Opioid drug abuse treatment-
Factors associated with opioid use type and retention in treatment

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Abstract

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The abuse of prescription type opiates is an emergent public health issue in Washington State and throughout the United States. Drug treatment admissions involving prescription type opiates as the primary drug of abuse have increased substantially in the past decade. However, the characteristics of this new patient population and their retention in treatment are poorly understood. This dissertation includes three research studies of clients in methadone maintenance treatment (MMT) programs in Washington State. The first study characterized the types of opiate users and found that those who use prescription type opiates only, predominately or equivalently to heroin are significantly more likely to have a chronic pain condition compared to those who reported only regular use of heroin when adjusting for other drugs used, demographic and social characteristics. The second study explored the impact of distance to treatment on 12 month retention and found that although primary prescription type opiate users lived significantly further from MMT their retention in treatment was not significantly different than for heroin users when adjusting for personal factors and controlling for the treatment agency in which they were served. The final paper found that prescription type opiate primary users do not have worse retention levels than heroin users when adjusting for other factors including demographics, stimulants usage, conduciveness of home to recovery, legal involvement and treatment agency utilized. In conclusion, prescription type opiate users do have significantly different characteristics than heroin users, however they have similar retention in MMT.

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CHAPTER 1
BACKGROUND AND MOTIVATION

Epidemiology of prescription type opiate abuse

Trends in prescription type opiate use, misuse and abuse

Prescription-type opiates may be legally used to treat pain or substance abuse, illegally for the affective state they may produce, or for both reasons. Prescription-type opiate use, abuse, morbidity and mortality have increased substantially over the past decade nationally (Gilson et al., 2004) and in the Seattle area (Banta-Green et al., 2007) . Heroin use and associated morbidity and mortality continue at moderately high levels, nationally (National Institute on Drug Abuse, 2006) and in the Seattle area (Banta-Green et al., 2008), relative to other drugs such as cocaine and methamphetamine.

Pain, a primary medical indication for opiate use, is common. Almost a quarter of U.S. adults reported moderate to extreme pain interference in the prior month according to a survey conducted in 2001 and 2002 (Wells et al., 2005). A large proportion of the population is prescribed opiates. An annual estimate of 65 million people were prescribed opiates in ambulatory care settings in 2000-2001 (Schappert and Burt, 2006) in the U.S.. Approximately 19% of adults covered by a major commercial insurer received at least one opiate prescription in 2005 (Von Korff et al., 2005).

Substantial increases in opioid use have been documented in Washington State and nationally in recent years. Substantial increases in the sale of several opioids to hospitals and pharmacies including hydrocodone (134% increase), oxycodone (464% increase) and methadone (577% increase) were seen throughout Washington State from 1997 through 2003, according to the DEA (Drug Enforcement Administration, 2004) . Regular users of prescription opiates were estimated to constitute 3% of adults in the U.S. in 2000-2001 (Wells et al., 2005).

The number and proportion of primary prescription type opiate users entering drug treatment has increased substantially throughout the United States from 0.9% (13,671) of all treatment admissions in 1992 to 4.2% (77, 780) in 2006 (Office of Applied Studies, 2008). In Washington State the number has increased more than 10 fold from 34 to 462 from 2001 to 2007 in publicly funded methadone maintenance treatment (MMT) clinics (Division of Alcohol and Substance Abuse, 2008). The estimated number of people initiating non-medical use of prescription pain medications increased significantly from 30,000 in 1999 to 79,000 in 2000 in Washington, as documented by the National Household Survey on Drug Abuse (Substance Abuse and Mental Health Services Administration, Office of Applied Studies, 2003). Drug caused deaths in which prescription type opiates were involved increased from 22 in 1997 in King County, WA to 148 in 2006 (Banta-Green et al., 2008). Mentions of prescription type opiates in emergency departments increased 114% in the greater Seattle area from 1997 to 2002 (Substance Abuse and Mental Health Services Administration, Office of Applied Studies, 2002).

Characteristics of problematic prescription type opiate users

Some of the better data on misuse of opiates include national surveys, drug treatment, and emergency departments though comparisons are severely limited by non-standardized definitions. The 2004 National Survey on Drug Use and Health reported the following characteristics of recent non-medical pain reliever use initiators ages 12 and older: 55% female, 75% white 28% family income more than $75,000 (Office of Applied Studies, 2005). 'Non-medical' use is a relatively low threshold of use indicating medicines were used for other than their intended purposes or did not belong to the user. They also reported that 13 percent had ever used cocaine, 0.7 percent heroin and 1.5% non-medical use of sedatives. Unfortunately they do not provide data tables which allow a comparison with other substances of abuse.

Factors associated with 'non-medical use of prescription opioid analgesics' in a large survey of college students included being white, male, and parents with a higher level

of education (McCabe et al., 2005). Note that parental education level is generally strongly associated with socioeconomic status.

Other studies have found associations between prescription type opiates and other substances including alcohol (McCabe et al., 2006), tobacco (Frosch et al., 2000) and other illicit drugs. It is critical to assess the population these data are drawn from as this impacts relationships between substances used. For instance, among pain patients prescribed opiates, a history of alcohol abuse has not been found to be associated with prescription opiate misuse (Schieffer et al., 2005).

Only recently have prescription opiates been explicitly included on many surveys. For instance in Washington State, 2006 was the first year that prescription opiates were a separate category for both the Healthy Youth Survey of school attendees and the student life survey at the University of Washington. An estimated 10% of 10^{th} graders reported any use of prescription type opiates 'to get high' in the past month (Banta-Green et al., 2007) and 6% of undergraduates reported any 'current' use of prescription type opiates 'not prescribed for you or … for the experience or feeling it caused' (McGhee and Lemire, 2006).

Data from 2005 for King County, Washington indicate that those entering drug treatment with prescription-type opiates as their primary drug were quite different from those who use other substances. A much higher proportion of prescription-type opiate users were female and white compared to primary alcohol and heroin users (Banta-Green et al., 2006). Emergency department data showed a similar pattern and also indicate an older group as well. Previous analyses of Washington State treatment data indicate that those using prescription type opiates generally had higher incomes than those heroin users who were entering private and public pay methadone maintenance treatment.

Overview of prescription opiate treatment options

Screening and early intervention for persons prescribed opiates

For those prescribed opiates about whom physicians have abuse concerns, there are clinical approaches that integrate monitoring and contracting. These approaches include pill counts to ensure medications are not taken too quickly, urinalysis to confirm that the prescribed medication is present and that others are not and writing a personal contract between the prescriber and the patient outlining the terms under which prescribing will continue (American Academy of Pain Medicine, 2007 and Fishman and Kreis, 2002). Unfortunately no standard approaches to screening for problematic use have been developed or implemented.

For those who are abusing there are a range of treatment services available. Treatment involves opiate substitution medications, drug counseling, support groups, or a combination of these.

Outpatient and Inpatient Treatment

At one end of the continuum is long term residential treatment for people who have impaired self-maintenance capabilities. These programs may or may not use opiate substitution medications. Other residential services include intensive inpatient which includes a concentrated program of counseling and education, often involving a patient's family as appropriate. Recovery houses provide housing as well as social, vocational and recreational activities to help people re-enter society. Outpatient drug treatment involves group and individual counseling, the intensity of which varies by program and client need. These programs are generally no different for persons misusing opiates than for people misusing others drugs.

Opiate Substitution Treatment

Treatment programs that are unique to persons misusing opiates are those which include an opiate substitution medication. Chronic opiate use induces tolerance and other physiological changes. The permanence of these changes on the body's ability to produce endogenous opiate like substances is unknown, but substantial impairment for long periods of time appears to be common and many believe that long term maintenance on opiate substitute medications is ideal for opiate addicted individuals. For this reason people who have used opiates chronically often find opiate substitution treatment (OST) to be appropriate. There are currently two main types of medications and settings for obtaining OST: methadone treatment clinics and buprenorphine prescribed by physicians in an office based setting.

Methadone maintenance treatment programs (MMT) dispense methadone as the replacement drug for whatever opiate(s) a person has been taking whether they were prescription-type, heroin or both (Ward et al., 1994). Methadone is generally dispensed as a liquid and taken daily. MMT facilities are very large programs which include dispensaries and offices for counseling, both individual and group. In Washington State each license for a MMT clinic allows 350 clients, some facilities are adjacent to each other and have 700 or more patients. These are physically large facilities which are hard to locate mostly because of the stigma associated with their clients and mission. Historically these facilities were designed to serve heroin addicts and are located in metropolitan areas. For instance in Washington there are seven clinics which are located in Seattle, Tacoma, Everett, Olympia, Yakima and Spokane and see mostly clients on public assistance. There are four private pay facilities as well; these centers do not accept public assistance clients and are located in several of the aforementioned cities. There are two Department of Veterans Affairs facilities in Seattle and Tacoma.

It is significant that MMT *dispense* methadone, but they do not prescribe it. The Drug Enforcement Administration (DEA) only allows MMT to dispense methadone for

addiction treatment, and physicians may not provide MMT outside of a MMT clinic (it may be prescribed for pain). Dispensing means that a person takes methadone in front of a clinic staff person, initially six days a week with a 'take home' for Sunday. Over the course of many months, and with progress in treatment, a person may be granted more take homes and have to attend the clinic less often. Methadone as a medication is very inexpensive and MMT is covered by several governmental financial assistance programs, with approximately 5,000 treatment slots at for-profit, non-profit and VA programs in Washington State in 2007.

Buprenorphine is another medication used in OST (McCance-Katzl, 2004). Buprenorphine is generally considered to be a safer medication than methadone, because it is a mixed opiate agonist-antagonist meaning that it is not possible to overdose on it when it is taken alone. (It can still be fatal when taken along with other central nervous system depressants.) It is also combined with an antagonist medication that is released if not taken orally, in order to discourage injection. Most patients take buprenorphine every other day, and the DEA has allowed more flexibility in how it is provided. Buprenorphine can be offered in an office setting by a physician not affiliated with a treatment program. For the past several years physicians have been limited to 30 patients on buprenorphine at any one time. One year from their initial approval to treat 30 patients providers may request an increase in their capacity to 100 patients. Over 200 Washington State physicians have taken the one day training necessary to obtain DEA approval to prescribe buprenorphine, so the increase in the number of patients allowed per physician is significant. The fact that it is prescribed, not dispensed, also allows people to obtain a 30 day supply at a time from a privately paid physician or up to 14 days for those on Medicaid. Buprenorphine is expensive and is not covered by governmental assistance programs at near the level that methadone is.

To summarize, of the two main types of OST, buprenorphine allows much more flexibility in terms of the number and location of potential providers and has many fewer restrictions compared to the highly regulated setting in which MMT is provided. Buprenorphine treatment, however, does not necessarily include substance abuse

counseling, and this is of real concern because addiction is more than a biological phenomenon. Additionally there is minimal funding currently available for low income persons to obtain buprenorphine.

Self-Help Groups

Self help groups, the most common of which are Alcoholics Anonymous and Narcotics Anonymous are another source of support. However, for those on OST medication they may not be welcome at many meetings because of the drug free stance they take- many consider opiate medications to be 'drugs' and do not welcome individuals who are in OST. Methadone anonymous meetings explicitly welcome people on methadone, however none are currently active in Washington State. People self-refer to 12 step programs which are not run or managed by professionals, though attendance may be mandated by some treatment programs.

Research questions and conceptual models

Given the emerging issue of prescription opiate abuse and the importance of MMT as a treatment modality for opiate addiction, three research studies were conducted to better understand the characteristics of those entering MMT and factors related to retention in MMT. The first paper (Chapter 2) describes the type of clients entering a single, large MMT between 2001 and 2006 in terms of their patterns of opiate use, chronic pain and personal characteristics. Paper 2 (Chapter 3) examines the impact of distance to treatment on retention in MMT, while the third paper (Chapter 4) examines differences in retention in MMT for primary prescription type opiate users compared to heroin users, Papers 2 and 3 utilize data for all persons admitted to not-for-profit MMT in Washington State in 2004 and 2005. A discussion of the conceptual models for these studies concludes this chapter.

Research question 1- Chronic pain and other factors associated with opioid use patterns at methadone maintenance treatment entry (Chapter 2)

Based upon epidemiological data, preliminary descriptive data and clinician anecdotes, it appears that those entering treatment for misuse of prescription-type opiates may represent a new type of client, about whom little is known. With greater exposure to prescription type opiates, legally or illegally, it is possible that those who might have a pre-disposition to opiate addiction are more likely to be exposed and ultimately addicted than a decade ago. That is, prescription type opiates may make it 'easier' to get hooked on opiates, providing a new access point whether via licit or illicit avenues. There may be either a new group of drug user, expanding drug abuse into a larger proportion of the population, or simply a new source and wider availability of a type of opiate, prescription form, for those who were already predisposed and likely to become addicted to heroin.

I sought to describe lifetime patterns of heroin and prescription-type-opioid use among those entering MMT for opioid dependence and to identify clinical and demographic factors associated with these lifetime patterns of opioid use. In particular, I was interested in the relationship between chronic pain conditions and various patterns of opioid use independent of other factors. These other factors included social and psychological issues that may be differentially associated with various opioid use patterns such as disability, incarceration history, psychiatric symptoms and medications.

Predisposition for addiction and psychopathology as well as pain perception have important biological bases. Psychological impacts on addiction, pain and medication use have been well documented. Social influences on health care utilization, addiction, pain and the manifestation of psychopathology are known to be significant. The biopsychosocial model has been shown to be salient in theories of chronic pain (Loeser, 1982 and Gatchel, 2004), psychopathology (Gatchel, 2004 and Substance Abuse and Mental Health Services Administration, 1994) and addiction (Donovan, 1998) as well as the dyadic relationships between each of these three conditions.

Shiffman (1989) placed the biopsychosocial model in a temporal context for his work in relapse to addictive behaviors (Donovan, 2005). This model is extended for the development of the current analytical framework so as to examine which of these factors are significantly different between various types of opiate users as defined by the pattern of lifetime opiate use (See Figure 1).

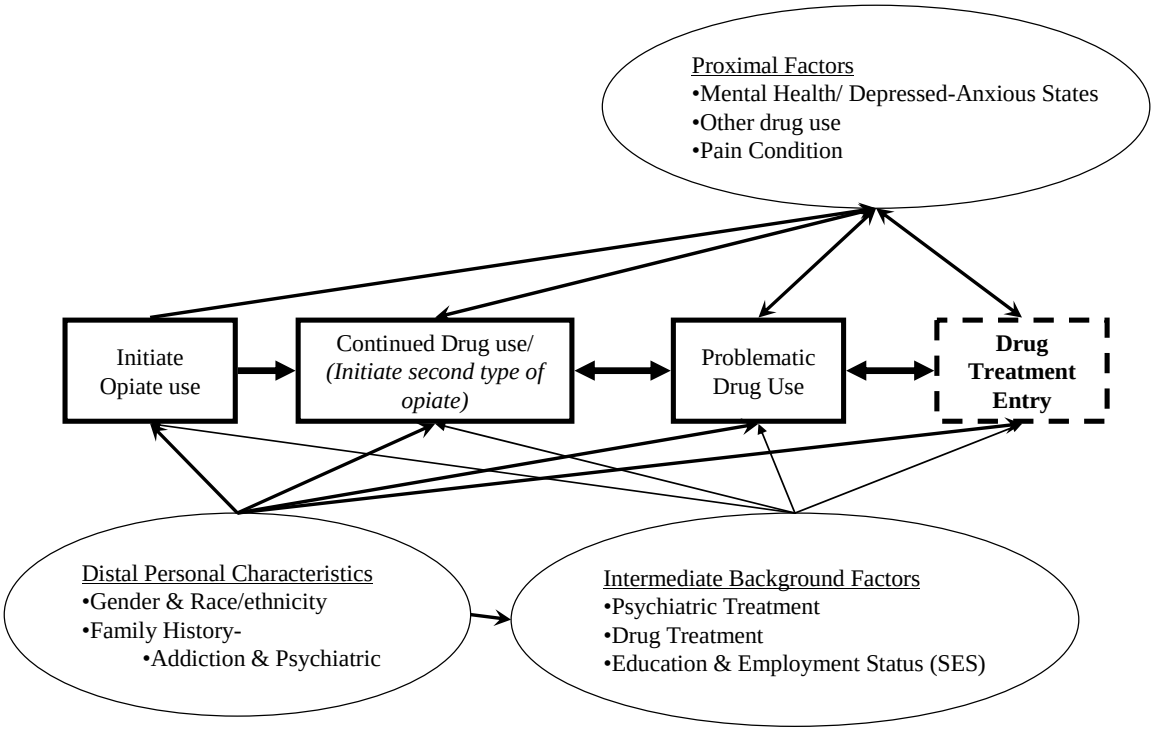


Figure 1. The Bio-Psycho-Social Model Applied to Opiate Use

The stages of opiate use are presented in the sequence of rectangles at the center of the diagram. The three different temporally bound constructs, of which the bio-psycho-social factors are components, are contained in the ovals. Distal characteristics, those most remote temporally, may impact initiation, escalation and continuation of opiate use as well as directly impacting intermediate background factors. These intermediate background factors may also directly act upon the opiate use trajectory. Proximal factors are those contemporary factors which impact opiate use progression and are also impacted by this progression. The analysis does not attempt to model the temporal or causal relationship between each of these variables given the cross-sectional nature

of the data. Rather the model is provided as background within which the larger conceptual issues are considered. The data source was the comprehensive bio-psycho-social assessment instrument, the Addiction Severity Index (McLellan et al., 1992) which included data elements related to each of these factors.

Retention in methadone maintenance treatment- associations with opiate type and distance to treatment

The purpose of these studies was to identify personal factors associated with MMT. A general depiction of the types of personal factors that influence treatment retention and the relationship between these factors is presented in Figure 2. Analyses are drawn from data for MMT agencies across Washington State; the exact number of agencies depends on the analysis, but is not fewer than 10 in any analysis. A substantial body of literature shows that treatment agency factors, such as clinic policies and average methadone dose, are strongly related to treatment outcomes (Brands et al., 2003). However, agency level factors are not the focus of these analyses and so fixed effects analyses were conducted. Treatment agency is adjusted for in regression analyses, so that all comparisons are only among persons in the same agency. In this way, the impact of the personal factors on retention is elucidated in the analyses, not agency level effects.

Research question 2- Does distance to MMT impact 12 month treatment retention? (Chapter 3)

The published research that exists on this topic indicates that greater distance to treatment is associated with significantly lower odds of drug treatment completion in outpatient treatment modalities, not including MMT (Beardsley et al., 2003). However, others have found no difference in MMT retention associated with living in the same versus adjacent or more distant counties than the one in which the MMT was located (Deck and Carlson, 2005). I measured distance in a more sophisticated manner, utilizing the population weighted centroid of the 5-digit zip code of the client's residence to the exact location of the MMT clinic.

Several important elements of physical access to treatment which have not previously been studied will be considered. By examining simultaneously multiple components of physical access to treatment, the most relevant factors should become clear (See Figure 2). Those enrolled in Medicaid can get reimbursed for their travel expenses to methadone treatment; this should increase treatment completion rates among all clients, but could make a bigger difference for those who live further away from treatment. Not having access to a car should increase a person's reliance upon other less convenient modes of transportation, resulting in lower treatment completion rates. The analysis was constructed to focus on this particular research question by selecting patients with stable housing and useable residential zip code information. Additionally, study variables, coding schemes, modeling procedure and interactions explored were focused on extracting as much information about distance to treatment and related factors as possible.

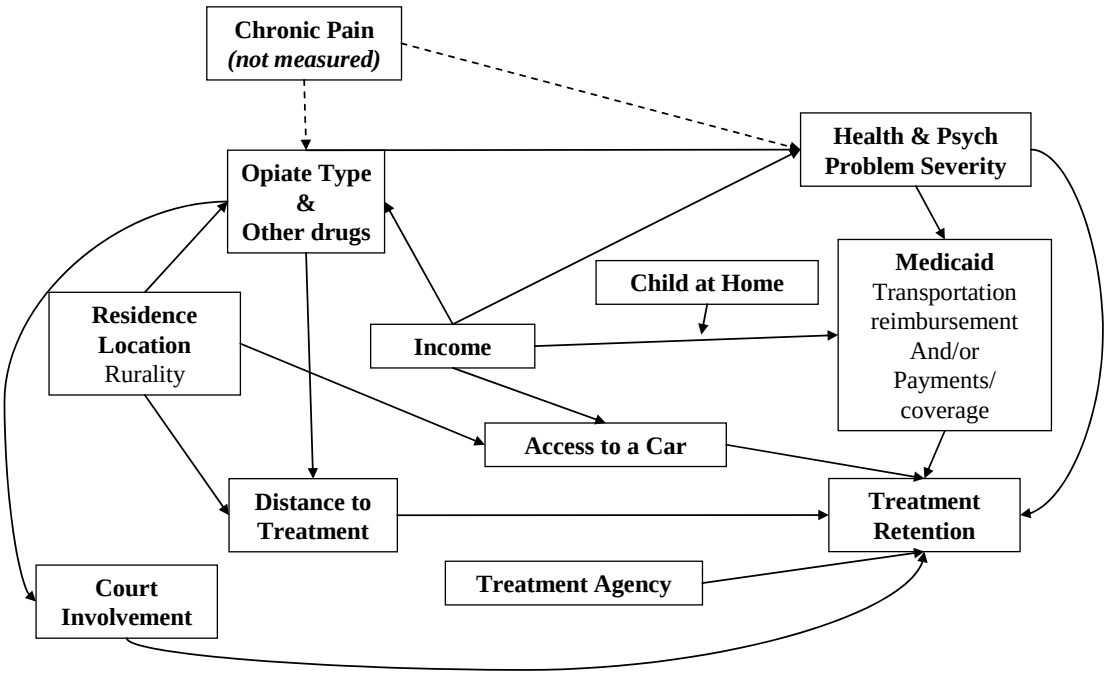


Figure 2. Measurement Model for Retention in Treatment Analyses

Research question 3- Does opiate use type impact 12 month treatment retention? (Chapter 4)

MMT is a long standing effective treatment modality. At a recent meeting of drug treatment researchers in Washington State sponsored by the Washington State Division of Alcohol and Substance Abuse (September 14, 2007) the question was raised- how effective are MMT programs at serving primary prescription type opiate users? The third analysis conducted for this dissertation addresses this question.

For this analysis it was important to clearly categorize clients by opiate use type. Those who reported any heroin use in the 30 days prior to treatment were considered heroin users and those who reported prescription type opiate use, but no heroin, were considered primary prescription type opiate users. The general conceptual model is the same as for research question 2 and is presented in Figure 2. However, the independent variable is different and the inclusion criteria and analysis plan were substantially different. Several factors are potentially related to the type of opiate used and these were considered carefully in constructing the analytic dataset and in the modeling procedure. Examples of potential confounders that might be related to treatment retention and opiate use type include legal system involvement and other drugs used. Most drug use, in particular among those seeking treatment, involves multiple substances either administered simultaneously or in close proximity to each other (poly drug use). These patterns of drug use and their relationship with personal and social factors were accounted for in the analysis. For the second and third research questions the data source was a comprehensive bio-psycho-social assessment based in part upon the Addiction Severity Index and implemented in a computer supported assessment process utilized by all MMT agencies that receive public funding in Washington State.

Summary

This chapter described the epidemiology of prescription type opiate use, the treatment options available to those abusing these drugs, and provided an introduction to the three studies that comprise the research findings of this dissertation. Chapters 2-4 are the three stand alone manuscripts addressing these research questions. Chapter 5 integrates the findings of these papers, discusses the policy and treatment implications and presents future research needs.

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CHAPTER 2

CHRONIC PAIN AND OTHER FACTORS ASSOCIATED WITH OPIOID USE PATTERNS AT METHADONE MAINTENANCE TREATMENT ENTRY

Background

Prescription-type-opioid use, abuse, morbidity and mortality have increased substantially over the past decade nationally (Gilson et al. 2004; Paulozzi et al. 2006) and in the Seattle area (Banta-Green et al., 2003 and 2007a). Heroin use and associated morbidity and mortality continue at moderately high levels nationally, (National Institute on Drug Abuse, 2006) and in the Seattle area relative to other drugs such as cocaine and methamphetamine (Banta-Green et al., 2007). While prescription-type-opioids can be legally used to treat pain or opioid dependence, illegally for the affective state they may produce, or for multiple reasons simultaneously, their use among those entering addiction treatment is poorly understood.

In the Seattle area, deaths and emergency department visits involving prescription-type-opioids have surpassed those for heroin in recent years (Banta-Green et al., 2006). The rate of prescription-type-opioid involved deaths increased 380% in the Seattle area from 1997 to 2005, to a rate of 7.7 deaths per 100,000 population compared to 4.1 per 100,000 for heroin. Nationally, the number of opioid analgesic poisoning deaths increased 91% from 1999 to 2002 (Paulozzi et al., 2006). Among those entering methadone maintenance treatment (MMT) programs in King County, prescription-type-opioids were the primary drug of abuse for 18% of patients in 2006, up from 3% in 1999 for those receiving public funds (Banta-Green et al. 2007). Those using primarily prescription opioids have generally been shown to more often be Caucasian, younger, higher income and female compared to users of other illegal drugs. Nationally, treatment admissions to all modalities of care for which prescription-type-opioids were primary increased from 20,555 to 59,056 from 1999 to 2004 (Office of Applied Studies, 2006).

Sales of prescription-type-opioids to hospitals, pharmacies and practitioners in Washington State has increased dramatically from 1997 through 2005, according to the DEA (1998-2005). Increases were seen for hydrocodone (166% increase), oxycodone (500% increase) and methadone (1042% increase). Methadone may be legally prescribed for pain conditions and the increase cited above is for pain related indications. Methadone may also be legally dispensed by methadone treatment programs as a component of opioid addiction treatment; methadone dispensed in this manner is not included in the data related to distribution.

The estimated number of people with past-month "non-medical use" of prescription pain medications in the United States was 6,405,000 according to the 2005 National Survey on Drug Use and Health (SAMHSA, 2006). The specific survey question asks about use of "any prescription pain reliever not prescribed for you or that you took only for the experience or feeling it caused". In 2005, this survey produced an estimate of 4.9% of people 12 and older with non-medical use of prescription pain relievers in the past year, however, only 12% of these past year non-medical users were estimated to meet criteria for abuse or dependence as opposed to 67% for past year heroin users.

The concerning trends in prescription-type-opioid misuse, abuse, dependence and the resulting morbidity and mortality highlight the need for improved understanding of the patterns of heroin and prescription-type-opioid use among those admitted for addiction treatment. We sought to describe lifetime patterns of heroin and prescription-type-opioid use among those entering methadone maintenance treatment for opioid dependence and to identify clinical and demographic factors associated with these lifetime patterns of opioid use. In particular, we were interested in the relationship between chronic pain conditions and various patterns of opioid use independent of other factors. These other factors included social and psychological issues that are potentially differentially associated with various opioid use patterns such as disability, incarceration history, psychiatric symptoms and medications. These data may inform treatment interventions geared specifically to the needs of various types of patients as well as providing information useful for preventing inappropriate initiation or escalation of prescription-type-opioids.

Methods

Data Source

Cross sectional data were collected at a single, large (capacity exceeded 750 patients throughout the period of data collection), private, not-for-profit opioid treatment program in the Seattle area. Approximately 80% of patients received some public funding for their treatment. Data were originally collected for clinical use and program evaluation from 2001-2006 by intake staff at the treatment program for all consecutive admissions. For clients who were readmitted only the initial intake data are utilized (n=1690). A total of 23 patients were excluded who reported they did not have at least one year of regular use of heroin or prescription-type-opioids, resulting in 1,667 patients for analyses. Human subjects approval and a waiver of signed consent were obtained from the University of Washington Institutional Review Board for these secondary analyses of de-identified data.

Measures

Data for this study are from the Addiction Severity Index (ASI) , a structured bio-psycho-social assessment (McLellan et al., 1992). Staff trained by a certified ASI trainer administered the instrument at the time of clients' admission to the program. We examined the lifetime pattern of regular use of prescription opioids and heroin use as documented with the ASI. The ASI definition of lifetime use refers to the time prior to the last 30 days and regular use requires use three or more times per week, binge use, or problematic irregular use in which normal activities are compromised. Clients are asked 'how many years in your life have you regularly used…" each of a list of drugs, which includes heroin, methadone and other opioids/analgesics as well as substances such as sedatives and amphetamine.. Examples of other opioids/analgesics provided include morphine, oxycodone and codeine. From the ASI we coded lifetime opioid use pattern as a three-category nominal variable: 1) prescription-type-opioid-only, more than or equal to heroin use, 2) heroin used more than prescription-type-opioids and 3) heroin only. These categories will be referred to as Rx>=Heroin, Heroin>Rx and Heroin-only.

Regular use of methadone is not included in the definition of lifetime opioid use pattern because the ASI does not distinguish between methadone dispensed as part of opioid drug treatment, prescribed for pain management, or obtained illicitly. This approach excludes those who received methadone for pain from the prescription opioid use groups, though most persons who have received opioids for a pain condition will have received other opioids prior to methadone, and this use of other types of opioids would be documented in the 'other opioids' category. The category of other opioids will be termed "prescription-type-opioids" to indicate the category of opioids, not heroin, and also to clearly indicate that the sources of such opioids is unknown and may well not have been via a prescription as the source of medications is not documented.

Any use of prescription-type-opioids or heroin in the prior 30 days was self reported at the time of intake. Patients reported their primary drug at the time of treatment entry with "more than 1 substance per day (including alcohol)" one of the response options. Drinking to intoxication was defined as 3 more drinks in one sitting, feeling "high" or having "got a buzz" from drinking alcohol. The variable 'first drug treatment' was derived from two questions: "how many times in your life have you been treated for" alcohol abuse and a parallel question for drug abuse. Treatment included: detoxification, halfway houses, in/outpatient counseling, and AA or NA meetings when 3 or more meeting had been attended in one month. The current drug treatment admission was considered the first drug treatment for persons who responded zero to both of these questions.

Chronic pain was derived from a text field that was completed for all clients who indicated "yes" to the question do you "have any chronic medical problems which continue to interfere with your life" with chronic medical condition defined as "a serious physical conditions that requires regular care , (i.e. medication, dietary restriction) preventing full advantage of their abilities.". The text field was examined for any overt mention of a chronic pain condition(s) e.g. "chronic back pain" and a newly created binary current chronic pain variable was coded accordingly.

Having a profession or trade was examined due to its greater relevance in terms of potential employability than years of education. All patients are asked whether they have a pension due to a physical disability. Having ever been in jail was coded as yes if the question “how many months were you incarcerated in your life” was greater than 0; if a person reported less than 1 month but 2 weeks or more this was rounded up to 1. Self-reported items included having ever been prescribed a medication for a psychiatric condition, experiencing a significant period of time with symptoms of depression or anxiety. All of these measures were determined a priori to be potentially important predictors or confounders of the relationship between opioid use pattern and chronic pain and were therefore included in regression analyses.

Analysis

Bi-variate associations were examined with chi-square tests used for binary variables and analysis of variance (ANOVA) for continuous variables. Multinomial logistic regression was utilized to determine the factors independently associated with the lifetime pattern of opioid use because the three-category variable is non-ordered. The reference category is heroin-only as the research question is focused on prescription-type-opioid use and this allows for a comparison with the only group of users with no regular prescription-type-opioid use. The estimation procedure fits maximum-likelihood multinomial logistic regression models. Multinomial logistic regression is similar to standard logistic regression that has a binary outcome. With multinomial logistic regression one group, in this case the heroin only group, is set as the referent group and parameter estimates for each outcome group are estimated relative to the referent group (Kohler and Kreuter, 2005). When exponentiated, these coefficient estimates can be reported as odds ratios, explaining the conditional odds of a person being in the particular opioid use pattern group compared to the referent group with regards to a single variable of interest while all other variables in the model are held constant. With multinomial logistic regression it is only possible to interpret the coefficients/odds ratios for each group relative to the referent group. All variables presented in table 1 were included in the initial regression model. The final model

shown in table 3 included only those variables with an individual Wald statistic significant at a 0.05 level in the initial model. SPSS 12.0.2 was utilized for all analyses.

Results

Of the 1,667 people entering drug treatment, 63% reported lifetime regular use of heroin and no regular use of prescription-type-opioids (Table 1). The remainder used prescription-type-opioids in a variety of ways. The largest group of prescription-type-opioid users (18.3%) used them for fewer years than heroin, that is, they were considered to be a 'heroin more than prescription type-opioid group' (i.e. Heroin>Rx in the table). Those who used prescription-type-opioids only (4.9%), more than heroin (9.9%) or an equal number of years as heroin (3.1%) were aggregated into a single category that totaled 17.8% of those entering treatment. Though there was some heterogeneity among these sub-groups, descriptive and multivariate analyses indicated that those who regularly used heroin and prescription drugs for an equal number of years were more similar to those with predominant or sole prescription opioid use than they were to those who used heroin exclusively or predominately (data not shown). Specifically, the strength and direction of associations detected with multivariate analyses were similar for the three groups categorized as Rx>= Heroin.

Socio-demographic characteristics of the population

Unadjusted bivariate analyses indicate that the three patterns of opioid use are associated with variation in age and ethnicity (Table 1). The lowest proportion of females was among the heroin-only group, however this difference was not statistically significant (p=0.15). Rx>=Heroin users were the youngest group and Heroin>Rx users the oldest. Heroin-only users were disproportionately Black and were less likely to

Table 1 Prevalence of Opioid Use Patterns and Characteristics of Users

	Rx >=Heroin	Heroin > Rx	Heroin only	*p*-Value
Total # (%)	298 (17.9)	307 (18.4)	1062 (63.7)	
Female	43.0	38.8	36.8	
Age Median (s.d.)	39.0(10.0)	45.0 (9.3)	42.0 (9.8)	*
Ethnicity				*
Hispanic	2.7	3.0	5.4	
Black	4.7	8.9	18.5	
Amer. Indian/Alaskan Native	7.7	7.3	7.7	
Asian/Pacific Islander	2.7	1.7	1.9	
White	82.2	79.2	66.4	
Profession/trade	79.5	79.5	71.7	*
Ever been in jail	39.8	74.9	74.9	*
Chronic Pain	48.3	39.1	21.8	*
Pension-physical disability	11.4	15.0	10.2	
Psych Prescription Ever	55.9	54.9	47.0	*
Depression Ever	63.4	69.4	61.4	**
Anxiety Ever	60.1	60.5	53.8	**
Ever IDU Any Drug	70.5	97.4	96.1	*
First drug treatment	22.1	7.8	9.9	*
Any regular lifetime use				
Alcohol to intoxication	58.4	72.1	64.3	*
Cocaine	47.8	60.9	56.4	*
Amphetamines	20.2	36.8	23.7	*
Sedatives	30.9	39.1	16.5	*

*P<0.01 **0.01<P<0.05

have a profession/trade compared to those who used prescription-type-opioids in any pattern. A history of being in jail was much more common among those who used heroin only or predominately.

Health and mental health characteristics

Chronic pain was least common among heroin-only users and most common among those who were Rx>=Heroin users (Table 1). A minority of patients were receiving a pension for physical disability at the time of the interview, with no significant differences by pattern of opioid use. Lifetime history of depression and anxiety symptoms as well as having ever been prescribed a psychiatric medication were common, with heroin-only users endorsing these items least often

Treatment history and drug using characteristics

A minority of patients reported that the current admission to treatment was their first, the Rx>=Heroin group reported this most often (Table 1). Having ever injected any drug was reported by almost all of the Heroin>Rx and heroin only groups, with a lower proportion, but still a majority of Rx>.=Heroin users reporting a history of injection drug use (IDU). Significant differences in the prevalence of lifetime regular use of alcohol and illegal drugs were evident between groups defined by opioid use pattern. Drinking to intoxication on a regular basis was most common among Heroin>Rx users. Cocaine and amphetamines were used least often by the Rx>=Heroin group. Any lifetime use of sedatives/barbiturates (e.g. alprazolam, diazepam, secobarbital) was most common among those who reported using Heroin>Rx and least often by those who used just heroin.

Opioid use patterns

As shown in Table 2, the years of use of prescription-type-opioids and heroin differed substantially for each of the lifetime opioid use patterns. The mean years of prescription-type-opioid use was 8.1 years (s.d. 5.3) for those who used Rx>=Heroin, compared with 3.0 years (s.d. 3.4) for those reporting more years of regular use of heroin than prescription-type-opioids. The average number of years of heroin use was

highest among the Heroin>Rx group, with a mean of 12.1 years, higher than for heroin-only users (2-sided t-test p=0.046) and much higher than those who used prescription-type-opioids-only-more-equal. The differences for both years of heroin and years of prescription-type-opioid use were significant across the groups (p<.001 for each).

The Rx>=Heroin group was least likely to report any heroin use in the past 30 days and most likely to report any prescription-type-opioid use. Almost all of those who reported that prescription-type-opioids were their primary drug were in the Rx>=Heroin group. Almost half of the Rx>=Heroin group reported heroin as their primary drug, lower than for the Heroin>Rx and heroin only groups. Interpreting self-reported primary drug of choice was complicated by the substantial minority who reported using more than 1 drug per day or a non-opioid substance as primary.

Table 2 Opioid use patterns- Past 30 days, Self-reported primary drug & Years of regular use

	Rx >= Heroin	Heroin >Rx	Heroin Only	*p*-Value
Rx opioids mean years of regular use (s.d.)	8.1 (5.3)	3.0 (3.4)	…	*
Heroin, mean years of regular use (s.d.)	2.0 (4.2)	12.1 (8.2)	11.0 (8.6)	*
Heroin any use past 30 days, %	63.4	88.9	91.9	*
Rx opioids any use past 30 days, %	61.4	34.3	20.4	*
Primary drug self-report				*
Rx opioids %	21.8	1.0	0.5	
Heroin, %	48.0	70.2	77.9	
Poly drug or non-opioid, %	30.2	28.9	21.6	

p-Value <0.001

Independent factors associated with opioid use patterns

The final multivariate model included chronic pain condition, age, race, jail ever in lifetime, having a profession/skill, ever IDU, first treatment admission, lifetime regular sedative use and lifetime regular amphetamine use. Race was recoded as a binary variable (white vs non-white) because the regression model would not resolve when

the all of the race categories were included in the model, this is likely due to some small cell sizes. The remaining variables in Table 1 were not significantly associated with lifetime opioid use pattern in the fully adjusted model. Removing them from the model made minimal difference in parameter estimates and associated significance test statistics.

Results of the final model indicate that having a chronic pain condition was strongly associated with being in Rx>=Heroin user with a lower but still highly significant odds ratio for Heroin>Rx users compared to heroin only users adjusting for all other variables in the model (see Table 3). Each 10 year increase in age was associated with a 21% lower odds (OR 0.79) of being a Rx>=heroin user as opposed to a heroin-only user. Conversely, Heroin>Rx users were more likely to be older than heroin-only users. Both groups with any history of regular prescription-type-opioid use had higher odds of being white compared with heroin-only users.

Table 3 Odds ratios of chronic pain on lifetime opioid use pattern, compared to heroin only users

	Rx >= Heroin			Heroin >Rx		
	O.R.	95% C.I.	*p*-Value	O.R.	95% C.I.	*p*-Value
Chronic Pain	3.21	(2.34 , 4.42)	*	1.97	(1.47, 2.63)	*
Age (10 year increment)	0.79	(0.67 , 0.93)	*	1.18	(1.01, 1.38)	**
White	2.15	(1.45 , 3.19)	*	1.70	(1.22, 2.37)	*
Have Profession/Skill	1.34	(0.93 , 1.92)		1.40	(1.01, 1.95)	**
Jail Ever	0.31	(0.22 , 0.42)	*	0.88	(0.64, 1.21)	
IDU ever any drug	0.13	(0.08 , 0.20)	*	1.24	(0.56, 2.73)	
First AOD treatment	1.55	(1.02 , 2.36)	**	0.94	(0.58, 1.52)	
Sedatives, regular use	2.52	(1.77 , 3.57)	*	2.51	(1.86, 3.39)	*
Amphetamine, regular use	0.82	(0.57 , 1.18)		1.62	(1.21, 2.17)	*

*P<0.01 **0.01<P<0.05

A history of having been in jail was much less common among Rx>=Heroin users compared with heroin only users, with Heroin>Rx users showing no difference. A history of any IDU was much less likely while the current treatment admission being their first was much more likely for Rx>=heroin users compared to heroin only users.

Regular sedative use was much more common among both of the groups which used prescription-type-opioids compared to heroin only users. Amphetamine use, however, was less likely among Rx>=heroin users compared to heroin-only users, while it was more likely among Heroin>Rx users compared to heroin-only users.

Discussion

The prevalence of chronic pain and much higher odds of having a chronic pain condition among those groups with regular use of prescription-type-opioid even after adjusting for potentially confounding factors, indicates the importance of pain and medical needs of such patients. Demographic, social and drug use patterns differ substantially by opioid use pattern defined by years of regular use of heroin and/or prescription-type-opioid. These findings show that those entering treatment with long term use of prescription-type-opioids may represent a different type of client than those who exclusively or predominately use heroin with whom MMT providers may be most familiar.

Current chronic pain conditions

Those with chronic pain conditions were much more likely to be in the two groups with regular prescription-type-opioid use compared to the heroin only group. To some degree this finding is tautological, those with pain are more likely to use pain medications. However, in this population of persons entering opioid addiction treatment the finding is significant because it implies that these are not people whose sole motivation for using prescription opioids is, or was, to experience euphoria. In a study of pain among methadone maintenance drug treatment patients Jamison et al. (2000) found that 61% had chronic pain and that those with pain were much more likely to take “oral narcotics”, though the authors did not describe the patterns of heroin and prescription-type-opioid use. The prevalence of chronic pain among our study population is likely lower because of the more conservative ascertainment of chronic pain status. Rosenblum et al. (2007) reported a 52% prevalence of chronic pain among patients reporting prescription-type-opioids as their primary drug, with an

adjusted odds ratio of 1.73 (99% C.I. 1.38, 2.17) for chronic pain compared to those reporting their primary drug as heroin. Our findings indicate a somewhat stronger association for chronic pain among those classified as Rx>=heroin users compared to heroin only users accounting for several of the same potential confounders as Rosenblum et al. (2007).

These data cannot determine whether the source of prescription opioids for patients with chronic pain is a legitimate prescription, family or friends', or illegal purchase. Potter et al. (2004) examined the manner in which controlled-release oxycodone was initially received among 48 inpatient drug treatment patients using this type of prescription-type-opioid. They reported that 31% initially received the medication via a legitimate prescription. Brands et al. (2004) examined prescription opioid abuse in a population entering a methadone maintenance program in Canada, categorizing users by their use of heroin or prescription-type-opioids as well as the initial sequence of use. Ongoing pain problems were most likely to be reported by those who used prescription-type-opioids only or initially.

Chronic pain is a prevalent condition. Chronic spinal pain, for instance, was estimated in the National Comorbidity Survey Replication to affect 19% of adults in U.S. in 2001-2002 (Von Korff et al. 2005). Prescription opioids are critical tools for pain management and concerns about misuse are negatively impacting patients and physicians (Merrill et al. 2003). The incidence of opioid misuse among those initiating them for chronic pain control varies depending upon the study and definitions of misuse. Among patients with back pain, estimates of the incidence of abuse of prescription opioids is between 5% and 25% (Mahowald et al., 2005; Ives et al. 2006). A history of substance abuse is strongly associated with abuse of prescription opioids among pain patients (Reid et al., 2002; Schieffer et al., 2005).

To be clear, neither the intended nor the unintended consequence of this work is to support the restriction of prescription opioid use among those needing them for chronic pain. Rather, these findings could be used by prescribers to enhance their understanding of which patients are at greater risk for misuse, so that they may engage

with these patients to ensure that their use of these medications remains as safe as possible.

Prevalence of opioid use patterns

A history of any regular lifetime use of prescription-type-opioids was reported by 37% of those entering opioid drug treatment. In total, the Rx>=heroin group constituted 18% (n=298) of clients. The relatively small size of this group is not surprising given that the data were obtained from a methadone maintenance drug treatment clinic and that this clinic is centrally located in a major urban area with a substantial level of heroin use. Additionally, physicians may not refer patients with primary prescription-type-opioid abuse to methadone maintenance programs because their addiction may go unrecognized, pain management may be a stronger focus, and pain patients with addiction may not accept methadone maintenance. Despite the relatively small proportion of prescription-type-opioid users in this study, the total number is quite large compared to several other studies which have examined aspects of prescription-type-opioid abuse (Brands et al., 2004; Trafton et al., 2004; Potter et al., 2004; Sigmon, 2006). Rosenblum et al. (2007) in a study of 5,663 patients at 72 MMT clinics in the United States, reported a median prevalence of past 30 day prescription opioid use of 69%, with an interquartile range of 50-98% across programs. We found that just 31% of all patients reported any prescription-type-opioid use in the past 30 days, though this varied significantly by lifetime-regular-opioid use type. The Rosenblum et al. (2007) study included the MMT clinic from which our data were obtained during 2005, when 24% (n=394) of the patients in our analyses were admitted.

Utility of categorizing patients by lifetime opioid use pattern

The degree to which the three groups of users as defined by pattern of lifetime opioid use are distinct is illustrated by differences in mean years of use, past 30 day use and self-reported primary drug. Poly drug use is the norm among those regularly abusing drugs and this approach to categorization incorporates this fact. The three categories do not perfectly and uniquely identify opioid use patterns, however they do provide a useful classification scheme utilizing the popular Addiction Severity Index. The

Rx>=heroin group, compared to the heroin only group, is significantly more likely to: be white, younger, have a skill/profession, not have an incarceration history, never injected drugs, never been in treatment before, and have a history of regular use of sedatives. The three groups defined by lifetime opioid use pattern have differences in drug use and other characteristics which are both statistically and clinically meaningful.

Limitations

The main potential limitation is the conceptualization of opioid use typologies based upon patterns of years of regular use of heroin and prescription-type-opioid use. This typology assumes that length of use reported on the ASI can be used to classify patients into meaningful groups. Use patterns are undoubtedly more complex in terms of patterns and motivations for use. This categorization scheme results in information loss. Despite this rather simple categorization scheme we found robust results and believe the scheme is easy to operationalize and of real world utility. A limitation of this study is that prescription opioid use may be appropriate, from medical and/or legal standpoints, or it may represent misuse. Ultimately, use was problematic, but the initial motivation is unknown. Additionally, self-report of drug use patterns is often suspect, however in this setting where the person is acknowledging their drug use and seeking treatment there is little motivation for falsification. These findings are not broadly generalizable due to the narrow population served in terms of local drug use practices (i.e. almost exclusive injection of heroin), low socio-economic-status and the utilization of data from one metropolitan area. The definition of prescription-type-opioids excludes methadone which could result in an underestimate of the prevalence of prescription-type-opioid use, however this would bias results in a conservative direction. Similarly, measurement of chronic pain was conservative, likely resulting in an underestimate of any associations between drug use patterns and pain. The advantages of using a large, secondary dataset of ASI's collected at intake seems a reasonable balance to the potential limitations of these data.

Implications

This study utilized an opioid use typology which incorporates poly-drug patterns and is based upon years of regular use of heroin and/or prescription-type-opioids. This typology is easily replicated by agencies and research projects utilizing the ASI. Chronic pain prevalence was relatively high overall, but was particularly high among the Rx>=heroin group which was younger and more treatment naïve than the heroin-only group. Comprehensive treatment services which address pain concomitant to addiction seem to be indicated. This points to a need for collaboration between drug treatment and health care systems. This collaboration might prove difficult under the best of circumstances, however among this group of low income clients financial access, let alone the coordination needed, may be particularly difficult to achieve. Future studies should examine whether addressing co-morbid concomitantly conditions improves drug treatment and other outcomes.

Notes to Chapter 2

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CHAPTER 3

DISTANCE TO METHADONE MAINTENANCE DRUG TREATMENT: USER CHARACTERISTICS AND RETENTION

Background

Methadone maintenance treatment (MMT) has been a modality used to provide drug treatment services to opiate addicted individuals for over 30 years. Historically, clients have been almost exclusively heroin users. Heroin users generally live in larger cities due to the greater availability of heroin and in turn MMT facilities have been located where demand for treatment is the highest. Heroin users have used prescription type opiates (PTO) to substitute for heroin when it was unavailable or to attempt to wean themselves off of heroin, but the primary use of PTO has been uncommon, especially among those entering MMT.

In the last decade there has been an increase in the amount of PTO consumed by members of the general population (Drug Enforcement Administration, 2006), an increase in misuse of the medications (National Survey on Drug Use and Health, 2005) and more recently an increase in admissions to MMT for people who were primary or sole users of PTO (Banta-Green et al., 2007). PTO are available throughout all regions of the United States as well as in rural and urban areas and there is increasing evidence that PTO abuse is more geographically heterogeneous than heroin use (National Survey on Drug Use and Health, 2006). In particular there is evidence that PTO abuse may be even more prevalent in rural areas than urban ones (Rosenblum et al. 2007; Knudsen et al. 2007).

Buprenorphine is another modality of opiate substitution drug treatment. Buprenorphine is provided by office based physicians as opposed to the large, freestanding clinics typical of MMT (Center for Substance Abuse Treatment, 2008).

The regulatory and administrative burden for providing buprenorphine is comparably much lower than for MMT. Conversely the cost of buprenorphine is substantially higher. As a result, despite the veritable explosion of potential buprenorphine providers, low income or disabled persons generally, and those receiving public assistance in particular, have very limited access to buprenorphine treatment in many states including Washington. Because of the lower cost and proven effectiveness of MMT it appears that this modality will continue to be widely utilized for some time to come.

The level of use of PTO in rural areas raises the possibility that access to appropriate treatment may by an issue, because of the need to travel greater distances to reach MMT programs. Research on distance to traditional outpatient, non-MMT, treatment in Baltimore indicated significantly higher odds of treatment completion for those closer to treatment facilities (Beardsley et al., 2003). Distance to care source has been shown to be negatively related to the initiation and the volume of outpatient mental health aftercare utilized following inpatient drug treatment (Schmitt et al., 2003). Deck and Carlson examined geographic proximity, as measured by county of residence compared to county of treatment facility, as a covariate in an analysis of MMT in Washington and Oregon (2005) with no effect shown in multivariate analyses. This is relatively crude measure of distance.

Washington State has been at the forefront of implementing an electronic information system for tracking service utilization among clients receiving public assistance and those receiving services at not for profit clinics including MMT. This information system, the Treatment Assessment and Report Generation Tool (TARGET), has been used for numerous studies of drug and alcohol treatment (e.g. Wickizer et al., 1994; Campbell et al., 2007). TARGET includes extensive data on substance abuse treatment services, substances used, and geographic identifiers and presents a unique opportunity to better understand factors associated with treatment retention.

The result of the various dynamics of drug abuse epidemiology, treatment services location and funding is that there appears to be a geographical disconnect between where services are located and where treatment demand appears to be emerging. This study will explore in detail the association among distance to MMT, drugs used and retention in treatment; we hypothesize that treatment retention will be positively associated with closer proximity to treatment. Retention in drug treatment is an important outcome variable, because it is associated with positive long term outcomes (French et al., 1993; Zhang et al. 2003).

Methods

Subjects

All adults who entered a fixed site, not-for-profit MMT program in Washington State between 2004 and 2005 were eligible. There were a total of 10 MMT facilities included of which 5 were located in the larger Seattle metropolitan statistical area which includes the two neighboring counties of Snohomish and Pierce, 4 in mid-size cities throughout Washington and one facility in a town 50 miles north of Seattle. Of the 49,015 who entered all modalities of drug treatment, 2,470 people entered MMT. A total 179 clients were excluded who were served at an out of state clinic, a mobile clinic, or had un-useable clinic identifier data. Those who moved out of their original zip code, n=269, during the episode were excluded as were those with unstable housing arrangements, e.g. homeless, living in a shelter (n=405). Lastly, those with no 12 month retention data were removed, n=23. The final analytic dataset contained 1,594 subjects.

Data source

All data for this retrospective cohort study were obtained from TARGET. Each treatment agency enters data into TARGET with data stored centrally. TARGET includes a comprehensive biopsychosocial assessment at intake, tracks changes to key milestones over time and records the date of treatment discharge. Comprehensive data

and identifiers are required to be submitted for all clients receiving services at not-for-profit clinics in Washington State. For profit clinics are required to enter intake data, however accurate identifiers are often missing, precluding longitudinal analyses. All variables of interest, with the exception of retention, were obtained at the time of intake into MMT. An episode of methadone care analysis was all methadone treatment admissions that occurred within 30 days of each other into a single episode of care. If a person had multiple episodes of care, the last episode was utilized. Each person was included in the analysis only once. Human subjects approval from the State of Washington was obtained in October of 2006.

Measures

12 Month Retention

The absence of a discharge record by day 366 following the date of intake into treatment was considered as evidence of retention in treatment (dependent variable) for at least 12 months. Retention has been used as an outcome variable in previous analyses of methadone treatment (Deck and Carlson, 2005; Ilgen et al., 2006; Campbell et al. 2007).

Distance to treatment

Distance to treatment (independent variable) for each individual was calculated using geographical information system software, ArcInfo 9.2 (Environmental Systems Research Institute, 2006) as the straight line distance in miles between the MMT clinic and the population weighted centroid for the client's 5-digit zip code of residence at the time of treatment entry. The population weighted centroid for each 5-digit zip code in Washington State was utilized to provide a more valid estimate of the likely distance to treatment. The mean geographic center of each of the census block groups in each 5-digit zip code tabulation area was used as the population weighted centroid. The difference between the geographic center and the population weighted center may be as much as 15 miles in some areas such as those on the periphery of mid-size, isolated

cities, where the population center may be at the geographic edge of 5-digit zip code area near the metropolitan area, but far from the geographic or geometric center. Once compiled, distance data were merged to the analytic dataset for statistical analyses.

Covariates

Indicator variables for each of the 10 treatment agencies (except an arbitrary, large "reference" agency) were included in the regression modeling procedure to adjust for treatment agency effects. A substantial body of research literature shows that several treatment agency level factors, such as clinic policies and average methadone dose, are strongly related to treatment outcomes (Brands et al., 2003) . Individual factors, not treatment factors, were of primary interest and the goal analytically was to adjust for treatment-agency factors, not explore them.

Public assistance types were aggregated to create a Medicaid funded group which included Title XIX, general assistance presumptive disability (GAX), temporary assistance for needy families (TANF), supplemental security income (SSI) and medical assistance only. In Washington State those who attend drug treatment and are receiving Medicaid are eligible for transportation reimbursement e.g. taxi, bus, fuel reimbursement; however, actual reimbursement was not documented. Medicaid eligibility has been shown to have a substantial positive impact on MMT retention (Deck and Carlson, 2005) though the exact mechanisms have not been detailed.

Ethnic groups were coded as White, Black and other. TARGET allows for great specificity in ethnic group membership, however the relatively small number of people in each of the other ethnic groups prevented regression models from resolving converging?.

Drugs of abuse include up to three drugs identified by the client as most problematic at the time of intake. Information on other drugs in addition to these three, either currently, or in the past is not documented. A drug use category of prescription type only primary (PTOP) was created. Individuals with PTOP included those who reported

PTO use but did not report any heroin or prescribed opiate substitute use. An additional category was created for those who did not identify heroin or prescription type opiate use, this is a catch all category that includes those whose only opiate type reported was the nebulous prescribed opiate substitute or who reported no opiate use. The prescribed opiate substitute category is rarely endorsed and the definition is not agreed upon by providers. It likely includes a combination of people who used prescribed opiate medications or those who transferred in from private pay buprenorphine treatment. Other major drugs of abuse are included, with those reported rarely e.g. Ecstasy, aggregated into an 'other' category. Cocaine has consistently been shown to be negatively associated with retention and other outcomes in MMT (Hser et al., 1998; Deck and Carlson 2005). Methamphetamine has long been a drug of abuse in Washington State and is a specific drug category. The category of amphetamines, is rarely endorsed and is included in the 'other' category. Methamphetamine has rarely been considered in analyses of MMT; however Deck and Carlson (2005) found it was negatively associated with retention in Oregon, but not Washington.

Rural urban commuting area (RUCA) codes for 5-digit zip codes were utilized. RUCA codes incorporate the geography and patterns of work commuting flows (Hart et al., 2005) and were aggregated into three categories: metro area core, metro area commuting and micropolitan/small town. While RUCA is related to distance to treatment it also represents the type of place in which people live.

The TARGET intake form asks "Is your current living environment conducive to recovery?" with a binary response option. Among the possible interpretations of this broad question is whether the person's home includes other drug users. The literature points to better treatment outcomes and lower drug use among MMT patients who have social networks which do not include drug users (Goehl, et al. 1993).

The impact of having children at home on treatment outcomes has been shown to be both positive and negative, but in both cases the effect was rather large (Peles et al.

2006; Scott-Lennox et al. 2000). A binary variable was created to indicate whether the client had children under the age of 12 living with them.

Current court/legal involvement was coded as positive if the client indicated he/she was: on probation or parole; enrolled in drug court; currently involved in a legal proceeding or DUI diversion; or had current child protective services involvement. Drug abuse treatment outcomes research generally and MMT in particular have shown negative effects of court/legal involvement on treatment outcomes (Saxon et al., 1996) though other literature shows that court referrals to treatment may be associated with better retention (Joe et al., 1999; Perron and Bright, 2008).

Statistical analyses

Descriptive statistics included t-tests and Chi^2 . A manual (non-automated), logistic regression analyses was utilized with variables entered in blocks based upon their conceptual relationship with each other. For instance, demographic variables and socio-economic-status variables were each entered as separate blocks of variables in consecutive logistic regression models. Variables were retained in the final model if they: reduced bias as indicated by changing the estimated odds ratio for distance to treatment substantially (Hosmer & Lemeshow, 2000) or if prior literature showed that the variable was strongly associated with MMT retention or distance to treatment. By including treatment agency explicitly in the model it was directly adjusted for as a fixed effect; this fixes the analysis of distance on retention to only compare those within the same agency.

Due to the substantial missing data for the covariate ‘do you have an automobile available?’ (missing 13%), multiple imputation procedures were implemented. Multiple imputation was utilized to fill in missing data for all variables, though only one other variable “do you have a valid driver’s license” (missing 1.4%) was missing for more than 1% of the study population. Imputed values for the missing observations were created by drawing from the posterior predictive distribution, as estimated by the method of multivariate imputation with chained equations (van Buuren and Oudshoorn,

2000). The bootstrap option was utilized to relax the typical assumption of multivariate normality on the distribution of regression coefficients. Missing values were imputed 5 times with the imputed values combined into one analytic dataset. The procedures for multiple imputation were based upon the work of Royston (2004). The micombine procedure in Intercooled Stata 9.2 was utilized to ensure proper point estimates and standard errors (Statacorp 2005).

Results

Bi-variate analyses (Table 4) indicated that the average distance to treatment for those who completed treatment was about the same as for those who did not complete treatment ($p=0.283$). The average distance to treatment varied by agency from 5.0 to 20.7 miles (data not shown). Other transformations of distance were explored including miles squared and categorizing distance into various increments, because previous literature showed a plateau effect (Beardsley et al., 2003) and it is possible that the impact of distance is non-linear. These alternatives did not provide a better fit to the data per the results of likelihood ratio tests of alternative models and so distance as a simple linear term was utilized.

Demographic characteristics of those not retained in treatment for 12 months indicate that they were younger, less likely female and more likely to be black in unadjusted analyses. Variables indicative of socio-economic-status were similar for education, employment and household income. Those with a home conducive to recovery were more likely to remain in treatment as were those with children under the age of 12 at home. Approximately a quarter of clients were married with no significant differences by treatment retention. The prevalence of psychiatric and medical concerns and Medicaid enrollment was similar . Those who stayed in treatment were somewhat more likely to have a valid driver's license. There was no significant difference in the proportion of those who reported having access to a car, before or after multiple imputation Those with current legal or court involvement were significantly less likely

to stay in treatment. Opiate use type did not differ significantly by retention status, but cocaine was significantly associated with leaving treatment. There was a higher proportion of methamphetamine users among those who did not complete treatment, but the difference was not statistically significant. Reported problematic use of alcohol, marijuana and sedatives was not associated with retention status. Lastly, the RUCA type was not associated with retention.

Table 5 provides descriptive statistics for the distance to treatment and RUCA type for drugs used. Opiate type is presented because MMT necessarily is for those dependent on opiates. Illicit stimulants were examined because of the consistent finding of their negative impact on retention and because the epidemiologic literature points to geographic differences in use and availability (National Institute on Drug Abuse, 2008; Northwest High Intensity Drug Trafficking Area, 2007). PTOP lived further from MMT facilities than heroin users, 12.6 compared to 9.9 miles respectively ($p=0.004$, $t(1,506)=-2.91$). Cocaine users lived significantly closer to MMT facilities, while there was no difference for methamphetamine users. There were, of course, significant differences by RUCA class, with those in metro core areas significantly closer to treatment on average. The distribution of drugs by RUCA type indicates that heroin users were more likely to live in metro core areas than either PTOP or no opiate users. A significantly higher proportion of cocaine users lived in metro core areas. Methamphetamine users were significantly less likely to live in metro core areas and 10% compared to 3% lived in micropolitan/small towns.

Table 4 Characteristics of clients by 12-month retention status

	Not in treatment at 12 months	In treatment at 12 months	p-value
	n=788	n=806	
Average distance in miles (sd)	10.6 (12.9)	9.9 (11.7)	0.283
Age (sd)	39.4 (10.1)	41.4 (10.8)	<0.001
Female (%)	49.6	55.6	0.017
Ethnicity (%)			
White	72.0	74.3	…
Black	13.6	9.6	0.016
Other	14.5	16.1	0.588
Educational /Technical Degree (%)	68.5	69.2	0.762
Household income >$500 mo. (%)	50.9	53.5	0.301
Employment (%)			
Employed	10.5	11.3	…
Unemployed	56.5	53.6	0.464
Other	0.3	0.9	0.135
Disabled	32.7	34.2	0.888
Home conducive to recovery (%)	72.7	81.4	<0.001
Kids under 12 at home (%)	19.7	22.5	0.173
Curently Married/Partnered (%)	25.5	24.2	0.514
Psych problem concerns (%)	59.9	58.3	0.076
Medical problem concerns (%)	47.8	50.1	0.085
Medicaid at intake (%)	63.5	63.2	0.901
Valid driver's license (%)	40.6	44.8	0.012
Access to a car (%)			
Yes	39.0	42.7	…
No	48.5	43.8	0.074
Missing	12.6	13.5	0.912
Legal/court involvement (%)	19.5	14.3	0.005
Heroin (%)	84.0	81.1	0.131
Rx-type opiates only (%)	11.0	13.0	0.223
No heroin or rx-type opiate (%)	5.0	5.8	0.436
Cocaine (%)	46.1	39.6	0.009
Methamphetamine (%)	8.9	6.6	0.084
Alcohol (%)	27.4	27.5	0.953
Marijuana (%)	15.9	16.1	0.885
Sedatives (%)	9.6	9.6	0.951
Rural Urban Commuting Area Designation of Residence			
Metro area core (%)	83.1	86.2	…
Metro area commuting (%)	13.3	10.4	0.070
Micropolitan/small town (%)	3.6	3.4	0.728

Table 5 Distance to treatment & RUCA Type by drugs used

		Distance in miles				Rural Urban Commuting Area type of Residential Zip Code (%)				
Past 30 day drug use	**# subjects**	**Mean**	**SD**	**p-value***	**test-statistic**	**Metro area core**	**Metro area commuting**	**Micro-politan/ small town**	**p-value***	**test-statistic**
Heroin user	1316	9.9	11.9	…		87.0	9.5	3.5	…	
Rx-type-only	192	12.6	14.2	0.004	t(1,506)=-2.91	74.5	21.9	3.7	<0.001	$X^2(2) = 26.26$
No opiate	86	10.4	13.6	0.696	t(1,400)=-0.39	72.1	25.6	2.3	<0.001	$X^2(2) = 22.32$
Cocaine	682	9.5	11.5	…		89.9	7.9	2.2	…	
No cocaine	912	10.8	12.8	0.044	t(1,592)=2.02	80.8	14.8	4.4	<0.001	$X^2(2) = 24.79$
Methamphetamine	123	11.4	13	…		78.9	11.4	9.8	…	
No methamphetamine	1471	10.1	12.2	0.271	t(1,592)=-1.10	85.2	11.9	2.9	<0.001	$X^2(2) = 15.92$
Metro area core	1350	8.3	9.8	…		…	…	…		
Metro area commuting	189	17.5	15.3	<0.001	t(1,537)=-11.15	…	…	…		
Micropolitan/small town	55	33.4	19.8	<0.001	t(1,403)=-17.58	…	…	…		

* p-values for 2-sided test & for comparison with referent group- heroin user or metro area core

Table 6 presents the results of the final logistic regression model using the imputed dataset. Distance to treatment was not associated with odds of retention adjusting for other factors. Two agencies had lower odds of retention compared to Agency 1, though the omnibus test statistic for differences among all agencies was not significant. Older age and being female were each significantly associated with higher odds of retention, with each 10 year increase in age associated with 30% higher odds of retention (95% CI 17%-46%) and being female associated with 34% higher odds of retention (95% CI 9%-66%) adjusting for other factors. Blacks were much less likely to remain in treatment for an entire year compared to whites among persons equivalent on all other variables. Living in a home conducive to recovery was strongly associated with retention (O.R. 1.62 95% C.I. 1.26, 2.08). Current court or legal involvement was negatively associated with retention (O.R. 0.75 95% C.I. 0.57, 0.98). Potential confounding was explored for blocks of variables and was shown to be slight (data not shown) so no variables were added solely for the purpose of reducing bias. Interactions between distance to treatment and opiate type, cocaine use, methamphetamine use, access to a car, and having a driver's license were examined for evidence of effect modification, no evidence was found. The odds ratio for the interaction term of distance and Medicaid eligibility was 1.008 (95% C.I. 0.991, 1.027).

Table 6 Factors associated with retention in MMT: Final Logistic Regression Model

	O.R.	**95% C.I.**	
Distance 10 mile increment	0.98	0.89	1.07
Agency 1	1.00	…	…
Agency 2	0.65	0.34	1.23
Agency 3	0.78	0.41	1.51
Agency 4	0.78	0.48	1.25
Agency 5	0.70	0.41	1.18
Agency 6	0.58	0.39	0.86
Agency 7	1.09	0.69	1.72
Agency 8	0.64	0.44	0.94
Agency 9	0.95	0.69	1.31
Agency 10	1.37	0.91	2.08
Age 10 year increments	1.30	1.17	1.46
Female	1.34	1.09	1.66
White	1.00	…	…
Black	0.57	0.40	0.81
Other ethnicity	1.09	0.81	1.47
Heroin, any use past 30 days	1.00	…	…
Rx type opiate only	1.20	0.85	1.69
No opiate use	0.99	0.62	1.59
Cocaine	0.81	0.65	1.00
Methamphetamine	0.70	0.46	1.04
Home conducive to recovery	1.62	1.26	2.08
Kids under 12 at home	1.31	0.99	1.73
Court/legal involvement current	0.75	0.57	0.98

Discussion

Summary of findings

Distance to treatment and retention

Distance to MMT was virtually unassociated with odds of retention in either unadjusted or adjusted analyses. Regression analyses which utilized RUCA type as the independent variable also did not show a relationship with retention (analyses not shown). Our findings are counter to the hypothesis posed and counter to published evidence for other forms of outpatient treatment in Baltimore (Beardsley et al. 2003) for clients with dependence on a range of substances. These negative results did parallel those found by Deck and Carlson (2005) which examined the impact of Medicaid funding on MMT retention with geographic proximity, measured in terms of county of residence compared to county where MMT was located. We thought that our more sophisticated measurement of distance to treatment might provide increased power to address this question. We also included variables which were conceptually related to mitigating the potential barriers imposed by distance to treatment- having access to a car, having a driver's license and Medicaid eligibility- none of these significantly impacted odds of retention in regression analyses.

In our study, all subjects were dependent on opiates and receiving opiate substitution treatment so among their motivations for staying in treatment was the very strong desire to prevent withdrawal from opiates. Literature has shown that those attending MMT have the highest rates of lifetime drug dependence and current drug use compared to other modalities of drug treatment (Hser et al., 1998). Beardsley's analysis (2003), which did not include MMT, included clients whose motivations for treatment were likely different and for which distance to treatment appears to have been a bigger barrier.

We found no significant difference in retention in treatment among those who initiated treatment. It is possible that distance acts as a barrier to initiating treatment. There is evidence from the health economics literature that distance to mental health treatment is a barrier to initiating treatment even after providing financial incentives (Lindrooth et al. 2006). The dataset we utilized, drug treatment data, does not allow for an investigation of whether distance to treatment is a barrier to initiating treatment.

Distance to treatment, RUCA and drugs of abuse

From an epidemiologic perspective the distance to treatment and RUCA types by various drugs of abuse were of interest. PTOP users were less likely to live in the urban core compared to heroin users. A multistate survey of MMT programs found that low urbanicity, per the Beale Urbanicity Coding scheme, of the MMT clinic was associated with prescription opiate abuse (Rosenblum et al. 2007) and Knudsen et al. (2007) found that rural MMT clinics in the United States were more likely to serve patients who used controlled release oxycodone. Similarly, the National Survey on Drug Use and Health reported that small metropolitan areas had the highest rates of past year misuse of pain relievers (NSDUH, 2006).

Cocaine users were more likely to live closer to treatment and in metro core areas than non-cocaine users. The relationship between cocaine use and urbanicity is substantiated by local law enforcement reports on the geographical distribution of cocaine use (Northwest High Intensity Drug Trafficking Area, 2006). In the present study the relationship was also likely related to the strong correlation between heroin and cocaine use; 48% of heroin users reported cocaine use compared with 19% of non-heroin users.

Methamphetamine users were less likely to live in metro core areas and more likely to live in micropolitan/small town areas, though they did not live any further from MMT than non-methamphetamine users. This finding is likely because methamphetamine users were more likely to access the MMT programs which were closer to smaller towns, for instance the average proportion of persons reporting methamphetamine use across all agencies was 8%, but the highest proportion, 28%, was for an agency much

closer to rural areas than agencies in the metro core areas. The National Survey on Drug Use and Health reported that metropolitan areas of the United States had the lowest rates of methamphetamine misuse (National Survey on Drug Use and Health, 2006).

While these drugs of abuse had a moderate, significant relationship with rurality and distance to treatment, their relationship with retention was weaker. Drugs of abuse were included in the final regression model because of the evidence in the published literature of the relationship between these drugs of abuse and treatment outcomes. Additionally, poly-drug use has been shown to be common among heroin users (Darke and Hall, 1995) so illicit stimulants were deemed integral to fully accounting for the effects of opiate use type. Cocaine and methamphetamine were both negatively associated with retention after adjusting for other factors, but these differences were not statistically significant. We found no differences in the odds of retention related to opiate type.

Limitations

The outcome of interest was 12 month retention in MMT as is commonly used. However, survival analyses would have incorporated more information on retention and may have revealed differential timing of dropout. Medicaid enrollment was used as a proxy for transportation reimbursement. TARGET did not contain data indicative of actually obtaining transportation nor the type of reimbursement e.g. bus tokens or taxi. Ideally street address data would be utilized for clients' residences to allow for exact distance calculations. Additionally, it would be of value to compare findings based on clients' self report of time traveled and electronic mapping estimates of travel time.

Data were only for those receiving treatment in programs receiving public funding. Given the higher prevalence of PTOP in private pay programs (Knudsen et al., 2007) and the potentially differential trajectories of use and impacts of socio-economic-status, it would not be appropriate to generalize these findings to all opiate users entering MMT. Treatment agency characteristics and treatment process variables have

generally been shown to have significant impacts on retention (Gerra et al., 2003; Magura et al., 1999; Peles et al., 2006; Gossop et al., 2003). We did not include any agency level variables, however we did conduct fixed effects analyses which adjusted for treatment agency, thereby comparing the effects of distance to treatment on retention only among those within the same clinic.

Future research directions

To strengthen analyses of those who have entered MMT it would be beneficial to directly assess patterns of transportation reimbursement and their impact on retention, rather than using the proxy of Medicaid eligibility which is dependent upon financial and disability status. Future studies should explore whether drug treatment initiation is affected by distance to treatment, for instance it would be of value to analyze the difference in enrollment in MMT among those screened as needing treatment by their proximity to treatment. Issues of treatment facility location, transportation reimbursement methods and funding levels for treatment and supportive services cannot be adequately addressed without further research.

Notes to Chapter 3

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CHAPTER 4
RETENTION IN METHADONE MAINTENANCE DRUG TREATMENT FOR PRESCRIPTION TYPE OPIATE PRIMARY USERS COMPARED TO HEROIN USERS

Background

The number and proportion of primary prescription type opiate users entering drug treatment has increased substantially throughout the United States from 0.9% (13,671) of all treatment admissions in 1992 to 4.2% (77, 780) in 2006 (Office of Applied Studies, 2008) . In Washington State the number has increased more than 10 fold from 34 to 462 from 2001 to 2007 in publicly funded methadone maintenance treatment (MMT) clinics (Division of Alcohol and Substance Abuse, 2008). This increase in treatment admissions has generally paralleled the increase in indicators of prescription type opiate abuse (Substance Abuse and Mental Health Services Administration, 2005; Paulozzi, 2007). Given that these indicators continue to increase it is likely that drug treatment demand will also continue to increase in coming years, making the issue of determining effective treatment modalities essential. MMT facilities have a long history, more than 30 years, of providing treatment to primary heroin users, however retention in treatment for the growing population of those with a primary addiction to prescription type opiates has not been assessed.

Several recent studies include information on treatment retention in opiate substitution treatment with buprenorphine, showing that prescription type opiate users have better retention than individuals using other types of opiates (Magura et al., 2007; Moore et al., 2007 and Torrnington et al., 2007); however, buprenorphine represents a very different treatment modality, the populations in these studies are relatively small, and multivariate analyses were not conducted.

The characteristics of prescription type opiate users have been well described in the literature (e.g. Rosenblum et al. 2007; Monga et al., 2007) indicating that this tends to

be a population that is more likely to be white, young, treatment naïve, socially stable and affected by a chronic pain condition heroin users. This is borne out in data specific to Washington State as well (Banta-Green et al. 2007). These demographic and social characteristics have generally been shown to be associated with positive outcomes in studies of MMT, while pain has been found to be associated with less improvement in social functioning over the course of treatment, though it was not associated with worse drug use outcomes (Trafton et al. 2004.). The overall impact of these characteristics on retention in MMT for prescription type opiate users has not been previously evaluated to the knowledge of these authors.

Washington State has a comprehensive substance abuse treatment information management system, the Treatment Assessment and Report Generation Tool (TARGET), which has been used for treatment services research (Wickizer et al., 1994) and epidemiological purposes for more than a decade (Jackson et al., 1999). These data are well suited to testing the hypothesis of interest: do prescription type opiate primary (PTOP) users have equivalent retention in MMT after adjusting for the following factors: demographics, treatment agencies, other drug use, public assistance type, social, legal and familial factors?

Methods

Study setting & population

A retrospective cohort study was used to examine the association between opiate type on twelve month MMT retention among adults admitted to treatment in not-for-profit clinics between January 1, 2004 and December 31, 2005 in Washington State. There are 11 not for profit MMT located in Washington State. Five of the clinics and a mobile clinic are located in the Seattle metropolitan statistical area, 4 are located in mid-size cities outside of the Seattle area and one is in a town 50 miles north of Seattle. Of the 49,015 who entered all modalities of drug treatment, 2,470 people entered

MMT. Excluding those who had only 'prescribed opiate substitute' use, no use of heroin or prescription-type opiates, an invalid agency name, no discharge status variable, who attended treatment at a facility that only served heroin users (meaning that they would drop out of multivariate analyses examining the impact of opiate type on retention), or who were missing co-variates of interest resulted in a final sample of 2,308. Conversations with methadone treatment administrators and staff responsible for the design and implementation of TARGET indicated that the 'prescribed opiate substitute' category was inconsistently used and that definitions were not agreed upon, impeding the interpretation of such data.

Data collection/data sources

Data were obtained from TARGET, an electronic information system. TARGET includes a comprehensive set of biopsychosocial questions in its admissions and discharge modules, tracks changes to important milestones over time and includes the date of discharge. Staff members at treatment agencies enter data directly into TARGET at their facility; data are transmitted electronically and stored at a central location. Discharge data were available beyond a year following the date of admission for all subjects. Human subjects permission to analyze de-identified, longitudinal data was obtained from the Washington State Institutional Review Board.

Variable description

Opiate use type (Independent variable)

Information was documented for the top 3 drugs of abuse as reported by the client. Two categories of opiate user type were created. Prescription type opiate only users were defined as those who reported prescription type opiate use and no heroin use in the 30 days prior to treatment entry. Those who reported any heroin use in the prior 30 days were categorized as heroin users, regardless of additional prescription type opiate use. Note that the term used throughout the paper is "prescription type opiate" to

emphasize that the type of opiate is a prescription form, not heroin, not that it was necessarily directly or indirectly obtained via prescription.

12 Month Treatment Retention (Dependent variable)

Retention in treatment for 12 months was defined as remaining in treatment at day 366 following admission to MMT. This meant that there was no discharge recorded in TARGET. Clients attend treatment facilities regularly for methadone dosing so dropouts are noted quickly in TARGET. A MMT 'episode' based analysis was utilized that combined the time in treatment for those who transferred directly (within 30 days) from one MMT to another. These transfers are often administrative and represent a person moving between two sub-units of the same agency at the same location. For those who had more than one MMT treatment episode, the final episode was utilized. Each person was included only once in the analysis.

Co-variates

All co-variates of interest were obtained at the time of intake into MMT. Subjects were categorized as either currently being married/partnered or not. Educational status was aggregated to high school education and above. Four ethnic categories were utilized: White, Black, Native American and other; the remaining ethnic groups were aggregated into the other category due to small numbers within the many, highly specific ethnic categories.

Public assistance type at intake was recorded as none (indicating self-pay), Temporary Aid to Needy Families (TANF) for low income parents, General Assistance Unemployable (GAU) for low income persons, General Assistance Presumptive Disability (GAX) and SSI were merged into a single category as they represent people with physical or mental disabilities, Medical Assistance Only, and an "other" category which included very small numbers of subjects who were receiving several other categories of public assistance.

Medical severity was based upon the Addiction Severity Index composite score (McGahan et al. 1986). A psychiatric severity composite score was created based on the three items parallel to the medical score- number of days with psychiatric problems in the past 30 days, self reported concern about these issues and self-evaluated need for treatment for these issues (note that not all of the items necessary for calculating the full ASI psychiatric composite score were available). The cutpoint for the medical severity score was 0.66 based upon literature showing that this cutpoint was associated with physical impairment (Calsyn et al. 2004.). The cutpoint for the psychiatric composite was 0.80 which was based upon receiver operating characteristic (ROC) analyses conducted with two other mental health variables available in the larger analytic dataset: current psychiatric treatment and current psychiatric medication utilization.

Housing status was recorded as stable for those who indicated they lived in a personal residence or single resident occupancy facility and unstable for those who indicated they were living on the street, in a shelter/mission or other unstable housing status. A single item asked if the current living situation was ‘conducive to recovery’. Current legal involvement was broadly defined to include any positive response to being on probation or parole, being enrolled in a drug court, current involvement in legal proceeding, DUI diversion, or having current child protective services involvement.

Drugs used at the time of intake in addition to opiates were derived from the 3 drugs of abuse self-reported by the client. The sedative category combined benzodiazepines and barbiturates. “Other drug” was a combination of the remaining drug categories which were infrequently endorsed e.g. hallucinogens.

Statistical analyses

Bi-variate statistics included chi2 tests and t-tests. A conceptually driven, manually (non-automated) implemented logistic regression model building procedure was utilized to explore the impact of adjusting for: 1) each of the different treatment agencies 2) demographics, 3) public assistance type, 4) psychiatric and health concerns, 5) alcohol and other drugs used, 6) social and familial factors such as living in a setting conducive to recovery and legal system involvement and 7) several exploratory two-way interactions of interest. Variables were included in the regression model based upon their conceptual relevance and statistical considerations, i.e. avoiding over-specification of the model or co-linearity. Variables were retained in the final model if they were integral to our conceptualization of the research question, if prior literature showed them to be strongly associated with opiate type and/or retention and if including the variable reduced bias. Because the research question was about retention in treatment and its association with opiate use type, we chose to adjust for treatment agency in all regression analyses so that the effect on retention above and beyond that which might be associated with the particular agency could be examined. Bias assessment (Hosmer & Lemeshow 2000) was conducted by examining the impact of adding variables in stages to the model on the odds of retention in treatment by opiate type. Stata 9.2 was utilized for all analyses (Statacorp, 2005).

Results

Bi-variate results

Unadjusted analyses indicated that primary prescription type opiate users were more likely to be retained in treatment for 12 months 54% vs. 46 % (p=0.023) compared to heroin users.

Prescription type opiate only users constituted 11.6% (N=270) of the study population overall and the prevalence of this group of opiate users varied between 4% and 38% among the 11 treatment agencies (Tables 7 and 8). The total number of subjects per treatment agency ranged from 47 to 565.

Table 7 Patient Characteristics by Opiate Use Type

	Rx-type only	**Heroin**	**p-value**
	n=269	n=2039	
Age average (s.d.)	34.3 (11.0)	41.5(9.9)	0.000
Female %	68.8	45.7	0.000
Ethnicity			
White	72.5	73.6	…
Black	3.4	13.5	0.000
Native American	11.5	3.9	0.000
Other	12.6	9	0.079
Married	32.7	20.5	0.000
Degree	65.4	70.2	0.107
Public Assistance Type			
None	26.0	27.9	…
Medical Assistance Only	12.6	5.4	0.000
GAU	6.3	15.5	0.002
TANF	32.7	11.2	0.000
GAX or SSI	21.9	39.7	0.004
Other	0.4	0.4	0.989
Psych problem concerns	36.1	40.7	0.351
Medical problem concerns	37.9	45.7	0.016
Heroin	0	100	0.000
Prescription type opiate	100	16.5	0.000
Cocaine	19.0	52.3	0.000
Methamphetamine	10.0	6.8	0.050
Alcohol	20.5	28.5	0.005
Marijuana	23.8	13.7	0.000
Sedatives	12.3	9.1	0.098
Other drug	7.8	4.1	0.005
No secondary drug	22.3	11.9	0.000
Stable housing	94.8	77.01	0.000
Children under age 12 at home	45.4	12.7	0.000
Home conducive to recovery	84.0	61.6	0.000
Legal system involvement	10.0	20.4	0.000
Ever IDU			
Continuously	9.7	92.8	…
Intermittently-rarely	14.5	4.2	0.000
Never	75.8	3.0	0.000
IDU past month	7.1	82.1	0.000

Table 8 Patient Characteristics by Opiate Use Type- Continued

	Rx-type only	Heroin	p-value
Agency 1 row %	3.7	96.3	…
Agency 2	38.3	61.7	0.000
Agency 3	11.3	88.7	0.010
Agency 4	13.7	86.3	0.000
Agency 5	16.7	83.3	0.000
Agency 6	28.5	71.5	0.000
Agency 7	32.1	67.9	0.000
Agency 8	9.6	90.4	0.001
Agency 9	5.3	94.7	0.206
Agency 10	10.8	89.2	0.000
Agency 11	4.9	95.1	0.646

In comparison to heroin users, PTOP users were significantly younger, more often female and married, and a higher proportion were Native American. Differences in public assistance enrollment were present by opiate type, with PTOP more likely to be on medical assistance only or TANF and heroin users much more likely to be on GAU or permanently disabled (GAX or SSI). Medical concerns were significantly more likely among heroin users while there was no significant difference in the prevalence of psychiatric concerns. PTOP were much more likely to indicate they had stable housing, that they had children under the age of 12 at home and that their living situation was conducive to recovery. Heroin users were much more likely to indicate they were currently involved with the legal system.

Cocaine use was the most common other drug of abuse for heroin users, reported by slightly more than half, much more prevalent than among PTOP. Marijuana was the most common other drug for PTOP, 24%, significantly more common than among heroin users, 14% ($p<0.001$). Recent methamphetamine use was reported by 10% of PTOP, a non-significant difference compared to the 7% of heroin users ($p=0.062$). Alcohol was more common among heroin users while there was no significant difference for sedative medications. Having no secondary drug of abuse was much more common (22%) among PTOP than heroin users (12%).

Injection drug use (IDU) was reported in the past month by 82% of heroin users and 7% of prescription type opiate only users. Lifetime IDU was reported by 97% of heroin

users and 24% of prescription type opiate only users. IDU history was not included in the regression analysis because it was so strongly correlated with opiate type used that it would not inform the primary research question.

Multivariate results

Table 9 presents a summary of the procedure utilized to determine the degree of confounding, or bias, accounted for by each of the types of variables. Overall, adjusting for potential confounders did not substantially change the magnitude or the direction of the odds ratio for the primary relationship of interest- treatment retention by opiate type used. The unadjusted and fully adjusted odds ratios were only 5% different, the largest change in the estimate as variables were introduced in blocks was 17% and the absolute value of the odds ratio was rather small. The degree of confounding accounted for by these variables was modest, however including them in the final model may decrease the amount of bias in the final estimate somewhat.

Table 9 Impact of Sequentially Adding Blocks of Variables to Logistic Regression Model on Odds of Retention in Treatment

	OR*	95% CI		Change in OR compared to unadjusted
Unadjusted	1.33	1.03	1.71	…
Agency	1.40	1.07	1.83	5%
Demographics	1.56	1.18	2.07	17%
Public Assistance	1.55	1.17	2.06	17%
Health/Psych Issues	1.54	1.16	2.05	16%
Other drugs used	1.41	1.05	1.89	6%
Social & Familial Factors	1.26	0.93	1.69	-5%

* Odds Ratio of retention in treatment for Prescription Type Opiate Primary compared with Heroin Users

The final logistic regression model is presented in Table 10. The odds of being retained in treatment for PTOP compared to heroin users adjusting for all other variables in the model was 1.25 (95% C.I. 0.93, 1.67), indicating there was no

statistically significant difference in treatment retention by opiate type; this compares with the unadjusted odds ratio of 1.33 (1.03, 1.71).

Table 10 Final Logistic Regression Model for Factors Associated with Retention in MMT at 12 Months

	Odds Ratio	95% C.I.		p-value
Rx opiate only	1.25	0.93	1.67	0.146
Agency 1	1.00	…	…	…
Agency 2	0.57	0.30	1.08	0.085
Agency 3	0.62	0.34	1.14	0.122
Agency 4	0.90	0.57	1.43	0.647
Agency 5	0.66	0.42	1.05	0.078
Agency 6	0.62	0.44	0.89	0.009
Agency 7	0.82	0.56	1.20	0.307
Agency 8	0.73	0.53	0.99	0.045
Agency 9	0.95	0.74	1.23	0.716
Agency 10	1.15	0.79	1.66	0.463
Agency 11	0.85	0.48	1.48	0.560
Age 10 year increments	1.27	1.15	1.40	0.000
Female	1.12	0.93	1.34	0.241
White (reference)	1.00	…	…	…
Black	0.69	0.52	0.91	0.008
Native American	0.95	0.62	1.44	0.808
Other race	0.96	0.72	1.30	0.806
Medical concerns	0.74	0.62	0.88	0.001
Cocaine	0.75	0.63	0.91	0.003
Methamphetamine	0.62	0.44	0.89	0.009
No public assistance	1.00	…	…	…
GAU (low income, temp. disabled)	1.58	1.19	2.09	0.001
TANF (parenting)	1.89	1.37	2.60	0.000
GAX or SSI (disabled)	1.86	1.48	2.35	0.000
Medical Assistance Only	1.06	0.71	1.59	0.768
Other	1.42	0.37	5.46	0.607
Home conducive to recovery	1.52	1.26	1.84	0.000
Kids under 12 at home	1.35	1.03	1.78	0.031
Legal system involvement	0.71	0.57	0.89	0.003

Adjusting for other factors including treatment agency, several co-variates of interest were significantly associated with treatment retention. Treatment retention did vary somewhat by agency and two of the agencies had significantly different odds of retention compared to the referent group (which had over 500 clients). Older patients

were more likely to stay in treatment, 27% higher odds of retention for each 10 year increase in age. Blacks were 31% less likely to be retained in treatment than whites, with no significant differences for Native Americans or other ethnicities. Those reporting medical concerns were less likely to stay in treatment. Illicit stimulant use, cocaine or methamphetamine, were both significantly associated with decreased odds of retention. Compared to those self-paying for treatment, those receiving public assistance because they were low income (GAU), parenting(TANF), or disabled (GAX or SSI) were much more likely to be retained in treatment. Living in a home conducive to recovery and having kids under the age of 12 at home were both significantly associated with retention. Current involvement with the legal system was associated with significantly lower odds of retention.

Effect modification/Interactions

Lastly, two-way interactions of interest were explored to assess effect modification, that is to see if the results differed for certain sub-populations. The interactions explored were: opiate type and ethnicity, opiate type and gender, opiate type and cocaine, opiate type and methamphetamine, opiate type and legal system involvement, home conducive to recovery and stable housing, or legal involvement and kids at home. None of these interactions approached significance at a significance level of $p<=0.10$.

Discussion

There has been the suggestion that primary prescription type opiate users may fare less well in MMT than heroin users because treatment policies and procedures as well as the social milieu of MMT programs have been driven by the historically predominant population of primary heroin users. Unadjusted analyses indicated just the opposite, that primary prescription type opiate users were more likely to be retained in treatment for one year. However, PTOP users have generally been found to have fewer health concerns and better social stability (Sigmon, 2006) which could conceivably be the reason for this difference in retention. Multivariate analyses which adjusted for demographic, treatment agency, illicit stimulant use, social and familial factors did attenuate the difference in retention. This indicates that the apparent better retention in treatment for PTOP is due, at least in part, to these factors.

Interestingly, public assistance which pays for MMT is strongly associated with retention in treatment even though these are populations facing significant barriers to attending and remaining in treatment including having young children at home or being disabled. This finding about the positive effects of public assistance has been shown in another analysis of MMT in the Pacific Northwest (Deck and Carlson, 2005). At the same time, the higher odds of retention for those with funding for MMT highlights the plight of those who are attempting to self-pay for treatment who, as the reference category in multivariate analyses, have lower likelihood of staying in treatment for a full 12 months. Concern about this group, which can be characterized as the working poor, has consistently been voiced by local providers and other community stakeholders. The finding regarding TANF funding for parenting clients does not appear to be due to added legal motivation as only 1.1% of clients had current involvement with child protective services (analyses not shown). Therefore it does not appear that the positive association between having children at home could be due to legal pressures; perhaps the better retention rates are due to internal motivation.

The finding that those who report living in a home conducive to recovery have better retention is not a surprise, but it is one of the biggest challenges for clients, and providers aiming to assist them, to overcome. Cocaine has consistently been shown to be associated with negative outcomes in MMT (Deck and Carlson, 2005; Hser et al., 1998). Some literature also points to the negative impact of methamphetamine use on retention (Deck and Carlson, 2005) though this area of study is limited by the relatively recent emergence of methamphetamine as a major drug of abuse and the geographic concentration of methamphetamine use to date. Continued drug use can be a reason for discharge for MMT and stimulants and prescription type sedatives are routinely tested for. Marijuana is generally not tested for and patients are typically only breathalyzed if alcohol use is suspected at the time of dosing or if the person has a known history of alcohol abuse.

African Americans are less likely to stay in treatment even after adjusting for many important factors related to other demographic variables, concurrent stimulant use, health severity and public assistance. How much this finding is due to the effects of persistent racism, community/ecological factors, entrenched poverty, disenfranchisement, other unmeasured treatment barriers or treatment variables such as therapeutic alliance is unknown. Similar findings regarding poor retention and other outcomes for Blacks are commonly seen in other multivariate analyses which have adjusted for important related variables (Deck and Carlson, 2005; Saxon et al., 1996).

Limitations

This study population received treatment in not-for profit clinics and is generally a very low-income population, in addition a sizeable proportion receive public assistance for disabilities, therefore these findings may not be generalizable to the entire population, especially those prescription type opiate users who are better off financially. A recent review of hundreds of MMT facilities in the U.S. indicated that prescription type opiate use was less prevalent in publicly funded not-for profit clinics (Knudsen et al., 2007). Only residents of Washington State were included in these analyses and heroin is

almost exclusively injected in Washington due to the low purity of the drug, limiting generalizability to other areas which have greater heterogeneity of routes of ingestion as the dynamics of use patterns within and between opiate types and characteristics of users may be associated with whether heroin is commonly inhaled or not.

Washington State has a high proportion of Whites and to the extent that opiate use type is related to ethnicity the power to detect this among less prevalent ethnic groups may be limited in this analysis. Conversely, Washington State has a relatively large proportion of Native Americans generally and this population was well represented in this analysis.

Treatment agency level variables are known to be important predictors of treatment success, e.g. therapeutic alliance (Simpson et al. 1997) and methadone dose (Brady et al. 2005), and these were not directly measured. However, these factors were accounted for as specific treatment agencies were adjusted for in analyses so analyses effectively compared people within the same agency to each other. The classification of prescription type opiate use was based on past 30 day use patterns and this in all likelihood classified some people as prescription type opiate primary users who had used heroin at some point, it is possible that a true difference in retention was obscured by this potential mis-classification of opiate use type. However, the magnitude of this mis-classification is likely small given that only 10% of PTOP reported a history of every injecting drugs regularly; among this population of opiate dependent individuals in Washington state, a history of regularly injecting drugs is likely an indication of heroin use.

Lastly, no information is available about the medical indication or source (e.g. prescription, street) for the use of these prescription-type opiates and while this would be of interest epidemiologically, the fact that these patients ended up needing drug treatment for their opioid use indicates that their use became problematic. Prescription type opiate use at entry to MMT has been shown to be associated with chronic pain

conditions (Trafton et al. 2004, Rosenblum et al. 2007); unfortunately no data elements were available that clearly indicated the presence of a pain condition.

Conclusion

Among the population studied, low income persons at MMT in Washington State, unadjusted analyses showed that primary prescription type opiate users appeared to have better retention in MMT compared to heroin users. However, multivariate analyses that adjusted for demographics, drugs used, treatment agencies, and social and familial factors indicated no difference in treatment retention indicating that the bi-variate association was explained at least in part by these other client characteristics. The findings of this study suggest that PTOP can be treated at MMT facilities at least as effectively as heroin users.

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CHAPTER 5
SUMMARY AND NEXT STEPS

This chapter summarizes and integrates the findings from the three research studies detailed in Chapters 2-4. Implications of the findings for policy and treatment services are presented and lastly suggested next steps for research are outlined.

Summary and integration of findings

Paper 1 detailed the characteristics of different opiate user types and showed that there were significant differences between these types in terms of chronic pain prevalence, demographics, history of incarceration and other drug use. While Rx>=Heroin users were generally less severe with regards to most factors, they had much higher odds of chronic pain. Paper 2 explored the relationship between distance to treatment and treatment retention. Negative findings resulted from this analysis indicating that there did not appear to be a relationship between distance to treatment and retention among the population studied after accounting for numerous other important factors. This is counter to literature on other forms of outpatient treatment, notably those that do not include an opiate substitution medication. This analysis also indicated no difference in retention by distance dependent upon the type of opiate used, despite the fact that prescription opiate users are further from treatment on average. Paper 3 showed that prescription type opiate primary users do not have worse retention levels than heroin users when adjusting for other factors including demographics, stimulants usage, conduciveness of home to recovery and legal involvement.

Taken together these studies show that prescription type opiate users do appear to be substantially different than heroin users in terms of many important characteristics. Treatment research conducted by Ilgen et al. (2006), however, indicates that although chronic pain is relatively prevalent in MMT it does not necessarily lead to worse

retention in treatment, though chronic pain patients did have poorer psychosocial functioning one year after admission. Though I was unable to integrate the domain of chronic pain into the retention analyses, there is a strong relationship between prescription opiate use and chronic pain. Overall, though prescription opiate users appear to have important differences from primary heroin users, they do seem to be amenable to treatment in MMT.

Policy and treatment implications

Chronic pain among MMT clients

The relatively high prevalence of chronic pain among MMT patients in general, and among Rx>=heroin users in particular, indicates the need for comprehensive medical services for MMT patients and for adequate pain treatment in particular. Ilgen et al.'s findings regarding worse psychosocial outcomes and evidence of the strong association with depression further supports the need for comprehensive services. Among those in MMT, chronic pain is likely to be poorly controlled by standard methadone dosing schedules due to the fact that the analgesic properties of methadone have a much shorter duration than its withdrawal alleviating properties. In fact, while methadone for drug treatment, that is to prevent withdrawal, is generally given once daily, methadone for pain is typically take 3-4 times per day. Little literature exists on the treatment of pain among those in MMT, though Alford et al. (2006) provide clinical recommendations for *acute* pain management in this population. This would be an area that would benefit from collaboration between addiction medicine and pain management physicians.

Distance to MMT

In the study presented in Chapter 3 distance to MMT appeared to have no impact on retention in treatment. The implications of this negative finding regarding distance to treatment on retention should be considered cautiously for three reasons: 1) those with unstable housing were explicitly excluded, 2) the nature of transportation reimbursement utilization was unknown and 3) only those who entered treatment were considered.

Excluding those with unstable housing was necessary from an analytic perspective because the independent variable was distance to treatment and the residential zip code, if any was given, was known to be unreliable (e.g. homeless patients are known to use the clinics' address as their own on occasion). The third analysis included those with unstable housing and though it was significantly related to retention in unadjusted analyses, it was not significantly associated in the fully adjusted model.

Though Medicaid eligibility was included as a co-variate, because it indicated the potential to obtain reimbursement for transportation costs, no data elements that documented the actual obtainment of transportation reimbursement were available. Nor, was the type of reimbursement available e.g. bus pass or taxi fare reimbursement.

It is possible that any impact of distance on treatment is manifest at the time of actually initiating services. That is, there may be a differential in initiating MMT among those in need of and eligible for services. Neither adequate data, nor comprehensive enough analyses, are yet available to inform policy related to transportation reimbursement for MMT clients.

Prescription type opiate primary clients in MMT

The findings of paper 3 indicate that prescription type opiate primary clients have retention in MMT at least equivalent to heroin users. From a treatment efficacy perspective it is appropriate to continue to fund MMT for primary prescription type

opiate users. There are other systems issues, for instance the possible displacement of heroin users by primary prescription type opiate users and the impact on public health more broadly, which these research results cannot inform. Clarification of terminology with regards to opiate types used will be important and is discussed below.

Future research directions

Distance to treatment and transportation reimbursement

The process of conducting these analyses and the findings points to several areas of improvement needed in this line of research. Future research investigating the impact of distance to treatment on retention should account for two critical issues: 1) the nature of the transportation reimbursement obtained and 2) whether the ability to initially access treatment is impacted by distance to treatment. Preliminary discussions with treatment providers and state data analysts suggest that both of these areas could be addressed with available data. To address the issue of the nature of transportation reimbursement it would be necessary to work with a local transportation broker who arranges these services and link client level data on transportation services received to clinic level data. This would likely be feasible as a prospective study with a limited number of treatment clinics. The second line of research, the impact of distance on initiating treatment, might be answered by exploring treatment initiation rates among all those assessed as needing MMT. The Alcoholism and Drug Addiction Treatment and Support Act (ADATSA) population is a potential study sample which receives a standard assessment. Additionally, qualitative work with patients about their transportation needs and how they access services should be conducted prior to initiating a large prospective study to inform the research questions and study design.

The utility of survival analysis in MMT treatment studies

The issue of transportation reimbursement highlights the importance of time dependent co-variates and the added value of survival analyses. Given the high frequency of visits required to MMT generally and in the first 90 days in particular, the timing of when transportation reimbursement begins could be critical. Survival analysis with time dependent co-variates would also allow for a more detailed analysis of distance to treatment for people who move during the course of treatment and/or for those whose housing status changes.

Measurement issues: chronic pain and opiate use patterns

Chronic pain is not documented in standard treatment intakes, though it is likely a component of medical intakes in some clinics. Given the importance of chronic pain it seems worthwhile to include an assessment of chronic pain in the standardized intakes required by the Washington State Division of Alcohol and Substance Abuse, at least for those reporting any opiate use. A similar conclusion was reported by Potter et al. (2008) in their paper *The value of screening for pain in patients with opioids dependence*. This would ensure that the issue is addressed for all clients and would provide necessary data elements for analyses. The variable used for chronic pain in the first paper was extracted from a more comprehensive intake assessment utilized by a single clinic. Significantly, data from this clinic had to be extracted from a text field associated with a question regarding chronic health problems. The open text field was completely un-standardized and necessitated a lengthy data extraction procedure. Perhaps a categorization scheme which aggregates International Classification of Disease (ICD) codes would be of utility in constructing response categories.

Ilgen et al. (2006) have conducted research on one year retention among MMT patients comparing those with and without significant pain. Unfortunately their study was quite small (n=200) and they did not explore in detail the relationship between opiate use

characteristics, pain and retention. There is a need for a larger, prospective study that integrates these domains and assesses each in a comprehensive manner.

Also needed is standardization is the terminology for prescription opiate type. Depending on the data source some of the possible categories included: other opiate, OxyContin, methadone, prescribed opiate substitute, and non-Rx methadone. These categories appear to have been added in a reactive manner as the issue of prescription opiate use among those entering treatment has become evident. It is time for providers, government administrators and researchers to develop a single, clear categorization scheme that can be incorporated into user manuals and training. It seems important to incorporate the motivation and source of the opioids into the categorization scheme. For instance, it is not currently possible to determine from existing secondary data whether patients are transferring into MMT after running out of money while attending either for-profit MMT clinics or for-profit buprenorphine providers. Understanding these marketplace dynamics in opiate substitution treatment has potentially profound implications for planning, policy and funding at the state and local level.

The need for data covering the complete population of those entering opiate substitution treatment in Washington State

Population coverage is a major issue. All analyses conducted for this dissertation used data from clients served at not-for-profit MMT clinics, the only complete data of its type readily available in Washington State. The total, average caseload for public pay MMT clients was 3,778 in 2007. Missing are private pay buprenorphine and MMT clients with capacity equal to 7,560 and an average caseload of 1,938 respectively in 2007 in Washington State. Only a few dozen buprenorphine clients in Washington State are currently receiving publicly funded care and almost none were during the time covered by these studies. The absence of private pay clients means we are increasingly missing a larger proportion of the (prescription) opiate using population. Conversations with key informants throughout Washington, and this author's analysis of the limited available data, indicates that these private pay clients are much more

likely to be prescription type opiate primary clients than those served in not-for-profit clinics. It is possible that as these people use up their personal or family's financial resources at for-profit clinics, they may transition to publicly funded clinics.

Addressing the large and growing population of those obtaining buprenorphine for drug treatment outside of the publicly funded system is a daunting problem. The State has no authority over these patients or providers to require treatment data and conducting provider level analyses would be extremely resource intensive.

At a minimum it will be important to add detail to assessment protocols for not-for-profit MMT clinics on the nature of opiate use and treatment history, so as to document the impacts of patients transitioning between private and public treatment systems. For-profit MMT clinics are required to input intake data into the State treatment database, unfortunately they routinely use fabricated patient identifiers, precluding the ability to conduct longitudinal analyses. The total caseload of publicly funded MMT clients in 2007 was 4,969, and totaled 2,692 at for-profit clinics. The potential capacity for buprenorphine treatment was 7,560 in 2007 throughout Washington. Some method for assigning consistent identifiers for private-pay clients seems warranted, particularly as the number of clients continues to grow and emerging evidence indicates they may be transferring to publicly funded treatment.

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