SOCIAL DETERMINANTS OF PSYCHIATRIC OUTCOMES

AN INVESTIGATION OF SOCIAL AND

BEHAVIOURAL FACTORS ASSOCIATED

WITH PSYCHIATRIC OUTCOMES

by

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ABSTRACT

Background: Social adversities are prevalent among those with psychiatric disorders and may be involved in poor outcomes among patients receiving treatment. Identification of social risk factors influencing outcomes will help provide targeted interventions for at-risk patients. This thesis explored the role of social and behavioural factors in relation to adverse psychiatric outcomes, specifically relapse to substance use and attempted suicide.

Methods: We used scoping study methodology to perform a comprehensive review to identify the gaps in the literature examining social functioning and MMT outcomes. This review informed our primary cohort study examining the association between social factors and continued opioid use in MMT. Lastly, we conducted a case-control study to identify risk factors for suicide attempts by comparing psychiatric patients with and without suicide attempt history (cases and controls, respectively). Multivariable logistic regression analyses were conducted in both primary studies to examine the association between predictors and outcomes.

Results: The review included 101 observational studies and determined the need for further research on social factors and MMT outcomes among a current sample of Canadian patients. Our cohort study included 1043 participants (mean age=38.4 years, standard deviation [SD]=11.06); 45.8% women) to investigate this and found that unemployment, criminal activity and interpersonal conflict with friends significantly increased odds of illicit opioid use. In examining risk factors for suicide attempts, we recruited 146 cases (mean age=45.18 years, SD=14.70 years; 55% female) and 104 control participants (mean age=45.01 years, SD=14.23 years; 50% female). No

sociodemographic differences existed between groups, however higher impulsivity and borderline personality symptoms significantly increased odds of attempted suicide.

Conclusions: Findings from these studies may indicate the need for structured monitoring of at-risk psychiatric patients. It may be important to develop tools to measure social and behavioural factors in clinical settings and promote further integration of social services in treatment settings.

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LIST OF ABBREVIATIONS

OUD	Opioid Use Disorder
MMT	Methadone Maintenance Treatment
SD	Standard Deviation
OR	Odds Ratio
CI	Confidence Interval
EMBASE	Excerpta Medica DataBase
CINAHL	Cumulative Index to Nursing and Allied Health Literature
GENOA	GENetics of Opioid Addiction
DISCOVER	Determinants of Suicidal Behaviour: Conventional and Emergent Risk
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
MAP	Maudsley Addiction Profile
MINI	Mini Neuropsychological Interview

DECLARATION OF ACADEMIC ACHIEVEMENT

I am the primary author of each study included in this sandwich thesis. I contributed substantially to each study by assuming the primary role in developing research questions, drafting study protocols, planning and conducting statistical analyses, and drafting each manuscript. Details of each author's contributions are presented at the end of each study.

CHAPTER 1

1.1 INTRODUCTION

1.1.1 Background

While many associate the development of health issues with biological processes, research has overwhelmingly shown the influence of social determinants on health (1). In fact, social factors are known to play an important role in the development and prognosis of mental illness and have a significant impact on morbidity and mortality (2-4). The prevalence of social adversity is disproportionately high among individuals with serious psychiatric disorders who require treatment or hospitalization (5-7). It remains important to elucidate the influence of social factors on treatment outcomes among these patients with serious chronic psychiatric illnesses. Uncovering social risk factors implicated in mental health treatment outcomes presents an opportunity for the implementation of broad public health prevention strategies and tailored treatment options for psychiatric patients. This thesis will investigate the impact of social and behavioural factors on adverse outcomes within two clinical populations: 1) patients with opioid use disorder receiving methadone maintenance treatment and 2) hospitalized patients with psychiatric illnesses with and without a history of attempted suicide.

1.1.2 Opioid use disorder and methadone maintenance treatment

Opioid use disorder (OUD) is serious chronic condition that affects 15.5 million

individuals worldwide and contributes significantly to the overall burden of disease in

North America (8). In North America, there has been a dramatic increase in the

prevalence of illicit opioid use with 25 million initiating nonmedical use of prescription

opioids from 2002 to 2011 (9). Illicit opioid use in Canada has reached epidemic

proportions and been linked to significant mortality (10-12). Corresponding to the

increase in opioid abuse, Canada has witnessed an influx of patients into methadone

maintenance treatment (MMT) programs for managing OUD (13). Though MMT is the

most commonly employed opioid substitution therapy in Canada, its effectiveness has

been largely examined in clinical trials of patients who primarily use heroin (11, 14). The

rise in prescription opioid dependence has significantly changed the demographic profile

of patients currently enrolled in MMT programs in Canada (15). For this reason, it is

important to conduct research on factors affecting treatment response, specifically the

prevalence and influence of social dysfunction within this novel cohort of patients.

1.1.3 Suicide attempts among patients with psychiatric disorders

Suicide takes the lives of 800, 000 individuals globally and attempted suicide is estimated

to occur up to 20 times more frequently (16, 17). Most studies assessing the risk factors of

suicide attempts compare individuals who have attempted suicide with the general non-

psychiatric population (7, 18-21). It is known that an estimated 90% of individuals who

attempt suicide have a psychiatric disorder while a small proportion of individuals with a

psychiatric disorder attempt suicide (17). Understanding the risk factors and warning

signs associated with suicide attempts among psychiatric patients is essential as these patients may be monitored in a clinical setting to prevent suicide completion. Sociodemographic, clinical and behavioural factors of suicide attempts are important to consider within a sample of psychiatric patients, in order to develop targeted interventions for at-risk patients. Also due to the documented sociodemographic similarities between psychiatric patients who have and have not attempted suicide, identifying warning signs associated with suicide attempts is important to better recognize patients at risk.

1.1.4 Thesis objectives

Given the devastating impact of these psychiatric conditions, research is warranted to improve outcomes for patients in treatment. This thesis combines three studies, Chapters 2 to 4, examining social and behavioural factors among psychiatric populations and their association with adverse treatment outcomes and attempted suicide. The papers included are submitted for publication or prepared for submission to peer-reviewed journals. The first paper is a scoping review describing the state of the literature assessing social factors in relation to outcomes in MMT globally, while the second paper is a cohort study assessing social factors and MMT outcomes among adults in MMT programs in Ontario, Canada. The third study is a case-control study comparing sociodemographic and behavioural characteristics of psychiatric patients who have or have not attempted suicide to identify risk factors within this population. Overall, these studies aim to assess the role of social and behavioural factors among individuals in treatment for OUD or other psychiatric disorders. Ultimately we aim to determine: how do social and behavioural factors influence outcomes for patients with serious mental illnesses? We examined this

research question by conducting a scoping review of the literature and obtaining primary data from multiple observational studies.

Chapter 2 is a scoping review of the literature that mapped the global distribution and yearly trend in publication of primary research assessing the influence of social factors on harm reduction outcomes in MMT patients. We assessed multiple social factors and harm MMT outcomes to summarize the state of published research. This review was used to identify areas where there is a paucity of research, in order to direct future research.

Chapter 3 is a multicentre prospective cohort study among adult MMT patients in Ontario. The purpose of this study was to determine the impact of social dysfunction on continued opioid use in MMT. We characterized social dysfunction by measuring past-month criminal activity, employment status and frequency of interpersonal conflict with partners, family and friends. Social factors were measured at baseline to determine whether they were associated with illicit opioid use at baseline assessment. Participants were also followed for three months to assess whether baseline social dysfunction predicted continued opioid use.

In Chapter 4, we conducted a case-control study to determine risk factors for attempted suicide in a psychiatric patient population. Here, we compared psychiatric inpatients who had attempted suicide in their lifetime to those who had never attempted suicide on sociodemographic and behavioural characteristics. Furthermore, we classified the individuals who had attempted suicide by intent to die and described the circumstances associated with the suicide attempt to identify suicide prevention strategies. This manuscript has been submitted to the journal *PLOS One*.

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CHAPTER 2
Study 1:
Social functioning in association with methadone maintenance treatment outcomes:
A scoping review of the literature

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2.1 ABSTRACT

Background: The rise in prescription opioid abuse has led to a changing demographic profile for methadone maintenance treatment (MMT) patients, previously consisting of mainly heroin users. It is important to characterize the primary research conducted on the influence of social factors on MMT outcomes to identify gaps in the literature and direct future research. This scoping review aimed to map the global distribution and yearly trend in publication of studies examining interpersonal conflict, criminal activity and employment in association with harm reduction outcomes in MMT.

Methods: Scoping study methodology described by Arksey and O'Malley was used to conduct this review. A team of 10 reviewers conducted title and abstract screening and full-text review independently in duplicate. Studies were classified into domains based on social factors, MMT outcomes, and methods used to measure the predictors and outcomes. Additionally, we determined whether studies adjusted for potential confounders in their statistical analyses. Results were summarized descriptively to determine gaps in the literature.

Results: We included 101 studies with 166,997 participants and mean age varying from 23.4 to 47 years across studies. The majority of studies included >50% male participants and were conducted in the United States, followed by China. Studies from Asian countries included heroin-using participants, and no included studies made distinctions in social characteristics between heroin and prescription opioid users. The majority of studies measured employment (i.e. employment status or related problems) as a predictor and treatment compliance as an outcome. Approximately half of the studies conducted for

each social factor domain performed statistical analyses that were adjusted for potential confounders.

Conclusions: In North America, further research on the impact of social dysfunction needs to be conducted among current samples of MMT patients. These studies should make distinctions between prescription opioid and heroin users in order to identify differences in MMT effectiveness. Harm reduction outcomes such as substance use, psychopathology, and quality of life should be prioritized for future research rather than treatment compliance alone. Future studies globally must conduct multivariate analyses assessing the association between social factors and MMT outcomes.

2.2 INTRODUCTION

Misuse of opioids, including prescription analgesics as well as heroin, has reached alarming proportions globally (1). The increasing prevalence of opioid use disorder (OUD) is a serious public health concern associated with overwhelming medical and social costs (2). The literature has noted an increased prevalence of social dysfunction among affected patients and subsequently physicians have urgently called for increased access to treatment (3, 4). While there have been marked increases in the number of patients enrolled in methadone maintenance treatment (MMT) programs, a significant amount of variability has been observed in treatment response (5, 6). Along with continued substance use, clinicians witness ongoing social adversities among patients in MMT (3, 7-9). These social issues may affect treatment compliance and inhibit the goal of harm reduction (10, 11), highlighting the importance of research related to social dysfunction among MMT patients.

Literature examining social factors is expected to differ based on geographic location, due to varying proportions of patients abusing heroin and prescription opioids (1, 12). In North America, there has been a substantial increase in the number of prescription opioid users with OUD in the past decade, with an analogous shift within treatment programs (13, 14). These patients represent a unique cohort of patients with different demographic and clinical profiles in comparison to heroin users (15). A scoping review will characterize the global distribution and yearly trend in published research, identify any knowledge gaps, and guide future research on social dysfunction with respect to various harm reduction outcomes in MMT.

This scoping review aimed to summarize the literature examining the association between social factors treatment outcomes during MMT for patients with OUD. The social predictors examined in this review were those identified by the Maudsley Addiction Profile (MAP) as common problem domains for patients with substance use disorders (16), consisting of 1) interpersonal conflict with intimate partners, family and friends (i.e. serious arguments; verbal, physical and sexual abuse or violence); 2) employment (i.e. employment status, problems with employment, missed days from work); and 3) criminal activity (i.e. criminal behaviour or offences, legal status, incarceration). Harm reduction outcomes of MMT, including substance use, psychopathology, quality of life and treatment compliance, were assessed in relation to the aforementioned social factors.

The objectives of the review were to:

1. Summarize the literature investigating the association between social functioning and methadone maintenance treatment outcomes by mapping global distribution and year of publication.

2. Identify critical knowledge gaps and limitations based on the literature and make recommendations for future research.

2.3 STUDY DESIGN AND METHODS

This review was conducted using a systematic scoping review approach, first described by Arksey and O'Malley (17). Scoping studies are similar to systematic reviews in that the methodology is reported with transparency to allow replication by other researchers and increase reliability of results. The framework for scoping reviews includes the following proposed stages: 1) identifying a research question, 2) finding relevant literature, 3) selection of studies based on eligibility criteria, 4) data extraction from included studies, and 5) summarizing and reporting of results. A systematic approach to the scoping review will allow us to provide a comprehensive assessment of the available evidence from the literature, while identifying major gaps in the literature to direct future research. Furthermore, proposing a research question, predefined eligibility criteria and study selection strategy will ensure that the review is thorough and objective. However, this scoping review differs from the traditional systematic review due to breadth of the research question, lack of formal quality assessment and descriptive data syntheses to summarize the findings.

2.3.1 Eligibility criteria

This review included observational studies (cross-sectional, prospective and retrospective cohort, and case-control studies) investigating predefined social factors and treatment outcomes among adult patients enrolled in MMT programs. Conference abstracts were included if sufficient information was available for data extraction. Randomized controlled trials (except relevant secondary reanalyses of trials), narrative reviews, qualitative studies, case reports, research letters and editorials were excluded.

Studies were excluded if they included patients in methadone detoxification rather than methadone maintenance. Studies examining changes in social dysfunction scores were excluded, as we wanted to consider studies examining the independent association of social dysfunction with MMT outcomes. Studies were excluded if they could not be retrieved in English. No restrictions were placed on date of publication.

Studies were eligible if they included the following social factors identified from the social functioning domain of the Maudsley Addiction Profile (MAP) (16):

1. ***Interpersonal conflict with family, partners or friends:*** intimate partner violence, physical abuse, sexual abuse that is *proximal to treatment* (does not included childhood abuse or history of violence), social functioning score measured as part of a validated questionnaire

2. ***Criminal activity:*** any measure of criminal behaviour such as arrests, offences in the past month, self-reported criminal activity, legal functioning score measured as part of a validated questionnaire

3. ***Employment:*** self-reported employment, number of days employed, employment related problems, employment score measured as part of a validated questionnaire

Studies examining the association of eligible social factors with the following MMT outcomes were included:

1. ***Treatment compliance:*** treatment retention or dropout from treatment, attendance in treatment, adherence to treatment

2. ***Substance use:*** continued opioid or heroin use during treatment; use of cocaine, illicit stimulants, benzodiazepine, cannabis, and other substances (excluding alcohol and nicotine)

3. ***Psychopathology:*** DSM criteria psychiatric disorder diagnosis, psychiatric disorders or psychopathology measured via validated questionnaire, suicidal ideation, measurements of mood or psychological symptoms

4. ***Quality of life:*** overall score measured via validated quality of life questionnaire

2.3.2 Data sources and search strategy

The literature search was performed using a comprehensive search strategy developed by the first author (M.B.) in consultation with a health sciences librarian (N.B.). Search terms included medical subject headings and keywords such as 'exp Opiate Substitution Treatment/', '((opioid or opiate) adj2 disorder).ti,ab.', '((opioid or opiate) adj (dependen* or addict* or abuse or misuse)).ti,ab.', 'methadone maintenance.mp' and variations of search terms for social factors (Appendix 1). The search strategy was adapted for the following electronic databases from inception to May 8th, 2016: MEDLINE, EMBASE, PsycINFO, Cumulative Index to Nursing and Allied Health Literature and Social Sciences Abstracts through Proquest.

2.3.3 Selection of studies

We formed a team of 10 reviewers to conduct title/abstract screening and full-text review based on the volume of citations retrieved from the search. Calibration exercises were conducted with the team to assess raw agreement and orient reviewers to the eligibility criteria. Calibration consisted of screening titles and abstracts of 100 retrieved

citations, followed by discussion between the first author and each team member regarding the level of agreement. Screening and full-text review were conducted in duplicate by independent reviewers and all disagreements were resolved by a third experienced author. Articles meeting eligibility criteria following full-text review were included for data extraction.

2.3.4 Data extraction

Data were extracted by independent authors on a pilot tested data extraction form. We extracted the following study characteristics: year of publication, country of study, study design (cross-sectional, prospective cohort, retrospective cohort, case-control), length of study if longitudinal, characteristics of study population (i.e. general MMT patient population, imprisoned MMT patients), total number of participants (including number of males and females), and mean age of participants. Information about all relevant social factors measured by the included studies and the instrument used for measurement was extracted, along with the MMT outcomes and methods of outcome measurement. As a surrogate for study quality, we extracted whether each study conducted multivariate analyses by adjusting for potential confounding variables (adjusted vs unadjusted analysis).

2.3.5 Data syntheses and reporting of results

Descriptive statistics were used to summarize all findings. Categorical variables were reported as counts or percentages. Continuous variables were summarized as means with standard deviations when normally distributed or medians with interquartile ranges when the distribution was skewed. The global distribution of included studies was

mapped, though we did not adjust for population density or prevalence of OUD within each continent. We also summarized the yearly trend in the number of published studies within each continent.

Social factors assessed in each study were classified under 'Interpersonal conflict', 'Criminal activity' or 'Employment'. Some studies assessed multiple social variables and were therefore included multiple times when assessing frequency of social factors examined in the literature. Studies examining MMT outcomes were categorized under pre-specified domains: 'Substance use', 'Psychopathology', 'Quality of life' and 'Treatment compliance'. Figures were presented to summarize the number of studies conducted for each social factor in association with each outcome domain. Furthermore, we characterized social factors based on the method of measurement in the study into 'self-report', 'validated questionnaire', or 'objective measure'. 'Self-report' referred to any yes/no question or single statement about the occurrence of social dysfunction in a given period of time. 'Validated questionnaire' referred to the use of a self-report questionnaire validated in MMT patients to measure the severity or frequency of social dysfunction. 'Objective measure' referred to any review of records (i.e. criminal records, employment history records) to confirm the occurrence of social dysfunction.

2.4 RESULTS

The initial search identified 13,577 potentially relevant citations (Figure 1). After removal of duplicates, 10,818 titles and abstracts were screened for eligibility. Following title and abstract screening, 2,994 full-texts were assessed and 101 studies were included in the review. The full data extraction form with information pertaining to each study is displayed in Appendix 2.

2.4.1 Characteristics of included studies

Across 101 studies, a total 166,997 participants were included with mean age ranging from 23.4 to 47.0 years. More than two thirds of the included studies had >50% men in the study sample and 11 studies included only male participants. Approximately half (48.5%) of the included studies had a prospective cohort design, with follow-up varying from one month to 30 years. This was followed by a cross-sectional design in 32.7% and retrospective cohort design in 17.8% of included studies.

Of the included studies, the majority were conducted in the United States (49.0%), followed by China (13.7%). Figure 2 shows the proportion of published studies by continent. It is also important to distinguish between studies published earlier than 2005 to those published within the last decade due to the documented changes in the sociodemographic characteristics of MMT patients in that year. Overall, 46 (45.5%) included studies were published before 2005 and included mainly heroin users. The remaining studies were published after 2005, however 48.2% of these studies were conducted in East Asian countries and also exclusively included heroin users. The trend in number of studies by year of publication within each continent is displayed in Figure 3.

Within North America, the majority of studies published after the rise of prescription opioid abuse (i.e. after 2005) were conducted in the United States (14/17=82.4%) with few in Canada (3/17=17.6%).

2.4.2 Social functioning and methadone maintenance treatment outcomes

Figure 4 summarizes the social factors and MMT outcomes examined by the included studies. A number of included studies measured multiple social factors and MMT outcomes. Employment was examined in 78 included studies primarily in relation to treatment compliance (33/78), followed by substance use (26/78), psychopathology (14/78) and quality of life (5/78). About half of the studies measuring employment conducted multivariate analyses, adjusting for potential confounding variables (53.8%). Crime was examined as a social factor in 67 studies in association with treatment compliance (29/67), substance use (24/67), psychopathology (11/67) and quality of life (3/67). Of 67 studies, 55.2% adjusted the analysis for potential confounders. Interpersonal conflict was assessed in 41 studies, with most studies investigating its association to treatment compliance (15/41) and substance use (14/41) followed by psychopathology (8/41) and quality of life (4/41). A greater proportion of studies examining conflict conducted multivariate analyses adjusting for confounders (65.9%). Figure 6 displays the proportion of adjusted compared to unadjusted studies.

When considering the measurement of social dysfunction, crime was measured by self-reports (41.8%), validated questionnaires (32.8%) and objective measures (25.4%) whereas employment was primarily measured by self-reports (76.9%). Interpersonal conflict was measured by both validated questionnaires (65.9%) and self-reports (34.1%).

2.5 DISCUSSION

This scoping review summarized the literature investigating social factors and MMT outcomes. As expected based on the high prevalence of OUD in North America, the majority of the research was conducted in the United States (1). Results showed that relatively few studies investigating social factors were conducted in Canada, despite the height of the opioid crisis in the country (Figure 6) (4, 13). There were no specific trends observed among the literature in Europe or Australia, however all studies from Asia were conducted after 2009 and included individuals with heroin dependence.

Few studies made the distinction between prescription opioid users and heroin users, yet it is likely there was an increase in the proportion of prescription opioid users in studies conducted after 2005 in North America (3, 13). Figure 6 shows a spike in the research examining social factors in MMT in the 1990s. However, it is important to conduct high calibre research in current MMT populations in both the United States and Canada due to the changing demographic of patients (15). The majority of included studies had over two times as many men as women in the study samples, which may not represent the current population of MMT patients. Recent data in Canada shows a growing proportion of women corresponding to the increase in prescription opioid abuse, which is important to investigate in future studies (13, 15).

This review also showed that studies predominantly examined crime, employment and interpersonal conflict in relation to treatment compliance. Treatment compliance plays an important role in effectiveness of MMT, such that patients retained in treatment exhibit show greater improvement in various areas (18, 19). However, it is also important

to examine psychopathology and substance use in combination with treatment compliance as these factors may be affected by social dysfunction and require additional therapy. A small proportion of studies examined social dysfunction in relation to quality of life. Considering that MMT is used largely as a harm reduction therapy, it is important for studies to evaluate quality of life using validated questionnaires to assess health status and overall functioning. It is especially important to determine the role of social factors in MMT response to add to the research examining MMT effectiveness in samples of individuals with prescription opioid and heroin dependence, as most current research has been conducted in samples of heroin users alone (4). MMT patients experiencing social issues may be at high risk of poor response and these factors need to be further investigated in longitudinal studies. Focusing on modifiable social risk factors such as interpersonal conflict, employment and crime can allow clinicians to develop targeted interventions to improve outcomes for these patients.

2.5.1 Limitations

We were unable to retrieve studies that were not available in English, which may not have captured research from areas outside of North America. Title assessment of the 17 studies unavailable in English indicated that the majority of studies were conducted in China. However, we were still able to capture a fair amount of research from China and the 17 studies represent a small proportion of studies that were eligible for inclusion. However, it is important to note that there may have been additional non-English studies, which were not indexed in the databases searched for this review.

2.6 CONCLUSIONS

This scoping review identified gaps in the literature that must be addressed by future research in order to aid in identifying patients who are at risk of poor outcomes in MMT. At the global level, studies should prioritize patient important outcomes along with treatment compliance. Observational studies investigating social risk factors should conduct multivariate analyses to account for potential confounding variables. Because of the shifting demographics, more research in the United States and Canada must be conducted among representative samples of MMT patients, and make distinctions between prescription opioid users and heroin users.

2.7 ACKNOWLEDGEMENTS, FUNDING, AND AUTHOR CONTRIBUTIONS

2.8 FIGURES AND TABLES

Figure 2.8.1 Flow diagram of study inclusion process
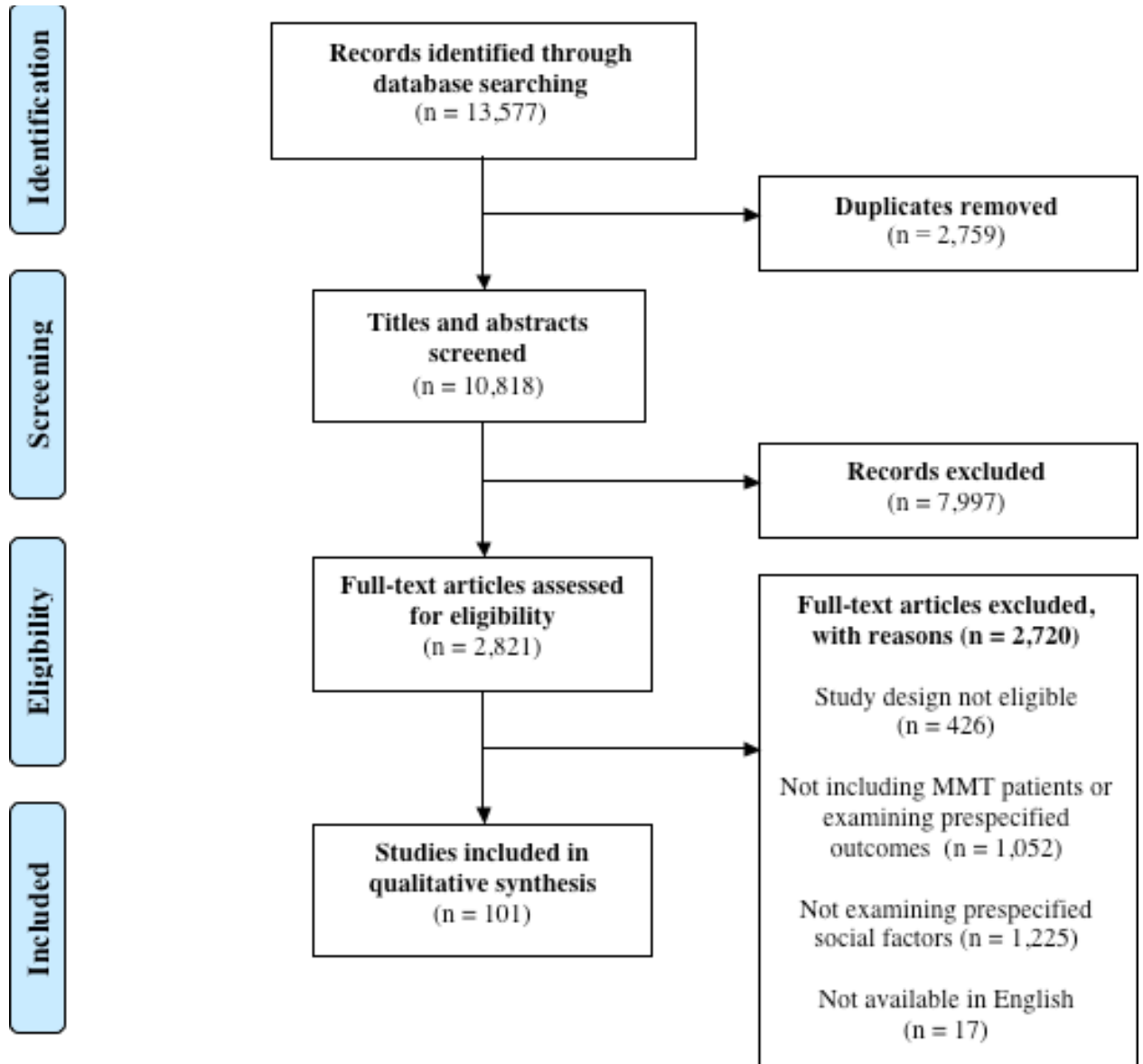
Figure 2.8.2 Global distribution of literature examining social factors related to methadone maintenance treatment outcomes.
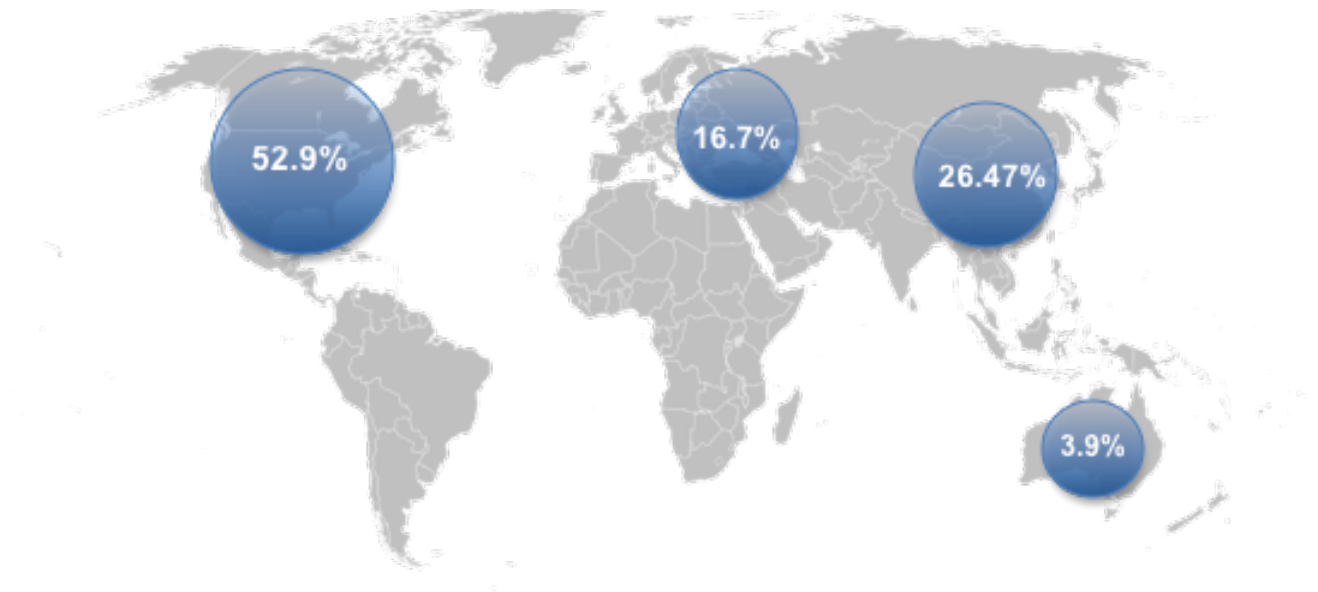
*N=102; one study was counted twice, as it was conducted in the Netherlands and United States.
Figure reports raw percentages, unadjusted for population density.

Figure 2.8.3 Trend in number of studies published on social factors related to methadone maintenance treatment outcomes from 1977-2016 by continent.
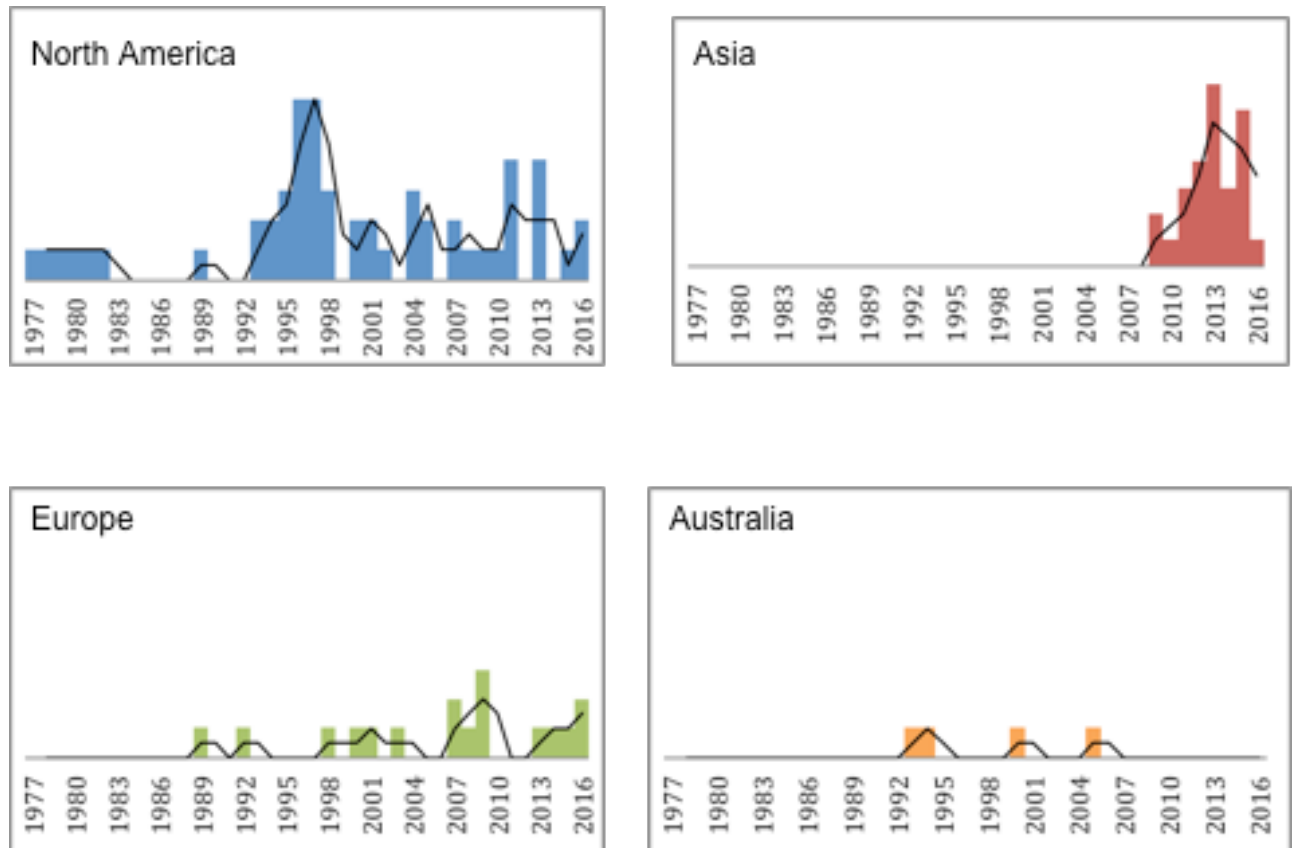
Figure 2.8.4 Social factors examined in published studies, shown per methadone maintenance outcome
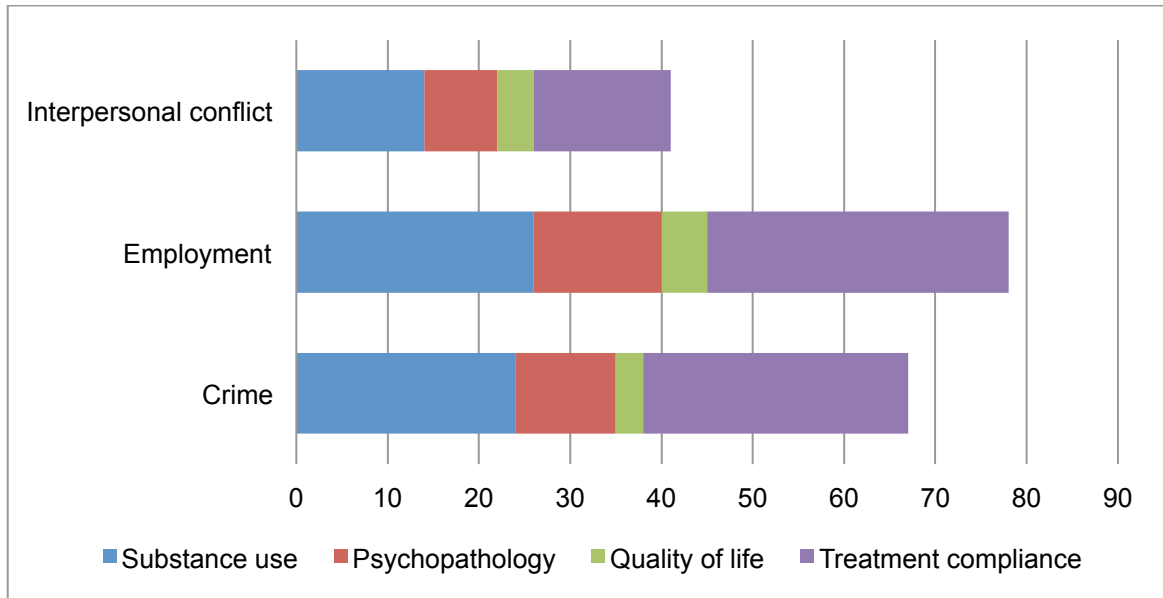
Figure 2.8.5 Statistical analyses of the association between social factors and methadone maintenance treatment outcomes in published studies.
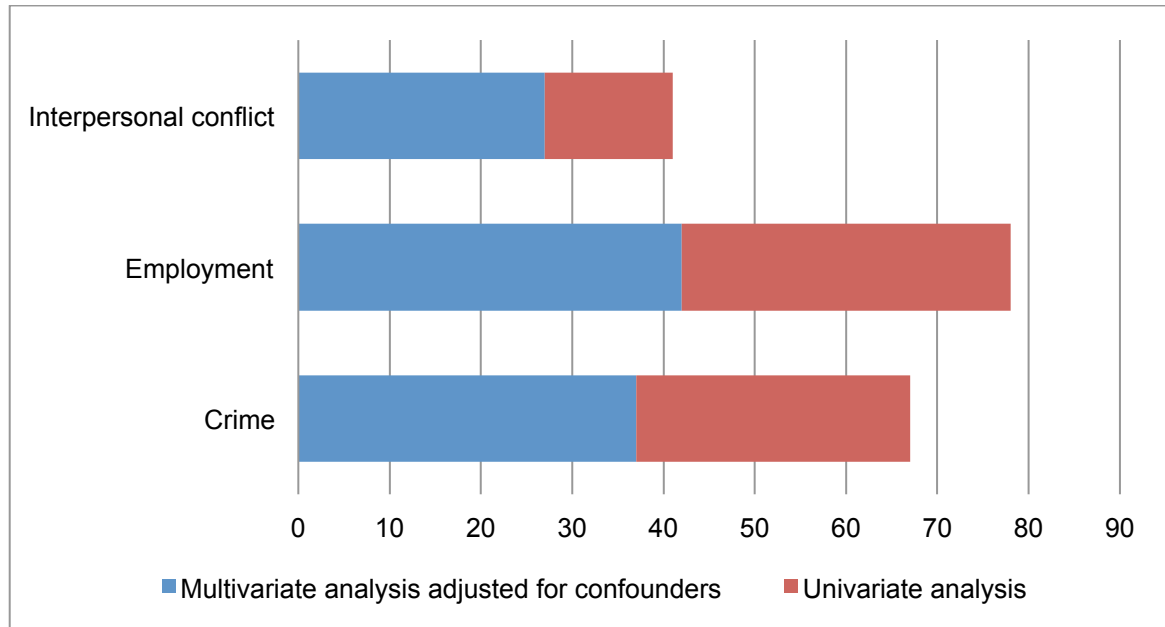
Figure 2.8.6 Trend in published studies on social factors and methadone maintenance treatment outcomes in the United States and Canada.
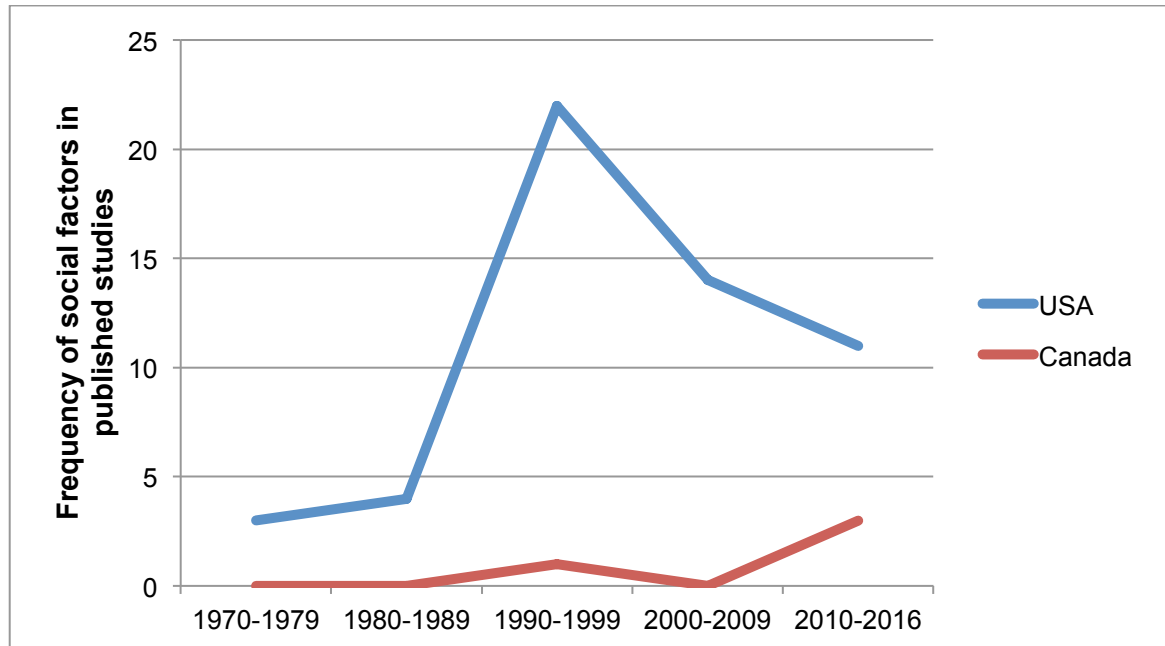
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CHAPTER 3

Study 2:

Association between social factors and continued opioid use among patients in methadone maintenance treatment: Results from a multicentre cohort study

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Competing interests: None to declare.

3.1 ABSTRACT

Background: Methadone maintenance treatment (MMT) is a widely prescribed treatment for opioid use disorders, yet there is significant variability in treatment outcomes. Social dysfunction is prevalent among MMT patients and may be implicated in treatment response. This study aims to determine the association between social factors and continued opioid use during MMT.

Methods: We conducted a multicentre, prospective cohort study of MMT patients in Ontario, Canada. We used multivariable logistic regression analyses to determine whether interpersonal conflict, criminal activity and employment status were associated with continued illicit opioid use at baseline entry to the study and three-month follow-up.

Results: We enrolled 1043 participants of mean age 38.4 years and 45.8% female. At baseline, criminal activity (odds ratio [OR]=2.61, 95% confidence interval [CI]=1.43–4.74) and interpersonal conflict with friends (OR=1.06, 95% CI=1.01–1.11) were associated with continued opioid use, while legal employment (OR=0.73, 95% CI=0.56–0.97) decreased odds of continued opioid use. At three-month follow- up, interpersonal conflict with friends remained significantly associated with continued opioid use (OR=1.06, 95% CI=1.01–1.12).

Interpretation: Criminal behaviour and interpersonal conflict with friends were associated with concurrent opioid use, while legal employment was associated with decreased odds of opioid use. Interpersonal conflict with friends was predictive of opioid use in the following three months. It is important to further assess peer groups of patients in MMT programs to determine whether it is beneficial to provide group treatment for

high-risk peer groups and identify tailored treatment approaches for patients who

continue to abuse opioids during treatment.

3.2 INTRODUCTION

The misuse of opioids is a serious global health concern, with opioid overdose being the predominant cause of drug-related mortality worldwide (1). Prescription opioids are highly liable for misuse, confirmed by evidence showing that 5.2% or 243,000 Canadians prescribed opioid pain relievers reported abusing them (2). Problematic patterns of opioid use often progress into opioid use disorder (OUD), a psychiatric disorder associated with severe individual and societal consequences, including increased criminal activity, psychiatric comorbidity, and mortality (3). Given the magnitude of this crisis, effective prevention and treatment strategies for OUD could provide significant social, healthcare, economic and personal benefits.

A recent world report concluded that prescription opioids are the most commonly abused substance, yet no 'gold standard' treatment has been established for OUD (4). Methadone maintenance treatment (MMT) is most commonly prescribed therapy for OUD in Canada (5, 6). While MMT has shown effectiveness (7), variability exists in treatment response and several patients continue to experience social issues, such as dysfunction within interpersonal relationships, unemployment, and continued criminal activity (8-15). Furthermore, a number of patients continue to use illicit opioids during treatment which, in combination with methadone, poses a major risk for overdose and death (16). Social dysfunction during MMT is related to poor psychological functioning, decreased quality of life, and poor treatment retention (11, 17). Identification of social risk factors for illicit opioid use during MMT will aid in the development of prevention strategies.

Much of the work examining social risk factors for MMT outcomes was conducted over a decade ago. However, there has been a shift in demographics within the MMT patient population, corresponding to the rise in prescription opioid rather than heroin use (18, 19). This change suggests different social factors may be implicated in MMT response; therefore it is important to characterize this association within a current sample of patients. This research will help identify aspects of MMT that must to be modified to meet the needs of current patients. This study aims to determine the association between social factors – interpersonal conflict with partners, family and friends, employment status and criminal activity – and illicit opioid use among adults with OUD enrolled in MMT programs.

3.3 STUDY DESIGN AND METHODS

3.3.1 Study Design & Recruitment

This study was approved by the Hamilton Integrated Research Ethics Board (HIREB; Study ID 11–056). Data were collected as part of the GENetics of Opioid Addiction (GENOA) research collaborative between the Population Genomics Program (PGP) at McMaster University and Canadian Addiction Treatment Centres (CATC). The CATC assesses opioid dependence according to DSM-IV criteria and provides treatment through daily, supervised methadone doses and medical follow-up visits. Detailed study methods for GENOA have been reported previously (20). GENOA has since expanded to include 17 clinics providing opioid substitution treatment.

Trained research personnel screened and recruited patients attending CATC for treatment of OUD using a consecutive sampling approach. To be included, patients had to be adults (≥18 years of age) receiving MMT and provide written informed consent. At the time of the study, methadone was the most widely prescribed opioid substitution treatment in Ontario and methadone services were covered under the Ontario Health Insurance Plan and Ontario Drug Benefit Plan, whereas other treatments such as buprenorphine/naloxone (trade name: Suboxone®) might have incurred additional costs. As such, there may have been socioeconomic differences between patients receiving methadone and Suboxone® treatments hence, the MMT inclusion criterion.

After providing written informed consent, participants underwent a structured baseline interview to collect information about demographics, medical and psychiatric comorbidity, clinical history and current treatment details. At the time of baseline

assessment, participants had been enrolled in MMT for varying lengths of time. Therefore we refer to 'baseline' as the start of the study recruitment. Research personnel also administered the Maudsley Addiction Profile (MAP) to assess multiple life domains such as frequency of substance use, personal and social functioning and health risk behaviours. The MAP questionnaire measures functioning across various domains related to addiction such as illicit substance use, physical and psychological health symptoms, social functioning, and health risk behaviours (22). It has shown adequate validity and reliability among MMT patients.

3.3.2 Social factors

For the present study, we used the MAP to assess social functioning at baseline and examine its association with continued illicit opioid use. The social functioning domain measured interpersonal conflict, employment, and criminal activity. For each variable, the frequency of occurrence was measured for the 30 days prior to baseline based on self-reports. Interpersonal conflict was defined as the number of days when "major arguments, verbal abuse, or violence" occurred with intimate partners, family, and friends. Criminal activity was defined as selling drugs, fraud/forgery, shoplifting, and theft from property or vehicle and was dichotomized to reflect any crime or no crime. Employment was defined as lawful work at the time of the interview.

3.3.3 Illicit opioid use

Illicit opioid use was the primary outcome of this study and was measured by once or twice weekly qualitative and semiquantitative urine analysis using the iMDx™ Analyzer and Prep Assay (NOVX Systems Inc, Richmond Hill, Ontario, Canada), as per

CATC protocol. The cut-off concentrations for detection by urinalysis were 300 ng/ml for opiates and 100 ng/ml for oxycodone. Urine samples were obtained and analyzed by trained clinic staff at the methadone clinic sites.

In this study, illicit opioid use was assessed as a binary outcome of any positive urine drug screens. Illicit opioid use was measured at baseline assessment (positive urine screens during three months prior to baseline interview) and at 3-month follow-up (positive urine screens three months prior to follow-up). The outcome was dichotomized to identify predictors of abstinence in this sample, as the combination of daily methadone dosing and continued opioid use could compromise patient safety. We included 1038 participants. Of these, 814 participants completed three-month follow-up with urine toxicology data. We did not conduct imputation for missing data, as missing data were not due to loss to follow-up but because participants had not yet reached the three-month follow-up point in the study.

3.3.4 Statistical Analysis

Study data were collected and managed using REDCap electronic data capture software (21). Descriptive statistics were reported to summarize demographic characteristics for the total sample. Continuous variables were reported as mean (standard deviation) and categorical variables as number (percentage).

We conducted multivariable logistic regression analyses to examine the association between the social factors and illicit opioid use, adjusting for age, sex, methadone dose and treatment duration. The first logistic regression model examined the baseline association between social factors and illicit opioid use, whereas a second model

examined the longitudinal association between social factors at baseline and illicit opioid use at 3-month follow-up. Multi-collinearity was assessed using the variance inflation factor (VIF), and variables with VIF>10 were excluded from the analysis. The Hosmer-Lemeshow test was used to assess the goodness-of-fit of the regression model. We reported adjusted odds ratios (OR), 95% confidence intervals (CI), and p-values from the regression models. The level of significance for hypothesis testing was set at alpha=0.05.

Logistic regression requires a minimum of 10 events per independent variable in order to achieve model stability (23). We included 9 independent variables in each regression model. The logistic regression model at baseline had 563 events (any positive opioid urine screens), and 422 events at follow up, indicating that there were an adequate number of events per variable.

All analyses were performed using Stata Version 13 (StataCorp LP, College Station, USA). We reported this study in accordance to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (24).

3.4 RESULTS

3.4.1 Baseline Demographic & Clinical Characteristics

A total of 1043 participants were included in the study. Table 1 provides an overview of participant characteristics. The mean age of the total sample was 38.4 years (SD=11.06) and about half of the participants were women (45.8%).

3.4.2 Social Factors and Illicit Opioid Use at Baseline

Results from the multivariable logistic regression models are presented in Table 2. Results showed a significant association between past-month criminal activity and illicit opioid use (OR = 2.61, 95% CI: 1.43-4.74, p=0.002). We also found a significant association between interpersonal conflict with friends and illicit opioid use (OR = 1.06, 95% CI: 1.01-1.11, p=0.024). Being legally employed was a protective factor, decreasing odds of illicit opioid use during treatment (OR = 0.73, 95% CI: 0.56-0.97, p=0.028). Interpersonal conflict with partners and family were not significantly associated with illicit opioid use (Table 2).

3.4.5 Social Factors and Illicit Opioid Use at Three-month Follow-up

Upon including the same social factors in the logistic regression model and assessing illicit opioid use at three-month follow-up, we found that interpersonal conflict with friends remained significantly associated with illicit opioid use (OR = 1.06, 95% CI: 1.01-1.12, p=0.023) whereas criminal activity (OR = 1.23, 95% CI: 0.67-2.26, p=0.499) and employment status (OR = 0.87, 95% CI: 0.64-1.19, p=0.392) no longer showed a significant association. Interpersonal conflict with partners and family were not significantly associated with illicit opioid use at three months (Table 2).

3.5 DISCUSSION

Findings from this study indicate that select social factors are associated with illicit opioid use in MMT, after controlling for age, sex, methadone dose and duration of treatment. Criminal activity at baseline more than doubled the odds of concurrent illicit opioid use but did not predict future opioid use. Employment at baseline was associated with a 27% decrease in odds of concurrent illicit opioid use. Additionally, we found that each additional day of interpersonal conflict with friends was associated with a 6% increase in odds of illicit opioid use both at baseline and three-month follow-up. We did not find that interpersonal conflict with friends or family were related to illicit opioid use at baseline or three-month follow-up.

To our knowledge, this is the largest prospective study investigating social factors and continued illicit opioid use in MMT patients within Canada. Other large studies have primarily assessed predictors of retention in treatment. While retention remains an important outcome of MMT, it is also important to identify risk factors for illicit opioid use during MMT – particularly social factors which may be modifiable with additional social support and counseling services. It is important to use the results of these studies to make comparisons with research in current MMT populations, given the shift in demographics among these patients associated with the growing burden of prescription opioid abuse. Our findings related to criminal activity and opioid use at baseline are aligned with the literature showing that criminal behaviour increases the risk of polysubstance use (25) and dropout from treatment (26-28). However, other studies examining continued opioid use (29, 30, 31) and retention in treatment (31) show no

association with criminal behaviour. Findings may be conflicted due to previous studies utilizing different definitions of criminal behaviour and differences in laws and regulations based on the study location. Our findings suggest that criminal activity is not significantly associated with opioid use at three months, such that criminal behaviour occurs concurrently with opioid use but does not predict future opioid use in MMT. It is likely that criminal activity involved selling opioids or theft of resources or money for purposes of obtaining opioids.

Considerable research has been conducted on intimate partner violence (IPV) among MMT patients (9, 10, 32-35), yet research on interpersonal conflict with friends or general social circles has been less prominent in relation to treatment outcomes. Results from this study show that interpersonal conflict with friends is associated with illicit opioid use at baseline and the following three months. Studies investigating conflict with friends exhibit inconsistency in findings, such that some studies show decreased treatment retention and poor psychiatric outcomes among MMT patients (36, 37), while others show no effect on psychopathology or substance use (38, 39). Conflicts between friends may be associated with opioid use if they occur as a means of obtaining opioids from friends (e.g. if participants consider drug dealers to be friends). Research shows that opioid users in treatment who surround themselves with substance-using friends are more likely to be coerced into using substances themselves (40). Our study also found a significant protective effect of legal employment on opioid use, though the literature examining employment status as a predictor of MMT response is largely conflicted. While some studies have also found employment to be a protective factor for MMT

outcomes (29, 41), most have found no association (26, 27, 31, 42, 43). Our study did not find a significant association between partner or family conflict and illicit opioid use in a large sample. The literature shows that women victimized by IPV are at higher risk of poor outcomes in MMT (32) and so it may be important to look at sex differences in this association. Studies among heroin users from East Asian countries have shown that family conflict is related to concurrent heroin use and lower treatment adherence (39, 44), while other studies have shown no significant association with polysubstance use (30) and treatment retention (26, 31). However, it is important to consider that these social factors may be related to other MMT outcomes, such as polysubstance use, psychological functioning and quality of life. If social factors influence multiple MMT outcomes, development of tools for screening social factors in clinical settings (i.e. interpersonal violence) may help identify those at risk of poor treatment outcomes to provide targeted interventions.

3.5.1 Limitations

Though steps were taken to reduce bias within the study, it is important to note the limitations of this study design. Biases may have occurred in the study due to self-reported measurements of social factors. Participants may have differently recalled interpersonal conflict or criminal activity although trained research personnel defined the variables during the interview. This may have resulted in systematic error if participants who experienced severe forms of interpersonal conflict were able to recall the incidents more easily. Due to the seriousness of the topics, participants may also have underreported criminal activity as well as interpersonal conflict. However, a validated

questionnaire was used in place of objective measures for a broad assessment of social issues, all of which may not have been captured by criminal records. As well, employment was measured at baseline to assess opioid use at three-month follow-up and we did not adjust for those who may have lost their employed position at three-months. The study was also limited in that we were not able to gather data for all participants at three-month follow-up. Nonetheless, we showed an adequate number of events per variable to conduct the analysis at three months with the available data.

3.6 CONCLUSIONS

In examining the association between social factors and illicit opioid use at baseline and three-month follow-up, we found that criminal activity is associated with concurrent illicit opioid use and legal employment is associated with decreased odds of concurrent opioid use, whereas neither variable predicts continued opioid use at three months. We also found interpersonal conflict with friends to be associated with concurrent opioid use as well as predictive of opioid use in the following three months. Future research should investigate the dynamics within friend groups of those who continue to use illicit opioids during MMT. If friend groups play a major role in continuing opioid use, it may be important to involve close friends in treatment programs utilizing similar approaches to family counseling. Additionally, it is important to further examine the positive effects of employment on MMT patients by implementing employment counseling programs and increasing access to employment for MMT patients. Our study shows that social factors play an important role in treatment response within a current MMT sample, consisting of both heroin and prescription opioid users. Future studies should investigate social factors in diverse MMT samples and prioritize the inclusion of Indigenous peoples to assess differences in social determinants of MMT outcomes. This can allow healthcare professionals to develop cost-effective and tailored treatment options to improve social circumstances and increase successful treatment outcomes.

3.7 ACKNOWLEDGEMENTS, FUNDING, AND AUTHOR CONTRIBUTIONS

3.8 FIGURES AND TABLES

Figure 3.8.7 Flow diagram of participant screening process
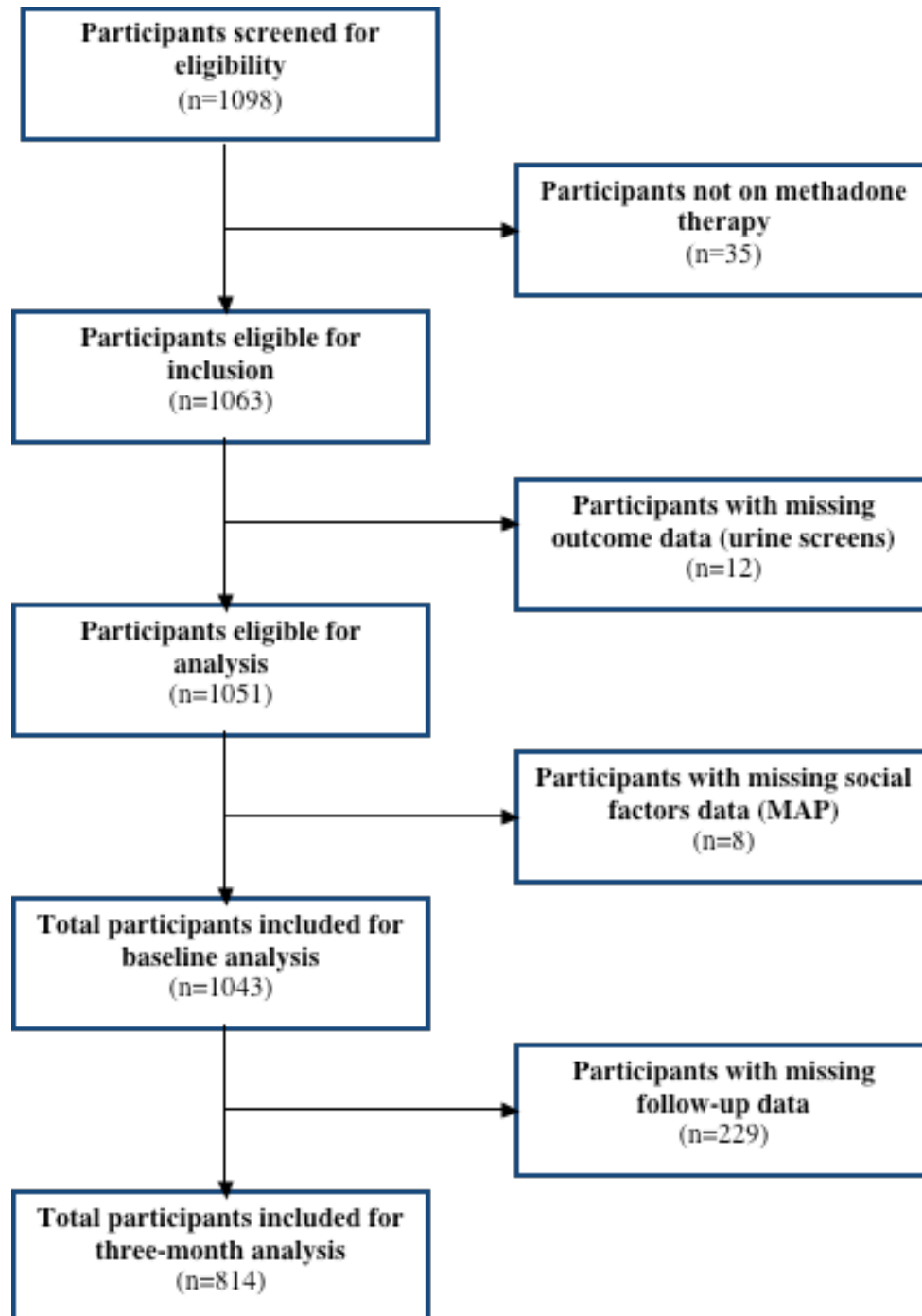
Table 3.8.1 Baseline participant characteristics based on opioid urine toxicology

	Total sample (n=1043)	Any opioid-positive urine screens (n=560)	No opioid-positive urine screens (n=483)
Demographic Characteristics			
Age, years; mean (SD)	38.31 (11.05)	37.41 (10.40)	39.36 (11.68)
Sex: female; n (%)	477 (45.73)	256 (45.71)	221 (45.76)
Ethnicity: Caucasian; n (%)	863 (83.38)	472 (84.89)	391 (81.63)
Marital status; n (%)			
Never married	482 (46.21)	265 (47.32)	217 (44.93)
Married/Common law/Living with partner	327 (31.35)	170 (30.36)	157 (32.51)
Widowed/Separated/Divorced	234 (22.44)	125 (22.32)	109 (22.57)
Education; n (%)			
Less than high school	227 (21.74)	140 (25.04)	87 (18.16)
High school	514 (49.71)	263 (47.05)	251 (52.40)
Trade school/College/University	297 (28.54)	156 (27.91)	141 (29.44)
Smoking status: current smoker; n (%)	884 (84.76)	498 (88.93)	386 (79.92)
Clinical Characteristics			
Age of onset of opioid abuse, years; mean (SD)	25.10 (8.74)	24.80 (8.44)	25.45 (9.06)
Prescribed by physician at onset; n (%)	487 (46.78)	257 (46.06)	230 (47.62)
Methadone dose, mg/day; mean (SD)	73.70 (44.47)	68.22 (42.52)	80.08 (45.86)
Treatment duration at baseline, years; mean (SD)	3.92 (4.03)	3.15 (3.78)	4.82 (4.12)
Opioids initially obtained by physician prescription; n (%)	487 (46.78)	257 (46.06)	230 (47.62)
Social Characteristics			
Employment status: currently working; n (%)	357 (34.23)	181 (32.32)	176 (36.44)
Interpersonal conflict, days; mean (SD)			
Partner	2.20 (6.09)	2.51 (6.69)	1.83 (5.29)
Family	1.63 (4.89)	1.73 (5.13)	1.52 (4.60)
Friend	0.71 (3.40)	0.98 (4.11)	0.41 (2.30)
Criminal activity, days; n (%)	68 (6.52)	52 (9.29)	16 (3.31)

SD: standard deviation
Notes: Number (percentage) is reported over the total number of participants for whom data is available for each variable. Social characteristics were measured in the 30-day period prior to baseline assessment.

Table 3.8.2 Results from multivariable logistic regression analysis for illicit opioid use at baseline and three-month follow-up.

Predictor	Odds Ratio	95% Confidence Interval	P-Value
Interpersonal conflict with partner			
Baseline	1.01	0.99 – 1.04	0.219
Three-month follow-up	1.02	0.99 – 1.05	0.169
Interpersonal conflict with family			
Baseline	1.00	0.97 – 1.03	0.971
Three-month follow-up	1.01	0.98 – 1.04	0.428
Interpersonal conflict with friend(s)			
Baseline	1.06	1.01 – 1.11	0.024*
Three-month follow-up	1.06	1.01 – 1.12	0.023*
Employment status: currently working			
Baseline	0.73	0.56 – 0.97	0.028*
Three-month follow-up	0.87	0.64 – 1.19	0.392
Criminal activity: present in past month			
Baseline	2.61	1.43 – 4.74	0.002*
Three-month follow-up	1.23	0.67 – 2.26	0.499
Age			
Baseline	1.00	0.99 – 1.01	0.857
Three-month follow-up	0.99	0.98 – 1.01	0.269
Sex: female			
Baseline	0.95	0.73 – 1.23	0.685
Three-month follow-up	1.09	0.81 – 1.46	0.565
Methadone dose			
Baseline	1.00	0.99 – 1.00	0.008*
Three-month follow-up	1.00	0.99 – 1.00	0.009*
Duration of treatment			
Baseline	0.90	0.87 – 0.93	<0.0001*
Three-month follow-up	0.93	0.89 – 0.97	<0.0001*

*significant at p<0.05
N (baseline): 1038
N (3-month follow-up): 813

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CHAPTER 4
Study 3:
Profile of suicide attempts and risk factors among psychiatric patients:
A case-control study

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4.1 ABSTRACT

Background: Suicidal behaviour remains challenging for clinicians to predict, with few established risk factors and warning signs among psychiatric patients.

Aim: We aimed to describe characteristics and identify risk factors for suicide attempts among patients with psychiatric disorders.

Methods: Multivariable logistic regression analysis, adjusted for clinically important confounders, was employed to determine risk factors for suicide attempts within a psychiatric patient population.

Results: The case (n=146) and control groups (n=104) did not differ significantly with regards to sociodemographic characteristics. The majority of the participants who had attempted suicide did so with *high* intent to die, and expected to die without medical intervention. The primary method of attempt was pharmaceutical overdose in 72.26% of patients. Individuals attempting suicide were not significantly different from the control group on sociodemographic characteristics. Results showed impulsivity (odds ratio [OR]=1.16, 95% confidence interval [CI]=1.03–1.30) and borderline personality symptoms (OR=1.06, 95% CI=1.00–1.12) were significantly associated with attempted suicide.

Conclusions: Our findings indicate that known risk factors for suicide may not apply within psychiatric populations. Prevention strategies for suicidal behaviour in psychiatric patients should focus on restriction of means available for suicide attempts such as pharmaceutical substances and target screening for high-risk personality and impulsivity traits.

4.2 INTRODUCTION

Suicidal behaviours are complex and can be challenging to foresee even among patients receiving medical and psychiatric care (1, 2). Suicide is the second leading cause of death among 15-29 year olds worldwide (3), with an even greater prevalence of non-fatal suicidal behaviour (4). Attempted suicide, defined as self-harm behaviour with intent to die (5), may occur up to 20 times more frequently than completed suicide (4, 6). Attempted suicide is associated with adverse, long-term outcomes, including psychiatric and medical comorbidity, hospitalization, repeated suicide attempts, poverty, chronic stress, and stigma (7, 8). Considering the personal and public health burden of suicide on global and local scales, it is necessary that preventive and rehabilitative strategies be developed to manage those presenting with suicidal behaviour.

While individuals with psychiatric illnesses represent the vast majority of the individuals who attempt suicide (4), only a small proportion of those with psychiatric illnesses attempt suicide. Known risk factors for suicidal behaviours are largely based on studies of general community populations and include prior suicide attempts, underlying psychiatric and substance use disorders, single marital status, unemployment, and major life stressors (8-12). However, reliable predictors of suicidal behaviour among populations with serious psychiatric disorders remain elusive. Wide-scale screening of psychiatric patients has been suggested as a method of early detection of suicidal behaviour (13), although feasibility greatly limits the ability to comprehensively screen all patients. Some studies have examined suicidal risk factors among patients with specific psychiatric disorders (14-16), yet suicidal risk factors among broad psychiatric

populations who typically presenting to clinical settings, including patients with multiple psychiatric diagnoses, are not yet clearly established. Defining high-risk psychiatric populations will allow clinicians to effectively screen patients for suicidal behaviour.

Moreover, given the difficulties of identifying those at risk of suicide from populations of psychiatric patients, identification of warning signs and behaviours associated with suicide among psychiatric patients can aid in suicide prevention. Patterns and behaviours associated with suicide attempts are important to characterize within psychiatric populations, in order to distinguish individuals in this group who attempt suicide from those with no history of suicide attempts. Identifying trends in behaviours, and methods of suicidal attempts, will aid in the movement towards developing large-scale suicide prevention methods.

The present study aimed to 1) describe the trends and circumstances associated with suicide attempts and 2) investigate risk factors of suicide attempts among adult inpatients with psychiatric disorders.

4.3 STUDY DESIGN AND METHODS

The participants and data used in this investigation were collected for the Study of Determinants of Suicide Conventional and Emergent Risk (DISCOVER) (17), a case-control study designed to investigate risk factors of attempted suicide. Participants were recruited between March 2011 and November 2014 in Hamilton, Ontario, Canada. Data were collected at St. Joseph's Healthcare and Hamilton Health Sciences hospitals. The study was approved by the Hamilton Integrated Research Ethics Boards (HIREB) (REB number 10-661 for St. Joseph's Healthcare Hamilton and 11-3479 for Hamilton Health Sciences Hospitals).

We included adults (≥ 18 years of age) who were able to provide written informed consent, communicate in English, and who were willing to follow study procedures. Figure 1 defines case and control groups and outlines the recruitment process. Cases included psychiatric inpatients who had made a suicide attempt, defined as self-directed injury with specific intent to die and that necessitated admission to a medical or psychiatric hospital ward. We had initially intended to recruit psychiatric inpatients who had made a suicide attempt within three months of recruitment (case-recent group). However, given the challenges of recruiting this particular patient population, we also included psychiatric inpatients who had a lifetime history of attempted suicide (case-past group). The control group matched by sex and age within 5 years to the cases consisted of adult psychiatric inpatients who had never attempted suicide and who were admitted to the same psychiatric hospital within the same time frame as the cases.

Potentially eligible inpatients were consecutively approached by trained research staff who inquired about their interest in participating in the study and provided study information. Patients who agreed to participate were asked to provide written informed consent. Research assistants conducted a structured face-to-face interview consisting of validated questionnaires. Participants were asked about sociodemographic characteristics including age, sex, education and socioeconomic status. We assessed intention to die as a result of the suicide attempt by asking the participants directly and the Pierce Suicide Intent Scale (18) was used to assess the level of intent associated with cases' most recent suicide attempt. Participants completed the 30-item Barratt Impulsiveness Scale (BIS) (19) to assess trait impulsivity and the 23-item Borderline Symptom List (BSL) (20) to assess borderline personality symptoms. The Mini International Neuropsychiatric Interview (M.I.N.I.) (21) was administered to assess the presence of psychiatric disorders.

STATA version 13 was used to perform all statistical analyses. For univariate analyses we used independent sample t-tests to compare means of continuous variables and chi-square tests to compare proportions of categorical variables between cases and controls. Non-parametric equivalents (i.e. Mann-Whitney-U tests) were used for continuous variables that were not normally distributed. Fisher's exact test was used to compare categorical variables that had an expected frequency of less than 5 in a particular cell. Simple Pearson's correlations were used to assess the linear relationship between two normally distributed variables and Spearman correlations were used for non-normally distributed variables. Multivariable logistic regression analysis was utilized to assess clinical risk factors associated with suicidal attempts, by comparing cases to controls.

Impulsivity (BIS) and borderline symptom (BSL) scores were inputted into the regression model as four-point increases in scores, which provided more meaningful results than a one-point increase on the questionnaires. We used a four-point interval because it was representative of an additional impulsive trait or borderline symptom on the questionnaires. The Hosmer-Lemeshow test was used to assess the goodness-of-fit of the regression model. The level of significance was set at alpha= 0.05, and we included clinically important variables based on the literature regarding psychiatric populations in the logistic regression model (14-16, 22). The reporting of this study is in accordance with the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) guidelines (23).

4.4 RESULTS

4.4.1 Study sample characteristics

The final sample comprised 250 individuals, including 146 psychiatric inpatients who had attempted suicide (cases) and 104 psychiatric inpatients who had never attempted suicide (controls). Figure 1 displays the number of individuals approached for recruitment and included in the final sample as well as the reasons for exclusion. The sociodemographic characteristics of the case and control groups are summarized in Table 1. The mean age of the case group was 45.18 years (standard deviation (SD) = 14.70 years, range 18-73 years) and the control group was 45.01 years (SD=14.23 years, range 18-82 years). The sample consisted of an approximately equal proportion of males and females (55% females in the case group, 50% females in the control group). In the univariate analysis, there were no significant differences in sociodemographic factors between cases and controls (p-values >0.05). The case group scored significantly higher on both BSL (p=0.0002) and BIS (p=0.0001) personality measures.

Psychiatric diagnoses were assessed using the M.I.N.I for 211 participants and we reviewed medical records of 20 participants with missing M.I.N.I data to determine the psychiatric diagnoses. Psychiatric diagnosis information was missing for 19 participants. Table 2 presents psychiatric diagnoses for the case and control groups. Total numbers are not reported, as a number of participants were diagnosed with multiple psychiatric disorders. Antisocial personality disorder (ASPD) was significantly more common among those who attempted suicide than among psychiatric controls (χ^2 =16.13, degree of freedom = 1, p < 0.0001). There were 20 participants in the case group and no

participants in the psychiatric control group with an ASPD diagnosis. There were no univariate differences in prevalence of mood disorders, anxiety disorders, psychotic disorders or substance use disorders among individuals who had attempted suicide compared to controls.

4.4.2 Objective 1: Description of suicidal attempts and associated circumstances

Tables 3 and 4 summarize the methods and details of the suicide attempts (Pierce Suicide Intent Scale, P-SIS). The majority of individuals attempted suicide by means of pharmaceutical overdose/pills (72.26%). Other methods included cutting (11.68%), hanging (5.15%), firearms/explosives (2.19%), and suffocation (2.19%). Certain participants also reported using multiple methods of attempting suicide.

The P-SIS assessed suicidal intent associated with an attempt based on circumstantial factors (e.g. alcohol consumption, suicide note), self-reported factors (e.g. patient's beliefs regarding the lethality of the attempt), and medical risk (e.g. objective likelihood of death) (Table 4). The P-SIS scored individuals as having low, moderate, and high intent to die as a result of the suicide attempt. According to P-SIS scores, 80.18% of the individuals who attempted suicide in our sample did so with high intent to take their lives. Furthermore, 62.70% of the participants who attempted suicide believed that they would have died from the attempt and more than half of the individuals were objectively assessed as high risk of death. Additionally, 47.69% of participants reported feeling glad that they had recovered since the attempt.

4.4.3 Objective 2: Risk factors for attempted suicide

A multivariable logistic regression model was used to determine factors associated with increased risk of attempted suicide. The model was adjusted for age, sex and smoking status. Furthermore, variables were included in the model based on clinical importance and significant findings in the literature among similar psychiatric samples (22). Diagnoses of mood disorders, psychotic disorders and substance use disorders were included, as well as personality measures, such as impulsivity and borderline personality symptom scores.

The regression model demonstrated a statistically significant association between impulsivity and attempted suicide (odds ratio (OR) 1.16, 95% confidence interval (CI) 1.03-1.30, p = 0.01), as well as borderline symptoms and attempted suicide (OR 1.06, 95% CI 1.00-1.12, p = 0.03) (Table 5). The results suggest that a four-unit increase on the BIS is associated with 16% increase in odds of attempted suicide, and a four-unit increase on the BSL was associated with 6% increase in odds of attempted suicide.

4.5 DISCUSSION

We sought to summarize characteristics and behaviours of adults associated with suicide attempts, which may help classify factors influencing suicidal behaviour in a clinical setting. We further aimed to make comparisons between individuals who had attempted suicide and a control group of psychiatric inpatients with no history of suicide attempts to identify risk factors among a vulnerable population. Our study found that adult psychiatric patients who had attempted suicide did not significantly differ from the psychiatric control group on sociodemographic characteristics or psychiatric diagnoses. The case group showed higher prevalence of maladaptive personality measures such as impulsivity, borderline symptoms and diagnosis of antisocial personality disorder. Factors such as single marital status, unemployment and low education level were not significantly different between the case and control groups in this study, but have been reported as significant risk factors in studies comparing cases to community controls (4, 8, 9). These findings indicate that known risk factors of suicidal behaviour may not be applicable within psychiatric inpatient populations, further confirming the necessity of identifying risk factors within psychiatric patients.

4.5.1 Behaviours associated with suicide attempts and implications on prevention

Identification of trends and behaviours such as suicidal attempt methods, potential precautions against discovery, and feelings related to recovery may be helpful in elucidating warning signs and prevention strategies of attempted suicide within this challenging population. Within our sample, the most common method of suicide attempt was ingesting pills or pharmaceutical overdose (72.26%). This may have been due to

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greater accessibility to medications in this sample, considering that participants had psychiatric comorbidities, as well as a modest prevalence of self-reported chronic pain (29.4%) and alcohol (21.2%) or substance use disorders (13.6%). The literature shows that access to methods of suicide may increase the risk of completed suicides (24-27) and limiting access to lethal methods can be an effective prevention strategy (28). A large ecologic study on survey-based data from the United States found higher rates of firearm suicides in states with high gun ownership, while non-firearm related suicides were equal across the states (27). Similar results have been found in studies of adolescent suicides examining access to firearms in the household (29, 30). An analogous trend may follow among psychiatric populations with access to high doses of pharmaceutical drugs. Furthermore, research in the United Kingdom exploring restricted access to over-the-counter pain relievers found that changing legislation to reduce pack sizes and enforcing a limit in purchasable tablets led to significant decreases in documented overdoses of these drugs over the following years (25). These strategies may be important to consider among Canadian psychiatric populations as a recent study in Toronto found that among cases of completed suicides by overdose, prescription medications (including opioid analgesics and psychotropic drugs) were involved in the majority of suicides (31).

Examination of suicide attempt behaviours revealed that almost half (45.03%) of the individuals attempting suicide had somebody "present" and "nearby or in contact" at the time of the suicide attempt. Furthermore, more than half (52.34%) the individuals who attempted suicide took no precautions against discovery. This demonstrates the importance of educating the families and friends of at-risk psychiatric patients regarding

warning signs and communication strategies. We also found that a large proportion (80.00%) of individuals attempting suicide took no final actions in anticipation of death (i.e. settling of affairs), which has been previously reported as a warning sign for suicidal behaviour (13). Approximately one-quarter of the participants who had attempted suicide left a note. Studies of individuals who completed suicide report a widely varying proportion of suicide notes from 18% to 37% and show that youth are more likely to leave notes (32).

The current study sample also showed that most cases of suicide attempts had serious intent to die and the majority of patients believed that the attempt would lead to death. However, the proportion of individuals attempting suicide with high intent to die in this sample appears greater than other samples, in which half of the participants report that they had low intent to die or attempted as a "cry for help" (10). This finding may be related to the higher severity of psychiatric illness in this sample, since all participants were psychiatric inpatients. While the majority of participants reported high intent to die at the time of attempt, 47.69% of patients who had attempted suicide stated they were "glad that they recovered". Given that a history of attempted suicide is among the strongest predictors of completed suicide (3), it is important to conduct future research among individuals reporting ambivalence related to physical and psychological recovery, as this may play a role in the prevention of repeat suicide attempts.

4.5.2 Personality variables associated with increased suicide attempt risk

Trait impulsivity and borderline personality symptoms were statistically significant risk factors for attempted suicide, when compared to psychiatric controls.

ASPD was only present in the case group, with no participants in the control group were diagnosed with ASPD. We did not include ASPD diagnosis in the adjusted regression model because it was completely associated with a suicide attempt, such that only the case group presented with ASPD. Other studies have found a significant association between antisocial personality symptoms and increased risk of attempted suicide (8, 33). Within this sample of psychiatric patients including participants with multiple psychiatric diagnoses, mood disorders, substance use disorders, and psychotic disorders were not found to be significantly associated with attempted suicide. This may be due to the similar prevalence and high severity of psychiatric disorders in the case and control groups, since included participants were all hospitalized patients. Findings regarding impulsivity and borderline personality symptoms are consistent with previous studies of psychiatric populations (34, 35), though some of these studies were conducted among patients with specific psychiatric disorders, such as major depression (36) or bipolar disorder (37).

Interestingly, trait impulsivity was associated with increased odds of attempted suicide yet no significant correlation was found between trait impulsivity and the self-reported impulsiveness of the suicide attempt itself. These findings suggest that trait impulsivity may not necessarily drive individuals to make impulsive suicide attempts. Baca-Garcia et al. found similar results when exploring the relationship between trait impulsivity and suicide attempt impulsivity (38). This may have clinical implications in increasing the feasibility of suicide attempt prediction among psychiatric patients, given the challenges associated with prevention of impulsive attempts. Additionally, these

findings indicate that development of clinical screening tools for trait impulsivity among psychiatric patients may be important in suicide attempt prevention.

4.5.4 Limitations

This study was limited by potential biases due to self-report measures as well as the case-control study design. Within the case group, the case-past group may have been differentially affected by recall bias related to the details of the suicide attempt. Furthermore, the cross-sectional design of the study did not allow us to determine the direction of the association risk factors and suicide attempts. For example, suicide attempts, particularly in the case-past group, may have occurred before the manifestation of borderline personality symptoms. However, it was expected that the measurement of trait impulsivity would remain fairly constant over time. Future prospective research among psychiatric inpatients is needed to identify factors than can be predictive of future suicide attempts. It is also important for future studies to collect information about specific pharmaceutical drugs or "pills" used to attempt suicide among psychiatric patients, as this may aid in developing prevention strategies.

4.6 CONCLUSIONS

Findings from this study indicate that those who attempt suicide may not differ significantly from psychiatric inpatients on sociodemographic factors such as unemployment, single marital status and living alone. Risk factors for suicide in this sample of psychiatric patients included impulsivity and borderline personality symptoms. A descriptive assessment of suicide attempts indicated that limiting access to methods of suicide and educating social supporters regarding behavioural trends may be effective suicide prevention strategies. Future qualitative research can identify themes associated with thought processes leading to suicide attempts and feelings related to recovery among high-risk psychiatric patients. Additionally, cohort studies among patients with serious psychiatric disorders (i.e. psychiatric inpatients) are needed to establish the temporal association between personality variables and attempted suicide and to further identify unique risk factors for suicide attempts in psychiatric populations.

4.7 ACKNOWLEDGEMENTS, FUNDING, AND AUTHOR CONTRIBUTIONS

4.8 FIGURES AND TABLES

Table 4.8.3 Study sample characteristics

	Cases (N=146)	Psychiatric Controls (N=104)	Univariate Test of Association
Age (years): mean (SD)	45.18 (14.69)	45.01 (14.23)	t= -0.09 df= 248 p =0.928
Sex: n (% female)	146 (55.48)	104 (50.00)	χ^2=0.73 df = 1 p=0.392
Education n (%)			
Elementary	8 (5.56)	8 (8.0)	χ^2=3.57 df=2 p=0.167
High-School	78 (54.17)	42 (42.00)	
Post-Secondary	58 (40.28)	50 (50.00)	
Employment Status n (%)			
Employed	34 (23.45)	33 (32.67)	χ^2=2.56 df=1 p=0.110
If Not Employed Then:			
Unemployed	29 (26.61)	21 (32.31)	χ^2=4.17 df=3 p=0.244
Retired	17 (15.60)	7 (10.77)	
On Disability	56 (51.38)	28 (43.08)	
On Social Security	7 (6.42)	9 (13.85)	
Marital Status n (%)			
Currently Married/Common Law/Live with Partner	39 (26.90)	31 (30.10)	χ^2=5.38 df=2 p=0.068
Never Married	45 (31.03)	43 (41.75)	
Widowed/Separated/Divorced	61 (42.07)	29 (28.16)	
Living Status n (%)			
Lives Alone	64 (46.38)	47 (46.08)	χ^2=0.0021 df=1 p=0.963
Doesn't Live Alone	74 (53.62)	55 (53.92)	
Smoking Status n (%)			
Current Smoker	59 (43.38)	35 (35.35)	χ^2=1.72 df=2 p=0.423
Former Smoker	34 (25.00)	26 (26.26)	
Never Smoked	43 (31.62)	38 (38.38)	
Personality Measures			
Borderline Symptom List Score: mean (SD)	65.03 (23.64)	53.23 (22.16)	t=-3.81 df=206 p=0.0002
Barratt Impulsivity Scale Score: mean (SD)	71.40 (12.03)	65.20 (10.23)	t=-4.14 df=213 p=0.0001

SD: standard deviation

Table 4.8.4 Psychiatric Disorders (DSM-IV Axis I Diagnosis)

	Cases, n	Controls, n	Univariate Test of Association
Mood Disorders	119	82	$\chi^2=1.68$ df=1 p=0.20
Anxiety Disorders	80	49	$\chi^2=2.36$ df=1 p=0.13
Antisocial Personality Disorder	20	0	$\chi^2=16.13$ df=1 p=<0.0001
Substance Use Disorders (including Alcohol Abuse/Dependence)	20	11	$\chi^2=0.71$ df=1 p=0.40
Psychotic Disorders	10	6	$\chi^2=0.17$ df=1 p=0.68

Notes: The total n is not in accordance with the sample size, as case and control participants were diagnosed with multiple psychiatric disorders.

Table 4.8.5 Method of suicide attempt

	n
Pills	99
Cutting	16
Hanging	7
Suffocating	3
Firearm/Explosive	3
Other*	9

*Other methods include alcohol consumption, starvation, intravenous drug use, and inducing collision.
Notes: The total n is not in accordance with the sample size, as some participants reported using multiple methods during the suicidal attempt.

Table 4.8.6 Suicide Intent Scale responses among case group

Suicide Intent Scale Question	n (%)
Circumstances (N)	
Did you drink alcohol at the time of attempt? (120)	
Yes	38 (31.67)
No	82 (68.33)
Isolation: Was anyone around at the time of attempt? (131)	
Somebody Present	25 (19.08)
Somebody Nearby or In Contact	34 (25.95)
No-One Nearby or In Contact	72 (54.96)
Timing: (118)	
Timed so that intervention is probable	38 (32.20)
Timed so that intervention is unlikely	38 (32.20)
Timed so that intervention is highly unlikely	42 (35.59)
Precautions against discovery: (128)	
No precautions	67 (52.34)
Passive precautions	26 (20.31)
Active precautions	35 (27.34)
Acting to gain help during or after attempt: (131)	
Notified helper regarding attempt	41 (31.30)
Contacted but did not specifically notify helper regarding the attempt	11 (8.40)
Did not contact or notify potential helper	79 (60.31)
Final acts in anticipation of death: settling of affairs (130)	
None	104 (80.00)
Partial preparation or ideation	13 (10.00)
Definite plans made (e.g. changes in will, taking out insurance)	13 (10.00)
Suicidal note: Was a suicidal note left? (130)	
No Note	95 (73.08)
Presence of Note	35 (26.92)
Self-Report (N)	
Patient's statement of lethality: Did you think that what you had done would kill you? (131)	
Thought that what he/she had done would not kill him or her	24 (18.32)
Unsure whether what she/he had done would kill him/her	25 (19.08)
Believed that what she/he had done would kill him/her	82 (62.60)
Stated intent: what was your intent at the time you made the attempt? (130)	
Did not want to die	2 (1.54)
Unsure	21 (16.15)
Wanted to die	107 (82.31)
Premeditation: did you consider attempting suicide prior to making the attempt? (130)	
Impulsive, no premeditation	47 (36.15)
Considered act for approx. 1 hour	7 (5.38)
Considered act for approx. 1 day	8 (6.15)
Considered act for more than 1 day	68 (52.31)
Reaction to act: how do you feel about the attempt now (130)	
Patient glad she/he had recovered	62 (47.69)
Patient uncertain whether she/he is glad or sorry	44 (33.85)
Patient sorry he she had recovered	24 (18.46)

Medical Risk (N)	
Risk predictable in terms of lethality of patient's act and circumstances known: (126)	
Survival certain	14 (11.11)
Death unlikely	33 (26.19)
Death likely or certain	79 (62.70)
Would death have occurred without medical treatment: (130)	
No	25 (19.23)
Yes	69 (53.07)
Uncertain	36 (27.69)

Notes: 'N' represents the total number of participants who responded to the question and 'n' represents the number of participants with a response to the specific question.

Table 4.8.7 Risk factors for attempted suicide: Multivariable logistic regression results (N=215)

Variables	Odds Ratio	95% Confidence Interval	P-value
Age (years)	1.01	0.98-1.03	0.64
Sex: Female	1.42	0.79-2.55	0.24
Smoking Status: Current Smoker	1.27	0.68-2.36	0.45
Mood Disorder Diagnosis	1.37	0.53-3.55	0.51
Psychotic Disorder Diagnosis	1.42	0.40-5.11	0.59
Substance Use Disorder Diagnosis	1.08	0.44-2.65	0.86
Borderline Symptom Score	1.06	1.00-1.12	0.03*
Barratt Impulsiveness Score	1.16	1.03-1.30	0.01*

*p-value<0.05

Notes: Age is interpreted as increase in one year. Borderline Symptom and Barratt Impulsiveness scores are interpreted as increases in four points on the questionnaires.

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CHAPTER 5

5.1 CONCLUDING REMARKS

5.1.1 Overview

Social dysfunction plays an important role in the development of mental illness and this thesis provides further evidence for the influence of social and behavioural factors on psychiatric outcomes. A comprehensive scoping review showed that social factors have largely been examined in relation to MMT outcomes within the United States, however there is a paucity of research in Canada after the rise of prescription opioid abuse. The changing demographic of MMT patients indicated the need for further research in Canada to establish the influence of social functioning on MMT outcomes. We conducted a large cohort study among adults in MMT in Ontario, Canada to explore this association and found that criminal activity and conflict with friends were associated with increased odds of illicit opioid use during treatment. However, legal employment was associated with decreased odds of opioid use. Of these social issues, only conflict with friends predicted opioid use at three months following entry to the study. Additionally, findings from our case-control study among patients hospitalized for psychiatric disorders showed that no sociodemographic factors were significantly associated with suicide attempts; however behavioural factors such as impulsivity and borderline personality symptoms were independent risk factors for attempted suicide within this sample. These findings

collectively add to the literature on the impact of social functioning on clinical outcomes among psychiatric patients in healthcare settings.

5.1.2 Social functioning and methadone maintenance treatment outcomes

Our comprehensive scoping review summarized research on social factors worldwide to inform the primary research question on the influence of social factors in a Canadian MMT program. The scoping review showed the majority of research was conducted on the association between social issues and treatment compliance, with less focus on harm reduction outcomes and lack of adjustment for confounders in statistical analyses. For the primary study, we employed a prospective cohort design and followed MMT participants for three months in treatment. For individuals maintained on methadone, we found that interpersonal conflict with friends measured at baseline increased the odds of continued opioid use at baseline and the following three months. Criminal activity was strongly associated with increased opioid use at baseline but this relationship was not significant at three months. Employment at baseline was related to decreased odds of illicit opioid use at baseline but was not significant at three months. It may be that criminal behaviour and distress in relationships with friends are a means of obtaining and using opioids. Given the overdose risk associated with daily methadone dosing and continued opioid use, it is important that these high-risk participants are monitored during treatment.

5.1.3 Sociodemographic and behavioural risk factors for attempted suicide

The case-control study that was conducted in this thesis compared a group of psychiatric inpatients with a history of attempted suicide to psychiatric patients with no history of suicide. Findings suggested no differences in sociodemographic characteristics between

the groups, which are considered to be important risk factors for suicide attempts within general non-clinical populations. Higher impulsivity and borderline personality symptoms significantly increased the risk of attempted suicide and may be important to monitor in clinical settings. Among the group of individuals who attempted suicide, we found pills to be the predominant method of suicide attempt. This finding may have implications for suicide prevention strategies, such as decreasing access to high quantities of medications among psychiatric patients. The importance of developing a national suicide prevention strategy has been emphasized by global organizations and further research among varying psychiatric samples is important to establish specific risk factors and warning signs.

5.1.4 Clinical implications and future directions

Studies included in this thesis determined that select social factors are associated with relapse to opioid use among OUD patients, while personality variables increase the risk of attempted suicide among psychiatric patients. Given these findings, it is important to conduct future research to further elucidate the role of these factors within these patient groups. Longitudinal studies among MMT patients can help understand the predictive effect of social dysfunction for various harm reduction outcomes, including polysubstance use, psychopathology and quality of life. Also among MMT patients, it is important to further explore the protective effect of employment to determine the benefit of programs directly increasing access to jobs. Case-control studies among psychiatric patients should investigate additional personality-related risk factors for suicide attempts and conduct sensitivity analyses for patients with a borderline personality disorder diagnosis in order to create a holistic suicide risk profile for psychiatric patients.

Considering that social factors are the basis of numerous health disparities, it is important to address and manage social issues by increasing access to psychosocial support and social services. Future studies can identify clinical tools to adequately monitor social issues and examine the effect of additional therapies for those experiencing social difficulties in treatment programs for addiction and psychiatric disorders. Among psychiatric patients, it may be useful to develop research tools into clinical instruments to measure behavioural factors (i.e. personality variables) to aid clinicians in identification of at-risk patients.

A key message from these projects is the importance of integrating social interventions into clinical settings to address mental health issues at their foundation. Understanding and management of social issues in healthcare settings can improve patient outcomes and reduce long-term medical costs.