

COVID-19 and Substance Use Disorders: Recommendations to a Comprehensive Healthcare Response. An International Society of Addiction Medicine (ISAM) Practice and Policy Interest Group Position Paper

Ali Farhoudian^{1,2}, Alexander Baldacchino³, Nicolas Clark^{4,5}, Gilberto Gerra⁶, Hamed Ekhtiari⁷, Geert Dom⁸, Azarakhsh Mokri¹, Mandana Sadeghi⁹, Pardis Nematollahi¹⁰, Maryanne Demasi¹¹, Christian G. Schütz¹², Seyed Mohammadreza Hashemian¹³, Payam Tabarsi¹⁴, Susanna Galea-singer¹⁵, Giuseppe Carrà¹⁶, Thomas Clausen¹⁷, Christos Kouimtsidis¹⁸, Serenella Tolomeo¹⁹, Seyed Ramin Radfar^{2,20*}, Emran Mohammad Razaghi¹

1. *Department of Psychiatry, Tehran University of Medical Sciences, Tehran, Iran*
2. *Substance Abuse and Dependence Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran*
3. *Division of Population and Behavioural Sciences, St Andrews University Medical School, University of St Andrews, UK*
4. *North Richmond Community Health, Melbourne, Victoria, Australia*
5. *Royal Melbourne Hospital, Melbourne, Victoria, Australia*
6. *Drug Prevention and Health Branch, Division for Operations, United Nations Office on Drugs and Crime, Vienna, Austria*
7. *Laureate Institute for Brain Research, Tulsa, OK, United States*
8. *Collaborative Antwerp Psychiatric Research Institute, University of Antwerp, Antwerp, Belgium*
9. *Aftab Mehrvarzi Substance Abuse Treatment Center, Tehran, Iran*
10. *Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*
11. *North Richmond Community Health, Victoria, Australia*
12. *Department of Psychiatry, University of British Columbia, Vancouver, BC, Canada*
13. *Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
14. *Clinical Tuberculosis and Epidemiology Research Center, National Research Institute for Tuberculosis and Lung Disease (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran*
15. *Institute for Innovation and Improvement, Waitemata DHB and Centre for Addictions Research, University of Auckland, Auckland, New Zealand*
16. *Department of Medicine and Surgery, Section of Psychiatry, University of Milan Bicocca, Milan, Italy*
17. *Norwegian Centre for Addiction Research (SERAF); University of Oslo, Oslo, Norway*
18. *General Secretariat of Prime Minister, Ministry of Health, Athens, Greece*
19. *Department of Psychology, National University of Singapore (NUS), Singapore*
20. *Integrated Substance Abuse Programs, University of California, Los Angeles, Los Angeles, CA, USA*

*** Correspondence:**

Seyed Ramin Radfar MD, MPH, NIDA/IAS Fellow

Email: raminradfar@yahoo.com

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Abstract:

Coronavirus disease 2019 (COVID-19) is escalating across the world with higher morbidities and mortalities in certain vulnerable populations. People who use drugs (PWUD) are a marginalized and stigmatized group with lower access to health care services, weaker immunity responses, vulnerability to stress, poor health conditions, and high-risk behaviours that put them at greater risk of COVID-19 infection and its complications. In this paper, an international group of experts on addiction medicine, infectious disease and disaster psychiatry explore the possible concerns raised and provide recommendations to manage the overlaps between COVID-19 and Substance Use Disorder (SUD).

Keywords: Coronavirus; COVID-19; Pandemic ; Public health; Substance use disorder; Addiction medicine; Harm reduction; Policy; Methadone; Opioid substitution therapy;

1. Introduction

Coronavirus disease 2019 (COVID-19) is a new member of the family of coronaviruses that infect humans[1] and which first emerged in the Wohan region of China in November 2019 [2]. By March 2020, the World Health Organization (WHO) assessed the global situation of COVID-19 as a pandemic. Cardiovascular disease, chronic respiratory disease, individuals aged 60 or older, and males have a higher risk of mortality than the rest of the population [3-5].

Frequently reported clinical symptoms at onset include pyrexia (83–98%), cough (46%–82%), myalgia or fatigue (11–44%), and shortness of breath (31%) [3-5]. Sore throat and, less commonly, sputum production, headache, hemoptysis, and diarrhea and have also been reported [6]. In more severe cases, COVID-19 can cause pneumonia, severe and acute respiratory syndrome and sometimes (1-3% of all infected cases death [7]. Currently, the medications under investigation for severe cases of COVID-19 include chloroquine phosphate [8] , hydroxychloroquine sulfate [9], lopinavir/ritonavir[10, 11], remdesivir [12], interferon-beta [13], oseltamivir and [11, 14] ribavirin [11] but none have been approved by regulatory authorities for use against COVID-19.

The most common strategies, as advised by WHO, include preventative measures such as quarantine and limitations of movement in infected areas [15, 16], interruption of human-to-human transmission, early identification and isolation, contact tracing of confirmed cases, providing appropriate care for patients, identifying and reducing transmission from the animal source, and minimizing social and economic impact through multispectral partnerships[17]. *Bai and colleagues* mentioned COVID-19 transmission from asymptomatic patients as a particular challenge for preventive activities [18].

In most countries, people who use drugs (PWUD) are a stigmatized and marginalized population with lower access to healthcare, they suffer from poorer health, weaker immune function, chronic infections, various issues with respiratory, cardiovascular and metabolic systems, as well as a range of psychiatric comorbidities [19, 20]. PWUD are often marginalized, experiencing a high rates of morbidity. Studies show the overall mortality rate

is three to five times higher in this marginalized group compared to the general population [21]. Cheung *et al* estimated that the risk of death among young PWUD homeless women in Toronto is 5 to 30 times higher than their housed counterparts [22, 23] . Substance use imposes different health problems which may complicate superimposed infection with COVID-19. For instance, chronic high alcohol consumption significantly increases the risk of acute respiratory distress syndrome [24]. During the 2009 H1N1 epidemic, a history of opium inhalation was identified as a risk factor for admission to an intensive care unit (ICU) with confirmed H1N1 [25]. Additionally it is important to understand how PWUD have a different perception of risk and risk taking behaviours during an epidemic, making them more risk averse [26, 27]. PWUD has a higher rate of smoking and different studies estimated current smoking rate of more than 70% [28-30]. Several studies found smoking as a significant risk factor for Middle East Respiratory Syndrome (MERS) transmission [31-33]

A literature search did not identify one article focusing around substance use disorder (SUD) and COVID-19. A group of international experts on addiction medicine, infectious disease and disaster management shaped a working group to explore the issues that might emerge when COVID-19 infection effects PWUD and identified the following recommendations for health service providers and policy makers

1.1. The system

Although the majority of COVID-19 infections are mild, the volume of severe cases in a pandemic has the potential to completely overwhelm any healthcare system. Consequently, health authorities may be required to repurpose health services and facilities away from PWUD. When such an incident occurs a business continuity protocol will cover several contingency measures so that organizations supporting PWUD will continue to provide its essential services. A response to both COVID-19 and drug use involves government, different sectors of the community and health authorities [34] to implement evidence-based prevention programs as well as engaging different stakeholders for policy coordination [35]. Generally, drug use prohibition and criminalization approaches result in higher stigmatization and discrimination against PWUD [36, 37]. This approach puts PWUD at a higher risk of viral transmission. Governments, health authorities and other relevant

stakeholders will need to identify provision of services for PWUD as essential services in order to support a comprehensive and proactive response to the challenges that COVID19 places on this population especially when they are in treatment [38].

1.2. The PWUD population

PWUD experience poor access to health services due to stigma and discriminations [19, 39, 40]. They are among one of the pervasive hard-to-reach populations, with studies showing that drug use is one of the major barriers for taking influenza vaccine [41, 42]. Many of the homeless PWUD communities live in crowded groups in shelters and/or shooting galleries with no or minimal air conditioning facilities. Additionally, poor hygiene, risky behaviours such as sharing drug using paraphernalia, and intoxication, put PWUD at greater risk of COVID-19 infection.

One of the other risk factors for PWUD and people who inject drugs (PWID) is a possible weaker immune system due a range of factors including, long term/ high dose administration of opioid drugs [43, 44], malnutrition [45, 46], homelessness [46], and long term alcohol and methamphetamine use [47-49]. Despite lacking evidence for introducing HIV as a risk factor for COVID-19 [50, 51] till now, there are some concerns regarding the access to treatment services for people living with HIV/AIDS (PLWHA) and their adherence to antiretroviral therapy [52] that could finally increase rate of mortality among PLWHA. On the other hand, respiratory infections among PWUD are common and in many cases do not present with recognized symptoms of the infections [53-55]. Tuberculosis is another respiratory infection that is more common among PWUD [56] even in high-income countries [57, 58].

1.3 The PWUD care provider

Care providers are at the front line of any outbreak response are not only at the risk of infection but are also prone to burnout and psychological distress. In a study that conducted on frontline staff involved in the sever acute respiratory syndrome (SARS) epidemic had high levels of burnout, psychological distress, and posttraumatic stress [59]. This is compounded with evidence that counsellors and therapist for PWUD were known that have higher rate of burnout[60] during normal practice. Staff working harm reduction settings

where most of the health service providers are peer groups it is essential that they are adequately supported to prevent cross viral exposure, psychological distress [61, 62], psychiatric disorders [63, 64], discrimination [65], and being the victim of physical and psychological violence [7]. Concerns regarding infection and the above mentioned stressful events may affect their effectiveness in an outbreak [66]. All staff need to access to Personal Protection Equipment (PPE).

They should perform hand hygiene frequently, use alcohol-based hand rub/gels if hands are not visibly soiled or with soap and water when hands are visibly soiled; keep at least one meter distance from affected individuals; wear a medical mask when in the same room with an affected individual; dispose of the material immediately after use; clean hands immediately after contact with respiratory secretions; covering the nose and mouth with a flexed elbow or disposable tissue when coughing and sneezing; refraining from touching eyes, nose or mouth with potentially contaminated hands [67] avoid close contact with anyone that has fever or cough [7], and finally improve airflow in living space by opening windows as much as possible [68]. Self-isolation of individual staff is paramount if there are signs of an infection[69-71], or exposure to infected cases.

PWUD staff still need to retain their crucial role of continuing at a distance either through digital technology or phone their PWUD management and treatment plan such as the provision of daily OST medication [72].

There is no convincing evidence that the paraphernalia and devices for drug use are major sources of virus transmissions in the latest epidemics of coronaviruses [73]. However, as the main source of viral transmission has been defined to occur through the droplets, it makes sense specifically to advise PWUD populations to avoid sharing cigarettes, pipes [47], water pipes and hookahs, etc. [74, 75]. One should continue providing clean needle and syringes and Take Home Naloxone (THN) when appropriate.

2. Early detection and referral systems and linkages to other community-based services

Infected patients are most virulent during the prodromal period, and in case of being mobile, and carrying on usual activities, they have an important role in infection spread to the other parts of the community [71]. In such conditions, it is very important to have an effective mechanism for the active and rapid detection of signs and symptoms and isolation [16, 76]. During the H1N1 pandemic in 2009, one of the risk factors for death or admission at intensive care units was delay in diagnosis [25]. Early detection in PWUD can be difficult as COVID-19 symptoms could be confused as part of a withdrawal syndrome [53-55]. It is highly recommended that a mechanism is in place for frequent screening of COVID-19 in PWUD within harm reduction and treatment settings [39, 40, 77].

3. Specific concerns around opioid substitution therapy

Any pandemic affects illicit drug distribution networks [78]. Sometimes this situation persuades PWUD to access treatment services for help but it is more likely that they will switch to a more hazardous consumption. For example the Iranian COVID pandemic generated the country's highest cluster of deaths due to methanol toxicity [79, 80]. However, provision of pharmacotherapies for the treatment of opioid dependence has become the main focus of the continuity plans around PWUD to make sure that such provision is not interrupted during the COVID-19 lockdown strategies being imposed by several governments.

3.1 Protocol for opioid pharmacotherapy provision:

3.1.1. Prescribing and dispensing of methadone and buprenorphine

Any close personal contact may be risky for COVID-19 transmission. Where possible, services should consider prescribing medications following telephone or video consultations. Prescriptions may be made for longer periods of time than usual, and can be delivered to

pharmacies by mail, email or fax. Take-home doses of medications can be provided for longer periods of time in situations of quarantine, self-isolation or lockdown and health service disruptions. Normal take-home policies should be relaxed and maximum periods of time for take-home doses of medications are recommended when the dose and social situation are stable. Treatment seeking individuals should be properly informed about the changes in practice and receive appropriate support in case of uncertainty and concerns. However, decisions should be taken on a case by case basis. Buprenorphine take-away doses are probably safer than methadone take-home doses.

If the person is in isolation and unable to pick up their medication personally, it can be delivered to their homes, or they can authorize someone else to collect the medication.

3.1.2. Optimal medical interventions for new patients

Opioid substitution therapy (OST) is among a category of treatment modalities that is normally considered to need regular and frequent supervision of patients, especially early in treatment. It is recommended that a more flexible OST program needs to be taken into account during the COVID pandemic [81].

Given the safety profile of buprenorphine, it would seem to be the preferred substitution treatment for individuals who want to initiate treatments. It is faster and safer [82] to reach an effective maintenance dose of buprenorphine compared to methadone, in fact it can be done on the first day of treatment. Some of the medications under consideration for the treatment of COVID-19 can significantly inhibit and/or stimulate methadone metabolism, putting patients at the risk of withdrawal or toxicity [83, 84]. Methadone specifically in high doses may prolong QT interval and cause fatal arrhythmias [85]. Possible cardiomyopathy in infected patients may increase the chance of Torsade's de Pointes arrhythmia and death [86], particularly if combined with chloroquine which also prolongs the QT interval.

Withdrawal symptoms from buprenorphine are milder than that of methadone in case of interruption to the supply of medication, at least in the short term.

Where available, the long acting (monthly) subcutaneous injections are an alternative to providing take home doses. Even transdermal buprenorphine should be considered where no

other alternatives exist. Multiple patches can be given simultaneously if necessary to achieve a therapeutic dose for opioid dependence treatment.

Additionally, benzodiazepine prescription for myalgia or stressful circumstances due to COVID-19 may also increase the risk of toxicity during methadone maintenance treatment (MMT). During the pandemic period, it is more likely that individuals with drug use disorders or those who are in treatment seek out benzodiazepines or other tranquilizers [87, 88]. Benzodiazepines misuse may mask signs and symptoms of COVID-19 infection and could escalate respiratory distress.

3.2. Considerations regarding different stages of maintenance therapy

3.2.1. Stage 1: Early Stabilization

Patients are at higher risk of methadone toxicity in the early stabilization period of methadone prescription [89, 90]. For MMT patients, the authors do not recommend relaxing the methadone dose protocol at this phase of treatment however they do suggest avoiding unnecessary visits and rigor, on a case by case basis. If accelerated induction is necessary, an additional dose of 30-40 mg can be followed by a further dose if someone has been observed 2 hours after their initial methadone dose. If they are still experiencing withdrawal at this time, they can safely be given a further dose. For buprenorphine, individuals can be rapidly inducted to optimal maintenance doses (16-24mg daily).

3.2.2. Stage 2: Late Stabilization

Clinicians should consider increasing the dose if the individuals are still experiencing has daily cravings, ongoing opioid use, or opioid withdrawal. However, clinicians should be sensitized in the differentiation between withdrawal syndrome including myalgia, insomnia, sweating, fatigue, and nausea with signs and symptoms of viral COVID19 infection. Pupil size is normally the best guide to distinguish opioid withdrawal from the symptoms of COVID-19 as COVID-19 infection does not affect pupil size. It should be possible to see pupil size even with video consultations.

3.2.3. Stage 3: Maintenance

Although the prescription period of anti-viral treatment is usually less than two weeks and the induction of hepatic metabolic enzymes takes more than the regular time for antiretroviral therapy (ART) prescription, clinicians should be careful about the change of methadone level in patients during and more specifically after termination or discharge of treatment for COVID-19. Changing from once daily dosing to a split dose twice daily is one strategy in patients who receive antiviral treatment. As a result of induction of methadone metabolism, some patients may need a mild increase in their previous methadone dosage after a few days of initiating antiviral treatment. For buprenorphine, double doses can be given every alternate day for people who are not considered safe to receive take-home doses.

3.2.4. Stage 4: Termination

In exceptional situations, some patients on MMT or BMT fulfil the criteria for termination of their OST. Termination is a stressful process [91] and needs close supervision and constant consultation. Besides, the emotional distress associated with opioid withdrawal may increase the risk of suicidal ideation. Termination of MMT and BMT increases the stress and more attendance at treatment centers are needed, so it is not recommended during the COVID-19 epidemic.

3.2.5. Detoxification

Some people who use opioids may wish to cease their opioid use during the epidemic, either due to reduced availability of opioids or due to the difficulty accessing treatment services. The simplest approach to detoxification, if available, would be a single high dose buprenorphine dose. Doses ranging from 32 to 96mg have been used for this purpose [92]. The long acting subcutaneous forms of buprenorphine can also be used in this way. Alternative approaches include clonidine, or a combination of symptomatic medications [93].

3.3. Urine/Saliva Drug testing

Individuals with moderate to severe signs of COVID-19 infection may need medications consisting of cocktail of ART, antimicrobials and analgesics. These medications may interfere with urine or saliva test results. For instance, Quinolones (e.g. moxifloxacin,

lomefloxacin, norfloxacin, ofloxacin, ciprofloxacin), rifampin, tolmetin (a nonsteroidal anti-inflammatory drug) may yield a false positive result in opiates urine drug screening [94]. Chloroquine [95] may result in amphetamine- false positive urine drug screens. Ibuprofen, naproxen, and efavirenz (antiretroviral medication used to treat and prevent HIV/AIDS.), may result in false positive in Δ 9-tetrahydrocannabinol (THC) and benzodiazepines screening tests [96-98]. In the duration of COVID-19 pandemic, the clinicians should assess the benefits of the urinary or saliva testing at this critical circumstance especially as this will potentially increase risks unnecessary due to close contacts.

4. Psychological consequences

In this pandemic, it seems that information is spreading more extensively and rapidly in comparison to when SARS broke out in 2003, which may result in exacerbation of public fear, panic, and distress. Social isolation may also make individuals susceptible to more psychological distress. Consequent economic depression after a pandemic also causes uncertainty and threats to future welfare [99]. The unpredictable future is exacerbated by myths and misinformation that are often driven by fake news and public misunderstanding [100]. Some patients will experience bereavement over the loss of a loved one.

The relationship between negative life events and brain stress systems have a prominent role in addiction disease [101-103]. PWUD are much more vulnerable to stress and crisis followed by lapse and relapse to ex-drug users [104-107]. As a result of stressful events and disasters, mental health problems emerge or exacerbate [108, 109]. In such circumstances, healthy individual may start drug use [107, 110], several patients may relapse into their previous drug use, start their high-risk behaviours [78, 110, 111]. Anxiety, worry, depression, irritability, and anger in in PWUD should be considered as a prodromal sign of lapse or relapse into new episode of drug use.

4.1. Psychological interventions

Psychosocial interventions are a key element in the treatment of PWUD especially in people using stimulants and with psychological problems [112]. In this period, telephone and internet-based psychotherapy is highly recommended as a replacement. Consultations by phone call, video chat, and short messages have great potential to make psychological

assessment and treatment more cost-effective. Computer-assisted therapy appears to be as effective as face-to-face treatment for treating anxiety disorders and depression[113] in some studies. It requires some very basic devices and knowledge and offers a good alternative for more isolated locations which have become relevant in this pandemic.

4.1.1. Cognitive Behaviour Therapy (CBT)

Negative emotional states that patients will experience during the COVID-19 pandemic include fear, anxiety and boredom as well as social withdrawal and/or isolation. CBT has been recognized as one of the most beneficial interventions for PWUD [114]. Stress reduction as a technique of CBT, either alone or in combination with pharmacotherapies, may prove beneficial in increasing quality of life and reducing cravings and promoting abstinence in clients seeking treatment for SUD [104]. Clinicians should help their patients to identify, manage, and reduce their negative emotional states that are associated with relapse and apply techniques of behavioural activation compatible with specific circumstances of each patient.

Coping skills training and crisis intervention are the most common types of CBT interventions to be recommended.

4.1.2. Matrix Model for ATS

Matrix Model is a multi-element package of therapeutic strategies to produce an integrated outpatient treatment experience[115, 116]. Treatment is delivered in an intensive outpatient program primarily in structured group sessions targeting the necessary skills. It is recommended that the sessions could be held individually instead of group format hoping to lessen the risk of infecting to COVID-19. The recommended parts based on the manual [117] for the period of COVID19 pandemic include:

RP17: Taking Care of Yourself

RP18: Emotional Triggers

RP20: Recognizing Stress

RP22: Reducing Stress

RP24: Acceptance

RP29: Coping with Feelings and Depression

RP Elective C: Recreational Activities

While face-to-face group work may be impossible during the COVID-19 pandemic, these sessions can also be conducted via group video chat, or individually.

4.1.3. Contingency Management

Incentive-based treatment approaches (i.e., contingency management (CM)) are effective interventions in reducing addictive behaviours in PWUD [114, 118-121]. There is also evidence showing that CM is highly beneficial for the treatment of these individuals targeting infectious disease control [122]. In order to take advantage of CM in the prevention of COVID-19, the desired behaviours (e.g. washing hands every hour, cleaning hands, etc.) and their scores or prizes (e.g. take-home doses) should be clearly defined and utilized into the list, just like other desired behaviours (e.g. negative urine test).

4.1.4. Enhancing social supports

Perceived social support from relatives and friends is a major predictor for retention in treatment for PWUD [123, 124] and the main factor of psychological resilience to disaster [125, 126]. Considering the importance of family support, it is recommended that clinicians engage family and carers more than ever during the pandemic, particularly is the person using drugs is forced into home isolation with family members. Attracting other sources of social support such as guaranteed wages, increase in social security payments will help the individual to pass this period with a better outcome.

5. PWUD pathology specific issues during treatment for COVID-19 infection

5.1. Respiratory illness

Opioids such as methadone are respiratory depressants and tolerance develops very slowly and incompletely. When patients undergoing MMT and acquire COVID-19, they should be

more closely monitored for both worsening respiratory functions and methadone toxicity. Abrupt cessation of methadone must be avoided, because anxiety and agitation due to withdrawal syndrome may induce or worsen cardiorespiratory complications [127, 128].

5.2. Renal insufficiency

The prevalence of kidney impairment in hospitalized COVID-19 patients are high and renal insufficiency increases the risk for in-hospital deaths [129].

Studies indicate that heroin users may suffer from nephropathy [130-132]. Other studies have found that individuals using amphetamine [47, 133, 134], cocaine [135-137], alcohol [138, 139], and strong cannabis [140, 141] are also more likely to suffer from renal failure. This may increase the risk of death in PWUD if they contract COVID-19.

5.3. Cardiovascular disorders

Heart disease increases the risk of death due to COVID-19 from approximately 1% in the general population to 6% in individuals with hypertension, 7.3% in diabetics, and 10.5% in patients with other cardiovascular disease [142, 143].

Individuals who have a history of alcohol or drug use are more likely to have cardiac pathology. Excessive alcohol consumption [144, 145] amphetamine [146, 147], heroin [148], and cocaine use [149] are all associated with increased risk of cardiac pathology.

5.4. Pain management

Contracting COVID-19 sometimes can result in moderate to severe pain including myalgia, sore throat, and headache that requires pain management. It is recommended that acute pain in PWID with COVID-19 is managed in consultation with pain or addiction specialists.

People who use opioids regularly will require additional opioids for the management of pain [150, 151]. Buprenorphine as a high-affinity partial agonist of mu-receptors has an analgesic effect in divided doses, but stops effecting other opioid analgesics and hinders acute pain management in case of necessity [152]. In this case, buprenorphine can be ceased and opioid analgesics used or buprenorphine can be continued and non-opioid medications such as clonidine, pregabalin/gabapentin and ketamine can be used [153].

6. Treatment system issues in a time of COVID-19

Health services will need to rapidly adapt to the COVID-19 situation. They will need to establish a mechanism of making decisions quickly and under stress, to identifying the essential services to be continued, to develop new mechanisms of patient flow (including screening, batching and referral), to redistribute staff from non-essential roles, and maintaining the continuity of essential supplies [154]. To reduce the risk of transmission, it is generally recommended that non-essential services close, or make their services available by telephone or on-line. When face-to-face services are required, some modifications may need to be made to the service system, for the identification of cases, the protection of staff, the reduction of transmission, and to ensure the continuity of essential services [155].

6.1. Case detection

When health services remain open in a pandemic, they should first invite all visitors to wash their hands before they touch anything. Then they should screen all new visitors with whatever SARS-CoV-2 screening mechanism is appropriate for the local conditions. This may include a combination of temperature (where possible measured with a non-touch thermometer), clinical symptoms (cough, shortness of breath, sore throat), and epidemiological criteria (recent travel, contact with cases, health care worker). Where, possible, patients meeting the testing criteria should be tested on-site and then directed to isolate themselves awaiting the results. For testing and any subsequent clinical interaction, staff should wear personal protective equipment (PPE) to protect themselves from transmission. If the client is coughing, it is preferable they should also wear a surgical mask [156].

6.2. Prevention of transmission in health services

Transmission is through to be mostly via droplet spread when people who are infected sneeze, cough or talk. Staff and patients should wash their hands frequently and be careful what they touch. Surfaces should be cleaned after they have potentially contaminated. Depending on the availability of PPE and the risk in the local community, it may be appropriate for staff to wear masks and gloves, or even gowns and eye protection. Patients with symptoms should wear a mask to prevent transmission through cough and sneezing. Patients can be divided into three risk

groups, those with confirmed SARS-CoV-2 virus, patients who meet criteria for testing awaiting test results, and other patients with differing levels of PPE depending on the availability of PPE. Preferably, patients with different risk levels should be treated in different parts of the health service. Staff and patients should keep a distance from each other[156].

6.3.Maintenance of essential services

In addition to providing OST, services should take the opportunity to encourage cessation of smoking by prescription of NRT, and by the distribution of naloxone and overdose resuscitation. In preparation of staff members being sick or isolated awaiting test results, each staff member involved in OST treatment should have at least one other staff member who can continue their role if they are sick. Where possible, staff may separate into different teams who have even less contact, so that if one person is sick then the risk of all needing to isolate themselves is reduced [157].

7. Conclusions and recommendations

PWUD are a marginalized hard-to-reach population living in crowded groups with lower access to healthcare who usually suffer from poorer health, weaker immune function, chronic infections, as well as various issues with physical and psychiatric comorbidities; consequently, they have higher risk of COVID-19 transmission and casualties. We believe that substance use and COVID-19 have a complex relationship with each other.

In summary we recommend the following recommendations:

- Health authorities should develop and apply specific strategies for PWUD for early identification and isolation, in order to interrupt transmission, providing appropriate care, attending medical issues and minimizing social negative impact.
- Health authorities continue to be responsible to provide adequate healthcare for PWUSs. They may be required to repurpose and reorient health services through a business continuity team that will be convened to implement evidence-based programs and decisions on how the organizations will continue to provide its services and make sure that all of the OST patients have adequate access to their opioid drugs.

- Treatment sectors should provide the essential requirements as well as software and programs like education tailored to their own clients' needs. Staff may also teach the patients hygiene rules, self-monitoring for signs of illness and rapid reporting the illness in case of occurrence.
- A mechanism for frequently screening for signs and symptoms of infection should be established. Internet and mobile based social media communications should be considered first line approaches for education and appropriate interventions.
- Opioid users face increased challenges; some concerns are about their take-home dose and repetitive visits that makes it impossible for them to stay at home. This pandemic could be considered as an extraordinary circumstance; the clinicians should facilitate OST protocol for clinically stable patients and cancel all group-based interventions/therapies.
- Healthcare workers in substance use treatment facilities are also facing increased risks of infection, burnout, distress, psychiatric disorders, discrimination, and being the victim of violence. The essential right for each service provider, no matter he/she is a peer group or professional service provider, is to be safe and secure, in both physical and mental health aspects.
- Misinformation, social isolation, consequent economic depression, and possible grief reactions may result in exacerbation of public fear, panic, and distress that can be followed by lapse and relapse in ex-drug users.
- Stress reduction, crisis interventions, coping skills training, motivational interviewing, and tailored and modified relapse prevention interventions, modification in contingency-based management for rewarding virus transmission preventive behaviours, attracting family support, managing patients' vocational problems are the main helpful psychosocial interventions.
- In this period, internet-based psychotherapy and phone counselling are highly recommended.

There are many medical considerations regarding PWUD that other physicians in charge of the management of COVID19 treatment should keep in their mind,

- Clinicians should be careful in the differentiation between withdrawal signs and symptoms and signs and symptoms of COVID19 infection.
- PWUD may have different clinical manifestations due to different etiologies. Healthcare providers should consider different possible manifestations and more importantly avoid any type of medical stigma or discriminations against PWUD.
- PWUD regularly self-medicate their physical and mental problems with drugs which may differently mask critical COVID19 symptoms.
- A number of drug-drug interactions between substance of use, addiction treatment medications and medications that are currently used for management of COVID-19 must be considered in terms of toxicity, withdrawal and exacerbation of fatal side effects.
- There is also possible overlap of pathological laboratory results of the CBC and liver enzymes in PWUD and people with COVID-19 infection. Histories of renal failure, cardiovascular, and metabolic diseases are more likely to emerged in PWUD which make them at higher risk of morbidity and mortality after contracting to COVID-19
- Pain management in PWUD specifically opioid users and patients under OST has its own complexity, which needs the involvement of joint expertise

8. Abbreviations:

BMT: Buprenorphine maintenance treatment

CBT: Cognitive Behaviour Therapy

CM: Contingency management

COVID-19: Coronavirus disease 2019

ICU: Intensive care unit

MERS: Middle East Respiratory Syndrome

MMT: Methadone Maintenance Treatment

OST: Opioid substitution therapy

PLWHA: People living with HIV/AIDS

PPE: Personal protection equipment

PWID: People who inject drugs

PWUD: People who use drugs

SARS: Sever acute respiratory syndrome

SUD: Substance Use Disorder

THC: Tetrahydrocannabinol

WHO: World Health Organization

9. Declarations:

9.1. Ethics approval and consent to participate:

Not applicable.

9.2. Consent for publication

Not applicable.

9.3. Availability of data and materials

Not applicable

9.4. Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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9.6. Authors' Contribution

AF and SRR, had original idea, wrote initial topics and headlines, and first draft. AB and NC finalized last version. All authors participated in the literature review, writing, editing, and revision of the report and reached consensus on conclusion. All of the authors declare no conflict of interest.

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Authors also respectfully, dedicate the article to the souls of all healthcare providers who lost their invaluable lives in the fight against COVID19.

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