

Review Paper: 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 Mokri⁹, Mandana Sadeghi¹⁰, Pardis Nematollahi¹¹, Maryanne Demasi¹², Christian G. Schütz¹³, Seyed Mohammadreza Hashemian¹², Payam Tabarsi¹³, Susanna Galea-Singer¹⁴, Giuseppe Carrà¹⁵, Thomas Clausen¹⁶, Christos Kouimtsidis¹⁷, Serenella Tolomeo¹⁸, Seyed Ramin Radfar^{2, 19*}, 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 Behavioral Sciences, St Andrews University Medical School, University of St Andrews, UK.
4. North Richmond Community Health, Victoria, Melbourne, Australia.
5. Royal Melbourne Hospital, Victoria, Melbourne, 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, Oklahoma, USA.
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. Department of Psychiatry, University of British Columbia, Vancouver BC, Canada.
12. Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
13. Clinical Tuberculosis and Epidemiology Research Center, National Research Institute for Tuberculosis and Lung Disease (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.
14. Institute for Innovation and Improvement, IWaitemā DHB, Centre for Addictions Research, University of Auckland, Auckland, New Zealand.
15. Department of Medicine and Surgery, Section of Psychiatry, University of Milan Bicocca, Milan, Italy.
16. Norwegian Centre for Addiction Research (SERAF); University of Oslo, Oslo, Norway.
17. General Secretariat of Prime Minister, Ministry of Health, Athens, Greece.
18. Department of Psychology, National University of Singapore (NUS), Singapore.
19. Integrated Substance Abuse Programs, University of California, Los Angeles, California, USA.



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ABSTRACT

Coronavirus disease 2019 (COVID-19) is escalating all over the world and has higher morbidities and mortalities in certain vulnerable populations. People Who Use Drugs (PWUD) are a marginalized and stigmatized group with weaker immunity responses, vulnerability to stress, poor health conditions, high-risk behaviors, and lower access to health care services. These conditions put them at a higher risk of COVID-19 infection and its complications. In this paper, an international group of experts on addiction medicine, infectious diseases, and disaster psychiatry explore the possible raised concerns in this issue and provide recommendations to manage the comorbidity of COVID-19 and Substance Use Disorder (SUD).

* Corresponding Author:

Seyed Ramin Radfar, MD., MPH., NIDA/IAS Fellow.

Address: Integrated Substance Abuse Programs, University of California, Los Angeles, California, USA.

Tel: +98 (913) 1946104

E-mail: raminradfar@yahoo.com

Highlights

- Health care providers in treatment and harm reduction settings must always have PPE.
- Screening of PWUD with COVID-19 is a priority with respects to human rights.
- Creative, evidence based and realistic approaches are needed for the current situation.
- Virtual context and mobile base platforms could facilitate mainstream interventions.
- Different clinical manifestations and drug interactions are major issues in PWUD with COVID19.

Plain Language Summary

The new coronavirus created a complex situation for all sections of the communities around the world. Health care providers are in the frontline of intervening to stop the spread of COVID-19. Meantime people who use drugs (PWUD) are at increased risk during this pandemic since they are a stigmatized and marginalized populations. Health service providers who are providing different needs for PWUD in treatment and/or harm reduction settings should always keep themselves safe with using standard PPE based on the WHO recommendations. Additionally PWUDs live in crowded locations and so screening and early identification of COVID-19 patients are important to break the cycle of transmission. It is recommended that protocols for opioid substitution therapy modify with complete adherence to patients' safety regarding both opioid drug risks and COVID-19 infections. It is important to have in mind that different stages of OST needs different approaches. PWUDs are more vulnerable to stress and other mental health problems. This makes psychological interventions such as cognitive-behavioral therapy and other modalities very important to have for PWUDs during these difficult and challenging times to assist and sustain treatment. Medical conditions such as respiratory illness, renal insufficiency, chronic pain and cardiovascular disorders are also important medical conditions that should be addressed appropriately among PWUDs with COVID-19. Health service providers in both fields of addiction treatment and COVID-19 treatment and prevention systems should be aware regarding special situations arising in the overlap of drug use and COVID-19 illness.

1. Introduction

Coronavirus Disease 2019 (COVID-19) is a new member of the coronavirus family that infect humans (Zhu et al., 2020). It first emerged in the Wuhan region of China in November 2019 (Lai Shih, Ko, Tang, & Hsueh, 2020). By March 2020, the World Health Organization (WHO) assessed the global situation of COVID-19 as a pandemic. Patients with cardiovascular diseases, chronic respiratory diseases, people aged 60 or older, and males have a higher risk of mortality than the rest of the population (Chen et al., 2020; Huang et al., 2020; Wang et al., 2020).

Frequently reported clinical symptoms at the onset of the disease include pyrexia (83%-98%), cough (46%-82%), myalgia or fatigue (11%-44%), and shortness of breath (31%) (Chen et al., 2020; Huang et al., 2020; Wang et al., 2020). Sore throat and, less commonly, sputum production, headache, hemoptysis, and diarrhea

have also been reported (Chan et al., 2020). In more severe cases, COVID-19 can cause pneumonia, severe and acute respiratory syndrome, and sometimes (1%-3% of all infected cases) death (World Health Organization, 2020b). Currently, the medications used for severe cases of COVID-19 include chloroquine phosphate (Gao, Tian, & Yang, 2020), hydroxychloroquine sulfate (Javadi et al., 2006), lopinavir/ritonavir (Li & De Clercq, 2020; Lim et al., 2020), oseltamivir (Li & De Clercq, 2020; Vetter, Eckerle, & Kaiser, 2020), and ribavirin (Li & De Clercq, 2020). 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 (Hellewell et al., 2020; Wu, Leung, & Leung, 2020), interruption of human-to-human transmission, early identification and isolation, providing appropriate care for patients, identifying and reducing transmission from the animal source, and minimizing the social and economic impact through

multispectral partnerships (World Health Organization, 2020a). Bai and colleagues mentioned some COVID-19 transmission from asymptomatic patients as a challenge for preventive activities (Bai et al., 2020).

In most countries, People Who Use Drugs (PWUD) are 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 (Ahern, Stuber, & Galea, 2007; Stuber, Galea, Ahern, Blaney, & Fuller, 2003). PWUD are a marginalized group who experience high rates of morbidities, three to five times higher compared to the general population (O'Connell, 2004). 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 (Bohnert & Ilgen, 2019; Fernandez-Quintana et al., 2019). 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 (McCarthy et al., 2020). During the 2009 H1N1 epidemic, a history of opium inhalation had been identified as a risk factor for admission to an Intensive Care Unit (ICU) with confirmed H1N1 (Tabarsi et al., 2011). Additionally, it is essential to understand how PWUD differently perceive danger and risk-taking behaviors during an epidemic, making them more risk averse (Manfredi & D'Onofrio, 2013; Rhodes, 1997). PWUD have a higher rate of smoking and different studies estimated the current smoking rate of more than 70% among them (Duan et al., 2017; Sutherland et al., 2016; Weinberger, Gbedemah, & Goodwin, 2017). Several studies found smoking a significant risk factor for Middle East Respiratory Syndrome (MERS) transmission (Alraddadi et al., 2016; Nam, Park, Ki, Yeon, Kim, & Kim, 2017; Sherbini Iskandrani, Kharaba, Khalid, Abduljawad, & Hamdan, 2017).

A literature review did not reveal even one article focusing on Substance Use Disorder (SUD) and COVID-19. Therefore, a group of international experts on addiction medicine, infectious diseases, and disaster management teamed up to explore the comorbidity of COVID-19 infection with substance use disorder and identify the necessary recommendations for health service providers and policymakers in this situation.

1.1. The system

Although the majority of COVID-19 infections are mild, the number of severe cases in a pandemic has the potential to 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 their essential services. A response to both COVID-19 and drug use involves government, different sectors of the community and health authorities (WHO Director-General's opening remarks at the media briefing on COVID-19 on March 5, 2020) to implement evidence-based prevention programs as well as engaging different stakeholders for policy coordination (Volkow, Poznyak, Saxena, Gerra, & UNODC-WHO Informal International Scientific Network, 2017). Generally, drug use prohibition and criminalization approaches result in higher stigmatization and discrimination against PWUD (Boyd & MacPherson, Vancouver Area Network of Drug Users, 2018; Santos da Silveira, Andrade de Tostes, Wan, Ronzani, & Corrigan, 2018). This approach puts PWUD at a higher risk of viral transmission. Governments, health authorities, and other relevant stakeholders should identify the provision of services for PWUD as essential services to support a comprehensive and proactive response to the challenges that COVID-19 places on this population, especially when they are under treatment (Ekhtiari et al., 2019).

1.2. The PWUD population

PWUD have poor access to health services due to stigma and discrimination (Ahern, Stuber, & Galea, 2007; Salamat, Hegarty, & Patton, 2019). They are among the pervasive hard-to-reach populations. For example, studies show that drug use is one of the significant barriers to taking the influenza vaccine (Bryant et al., 2006; Kong, Chu, & Giles, 2020). Many homeless PWUD communities live in crowded groups in shelters and or shooting galleries with no or minimal air conditioning facilities. Additionally, poor hygiene, risky behaviors such as sharing drug-using paraphernalia and intoxication put PWUD at higher risk of COVID-19 infection.

One of the other risk factors for PWUD and People Who Inject Drugs (PWID) is their weaker immune system due to a range of factors. These factors include long-term/high-dose administration of opioid drugs (Liang, Liu, Chen, Ji, & Li, 2016; Sacerdote, Franchi, Gerra, Leccese, Panerai, & Somaini, 2008), malnutrition (Haber, Demirkol, Lange, & Murnion, 2009; Vila et

al., 2019), homelessness (Haber et al., 2009), and long-term alcohol and methamphetamine use (Nelson, Zhang, Bagby, Happel, & Raasch, 2008; Radfar & Rawson, 2014; Roy et al., 2011). Despite lacking evidence for introducing HIV as a risk factor for COVID-19 (British HIV Association, 2020), there are some concerns regarding the access to treatment services for People Living With HIV/AIDS (PLWHA) and their adherence to antiretroviral therapy (Dadkha, Mohammadi, & Mozafari, 2008). This situation could finally increase the 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 these diseases (Dimassi & Rushton, 2009; Bradley Drummond et al., 2011; Gordon & Lowy, 2005). Tuberculosis is another respiratory infection that is more common among PWUD (Perlman, Salomon, Perkins, Yancovitz, Paone, & Jarlais, 1995) even in high-income countries (de Vries et al., 2017; Heuvelings et al., 2017).

1.3. The PWUD care provider

Care providers are at the front line of any outbreak response. They are not only at the risk of infection but are also prone to burnout and psychological distress. In a study conducted on frontline staff involved in the Severe Acute Respiratory Syndrome (SARS) epidemic, it was found that they had high levels of burnout, psychological distress, and posttraumatic stress (Maunder et al., 2006). This situation is compounded with evidence that counselors and therapists for PWUD are well-known as having a higher rate of burnout (Vilardaga et al., 2011) during usual practice. Staff working in harm reduction settings, where most of the health service providers are peer groups, should be adequately supported. This support should prevent cross-viral exposure, psychological distress (Hashemian et al., 2015; Lancee, Maunder, & Goldbloom, 2008), psychiatric disorders (Tang, Pan, Yuan, & Zha, 2017; Zhu et al., 2020), discrimination (Gilchrist et al., 2011), and physical and psychological violence (World Health Organization, 2020b). Concerns regarding infection and the above mentioned stressful events may affect their effectiveness in an outbreak (Abolfotouh, AlQarni, Al-Ghamdi, Salam, Al-Assiri, & Balkh, 2017). All staff should have access to Personal Protection Equipment (PPE).

They should perform hand hygiene frequently, use alcohol-based hand rub/gels if their hands are not visibly soiled or with soap and water when they are visibly soiled. They must keep at least one meter distance from affected individuals, wear a medical mask when in the same room with an affected individual, and dispose of

the material immediately after use. They should clean their hands immediately after contact with respiratory secretions, cover the nose and mouth with a flexed elbow or disposable tissue when coughing and sneezing, and refrain from touching eyes, nose, or mouth with potentially contaminated hands (World Health Organization, 2020b). Also, they must avoid close contact with anyone that has fever or cough (World Health Organization, 2020b) and finally improve airflow in living space by opening windows as much as possible (World Health Organization, 2020b). Self-isolation of individual staff is paramount if there are signs of an infection (Heymann & Shindo, 2020; World Health Organization, 2020a).

PWUD staff still need to retain their crucial role at a distance either through digital technology or phone and continue their PWUD management and treatment plan, such as the provision of daily OST medication (Tschakovsky, 2009).

There is no convincing evidence that the paraphernalia and devices for drug use are the primary sources of virus transmissions in the latest epidemics of coronaviruses (Alagaili, Briese, Amor, Mohammed, & Lipkin, 2019). However, as the main source of viral transmission has been defined to occur through the droplets, it makes sense to advise PWUD populations to avoid sharing cigarettes, pipes (Radfar & Rawson, 2014), water pipes and hookahs, and so on (Knishkowsky & Amitai, 2005; Munckhof, Konstantinos, Wamsley, Mortlock, & Gilpi, 2003). 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. In the case of being mobile and carrying on usual activities, they play an essential part in spreading the infection to the other parts of the community (Heymann & Shindo, 2020). In such conditions, it is imperative to have an effective mechanism for the active and rapid detection of signs and symptoms and patient's isolation (Hellewell et al., 2020; Shamaei et al., 2009).

During the H1N1 pandemic in 2009, one of the risk factors for death or admission at intensive care units was a delay in diagnosis (Tabarsi et al., 2011). Early detection in PWUD can be difficult as COVID-19 symptoms could be confused with a withdrawal syndrome (Dimassi & Rushton, 2009; Bradley Drummond et al., 2011; Gordon & Lowy, 2005). It is highly recommended that

a mechanism be implemented for the frequent screening of COVID-19 in PWUD within harm reduction and treatment settings (Salamat, Hegarty, & Patton, 2019; Van Olphen, Eliason, Freudenberg, & Barnes, 2009).

3. Specific Concerns Around Opioid Substitution Therapy

Any pandemic affects illicit drug distribution networks (Rahimi Movaghar, Farhoudian, Rad Goodarzi, Sharifi, Yunesian, & Mohammadi, 2006). Sometimes this situation persuades PWUD to seek treatment services for help, but usually, they switch to a more hazardous consumption. The Iranian COVID pandemic generated the highest incidence of mortality secondary to methanol toxicity (At least 44 dead from drinking toxic alcohol in Iran after coronavirus cure rumor, 2020; Tainted alcohol claims more lives than coronavirus in Khuzeestan Province, Iran, 2020). However, opioid substitution therapy (OST) provision of controlled medication 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 harmful and risky for COVID-19 transmission. Methadone syrup and buprenorphine tablets or film are often provided to PWUD after bringing out their blister packs. Despite no evidence, this action might increase the chance of viral transmission by exposing both staff and PWUD. It is recommended that dispensing clinics be trained to handle the process of tablet delivery with minimum hand contact.

Take-home doses of medications can be provided for more extended periods in situations of quarantine, self-isolation, or lockdown and health service disruptions. The maximum time for take-home doses of drugs is recommended when the dose and social situation are stable. Treatment seeking individuals should be adequately informed about the changes in the practice, and they should receive appropriate support in case of uncertainty and concerns. However, decisions should be taken on a case by case basis. In summary, individuals under Buprenorphine Maintenance Treatment (BMT) can receive accelerated take-home doses after two weeks of initiation. In particular, the people can receive this protocol who are at least on 60 mg methadone or 8 mg daily bu-

prenorphine and have no signs of withdrawal symptoms, do not experience craving (Mokri, Ekhtiari, Edalati, & Ganjgahi, 2008), are abstinent based on self-reporting, and provide negative toxicological tests. This condition should be reviewed every 14 days if the individuals provided with take-home doses are not showing the stability mentioned above. Buprenorphine take-home 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 (Blake & Lyons, 2016).

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 (Maremmani & Gerra, 2010) 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 (Lüthi, Huttner, Speck, & Muelle, 2007; Winton & Twilla, 2013). Methadone specifically in high doses may prolong QT interval and cause fatal arrhythmias (Krantz, Lewkowicz, Hays, Woodroffe, Robertson, & Mehle, 2002). Possible cardiomyopathy in infected patients may increase the chance of Torsade's de Pointes arrhythmia (Lüthi et al., 2007) and, 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 (Dorn, Yzermans, & van der Zee, 2007; Fassaert et al., 2007). 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 a higher risk of methadone overdose in the initial stabilization period of methadone prescription (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010; Degenhardt, Randall, Hall, Law, Butler, & Burns, 2009). 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 (16-24 mg daily).

3.2.2. Stage 2: Late stabilization

Clinicians should consider increasing the dose if the individuals are still experiencing daily cravings, ongoing opioid use, or opioid withdrawal. However, clinicians should be sensitized in the differentiation between withdrawal syndromes, including myalgia, insomnia, sweating, fatigue, and nausea with signs and symptoms of viral COVID-19 infection. Pupil size is the best guide to distinguish opioid withdrawal from the symptoms of COVID-19 as this 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, the clinicians should be careful about the changes of methadone level in these patients during and more specifically after termination or discharge of the treatment for CO-

VID-19. Change from split doses to multiple daily doses is a strategy in patients who receive antiviral therapy. As a result of the 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 other 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 fulfill the criteria for completion of their OST. Termination is a stressful process (Berger & Smith, 1978) 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, so more attendance at treatment centers are needed, and 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 outbreak, either due to reduced availability of opioids or the difficulty accessing treatment services. The most straightforward approach to detoxification, if available, would be single high dose buprenorphine. Doses ranging from 32 to 96 mg have been used for this purpose (Ahmadi, Jahromi, Ghahremani, & London, 2018). Alternative approaches include clonidine or a combination of symptomatic medications (World Health Organization, 2009).

3.3. Urine/Saliva drug testing

Individuals with moderate to severe signs of COVID-19 infection need medications consisting of a 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 non-steroidal anti-inflammatory drug) may yield a false-positive result in opiates urine drug screening (Reisfield, Goldberger, & Bertholf, 2009). Chloroquine (Lora-Tamayo, Tena, Rodriguez, & Moren, 2002) 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 (Blank, Hellstern, Schuster, Hartmann, Matthée, Burhenne, 2009; Rossi, Yaksh, Bentley, van den Brande, Grant, & Ellis, 2006; Sait-

man Park, & Fitzgerald, 2014). During the 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 unnecessary risks due to close contacts.

4. Psychological Consequences

In this pandemic, it seems that information is spreading more extensively and rapidly in comparison to the SARS outbreak in 2003. However, this condition may result in a worsening 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 (Strong, 1990). The unpredictable future is exacerbated by myths and misinformation that are often driven by fake news and public misunderstanding (Bao, Sun, Meng, Shi, & Lu, 2020). Some patients will experience grief over the loss of loved ones.

The relationship between adverse life events and brain stress systems have a prominent role in addiction disease (Koob, 2008, 2009, 2013). PWUD are much more vulnerable to stress and crisis followed by lapse and relapse to ex-drug users (Goeders, 2003; Koob et al., 2014; Miliwojevic & Sinha, 2018; Somaini et al., 2012). As a result of stressful events and disasters, mental health problems emerge or exacerbate (Farhoudian, Hajebi, Bahramnejad, & Katz, 2013; Farhoudian, Rahimi Movaghar, Rad Goodarzi, Younesian, & Mohammad, 2006). In such circumstances, healthy individuals may start drug use (Farhoudian et al., 2006; Somaini et al., 2012), and several patients may relapse into their previous drug use and start their high-risk behaviors (Brandon, Vidrine, & Litvin, 2007; Farhoudian et al., 2006; Rahimi Movaghar, et al., 2006). Anxiety, worry, depression, irritability, and anger in PWUD should be considered as a prodromal sign of lapse or relapse into a new episode of drug use.

4.1. Psychological interventions

Psychosocial interventions are a vital element in the treatment of PWUD, especially in people using stimulants and having mental problems (De Crescenzo et al., 2018). In this period, internet-based psychotherapy is highly recommended as a replacement. Internet consultation, including phone calls, 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 a face-to-face treatment for treating anxiety disorders and depression (Taylor & Luce, 2003). Although it requires some

equipment and knowledge, it offers a good alternative for more isolated locations, which is relevant in this pandemic.

4.1.1. Cognitive Behavior Therapy (CBT)

Negative emotional states, including fear, anxiety, and boredom, as well as social withdrawal and or isolation, are the main emotions that patients will experience during the COVID-19 pandemic. CBT has been recognized as one of the most beneficial interventions for PWUD (Lee & Rawson, 2008). 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 (Goeders, 2003). Clinicians should help their patients to identify, manage, and reduce their negative emotional states associated with relapse and apply techniques of behavioral 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 (Rawson & McCann, 2005; Rawson et al., 1995). Treatment is delivered in an intensive outpatient program primarily in structured group sessions targeting the necessary skills. It is recommended that the meetings could be held individually instead of group format, hoping to lessen the risk of COVID-19 infection. The recommended parts based on the manual (Services among Iranian people living with HIV and AIDS: A qualitative study, 2019) for the period of COVID19 pandemic include: 1. RP17: Taking care of yourself; 2. RP18: Emotional triggers; 3. RP20: Recognizing stress; 4. RP22: Reducing stress; 5. RP24: Acceptance; 6. RP29: Coping with feelings and depression; 7. RP Elective C: Recreational activities.

4.1.3. Contingency management

Incentive-based treatment approaches (i.e. Contingency Management [CM]) are effective interventions in reducing addictive behaviors in PWUD (Ainscough, McNeill, Strang, Calder, & Brose, 2017; Benishek et al., 2014; Lee & Rawson, 2008; Messina, Farabee, & Rawson, 2003; Rawson et al., 2006). Evidence also supports the CM beneficial effect on the treatment of these individuals targeting infectious disease control (Herrmann, Matusiewicz, Stitzer, Higgins, Sigmon, & Heil, 2017).

To take advantage of CM in the prevention of COVID-19, the desired behaviors (e.g. washing hands every hour, cleaning hands, etc.) and their scores or prizes (e.g. take-home doses) should be clearly defined and inserted into the list, just like other desired behaviors (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 (Radfar & Rawson, 2014; Shirinbayan, Rafiey, Vejdani Roshan, Narenjiha, & Farhoudian, 2010) and the main factor of psychological resilience to disaster (Radfar, Nematollahi, & Arasteh, 2016; Rodriguez-Llanes, Vos, & Guha-Sapir, 2013). Considering the importance of family support, clinicians are advised to engage family and care providers more than ever during the pandemic. Attracting other sources of social support such as guaranteed wages and an increase in social security payments will help the individual to pass this period with a better outcome.

5. PWUD Specific Pathology 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 under MMT 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 (Friedman, Kamel, Perez, & Hamada, 2003; Kienbaum, Thurauf, Michel, Scherbaum, Gastpar, & Peters, 1998).

5.2. Renal insufficiency

The prevalence of kidney impairment in hospitalized COVID-19 patients is high, and renal insufficiency increases the risk for in-hospital deaths (Cheng et al., 2020).

Studies indicate that heroin users, especially PWID, suffer from nephropathy (Cunningham, Brentjens, Zielezny, Andres, & Venuto, 1980; do Sameiro Faria, Sampaio, Faria, & Carvalho, 2003; May, Helderma, Eigenbrodt, & Silva, 1986). Other studies confirm that individuals using amphetamine (Ginsberg, Ertzman, & Schmidt-Nowara, 1970; Radfar & Rawson, 2014; Rifkin, 1977), cocaine (Merigian & Roberts, 1987; Norris et al., 2001; Sharff, 1984), alcohol (De Marchi, Cecchin, Basile, Bertotti, Nardini, & Bartoli, 1993; Perneg-

er, Whelton, Puddey, & Klag, 1999), and potent cannabis (Abodunde, Nakda, Nweke, & Veera, 2012; Gudsoorkar & Perez Jr, 2015) are more likely to suffer from renal failure. It might be logically concluded that people with a history of drug consumption are more prone to contract renal insufficiency when they are infected to COVID-19; however, there is not any revealing evidence so far.

Evidence suggests that renal insufficiency does not affect the metabolism of methadone in MMT patients (Murtagh, Chai, Donohoe, Edmonds, & Higginson, 2007). Despite this issue, patients in acute renal failure due to COVID-19 should be monitored for signs of methadone toxicity because of other reasons for renal insufficiency.

5.3. Cardiovascular disorders

Heart diseases increase the risk factors of death due to COVID-19 to 6% in affected individuals with hypertension, 7.3% in diabetics, and 10.5% in patients with other cardiovascular diseases (Murtagh et al., 2007).

Individuals with a history of alcohol or drug use are more likely to have cardiac pathology. Excessive alcohol consumption (Fabrizio & Regan, 1994; Mirijello et al., 2017), amphetamine (Giv, 2017; O'neill et al., 2004), heroin (Routsis et al., 2007), and cocaine (Barton Duell, 1987) are all associated with the 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 (Athanasos, Smith, White, Somogyi, Bochner, & Ling, 2006; Doerty et al., 2001). 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 (Harrington & Zaydfudim, 2010). 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 (Goel et al., 2019).

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 (Communications, 2020). 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 (Interim Guideline for Healthcare Facilities, 2020).

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 (World Health Organization, 2020c).

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 (World Health Organization, 2020c).

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 (Guide on Business Continuity Planning for COVID-19, 7 February, 2020).

7. Conclusions and Recommendations

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

In summary, we suggest the following items:

Health authorities should develop and apply specific strategies for PWUD for early COVID-19 identification and patient isolation, interrupting transmission, providing appropriate care, attending medical issues, and minimizing negative social impact.

Health authorities are responsible for providing adequate healthcare for PWUDs. They may be required to repurpose and reorient health services through a business continuity team. This team implements evidence-based programs and makes decisions on how the organizations will continue to provide their services. Also, they make sure that all OST patients have adequate access to their opioid drugs.

Treatment sectors should provide essential requirements, as well as software and programs tailored to their

own clients' needs. Staff may also teach the patients the hygiene rules, self-monitoring for signs of illness, and rapid reporting of the disease 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 as the first-line approaches for education and appropriate interventions.

Opioid users face increased challenges; some concerns are about their take-home doses and repetitive visits that make 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 or therapies.

Healthcare workers in substance use treatment facilities are also facing a higher risk of infection, burnout, distress, psychiatric disorders, discrimination, and violence. The essential right for each service provider, no matter a peer group or professional service provider, is to be safe and secure, in both physical and mental health aspects.

Misinformation, social isolation, ensuing 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 counseling are highly recommended.

There are many medical considerations regarding PWUD that other physicians in charge of the management of COVID-19 treatment should keep in their minds.

Clinicians should be careful in the differentiation between withdrawal signs and symptoms and those of COVID-19 infection.

PWUD may have different clinical manifestations due to various etiologies. Healthcare providers should consider different possible manifestations and, more impor-

tantly, avoid any type of medical stigma or discrimination against PWUD.

PWUD regularly self-medicate their physical and mental problems with drugs, which may mask critical COVID-19 symptoms.

A number of drug-drug interactions between substance of use, addiction treatment medications, and COVID-19 medications must be considered in terms of toxicity, withdrawal, and exacerbation of fatal side effects.

There is also a 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 emerge in PWUD that put them at higher risk of morbidity and mortality after contracting COVID-19

Pain management in PWUD, specifically opioid users and patients under OST, has some complexity, which calls for the involvement of joint expertise.

Ethical Considerations

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Authors' contributions

Ali Farhoudian and Seyed Ramin Radfar had the original idea, wrote initial topics and headlines, and the first draft. All authors participated in the literature review, writing, editing, and revision of the report and reached consensus on the conclusion. All authors declare no conflict of interest.

Conflict of interest

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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