. It is debatable whether these results could be replicated in the community setting. In fact, it is likely that methadone overdoses could occur in the streets, homeless shelters, and supported accommodation. Evidence from Canada indicates that most drug overdoses occurred indoors (Mackinnon et al., 2020).

Several patients were on additional psychotropic medications. Although it is known that some of these medications could have side effects like fever, cough, and dyspnea that mirror COVID-19 symptoms (Javelot, Llorca, Drapier, et al., 2020), there is lack of evidence on the interaction between psychotropic medications and COVID-19 infection (Javelot, Llorca, Meyer, et al., 2020). Although this was not the aim, this study has also shown that psychotropic medications are safe among patients with COVID-19, more so in combination with OST.

Recommendations

No studies have been carried out to determine the rates of COVID-19 infections in prisons as compared with the general population. However, prisons are likely to experience

outbreaks of infections because of structural risk factors such as overcrowding, reduced ventilation within cells, lack of social distancing among prisoners and prison officers, and poor environmental hygiene characterized by sharing of toilets, bathrooms, and items such as vapes among prisoners. In addition, prisoners who have reported COVID-19 symptoms are often locked and isolated in cell with a cellmate whether they have symptoms or not. Furthermore, remand prisons have a higher rate of prisoner admission, with most being brought in from the general population as opposed to transfers from other prisons, as well as increased movement through Wings, increasing the risk of the spread of COVID-19. We recommend that studies are needed to determine rates of infections and factors that influence the spread of COVID-19 in prisons. In addition, as is happening in prisons in the United Kingdom, persons entering addiction treatment and recovery support services should be routinely screened for COVID-19.

The uptake of vaccine among SUD populations is likely to be low within the community because of lack of primary and secondary health engagement. There should be investment in promotion and development of trust in vaccination among this population as they would become reservoirs of future infections as they face structural barriers characterized by homelessness, frequent incarcerations, discrimination, and stigma despite being a group with a high COVID-19 risk. Prisoners with drug misuse disorders are faced with structural barriers in terms of access to healthcare and should be offered vaccination as a matter of routine before they leave prison as they are most likely not to engage with services in the community. As such, prison offers a rare but important window of opportunity.

Although the highest prevalence of crack cocaine use within Europe is in the United Kingdom, there is a low amount of crack pipes (EMCDDA, 2019). As crack cocaine is mainly smoked, this has led to users having to create and share makeshift pipes, increasing the risk of transmission of COVID-19 (Harris, 2020). We recommend that it is also worth the consideration for community services to provide "crack pipes" in a similar scheme to "needle exchange" to help reduce COVID-19 transmission among SUD populations.

We need further research on the effects of SUD recovery status on COVID-19 infection, hospitalization, and death risk. Because of lack of robust studies, much remains to be learnt regarding the relationship between COVID-19 and alcohol and other substances of abuse.

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