OPIOID AGONIST THERAPY DISCONTINUATION IN BRITISH COLUMBIA: A CROSS-SECTIONAL STUDY OF PEOPLE WHO ACCESS HARM REDUCTION SERVICES

by

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Abstract

Background: The opioid overdose crisis has been contributing to increasing mortality rates in North America, with 2236 deaths in 2021 compared to 1768 in 2020, in British Columbia (BC) alone. Research has shown significant reductions in opioid overdose mortality rates among those who receive opioid agonist therapy (OAT), while OAT discontinuation has also been recognized as a period of high risk for overdose. This study assesses a provincial sample of individuals who use substances and access harm reduction supply distribution sites, with the objective to investigate the prevalence and correlates of OAT discontinuation across BC.

Methods: This study utilizes data from the cross-sectional provincial-level Harm Reduction Client Survey (HRCS) administered in 2019, among individuals who use substances and are aged 19+. The outcome of OAT discontinuation included 2 levels: individuals who did and did not indicate discontinuing OAT in the past 6 months. Prevalence of potential correlates and their association with the OAT discontinuation outcome was assessed using Chi-squared or Fisher's Exact test. Bivariate and multivariable analyses using logistic regression models examined associations between potential demographic, socioeconomic, accessibility, drug use and harm reduction correlates with the outcome.

Results: Among the 194 participants included in the sample, 59.8% identified as cis man, 37.6% identified as indigenous and 38.1% were between the ages of 30-39 years old. Multivariable logistic regression analyses identified that: being aged ≥50 and taking the survey in medium/large urban areas was associated with lower odds of OAT discontinuation, while having experienced an overdose in the past 6 months was associated with greater odds of OAT discontinuation. Substance use, including opioids and stimulants, was similar among those who continued and discontinued OAT.

Conclusion: Prevention of OAT discontinuation among individuals using substances in BC should address disparities in healthcare accessibility in remote and rural areas, while targeting younger individuals who have a history of overdose or are at higher risk of overdose, following OAT discontinuation. Equitable and continued access to harm reduction services can allow for safe consumption of various substances, that may continue among individuals enrolled in OAT programs.

Lay Summary

Opioid Agonist Therapy (OAT) has been recognized as the first line of treatment for individuals experiencing opioid use disorder. OAT discontinuation is a period of high risk of fatal overdose; however, understanding OAT discontinuation in BC has often been limited to large urban areas and medication trials. Individuals who use substances face many barriers to accessing care that may contribute to lower treatment retention. This study used a sample of individuals who use substances and access harm reduction supply distribution services across BC, to better characterize OAT discontinuation. Being younger, living in rural areas and having experienced an overdose in the past 6 months was associated with OAT discontinuation. Youth specific programs, increased availability of staff and programs in rural communities, as well as structured plans and follow-up for patients admitted with an overdose should be considered in providing the resources individuals may need to continue in treatment.

Preface

This study analyzes data from a cross-sectional survey of individuals who use substances and access harm reduction supply distribution sites across British Columbia, Canada (Harm Reduction Client Survey [HRCS], 2019). The HRCS research team, epidemiologists, and statisticians at BC Centre for Disease Control's (BCCDC) Harm Reduction Unit performed all data entry, coding and cleaning. Data collection was completed by staff and volunteers at respective harm reduction supply distribution sites and overseen by the HRCS research team. The HRCS and this thesis has been approved by the University of British Columbia (UBC) Behavioural Research Ethics Board and other relevant local boards (BREB H07-00570 "More Than Just Needles: An Evidence-informed Approach to Enhancing Harm Reduction Supply Distribution in BC").

I devised and conceptualized the research and analysis design (Chapters 2 and 3) with guidance from my supervisory committee (Dr. Jane Buxton, Dr. Michael Otterstatter, and Dr. Daniel Vigo). In collaboration with all committee members and the epidemiologists at BCCDC's Harm Reduction Unit, I developed a data analysis plan that was approved by committee members. I performed all statistical analyses using R version 4.1.2 (2021-11-01) and created all figures and tables in the thesis.

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List of Abbreviations

aHR	Adjusted Hazard Ratio
AIC	Akaike Information Criterion
aOR	Adjusted Odds Ratio
BC	British Columbia
BCCDC	BC Centre for Disease Control
CIHR	Canadian Institutes of Health Research
DTES	Vancouver's Downtown Eastside
FNHA	First Nations Health Authority
GSDOA	Good Samaritan Drug Overdose Act
HCV	Hepatitis C Virus/Infection
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
HRCS	Harm Reduction Client Survey
LRT	Likelihood Ratio Test
MMT	Methadone Maintenance Treatment/Therapy
OAT	Opioid Agonist Treatment/Opioid Agonist Therapy
OPS	Overdose Prevention Services
OR	Odds Ratio
OUD	Opioid Use Disorder
PWID	People who Inject Drugs
PWUD	People who Use Drugs
REDCap	Research Electronic Data Capture

SCS	Supervised Consumption Site
SROM	Slow-release oral morphine
UBC	University of British Columbia
VANDU	Vancouver Area Network of Drug Users

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Dedication

To all the HRCS participants, who have contributed to research, policy, and healthcare system development over many years in countless ways and are deserving of much better care and support than our system has provided them with.

Chapter 1: Introduction

1.1 Background and Objectives

The opioid overdose crisis has been an evident contributor to increasing mortality rates in North America. On April 14, 2016, the provincial health officer of British Columbia (BC), Dr. Perry Kendall declared a public health emergency due to the increase in opioid-related overdose deaths across the province (1). In British Columbia alone, there were 2236 deaths or 43.0 per 100,000 in 2021, which was more than the number of deaths caused by suicide, motor vehicle incidents, homicides and prescription drugs combined (2). This number was almost double that of 2020 (1768 deaths or 34.3 per 100,000). Additionally, illicit drug toxicity was identified as the leading cause of mortality among young individuals, ages 19-39, and the second leading cause of years of life lost from 2020-2022 (3). It is important to recognize that drug use and drug-related mortality are often underestimated, due to the stigma faced by individuals who use substances; this stigma can often create a disconnect between individuals who use drugs and systems of care, which can lead to hesitancy in reporting drug use behaviors (4).

According to the Provincial Guidelines for treating opioid use disorder (OUD), opioid agonist treatment (OAT) is the recommended first-line therapy in BC (5). OAT has been defined by BC Mental Health and Substance Use Services as a safe and effective medication-based treatment, involving opioid agonists, which work slowly in the body to reduce withdrawal and craving symptoms for opioid drugs (6). Research has shown significant reductions in opioid overdose mortality rates among those who receive OAT treatment (7). In May 2021 for example, the National Institute on Drug Abuse reported that among nearly 50,000 adults receiving outpatient treatment for opioid use disorder, overdose deaths were significantly reduced by about 5 folds among those treated with OAT medications compared to those treated with non-

medication approaches (8). At the same time, discontinuation of OAT creates a period of high risk for overdose and mortality. The same study found that among those receiving outpatient OAT for opioid use, the protective effects of opioid agonist medications were lost following discontinuation of treatment with increased overdose fatalities, suggesting that long-term retention and continuation on OAT is necessary to prevent overdose deaths (8). Ideally, OAT should be combined with behavioral and social supports to optimize treatment outcomes and address concurrent psychosocial factors that may be contributing to the patient's substance use and quality of life (9).

Many individuals who use illicit substances are at an increased risk of experiencing an overdose following OAT discontinuation (8,10). In BC in particular, retention rates in OAT have been low. Two retrospective cohort studies from 2020, with approximately 50,000 participants found that less than 16% of individuals are retained on OAT for more than a year in BC (11), with less than 40% retention rate prior to treatment induction and over 50% of participants never reaching the minimum effective dose (12).

Several factors have previously been associated with increased discontinuation among patients seeking OAT, though most of these findings have been limited to single studies or clinical trials with high variability across settings. Limited access to healthcare services for example, including outpatient and acute settings, have been associated with lack of engagement with OAT programs and higher rates of discontinuation, which can in turn lead to greater risks of overdose among this highly vulnerable population group (11). Additional correlates of OAT continuation and discontinuation are discussed in Chapter 1.6. The knowledge gap in understanding factors contributing to OAT discontinuation is critical, especially now, with overdose deaths being higher than ever in British Columbia.

Globally and in Canada, treatment access and distribution for individuals with opioid use disorder is not equitable. A strong body of recent evidence has suggested that a variety of structural and systemic factors contribute to barriers in accessing addiction care. On the structural level, lack of treatment programs in rural and smaller communities in Canada has restricted accessibility to care for individuals who use opioids. These include limited access to supervised consumption services, safer supply, and OAT programs, in addition to housing and social supports (13). Additionally, those with a history of incarceration have an elevated risk of fatal overdose (14–16), often due to lack of overdose prevention, harm reduction and addiction treatment supports, both within prison systems and following release from incarceration. A recent study in BC, from 2015-2018, found that among those who were released from prison in the prior 30 days, those with access to community healthcare had a higher hazard of healthcare-attended nonfatal overdose (aHR 2.83) and a lower hazard of fatal overdose (aHR 0.58), suggesting that accessibility to healthcare services (15), including those that address psychosocial outcomes (16) can help mitigate the risk of fatal overdose among those with a history of incarceration.

Individuals who use illicit substances often face a multitude of social and structural barriers including unstable housing, concurrent mental health, and concurrent physical disorders, such as hepatitis C and HIV, limited access to treatment programs that are culturally relevant and peer-led (particularly for indigenous populations), as well as social stigma (17–21). The intersection of these factors can contribute to limited access and use of treatment services and increase the potential for treatment discontinuation. In BC, individuals with younger age, male sex, from urban areas, lower income levels, and those who may be experiencing homelessness have been shown to have increased OAT engagement (11). Limited studies have assessed OAT

discontinuation in a comprehensive manner, since most studies are often restricted to retention rates in active clinical trials, with limitations on patient inclusion criteria.

The Harm Reduction Client Survey (HRCS) is a cross-sectional, unique cohort of individuals in BC who access harm reduction supply distribution sites (described in more detail in Chapter 1.3). The wealth of data and variables in HRCS, particularly with regards to treatment access and drug use behaviors, is well-suited for studying OAT discontinuation rates and contributors to this outcome among individuals with illicit opioid use in BC.

Another unique aspect of this work is its focus on identifying characteristics and correlates of individuals who discontinue OAT to help inform action steps in responding to the overdose crisis, by targeting individuals who have higher risk factors for lower retention in treatment. The findings of this study can therefore be translatable to treatment providers, policy makers, and other knowledge users within the province and country.

There are 2 main questions that this study attempts to address. Among the survey participants that are accessing harm reduction supply distribution sites and who had indicated having been prescribed OAT medication in the past 6 months:

1. What are the characteristics of participants who report having discontinued OAT compared to those who do not report discontinuation in the past 6 months?
2. What are the sociodemographic, drug use, accessibility and harm reduction service access correlates of continuation and discontinuation among these participants?

1.2 Conceptual Framework

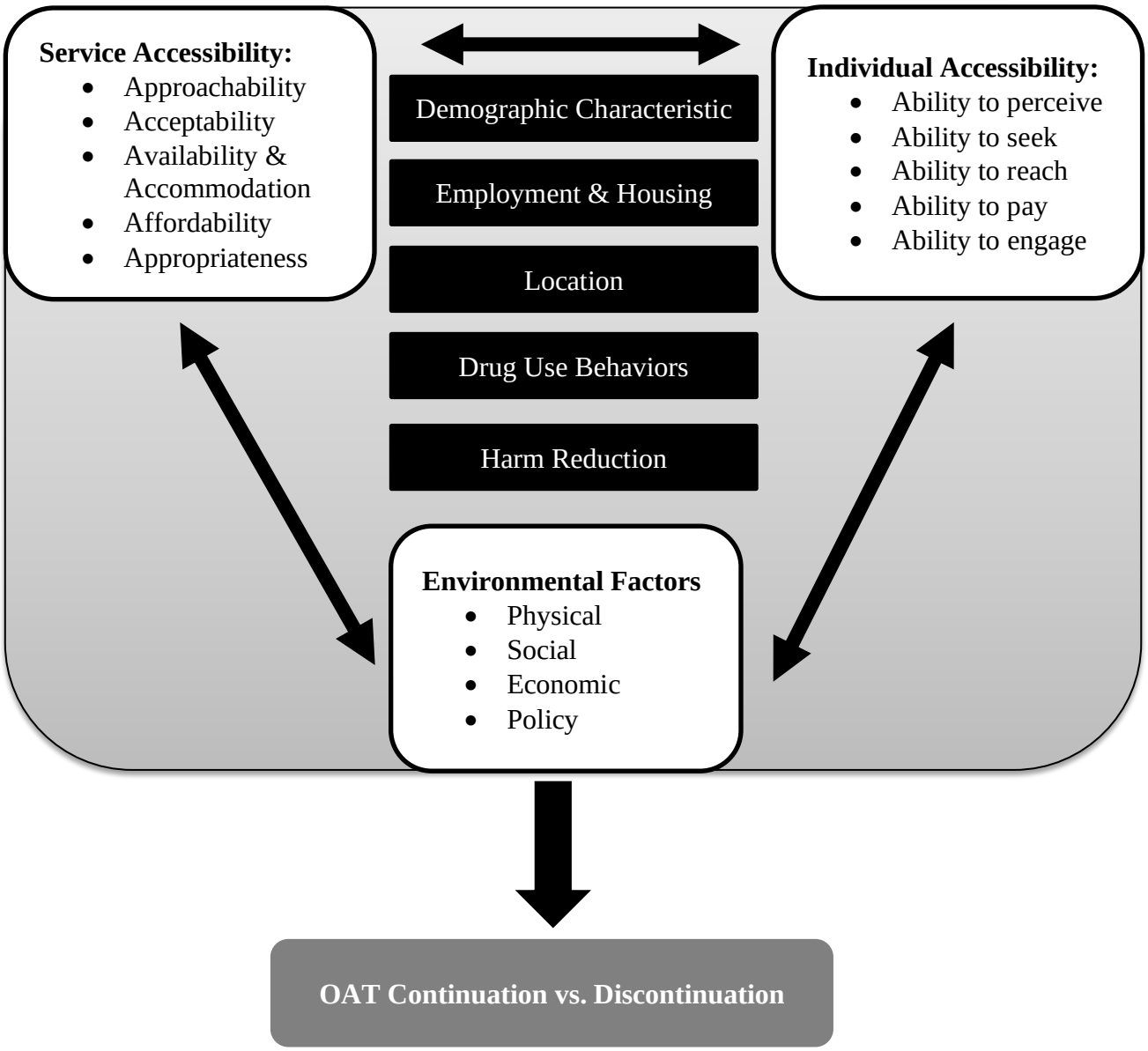

Figure 1.1[1] Theoretical and Conceptual Framework.

The theoretical and conceptual framework for this dissertation (Figure 1.1) was built upon Levesque et al.'s (2013) concept on access to healthcare services (22), and Rhodes et al.'s (2002)

[1] Adapted from Levesque at al. (2013) and Rhodes et al. (2002) (22,23).

Risk Environment Framework (23). This thesis uses OAT discontinuation as the main outcome for understanding prevalence of covariates (Chapter 2) and the association of these covariates with the outcome (Chapter 3). For question 1, Chapter 2 of this dissertation describes the prevalence of various systemic, structural and individual covariates that have previously been identified and can potentially be associated with OAT continuation and discontinuation. For question 2, Chapter 3 of this dissertation uses OAT continuation versus discontinuation as an outcome, and assesses individual, structural, and systemic covariates as explanatory variables to characterize individuals who are likely to discontinue vs continue OAT.

Levesque's conceptual framework of access involves five dimensions related to healthcare service provision, including (1) approachability, (2) acceptability, (3) availability and accommodation, (4) affordability, and (5) appropriateness (22). A unique aspect of Levesque's framework is that it assesses accessibility from both perspectives of service provision and the corresponding abilities of persons to interact with the abovementioned dimensions. The five dimensions of abilities include (a) ability to perceive, (b) ability to seek, (c) ability to reach, (d) ability to pay, and (e) ability to engage (22). An individual's demographic, socioeconomic, and health status interact with systemic and structural factors to determine one's ability to overcome barriers such as stigma and continue accessing services, such as OAT.

Table 1.1 has been adapted from Levesque's conceptual framework and outlines the five dimensions of service accessibility and how they relate to the five corresponding abilities of persons that interact with those dimensions while accessing healthcare services.

Table 1.1 Five dimensions of service accessibility and their relation to five corresponding abilities of individuals accessing healthcare services according to Levesque et al. (2013) (22)**.**

Dimensions of health service accessibility	Definitions	Abilities of individuals to interact
Approachability →	Services are transparent, provide information and outreach activities and individuals can trust and identify them. ←	Ability to perceive
Acceptability →	Services are culturally and socially appropriate and individuals have autonomy to seek care without stigma or discrimination. ←	Ability to seek
Availability and accommodation →	Services are evenly distributed and available in a timely manner and individuals have adequate mobility and means to access. ←	Ability to reach
Affordability →	Services have affordable direct; indirect and opportunity costs and individuals have sufficient income and insurance to afford. ←	Ability to pay
Appropriateness →	Services are of high technical and interpersonal quality and individuals can seek services that are effective for their needs. ←	Ability to engage

In terms of approachability and ability to perceive need for care, living in areas with high concentration and abundance of harm reduction and addiction treatment services, in addition to having a stable living environment can make it easier to identify and access addiction services, compared to individuals that live in temporary housing or in neighborhoods with lower outreach efforts and less transparency of information regarding available services. The approachability of available OAT services and the living circumstances of individuals trying to access such services can therefore affect their likelihood to continue and remain in treatment. The acceptability of services and the ability to seek healthcare depends on social and cultural norms. Discrimination and stigmatization against individuals who use substances (24), are experiencing homelessness, and those who are ethnic, racial or gender minorities can prevent marginalized groups from

seeking care due to negative experiences (25,26). Since OAT is a long-term treatment program, negative experiences of stigma and discrimination can impact an individual's tendency to discontinue treatment, and therefore further understanding the demographic, socioeconomic and substance use characteristics, especially among those that have historically been subject to stigmatization within healthcare systems, is important in better addressing OAT discontinuation rates. Availability and accommodation and the ability to reach healthcare, I argue, is one of the most important determinants of access and continuation on OAT. This dimension of accessibility determines location, hours of operation, wait times, appointment policy and individual abilities to transport to such services. When it comes to OAT, many individuals who use substances are at a disadvantage in their ability to reach services. Individuals who live in rural communities are often located far from larger centers, which often have more availability for treatment programs (13). Additionally, many individuals who use substances live in unstable situations, such as temporary shelters and do not necessarily have stable employment or flexible working hours, which limits their ability to reach the necessary services and continue such treatments (22). On the service end, wait times for OAT vary greatly in Canada (27), and demand is always higher than availability, which means oftentimes the healthcare system is unable to meet individuals where and when they need to be met to enter treatment. Given the mechanism of addiction and the difficulty in having the autonomy and empowerment to seek addiction care in the first place, not being able to provide care in a timely manner when individuals need it can very likely impact their desire and ability to continue treatment. Affordability and the ability to pay for healthcare may also affect OAT accessibility. Although government benefits in Canada may offset the direct costs of treatment programs, insufficient benefits can affect the quality of care (appropriateness) some individuals may receive. Additionally, individuals who live in remote or

rural areas with lower concentration of OAT programs (availability and accommodation) need to consider additional travel costs that can often be a barrier for individuals who may also be experiencing homelessness and employment instability in addition to substance use disorder (13). It is important to consider that many individuals who seek addiction care are also on income assistance programs, where finding food and shelter for themselves and their dependents takes priority over accessing high quality medical services, ultimately limiting their ability to continue on OAT programs (28,29). Appropriateness of services and the ability of patients to engage in healthcare ensures that healthcare accessibility is sufficient to provide effective care to patients. While there are many measures of effectiveness for addiction treatment, in terms of OAT, continuation or long-term retention in treatment is one of the common measures used to determine effectiveness of programs. Additionally, urinalyses and self-reported drug use measures are used to assess changes in patients' drug use while engaged in OAT (30). One of the main objectives of this thesis is to better characterize drug use behaviors of patients continuing and discontinuing OAT to better understand treatment effectiveness in BC. Health literacy and self-management are necessary aspects of ensuring a patient's ability to engage in appropriate healthcare (22). Many patients enter the addiction treatment system without fully understanding the scope and implications of treatments available to them; many are brought into the emergency department after an overdose event, provided antagonist medications to counteract the overdose, and offered limited treatment options after, which oftentimes include buprenorphine/Suboxone and more recently, the microdosing regimen (31). It is important to consider that those who might be more prone to discontinuing OAT, likely include patients who have been initiated on the treatment without prior preparation and voluntary admission, particularly those with no follow-up treatment plan (32).

Rhodes's 'risk environment' framework is another well-established framework that I have used to inform my work in understanding drug-related harm and harm reduction methods for drug abuse. Rhodes's model consists of two key dimensions: types of environments and level of environmental influence. The four types of environments include (1) physical environment, (2) social environment, (3) economic environment, (4) policy environment. The two ideal levels of environmental influence include (a) micro environment, (b) macro environment. Rhodes emphasizes the interplay between these two environmental dimensions to emphasize not only the presence of a 'risk environment' but also creating environments that enable more effective approaches to harm reduction (23). Like Levesque (22), Rhodes also emphasizes the significance of interactions between individuals and environments in creating harm in social contexts; through better understanding environmental-level harms, Rhodes emphasizes the importance of taking away shame and blame from the individual by looking at the broader environment that can impact individual-level behavior. It is the interaction between the individuals and their environments at various levels that affect the presence and absence of drug-related harms (23,33).

Table 1.2 has been adapted from Rhodes's framework (23,33), outlining the two environmental dimensions, how they interact with one another, and an example of harm risk and risk mitigation/harm reduction strategy for each. Examples mainly include harms and interventions associated with individuals who use substances.

Table 1.2 Four types of environments and their relation to the two levels of environmental influence, along with an example of risk and intervention for each, according to Rhodes et al. (2002) (23)**.**

	Micro-environment	Macro-environment
Physical environment		
Risk	Location and method of drug use	Drug trafficking and distribution routes
Intervention	Availability of harm reduction and overdose prevention sites	Adaptable testing, use and distribution policies based on changing drug markets
Social environment		
Risk	Access to outreach and health services; peer groups and drug use alone	Stigmatization and marginalization based on drug use behaviors, demographics, and social status
Intervention	Availability of peer-based, low threshold treatment and harm reduction programs	Collective action and education towards destigmatization and harm reduction measures
Economic environment		
Risk	Unemployment, homelessness, transportation costs for treatment access	Economic inflation at healthcare system level
Intervention	Supply distribution sites, government-subsidized treatment, and housing programs	Increased economic investments towards harm reduction and treatment programs
Policy environment		
Risk	Low accessibility and capacity of harm reduction and treatment programs	Criminalization of drug possession and drug use
Intervention	High-capacity housing and harm reduction programs at community level	Decriminalization of drug use and community involvement in mitigating drug use risk

In terms of the physical environment, individual circumstances, and drug use behaviors, at the micro level, and drug markets and contaminated supply distribution, at the macro level can impact risk. For example, individuals with higher tendency to inject opioids, either as standalone or in combination with other substances, are at a higher risk of both overdose and injection-related comorbidities, such as HIV and HCV, commonly seen in this population group (34,35). Additionally, people who inject drugs (PWID) who are experiencing comorbidities have been

found to experience gaps and lower accessibility to addiction treatment programs, as well as lower OAT engagement (36). The rapidly changing drug markets in BC and around the world have also introduced higher levels of fentanyl on the streets (37,38). Additionally, contaminated opioid supplies that contain benzodiazepines have led to increased risk of overdose due to the drug's unresponsiveness to common antagonist agents such as naloxone (39). While OAT is an effective treatment approach for individuals with opioids use disorder, the availability of harm reduction measures for individuals who are in treatment is important to help mitigate risks associated with substance use (40). The social environment micro and macro level risks involve system-level marginalization and stigma, and the use of peer groups to break communication barriers and provide culturally safe and appropriate care. Peer-level interventions can be effective in overcoming stigma within healthcare systems, since stigma is often perceived to come from those of higher social positions with greater social control, and historically, individuals who use substances have been more prone to stigmatization and negative attitudes from those in higher social positions (41–43). Therefore, provision of community-level outreach programs and peer support can often be effective in providing safe environments for marginalized populations who use substances without feeling judged and stigmatized (44,45). Additionally, collective action and involvement of those in higher social positions in advocating for and supporting harm reduction approaches and risk mitigation can help break stigmatizing barriers in accessing healthcare by those who are often victimized, which can include the providers themselves as well (46). Economic environment risk assesses costs associated with micro and macro level environments and how these costs affect individuals who use substances and increase the risk of harms they experience. For example, substance use has often been correlated with unemployment and homelessness (47,48). Although addiction care is

government-subsidized in Canada (49), individuals who live in rural communities have more limited access to care with fewer treatment options, which can impact the quality and availability of care they receive (50). Lack of choice in medication and treatment received has previously been associated with lower retention outcomes in OAT, higher risk of dropout, relapse, and overdose (44). One-stop services addressing multiple medical care needs, along with food, housing and transportation has been recommended as an effective way to encourage engagement with the healthcare system and improve health outcomes (51). Over the years, BC has invested additional resources in expanding harm reduction programs across the province that can help mitigate the risks and harms associated with substance use, including distribution of take-home naloxone kits and training in naloxone administration (supporting peer social interactions) (52), and expanding supply distribution, safe injection, and overdose prevention sites (53). The micro and macro level policy environments concern policies surrounding availability and capacity of harm reduction programs and the laws governing drug use and possession. At the micro level, policies supporting community-level treatment and harm reduction programs can help increase accessibility and reduce harms associated with risks of drug use; an example of this would be take-home OAT doses, which allows patients to minimize transportation costs (economic environment) and those living in rural communities with lower accessibility to clinic and treatment centers to avoid long trips for treatment (54). At the macro level, the federal Good Samaritan Drug Overdose Act (GSDOA), which provides legal protection for individuals who seek emergency help during an overdose event, may be used as an example of policy change supporting decriminalization and protecting rights of individuals who use substances, while encouraging peer and community support (55,56).

1.3 The Harm Reduction Client Survey (HRCS)

This work is based on a secondary analysis of the 2019 British Columbia (BC) Harm Reduction Client Survey (HRCS), prior to the start of the COVID-19 pandemic (Appendix A).

The HRCS is a cross-sectional survey of clients at participating harm reduction supply distribution sites, who use drugs and are aged 19 years and older, across the 5 regional health authorities of BC (57). The objective of the HRCS was to gain more comprehensive province-wide information regarding drug use, related harms, stigma and availability and accessibility of harm reduction services for individuals who use substances (58). The survey is particularly unique, because it samples beyond the two major cities of Vancouver and Victoria, and allows for evaluation across all health authorities (58). Additionally, the sample includes a specific population of individuals who are accessing harm reduction supply distribution sites that are connected to harm reduction services. The survey has been developed with extensive collaboration with representative organizations, including the First Nations Health Authority (FNHA) and people with lived and living experiences, including the Vancouver Area Network of Drug Users (VANDU), to ensure questions are culturally safe and relevant, and trying to avoid potential triggering and stigmatizing questions surrounding substance use, living circumstances, and access to services. The HRCS is used to evaluate programs, explore timely and relevant concerns, in addition to informing harm reduction program accessibility across the province (57).

The HRCS began as a pilot in 2012 and continued annually until 2015 and then resumed in 2018, 2019 and 2021. The average number of respondents each year is about 700, with an average of 30 participating distribution sites. For 2019 specifically, there was a total of 22 harm reduction distribution sites and a total of 621 participants who completed the survey. The 2019 survey inquired about drug use in the past 3 days, in addition to questions evaluating use of

fentanyl, harm reduction sites (overdose prevention sites (OPS)), frequency of obtaining harm reduction supplies, owning naloxone kits and enrollment in OAT in the past 6 months. Self-reported past 3-day substance use is assessed alongside urinalysis data for better comparison of substances detected versus reported in the survey. This thesis does not included any analyses from the survey's urinalysis data.

Additional questions regarding experiencing and/or witnessing opioid and/or stimulant overdose in the past 6 months was also included (57). For this study, we will utilize questions that pertain to OAT discontinuation, sociodemographic characteristics, drug use patterns, and harm reduction service use for our analyses. Many of these variables are considered proxies for factors impacting individual accessibility to services and will be used to inform a discussion around accessibility to addiction services among these vulnerable population groups. We will assess the characteristics of clients that are associated with OAT discontinuation versus continuation. All responses within the survey are self-reported and collected cross-sectionally. Sites received $5 CAD per participant recruited and each participant received $10 CAD for participation as compensation (59). HRCS is conducted under the Harm Reduction Unit at the BC Centre for Disease Control (BCCDC), and data access agreements have been arranged accordingly. This project has been approved by the University of British Columbia (UBC) Behavioural Research Ethics Board and other relevant local boards (BREB H07-00570 "More Than Just Needles: An Evidence-informed Approach to Enhancing Harm Reduction Supply Distribution in BC"). All data from the 2019 survey were managed and stored securely using UBC's Research Electronic Data Capture (REDCap) platform (60,61).

The correlates that will be assessed in relation to OAT discontinuation in this dissertation include participant demographics, socioeconomic status, accessibility to services, including harm

reduction programs and supply distribution sites, type of drugs used, preferred mode of drug use, history of overdose, and characteristics of OAT treatment. Further information regarding variable selection and inclusion can be found in Chapter 2.2.2.

1.4 Current State of Opioid Agonist Therapy in Canada

Current OAT treatments in Canada are available in a variety of forms, including methadone (Methadose), buprenorphine/naloxone (Suboxone), slow-release oral morphine (Kadian), diacetylmorphine (heroin), hydromorphone (pill form and injectable liquid). Methadone is offered widely; however, currently in BC, it is clinically recommended only when Suboxone is not preferable due to intolerance, patient preference, challenging induction, and inadequate response to buprenorphine/naloxone (9). Methadone has been regarded a successful OAT medication for years, particularly when used in conjunction with other supports. Those maintained on methadone tend to have reduced withdrawal, crime risk, risk of death and overdose. In 2019, when the survey was conducted, close to 15,000 individuals were receiving methadone in BC; however, since the medication is no longer considered first line of treatment, there has been a slow decline in numbers receiving this OAT drug over the years (62). In BC, buprenorphine/naloxone (Suboxone) is available as the first line of treatment for patients with opioid use disorder, which can be through standard induction regimens of 2-4 mg or microdosing starting at 0.5 mg twice daily or rapid microdosing of 0.5-1 mg at shorter intervals. In 2019, there were about 6,000 individuals on Suboxone in BC (62). Precipitating withdrawal is one of the main issues associated with standard induction of Suboxone. This is partly because during the induction phase of the Suboxone medication, the patient needs to be in a moderate to severe withdrawal stage. Reaching this level of withdrawal can often cause discomfort for many individuals. Additionally, giving too high a dose at once or leaving long intervals between doses

can precipitate withdrawal (9). Because of this issue, the microdosing regimens are preferred by some patients (31,63). Slow-release oral morphine (SROM) is recommended when methadone and Suboxone have been ineffective, are contraindicated or not preferred (9). A few programs also offer supervised injectable OAT, including diacetylmorphine and hydromorphone for patients who do not respond to any of the previously discussed medications (9,64). One of the aims of this study is to assess the association between the type of OAT medication and discontinuation rates. Data regarding treatment retention among methadone, Suboxone and SROM has been mixed over the years (5). A meta-analysis in 2021 found that retention was generally equal for methadone and Suboxone, though the average retention rates across studies was highly variable and the quality of evidence was marked as low (65). A recent population-based study in British Columbia from 2008-2018 found that the odds of completing OAT induction improved over time for Buprenorphine and surpassed that of methadone by 2018. However, among those who completed induction, being on buprenorphine was associated with shorter time to discontinuation through the study period, with an overall low rate of completing OAT induction, and low rates of reaching the minimum effective dose among the cohort (12). Additionally, a retrospective study of OAT discontinuation among people with opioid use disorder in BC identified a consistently higher rate of discontinuing treatment among those accessing Suboxone compared to methadone (10). While the push towards Suboxone over methadone over the years has been mainly due to the safer profile of the drug, one wonders if the treatment recommendations align with the patients' wishes or if they are made by physicians alone. It is also important to consider that Suboxone has the potential of being a more accessible drug, as it limits the need for the patient to make daily visits to the pharmacy, which is often challenging for patients who may be experiencing challenges beyond drug abuse, such as

homelessness or needing to work (66). Recently, BCCSU released an updated report on OAT practice, recommending prescribers to work more closely with each patient to determine the medication that is most therapeutically suitable for them, based on their life circumstances and previous treatment experiences (5).

1.5 Drug Use Behaviors Among Individuals on Opioid Agonist Therapy

While OAT has been shown to significantly reduce the risk of overdose mortality (8), use of illicit and non-illicit substances during OAT often continues. There are a variety of reasons why individuals may use other substances, while on OAT. These include but are not limited to: managing the side effects of OAT medications (often by using stimulants or uppers), lack of sufficient dosage and experiences of opioid withdrawal, which leads to other illicit opioid use in addition to the OAT medication to supplement the dosage, in addition to lack of energy brought on by OAT medications, which may be counteracted by the use of stimulants (67).There are also inconsistent guidelines across Canadian provinces in terms of urine drug screening during opioid agonist therapy (OAT), which means individuals in different treatment programs might be continuing use of various illicit substances while in treatment, depending on the restrictions (68). Previous studies have reported variations in continued drug use during OAT. A study in Ukraine found that among a random sample of 434 patients receiving methadone and buprenorphine maintenance treatment, 23% reported concurrent drug injections. Of those, 100% injected opioids and 24% injected stimulants (69). A recent Canadian study in a Vancouver cohort from 1996-2018 observed decreasing trends for use of heroin, illicit prescription opioids and benzodiazepines after OAT engagement but no significant difference in cocaine, crack cocaine, crystal methamphetamine and cannabis use, and a growing rate of alcohol use post OAT was reported (70). Another study in Vancouver estimated the association of daily cannabis use on the

likelihood of retention in OAT therapy of methadone and buprenorphine among 820 people who used illicit drugs and found that daily cannabis use was associated with approximately 21% greater odds of retention in treatment (71). Additionally, a study of 875 participants in Vancouver found a significant portion of participants on methadone reported more than weekly crystal methamphetamine use, which was associated with an increased risk of methadone discontinuation (72). Finally, a cross-sectional study of 105 patients in a psychiatric hospital in Zurich found concomitant illicit drug use, including heroin and cocaine, among patients receiving OAT, with reduced opiate consumption among those on buprenorphine maintenance (73). Overall, there appears to be high variation in the patterns of substance use among those receiving OAT. This study aims to uncover additional information, on a province-level, regarding concomitant OAT treatment and illicit substance use. This information is critical in better understanding the effectiveness of OAT in reducing substance use and the interplay between harm reduction programs and OAT in providing safer modes of substance use.

1.6 Previously Identified Correlates of Opioid Agonist Therapy Retention

Studies have previously reported some correlates of OAT continuation and discontinuation, among those receiving methadone, buprenorphine and SROM. Previous studies have found that injection drug use, incarceration in the past 12 months, recent receptive syringe or injection equipment sharing and being male was associated with significantly higher discontinuation rates (29,74,75). Another study reported that regular contact with the healthcare system in outpatient or acute setting was associated with lack of engagement in OAT (11). Additionally, being of aboriginal decent and of younger age has been associated with an increased risk of leaving treatment (75,76). An older study in the US from 2010 found lower treatment retention rates in OAT among participants who lost access to a harm reduction program during the study (77).

Additionally, a retrospective cohort study of 16,576 participants in New South Wales, Australia identified experiences of homelessness as significant predictors of retention in OAT treatment (78), while a prospective cohort study of people who use drugs in Vancouver, identified homelessness as a predictor of treatment discontinuation (29). Another study in Vancouver found that employment was significantly associated with OAT engagement among patients (79), while another study found that not being on income assistance was positively associated with OAT discontinuation (29). Although our current study has limitations regarding the variables that were measured, I will use the available literature to inform the inclusion of variables as covariates and correlates of OAT discontinuation in our models.

There are limited province-level studies in Canada that have assessed OAT retention rates, and characterization of individuals who are likely to continue vs. discontinue treatment has been largely limited to single trials or cohorts in larger cities, such as Vancouver's Downtown Eastside. Studies have often focused on single attributes of individuals in OAT, such as drug use behaviors, access to services or demographics without considering the interplay between these social structural factors in informing access and ability to continue OAT. Understanding the combined effects of these factors as proxies of health service access can help us better understand the structural barriers present within the addiction treatment system of BC to better inform future services. The HRCS represents a diverse cohort of individuals who use substances across urban and rural areas of the province. This study will provide quantitative evidence on populations from various areas of the provinces and can help inform healthcare providers and policy makers across BC regarding factors that may impact OAT discontinuation among people who use drugs to identify those who are most vulnerable and likely to drop out of treatment.

Chapter 2: Characteristics of Individuals who Continued vs. Discontinued on Opioid Agonist Therapy

2.1 Introduction

Illicit drug use has been a major contributor to mortality and disability in BC and worldwide (8). Use of illicit and non-illicit substances often continues during OAT treatment (70,80,81). Studies in Vancouver-based cohorts have shown great variations in substance use among those who enter OAT treatment; however, there generally appears to be a decrease in use of heroin and illicit prescription opioids, but no significant difference in use of cocaine, crack cocaine, crystal methamphetamines and cannabis, while alcohol use has been shown to increase in some cohorts of individuals engaged in OAT (70,72,79). Additionally, method of use may put individuals who use drugs at higher risk of overdose and other related harms (82). For example, individuals who are more likely to inject drugs, are at a higher risk of both overdose and injection-related comorbidities, including HIV and HCV infections (34,35). Understanding type and method of substance use, along with access to and use of harm reduction services that can help mitigate risks is therefore of great importance among clients accessing OAT services.

In BC, there is a knowledge gap in identifying drug use patterns and behaviors among those accessing OAT and harm reduction services, particularly outside major cities of Vancouver and Victoria, where most studies are often concentrated. This chapter aims to add to the existing literature by providing a comprehensive description of individuals who continue and discontinue on OAT across the province, in an aim to inform public health responses to the growing problem of the overdose crisis in North America.

The main objective of this chapter is to identify substances that are commonly used by clients who are accessing harm reduction supply distribution sites across the province's five health regions and have indicated being prescribed at least one OAT medication in the past 6 months (Question 37a, Appendix A). The sample was stratified by whether the individual reported having continued or discontinued on OAT in the past 6 months prior to taking the HRCS survey (Question 37b, Appendix A) (57,58).

2.2 Methods

2.2.1 Primary outcome variable

The outcome variable (OAT discontinuation) was taken from the HRCS survey (Appendix A) as follows:

a. In the last 6 months, did any of the following make it difficult for you to access Opioid Agonist Treatment (OAT)/Opioid Substitution Treatment (OST) (eg. methadone, buprenorphine/naloxone, etc)?

Those who had responded "I do not use opioids" and/or "I did not try to access OAT/OST" were excluded.

b. In the last 6 months, were you prescribed any of the following OAT/OST?

Those who had responded "I wasn't prescribed any OAT/OST" and/or "Prefer not to say" were excluded.

c. In the last 6 months, did you discontinue OAT/OST?

This final question was used to define the sample for this study. Figure 2.1 shows a flowchart describing how the final analytic sample was derived for the main outcome variable of OAT discontinuation.

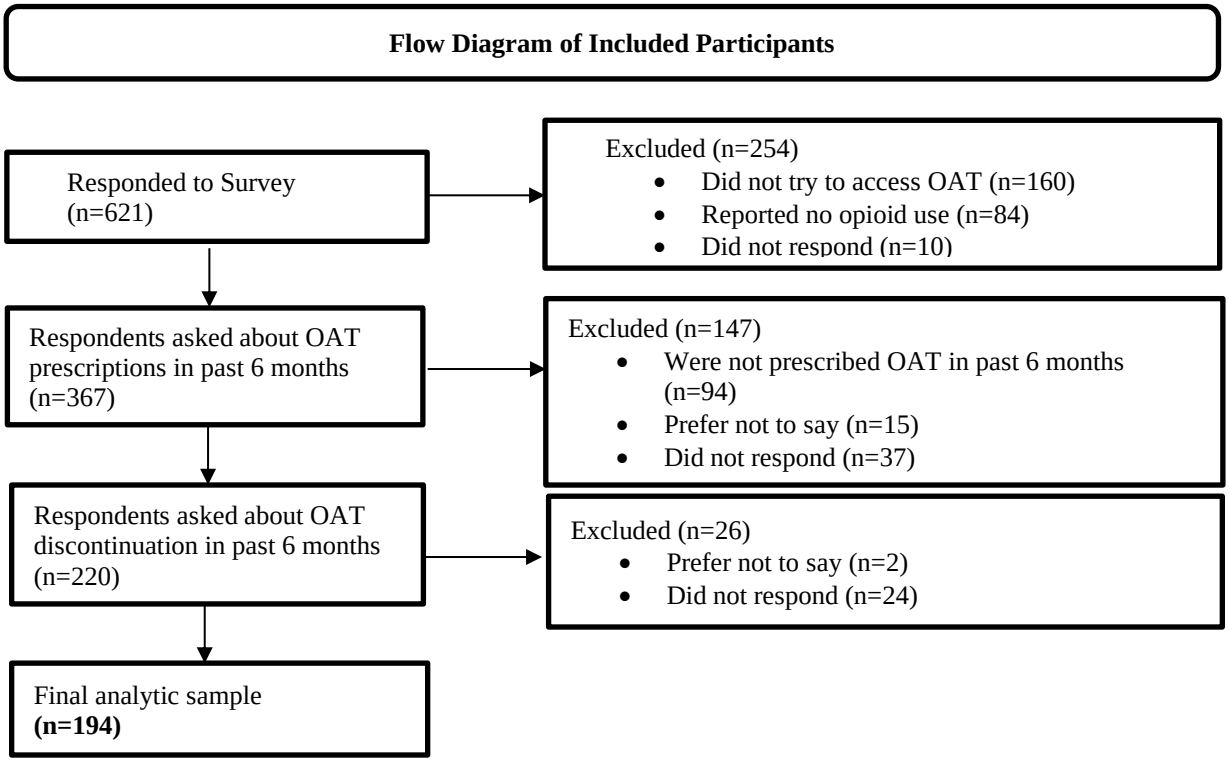

Figure 2.1 Inclusion criteria for OAT discontinuation/continuation outcome among HRCS participants.

All the above questions allow for multiple selections by the participants; because of this, rather than including participants based on responses, those who did not respond or responded no at every step were excluded to arrive at the final analytical sample. The outcome questions have been previously validated and included as part of the survey in prior years and were further modified based on consultation with on-site and research team members to better address the target population. The 6-month time limit has been determined based on the prior analyses of the survey and other questions mostly limited to the prior 6 months, in addition to other study timelines, to allow for better comparison.

2.2.2 Explanatory Variables

As detailed previously in Chapter 2.1, the main explanatory variable in this chapter was past 3-day drug use by the participant. Additional variables that were assessed in relation to OAT continuation vs. discontinuation included demographics, socioeconomic status, access to services, drug use characteristics, as well as the OAT medication prescribed. Additional details regarding each variable group are outlined below. The categories of each variables are shown in brackets, in front of the variable name.

1. Demographics
    a. Age (19-29, 30-39, 40-49, >50, missing)
    b. Gender (cis woman, cis man, transgender, and gender expansive, prefer not to say, missing)
    c. Self-reported indigeneity (First Nations, Metis, non-indigenous, prefer not to say, missing)
2. Socioeconomic status
    a. Housing Status (currently stably housed, currently not stably housed, prefer not to say, missing); stable housing refers to living in a private residence alone or with others, as well as other public residences such as hotels, shelters, rooming houses, etc. Unstable housing was defined as individuals who indicated not having a regular place to stay (Question 4, Appendix A).
    b. Employment Status (currently employed, currently not employed, prefer not to say, missing); currently employed refers to any form of paid employment full time or part time.
3. Overall accessibility to services

The following variables were used as proxies for accessibility to services:

a. Urbanicity (medium/large urban, small urban, rural); urbanicity of sites was derived using a classification system developed by the BC Ministry of Health specific to communities in BC, which combined definitions of urbanicity set by Statistics Canada with indicators of remoteness, population density and proximity to urban areas. Urbanicity was defined based on the location the survey was administered and was assumed to represent living location for most participants, when making inferences.
b. Health Authority (Vancouver Coastal Health, Fraser Health, Interior Health, Island Health, Northern Health)

4. Types of Drugs Used (recorded as used, not used, or missing in the past 3 days, independent of method of use)
    a. Methadone (yes, no, missing)
    b. Buprenorphine (yes, no, missing)
    c. Dilaudid (yes, no, missing)
    d. Oxycodone (yes, no, missing)
    e. Morphine (yes, no, missing)
    f. Prescription opioids[2] (methadone + buprenorphine/Suboxone + hydromorphone/Dilaudid + oxycodone + morphine) (yes, no, missing)
    g. Heroin (yes, no, missing)

[2] Prescription opioids include opioids that tend to be medically prescribed; however, may be used illicitly in the sample or may be obtained through prescription. Additional information regarding proportion of participants who indicated OAT prescription in past 6 months and indicated using the same opioid in the past 3 days may be found in Table B.1 in Appendix B.

h. Fentanyl (yes, no, missing)

i. Heroin and/or fentanyl (heroin + fentanyl) (yes, no, missing)

j. Any opioid (methadone + buprenorphine + Dilaudid + oxycodone + morphine + heroin + fentanyl) (yes, no, missing)

k. Xanax (yes, no, missing)

l. Benzodiazepines other than Xanax (yes, no, missing)

m. Any Benzodiazepines (Xanax + benzodiazepines other than Xanax) (yes, no, missing)

n. Stimulants (Ritalin/Adderall) (yes, no, missing)

o. Crystal Meth (yes, no, missing)

p. Cocaine (yes, no, missing)

q. Crack (yes, no, missing)

r. MDMA (yes, no, missing)

s. Any Stimulant (stimulants + crystal meth + cocaine + crack + MDMA) (yes, no, missing)

t. Cannabis or Hash (yes, no, missing)

u. Tobacco (yes, no, missing)

v. Alcohol (yes, no, missing)

5. Drug Use Characteristics

    a. Preferred method of drug use (smoking/inhalation, injection, other, prefer not to say, missing)

    b. History of overdose in the past 6 months (stimulants, opioids, both, no, don't know, prefer not to say, missing)

c. Owning a naloxone kit (yes, no, prefer not to say, missing)
d. Frequency of obtaining harm reduction supplies in the past 6 months (frequent, occasional/never, prefer not to say, missing)
e. Overdose Prevention Services (OPS)/ Supervised Consumption Site (SCS) use in the past 6 months (yes, no, prefer not to say, missing); overdose prevention services, including safe consumption sites, were introduced in the province by the health minister, under the emergency declaration, in response to increasing overdose rates (83).

6. OAT medication characteristics
    a. OAT medications prescribed in the past 6 months (methadone, buprenorphine/naloxone (Suboxone), slow-release oral morphine, more than 1 medication, missing)

2.2.3 Statistical Analysis

Descriptive statistics were calculated and stratified by the OAT discontinuation vs. continuation outcome. Participants who had not indicated a response to the respective question were tabulated under "missing" and those who had indicated "prefer not to say" on the survey were also grouped separately in analyses. This decision was made to account for and assess underreporting, particularly since many of the selected variables for our study are often underreported in studies, due to the sensitive nature of the questions. All variables were summarized as frequencies and proportions. P-values were calculated using Pearson's chi-squared test or Fisher's exact test (where appropriate) for comparison of all categorical data. All data manipulation and statistical analyses were conducted in R version 4.1.2 (2021-11-01).

2.3 Results

Table 2.1 describes the demographics, socioeconomic, structural and accessibility characteristics of participants in the HRCS cohort. The sample included a total 194 participants, who were included based on their response to the OAT continuation vs. discontinuation question, as shown previously in Figure 2.1. The larger proportion of participants (38.1%, n=74) were between 30-39 years of age; 59.8% (n=116) identified as cis man, 36.6% (n=71) as cis woman and 1.5% (n=3) identified as transgender and gender expansive. Overall, 37.6% (n=73) of participants identified as Indigenous. Much of the sample indicated being stably housed and experiencing unemployment (70.1%, n=136), at the time of taking the survey. Most participants took the survey at medium/large urban locations (70.6%, n=137), and there was a relatively equal spread of participants across all health authorities (p=1.00).

Bivariate analyses identified age as statistically significant ($p<0.05$) in its association with OAT discontinuation, where the ≥ 50 age group had a higher proportion of participants (82.9%, n=34) continuing OAT, compared to other age categories.

Table 2.2 shows the past 3-day types of drugs used by participants and the OAT medication received in the past 6 months. Of the 194 participants, 57.7% (n=112) indicated being prescribed methadone in the past 6 months, followed by 17.5% (n=34) indicating buprenorphine/naloxone prescription. 10.3% (n=20) indicated being prescribed more than 1 OAT medication in the past 6 months. Most participants indicated some stimulant use in the past 3 days (78.9%, n=153) with 69.6% (n=135) indicating crystal meth, and 20.6% (n=40) indicating cocaine and/or crack use. Most participants (71.1%, n=138) also indicated heroin and/or fentanyl use in the past 3 days, including 53.1% (n=103) indicating heroin and 61.3% (n=119) indicating

fentanyl use specifically. Cannabis, tobacco, and alcohol use was also commonly reported among participants at 53.6% (n=104), 85.6% (n=166) and 30.4% (n=59), respectively.

Bivariate analyses identified the following variables as statistically significant ($p<0.05$) in their association with OAT discontinuation: methadone use in the past 3 days ($p<0.01$), prescription opioid use in past 3 days ($p<0.01$), heroin and/or fentanyl use in past 3 days ($p<0.01$), and OAT medication prescribed in the past 6 months ($p<0.01$). OAT discontinuation was similar among individuals who reported heroin (58.3%), fentanyl (52.1%), and heroin or fentanyl use combined (51.4%).

Table 2.3 shows descriptive statistics for preferred mode of drug use, experiences of overdose in the past 6 months, and harm reduction variables. 22.1% (n=38) of participants indicated experiencing an overdose with 13.4% (n=26) indicating experiencing an opioid overdose, 4.6% (n=9) indicating having experienced a stimulant overdose and 4.1% (n=8) indicating having experienced both stimulant and opioid overdose in the past 6 months. Of the 194 participants, 62.4% (n=121) indicated smoking/inhalation and 32.0% (n=62) indicated injection as their preferred method of drug use. 57.2% (n=111) of participants indicated frequently accessing harm reduction supplies and 43.3% (n=84) indicated using overdose prevention sites in the past 6 months, in addition to 75.8% (n=147) indicating owning a naloxone kit.

Bivariate analyses identified the following variables as statistically significant ($p<0.05$) in their association with OAT discontinuation: experience of overdose in the past 6 months ($p<0.01$), use of an overdose prevention site in the past 6 months ($p<0.05$). Additional data regarding prescription OAT medication in the past 6 months and substance use in the past 3 days may be found in Appendix B.

Table 2.1 Demographic, socioeconomic, structural and access characteristics of included participants, stratified by continuation vs. discontinuation of OAT in the past 6 months (n=194).

Characteristics	OAT Status		Total (n=194) n (%)[G]	Chi-Square *P*-value[A]
	Continued (n=109) n (%)[F]	Discontinued (n=85) n (%)[F]		
Gender				0.62
Cis woman[B]	38 (53.5%)	33 (46.5%)	71 (36.6%)	
Cis man[B]	67 (57.8%)	49 (42.2%)	116 (59.8%)	
Transgender and gender expansive[C]	1 (33.3%)	2 (66.7%)	3 (1.5%)	
Prefer not to say	0	0	0 (0.0%)	
Missing	3 (75.0%)	1 (25.0%)	4 (2.1%)	
Age category				**<0.001*** **
19-29	17 (48.6%)	18 (51.4%)	35 (18.0%)	
30-39	33 (44.6%)	41 (55.4%)	74 (38.1%)	
40-49	23 (57.5%)	17 (42.5%)	40 (20.6%)	
≥50	34 (82.9%)	7 (17.1%)	41 (21.1%)	
Missing	2 (50.0%)	2 (50.0%)	4 (2.1%)	
Indigenous identity[D,E]				0.33
First Nations	25 (48.1%)	27 (51.9%)	52 (26.8%)	
Metis	14 (66.7%)	7 (33.3%)	21 (10.8%)	
Non-Indigenous	63 (56.2%)	49 (43.8%)	112 (57.7%)	
Prefer not to say	0	0	0 (0.0%)	
Missing	7 (77.8%)	2 (22.2%)	9 (4.6%)	
Currently stably housed				0.11
Yes	82 (60.3%)	54 (39.7%)	136 (70.1%)	
No	27 (46.6%)	31 (53.4%)	58 (29.9%)	
Prefer not to say	0	0	0 (0.0%)	
Missing	0	0	0 (0.0%)	
Currently employed				0.22
Yes	33 (63.5%)	19 (36.5%)	52 (26.8%)	

No	73 (53.7%)	63 (46.3%)	136 (70.1%)	
Prefer not to say	3 (75.0%)	1 (25.0%)	4 (2.1%)	
Missing	0	2 (100.0%)	2 (1.0%)	
Urbanicity				0.51
Medium/large urban	80 (58.4%)	57 (41.6%)	137 (70.6%)	
Rural	9 (45.0%)	11 (55.0%)	20 (10.3%)	
Small urban	20 (54.1%)	17 (45.9%)	37 (19.1%)	
Health authority				1.00
Fraser Health	28 (57.1%)	21 (42.9%)	49 (25.3%)	
Interior Health	25 (58.1%)	18 (41.9%)	43 (22.2%)	
Island Health	16 (53.3%)	14 (46.7%)	30 (15.5%)	
Northern Health	13 (56.5%)	10 (43.5%)	23 (11.9%)	
Vancouver Coastal Health	27 (55.1%)	22 (44.9%)	49 (25.3%)	

[A]*P*-values reflect significance of Chi-squared test or Fisher's exact test (where appropriate).

[B]A cis or cisgender person is one whose gender identity matches their sex assigned at birth.

[C]Transgender and gender expansive includes people that identified as transgender men, transgender women, or gender non-conforming people.

[D]No participants who identified as Inuit reported their OAT status.

[E]We recognize that Indigenous identity is often a proxy for factors like intergenerational trauma, systemic racism, and socioeconomic status.

[F]Indicates row percentages.

[G]Indicated column percentages.

[***] Indicates p-value significance level of ≤0.001.

Table 2.2 Past 3-day drug use and OAT medication received among included participants, stratified by continuation vs. discontinuation of OAT in the past 6 months (n=194).

Characteristics	OAT Status		Total (n=194) n (%)[C]	Chi-Square *P*-value[A]
	Continued (n=109) n (%)[B]	Discontinued (n=85) n (%)[B]		
Methadone				**<0.01****
Yes	64 (77.1%)	19 (22.9%)	83 (42.8%)	
No	11 (37.9%)	18 (62.1%)	29 (14.9%)	
Missing	34 (41.5%)	48 (58.5%)	82 (42.3%)	
Buprenorphine				0.35
Yes	8 (47.1%)	9 (52.9%)	17 (8.8%)	
No	26 (50.0%)	26 (50.0%)	52 (26.8%)	
Missing	75 (60.0%)	50 (40.0%)	125 (64.4%)	
Dilaudid				0.44
Yes	5 (55.6%)	4 (44.4%)	9 (4.6%)	
No	23 (47.9%)	25 (52.1%)	48 (24.7%)	
Missing	81 (59.1%)	56 (40.9%)	137 (70.6%)	
Oxycodone				0.16
Yes	0	2 (100.0%)	2 (1.0%)	
No	27 (50.9%)	26 (49.1%)	53 (27.3%)	
Missing	82 (59.0%)	57 (41.0%)	139 (71.6%)	
Morphine				0.58
Yes	21 (61.8%)	13 (38.2%)	34 (17.5%)	
No	21 (50.0%)	21 (50.0%)	42 (21.6%)	
Missing	67 (56.8%)	51 (43.2%)	118 (60.8%)	
Prescription opioids				**<0.01****
Yes	90 (72.0%)	35 (28.0%)	125 (64.4%)	
No	3 (18.8%)	13 (81.2%)	16 (8.2%)	
Missing	16 (30.2%)	37 (69.8%)	53 (27.3%)	
Heroin				**<0.01****

Yes	43 (41.7%)	60 (58.3%)	103 (53.1%)	
No	10 (62.5%)	6 (37.5%)	16 (8.2%)	
Missing	56 (74.7%)	19 (25.3%)	75 (38.7%)	
Fentanyl				**<0.01****
Yes	57 (47.9%)	62 (52.1%)	119 (61.3%)	
No	7 (70.0%)	3 (30.0%)	10 (5.2%)	
Missing	45 (69.2%)	20 (30.8%)	65 (33.5%)	
Heroin or fentanyl				**<0.01****
Yes	67 (48.6%)	71 (51.4%)	138 (71.1%)	
No	4 (66.7%)	2 (33.3%)	6 (3.1%)	
Missing	38 (76.0%)	12 (24.0%)	50 (25.8%)	
All opioids				1.00
Yes	101 (55.8%)	80 (44.2%)	181 (44.2%)	
No	2 (66.7%)	1 (33.3%)	3 (1.5%)	
Missing	6 (60.0%)	4 (40.0%)	10 (5.2%)	
Xanax				0.26
Yes	2 (28.6%)	5 (71.4%)	7 (3.6%)	
No	27 (52.9%)	24 (47.1%)	51 (26.3%)	
Missing	80 (58.8%)	56 (41.2%)	136 (70.1%)	
Benzodiazepines other than Xanax				0.36
Yes	10 (47.6%)	11 (52.4%)	21 (10.8%)	
No	23 (50.0%)	23 (50.0%)	46 (23.7%)	
Missing	76 (59.8%)	51 (40.2%)	127 (65.5%)	
All Benzodiazepines				0.35
Yes	12 (48.0%)	13 (52.0%)	25 (12.9%)	
No	22 (50.0%)	22 (50.0%)	44 (22.7%)	
Missing	75 (60.0%)	50 (40.0%)	125 (64.4%)	
Stimulants				0.35
Yes	9 (69.2%)	4 (30.8%)	13 (6.7%)	
No	25 (49.0%)	26 (51.0%)	51 (26.3%)	
Missing	75 (57.7%)	55 (42.3%)	130 (67.0%)	

Crystal Meth				0.10
Yes	69 (51.1%)	66 (48.9%)	135 (69.6%)	
No	8 (66.7%)	4 (33.3%)	12 (6.2%)	
Missing	32 (68.1%)	15 (31.9%)	47 (24.2%)	
Cocaine				0.72
Yes	22 (55.0%)	18 (45.0%)	40 (20.6%)	
No	21 (51.2%)	20 (48.8%)	41 (21.1%)	
Missing	66 (58.4%)	47 (41.6%)	113 (58.2%)	
Crack				0.85
Yes	21 (52.5%)	19 (47.5%)	40 (20.6%)	
No	24 (55.8%)	19 (44.2%)	43 (22.2%)	
Missing	64 (57.7%)	47 (42.3%)	111 (57.2%)	
MDMA				0.61
Yes	3 (50.0%)	3 (50.0%)	6 (3.1%)	
No	28 (50.9%)	27 (49.1%)	55 (28.4%)	
Missing	78 (58.6%)	55 (41.4%)	133 (68.6%)	
All Stimulants				0.22
Yes	82 (53.6%)	71 (46.4%)	153 (78.9%)	
No	5 (83.3%)	1 (16.7%)	6 (3.1%)	
Missing	22 (62.9%)	13 (37.1%)	35 (18.0%)	
Cannabis or Hash				0.25
Yes	53 (51.0%)	51 (49.0%)	104 (53.6%)	
No	16 (66.7%)	8 (33.3%)	24 (12.4%)	
Missing	40 (60.6%)	26 (39.4%)	66 (34.0%)	
Tobacco				0.23
Yes	91 (54.8%)	75 (45.2%)	166 (85.6%)	
No	4 (44.4%)	5 (55.6%)	9 (4.6%)	
Missing	14 (73.7%)	5 (26.3%)	19 (9.8%)	
Alcohol				0.70
Yes	31 (52.5%)	28 (47.5%)	59 (30.4%)	
No	25 (61.0%)	16 (39.0%)	41 (21.1%)	
Missing	53 (56.4%)	41 (43.6%)	94 (48.5%)	

OAT Medication			**<0.01****
Methadone (Methadose)	67 (59.8%)	45 (40.2%)	112 (57.7%)
Slow-release oral morphine	16 (84.2%)	3 (15.8%)	19 (9.8%)
Buprenorphine/naloxone	15 (44.1%)	19 (55.9%)	34 (17.5%)
More than 1 medication	4 (20.0%)	16 (80.0%)	20 (10.3%)
Missing	7 (77.8%)	2 (22.2%)	9 (4.6%)

[A]*P*-values reflect significance of Chi-squared test or Fisher's exact test (where appropriate).

[B]Indicated row percentages.

[C]Indicates column percentages.

** Indicates p-value significance level of ≤0.01.

Table 2.3 Preferred mode of drug use, experiences of overdose and use of harm reduction services in the past 6 months, among included participants, stratified by continuation vs. discontinuation of OAT in the past 6 months (n=194).

Characteristics	OAT Status		Total (n=194) n (%)[C]	Chi-Square
	Continued (n=109) n (%)[B]	Discontinued (n=85) n (%)[B]		*P*-value[A]
Preferred mode of drug use				0.84
Injection	35 (56.5%)	27 (43.5%)	62 (32.0%)	
Smoking/inhalation	67 (55.4%)	54 (44.6%)	121 (62.4%)	
Other	6 (66.7%)	3 (33.3%)	9 (4.6%)	
Prefer not to say	0	1 (100.0%)	1 (0.5%)	
Missing	1 (100.0%)	0	1 (0.5%)	
Drug use alone				0.22
Yes	89 (54.3%)	75 (45.7%)	164 (84.5%)	
No	19 (70.4%)	8 (29.6%)	27 (13.9%)	
Prefer not to say	1 (33.3%)	2 (66.7%)	3 (1.5%)	
Missing	0	0	0 (0.0%)	
Experienced an overdose in the last 6 months				**<0.01****
Stimulants	3 (33.3%)	6 (66.7%)	9 (4.6%)	
Opioids	9 (34.6%)	17 (65.4%)	26 (13.4%)	
Both	2 (25.0%)	6 (75.0%)	8 (4.1%)	
No	91 (64.1%)	51 (35.9%)	142 (73.2%)	
Don't Know	1 (50.0%)	1 (50.0%)	2 (1.0%)	
Prefer not to say	0	0	0 (0.0%)	
Missing	3 (42.9%)	4 (57.1%)	7 (3.6%)	
Naloxone kit possession				0.80
Yes	84 (57.1%)	63 (42.9%)	147 (75.8%)	
No	23 (53.5%)	20 (46.5%)	43 (22.2%)	
Prefer not to say	0	1 (100.0%)	1 (0.5%)	

Missing	2 (66.7%)	1 (33.3%)	3 (1.5%)	
Frequency of accessing harm reduction supplies				0.10
Frequent	56 (50.5%)	55 (49.5%)	111 (57.2%)	
Occasional/never	52 (63.4%)	30 (36.6%)	82 (42.3%)	
Prefer not to say	1 (100.0%)	0	1 (0.5%)	
Missing	0	0	0 (0.0%)	
Used an overdose prevention site (OPS) in the last 6 months				**0.01****
Yes	38 (45.2%)	46 (54.8%)	84 (43.3%)	
No	70 (64.8%)	38 (35.2%)	108 (55.7%)	
Prefer not to say	0	0	0 (0.0%)	
Missing	1 (50.0%)	1 (50.0%)	2 (100.0%)	

[A]*P*-values reflect significance of Chi-squared test or Fisher's exact test (where appropriate).

[B]Indicated row percentages.

[C]Indicates column percentages.

** Indicates p-value significance level of ≤0.01.

2.4 Discussion

In this chapter, we assessed demographic, socioeconomic, drug use characteristics and use of harm reduction services in a sample from the HRCS that had indicated continuation or discontinuation of OAT in the past 6 months. In our sample, most participants indicated using at least one type of drug, including opioids, stimulants, cannabis or hash, tobacco and/or alcohol within the past 3 days. According to Chi-squared analyses, older age, past 3-day use of methadone and all prescription opioids combined, being prescribed a methadone OAT medication, and not using an OPS site in the past 6 months was associated with OAT continuation, while missing responses to past 3-day heroin and/or fentanyl use and experiencing stimulant and/or opioid overdose in the past 6 months was associated with OAT discontinuation.

Significant associations were found between age category and OAT discontinuation in our sample with a higher percentage of older (≥50) age group continuing OAT. Previous studies support our findings where younger age was associated with an increased risk of leaving OAT treatment (75,76). A study in BC from 2020 found that compared to those ever engaged in OAT, people with opioid use disorder currently engaged in OAT were more often between the age of 35-44 years (compared to ≥45). In our sample, the 30–39-year age groups were equally distributed across the continuation and discontinuation cohort; however, this group did form the highest percentage of the sample (38.1%), which consists of individuals having enrolled in OAT treatment in the past 6 months (11).

Drug use variables that were significantly different among the continued vs. discontinued groups included methadone, prescription opioids, heroin, and fentanyl (assessed both individually and combined), in addition to the OAT medication prescribed in the past 6 months. A higher percentage of participants who continued OAT reported methadone (77.1%) and

prescription opioid (72.0%) use in the past 3 days, which is consistent with the sample having been restricted to those who indicated receiving OAT in the past 6 months, and methadone being the most prevalent OAT prescription in the sample (57.7%). Prevalence of past 3-day heroin, fentanyl and heroin and/or fentanyl use combined was high across the sample overall, with a greater percentage of participants indicating using these opioids in both the continued and discontinued groups. Of note however is that among those who indicated not having used either fentanyl, heroin, or the combination of the two, the majority had also indicated continuing on OAT. Our findings were supported by the urinalysis testing conducted on the larger HRCS cohort (84). The urinalysis results showed that 77.7% of individuals who had methadone and 59.4% of individuals who had buprenorphine detected in their urinalysis also had co-detected fentanyl in their urine, which support our findings of continued use of fentanyl among individuals who are actively enrolled in OAT. A previous cohort study in Vancouver, from 1996-2018, had shown decreasing trends for heroin and illicit prescription opioid use among individuals engaged in OAT (70). Due to the cross-sectional nature of our study and having limited our sample to individuals who accessed OAT in the past 6 months, it is difficult to determine whether illicit opioid use significantly decreased following OAT engagement among our sample and our comparisons are limited to individuals who continued and discontinued, following initial OAT engagement in the prior 6 months. A cohort analysis from the United States in 2018 found significant use of illicit opioids during treatment with buprenorphine/naloxone, with compliant patients more likely than noncompliant patients to be abstinent during treatment (85). These findings can partially explain the associations seen in our sample with a greater proportion of participants who did not report illicit opioid use having continued OAT, if continuation on OAT also implied treatment compliance in our sample.

There were no differences observed between the continuation and discontinuation groups in terms of past 3-day use of benzodiazepines, stimulants, cannabis, tobacco, and alcohol. Multiple studies in the past have shown continued use of stimulants among individuals receiving OAT (69,70,72,73). A recent publication on a sample from HRCS, administered in 2019, found that over half of the participants who reported opioid and/or stimulant use in the past 3 days used both drugs concurrently (67). Individuals with concurrent opioid and stimulant use are more likely to experience both fatal and non-fatal overdose (67,86–90); therefore, considering a large percentage of these individuals are also engaged in OAT, tailored treatment services and harm reduction programs that help individuals with such unique needs and mitigate the increased risk of overdose and other drug-related harms associated with concomitant opioid and stimulant use are necessary. Cannabis use was similar across the continuation and discontinuation groups in our sample. A previous cohort study in Vancouver, from 1996-2018, also found no significant difference in cannabis use, following OAT engagement, which helps support our findings (70). This finding is also consistent with some studies suggesting that cannabis use may be associated with decreased craving and use of opioids and higher retention in OAT (71), therefore individuals receiving OAT may use cannabis to reduce cravings for opioids. There were no significant differences associated with OAT discontinuation and reported alcohol use in our sample. Previous studies have at times found growing rates of alcohol use following OAT engagement (70). While the treatment mechanism of OAT medications is not expected to impact drug use beyond opioids, it is important to consider use of other substances alongside opioids among those engaged in or discontinuing OAT. This chapter helped highlight some of the most used substances among individuals that are continuing or discontinuing OAT in HRCS in 2019. While use of many substances was not associated with OAT discontinuation, these findings help

highlight the importance of access to harm reduction services and treatment strategies that help target substance use, beyond opioid use, among individuals accessing OAT to better mitigate risk of overdose and harms associated with polysubstance use.

In our sample, 73.2% did not report having experienced an overdose in the past 6 months; however, 22.1% reported a stimulant, opioid, and stimulant and/or opioid overdose combined (Table 2.3). Of those who reported an overdose in the past 6 months, the majority had also indicated discontinuing OAT in the past 6 months, while the majority of those who indicated not having experienced an overdose had continued OAT. Of the 13.4% that reported experiencing an opioid overdose, 2/3 also reported having discontinued OAT in the past 6 months. A previous study from the United States found an association with increased risk of overdose following OAT discontinuation (8), suggesting that long-term retention and continuation on OAT helps prevent overdose (8,10), which is in-line with our findings. Another large retrospective cohort study of 55,347 people in BC, from 1996-2018, found that the all-cause standardized mortality ratio was substantially lower among individuals taking OAT compared to off/discontinuing OAT, with risk of mortality remaining high among individuals who stop OAT treatment (91).

OPS/SCS use in the past 6 months was reported by 43.3% of participants, while 55.7% did not report using OPS/SCS; however, among those who did report using a site, the majority indicated having discontinued OAT in the past 6 months, while the majority of those who did not report using the site reported having continued OAT. These findings have important implications for healthcare policy around accessibility of harm reduction sites, particularly overdose prevention services. It is important to consider that most individuals who are discontinuing OAT are continuing to access OPS/SCS. Given our findings that most individuals who are discontinuing treatment are also experiencing increased rates of stimulant and opioid overdose, it

is important to ensure accessible OPS/SCS for individuals who discontinue treatment, as it is an actively sought service that can help mitigate the harms associated with toxic substance use. Of concern is the number of participants who indicated continuing OAT and not accessing OPS/SCS. While the reason for not using OPS/SCS among those who are in OAT is not clear from the survey, as previously discussed, a high percentage of individuals who continue OAT are actively using opioids and stimulants in our sample; therefore, it is also important to ensure continuous access to OPS for individuals who continue OAT, to help mitigate risks of overdose mortality while in treatment. Use of OPS/SCS may also be occasional, and individuals may still choose to use substances outside of an OPS/SCS facility. Qualitative studies in this area may help shed additional light on why participants may be choosing to not access OPS/SCS or not having the means to access OPS/SCS during OAT treatment. Additional information regarding harm reduction measures and services may be found in Chapter 4.2.3.

While we did not find any significant associations between other harm reduction variables and OAT discontinuation, such as naloxone kit possession and frequency of accessing harm reduction supplies, most participants in our sample indicated owning a naloxone kit (75.8%) and frequently accessing harm reduction supplies (57.2%), in both the continuation and discontinuation groups. These findings have positive implications, given the increased efforts to expand access to harm reduction services across the province. Given the number of participants who indicated using heroin and/or fentanyl in the past 3 days, while continuing OAT, ensuring access to naloxone kits is an important harm reduction measure for this population group to help minimize the risk of an opioid overdose fatality. Similarly, accessibility to harm reduction supplies, such as clean and unused needles, is an important measure to be available to individuals that may be continuing or discontinuing OAT. In our sample specifically, 32.0% of participants

indicated injection as their preferred method of drug use; therefore, accessibility to harm reduction supplies, particularly unused needles, is important in helping mitigate the harms associated with injection substance use while in treatment. Our findings need to be further assessed within the context of the COVID-19 pandemic, as the survey was conducted prior to the introduction of many of the newer public health restrictions. For example, a recent study of semi-structured interviews conducted in Australia, in 2020, found that while improvements in opioid agonist therapy prescriptions during the pandemic were noted as positive, disruptions in the delivery of harm reduction and sterile injecting equipment increased difficulties in adapting to changes in service access, increased levels of social isolation and injecting risk behaviors (92). Another recently published study of PWID between 2003-2019 from Quebec, Ontario, Saskatchewan, and British Columbia found gaps in engagement in harm reduction programs across Canadian provinces, including needle and syringe programs (58-70%), OAT engagement (8-26%), as well as supervised injection sites (1-15%) (93). It is important to consider that the HRCS samples from participants accessing harm reduction supply distribution sites; therefore, it is expected that a higher percentage of our sample would have access to harm reduction services, compared to the broader population of people who use drugs (PWUD) across British Columbia and Canada.

Many participants did not indicate a response to the drug use variables that were measured in the survey. There was a large range, from 4.6% not indicating a response to the question about OAT medication prescription in the past 6 months to 71.6% not indicating a response to the oxycodone use question in the past 3 days. Since missing values included a large proportion of participants, a decision was made to include missing responses as a category in both the bivariate (Chapter 2) and multivariable (Chapter 3) analyses in this thesis. Additionally,

it is possible, due to the formatting of the survey (Appendix A), that many participants did not indicate “no” responses and instead skipped questions regarding drugs that did not pertain to them. This would have yielded a missing response for those drugs, where in fact the participant may have only used certain drugs on the list and chose to skip providing a response to others, instead of marking a “no” answer. While survey administrations are assisted by volunteers, this is a data collection limitation that may have occurred and potentially impacted our findings. An approach that we used to account for this was grouping the smaller drug groups into larger umbrella groups, including prescription opioids, heroin and/or fentanyl, all opioids, all benzodiazepines and all stimulants. As presented in Table 2.2, the number of missing responses was much lower within the larger umbrella groups, as it was more likely that a participant would have indicated a “yes” or “no” response to at least one of the drugs. While we cannot definitively confirm that these individuals may have skipped responses to some questions and only indicated “yes” to the ones they were using, to minimize the number of missing responses in the multivariable analyses, only the larger umbrella drug groups were included in our model (Chapter 3). Additional information regarding statistical limitations and considerations may be found in Chapter 4.3.3.

Our findings have several other strengths and limitations. Since all measures in the survey are self-reported, this may introduce reporting bias due to social desirability and recall inaccuracy. Recall bias is particularly an issue with the more long-term questions surrounding the past 6 months, while it is unlikely to be an issue with the past 3-day drug use variables; however, reporting bias may still be an issue, given the sensitive nature of the questions and the stigma associated with substance use. We tried to minimize the effects of reporting and recall bias, by including individuals who did not respond to questions or indicated they preferred not to

respond in our analyses. Additionally, since the survey was conducted at harm reduction sites, it is possible that participants felt more comfortable within the community-level environment, which can help reduce chances of bias. The convenience method of sampling overrepresented individuals with access to harm reduction supply distribution services in the province, which is not necessarily generalizable to all people who use drugs or are prescribed OAT across BC. Additionally, given our inclusion criteria, many individuals were excluded from the final analytical sample, which led to a very low sample size for some of the variables; because of this, larger umbrella drug groups were included for the multivariable analysis (Chapter 3) to maximize statistical power. Additionally, we have provided a quantitative approach to describing the participants in our sample, while many questions around substance use and accessibility to addiction services may be better resolved through qualitative approaches. The strength of our analysis is that we provided an overview of all substances used within our sample, and we highlighted the lack of difference in active substance use, despite engagement in OAT, which has important implications in ensuring continuous access to harm reduction measures for individuals in treatment.

To conclude, this chapter highlighted prevalent substance use among individuals who continued or discontinued OAT in BC. Our findings highlighted the need for continuous harm reduction interventions for individuals that are both continuing and discontinuing OAT to help mitigate the harms associated with various types of substance use. Patient-centered, safe, and supportive treatment and harm reduction programs that provide stable resources for individuals who use substances can promote access to health services, alleviate risks and cultivate positive connections among peers and communities. Chapter 3 will add to our current findings by

modelling covariates of OAT discontinuation through a multivariable logistic regression approach.

Chapter 3: Correlates of OAT Discontinuation Among HRCS Participants

3.1 Introduction

OAT discontinuation rates have been high over the past years across BC. A cohort of 55,470 individuals in BC, diagnosed with opioid use disorder, identified only 33% who were engaged in OAT as of 2017, even though 71% had previously received treatment, and only 16% were retained in treatment for at least 1 year (11). Another study of 37,207 individuals in BC, diagnosed with opioid use disorder, found monthly discontinuation rates of 10.6% to 14.9% from 2012-2018, with discontinuation rates for buprenorphine/naloxone being almost double (21.2%) that of methadone (10.0%) (10). In our HRCS sample, 85 of 194 (43.8%) participants who had reported receiving OAT in the past 6 months reported having discontinued OAT in the past 6 months. This rate was highest among those having received buprenorphine/naloxone (58.3%), followed by 45.7% among those receiving methadone and 19.4% among those receiving other OAT medications, including slow-release oral morphine and hydromorphone (Table 2.2).

OAT discontinuation has been associated with an increased risk of overdose mortality (8). In a recent population-based study from Ontario, Canada, OAT discontinuation rates following the COVID-19 pandemic were assessed (94). Weekly prevalence of OAT discontinuation ranged from 0.6-1.1% among those stable (>60 continuous days on treatment) and 7.3-16.6% among those not stable on treatment. Mortality rate in this study was 1.4% among those discontinuing methadone and 0.8% among those discontinuing buprenorphine/naloxone, considering deaths within 30 days of discontinuation (94). In our sample, 22.2% (n=43) indicated having experienced an overdose in the past 6 months, of whom 67.4% had indicated discontinuing OAT, compared 35.9% of those who had not indicated experiencing an overdose in the past 6 months (73.2%, n=142) discontinuing treatment (Table 2.3).

Our sample consists of individuals who received OAT in the past 6 months, but are also accessing harm reduction supply distribution sites, indicating possible continued use of illicit substances while in treatment. In Chapter 2, we identified variables that were associated with OAT discontinuation, through bivariate Chi-squared or Fisher's Exact tests (where appropriate). Variables that were identified as significantly associated with OAT discontinuation included having experienced an overdose and having accessed an overdose prevention site in the past 6 months (Table 2.3). Variables that were identified as possibly protective against OAT discontinuation included being of age ≥50 years, having indicated methadone use and other prescription opioid use combined within the past 3 days, and having received slow-release oral morphine as an OAT medication within the past 6 months. Discontinuation was also lower among those with a missing response to use of heroin, fentanyl, and heroin and/or fentanyl use variables combined (Table 2.2). However, these analyses only consider bivariate associations and thus do not control for possible confounding relationships among variables.

This chapter aims to build on the descriptive results reported in Chapter 2, by providing a comprehensive understanding of the correlates associated with OAT discontinuation through a multivariable logistic regression model (57,58).

3.2 Methods

3.2.1 Primary outcome variable

The outcome variable (OAT) discontinuation was taken from the HRCS survey (Appendix A), as described in Chapter 2.2.1. Analyses of the OAT discontinuation outcome were restricted to the 194 participants who indicated a yes or no response to the OAT discontinuation question (Figure 2.1). In this chapter, for the purposes of the multivariable model, the outcome was coded as 1=yes to OAT discontinuation and 0=no to OAT discontinuation. Although OAT discontinuation

was selected as the outcome variable in the model, we recognize that due to the nature of some of the variables, the temporality of the associations (cause vs effect) cannot be determined. Hence, the conclusions and inferences made in this chapter are based only on whether associations exist between variables, not the direction of these associations.

3.2.2 Explanatory variables

This chapter assesses OAT discontinuation, through a multivariable logistic regression model. Since our aim is to characterize OAT discontinuation by identifying the correlates associated with the outcome, we do not focus on any single explanatory variable as the primary variable of interest.

3.2.3 Potential covariates of interest

Covariates were selected for our modeling, using a combination of literature support and the descriptive data from Chapter 2.3. Variables were categorized into 5 groups to allow for an organized stepwise approach to model building.

3.2.3.1 Demographics

The demographic variables tested in the model included age, gender, and self-reported indigenous identity.

a) Age: The age variable was categorized into five groups: 19-29, 30-39, 40-49, ≥50, unknown. The unknown group consisted of individuals who did not report their age in the survey. The youngest age group (19-29) was set as the reference for both the bivariate and multivariable regression models.
b) Gender: Self-reported gender included cis woman, cis man, transgender and gender expansive, and unknown. The unknown group consisted of individuals who did not respond to the gender identity question in the survey (Question 1, Appendix A). The cis

man category was set as the reference for both bivariate and multivariable regression models.

c) Self-reported indigenous identity: Self-reported indigenous identity included 3 categories: indigenous, non-indigenous, unknown. The indigenous category consisted of all individuals who identified as First Nations or Metis in the survey. Non-indigenous included individuals who responded "no" to identifying as indigenous (Question 3, Appendix A). The unknown category included individuals who did not respond to Question 3 of the survey, regarding indigenous identity (Appendix A). The non-indigenous category was set as the reference for both the bivariate and multivariable regression models.

3.2.3.2 Socioeconomic status

The socioeconomic related variables tested in the model included housing and employment status.

a) Housing status: The housing status variable included 2 categories: stably housed, not stably housed. Housing stability was determined in the same manner as described in Chapter 2.2.2. The non-stable housing category was set as the reference for both bivariate and multivariable regression models.

b) Employment status: Employment status included 3 categories: currently employed, currently unemployed, unknown. The currently employed and unemployed categories were determined in the same manner as Chapter 2.2.2. The 'prefer not to say' and missing categories from Table 2.1 were combined to create the unknown category with a larger sample size for the multivariable model. The unemployed category was set as the reference for both the bivariate and multivariable regression models.

3.2.3.3 Accessibility

Two variables were selected as proxies for accessibility to treatment in the model: urbanicity and regional health authority.

a) Urbanicity: Urbanicity included 3 categories: medium/large, small urban and rural. The categories were determined in the same manner as described in Chapter 2.2.2, based on the location the participants were taking the survey. The rural category was set as the reference for both the bivariate and multivariable regression models.
b) Health authority: Health authority included 5 categories: Fraser Health, Interior Health, Island Health, Northern Health, and Vancouver Coastal Health. The categories were determined in the same manner as described in Chapter 2.2.2. The Fraser Health category was set as the reference for both the bivariate and multivariable regression models.

3.2.3.4 Drug use

Four variables were included to assess past 3-day drug use in the sample: heroin and/or fentanyl, stimulants, cannabis, and alcohol.

a) Heroin and/or fentanyl: Past 3-day heroin and/or fentanyl use was categorized as: yes, no, and unknown. The categories were determined in the same manner as described in Chapter 2.2.2, where the yes category included anyone who indicated using heroin and/or fentanyl, the no category included anyone who indicated not using either heroin nor fentanyl, and the unknown category included anyone who did not respond yes to either heroin or fentanyl and did not indicate no to both drugs either. Heroin and fentanyl use were combined as a variable, based on knowledge that most street drugs available as heroin contain a high percentage of fentanyl, therefore it is difficult to ensure heroin use alone among the sample. Additionally, the distribution of both heroin and fentanyl drug

use (Table 2.2) was similar, allowing the two to be combined, with minimal effects on analyses. The no category was set as the reference for both the bivariate and multivariable regression models.

b) Stimulants: Past 3-day stimulant use was categorized as: crystal meth, other (crack, cocaine, MDMA, Ritalin/Adderall), no, and unknown. The categories were determined using results from Table 2.2. Crystal meth included any individual who responded yes to using crystal methamphetamines in the past 3 days. The other category included any individuals who responded yes to any other stimulant drug. Drugs other than crystal meth were combined in the other category, due to similarities in their distribution from Table 2.2. Sensitivity analyses confirmed that combining the drugs or testing them as individual levels did not affect the results of either the bivariate or the multivariable models, therefore categories were combined to increase sample size for analysis. The no category included individuals who responded no to all stimulant drugs. The unknown category included individuals who did not respond yes to any stimulant drug and did not respond no to all of them. The no category was set as the reference for both the bivariate and multivariable regression models.

c) Cannabis: Past 3-day cannabis use was categorized as: yes, no, and unknown. The categories were determined in the same manner as described in Chapter 2.2.2. The unknown group included individuals who did not respond yes or no to cannabis use in the past 3 days. The no category was set as the reference for both the bivariate and multivariable regression models.

d) Alcohol: Past 3-day alcohol use was categorized as: yes, no, and unknown. The categories were determined in the same manner as described in Chapter 2.2.2. The

unknown group included individuals who did not respond yes or no to alcohol use in the past 3 days. The no category was set as the reference for both the bivariate and multivariable regression models.

3.2.3.5 Harm reduction

The harm reduction related variables to be tested in the model included preferred mode of drug use, using drugs alone, history of opioid or stimulant overdose, owning a naloxone kit, frequency of obtaining harm reduction supplies, and using an OPS/SCS site.

a) Preferred mode of drug use: Preferred mode of drug use was categorized as: smoking/inhalation, injection, other. Variable categories were determined in the same manner as in Chapter 2.2.2. The other level combined those who preferred not to answer, missing responses, and those who did not choose injection or smoking/inhalation as their preferred mode of substance use, to increase sample size. Sensitivity analyses confirmed no difference in final model outcome, from this combination of variable levels, compared to keeping the unknown category separate. The smoking/inhalation category was set as the reference for both the bivariate and multivariable regression models.

b) Drug use alone: Drug use alone was categorized as: yes, no, and unknown. The categorization was in the same manner as described in Chapter 2.2.2. The yes category included anyone who responded using drugs alone occasionally, often, or always (Question 17, Appendix A). The no category included individuals who responded never to the same question. The unknown category included individuals who preferred not to answer or were missing responses to the question. The no category was set as the reference for both the bivariate and multivariable regression models.

c) History of overdose: History of opioid and/or stimulant overdose in the past 6 months was categorized as: yes, no, and unknown. The yes category combined individuals who responded yes to having overdosed on stimulants, opioids, or both (Table 2.3). The no category included individuals who responded no to both stimulant overdose (Question 19) and opioid overdose (Question 20) (Appendix A). The unknown category combined prefer not to say, don't know and missing categories (Table 2.3). The decision to combine various levels based on the results from Table 2.3 was made to increase sample size, ensuring the categories that were combined had similar distribution and would not affect the results of the analyses. The no overdose category was set as the reference for both the bivariate and multivariable regression models.

d) Owning a naloxone kit: Owning a naloxone kit was categorized as: yes, no, and unknown. The categorization was in the same manner as described in Chapter 2.2.2, except the unknown category combined prefer not to say and missing categories from Table 2.3 (Question 24, Appendix A), to increase sample size. The no category was set as the reference for both the bivariate and multivariable regression models.

e) Frequency of obtaining harm reduction supplies: Frequency of obtaining harm reduction supplies in the past 6 months was categorized as: frequent and occasional/never. The categorization was in the same manner as described in Chapter 2.2.2; however, the 1 individual who indicated prefer not to respond (Question 26, Appendix A) was combined with the occasional/never group to increase sample size for analyses. The occasional/never category was set as the reference for both the bivariate and multivariable regression models.

f) Overdose Prevention Service (OPS)/Supervised Consumption Site (SCS) use: Use of an OPS/SCS in the past 6 months was categorized as: yes and no. The categorization was in the same manner as described in Chapter 2.2.2; however, the 2 individuals who were missing responses (Question 31, Appendix A) were combined with the no group to increase sample size for analyses. Since one of these individuals was in the continued, and the other in the discontinued outcome levels, this combination of variable levels did not impact findings. The no category was set as the reference for both the bivariate and multivariable regression models.

Figure 3.1 shows a concept map of the variables that were tested in the bivariate and multivariable regression models, within their respective categories.

3.2.4 Statistical Analysis

A concept map (Figure 3.1) was developed, using existing literature, to assess variables for inclusion in the multivariable model. Links between variables were informed by a literature review (Chapter 1). The relevant categories of variables included in the concept map have been previously described in Section 3.2.3 of this chapter. Bivariate regression models were used to examine associations between multiple variables and the outcome. I expected results from the bivariate regression to be different from the results of the Chi-squared tests in Chapter 2, since some variable categories were combined, and the reference category may have changed for the multivariable analysis in Chapter 3. In cases where the variables had the same categories as the descriptive statistics, then the bivariate and Chi-squared test results were the same. Stepwise model selection was used to determine the model with the best fit, as indicated by the lowest Akaike Information Criterion (AIC) (95). The order the blocks and variables were added to the model were switched around to confirm no effect on final model outcomes. Certain variables

were considered conceptually relevant regardless of their statistical significance (i.e., gender, housing status, urbanicity, stimulant use, alcohol use) and were retained in the multivariable model regardless of AIC. Sensitivity analyses were conducted to ensure this forcing of variables did not affect the conclusions of the model. The explanatory merit of the model at each stage was estimated using McFadden's likelihood ratio R^2 (96). Model fit was compared using Likelihood Ratio Test (LRT), with each model being compared to the previous model, nested within; the first model (demographics block) was compared to a null model (97). LRT was not used as a measure to include or exclude variables, but rather as an informative measure to compare models, to assess how the model would change with the addition of each block of variables. Odds ratios (OR), adjusted odds ratios (AOR) and 95% confidence intervals (CI) were presented. All data manipulation and statistical analyses were conducted in R version 4.1.2 (2021-11-01).

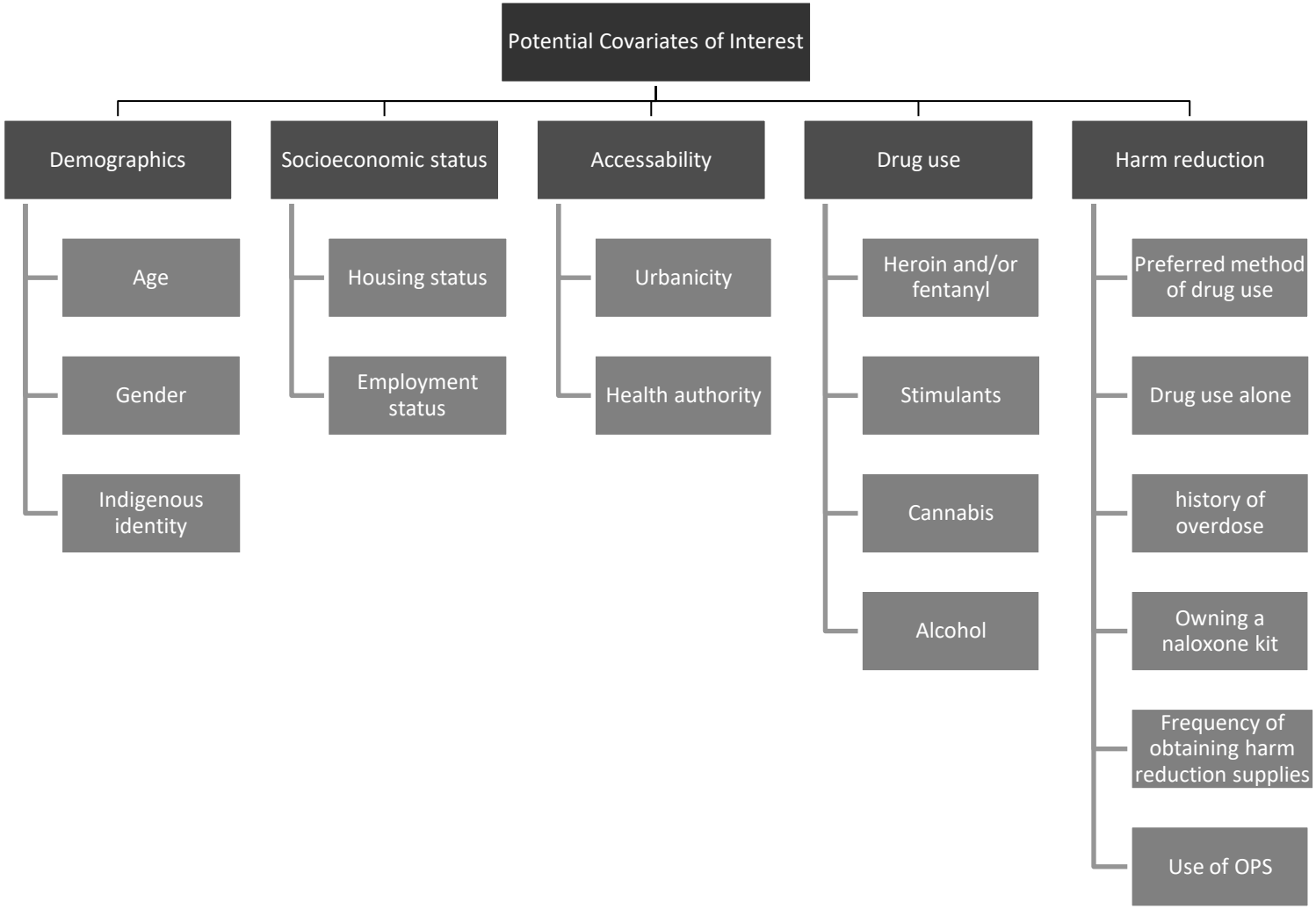

Figure 3.1 Concept map of variables tested in the bivariate and multivariable models.

3.3 Results

Table 3.1 describes the distribution and unadjusted odds ratios of variables that were tested for inclusion in the multivariable model based on the concept map shown in Figure 3.1. Bivariate logistic regression identified that being ≥50 years old (compared to 19-29 years old) was associated with lower odds of having discontinued OAT in the past 6 months ($p<0.01$). Additionally, having experienced an opioid and/or stimulant overdose in the past 6 months (compared to not having experienced an overdose) ($p<0.001$), and having used OPS/SCS in the past 6 months (compared to not having used OPS/SCS) ($p<0.01$), was associated with greater odds of having discontinued OAT in the past 6 months.

Table 3.2 shows the multivariable model results, following the addition of each block of variables to the model. AOR, McFadden's Pseudo-R^2 and changes in Pseudo-R^2 values following the addition of each block of variables are presented to better understand the effects of the addition of each variable block to the model. The final column (highlighted grey) shows the final included model, while the first column shows bivariate results and unadjusted OR values for comparison. After adjusting for other variables, the multivariable model revealed a positive association between having experienced an opioid and/or stimulant overdose in the past 6 months (relative to not having experienced an overdose) and OAT discontinuation (AOR=3.77, 95% CI (1.57-9.03)). Being aged ≥50 years (relative to 19-29 years old) was negatively associated with OAT discontinuation, after adjusting for other variables (AOR=0.12, 95% CI (0.03-0.45)). Additionally, having taken the survey in a medium/large urban area (relative to a rural community) was also negatively associated with OAT discontinuation, after adjusting for other variables (AOT=0.27, 95% CI (0.07-0.98)). The final adjusted multivariable model (Table 3.2) had a McFadden Psuedo-R^2 value of 0.20, indicating moderate explanatory power (96).

The sensitivity analysis (Appendix C.1) confirms the robustness of the model despite forcing certain variables (i.e., gender, stable housing, urbanicity, past 3-day stimulant and alcohol use). In our sensitivity analysis, the stepwise model selection process using AIC arrived at a best-fit model that included age, past 3-day heroin and/or fentanyl use, history of opioid and/or stimulant overdose and use of OPS in the past 6 months. Compared to the final model shown in Table 3.2, Table C.1 confirms that both age and history of heroin and/or stimulant overdose in the past 6 months remain significantly associated with the outcome, despite forcing in additional variables. The analysis also confirms that the additional variables that were included in the model help increase the explained variability by the model (higher McFadden R^2), in addition to the models not being significantly different from one another (LRT not significant). Therefore, the additional variables were included in the final model to help explain additional variability, in addition to the variables being conceptually important based on prior literature review. Additional sensitivity analyses may be found in other sections of Appendix C. These additional analyses confirm that the modeling outcome remains qualitatively the same as the final model shown in Table 3.2.

Table 3.1 Estimated distributions and unadjusted odds ratios (OR) for potential correlates of OAT discontinuation among HRCS participants, for further testing in the multivariable model.

	OAT Status				
	Continued n (%)[C]	**Discontinued n (%)[C]**	**Total n (%)[D]**	**Simple Bivariate OR (95% CI)**	***P*-value[A]**
Demographic Characteristics					
Age (years)					
19-29	17 (48.6%)	18 (51.4%)	35 (18.0%)	---	---
30-39	33 (44.6%)	41 (55.4%)	74 (38.1%)	1.17 (0.52,2.63)	0.70
40-49	23 (57.5%)	17 (42.5%)	40 (20.6%)	0.70 (0.28,1.74)	0.44
≥50	34 (82.9%)	7 (17.1%)	41 (21.1%)	0.19 (0.07,0.56)	**<0.01****
Unknown	2 (50.0%)	2 (50.0%)	4 (2.1%)	0.94 (0.12,7.48)	0.96
Gender					
Cis man	67 (57.8%)	49 (42.2%)	116 (59.8%)	---	---
Cis woman	38 (53.5%)	33 (46.5%)	71 (36.6%)	1.19 (0.66,2.15)	0.57
Transgender and gender expansive	1 (33.3%)	2 (66.7%)	3 (1.5%)	2.73 (0.24,31.02)	0.42
Unknown	3 (75.0%)	1 (25.0%)	4 (2.1%)	0.46 (0.05,4.51)	0.50
Self-reported indigenous identity					
Indigenous	39 (53.4%)	34 (46.6%)	73 (37.6%)	1.12 (0.62,2.03)	0.71
Non-Indigenous	63 (56.2%)	49 (43.8%)	112 (57.7%)	---	---
Unknown	7 (77.8%)	2 (22.2%)	9 (4.6%)	0.37 (0.07,1.85)	0.22
Socioeconomic Characteristics					
Stable housing					
Yes	82 (60.3%)	54 (39.7%)	136 (70.1%)	0.57 (0.31,1.07)	0.08
No	27 (46.6%)	31 (53.4%)	48 (29.9%)	---	---
Currently Employed					
Yes	33 (63.5%)	19 (36.5%)	52 (26.8%)	0.67 (0.35,1.29)	0.23
No	73 (53.7%)	63 (46.3%)	136 (70.1%)	---	---
Unknown	3 (50.0%)	3 (50.0%)	6 (3.1%)	1.16 (0.23,5.95)	0.86
Accessibility Characteristics					

Urbanicity					
Medium/large urban	80 (58.4%)	57 (41.6%)	137 (70.6%)	0.58 (0.23,1.50)	0.26
Small urban	20 (54.1%)	17 (45.9%)	37 (19.1%)	0.70 (0.23,2.07)	0.52
Rural	9 (45.0%)	11 (55.0%)	20 (10.3%)	---	---
Health authority					
Fraser Health	28 (57.1%)	21 (42.9%)	49 (25.3%)	---	---
Interior Health	25 (58.1%)	18 (41.9%)	43 (22.2%)	0.96 (0.42,2.20)	0.92
Island Health	16 (53.3%)	14 (46.7%)	30 (15.5%)	1.17 (0.47,2.91)	0.74
Northern Health	13 (56.5%)	10 (43.5%)	23 (11.9%)	1.03 (0.38,2.79)	0.96
Vancouver Coastal Health	27 (55.1%)	22 (44.9%)	49 (25.3%)	1.09 (0.49,2.41)	0.84
Past 3-Day Drug Use					
Heroin and/or fentanyl					
Yes	67 (48.6%)	71 (51.4%)	138 (71.1%)	2.12 (0.38,11.95)	0.39
No	4 (66.7%)	2 (33.3%)	6 (3.1%)	---	---
Unknown	38 (76.0%)	12 (24.0%)	50 (25.8%)	0.63 (0.10,3.89)	0.62
Stimulants					
Crystal Meth	69 (51.1%)	66 (48.9%)	135 (69.6%)	4.78 (0.54,42.03)	0.16
Other (crack, cocaine, MDMA, etc.)	13 (72.2%)	5 (27.8%)	18 (9.3%)	1.92 (0.18,20.82)	0.59
No	5 (83.3%)	1 (16.7%)	6 (3.1%)	---	---
Unknown	22 (62.9%)	13 (37.1%)	35 (18.0%)	2.95 (0.31,28.14)	0.35
Alcohol					
Yes	31 (52.5%)	28 (47.5%)	59 (30.4%)	1.41 (0.63,3.17)	0.40
No	25 (61.0%)	16 (39.0%)	41 (21.1%)	---	---
Unknown	53 (56.4%)	41 (43.6%)	94 (48.5%)	1.21 (0.57,2.55)	0.62
Cannabis					
Yes	53 (51.0%)	51 (49.0%)	04 (53.6%)	1.92 (0.76,4.89)	0.17
No	16 (66.7%)	8 (33.3%)	24 (12.4%)	---	---
Unknown	40 (60.6%)	26 (39.4%)	66 (34.0%)	1.30 (0.49,3.47)	0.11
Harm Reduction Characteristics					
Opioid and/or stimulant overdose in past 6 months					
Yes	14 (32.6%)	29 (67.4%)	43 (22.2%)	3.70 (1.79,7.62)	**<0.001*** **
No	91 (64.1%)	51 (35.9%)	142 (73.2%)	---	---

Unknown	4 (44.4%)	5 (55.6%)	9 (4.6%)	2.23 (0.57,8.68)	0.25
OPS use in past 6 months					
Yes	38 (45.2%)	46 (54.8%)	84 (43.3%)	2.20 (1.23,3.94)	**0.01****
No	71 (64.5%)	39 (35.5%)	110 (56.7%)	---	---
Preferred mode of drug use					
Smoking/inhalation	67 (55.4%)	54 (44.6%)	121 (62.4%)	---	---
Injection	35 (56.5%)	27 (43.5%)	62 (32.0%)	0.96 (0.52,1.77)	0.89
Other	7 (63.6%)	4 (36.4%)	11 (5.7%)	0.71 (0.20,2.55)	0.60
Drug use alone					
Yes	89 (54.3%)	75 (45.7%)	164 (84.5%)	2.00 (0.83,4.83)	0.12
No	19 (70.4%)	8 (29.6%)	27 (13.9%)	---	---
Unknown	1 (33.3%)	2 (66.7%)	3 (1.5%)	4.75 (0.38,60.14)	0.23
Owning a naloxone kit					
Yes	84 (57.1%)	63 (42.9%)	147 (75.8%)	0.86 (0.44,1.71)	0.67
No	23 (53.5%)	20 (46.5%)	43 (22.2%)	---	---
Unknown	2 (50.0%)	2 (50.0%)	4 (2.1%)	1.15 (0.15,8.93)	0.89
Frequency of obtaining supplies in past 6 months					
Frequent	56 (50.5%)	55 (49.5%)	111 (57.2%)	1.74 (0.97,3.11)	0.06
Occasional/never	53 (63.9%)	30 (36.1%)	83 (42.8%)	---	---

Reference categories are denoted by "---"

[A]*p<0.05, **p<0.01, ***p<0.001

[B]Self-reported indigenous identity included individuals who identified as First Nations and/or Metis.

[C]Indicates row percentages.

[D]Indicates column percentages.

Table 3.2 Estimated unadjusted odds ratios (OR) and adjusted odds ratios (AOR) for correlates of OAT discontinuation among HRCS participants as determined by logistic regression.

	OAT Discontinuation[a]					
	Simple Bivariate OR (95% CI)	Block 1 (Demographics) AOR (95% CI)	Block 2 (Socioeconomic) AOR (95% CI)	Block 3 (Accessibility) AOR (95% CI)	Block 4 (Drug Use) AOR (95% CI)	Block 5 (Harm Reduction) AOR (95% CI)[b]
Demographic Characteristics						
Age (years)						
19-29	---	---	---	---	---	---
30-39	1.17 (0.52,2.63)	1.13 (0.51,2.55)	1.14 (0.51,2.57)	1.12 (0.48,2.54)	1.28 (0.52,3.16)	1.02 (0.39,2.68)
40-49	0.70 (0.28,1.74)	0.71 (0.28,1.89)	0.74 (0.29,1.87)	0.72 (0.28,1.84)	0.82 (0.30,2.21)	0.56 (0.19,1.65)
≥50	**0.19 (0.07,0.56)****	**0.19 (0.06,0.54)****	**0.20 (0.07,0.59)****	**0.18 (0.06,0.55)****	**0.18 (0.05,0.58)****	**0.12 (0.03,0.45)****
Unknown	0.94 (0.12,7.48)	1.14 (0.13,9.99)	1.29 (0.15,11.42)	1.30 (0.15,11.49)	1.17 (0.12,11.59)	0.97 (0.10,9.72)
Gender						
Cis man	---	---	---	---	---	---
Cis woman	1.19 (0.66,2.15)	0.92 (0.49,1.74)	0.94 (0.50,1.78)	0.92 (0.49,1.74)	0.70 (0.35,1.40)	0.72 (0.35,1.47)
Transgender and gender expansive	2.73 (0.24,31.02)	3.23 (0.22,46.68)	3.66 (0.26,52.43)	2.93 (0.22,38.48)	2.36 (0.18,31.40)	2.80 (0.20,39.29)
Unknown	0.46 (0.05,4.51)	0.47 (0.04,5.60)	0.52 (0.04,6.19)	0.56 (0.05,6.81)	0.84 (0.06,11.59)	1.25 (0.09,16.87)
Socioeconomic Characteristics						
Stable housing						
Yes	0.57 (0.31,1.07)		0.67 (0.35,1.29)	0.69 (0.35,1.32)	0.86 (0.42,1.76)	1.08 (0.49,2.36)
No	---		---	---	---	---
Accessibility Characteristics						
Urbanicity						
Medium/large urban	0.58 (0.23,1.50)			0.51 (0.18,1.42)	**0.24 (0.07,0.84)***	**0.27 (0.07,0.98)***
Small urban	0.70 (0.23,2.07)			0.61 (0.18,2.03)	0.35 (0.08,1.45)	0.42 (0.09,1.91)
Rural	---			---	---	---
Past 3-Day Drug Use						
Heroin and/or fentanyl						
Yes	2.12 (0.38,11.95)				0.58 (0.07,4.89)	0.59 (0.05,6.63)
No	---				---	---

Unknown	0.63 (0.10,3.89)				0.12 (0.01,1.30)	0.16 (0.01,2.17)
Stimulants						
Crystal Meth	4.78 (0.54,42.03)				5.81 (0.50,67.80)	8.05 (0.52,124.60)
Other (crack, cocaine, etc.)	1.92 (0.18,20.82)				3.09 (0.23,42.25)	5.52 (0.30,100.58)
No	---				---	---
Unknown	2.95 (0.31,28.14)				7.51 (0.51,109.60)	12.25 (0.64,235.59)
Alcohol						
Yes	1.41 (0.63,3.17)				1.54 (0.57,4.12)	1.45 (0.52,4.02)
No	---				---	---
Unknown	1.21 (0.57,2.55)				1.68 (0.63,4.51)	1.63 (0.58,4.58)
Harm Reduction Characteristics						
Opioid and/or stimulant overdose in past 6 months						
Yes	**3.70 (1.79,7.62)*** **					**3.77 (1.57,9.03)** **
No	---					---
Unknown	2.23 (0.57,8.68)					1.87 (0.42,8.26)
OPS use is past 6 months						
Yes	**2.20 (1.23,3.94)** **					1.80 (0.89,3.65)
No	---					---
McFadden Pseudo-R^2		0.07	0.08	0.09	0.15	0.20
Pseudo-R^2 change[c]		**0.07****	0.01	0.01	**0.06***	**0.05****

Reference categories are denoted by "**---**"

*p<0.05, **p<0.01, ***p<0.001

[a]Final model size N=194

[b] Shows final model

[c]Significant values indicate significance of LRT, comparing each model to the model in the previous column, to assess the effects of adding each block of variables to the model.

3.4 Discussion

This chapter examined the associations between various correlates, chosen based on prior literature support, and OAT discontinuation using multivariable logistic regression modelling. The blocks/categories of variables that were tested included: demographics, socioeconomic status, accessibility, drug use, and harm reduction. Chapter 2 identified several variables that were significantly associated with OAT discontinuation: being aged ≥50 years old, past 3-day methadone use, past 3-day prescription opioid use combined, missing responses to past 3-day heroin use, missing responses to past 3-day fentanyl use, missing responses to past 3-day heroin and/or fentanyl use combined, OAT medication prescribed in the past 6 months, experience of overdose in the past 6 months, and use of OPS/SCS in the past 6 months. This chapter further examined the associations between conceptually relevant variables and OAT discontinuation. The use of a multivariable model allowed assessment of the independent effects of each variable, while accounting for the simultaneous impacts of other potentially confounding variables. The findings suggest a need towards targeting individuals with prior experiences of overdose, those who are younger and living in rural communities, allowing for OAT services that meet unique needs of these individuals to allow for continuation of treatment, through equitable access.

Multivariable analyses showed that being older (≥50 years old), compared to 19-29 years of age was associated with lower odd of OAT discontinuation in the past 6 months. These findings were consistent with those shown in Chapter 2 (Table 2.1). A systematic review of randomized clinical trials and observational cohort studies reporting on retention rates found that older age was generally associated with increased retention in OAT, though the results were heterogenous across studies (98). A study in the United States found that retention rates were generally low among adolescents (mean age 19.2), who were enrolled in

buprenorphine/naloxone treatment, with about 45% retaining at 60 days and only 9% retaining at 1 year follow-up (99). Another study in the United States also supported those emerging adults (18-25 years old) are often poorly retained in substance use disorder treatment, and compared to older adults, retention in treatment was significantly lower at 3 months (56%) and 12 months (17%). Younger adults were also significantly more likely to test positive for illicit opioids, relapse and have lower treatment retention, compared to older adults (100). A study assessing adherence to medication for opioid use disorder among adolescents found that younger age was consistently associated with shorter retention, particularly among those with concurrent substance use, family conflict and lower flexibility in dosage and regimen of the treatment being delivered (101).

The multivariable analysis also revealed an association between living in medium/large urban areas (compared to rural communities) and lower odds of OAT discontinuation in the past 6 months. These findings were not seen in Chapter 2 (Table 2.1) and only appears after controlling for other variables with our model, specifically, upon the addition of the drug use block (Table 3.2). It may be that drug use characteristics tend to confound and mask the true effects of urbanicity on OAT discontinuation; once these variables are controlled for in our model, the true relationship between urbanicity and OAT discontinuation can be seen. Assuming the location where the participant took the survey is a proxy for where they live, this finding is consistent with other studies, which show that living in remote and rural communities is often associated with lower accessibility to treatment services (13). Accessibility barriers to healthcare in rural communities of Canada has been an ongoing issue (102). While around 18% of Canadians live in rural communities, only 8% of physicians practice in these communities, which significantly affects access to healthcare and exacerbates poorer health outcomes in these

communities (103). A study from 2018 in rural Southwestern Ontario assessed the perceived barriers and facilitators to providing methadone maintenance treatment (104). The main identified barriers were increased workload and extended operating hours due to shortage of staff within the community, including pharmacists and physician prescribers. Additionally, slower emergency-response rates within rural communities were expressed as a concern for safety for those who use opioids and other substances, where they might be at a greater risk of fatal overdose (104).

Another association in the multivariable model was increased odds of OAT discontinuation associated with experiences of opioid and/or stimulant overdose (compared no experience of overdose) in the past 6 months; however, the order of association between these two variables is not clear, since the survey variables were measured cross-sectionally and both OAT discontinuation and experiences of overdose variables were inquired about within the past 6 months. These findings were consistent with those shown in Chapter 2 (Table 2.1) and continued to hold after adjusting for other variables in the model. A previous Australian cohort study from 2001-2020 found that OAT provision reduced overdose by 52.8%, and approximately 1.2 deaths averted, and 9.7 life-years gained per 100 person-years on OAT (105). A recent review of literature also suggested that multiple randomized controlled trials of both buprenorphine and methadone maintenance therapy have shown decreased illicit opioid use and mortality, with discontinuation of OAT being associated with increased rates of relapse and mortality (106). Although our results are consistent with these findings and continuing on OAT is safer in terms of overdose than discontinuing, I cannot infer the direction of cause and effects from our analyses. While experience of overdose in the past 6 months was significantly associated with OAT discontinuation in our sample, illicit opioid use (heroin and/or fentanyl) in

past 3 days was the same among those who continued and discontinued on OAT, both in the bivariate and multivariable analyses. This is expected, since our sample was obtained from individuals accessing harm reduction supply distribution sites, which suggests these individuals are likely actively using substances, while engaged in treatment. While the general population of individuals who access OAT may be more likely to reduce illicit opioid use while in treatment, persistent illicit substance use within our sample supports the necessity for continued access to harm reduction supplies and services, among those in treatment, to ensure reduced risks of overdose and safer consumption of substances with reduced harms.

Understanding the dimensions of access to addiction care can be crucial in successfully engaging and retaining individuals in opioid agonist therapy, delivering adequate primary care, and achieving better health outcomes. As previously described in Chapter 1.2 (Figure 1.1, Table 1.1), according to Levesque et al.'s (2013) framework, access may be broken down to five dimensions from the perspective of individuals who are seeking care (22). Understanding access to addiction care both from the perspective of the health services being provided and the ability of individuals to interact with such services (22), can help delineate the ways in which individual barriers can function as barriers to health services access, and help with understanding how to best approach individualizing health service provision to more vulnerable populations. For example, for individuals seeking care in rural communities, multiple factors may increase barriers to care, including limited access to physicians who prescribe OAT, medications requiring daily observations at pharmacies and increased travel distance to obtain such medications, which for many individuals may also interfere with regular employment hours. Since this survey was conducted prior to the COVID-19 pandemic, many patients had to travel for in-person care visits and take-home safe supply OAT medications were not yet available. For

approachability, individuals who are experiencing homelessness or housing instability with frequent moving may find it challenging to identify addiction services, and individuals often rely on limited outreach services or services provided through shelter and temporary housing facilities (107). One issue is that many of these facilities are not available at times when individuals need them, preventing continuous access to care when necessary. While stable housing was not associated with OAT discontinuation in our sample, it is important to consider the uniqueness of our sample, in terms of access to ham reduction supply distribution facilities. It is likely that those within our sample were more connected to housing and harm reduction services then the general population of individuals who access addiction care, since housing instability was lower in our sample (29.9%) compared to 67.7% of individuals who reported addiction or substance use across Canada (108). For acceptability of services, social and cultural barriers limit the care available to individuals who use substances, as they are often marginalized and face a variety of stigma and discrimination based on their housing status, ethnicity, gender and other comorbidities. These negative experiences with healthcare systems may deter individuals from seeking care (24–26,28), and understanding such disparities in healthcare delivery are necessary to address OAT discontinuation within communities. Availability and accommodation are important contributors to barriers in accessing timely addiction treatment. The location, hours of operation, wait times, and individual ability to access transportation to such services all determine accessibility to OAT (109). Individuals who use substances may be at a particular disadvantage, especially if they live in rural communities with limited availability of OAT programs (13), and are not able to access services during flexible hours that work with their schedules (22). Additionally, the high range of wait times across Canada (27) makes it difficult for individuals to access treatment when they need it, which can in turn deter the desire to enter

treatment and even exacerbate dropout and discontinuation (28). For affordability, even though Canada operates on a universal healthcare system, where addiction care is government-subsidized, daily living expenses such as food and shelter, may compete with costs of travelling for treatment or even receiving better and more high-quality care, when needed (13,28,29). Finally, when it comes to appropriateness, the ability of patients to engage in healthcare may ultimately determine their likelihood of continuation and retention on OAT. When there is limited communication and knowledge-sharing between the provider and patient, the likelihood of treatment dropout may increase (110). As suggested by the framework in Figure 1.1 and the dimensions of accessibility described in Chapter 1.2, understanding OAT discontinuation requires an in-depth understanding of individual patient accessibility to addiction care and how the various factors associated with OAT discontinuation may be informed by access to care. Addressing OAT discontinuation therefore requires an in-depth evaluation both at a system and individual level.

There are several strengths and limitations to our study in this chapter. Just as with Chapter 2 (Section 2.4), self-reported measures in the survey may introduce reporting bias due to social desirability and recall inaccuracy. Additionally, convenience sampling from harm reduction supply distribution sites may have overrepresented individuals with active substance use while receiving OAT, which is not necessarily generalizable to all people who use drugs across BC. The relatively small sample size (N=194) likely limited statistical power in the multivariable analysis (Table 3.2); however, we demonstrated the robustness of our findings by conducting multiple sensitivity analyses (Appendix C), and the additional variables kept in the model ultimately helped increase the explanatory power. There are other methods of analysis and certain improvements that may be considered in future analyses (these have been described in

Chapter 4.3.3). Despite the limited data, our model and findings are strongly supported by the literature and represent one of the few analyses conducted on a unique sample of individuals accessing harm reduction distribution sites while on OAT. Our findings therefore serve as a contributor for future qualitative and quantitative analyses to better understand individual and systemic contributors to OAT discontinuation among those using substances and accessing harm reduction services in BC.

To conclude, this study added to Chapter 2, by assessing OAT discontinuation through a multivariable logistic regression analysis, among a sample of individuals who use substances and access harm reduction supply distribution sites across BC. The mechanisms by which accessibility to healthcare services may have impacted access to addiction care and ultimately OAT retention was discussed according to the framework laid out in Figure 1.1. Improving OAT retention and lowering dropout and discontinuation rates is therefore dependent on understanding and addressing both unique individual risk factors (such as age, urbanicity and previous experiences of overdose), in addition to system-level risk factors (such as individualization of available treatment for younger populations, increasing availability and accessibility of healthcare services in rural communities, as well as providing adequate supplies and safe consumption space for individuals who continue to use illicit substances with high risk of overdose, while receiving OAT). Additional recommendations and improvements have been discussed in Chapter 4.2.

Chapter 4: Final Discussion, Conclusions and Recommendations

4.1 Summary of Findings

There is limited evidence regarding OAT discontinuation among individuals who use substances in BC, particularly among those who are actively seeking harm reduction services. Majority of studies are often limited to clinical trials of medications or cohorts centered in large urban communities, such as Vancouver's DTES and Victoria. This thesis aimed to fill an important gap in literature by assessing OAT discontinuation among a sample of individuals who use substances across the province of BC but are also actively seeking harm reduction services. The objectives addressed by this work included: characterizing individuals who continued versus discontinued OAT in the past 6 months (Chapter 2), identifying sociodemographic, drug use, accessibility, and harm reduction service correlates of OAT discontinuation among the sample (Chapter 3).

Chapter 2 revealed a high prevalence of substance use among individuals who continued and discontinued on OAT in the past 6 months. Chi-squared or Fisher's exact tests (where appropriate) revealed significant associations between age, past 3-day methadone use, past 3-day prescription opioid use combined, past 3-day fentanyl use, past 3-day heroin use, past 3-day heroin and/or fentanyl use combined, OAT medication prescribed in the past 6 months, experiences of opioid and/or stimulant overdose, and accessing OPS/SCS in the past 6 months with the OAT discontinuation outcome. Our discussion focused on describing the sample, the continued use of illicit substances among those enrolled in OAT, and the significance of continuous access to harm reduction services for those receiving addiction treatment.

Chapter 3 built on Chapter 2 findings by conducting a multivariable block stepwise logistic regression analysis, using OAT discontinuation in the past 6 months as the outcome.

Findings revealed positive associations between younger age, taking the survey in rural communities and past 6-month experiences of opioid and/or stimulant overdose with higher odds of OAT discontinuation. Our discussion was guided by the accessibility framework, laid out in Figure 1.1, where we discussed the importance of individual and system-level understanding of addiction care to address OAT discontinuation in the province.

In this final chapter, I will reflect on our findings, discuss relevant action steps towards providing more equitable and accessible care, and address alternative data collection and analysis methods that may be used to build on our findings.

4.2 Improving Addiction Care and OAT Retention Rates in BC

Improving OAT retention is crucial to improving addiction care outcomes among individuals who use substances. Our study showed that 85 (43.8%) individuals who had received at least one OAT medication had also indicated discontinuing treatment in the past 6 months (Chapter 2.3). We also identified that being younger, taking the survey in a rural community and having had past experiences of opioid and/or stimulant overdose was associated with greater odds of OAT discontinuation in the past 6 months (Chapter 3.3). This section will use findings from the literature to discuss strategies in addressing OAT discontinuation and retention, based on individual-level and system-level risk factors.

4.2.1 Targeting Individuals at Greater Risk of OAT Discontinuation

In our sample, we identified 3 factors that were associated with greater odds of OAT discontinuation: being of younger age, having taken the survey in a rural area, and having experienced opioid and/or stimulant overdose in the past 6 months. In this section, I will address some ways in which we can target some of these risk factors at the individual level to provide more individualized and tailored care to aim for better retention outcomes.

In our study, we found that individuals aged ≥50 years old had 0.12 times the odds of having discontinued OAT in the past 6 months, compared to those aged 19-29 years. In Canada, youth have the highest rate of substance use disorder compared to any other age group (111). Studies have suggested multiple risk factors that could contribute to increased rates of substance use among adolescent individuals, including brain development, peer pressure, living environment and social dynamics at home, as well as not having developed sufficient and healthy coping mechanisms for various emotional stressors (112,113). Age has consistently been associated with retention outcomes in substance use treatment, where low retention rates are often seen among those who are younger (114,115). One of the main issues contributing to low rates of retention among youth receiving addiction treatment, is that oftentimes adults and youth are offered similar treatment regimens (114,115). This approach may be problematic as it ignores the various causes and motivators of substance use, and how these may be different among adolescents and older adults (114,115). For example, many youths may be using substances as a means to cope with mental and physical comorbidities, environmental and social stressors, in addition to early exposure and experimentation with new substances (115).

One of the ways in which programs can begin addressing age-related risk factors of OAT discontinuation include implementing programs that are specific to the needs of youth. Previous studies have identified that cognitive behavioral therapy paired with OAT may help with greater retention in treatment among youth (115). Although provision of psychosocial treatment alongside OAT has been continuously recommended in the Canadian healthcare system, these recommendations are often not carried out, and many individuals do not have access to centers that can provide a combination of psychosocial therapy and medication treatments (9). Youth may also be receiving lower rates of OAT prescriptions in general, compared to adults, due to

lower availability of medication options for younger age groups. A cross-sectional study assessing OAT prescriptions among youth with OUD in the years 2014-2016 across 6 states found that medication-assisted treatment for OUD was generally low among youth, at around 14% for those 16-17 years of age and 39% for those 22-25 years of age (116). Conceptualization and implementation of programs, at least for youth, where they are provided psychosocial support with focus on effective and individualized coping mechanism strategies, in addition to opioid agonist medications with support for other substance use, is an essential action step towards improving OAT retention rates among younger individuals in the province.

Another finding from our study was that having taken the survey in a medium/large urban area was associated with 0.27 times the odds of having discontinued OAT in the past 6 months, compared to those from rural communities. We assumed that the location where the survey was taken was a proxy for the location where the participant is living. In Canada, lack of program funding for addiction treatment services in rural communities has increased inaccessibility and wait times in the region (117). Additionally, living in rural areas is often associated with longer commute times for treatment access, lower number of staff within communities, and concerns regarding stigma, confidentiality, and safety (118,119). These factors combined have contributed to lower accessibility to addiction care and lower retention rates in rural areas (13).

A few studies in Canada have assessed novel approaches to addressing lower accessibility to addiction care in rural communities. A study in Kelowna and Kamloops, BC from 2019, assessed service utilization of two mobile SCS (120). Over 90% of clients reported a positive experience in terms of access to services; however, challenges in terms of hours of operation, continuity and quality of service were identified (120). Another study in Ontario, Canada, from 2018, identified greater engagement of community pharmacists in providing

medication-assisted treatment, such as MMT, as a factor in helping to bridge service gaps and minimize stigmatization associated with attending addiction treatment clinics in rural communities (104). While multiple approaches have been assessed to increase access to care in rural communities, disproportional access to addiction care, particularly OAT, continues to be a problem in these areas. Identifying individuals from rural communities and coordinating among centers and individual staff, to ensure appropriate hours of accessibility to service, may be a beneficial next step towards more equitable and accessible addiction care in the province.

In our study, we also found that individuals with previous experiences of opioid and/or stimulant overdose had 3.77 times the odds of having discontinued OAT in the past 6 months, compared to those who did not have experiences of overdose in the past 6 months. Since our study was cross-sectional and we inquired regarding experiences of overdose and OAT discontinuation in the past 6 months, it is difficult to deduce temporality. For example, it could be the case that individuals with prior experiences of overdose are also more likely to discontinue OAT. This may be more related to the way in which care is delivered to individuals who experience overdose. Oftentimes, patients enter the treatment system after an overdose event, without fully understanding the scope and implications of the care that is available to them. Many patients are brought into the emergency room following an overdose event and immediately provided an antagonist medication, such as naloxone, to counteract the overdose, and from there on, options for follow up care is often limited to buprenorphine/naloxone or the microdosing regimen (31). Other treatment options may require outpatient clinic visits or longer wait times, in which case many patients may need to discontinue treatment without proper follow up care (32). Additionally, OAT discontinuation itself has been associated with greater vulnerability to risk of overdose, as the effects of the opioid agonist medication begin to wear off

and illicit opioid use can increase the risk of fatal and non-fatal overdose (8,10). Additionally, in our sample, many patients were using opioids, while on OAT; in cases where physicians may discontinue OAT if the urinalysis shows other opioid use, this may also increases the risk of an overdose.

A few approaches may be taken to help identify and mitigate the risk of overdose for individuals who are enrolling in OAT and using substances. First, continued access to OPS/SCS, even for individuals who are actively engaged in OAT is necessary. In our sample, we saw a large proportion of individuals who were continuing illicit substance use, while in treatment, including 55.8% indicating past 3-day opioid use and 53.6% indicating past 3-day stimulant use. Those who discontinue treatment may be at an especially increased risk of overdose, which makes access to OPS/SCS critical. A recent study from Ontario, Canada, from 2021, among individuals receiving outpatient methadone agonist therapy identified that individuals with shorter treatment duration, were at a higher risk of experiencing an overdose while receiving treatment (121). This suggests that access to OPS/SCS is particularly important for individuals during their early stages of treatment. Additionally, both emergency physicians and addiction specialists should work more closely with patients (5) to implement a plan that works with their unique circumstances, paying particular attention to individuals who have had a history of overdose, OAT discontinuation, relapse, and risk factors for low retention.

4.2.2 Addressing System and Institutional Barriers to Care

On the system's level, improving transition from different institutions and creating a more coherent system of care can help minimize treatment discontinuation and improve retention rates. For many individuals who use substances, system-level barriers may include unapproachability of programs, due to lack of information, making it difficult for individuals to

perceive the need and how to use the care available to them (22). Additionally, individuals may have trouble navigating multiple systems, especially since the hours of operation and location of programs tend to vary greatly, making it difficult for individuals to get care when needed (22). Lack of coherency among systems of care is another barrier faced by many individuals, particularly in housing and social support programs, where one might find themselves repeating information multiple times, instead of making progress toward improving their outcomes. Language and cultural barriers are also an important contributor to acceptability of services and the ability of individuals to seek the program and care that most benefits them (22). Some individuals who use substances may also experience additional barriers beyond substance use, such as physical and psychological comorbidities and disadvantaged socioeconomic status (17–19,34,35,91). Individuals with comorbidities, such as HIV and HCV, may also face additional stigma when accessing housing and government benefit programs (17–19,34,35,91). Some frameworks that may benefit in addressing some of these barriers include having a client-centered approach, low barrier programs that do not stigmatize or discriminate based on substance use, mental health or physical health status, integration of harm reduction and housing programs within treatment programs, as well as an emphasis on patient choice (122). In our study, we identified previous experiences of overdose as a factor contributing to increased odds of OAT discontinuation, which suggests emergency response teams and hospitals as a potential point of intervention to allow for increased retention rates. Having accessible program options (both inpatient and outpatient), as part of the discharge plan, including connecting patients with social and housing support workers can also aid with patients following through with their treatment plans and increasing retentions rates.

4.2.3 Harm Reduction Programs

Harm reduction is a necessary risk mitigator for harms associated with substance use. As was seen in both Chapters 2 and 3, substance use rates were high in our sample, despite OAT engagement status. This finding supports the necessity for continuous access to harm reduction programs, including take-home naloxone kits, supplies (such as clean syringe needles), and OPS/SCS locations. In our sample, most individuals indicated accessing harm reduction programs, including 76% reporting naloxone kit possession, 57% reporting frequently accessing harm reduction supplies and 43% reporting use of OPS/SCS in the past 6 months (Table 2.3).

Individuals may access harm reduction programs through their housing units; however, not all housing programs provide harm reduction measures, and some require abstinence, which not only takes away individual choice when it comes to substance use, but also takes away access to housing and shelter in this case. It is therefore important to ensure availability of low-barrier housing options for individuals who continue to use substances while in treatment, and for those who have not chosen or have not had the means to enter treatment programs. Additionally, it is necessary for housing programs to offer supervised check-ins and consumption rooms for individuals who use substances, to minimize the risk of overdose, in addition to allowing for non-discriminatory and optional screening methods for substances and helping connect individuals with the appropriate health services when needed (123). Another way to develop and encourage programs that are relevant, helpful, and equitable for individuals who use substances, is to encourage active peer engagement and involvement of community members, people with lived and living experiences alongside professionals, when developing harm reduction strategies and delivering programs within communities (124). Peer-level interventions

can be effective in overcoming stigma within healthcare systems and can help provide safer environments for marginalized populations who use substances (44,45).

In our sample, it is possible that OAT medications may have been used as a harm reduction measure as well. The bivariate analyses showed positive associations between OPS/SCS use and OAT discontinuation in the past 6 months (Table 3.1), suggesting important harm reduction steps taken by individuals to try and reduce risks related to substance use, particularly among those who may not have access to OAT. Considering the substantial number of individuals that reported illicit substance use, while on OAT, it is also possible that OAT medications are being used as a harm reduction measure to reduce craving and withdrawal symptoms, and toxic levels of illicit substance use. This is an important consideration, particularly for practices, where positive urine tests result in discontinuation of OAT by prescribers, in which case the choice of substance use, while using OAT as a harm reduction measure, is taken away.

4.3 Strengths, Limitations, and Statistical Considerations

4.3.1 Strengths

The main strength of this study was its unique sample composition, community-based research design, and large-scale provincial level setting. Our study sampled beyond Vancouver's DTES and assessed OAT discontinuation across all 5 regional health authorities in BC. The survey was developed with extensive collaboration with representative organizations, including FNHA and people with lived and living experiences, through VANDU and PEEP, to ensure culturally safe and relevant questions surrounding substance use, living circumstances and access to services. Since surveys are filled out annually at harm reduction sites within communities, the familiarity of staff and participants with the survey makes for a less stigmatizing/judgmental collaboration

and allows for a stronger rapport to be built among community members. Additionally, this setting could help mitigate reporting bias, particularly for questions that are often underreported due to social desirability, such as substance use behaviors.

The survey questionnaire itself captures great detail regarding participant demographics, socioeconomic status, substance use behaviors and access to harm reduction services and treatment programs. Although the small sample size limited our ability to include all desired variables and relationships in our model, multiple studies have previously been published on the HRCS, which helped inform our methodology and discussion (57,59,67,84,125). Another strength of our study was the application of Levesque et al.'s (2013) concept on access to healthcare services (22) and Rhodes et al.'s (2002) Risk Environment Framework (23), to better understand how inaccessibility may be affecting OAT discontinuation in our sample (Figure 1.1).

Our results concern implications around organizational structures, training of staff, as well as sensitivity and understanding towards more vulnerable populations who may be more likely to discontinue OAT. Through our collaborations with sites across the province, we will be sharing our findings to determine how to best address the needs of clients within each health region. Additionally, our findings can inform policy makers and stakeholders regarding service provision across the province to help maximize engagement within addiction treatment programs; in that regard, our findings are relevant both within the context of monitoring and service provision policy, as well as individual practices of service providers.

Finally, findings from the HRCS are used to inform future surveys, by targeting more relevant areas and questions. Our collaborators at FNHA, VANDU and PEEP also provide input for future surveys based on our findings and provide feedback on survey content development to help us further contextualize and interpret our findings.

4.3.2 Limitations

One of the main limitations of this study was that we could not infer causality or temporality. This limited our interpretation for some of our findings, particularly with regards to prior experiences of overdose and OAT discontinuation; however, our study may also act as a base point for future qualitative studies that stem from the HRCS to better understand the mechanisms and associations between the various variables that we found significant in our study.

Our results are likely not generalizable to all individuals who use substances across BC, as the HRCS conveniently samples from individuals who access harm reduction supply distribution sites. This means that most individuals in our sample are actively using substances, regardless of their engagement in OAT, which is not always the case, as some programs require negative urinalysis checks to allow for treatment continuation (68).

Due to the large array of services and inter-provincial differences in healthcare delivery, the results of this project will only be generalizable to populations who use drugs in BC, as well as other provinces and territories with similar harm reduction and treatment approaches. Of special interest would be to compare our results to other provinces and territories with similar harm reduction and treatment program availabilities to see if there might be difference in terms of both correlates and prevalence of OAT discontinuation across Canada. Certain groups, potentially those with riskier drug use behaviors, who may avoid harm reduction sites, may not have been targeted with our sampling method, and therefore results should be generalized across BC with caution, bearing in mind that groups who do not access the survey sites are likely being excluded from the study. Additionally, since individuals were sampled at harm reduction sites, it is more likely that those with illicit substance use while in treatment were oversampled, and individuals receiving OAT who may not have been using illicit substances were likely excluded

from our sample. It is also important to note that all survey measures used in our analysis are self-reported. In that regard, generalizations should be considered with caution as the measures are not objective in nature. Additionally, there may be context-dependent mediation with our methods of conducting the survey, in that if the survey was conducted in a different context with potentially different research groups or collaborators, our target reach and therefore results may have been different.

4.3.3 Methodology and Statistical Considerations

The power of analysis in our study was limited due to the small sample size; however, we conducted multiple sensitivity analyses to confirm the robustness of our findings and alternated the order in which the variables and blocks were added into the model to confirm it did not impact our results. I also tried to limit the impact of missing data on analysis power, by including individuals with unknown and missing responses in the model, either by combining them with other levels (if statistically supported) or keeping them as a separate level in the model. This approach has been used in publications in the past, where the percentage of missing data is higher than expected (>5-10%) (59). Additionally, missing data was under 5% for all the variables that were significantly associated with the outcome, which makes it unlikely that it would have affected outcomes for those variables, and our findings were supported by other study findings as well (Table 3.1).

Although missing values were included in the analyses, for certain variables, there was an overwhelming number of individuals who did not respond to the question. This was mainly seen for the past 3-day drug use variables. The main issue this caused with our analysis was lower variability, which widened our confidence intervals in the model. Additionally, it is difficult to say whether these individuals chose to solely respond yes to substances they were using and skip

other substances on the list (Question 10, Appendix A), or if they deliberately chose to skip those substances due to greater stigma associated with their use. Since the proportion of unknown and missing data was high across all drug use variables (Table 2.2), it is difficult to determine whether stigma associated with illicit drugs may have been a contributing factor with certainty. Another way I could have dealt with the missing data in the analyses was to exclude them from the multivariable model (67); however, this approach is often used when the percentage of missing data across the sample is low (5-10%) and would have led to a very low sample size in our work. Another approach would be to impute the missing data in our dataset, by assuming the proportion of the levels of each variables remain consistent among the unknown and missing values (126); however, this assumption may cause issues, especially when the missing values are mostly seen in variables associated with high levels of stigma and reporting bias. The presence of missing data in this case provides valuable insight into the methods of data collection used in public health surveys. Although our surveys are assisted by volunteers at the collection sites, future HRCS surveys should attempt to cross-check skipped responses with the client, prior to them leaving the facility if possible. While still allowing the client to skip responses if they choose to do so, double-checking if the questions they left blank were deliberate or not can help with future analyses and interpretations. An alternative method would be to provide a skip option on the survey and volunteers could double check with individuals who did not select the skip option but did not provide an answer either if they meant to skip the question or provide an alternative response. These recommendations would ideally help create a dataset with fewer unknown and missing values; however, practically implementing such approaches in human subject research may be more challenging than described above.

Another statistical limitation of our study was that we did not assess intersectionality and effect modification by assessing interaction terms or mediators in the model. This was primarily due to the small sample size of our model, where addition of extra interaction terms made the model very unstable. Future qualitative studies should aim to understand the complex intersecting factors that contribute to OAT discontinuation to better inform health service provision.

Finally, I acknowledge that there were numerous other statistical and modelling approaches to analyzing our data. Our sensitivity analyses (Appendix C) helped shed some light on the robustness of our results; however, there are numerous other approaches we could have taken that may not have been assessed in this thesis. One alternative approach that should be considered in future cross-sectional studies, where temporality is not clear, is a clustering analysis approach. With this approach, we may find additional groupings of variables in our sample, without forcing certain variables as outcomes or independent factors in the model.

4.4 Conclusion

This study made important contributions to the literature by characterizing OAT discontinuation across the 5 regional health authorities in BC, in a unique sample of individuals who access harm reduction supply distribution services. People who access OAT have diverse personal and system-level experiences that may or may not contribute to treatment retention and discontinuation. Our study helped highlight several factors associated with OAT discontinuation in the province. Being younger, living in rural communities and having experienced opioid and/or stimulant overdose was associated with increased odds of OAT discontinuation in our sample.

To address OAT discontinuation, structural-level interventions need to address the root causes of substance use, including unstable housing, socioeconomic stressors, coping with physical and mental health comorbidities and many others. At the system level, comprehensive planning at every level of care needs to ensure that support is available to individuals by choice and when needed, with minimal wait times and additional complications, to reduce loss of motivation and discontinuation. Early intervention programs should aim to target youth, who are at increased risk of substance use and treatment discontinuation, by providing alternative treatment routes in combination with psychosocial support. Cultural safety, cultural humility, and harm reduction programs free of stigma and judgment can help provide support to individuals with diverse needs, while working with housing and social support workers to make a plan that is in line with the individual's goals.

Involvement of peers and individuals with lived and living experiences is critical in facilitating relevant and informative research, policies, and health services to address inaccessibility and inequities within the Canadian addiction care system. While numerous efforts have been made to provide more culturally safe and supportive care to individuals who use substances in BC, additional efforts are needed to minimize stigma and ensure equitable access for individuals with diverse backgrounds and needs.

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Appendices

Appendix A

2019 Harm Reduction Client Survey

This survey is being conducted to help improve harm reduction services. No personal identifying information will be collected and your responses will be kept confidential. Your participation is voluntary and you are free to only answer the questions you are comfortable with. The survey will take roughly 20 minutes of your time. Please note that you can only complete the survey once.

To participate in this survey you must have used an illegal drug other than cannabis within the last 6 months.

1. What is your current GENDER identity? (Select one)
❑ Woman ❑ Man ❑ Trans man ❑ Trans woman ❑ Gender non-conforming
❑ Other, specify: _____ ❑ Prefer not to say
2. How old are you? _____ (years) ❑ Prefer not to say
3. Do you identify yourself as any of the following? (Select one)

❑ First Nations ❑ Métis ❑ Inuit ❑ No ❑ Prefer not to say
4. Do you live: (Select one)
❑ In a private residence, alone ❑ In a private residence, with someone else
❑ Other residence (hotels, motels, rooming houses, single room occupancy (SRO), shelters, social/supportive housing etc.)
❑ I have no regular place to stay (homeless, couch surf, No Fixed Address)
❑ Other, specify _____ ❑ Prefer not to say
5. How long has this been your living situation? (Select one)
❑ More than 1 year ❑ 7-12 months ❑ 1-6 months ❑ Less than 1 month ❑ Prefer not to say
6. Are you currently employed? (Select all that apply)
❑ Yes, paid volunteer ❑ Yes, part -time ❑ Yes, full-time ❑ No ❑ Prefer not to say
7. Do you have a cellphone? (Select one)
❑ Yes ❑ No ❑ Prefer not to say
8. How did you get here today? (Select one)
❑ Walked ❑ Biked ❑ Drove Myself ❑ Bus/ Skytrain/ Transit ❑ Taxi
❑ Someone drove me ❑ Mobile Site / Outreach came to me ❑ Prefer not to say
9. How long, in total, did it take you to get here today? (Select one)
❑ Outreach came to me ❑ 1 - 10 minutes ❑ 11 - 30 minutes
❑ 31 - 60 minutes ❑ Over 1 hour ❑ Prefer not to say

10. Did you use any of these in the LAST 3 DAYS?			**IF YES ➔** (Circle all that apply)						
			How did you use it?					**Did you have a prescription for it?**	
Methadone (Methadose/Metadol)	No	Yes	Smoke	Snort	Inject	Swallo	Other	No	Yes

						w			
Buprenorphine/Naloxone (Suboxone)	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Hydromorphone (Dilaudid)	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Oxycodone	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Morphine	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Heroin	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Fentanyl	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Xanax	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Other Benzos (Ativan/Valium)	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Stimulant (Ritalin/Adderall)	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Crystal Meth/Methamphetamine	No	Yes	Smoke	Snort	Inject	Swallow	Other		
Cocaine (powder)	No	Yes	Smoke	Snort	Inject	Swallo	Other		

						w			
Crack	No	Yes	Smoke	Snort	Inject	Swallow	Other		
MDMA	No	Yes	Smoke	Snort	Inject	Swallow	Other		
Cannabis/Hash	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Tobacco (cigarettes)	No	Yes	Smoke	Snort	Chew	Swallow	Other		
Alcohol	No	Yes				Swallow			
Other 1:	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes
Other 2:	No	Yes	Smoke	Snort	Inject	Swallow	Other	No	Yes

11. In the <u>last 3 days</u>, did you use both uppers (e.g. crystal meth) and downers (e.g. heroin) one after the other or together? (Select all that apply)

❑ No ❑ Yes, downers then uppers. If so, specify why: _____

_____

❑ Yes, uppers then downers. If so, specify why: _____

_____

❑ Yes, I mix uppers and downers together. If so, specify why: _____

_____

❑ Other, specify:_____ ❑ Prefer not to say

12. In the *past month*, how often did you use drugs by any mode (excluding cannabis, alcohol, or tobacco)?

❑ Every day ❑ A few times a week ❑ A few times a month ❑ Prefer not to say

13. If you use down, what would you prefer to use? (Select one)

❑ Heroin ❑ Fentanyl ❑ Morphine ❑ Oxycodone
❑ Hydromorphone (Dilaudid) ❑ Methadone/Methadose ❑ Buprenorphine/naloxone (Suboxone)
❑ I don't use down ❑ Prefer not to say

14. If you use uppers/stimulants, what would you prefer to use? (Select one)

❑ Crystal Meth/Methamphetamine ❑ Cocaine (powder) ❑ Crack ❑ MDMA
❑ Stimulants (Ritalin/Adderall) ❑ I don't use stimulants ❑ Prefer not to say

15. If your drugs tested positive for fentanyl (before you use), would you change the amount you use? (Select One)

❑ Yes, would use less ❑ Yes, would use more ❑ No, nothing would change ❑ Prefer not to say

16. What is your preferred method of using drugs? (Select one)

❑ Smoking/inhalation ❑ Snorting ❑ Injecting ❑ Swallowing
❑ Other, Specify: _____ ❑ Prefer not to say

17. How often do you use drugs alone? (Select one)

❑ Never ❑ Occasionally ❑ Often ❑ Always ❑Prefer not to say

18. What are some of the reasons YOU use drugs alone? (Select all that apply)

❑ It's safer to be alone ❑ It's more convenient and comfortable to use at home

❑ I don't want to share ❑ I don't want others to know that I'm using drugs

❑ I don't have anyone else to use with ❑ I never use alone

❑ Other, Specify: _____ ❑ Prefer not to say

19. In the last 6 months, have YOU overdosed (overamped) by accident from using a stimulant (eg. Crystal meth, crack)? (Select one)

❑ Yes ❑ No ❑ Don't know ❑ Prefer not to say

20. In the last 6 months, have YOU overdosed by accident from using any opioids (eg. fentanyl, heroin)? (Select one)

❑ Yes ❑ No *(skip to #22)* ❑ Don't know *(skip to #22)* ❑ Prefer not to say *(skip to #22)*

21a. In the last 6 months, how many times did you overdose by accident from using opioids? (Select one)

❑ Once ❑ 2 times ❑ 3 times ❑ 4 times ❑ 5 or more times ❑ Prefer not to say

21b. In the last 6 months, when you had the most recent opioid overdose were you given Naloxone/Narcan?

(Select one)

❑ Yes ❑ No *(skip to #22)* ❑ Don't know *(skip to #22)* ❑ Prefer not to say *(skip to #22)*

21c. When you were given Naloxone/Narcan most recently, was it given to you by: (Select all that apply)

❑ Paramedic or emergency responder ❑ OPS/ SCS Staff ❑ Friend / family member
❑ Stranger who happened to be there ❑ Housing worker ❑ Nurse/health worker in hospital

❑ Other, specify_____ ❑ Don`t know ❑ Prefer not to say

22. In the last 6 months, have you SEEN an accidental overdose in someone using any opioids? (Select one)

❑ Yes ❑ No *(skip to #24)* ❑ Don't know *(skip to #24)* ❑ Prefer not to say *(skip to #24)*

23a. Did you give Naloxone/Narcan to the person that overdosed during the last opioid overdose you witnessed? (Select one)

❑ Yes *(skip to #23c)* ❑ No ❑ Prefer not to say *(skip to #23c)*

23b. Why did you not give Naloxone/Narcan to the person experiencing an overdose? (Select all that apply)

❑ Some else gave Naloxone/Narcan ❑ Situation seemed under control
❑ Don't know how to use Naloxone/Narcan ❑ Naloxone/Narcan was not available
❑ Other, specify:_____ ❑ Prefer not to say

23c. Was 9-1-1 called during the last opioid overdose you witnessed? (Select one)

❑ Yes *(skip to #24)* ❑ No ❑ Don't know *(skip to #24)* ❑ Prefer not to say *(skip to #24)*

23d. Why was 9-1-1 not called? (Select all that apply)

❑ Didn't have a phone/phone not available ❑ Situation seemed under control
❑ Worried about family services being notified
❑ Worried about neighbors/landlord knowing about drug use
❑ Worried about police coming. If so, specify why:_____
❑ Other, specify:_____
❑ Prefer not to say

24. Do you have a Naloxone/Narcan kit? (Select one)

❑ Yes ❑ No, I do not have a kit but I want one ❑ No, I don't have a kit and I don't want one ❑ Prefer not to say

25. In the last 6 months, did any of the following make it difficult for you to get a Naloxone/Narcan kit? (Select all that apply)

❑ Had no difficulties ❑ I don't need a kit ❑ The site where I can get a kit is too far away
❑ Worried about being stigmatized ❑ I don't know where to get a kit
❑ Other, Specify _____

❑ Prefer not to say

26. In the last 6 months, how often did you pick up supplies (e.g. needles) from any site/outreach, either for yourself or another person? (Select one)

❑ Every day ❑ A few times a week ❑ A few times a month ❑ Less than once a month

❑ Never ❑ Prefer not to say

27. In the last 6 months, did any of the following make it difficult for you to pick up supplies from any site/outreach?

(Select all that apply)

❑ Had no difficulties ❑ Site not open ❑ Site too far away ❑ Staff had negative attitude
❑ Concerned about confidentiality ❑ Site didn't have the supplies I needed, specify:_____
❑ Other, specify: _____ ❑ Prefer not to say

28. In the last 6 months, did any of the following make it difficult for you to dispose of used supplies at any site/outreach/drop box? (Select all that apply)

❑ Had no difficulties ❑ Not enough disposal locations nearby ❑ Disposal site hours were too short
❑ Worried about being stigmatized ❑ Other, specify: _____ ❑ Prefer not to say

29. In the last 6 months, have you injected any type of drug? (Select one)

❑ Yes ❑ No *(skip to #31)* ❑ Prefer not to say *(skip to #31)*

30a. In the last 6 months, did you have any trouble getting unused needles? (Select one)

❑ Yes ❑ No ❑ Prefer not to say

30b. In the last 6 months, have you fixed with a needle that had been used by someone else? (Select one)

❑ Yes ❑ No ❑ Prefer not to say

31. In the last 6 months, have you used drugs at an overdose prevention site (OPS)/supervised consumption site (SCS)? (Select one)

An OPS/ SCS is a place (fixed or mobile) where drug consumption is supervised by staff or volunteers to reduce overdose related deaths.

❑ Yes ❑ No *(Skip to #33)* ❑ Prefer not to say *(Skip to #33)*

32a. How often are you using an OPS/SCS? (Select one)

❑ Every day ❑ A few times a week ❑ A few times a month ❑ Less than once a month ❑ Prefer not to say

32b. In the last 6 months, what type of OPS/SCS have you used? (Select all that apply)

❑ Shelter or housing ❑ Community Health Centre/Health Clinic ❑ Stand-alone OPS/SCS facility

❑ Mobile Site ❑ Community Organization ❑ I wouldn't use a OPS/SCS

❑ Other, specify: _____ ❑ Prefer not to say

33. In the last 6 months, did any of the following make it difficult for you to use an OPS/SCS? (Select all that apply)

❑ Had no difficulties ❑ I don't need to use an OPS/SCS ❑ Service not available nearby

❑ Concerned about confidentiality ❑ Worried about being stigmatized at OPS/SCS ❑ Staff had negative attitude

❑ Not allowed to smoke/snort drugs there ❑ Other, Specify: _____

❑ Prefer not to say

34. In the last 6 months, have you used a glass pipe (meth or crack) to smoke any drug? (Select all that apply)

❑ Yes, crack pipe ❑ Yes, meth pipe ❑ No, used something else to smoke (ie. light bulb, metal pipe)

❑ I don't use a pipe ❑ Prefer not to say

35. What do you do when you can't get a new (unused) pipe to smoke any drug? (Select all that apply)

❑ I don't use a pipe ❑ Inject instead ❑ Snort/swallow instead ❑ Wait until I find a new pipe
❑ Share, buy, or borrow a used pipe ❑ Smoke without a pipe using (specify): _____
❑ I have never had a problem getting pipes ❑ Prefer not to say

36. In the last 6 months, did any of the following make it difficult for you to access Opioid Agonist Treatment (OAT)/Opioid Substitution Treatment (OST) (eg. methadone, buprenorphine/naloxone, etc)? (Select all that apply)

OAT/OST are drug therapies that counter opioid withdrawal symptoms and act as a substitute for the opioids you were previously taking

❑ Had no difficulties ❑ I did not try to access OAT/OST *(skip to #38)*
❑ I do not use opioids *(skip to #38)* ❑ Could not find a prescribing physician

❑ There were no pharmacies nearby ❑ Could not get prescription because of positive urine test
❑ Clinic fees were too high ❑ Worried about being stigmatized at clinic
❑ Wasn't offered preferred OAT/OST ❑ Other, specify: _____
❑ Prefer not to say

37a. In the last 6 months, were you prescribed any of the following OAT/OST? (Select all that apply)

❑ Methadone (Methadose) ❑ Buprenorphine/naloxone (Suboxone) ❑ Slow-release oral morphine (Kadian)

❑ Diacetylmorphine (heroin) ❑ Hydromorphone, pill form (generic) ❑ Hydromorphone, pill form (Dilaudid)

❑ Hydromorphone, injectable liquid (Dilaudid)

❑ Other, Please specify: _____

❑ I wasn't prescribed any OAT/OST *(skip to #38)* ❑ Prefer not to say *(skip to #38)*

37b. In the last 6 months, did you discontinue OAT/OST? (Select one)

❑ Yes ❑No *(skip to #38)* ❑ Prefer not to say *(skip to #38)*

37c. Why did you discontinue OAT/OST? (select all that apply)

❑ Couldn't get to pharmacy during open hours ❑ Couldn't make clinic appointment time

❑ Treatment wasn't effective ❑ Switched treatment

❑ Clinic was too far away ❑ Challenges with transportation/travel

❑ Clinic staff had negative attitude ❑ Clinic fees were too high
❑ Prefer not to say ❑ Other, Please Specify:

38. Have you heard about the Good Samaritan Drug Overdose Act? (Select all that apply)

❑ Yes ❑ No *(skip to end)* ❑ Prefer not to say *(skip to end)*

39. Do you believe the GSDOA protects the following people from being arrested for simple possession of substances (small amount of drugs for own use) at the scene of an overdose? (Select all that apply)

a. The person who calls 9-1-1
❑ Yes ❑ No ❑ Prefer not to say

b. The person who overdoses
❑ Yes ❑ No ❑ Prefer not to say

c. Anyone at the scene of an overdose

❑ Yes ❑ No ❑ Prefer not to say

40. Imagine there is an overdose in a public place; 9-1-1 is called and the police come to the scene. Do you think the police can legally arrest a person if they: (Select all that apply)

a. Have a larger amount of drugs on them or items (eg. scale) that may look like they are involved in drug dealing
❑ Yes ❑ No ❑ Prefer not to say

b. Are in a red/no-go zone they received for a previous charge that was not simple drug possession (eg. theft)
❑ Yes ❑ No ❑ Prefer not to say

c. Have an outstanding warrant for something other than simple drug possession (eg. theft)
❑ Yes ❑ No ❑ Prefer not to say

*Now I'd like to tell you about the **Good Samaritan Drug Overdose Act**, which was made law in May 2017. It protects the person who overdoses, the person who calls 9-1-1, and anyone else at the scene of an overdose from being arrested for 'simple' possession that means having illegal drugs for their own personal use. It does not protect anyone at an overdose from being arrested for outstanding warrants, controlled substance trafficking or production, or any other serious offense. (Please provide the participant with a Good Samaritan Drug Overdose Act info card at this point.)*

Appendix B

Table B.1 Proportion of participants indicating OAT prescription in the past 6 months (Appendix A, Question 37a), taking the opioid in the past 3 days (Appendix A, Question 10), and proportion of those who indicated OAT prescription in the past 6 months also indicating taking the opioid in the past 3 days.

OAT Medication	**Indicated prescribed medication in past 6 months n (%)**	**Indicated taking in past 3 days n (%)**	**Indicated prescribed in past 6 months and taking in past 3 days n (%)[a]**
Methadone	123 (63.4%)	83 (42.8%)	75 (61.0%)
Buprenorphine	48 (24.7%)	17 (8.8%)	17 (35.4%)
Morphine	25 (12.9%)	34 (17.5%)	14 (56.0%)
Dilaudid	4 (2.1%)	9 (4.6%)	2 (50.0%)

[a]Percentage is the proportion of the individuals who indicated being prescribed the opioid in the past 6 months (denominator is the second column of the table).

Appendix C

C.1 Effects of forcing in conceptually significant variables into the multivariable regression model (compare to Table 3.2 in the main text)

Table C.1. Estimated odds ratios (OR) and adjusted odds ratios (AOR) for correlates of OAT discontinuation among HRCS participants as determined by stepwise block selection logistic regression, comparing final included model and model including only variables statistically selected for through stepwise selection and lowest AIC values.

	OAT Discontinuation[a]		
	Simple Bivariate OR (95% CI)	Final Included Model AOR (95% CI)	Sensitivity Analysis AOR (95% CI)
Demographic Characteristics			
Age (years)			
19-29	---	---	---
30-39	1.17 (0.52,2.63)	1.02 (0.39,2.68)	1.07 (0.44,2.60)
40-49	0.70 (0.28,1.74)	0.56 (0.19,1.65)	0.61 (0.22,1.69)
≥50	**0.19 (0.07,0.56)****	**0.12 (0.03,0.45)****	**0.17 (0.05,0.55)****
Unknown	0.94 (0.12,7.48)	0.97 (0.10,9.72)	1.01 (0.12,8.70)
Gender			
Cis man	---	---	
Cis woman	1.19 (0.66,2.15)	0.72 (0.35,1.47)	
Transgender and gender expansive	2.73 (0.24,31.02)	2.80 (0.20,39.29)	
Unknown	0.46 (0.05,4.51)	1.25 (0.09,16.87)	
Socioeconomic Characteristics			
Stable housing			
Yes	0.57 (0.31,1.07)	1.08 (0.49,2.36)	
No	---	---	
Accessibility Characteristics			
Urbanicity			
Medium/large urban	0.58 (0.23,1.50)	**0.27 (0.07,0.98)***	
Small urban	0.70 (0.23,2.07)	0.42 (0.09,1.91)	

Rural	---	---	
Past 3-Day Drug Use			
Heroin and/or fentanyl			
Yes	2.12 (0.38,11.95)	0.59 (0.05,6.63)	1.49 (0.18,12.41)
No	---	---	---
Unknown	0.63 (0.10,3.89)	0.16 (0.01,2.17)	0.65 (0.07,5.92)
Stimulants			
Crystal Meth	4.78 (0.54,42.03)	8.05 (0.52,124.60)	
Other (crack, cocaine, etc.)	1.92 (0.18,20.82)	5.52 (0.30,100.58)	
No	---	---	
Unknown	2.95 (0.31,28.14)	12.25 (0.64,235.59)	
Alcohol			
Yes	1.41 (0.63,3.17)	1.45 (0.52,4.02)	
No	---	---	
Unknown	1.21 (0.57,2.55)	1.63 (0.58,4.58)	
Harm Reduction Characteristics			
Opioid and/or stimulant overdose in past 6 months			
Yes	**3.70 (1.79,7.62)*** **	**3.77 (1.57,9.03)** **	**3.46 (1.56,7.71)** **
No	---	---	---
Unknown	2.23 (0.57,8.68)	1.87 (0.42,8.26)	1.90 (0.46,7.88)
OPS use is past 6 months			
Yes	**2.20 (1.23,3.94)** **	1.80 (0.89,3.65)	1.82 (0.93,3.54)
No	---	---	---
McFadden Pseudo-R^2		0.20	0.16
Pseudo-R^2 change			0.04

Reference categories are denoted by "---"
*p<0.05, **p<0.01, ***p<0.001
[a]Final model size N=194

C.2 Effects of adding in past 3-day prescription opioid use to the multivariable regression model (compare to Table 3.2 in the main text)

Table C.2. Estimated odds ratios (OR) and adjusted odds ratios (AOR) for correlates of OAT discontinuation among HRCS participants as determined by stepwise block selection logistic regression comparing the final included model and model including past 3-day prescription opioid use.

	OAT Discontinuation[a]		
	Simple Bivariate OR (95% CI)	Final Included Model AOR (95% CI)	Sensitivity Analysis AOR (95% CI)
Demographic Characteristics			
Age (years)			
19-29	---	---	---
30-39	1.17 (0.52,2.63)	1.02 (0.39,2.68)	1.52 (0.48,4.80)
40-49	0.70 (0.28,1.74)	0.56 (0.19,1.65)	1.13 (0.32,4.01)
≥50	**0.19 (0.07,0.56)****	**0.12 (0.03,0.45)****	**0.14 (0.03,0.68)***
Unknown	0.94 (0.12,7.48)	0.97 (0.10,9.72)	1.81 (0.13,25.01)
Gender			
Cis man	---	---	---
Cis woman	1.19 (0.66,2.15)	0.72 (0.35,1.47)	0.69 (0.30,1.57)
Transgender and gender expansive	2.73 (0.24,31.02)	2.80 (0.20,39.29)	2.95 (0.14,60.65)
Unknown	0.46 (0.05,4.51)	1.25 (0.09,16.87)	0.32 (0.02,5.50)
Socioeconomic Characteristics			
Stable housing			
Yes	0.57 (0.31,1.07)	1.08 (0.49,2.36)	1.80 (0.73,4.44)
No	---	---	---
Accessibility Characteristics			
Urbanicity			
Medium/large urban	0.58 (0.23,1.50)	**0.27 (0.07,0.98)***	**0.26 (0.07,0.99)***
Small urban	0.70 (0.23,2.07)	0.42 (0.09,1.91)	0.42 (0.09,1.91)
Rural	---	---	---
Past 3-Day Drug Use			
Prescription opioids			

Methadone			**0.02 (0.00,0.17)*** **
Buprenorphine			0.10 (0.01,1.02)
Other			**0.04 (0.00,0.41)** **
No			---
Unknown			0.22 (0.03,1.83)
Heroin and/or fentanyl			
Yes	2.12 (0.38,11.95)	0.59 (0.05,6.63)	3.89 (0.26,58.69)
No	---	---	---
Unknown	0.63 (0.10,3.89)	0.16 (0.01,2.17)	1.27 (0.07,23.53)
Stimulants			
Crystal Meth	4.78 (0.54,42.03)	8.05 (0.52,124.60)	2.11 (0.13,33.86)
Other (crack, cocaine, etc.)	1.92 (0.18,20.82)	5.52 (0.30,100.58)	1.34 (0.06,28.33)
No	---	---	---
Unknown	2.95 (0.31,28.14)	12.25 (0.64,235.59)	4.35 (0.20,95.11)
Alcohol			
Yes	1.41 (0.63,3.17)	1.45 (0.52,4.02)	1.09 (0.32,3.66)
No	---	---	---
Unknown	1.21 (0.57,2.55)	1.63 (0.58,4.58)	1.15 (0.33,4.03)
Harm Reduction Characteristics			
Opioid and/or stimulant overdose in past 6 months			
Yes	**3.70 (1.79,7.62)*** **	**3.77 (1.57,9.03)** **	**4.33 (1.60,11.73)** **
No	---	---	---
Unknown	2.23 (0.57,8.68)	1.87 (0.42,8.26)	2.53 (0.47,13.56)
OPS use is past 6 months			
Yes	**2.20 (1.23,3.94)** **	1.80 (0.89,3.65)	1.83 (0.81,4.13)
No	---	---	---
McFadden Pseudo-R^2		0.20	**0.34**
Pseudo-R^2 change			**0.14*** **

Reference categories are denoted by "---"
*p<0.05, **p<0.01, ***p<0.001
[a]Final model size N=194