

## CASE REPORT

# Treatment of opioid use disorder in an innovative community-based setting after multiple treatment attempts in a woman with untreated HIV

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## SUMMARY

Opioid use disorder is associated with significant health and social harms. Various evidence-based interventions have proven successful in mitigating these harms, including harm reduction strategies and pharmacological treatment such as methadone. We present a case of a 35-year-old HIV-positive woman who was off antiretroviral therapy due to untreated opioid use disorder, and had a history of frequently self-discharging from hospital against medical advice. During the most recent hospital admission, the patient was transferred to an innovative community-based clinical support residence that supported harm reduction. Initially, she received methadone to only manage the withdrawal symptoms rather than for long-term maintenance therapy. However, with gradual dose increases to treat cravings and withdrawal, she ultimately discontinued all drug use and reinitiated antiretroviral therapy. This case highlights that patients whose goal is not abstinence can be successfully treated for acute medical illnesses and comorbid substance use disorders using harm reduction approaches, including appropriate dosing of pharmacotherapy.

## BACKGROUND

Opioid use disorder poses a comparatively higher risk than other addictive disorders for significant health and social harms, such as morbidity and mortality related to opioid overdose and untreated HIV.<sup>1-3</sup> Methadone maintenance treatment (MMT) is one of the most common treatment approaches for opioid use disorder as it has been shown to improve rates of retention in addiction treatment, reduce illicit opioid use and subsequently reduce fatal overdose and other health and social harms related to opioid dependence.<sup>4-6</sup> Particularly, in the context of HIV infection, the benefits of MMT in reducing HIV risk behaviours, increasing adherence to antiretroviral therapy and improving virological outcomes have been well established.<sup>7-11</sup> However, there are a number of considerations regarding dosing, pharmacokinetic interactions, patient motivation and structural considerations to be considered when treating patients with comorbid HIV and opioid use disorder.

## CASE PRESENTATION

A 35-year-old HIV-positive First Nations woman was admitted to the urban health unit of a major teaching hospital in Vancouver, Canada, on several occasions for severe bilateral lymphedema

secondary to severe long-standing intravascular Kaposi sarcoma. During her most recent admission, she re-presented to hospital with a soft-tissue infection in her lower extremities and significant immunosuppression (CD4 absolute count=70, HIV viral load=120 000 copies/mL). For the 2.5 weeks prior to admission, she had not taken her antiretroviral therapy (ART) or any of her other prescribed medications, including dapsone (for pneumocystis pneumonia prophylaxis due to an allergy to trimethoprim-sulfamethoxazole), ipratropium, salbutamol, ferrous gluconate or multivitamins.

Review of this patient's substance use history demonstrated that the patient had a long-standing history of opioid use disorder with multiple hospital admissions and treatment attempts with MMT and buprenorphine/naloxone. No history of psychiatric comorbidity was noted. In terms of her substance use history, the patient did not report intravenous drug use. She had first used opioids 17 years ago, and she reported presently smoking ~0.5 g of heroin per day. She denied past or present illicit use of methadone or opioid analgesics. In terms of her stimulant use, the patient reported presently smoking ~1 g of crack cocaine per day. She denied any past or present use of crystal methamphetamine or prescription stimulants. Regarding other drug use, the patient reported smoking one pack of cigarettes per day. She reported using cannabis and alcohol in her teenage years, but denied any recent use of the same. She also denied any past or present use of hallucinogens or benzodiazepines.

In terms of her social history, the patient had a history of financial strain leading to survival sex work, and had outstanding warrants related to her illicit drug use and was currently enrolled in Drug Court Counsel. Owing to these legal issues, the patient had lost her occupancy at her previous supportive housing residence, and was no longer receiving government income assistance.

## INVESTIGATIONS

Consultation with the hospital's Addiction Medicine Consult Team revealed that the patient was precontemplative with regard to her substance use. According to Prochaska's Transtheoretical Model of Health Behavior Change, precontemplation is 'the stage in which people are not intending to take action in the foreseeable future'.<sup>12</sup> This was evidenced by the patient being willing to take



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methadone for withdrawal management only and to reduce drug use while in hospital, but having no interest in abstaining from heroin or cocaine as she felt the need to use drugs to escape from her life stressors (eg, financial strain leading to survival sex work, relationship strains and pain related to her poor physical health). As such, methadone was the superior option for in-hospital withdrawal management for this patient given that she would have likely been unable or unwilling to abstain from opioid use long enough to avoid precipitated withdrawal using buprenorphine/naloxone. She had previously attempted community-based opioid agonist treatment (OAT) with methadone and buprenorphine/naloxone several times over the past 8 years, but was unable to adhere to treatment for sustained periods of time. In past admissions, the patient had frequently self-discharged from hospital against medical advice (AMA) due to opioid withdrawal. As such, she was considered to be at high risk for leaving AMA during her most recent hospital admission.

**TREATMENT**

The patient was referred to the Community Transitional Care Team (CTCT), an innovative, harm reduction based community clinical support residence for individuals in Vancouver’s Downtown Eastside who require long-term intravenous antibiotic therapy, or stabilisation of acute or chronic health issues.<sup>13</sup> Patients have access to drug treatment programmes; however, admission to the CTCT is not dependent on drug abstinence or committing to treatment aimed at drug use cessation. The CTCT was created to address the high rates of failure to complete antibiotic treatment among active drug users. This care plan was a suitable option for this patient given her poor health status, and the fact that she had lost her previous housing due to legal issues stemming from her illicit drug use.

On admission to the CTCT, the patient was noted to present as guarded and reluctant to fully engage with staff. The patient’s methadone dose was gradually titrated upwards (table 1) with the initial aim to manage her withdrawal. However, as the patient’s methadone dose increased, she reported reduced craving and use of both heroin and crack cocaine, which was confirmed by negative urine drug tests. At a higher, more therapeutic maintenance dose of daily methadone, the patient no longer experienced the discomfort of drug cravings or withdrawal from opioids or stimulants, was agreeable to and engaged in her maintenance therapy, and eventually chose to stop all illicit drug use.

The clinically supportive environment at the CTCT allowed for carefully monitored methadone titration through regular staff availability to address ongoing pain and changes in ART that affected methadone metabolism. Owing to inconsistent adherence to previous ART (efavirenz/emtricitabine/tenofovir disoproxil umarate), the patient was switched to a regimen of atazanavir, ritonavir and FTC/tenofovir, a less potent inducer of methadone metabolism.<sup>14</sup> To avoid toxic accumulation of methadone, the patient’s methadone dose was decreased by 20 mg during this transition period (table 1, day 90), and she was monitored for toxicity following each dose. Also, since the patient had severe persistent pain secondary to her chronic lymphedema, her daily methadone dose was split into thrice or twice daily doses in order to optimise the analgesic benefits of methadone administered in divided doses.<sup>15–19</sup>

**OUTCOME AND FOLLOW-UP**

Having initially presented to the CTCT as guarded and reluctant to engage with staff, the patient increasingly began to develop

**Table 1** Methadone dosages administered in hospital and community-based treatment for a 35-year-old patient with HIV and opioid dependence

Day*	Clinical care setting	Daily methadone dose	PRN Methadone dose	Split-dosing schedule
1	Hospital	30 mg/day	10 mg Two times a day PRN	
3	Hospital	40 mg/day	2×10 mg PRN	
8	Hospital	40 mg/day	10 mg PO q3h PRN (max 2 doses/24 hours)	
8	CTCT†	60 mg/day		
12	CTCT	70 mg/day		50-10-10
16	CTCT	80 mg/day		50-10-20
27	CTCT	90 mg/day		60-10-20
43	CTCT	90 mg/day		70-20
57	CTCT	100 mg/day		80-20
70	CTCT	100 mg/day		80-20
76	CTCT	110 mg/day		90-20
90	CTCT	90 mg/day		60-30
104	CTCT	100 mg/day		70-30
112	CTCT	110 mg/day		80-30
120	CTCT	110 mg/day		
124	CTCT	110 mg/day		

\*Day 1=First dose of methadone given during most recent hospital admission.  
 †CTCT=Community Transitional Care Team.  
 PRN, as needed.

trust and positive rapport with the care team as her primary concerns were addressed. Specifically, in addition to the healthcare team effectively helping to manage the patient’s opioid withdrawal, pain and HIV care, the patient’s case manager was also able to successfully negotiate with the patient’s Drug Court Counsel lawyer that the patient’s outstanding warrants be vacated, and her income assistance reinstated given her recent health concerns. Had this not been the case, the significant improvements the patient had made in regard to her recent adherence to OAT and ART could have been compromised given the poor health outcomes associated with incarceration in this population.<sup>20</sup>

Of note, during her admission at the CTCT, the patient also reconnected with her mother and siblings after more than 14 years of estrangement. The patient decided to move back home with her family (who lived in another province). Thus, the healthcare team at the CTCT transitioned the patient back to single daily dosing of methadone, and arranged new health providers for the patient in preparation for this transition of care. The patient was then discharged from the CTCT, reunited with her family, and reports sustained abstinence and good health at the time of writing (3 months post discharge).

**DISCUSSION**

The present case highlights the importance of harm reduction strategies within healthcare settings, and continued access to evidence-based addiction treatment for precontemplative patients with major health concerns associated with substance use, such as untreated HIV. Over the course of 17 weeks, this patient presenting to hospital with severe comorbidities secondary to ART non-adherence and initially precontemplative with respect to her untreated opioid use disorder<sup>12</sup> was able to achieve a therapeutic dose of methadone in a low-threshold, community-based treatment setting, and subsequently able to

re-start a new ART regimen and abstain from illicit opioid and stimulant use. The patient also had her legal warrants vacated and income assistance reinstated, allowing her to reunite with family from whom she had been estranged for over a decade.

This case emphasises the importance of a comprehensive and non-judgemental approach to caring for individuals with opioid use disorder, as well as appropriate dosing for patients on MMT or other OAT approaches in order to achieve optimal therapeutic benefits. Several meta-analyses have found that higher methadone doses (ie, >50 or 60 mg/day) significantly improve retention in MMT and reduce illicit opioid use compared to lower methadone doses;<sup>21–23</sup> several studies have also found that methadone doses at or well above 120 mg/day may be required to fully block opioid-related euphoria and fully suppress withdrawal.<sup>24 25</sup> In this context, it has been suggested that methadone is often prescribed at doses that are sufficient to ameliorate withdrawal symptoms; however, these doses are often insufficient for effectively neutralising the euphoric effects of opioids, and hence the rationale for high-dose treatment.<sup>22</sup> Furthermore, as demonstrated in the present case, flexible dosing has also been found to improve retention in MMT compared to fixed dosing strategies.<sup>21</sup> Thus, physicians in acute and community addiction treatment settings may benefit from increased education on the variability of the methadone dose for achieving optimal therapeutic effects.

Higher methadone doses have also been found to be more effective in reducing cocaine use among people who use heroin and cocaine concurrently,<sup>22</sup> as was also observed in the present case. Among people who use illicit drugs, rates of concurrent heroin and cocaine use as high as 50% have been previously documented.<sup>26</sup> Potential reasons for cocaine use in individuals with opioid dependence may include seeking antagonism of sedative opioid effects, seeking euphoria that is not blocked by methadone or seeking to suppress opioid withdrawal symptoms.<sup>22</sup> Thus, by treating opioid dependence via MMT, patients may in turn reduce their frequency or intensity of cocaine use, which further reduces the risk of significant health and social harms associated with cocaine use.<sup>27–32</sup>

While high methadone doses are often required to achieve therapeutic benefits, significantly higher doses are often observed in patients on MMT with comorbid chronic pain.<sup>19</sup> While opioid-induced hyperalgesia (ie, increased sensitivity to pain and/or decreased tolerance for pain, secondary to consistent exposure to opioids) may be one reason for the higher doses often seen in MMT patients with chronic pain,<sup>33 34</sup> several studies have found that chronic pain is often under-treated in MMT patients,<sup>35–38</sup> suggesting that higher MMT doses may be beneficial for treating concurrent chronic pain and opioid dependence. The average duration of action for analgesia using methadone is markedly shorter (~4–8 hours) than its duration of action for suppression of opioid withdrawal (~24–48 hours).<sup>39 40</sup> As demonstrated in the present case, an alternative dosing approach for MMT patients with acute or chronic pain is to administer split methadone dosing rather than an once daily dose for clinically stable patients, which may facilitate more consistent pain control. Although the practice of split methadone dosing for pain is frequently seen in clinical practice and scientific literature,<sup>15–19</sup> it should be noted that the effects of this approach have not yet been empirically quantified with respect to improved analgesia, and therefore this represents an area for future research.

In HIV-positive patients, as in the present case, additional methadone dosing considerations must be taken into account as methadone has pharmacokinetic interactions with several

antiretroviral medications (eg, zidovudine, didanosine, stavudine, abacavir, nevirapine, efavirenz, nelfinavir) that may result in symptoms of opioid withdrawal, opioid overdose, reduced antiretroviral efficacy or increased antiretroviral-related toxicity, depending on the antiretroviral in question.<sup>41</sup> Therefore, after assessing the potential for such interactions in patients on concurrent methadone and antiretroviral therapy, dosage adjustments may be required and follow-up antiretroviral resistance testing is recommended. Despite the potential interactions between methadone and certain antiretrovirals, the overwhelming benefits of MMT (or other OAT) provision in the context of HIV (eg, reduced HIV risk behaviours, increased adherence to ART, improved virological outcomes, reduced ART-related side effects) have been well established.<sup>7–10 42</sup>

Ultimately, methadone dosing should be informed by clinical judgement based on a variety of individual factors such as metabolism, comorbidities including prolonged QT<sup>43</sup> and drug–drug interactions.<sup>44</sup> Furthermore, even if therapeutic doses are achieved, patients may still relapse to opioid use, and multiple attempts with OAT (or alternative treatments for severe opioid use disorder such as slow-release oral morphine, diacetylmorphine or naltrexone) are often necessary in order to facilitate sustained abstinence.<sup>45</sup> However, encouraging results from a study of heroin abstinence durations found that periods of abstinence appear to become successively longer for each subsequent treatment attempt.<sup>46</sup> Certainly, in the present case, the patient had previously attempted OAT several times, but was unable to maintain a sustained period of abstinence from illicit opioid use until the most recent treatment attempt described above. The potential benefits of comprehensive, flexible harm reduction programmes for OAT that facilitate cycling into and out of treatment have also been described in other settings.<sup>47 48</sup>

The present case also demonstrates the role of OAT in supporting either harm reduction or abstinence, depending on the patient's preference, and the importance of aligning treatment approaches with patient goals. For many individuals with opioid use disorder, abstinence-only approaches may not be feasible if the individual is unwilling to completely terminate all substance use at once. In the present case, the patient was initially willing to take methadone for withdrawal management and reduction of drug use, but had no interest in fully abstaining from heroin or cocaine use. However, as the patient's health and sociostructural circumstances began to improve and her methadone dose continued to increase, so did her ability to abstain from illicit drug use and finally she no longer felt the need to use heroin or cocaine. Thus, this case presents the potential for OAT to facilitate a shift from a harm reduction paradigm to a treatment paradigm in the context of opioid addiction in the healthcare setting.

Indeed, as an alternative to traditional abstinence-only approaches to addiction care, which tend to be punitive in nature for individuals who do not wish to fully cease illicit opioid use, the provision of OAT may be a means of supporting a harm reduction model of care. As exemplified in the present case, supporting withdrawal management—particularly for patients admitted to hospital—helps to establish trust and rapport, mitigates the risk of patients leaving hospital AMA to self-manage their withdrawal,<sup>49</sup> and engages patients in addiction treatment that they may optimally wish to continue in community-based treatment settings. Thus, while acute care environments may certainly be seen as 'risk environments' if addiction issues are poorly managed,<sup>50</sup> these may also conversely be seen as opportunistic environments that facilitate engagement in healthcare and psychosocial support, particularly

for extremely marginalised populations that tend to avoid conventional community healthcare services until severe health concerns emerge that may require them to present to emergency departments and hospital settings.

In this context, this case presents an excellent example of an effective non-conventional community health service via an innovative, low-barrier, multidisciplinary supportive transitional housing programme via the CTCT. The CTCT is a community-based care model that was designed primarily as an alternative to hospital-based treatment for administering long-term intravenous antibiotic treatment in a home-like residential care setting for individuals in Vancouver's Downtown Eastside, a postindustrial neighbourhood with an established drug market and widespread illicit drug use, poverty, poor housing conditions and infectious diseases such as HIV and hepatitis C.<sup>13 51</sup> The CTCT employs a harm reduction approach so that patients are able to continue using drugs without fear of retribution or dismissal from the health facility, as is often the case in hospital environments.<sup>50</sup> In fact, the CTCT is very close in proximity to a supervised injection site that has been shown to reduce the health and social harms associated with injection drug use.<sup>52–58</sup> By facilitating access to harm reduction services, healthcare providers are able to work 'with' instead of 'against' people who use drugs, in contrast to the zero-tolerance policies that further marginalise and stigmatise this population.<sup>59</sup> Indeed, in the present case, the patient continued to use heroin and cocaine during the early stages of her admission to CTCT while her methadone dose was being titrated upward, until she no longer felt the need to use and became abstinent. If the patient had

been discharged from care due to her on-going drug use early on, her treatment outcomes may not have been as positive (ie, achieving abstinence and re-starting antiretroviral treatment). Thus, facilitating transitional care from the hospital setting to low-barrier community-based care models has the potential to promote adherence to treatment, improve treatment completion, reduce lengths of hospital admission, reduce rates of self-discharge from hospital against medical advice, improve access to stable housing, reduce perceived stigma and increase patient satisfaction.<sup>13</sup>

To sum up, this case highlights that despite the stage of change, medically ill patients can be successfully treated for comorbid addiction in a relatively short period of time given the consideration for appropriate dosing of pharmacological treatments, and with appropriate psychosocial and culturally appropriate supports as was carried out here in the context of harm reduction.

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### Patient's perspective

"She has improved immensely, she is still on 110 mgs of methadone and she states she is fine ... The family are all happy to have her home however understand that (she) still has a long road ahead for her recovery but are all standing behind her and helping in any way." –Patient's mother.

### Learning points

- ▶ Multiple attempts and appropriate dosing (ie, therapeutic dosage, consideration of pharmacokinetic interactions) are often required for successful treatment of substance use disorders.
- ▶ Traditional abstinence-based approaches to substance dependence may not be feasible for all patients; thus, opioid agonist treatment also plays a role in the context of harm reduction (eg, reduced illicit opioid use, improved pain management, retention in care and prevention of self-discharge against medical advice).
- ▶ Even the precontemplative patient can be successfully treated for addiction in a relatively short period of time through consideration for appropriate dosing of pharmacological treatments and with appropriate supports in the context of harm reduction.
- ▶ Harm reduction approaches may be beneficial not only in addiction services, but also in all health settings where drug using individuals present.

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