University of Alberta

Characterizing Opioid Overdoses in Alberta

by

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Your file Votre référence
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For the staff and clients at Streetworks, who have taught me that more generosity exists in the face of poverty than anywhere else.

Abstract

This research examined opioid overdoses in Alberta in 2004, using a combination of secondary analyses of administrative data and primary data collection. The Narcotic Overdose Registry of Alberta described deaths from opioid use. Most deaths occurred in a private location (72%); another drug was taken in 83% of cases. Bystander resuscitation was attempted in 13% of cases. The Narcotic Overdose Registry of Edmonton described opioid overdoses presenting to five emergency departments (EDs). Coingestants were common (82%) and most patients (51%) required emergent physician assessment. Most (77%) were discharged from the ED after prolonged observation. The Narcotic Overdose Respondent Intervention Survey documented the overdose experiences of a cohort of community drug users. Respondents had experienced a median of one overdose (IQR: 0,4) and had witnessed a median of two overdoses (IQR: 1, 10). Over 30% of respondents avoided calling the ambulance. Support for a community based naloxone program was widespread (80%).

Preface

This thesis is presented in the paper format. It consists of five chapters, including an introductory chapter on opioid overdoses and a chapter summarizing conclusions and future research directions. Chapters two, three and four are presented in a format appropriate for medical journal publication with a separate bibliography.

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Table of Contents

List of Tables

List of Figures

List of Symbols and Abbreviations

CCENDU	Canadian Community Epidemiology Network on Drug Use
CH	Capital Health Region of Alberta
CI	confidence interval
CIHI	Canadian Institute for Health Information
CPR	cardiopulmonary resuscitation
CTAS	Canadian Triage and Acuity Scale
ED	emergency department
EMS	emergency medical services
HIV	human immunodeficiency virus
ICD-9	International Classification of Disease, Injuries and Causes of Death, 9th Ed.
ICD-10	International Classification of Disease, Injuries and Causes of Death, 10th Ed.
IDU	injection drug user
IQR	interquartile range
κ	kappa
ME	Medical Examiner
NORA	Narcotic Overdose Registry of Alberta
NORE	Narcotic Overdose Registry of Edmonton
NORIS	Narcotic Overdose Respondent Intervention Survey
PYLL	potential years of life lost
RMO	registry of refused, missed, or other study exclusions
SD	standard deviation
VIDUS	Vancouver Injection Drug User Study

YPLL years of productive life lost

Chapter 1

Introduction to Opioid Overdoses

1.1 Injection Drug Use in Canada: Epidemiology

Although it is difficult to obtain accurate information on rates and patterns of illicit drug use in the general population, it has been estimated that 50,000 to 90,000 Canadians were injection drug users (IDUs) in 1996 (1). This translates into a rate of 2.5-4.6 Canadians engaging in IDU per 1,000 population aged 15-54 (2). A recent study also estimated that there were more than 80,000 regular illegal opiate users in Canada in 2003 (3). These numbers, however, likely underestimate the scope of the problem since drug use is under-represented in telephone and mail population surveys because of the illegal nature of users' activities and limited coverage of such 'hidden' populations in telephone and mail-based sampling frames.

IDUs face many health challenges. In this population, rates of HIV and Hepatitis B and/or C are high. Rates of HIV in the IDU population were found to be 16-20% in Montréal, 10% in Toronto and 23-30% in Vancouver with overall rates of Hepatitis B or C of 80% (2). In Alberta, the age-adjusted rate of newly reported cases of HIV infection was 5.7 per 100,000 population in 2001; the most commonly reported exposure category for both men and women was injection drug use (35.2% of men and 52.8% of women) (4). One surveillance study anonymously tested the leftover blood of all patients requiring blood work for other reasons who presented to one of two emergency departments (EDs) in an urban Canadian centre. They found HIV rates of 1% overall (82% of these were previously known to be HIV positive) and Hepatitis C rates of 10% (only 44% of these were previously known to be Hepatitis C positive) (5). In addition to

blood borne infection, IDUs are also at risk for other infections, predominantly abscesses, skin infections and cellulitis as a result of non-sterile injection practices. In a recent study conducted in Vancouver, this was the most common reason cited for visiting an ED and accounted for 18% of ED visits in this group (6).

IDUs are also at high risk of experiencing traumatic injuries. These can occur either as a result of assault, risky activities during drug procurement, or during an overdose episode (6, 7). Canadian data on the morbidity associated with overdose is limited; however, one Australian study suggests that up to 40% of overdoses may result in a physical injury sustained while falling, and up to 14% of overdose victims may be subject to assault while unconscious (7).

Finally, IDUs are also at risk of experiencing both fatal and non-fatal overdose. In a recent prospective cohort study of 679 illicit opioid users in five Canadian cities (Vancouver, Edmonton, Toronto, Montréal and Québec City), 17.2% of subjects reported an episode of overdose in the preceding 6 months, and of these, 37.8% had overdosed on more than one occasion (8). Risk factors associated with overdose included homelessness, non-injection use of hydromorphone in the past 30 days, and involvement in drug treatment in the past 12 months (8). These findings are consistent with other Canadian data on opiate users in Toronto who reported lifetime rates of overdose of 50% and rates of overdose of 4.1% in the last month (9). Participants involved in the Vancouver Injection Drug User Study (VIDUS) reported rates of non-fatal overdose in the preceding 6 months of 9.7% (10).

Because of the many health challenges faced by this population, IDUs are frequent users of ED and primary care services. In a prospective cohort study of IDUs in

Vancouver, 78% had visited a primary care clinic in the past year and 60% had visited the ED in the preceding two years. The most common reasons for visiting the ED were abscesses or cellulitis, wounds or lacerations and substance use or overdose (6). Rates of ED use by this population have been estimated to be 30% higher than demographically similar non-drug using controls (11).

1.2 The Pharmacology of Opioid Use

A variety of compounds are classified as *opioids*. Heroin (street names: smack, "H," "skag," and "junk") is the most commonly used illicit opiate; however, other opiates found on the street include morphine, hydromorphone (Dialudid®; street name "drug store heroin," "Little D," and "Dillies"), oxycodone (Percodan® and Percocet®), and codeine. Opiates produce their effects by acting as agonists on the mu, kappa, and delta receptors in the central nervous system. Their effects include euphoria, analgesia, respiratory depression, delayed gastrointestinal motility and miosis. The respiratory depression seen with opioid overdose results from a direct effect of the drug on the brainstem respiratory centers, primarily mediated through a reduction in responsiveness to carbon dioxide (12).

Heroin is rapidly absorbed through all routes of administration – intravenous heroin peaks in less than one minute, intranasal and intramuscular heroin peak in 5-10 minutes. Heroin is more lipid soluble than other opiates and thus crosses the blood-brain barrier within 15-20 seconds and achieves relatively high brain concentrations (12). Once inside the brain, heroin is rapidly metabolized to 6-monoacetylmorphine and then to morphine. Both of these compounds are mu opioid receptor agonists. Morphine itself

is much slower to cross the blood-brain barrier, and so heroin can be viewed as a pro-drug which serves to transport morphine directly into the central nervous system (13).

Morphine is broken down by glucuronidation, primarily in the liver, but also in the brain. The rate of glucuronidation is known to be affected by many other drugs including rifampin, antidepressants and alcohol. Genetic variation in the enzymes involved in glucuronidation have also been documented and it has been suggested that some individuals may be genetically more susceptible to overdose (13). Thus, the ability of an individual to metabolize heroin and other opiates may be affected by concurrent drug use and their genetic make up. Active liver disease may also impair the body's ability to metabolize opioids (14). These effects, combined with users' tolerance toward the drug, result in significant intra- and inter-subject variability in responses to heroin and other opiates (13).

Tolerance refers to the body's physical adjustment to a drug and the need over time to use more of a drug to achieve the same intoxicating effects. Tolerance to opiates does occur to their euphoric effects, but less rapidly to the drug's effect on respiration. This means that chronic drug users will often inject increasing amounts of a drug to achieve the same euphoric effect; however, this pattern of use increases the risk of respiratory depression. The margin of safety for chronic opiate users may be very small. If drug use is stopped abruptly, chronic users can also experience unpleasant withdrawal symptoms such as anxiety, sweating, and diarrhea; however, after a period of abstinence tolerance will gradually decline (13, 14).

The central effect of opioids on respiration may be enhanced by the concurrent use of other drugs. Benzodiazepines and alcohol both act on the GABA receptor site,

which also plays a major role within the respiratory control centers. Thus, there is the potential for significant respiratory depression and death if drugs such as opioids, benzodiazepines and alcohol are combined (13-15).

1.3 Mortality and Morbidity Associated with Opioid Use in Canada

Systematic Review Methods: A systematic review was performed to gather empirical studies designed to answer the following question: "Among regular users of illicit opioids in Canada, what is the excess morbidity and mortality attributable to their drug use?" A PubMed search, from 1966 to July Week 3 2006, was performed. Search terms were comprehensive and inclusive (please refer to Appendix 1 for search terms). EMBASE, PsycInfo, DARE and the Cochrane Central Register of Controlled Trials were also queried using a similar approach. No hand searching of journals or bibliographies was undertaken and no effort was made to obtain unpublished works; as a result, the review may suffer from publication bias. Articles were deemed suitable for inclusion on the basis of one reviewer's opinion only. A total of 189 articles were identified; of these only two attempted to quantify the morbidity and mortality attributable to illicit opioid use among Canadian drug users (please refer to Table 1-1). Each of these studies is described in the following paragraphs.

The OPICAN study is a prospective cohort study of 679 regular opiate users across five sites (Edmonton, Montréal, Québec City, Toronto and Vancouver) in Canada. Baseline data, including biological verification of opiate use, were collected upon entry to the study. The average age of study participants was 34.8 years and 67% of the sample were men. Participants were asked to report their personal health status; 50% rated their

health as "good or better" and 50% rated it as fair or poor. The most serious health problems reported by this group were hepatitis (34%) and pain (15%). Thirty-two percent of participants reported a mental health problem; however, 49% tested positive on a standardized screen for depression. One limitation to this study is that no control group was used, making it difficult to assess how much of this morbidity is directly attributable to drug use or is a result of other social factors (16).

Recognizing that information on the morbidity and mortality attributable to opioid use in Canada is extremely limited, Popova et al. attempted to provide an overview of illegal opioid use and health service utilization among illegal opioid users across Canada. A combination of statistical data and survey data from key informants was used. They estimated that there were a total of 3,245 hospitalizations for illegal opioid use in 2000-2001 (21.0 admissions per 100,000 population aged 15-49 years). They also estimated that there were 958 deaths in Canada in 2002 attributable to illegal drugs; this corresponds to a rate of overdose death of 5.9 per 100,000 in the population aged 15-49 years. The proportion of overdose deaths in the estimated opioid users population was 1.1. Again, due to lack of a control group, it is difficult to determine how much of this morbidity and mortality is directly attributable to opioid use and addiction as opposed to other coexistent factors, such as social marginalization (3).

Other Canadian data have attempted to quantify the morbidity and mortality associated with illicit drug use in general. The Canadian Community Epidemiology Network on Drug Use (CCENDU) collects data on hospital admissions and death related to alcohol and drug use in Canada from administrative databases found in all the provinces and territories. In 1999, there were 517 deaths in Canada related to illicit drug

use; this represents an increase from 497 deaths in 1998. These data were derived from the Vital Statistics Database which contains only the "underlying cause of death" data, and the information is coded based on the International Classification of Disease, Injuries and Causes of Death, 9th revision (ICD-9) (17). Consequently, this information likely significantly under-represents the mortality burden of illicit drug use on Canadians. Medical examiner data are also difficult to interpret – one Canadian independent review found poor overall agreement (Kappa [κ] = 0.27) between a toxicologist and a medical examiner in determining overdose as the cause of death (18). CCENDU data on the morbidity of illicit drug use on Canadians is derived from the Canadian Institute for Health Information, Hospital Morbidity Database. In 2000-01, there were an estimated 25,908 hospital admissions in individuals 15 years and older with a primary diagnosis related to illicit drug use. A further 29,214 admissions listed illicit drug use as a secondary cause of hospitalization (17). An Ontario study which examined all hospital admissions from 1985-1986 estimated that, compared to age and sex matched controls and after adjusting for multiple diagnoses, the standardized morbidity ratio for illicit drug users was 8.87 for those with a primary diagnosis related to illicit drug use and 4.74 for those with a secondary diagnosis related to drug use (19).

Despite the limited Canadian data available, it seems clear that regular opioid users are at substantial risk of experiencing death, hospitalization, and psychiatric co-morbidity.

1.4 Mortality and Morbidity Associated with Opioid Use Internationally

Mortality: Living a life complicated by opioid addiction can be associated with chaotic housing situations, poor health, incarceration, and premature mortality. Several key international studies have attempted to quantify mortality attributable to opioid addiction. One of the longest running studies followed a group of 128 primarily heroin addicts for 22 years in London, UK. Over the course of follow up, 38% of subjects died giving an overall death rate of 1.84% annually. Compared to an age- and sex-matched sample of the general population this represents an excess mortality ratio of 11.9 (95% CI not reported). The mean age at death was 38 years; overdose was by far the most common cause of death, accounting for 44% of deaths in the group, and other drug-related causes accounted for a further 24% of cases (20). A more recent study in London found a similar standardized mortality ratio of 17 (95% CI 10 - 28) for women and 16.8 (95% CI 11 - 23) for men, again with overdoses accounting for the largest proportion of excess mortality (52%) (21).

A similar sample of 459 IDUs in Glasgow was followed for an average duration of 5.5 years. Within this sample, 69% used heroin as their principal drug of choice. Over this time period the average annual mortality rate was also 1.8%; however, the excess mortality ratio was 22.0 (95% CI 16.5 - 28.8) due to a much lower average age of death (26.3 years). Again, overdose accounted for the vast majority of deaths (22).

In an attempt to more precisely define the excess mortality attributable to heroin use, Hulse et al. conducted a meta-analysis of 12 studies published between 1966 and 1996 which either reported standardized mortality ratios or death rates of illicit opioid users. Their work included reports from the UK, USA, Sweden, Scotland, Italy and Denmark; however, no Canadian studies were included. Overall, the pooled standardized

mortality ratio was 13.2 (95% CI 12.3 – 14.1). While not all studies reported on the cause of mortality, four major causes of mortality were identified for those that did: accidental overdose, suicide (either by drug or other method), violence and accident/injury, and medical condition (often related to drug use). With the exception of one study claiming 77% of all deaths were due to accidental overdose, the other studies reported overdose as the cause of death in 23 – 49% of cases (23).

Despite difficulties in quantifying the problem, it seems clear from multiple sources that illicit opioid use is associated with a significant mortality burden, and due to the young age of those involved, the years of productive life lost (YPLL) is staggering. A significant proportion of this excess mortality is directly attributable to overdose.

Morbidity: The morbidity associated with opioid use has been even less fully characterized than the associated mortality. Non-fatal overdoses are a common occurrence among heroin users, with 17.2% of subjects in the OPICAN study reporting an overdose event in the preceding 6 months; among these 37.8% reported multiple episodes of overdose (8).

A cross-sectional survey of 198 heroin users in Sydney, Australia suggests that the morbidity associated with non-fatal heroin overdose is significant. In this study group, 69% of participants had ever overdosed; the median number of overdoses was three. In the preceding 12 months, 28% of subjects had overdosed at least once. The most common cause of overdose related morbidity was physical injury such as broken limb bones or head injuries sustained when falling from the overdose. Other common occurrences included burns, assault while comatose, peripheral neuropathy, vomiting and chest infection. Over three-quarters (82%) of those who had overdosed experienced at

least one overdose-related morbidity symptom. The incidence of these events was no different between those individuals who received medical attention and those who didn't (7). Other less common causes of morbidity in opioid overdose include pulmonary edema, cardiac arrhythmia, rhabdomyolysis and compartment syndrome (14). The relationship of multiple non-fatal overdoses and possible anoxia to cognitive impairment is not clearly understood; however, one study found a significant association between the number of non-fatal overdoses and decreased performance on neuropsychological testing between a group of methadone maintenance patients and controls (24).

In summary, illicit opioid use extracts a high mortality toll, as well as being a major cause of morbidity in this population. Non-fatal episodes of overdose are common and are associated with injury, burns, assault, peripheral neuropathy, pulmonary edema or infection and long-term cognitive impairment. The additional burdens of homelessness and poverty have yet to be fully quantified in this population.

1.5 Overdose: Prevalence, Risk Factors and Circumstances

While death from opioid overdose is a common occurrence, some opiate users seem to be at greater risk for death than others. Several risk factors for overdose death have been identified.

Recent period of abstinence: Heroin users with a recent period of opioid abstinence, usually due to incarceration or enrolment in a drug treatment program, are at significant risk of overdosing when they return to regular drug use (8, 25-28). This is thought to be due to changes in tolerance, and an immediate resumption of their pre-abstinence doses of heroin. This theory is supported by hair analysis studies which found

that mean hair morphine concentrations of individuals who died from opiate overdose were in between those of active heroin users and abstinent former addicts (29, 30). One study found that those patients who "successfully" completed inpatient detoxification programs were much more likely than other patients to die within one year of treatment (26).

Polydrug use: Taking heroin in combination with other central nervous system depressants has also been associated with an increased risk of overdose death. In a retrospective review of all heroin related fatalities that occurred from 1992 – 1994 in Australia, 76% were associated with ingestion of another drug. The most common coingestants were alcohol, benzodiazepines, antidepressants and cocaine (28). Similar studies in subsequent years suggest that the rate of polysubstance use culminating in death is increasing (31-33). These results are also consistent with data from New York City, where 58% of overdose deaths from 1990 – 1998 were associated with more than one drug (34).

Route of administration: Those patients who use heroin primarily by non-injecting routes (smoking or inhaling) appear to be at less risk for overdose death. In one study, they also tended to be younger, have higher levels of education, were more likely to be employed, and had shorter heroin using careers. The lifetime rates of overdose in this group were 13% for non-injectors compared to 58% for injectors. Reports of recent overdose were also lower (2% vs. 29%) (35).

Psychiatric co-morbidities: The addiction literature in general assumes that most drug overdoses are unintentional or "accidental"; however, this may not always be the case. Several studies suggest that 10 – 34% of heroin users may have had at least one

intentional overdose incident (36-38). The reasons given for intentional overdose include a situational crisis preceding the overdose or an unhappy emotional state (36, 39). Thus, some overdoses may be intentional attempts at self-harm or suicides.

Changes in heroin supply: Fluctuations in the supply of heroin in Australia has afforded the opportunity to study the effect of several heroin "droughts" on the rates of death from opioid overdose. In two such cases, reductions in the supply of heroin resulted in a clear decrease in opioid related deaths (40) and opioid related presentations to emergency departments (41). There was an increase in the use of other drugs such as cocaine and methamphetamines; however, mortality rates from these drugs were lower (41). The heroin droughts in Australia also corresponded to a 35% reduction in overdose deaths and a 45% reduction in naloxone use in British Columbia; this suggests that global heroin supply is a significant factor in overdose related mortality (42). Large seizures of heroin by law enforcement officials have not been shown to have a similar effect (43). There is also evidence to suggest that changes in the purity of available heroin can lead to an increase in overdose rates, although this has not been systematically studied (44).

Circadian differences: Circadian differences in the response to opiates may exist. Despite no significant change in plasma morphine levels over a 24 hour period, the risk of death from an opioid overdose is significantly higher from 03:00 to 08:59, while the risk of non-fatal overdose is highest in the afternoon to early evening (45). EMS data also support this hypothesis and have highest rates of call volume for opioid related problems in the afternoon to early evening (46). What is unclear from these papers is whether these increased rates of EMS use and death are simply due to increased rates of use during these periods.

Homelessness: The effect of being homeless on the incidence of overdose has not been well studied. Several studies have found an association between risk of overdose and being homeless (8, 27).

Duration of heroin use: Long-term dependent users are at an increased risk of death compared to novice users (47). This may be due to the fact that as tolerance increases from chronic use, the margin of safety between the effective dose and the lethal dose becomes dangerously narrowed.

Circumstances surrounding the overdose: Fatal and non-fatal opioid overdoses are common among heroin and other opioid users. Most overdoses, however, seem to be witnessed by other people and do not occur in isolation. One study reported that up to 88% of these overdoses occur in the presence of other people (33). Most users (70% - 86%) have witnessed someone else's overdose, and of those that have witnessed overdoses, the median number of overdoses they have seen is between three and six (33, 48).

Pre-hospital interventions: A few studies have attempted to determine the actions taken by other users at the scene of an overdose. In one Australian study, the most common initial response was to check the individual's level of consciousness, followed by checking their breathing and/or pulse. Only 9% called an ambulance initially; however, another 36% of individuals did so as a subsequent action. A total of 39% of people attempted either mouth-to-mouth or cardiopulmonary resuscitation (CPR) at some point (33).

Other Australian studies have found much lower rates of bystander assistance – in New South Wales, the ambulance was called while the subject was alive in only 10% of

cases and CPR was attempted in only 11% (49). Other studies based on Medical Examiner data from the US are even more disturbing in that only 6% of fatal overdoses received any type of basic life support or CPR (50). Bystander CPR in the setting of heroin overdose has been shown to significantly affect patient outcomes. In one study there was a significantly lower rate of hospitalization after overdose in those cases that received bystander CPR compared to those who did not (51).

Aside from basic life support measures, bystanders will frequently try other actions to reverse the overdose. These include injecting the victim with salt water, putting ice on the victim or taking them into a cold shower, injecting them with other drugs like cocaine, inflicting pain or walking the person around (48, 52, 53).

In many overdose situations, requesting formal medical assistance is delayed or prevented. In one study, 40% of bystanders were delayed or prevented from getting help at the scene of their latest witnessed overdose. A fear of police involvement was cited as a barrier to obtaining assistance by 80% of these people; more specifically concerns about outstanding warrants and fear of manslaughter charges predominated (33). Studies from the US have suggested that this barrier to obtaining help may be even more of an issue with one survey reporting that 75% of respondents hesitated to call for emergency assistance for fear of being arrested. In this setting, many attempted to resuscitate overdosed companions on their own or left overdose victims in public places hoping that they would be found and helped by others (54). Distrust of medical institutions also appears to be deeply ingrained among drug users and is another barrier to calling for medical assistance (53).

These findings are supported by Canadian drug user surveys. In Toronto, one third of opiate users who had ever overdosed had *never* received any medical treatment for these incidents (9). The OPICAN study also reported that 24.1% of overdose victims did not receive any type of formal or informal medical assistance in response to this urgent health threat (8).

Summary: Opioid overdoses are rarely instantaneously fatal (49). In most cases, death occurs slowly over hours, giving ample opportunity for bystander and medical assistance to prevent death from occurring. As Davidson aptly comments, "When bystanders are present, willing, and able to act effectively, overdose fatalities should therefore be extremely rare. That overdose deaths are frequent suggests that one or more of these three factors is commonly missing, and that the social context of overdoses may be as important as the biomedical context in understanding and preventing fatalities."(50), p. 262.

1.6 Addiction Interventions

There are three general approaches to illegal drug use and addiction: the *traditional or mechanistic*, the *libertarian,* and the *harm reduction* approach (55). The *traditional* response to drug addiction in Canada has been criminalization, incarceration and abstinence-oriented treatment programs. Critics of this response point out that this approach includes, "moral arbitrariness in dividing drugs into licit and illicit ones, marginalization of drug users, straining of the criminal justice system, infringement of the civil rights of citizens, [*and*] indirect sustenance of a black market" (55), p. 1698-9.

Many physicians also feel that this approach does not adequately deal with the urgent medical issues faced by this population (56).

Others call for a *libertarian* approach involving legalization of all illicit drugs. This, they argue, would wipe out the need to engage in contact with an illegal market, allow governmental regulation of the content and distribution of drugs, and divert resources from enforcement to treatment and counseling. This approach, however, is felt by many to be too liberal, untested, and an orientation that may increase population levels of drug use (55).

The *harm reduction* approach to dealing with addictions has been advocated as a method that lies in between these two extremes. Conceptually, harm reduction approaches take a value-neutral approach to drug use, do not insist on abstinence, and focus on the more immediate harmful consequences of drug use (55). Harm reduction programs are therefore characterized as a more humane, pragmatic, and locally responsive approach. In this model, addictions are treated like other traditional chronic diseases (such as diabetes, asthma, etc.), where exacerbations are expected and treated accordingly. Service delivery is characterized as 'low threshold', i.e. health services are designed to be easily accessible to clients and incorporate policies and practices to encourage health service use. Examples of low threshold policies and practices include user-friendly clinic operating hours, tolerance of drug use or intoxication, or outreach activities that bring the health services to the client (2). The overall goal of harm reduction is to "decrease adverse health, social and economic consequences of drug use without requiring a decrease in drug use" (55), p. 1698. Table 1-2 outlines some common harm reduction strategies that have been applied to drug use (2). Harm

reduction strategies are an important component of national drug plans, such as Canada's drug strategy, that also include prevention, treatment and law enforcement.

1.7 Intervention: Community Based Naloxone Programs

Naloxone or Narcan ©: Naloxone is an opioid antagonist that reverses the effects of opioids including the respiratory depression which can lead to death. It is essentially a pure opioid antagonist and does not exhibit mixed agonist/antagonist properties. In the absence of opioids it exhibits essentially no pharmacologic activity. It has not been shown to produce tolerance or to cause physical or psychological dependence. When used in individuals with physical dependence on opioids, however, it will produce withdrawal symptoms. It has no effect on the respiratory depression caused by drugs other than opioids (57).

Naloxone has been used safely in the hospital and pre-hospital setting for years to reverse the effects of opioid overdose (58-61). Serious adverse reactions temporally associated with naloxone have included pulmonary edema, seizure and arrhythmia however these reactions occur in < 1% of individuals given naloxone and have mainly been reported in individuals undergoing elective surgeries and not those with a symptomatic narcotic overdose (58-60, 62-66). Acute pulmonary edema is also a well documented side effect of heroin overdose in the absence of naloxone administration (67, 68). One concern about naloxone has been that the half-life of naloxone (60 minutes) is shorter than that of heroin (90 minutes) and other longer acting opiates. This means that there is the potential for the naloxone to wear off and individuals could re-enter an overdose state. Considerable debate exists in the literature over how long individuals

need to be watched after receiving a dose of naloxone (69-72). One Canadian centre has developed a clinical prediction rule to help determine which patients can be safely discharged one hour after the administration of naloxone for a presumed opioid overdose. They concluded that patients can be safely discharged if: 1) they can mobilize as usual; 2) have an oxygen saturation on room air of > 92%; 3) have a respiratory rate of > 10 breaths/min and < 20 breaths/min; 4) have a temperature of > 35.0^0C and < 37.5^0C; 5) have a heart rate > 50 beats/min and < 100 beats/min; *and* 6) have a Glasgow Coma Scale score of 15 (70). While promising, these clinical guidelines have yet to be prospectively validated.

Community based naloxone programs: Community based naloxone programs have been proposed as a method of reducing the morbidity and mortality associated with opioid overdose. A systematic review of the literature was performed to document the available evidence for such programs. Searches were carried out in PubMed, EMBASE, PsycInfo, Cochrane and DARE databases and included all articles published up until February Week 2, 2005. Search terms were comprehensive and inclusive (please refer to Appendix 2 for search terms).

A total of 726 possible articles were identified. Only articles that directly addressed community based naloxone programs were eligible for inclusion in the review. The abstracts were independently reviewed by two investigators (DL and KD), and disagreements were resolved by reviewing entire articles and by consensus. Because of the limited amount of information published in this area and the methodological variability, an assessment of quality was not performed. A total of 22 relevant articles were initially identified. The search was updated on July Week 3, 2006 and five more

articles were included at the discretion of one reviewer (KD); thus a total of 27 articles are included in this review. A recent review of the literature on this topic has also been published (73).

Due to the mortality and morbidity burden of opiate overdose and the current lack of formal health service response, many of the articles simply propose that drug users be trained in the provision of basic life support measures and naloxone administration, but do not include a formal evaluation of such a program (52, 74-81). Several studies have documented user acceptability of a community based naloxone program, with levels of support ranging from 70 – 90 % (48, 82, 83). The majority of drug users (88.5%) in a recent survey expressed willingness to administer a medication to another drug user in the event of an overdose (84). There is also preliminary evidence of health care provider and community worker support for such programs (85, 86); however, others feel that such programs may not be of benefit or do more harm than good (87, 88). In a recent survey of EMS providers in Baltimore, 56% felt that training drug users to administer naloxone would not be effective in reducing overdose deaths; concerns included drug users' ability to properly administer the drug, perceptions that community based naloxone programs condone and promote drug use, and the unsafe disposal of used needles (89). There is also some concern in the literature that easy availability of naloxone may increase the amount of drug used because of the possibility of easy rescue (90); however, only 5- 6% of users said that this would influence their drug taking practices. Reasons for this included the unpleasant withdrawal symptoms precipitated by naloxone, and the fact that heroin was too expensive to waste by taking more of it than was needed (75, 82).

The risk of Hepatitis C transmission during naloxone administration with unclean needles has also been proposed (91), although never empirically evaluated.

Community based naloxone programs already exist in many parts of Europe and the US. The longest running program exists in Italy, where naloxone has been sold over the counter for more than 12 years and distributed by needle exchange programs since 1995 (92). American community based naloxone programs are currently operating in Chicago, Salt Lake City, New Mexico, San Francisco, Baltimore and New England (86, 93, 94). There have been limited evaluations of these programs since many are clandestine and unsanctioned (95); moreover, these evaluations are often descriptive and use weak research designs. There are, however, published reports of lives saved by such programs.

The program in Berlin, Germany has reported 29 lives saved (96). The program in Jersey, UK has reported 5 lives saved (96). The Chicago Recovery Alliance probably runs the largest community based naloxone program in the US and has recently reported 260 lives saved (93). Two recent pilot studies have demonstrated the ability of drug users to perform CPR and administer naloxone in overdose situations; in both these studies all the overdose victims survived (97, 98). To date, a community based naloxone program has not been initiated in Canada.

In summary, the evidence for community based naloxone programs is mainly anecdotal. Recent pilot studies demonstrating that drug users can be trained in CPR and naloxone administration and perform these skills in the setting of a witnessed overdose are very promising. Further studies are needed to determine the efficacy and safety of community based naloxone programs.

1.8 Research Questions

Opioid users face significant morbidity and mortality burdens as a consequence of their drug use, particularly as a result of overdose. Despite the fact that most opioid overdoses are witnessed, the response to this immediate health crisis is less than ideal, with low rates of bystander CPR and formal emergency medical service or other medical assistance. Naloxone has been used safely in the hospital and pre-hospital setting for years to reverse the effects of opioid overdose and the respiratory depression that leads to death and disability.

There is a need to develop innovative health promotion strategies to increase the availability of this treatment to opiate users, especially in Canada. Several jurisdictions in Europe and the United States have implemented community based naloxone programs where users are trained in basic life support measures and naloxone administration. There have been many anecdotal reports of lives saved; however, evaluation has been infrequent. Moreover, no such program has been implemented in Canada. In fact, little is known about the experience of Canadian opiate users, and there has been no local research on this issue in the Capital Health region of Alberta. This thesis is designed to fill this information gap.

This thesis is presented in three parts and is designed to answer the following questions:

Part I: Narcotic Overdose Registry of Alberta (NORA): NORA is a registry of fatal events attributed to opioid use in Alberta over a one year period. The main goals of this study were: (1) to determine the mortality associated with opioid overdose in

Alberta; (2) to determine the circumstances surrounding fatal opioid overdoses; and (3) to compare rural and urban overdoses.

Part II: Narcotic Overdose Registry of Edmonton (NORE): NORE is a registry of all opioid overdose patients seen in five Capital Health emergency departments over a one year period. The main goals of this study were: (1) to present the epidemiology of opioid overdoses in Edmonton, AB; (2) to determine the morbidity/mortality associated with these opioid overdoses; and (3) to describe interventions reported in conjunction with these opioid overdoses.

Part III: Narcotic Overdose Respondent Intervention Survey (NORIS): NORIS is a survey of 150 opioid and non-opioid using clients seen at the Streetworks Needle Exchange Program in Edmonton, AB. Respondents were asked about their experience with drug use, addiction, and overdose. The main goals of this study were: (1) to determine the overdose experiences of drug users in Edmonton, AB; and (2) to determine the perceptions of drug users in Edmonton, AB of a community based naloxone program.

Table 1-1: Summary of the morbidity and mortality associated with illicit opioid use in Canada

Author, yr	Location	Design	N/Age	Drugs	Follow-up	Outcome
Fischer, et al., 2005(16)	Edmonton, Montréal, Québec City, Toronto, Vancouver	Prospective cohort	679/ 34.8 years	Regular opiate use for at least one year	n/a	Personal health assessment, 50.4% fair or poor; Depression, 49.2%
Popova, et al., 2006(3)	Canada	Survey of key informants/ administrative data	n/a	Illegal opioid users	n/a	Hospitalization rate 21.0 / 100,000 population aged 15-49; proportion of overdose deaths in estimated opiate users population was 1.1

Table 1-2: Main types of harm reduction initiatives relevant to injection drug use

Initiatives	*Proposed Immediate Objectives*
Education about Overdose prevention Safer injection techniques Risks of needle sharing Safe sex	 Reduce deaths due to overdose Reduce abscesses and infections; reduce damage to veins Reduce needle sharing and HIV, Hepatitis C transmission
Needle exchange programs or other methods of needle distribution such as pharmacies, needle dispensing machines, mobile vans	Reduce needle sharing and related infectious problems Reduce spread of blood borne disease
Distribution of bleach	Reduce risk of infection if needle sharing occurs
Supervised injection sites	Reduce deaths due to overdose Reduce sharing of needles and associated problems Reduce public exposure to self-injection Access to counseling and other health/social services
Drop-in centers Shelters	Provide food and/or shelter Improve self-care and access to services Reduce public exposure to self-injection Provide counseling
Outreach Professional Peer	Provide food/blankets/condoms Intervene in emergency situations Dispense needles/bleach/methadone
Low-threshold methadone	Reduce need for drugs by injection Reduce use of illegal drugs Stabilization, improved health and social integration
High-threshold methadone	Reduce/eliminate need for drugs by injection Reduce use of illegal drugs Stabilization, improved health and social integration
Prescription of other non-injectable or injectable maintenance drugs LAAM (a long acting opioid agonist), buprenorphine, codeine, heroin	Reduce/eliminate need for drugs by injection Reduce use of illegal drugs Improvements in other life areas
Prescription of preferred drugs for self injection Opiates, amphetamines, cocaine	Reduce/eliminate use of illegal drugs Improvements in other life areas
Drug-use tolerance zones	Geographical containment of drug use

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Chapter 2

Characterizing Alberta Opioid Deaths: Results from the Narcotic Overdose Registry of Alberta (NORA)

2.1 Introduction

Injection drug use is an important health problem in Canada and the United States. Although it is difficult to obtain accurate information on rates and patterns of illicit drug use, conservative estimates suggest that there are 50,000 to 90,000 injection drug users (IDUs) in Canada alone (1, 2). This translates into a rate of 2.5 – 4.6 Canadians who use injection drugs per 1,000 population aged 15-54 years (3). Given the many health challenges faced by this population, IDUs are frequent users of the emergency department (ED) and primary health care services; one study estimated rates of ED use 30% higher than demographically similar non-drug using controls (4). In a Vancouver study of a prospective cohort of IDUs, 78% had visited a primary care clinic in the past year and 60% had visited the ED in the preceding two years. The most common reasons for ED visits were abscesses or cellulitis, wounds or lacerations and substance use or overdose (5).

Although many different drug classes can be used intravenously, intravenous opiate use is associated with particularly excessive morbidity and mortality. Opiates produce their effects by acting as agonists on the mu, kappa and delta receptors in the central nervous system. Their effects include euphoria, analgesia, respiratory depression, delayed gastrointestinal motility and miosis. The respiratory depression, which leads to death in opioid overdose, results from a direct effect of the drug on the brainstem respiratory centers, primarily mediated through a reduction in responsiveness to carbon

dioxide (6). This central effect on respiration can be enhanced by the use of other drugs such as benzodiazepines and alcohol (7-9).

Many studies have attempted to quantify the excess mortality attributable to illicit opioid use. One meta-analysis has estimated the excess mortality ratio to be 13.2 (95% CI 12.3 – 14.1) for heroin users. In this particular study four major causes of mortality were identified: accidental overdose, suicide (either by drug or another method), violence and accident/injury, and medical conditions (often related to drug use). Overdose was the cause of death in approximately 23-49% of cases (10). Non-fatal overdoses are also common among heroin users, with up to 69% having ever overdosed and a median of three overdoses for those who had overdosed (11). These findings are consistent with recent Canadian data indicating that 17.2% of opioid users had overdosed in the preceding six months and, of those that had overdosed, 37.8% had experienced multiple overdose episodes (12). Australian data suggest that overdoses are also commonly witnessed by other individuals present at the time of the drug use. One study reported that up to 88% of opioid overdoses occurred in the presence of other people (13). Most users (70-86%) have witnessed someone else's overdose, and of those who have witnessed overdoses, a range of three to six have been witnessed (13, 14).

Heroin overdoses are rarely instantaneously fatal (15). In most cases, death occurs slowly over hours, giving ample opportunity for bystander and medical intervention(s). As Davidson aptly comments, "When bystanders are present, willing, and able to act effectively, overdose fatalities should therefore be extremely rare. That overdose deaths are frequent suggests that one or more of these three factors is commonly

missing, and that the social context of overdoses may be as important as the biomedical context in understanding and preventing fatalities."(16), p. 262.

Canadian data on the true mortality attributable to opioid use is limited. The Canadian Community Epidemiology Network on Drug Use (CCENDU) collects data on hospital admissions and death related to alcohol and drug use in Canada from administrative databases; however, it is suspected that this source significantly under-represents the burden of disease in this population (17). One recent study reported a total of 958 illegal drug and combined drug and alcohol related deaths in Canada in 2002; however, the role of opioids in these deaths is unclear (2). To our knowledge there has been no formal study designed to document the circumstances associated with fatal opioid overdose in a Canadian setting. The purpose of this study is to fill this information gap by describing the circumstances of opioid related fatalities in a Canadian province.

2.2 Methods

Study Design: This was a retrospective chart review of all Medical Examiner (ME) cases for the year 2004 in the province of Alberta, Canada. Cases were eligible for analysis if opiates or their metabolites were quantitatively or qualitatively determined to be present at the time of death. There were no specific exclusion criteria, although non-opiate overdose cases were not included. Routine toxicology screening is not performed in this province; in fact, it is the policy of the Office of the Chief Medical Examiner that any request for toxicology screening, beyond a blood alcohol level, must be justified

based on historical or physical examination findings. This study was approved by the Health Research Ethics Board at the University of Alberta.

Study Setting and Population: In 2004, Alberta had a population of 3,066,257 persons (18), which represents approximately 10% of the total Canadian population. There are two main urban areas in Alberta: Edmonton with an estimated metropolitan population of 666,104 persons in 2004; and Calgary with an estimated metropolitan population of 933,495 persons in 2004 (18). The remainder of the population lives in predominantly rural or smaller urban settings.

Study Protocol: In collaboration with treating physicians, local MEs arbitrate on the cause of death across the Province of Alberta. The Office of the Chief Medical Examiner maintains a database of all deaths that occur in the province during the year. All deaths with a positive opiate screen from January 1, 2004 to December 31, 2004 were identified by searching this database. Opiates or their metabolites that could be identified by toxicology screening included heroin, morphine, codeine, hydromorphone, oxycodone, methadone, fentanyl, propoxyphene and meperidine. Samples for toxicological testing were obtained from various sites (including, but not limited to blood, urine, vitreous, liver, bile and gastric contents), and may have been taken pre- or post-mortem; any opioid identified in the sample (either qualitative or quantitative) was considered positive and these patients were included in the study. ME charts typically included an autopsy or Medical Examiner's report, a police report, and where emergency medical services (EMS) was called to the scene, a full EMS report. Data were abstracted using a standardized form by two reviewers (DL and KD). A copy of the data abstraction form can be found in Appendix 3. Ten percent of the charts were reviewed by both

individuals and the inter-rater reliability (kappa [κ]) on seven study variables was calculated.

Measures: This study collected information on patient demographics, location of death, circumstances surrounding the overdose, coingestant use, EMS activation and prehospital care. Race (aboriginal vs. non-aboriginal) was determined by information contained in the police report, as well as visual inspection or information provided by the family. Deaths were considered urban if they occurred within the city limits of Calgary or Edmonton; all other deaths were considered rural. One *a priori* subgroup analysis was planned to compare urban vs. rural deaths on the basis of age, gender, location of death, coingestant use, and EMS activation. Once it became apparent that some of the patients included in the study did not die as a direct result of drug overdose (for example, one patient died in a motor vehicle collision after taking two tablets of acetaminophen with codeine), a second subgroup analysis was performed to compare those with a primary cause of death related to "overdose" or "toxicity" vs. those that died from non-overdose related causes. These two groups were also compared on the basis of age, gender, location of death, coingestant use and EMS activation.

Data Analysis: Statistics were calculated using SPSS (SPSS Inc., Chicago, IL). Categorical variables are described with percentages, while continuous variables are described with means and standard deviations (SD) or medians and interquartile ranges (IQR), where appropriate. When comparing groups, chi-square analyses were used for categorical variables and two-sample t-tests were used for continuous variables. In order to avoid inflated Type I error rates due to multiple statistical tests, a Bonferroni correction ($p<0.01$) was used to determine significance when multiple comparisons were

made across study groups. Potential years of life lost (PYLL) were calculated by determining the difference between the age of death and 75 years, the average life expectancy for men and women in Canada. Age specific death rates were calculated by dividing the number of deaths in this cohort per age group by the 2004 Alberta population per age group.

2.3 Results

Demographics: There were a total of 352 deaths in the province of Alberta in 2004 in which there was a positive opioid screen at the time of death; all charts were available for review. A total of 30 charts were reviewed by two individuals and the inter-rater reliability on 7 variables was acceptable ($\kappa = 0.86$).

The median age at death was 46 years (IQR 36.0, 53.0) and 211 of the cases (60%) were male. Most victims were Caucasian (290; 82%) or Aboriginal/Métis (52; 15%). The majority of deaths (209; 59%) occurred in either Calgary or Edmonton. The most common location of death was at home or in another private residence (255; 72%). Seventy-one patients (20%) died in hospital and only 14 (4%) deaths occurred in a public location. Further demographic details of the study sample are documented in Table 2-1.

Overdose Circumstances: Drug use was clearly witnessed in 47 (13%) of cases. Bystander CPR was performed in 46 (13%) cases and support of the airway or rescue breathing alone was performed in 9 (3%) cases. Coingestants were frequent, with benzodiazepines (46%), acetaminophen (39%), alcohol (31%) and cocaine (24%) being the most commonly identified in the case files.

Health Care Services: EMS was activated in 285 (81%) cases; however, in 143 (41%) cases, the individual was declared dead at the scene. Pre-hospital naloxone was given in 12 (3%) cases; it was ineffective in 8 cases and had an unclear effect in the remaining 4 cases.

Subgroup Analyses: The cohort was divided into primary vs. secondary overdose diagnoses as the immediate cause of death for subgroup analyses. A total of 238 individuals (68%) were determined to have died as a primary result of overdose. These two subgroups did not differ with respect to sex ($x^2(1) = 1.73$, p=0.19) or EMS activation ($x^2(1) = 0.91$, p=0.34). Those with a primary diagnosis of overdose, however, were significantly younger than cases with a secondary overdose diagnosis (43 years vs. 50 years, $t = 4.59$, $p < 0.001$), more likely to die at home or in another private residence (78% vs. 61%; $x^2(1) = 12.0$, p=0.001) and more likely to have consumed other drugs or medications (87% vs. 75%, $x^2(1)= 7.35$, p=0.007). A second subgroup analysis comparing those who died in an urban vs. rural setting did not demonstrate any significant differences in age, gender, location of death, rates of EMS activation or the use of coingestants.

PYLL and Age Specific Death Rates: There were a total of 10,522 PYLL in this cohort; this represents an average of 29.9 years/person. If just those individuals with a primary cause of death related to overdose are considered, the average PYLL is 32.0 years/person. Overall, males experienced higher age specific rates of death than females (13.0 per 100,000 vs. 8.9 per 100,000). In males, the 45-49 year group had the highest age specific death rate at 28.3 deaths/100,000 persons. In females, the 50-54 year group

had the highest age specific death rate at 29.6 deaths/100,000 persons. Please refer to Figure 2-1.

2.4 Discussion

Opioid-related fatalities, as in this and other studies, commonly occur in relatively young individuals with many years of potential life remaining (10). Since most deaths from opioid overdose do not occur immediately, there is an opportunity to intervene and prevent death from occurring (15). In order to determine which interventions would be most appropriate in preventing death, it is important to understand the circumstances that surround opioid related deaths. Unfortunately, very little is known about where and how these deaths transpire.

This study highlights that the vast majority of opioid related deaths occur at home or in another private residence (72%). This suggests that family members or friends of opiate users represent the key groups for targeting intervention strategies. For example, training such individuals in overdose recognition, basic life support measures and EMS activation may prove effective at reducing the death toll from this problem. In this study, bystander CPR was only performed in 13% of cases. Other studies have reported rates of bystander CPR in this setting ranging from 6 - 39% (13, 15, 16). As in other settings of cardiac or respiratory arrest, bystander CPR has been shown to significantly reduce the morbidity associated with opioid overdose (19).

The high proportion of coingestants found in this study (83%) are consistent with other reports; however, this proportion is higher than those of 58-76% which were reported in American and Australian studies of fatal opioid overdoses during the 1990's

(20, 21). These results would suggest that polysubstance use culminating in death may be increasing (13, 22, 23), although longitudinal data is required to support this inference. Overdose prevention programs need to educate users about the dangers of using multiple substances simultaneously.

One component that cannot be overlooked is the social setting in which these deaths occur. In many cases, bystanders are prevented or delayed from obtaining formal medical assistance due to fear of police involvement. Concerns over outstanding warrants and fear of manslaughter charges have been cited as barriers to calling for emergency medical assistance (13, 24). Distrust of medical institutions also seems to be deeply ingrained among drug users and is another barrier to calling for medical assistance (25). Once those present at the scene determine that an overdose has occurred, if unable to revive the individual themselves, they may flee the scene or leave the individual to be found by someone else. This may explain the large discrepancy between the results of this study where only 13% of overdoses were clearly witnessed and other Australian survey data suggesting that up to 88% of opioid overdoses are witnessed (13). While EMS was activated 81% of the time in this study, in 41% of deaths the individual was declared dead at the scene suggesting that the call for medical assistance was made at a futile point in the overdose continuum.

In summary, opioid overdoses seem to occur in young males, in a private location. Most victims do not receive bystander CPR and formal EMS services, if activated, arrive too late for successful resuscitation to occur.

2.5 Limitations

There are several limitations of this study that warrant discussion. First, these results represent only one Canadian province over the period of one year and may not reflect the circumstances present in other locations or trends over time. Opioid related deaths are known to fluctuate with the supply of the drug and also with location (26, 27), and other centers are encouraged to examine the epidemiology of fatal opioid overdoses to identify differences with these data.

We included all individuals that were found to have positive opioid screens at the time of death. It is impossible to know how many individuals died from a narcotic overdose yet did not receive a toxicology assessment. This could transpire when the death seemingly occurred from natural causes. Moreover, elevations in opioid metabolites may occur in patients consuming small quantities of narcotic analgesics, so these data may over-estimate the magnitude of the problem. There is evidence, however, to suggest chronic opiate use is dangerous to apparently healthy people, and their use is strongly associated with death (10, 28-30).

This study also has the limitations common to retrospective reviews. While Medical Examiner charts contain robust physical information about the deceased, a variable amount of other information about the circumstances surrounding the death are available. We often found that the individual was discovered by others staying at the same location, but that very little was known about when the drug use occurred, and whether others were present at the time of the overdose and fled the scene. This may reflect an individual's lack of willingness to become involved once they realize that a severe overdose has occurred. Consequently, the proportion of witnessed overdose, bystander CPR or airway support reported in this study may be underreported. In some

cases, it is also difficult to determine the relative contribution of the narcotic to the cause of death when trauma or other circumstances are present. One Canadian independent review found poor overall agreement (Kappa [κ] = 0.27) between a toxicologist and a Medical Examiner in determining overdose as the cause of death (31). The results of our study rely on the interpretation of available information by the Medical Examiner at the time of death; however, the inter-rater reliability in determining the immediate cause of death in this study is not known. By including all deaths with a positive opioid screen regardless of immediate cause of death, and doing a secondary analysis of the data based on cause of death, we hoped to eliminate some of this uncertainty in the results.

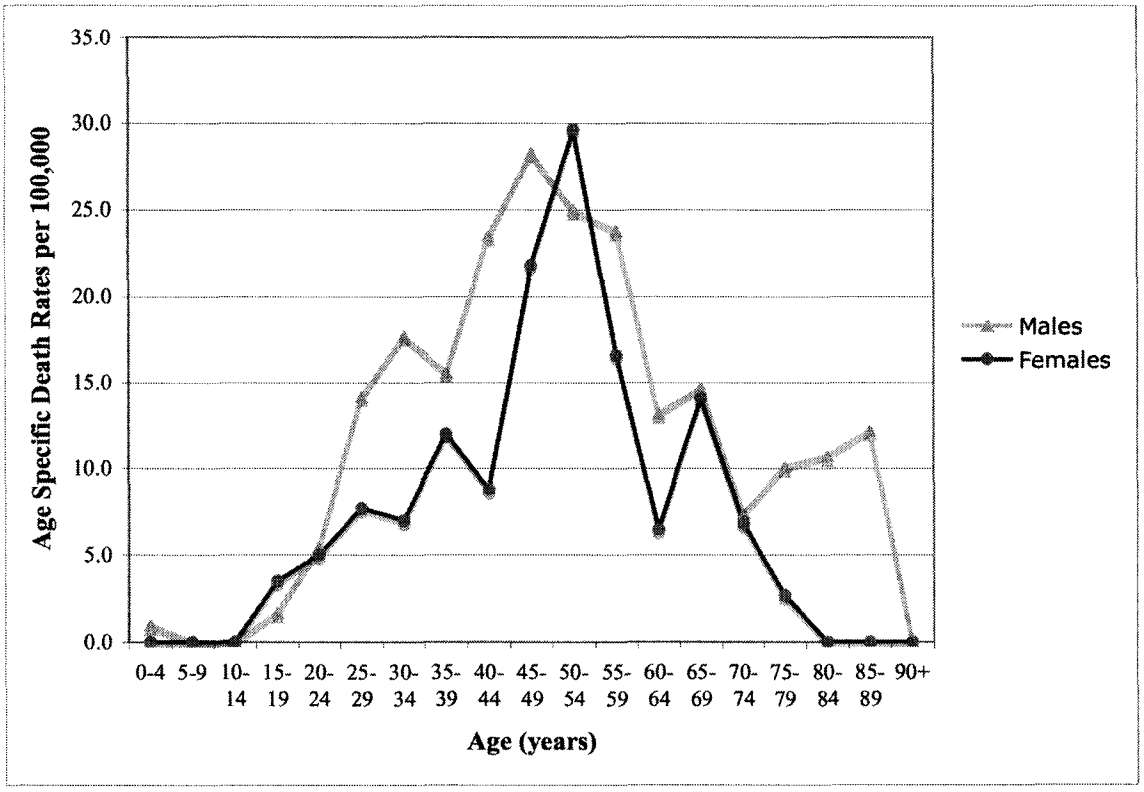
2.6 Conclusions

What is clear from this study is that fatal opioid overdose is a serious problem in this province. Moreover, innovative educational and training programs must be devised to reduce the mortality associated with opioid overdose. A harm-reduction approach has been advocated as a method of reducing the morbidity and mortality seen with injection drug use (32, 33). Conceptually, harm reduction approaches are value-neutral, do not insist on abstinence and focus on the more immediately harmful consequences of drug use (32). Culturally sensitive educational programs need to be designed to warn users of the dangers of poly-substance use and also to train them in basic life support measures and CPR. EMS activation must occur in a setting free from fear of arrest or persecution. Community based naloxone programs in which users are trained to administer an intramuscular injection of naloxone to reverse the lethal effects of the opioid have also been proposed (34).

Table 2-1: Baseline characteristics of all deaths with a positive opioid screen in the province of Alberta, Canada in 2004

Factor	Summary Results
Age	45 years (SD=13.1)
Gender:	
Male	211 (60%)
Female	141 (40%)
Race:	
Caucasian	290 (82%)
Aboriginal	39 (11%)
Métis	13 (4%)
Other	6 (2%)
Missing	4 (1%)
Time of Death:	
08:01 – 16:00	172 (49%)
16:01 – 24:00	103 (29%)
00:01 – 08:00	75 (21%)
Day of Week of Death:	
Weekend (Saturday 00:00 – Sunday 23:59)	109 (31%)
Weekday (Monday 00:00 – Friday 23:29)	243 (69%)
Location of Death:	
Home or other Private Residence	255 (72%)
Hospital	71 (20%)
Public Location	15 (4%)
Police Custody	1 (< 1%)
Other	10 (3%)
Site:	
Edmonton	126 (36%)
Calgary	83 (24%)
North Rural	59 (17%)
South Rural	84 (24%)

Figure 2-1: Age specific death rates per 100,000 due to opioid overdose for men and women in Alberta, Canada in 2004



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Chapter 3

Characterizing Opioid Overdoses: Results from the Narcotic Overdose Registry of Edmonton (NORE)

3.1 Introduction

Injection drug use is an important problem in Canada and the United States. Although it is difficult to obtain accurate information on rates and patterns of illicit drug use, conservative estimates suggest there are 50,000 to 90,000 injection drug users (IDUs) in Canada alone (1, 2). This translates into a rate of 2.5 – 4.6 Canadians who use injection drugs per 1,000 population aged 15-54 years (3). Given the many health challenges faced by this population, IDUs are frequent users of the emergency department (ED); one study estimated rates of ED use 30% higher than demographically similar non-drug using controls (4). In a Vancouver study of a prospective cohort of IDUs, 78% had visited a primary care clinic in the past year and 60% had visited the emergency department in the preceding two years. The most common reasons for visiting the ED were abscesses or cellulitis, wounds or lacerations and substance use or overdose (5).

While many different drug classes can be used intravenously, intravenous opiate use is particularly important since it is associated with increased morbidity and mortality. Opiates produce their effects by acting as agonists on the mu, kappa and delta receptors in the central nervous system. Their effects include euphoria, analgesia, respiratory depression, delayed gastrointestinal motility and miosis. The respiratory depression, which may lead to respiratory arrest and death in opioid overdose, results from a direct effect of the drug on the brainstem respiratory centers, primarily mediated through a

reduction in responsiveness to carbon dioxide (6). This central effect on respiration can be enhanced by the use of other drugs such as benzodiazepines and alcohol (7-9). While the excess mortality attributable to opioid overdose has been relatively well quantified (10), the morbidity associated with opioid addiction has not been as well studied. Non-fatal overdoses appear to be particularly common among heroin users. For example, in Australia, 69% of heroin users admitted to ever overdosing, with a median of 3 overdoses per person (11). In Canada, 1 in 7 opioid users reported overdosing in a six month period prior to assessment and multiple overdoses were also common (12). Many non-fatal overdoses are associated with complications, including physical injury (e.g. fractures, dislocations, lacerations and/or head injuries) sustained when falling. Over three-quarters (82%) of those who overdose experience at least one overdose-related health complication (11). Other, less common causes of morbidity in opioid overdose include pulmonary edema, cardiac arrhythmia, rhabdomyolysis and compartment syndrome (8).

Canadian data on the morbidity attributable to opioid use is limited. The Canadian Community Epidemiology Network on Drug Use (CCENDU) collects data on hospital admissions and death related to alcohol and drug use in Canada from administrative databases. CCENDU data on the morbidity of illicit drug use is derived from the Canadian Institute for Health Information (CIHI), Hospital Morbidity Database. In 2000-01, there were an estimated 25,908 hospital admissions in individuals 15 years and older with a primary diagnosis related to illicit drug use. A further 29,214 admissions listed illicit drug use as a secondary cause of hospitalization (13). One weakness of the CIHI database is the lack of ED data on which to base morbidity estimates. To our knowledge there has been no formal review to document the

circumstances of opioid overdoses that present to the ED, where admission may not occur in all cases. Thus, the purpose of this study is to describe the circumstances of opioid overdose that present to EDs in an urban Canadian centre.

3.2 Methods

Study Design: Retrospective chart review of all opioid overdoses presenting to any one of five emergency departments in an urban Canadian centre from January 1, 2004 through December 31, 2004. This study was approved by the Health Research Ethics Board at the University of Alberta.

Study Setting and Population: This study was conducted in the Capital Health (CH) region of Edmonton, Alberta, Canada. The CH region provides services for approximately one million people and includes a large inner-city teaching hospital. Edmonton has a large intravenous drug using population – the local needle exchange program serves approximately 400 unique users per month, and due to group exchanges, exchanges 2000 needles per user per year (14).

Study Protocol: Patients included in the analysis met the following criteria: (1) presented to one of the five participating EDs between January 1, 2004 and December 31, 2004; (2) were 13 years of age or older; and (3) had a diagnosis of toxic ingestion of opioids (consecutive ICD-10 codes between T40.0 to T40.6) recorded as their discharge diagnosis. All ED charts are reviewed by trained nosologists in the Health Records department at each of the Capital Health hospitals. Each patient visit is coded with up to 10 diagnosis codes. The diagnosis codes in all 10 fields were reviewed to identify the patients included in this study. Patients were excluded from the analysis if they: (1) left

without treatment; (2) were transferred from another facility outside the Capital Health region; or (3) if they ingested only cocaine without an opioid (ICD-10 code T40.5). The charts were reviewed in detail and data abstracted using a standardized form. Please see Appendix 4 for a copy of the data abstraction form. The data were abstracted by one of three trained data abstractors. Ten percent of the charts were reviewed by two individuals and the inter-rater reliability (kappa [κ]) on 8 variables was calculated. Disagreements were resolved by consensus.

Measures: This study is predominantly descriptive in nature. Key measures include the location of the overdose, frequency of coingestants, initial triage score, disposition and length of stay in the emergency department. On arrival to the study hospitals, the Canadian Triage and Acuity Score (CTAS) was used to determine the priority with which patients were assessed. Patients with a CTAS score of 1 indicates a *resuscitation* and immediate physician assessment is advised; a score of 2 is considered *emergent* and physician assessment is advised within 15 minutes; a score of 3 is considered *urgent* and physician assessment is advised within 30 minutes. CTAS 4 and 5 scores are less urgent and physician assessment is advised within 60 and 120 minutes, respectively (15).

Comparative Data: Data on all 240,867 ED visits for the participating CH region hospitals were obtained for the 2004 calendar year from the Health Services Planning and Information department (Chris Houston, Capital Health). This information was used to compare the study sample with all patients receiving ED services with respect to CTAS scores, admission proportions and lengths of stay.

Data Analysis: Statistics were calculated using SPSS (SPSS Inc., Chicago, IL). Categorical variables are described with percentages, while continuous variables are described with means and standard deviations (SD) or medians and interquartile ranges (IQR). Chi-square analyses were used to test for significant differences between groups.

3.3 Results

Sample: There were a total of 570 ED visits for opioid overdose identified. Of these, 563 (98.8%) were available for review. One hundred and thirty-six (24%) charts met the exclusion criteria and were not included in the primary analysis (Figure 3-1). A total of 60 charts were reviewed by two individuals and the inter-rater reliability on 8 variables was adequate ($\kappa = 0.60$).

Demographics: A summary of the patients included in the study can be found in Table 3-1. The median age of presentation was 37.0 years (IQR 28.0, 47.0). Females presented to the ED more commonly than males with opioid overdose (56% vs. 44%, $x^2(1) = 442.8$, $p \leq 0.001$). Overdoses occurred commonly at home or in another private residence (244, 58%). Only 65 (15%) overdoses occurred in a public place; however, it was impossible to determine the location of the overdose from the ED record in 101 (24%) cases.

Coingestants were extremely common in the sample with a total of 348 (82%) individuals taking at least one other drug in addition to an opioid (Table 3-2). The most common coingestants were acetaminophen, ethanol, benzodiazepines and cocaine (50%, 27%, 21% and 8%, respectively; Table 3-3). EMS transport to hospital occurred in 373 (71%) cases.

In this study, 23 (5%) patients received a CTAS score of 1 and 196 (46%) received a score of 2. This compares to < 1% and 12% for all ED visits to these CH region hospitals over the same time period, respectively. This translates into 51% of patients presenting to the ED with an opioid overdose in this study requiring emergent physician assessment within 15 minutes, compared to 12% for all ED visits. Figure 3-2 provides a comparison of the CTAS distributions for this study and all ED visits.

Interventions: Pre-hospital naloxone was administered in 81 (19%) cases; it was effective at improving the patient's respiratory rate or level of consciousness in 67 (83%) of those cases. Naloxone was administered in the ED in 85 (20%) cases and was effective at improving the patient's respiratory effort or level of consciousness in 53 (62%) those cases. A naloxone infusion was started in 22 (5%) cases.

Outcomes: Most patients (330, 77%) were discharged from the ED; 93 (22%) were admitted to hospital. This admission burden is higher than for all patients presenting to these EDs in the CH region (22% vs. 14.5%). Only 4 (<1%) patients died while in the ED or while admitted to hospital. The median length of stay for those patients that were discharged from the ED was 8.7 hours (IQR 4.7 – 13.7 hours). By comparison, the average length of stay for all patients presenting to these EDs in the CH region who were subsequently discharged was 5.8 hours.

3.4 Discussion

This retrospective review of ED opioid overdoses across an integrated Canadian health region identified that most overdoses presenting to the ED occur in a private location, are transported by EMS, require emergent physician assessment on arrival and

have prolonged lengths of stay in the ED. Due to lack of documentation on the ED chart, it was not possible to determine how many of these overdoses were witnessed; however, previous research suggests that up to 88% of opioid overdoses occur in the presence of other people and that most users have witnessed someone else's overdose (16, 17). EMS activation was also common in this population, with EMS transporting 71% of the patients in this study to the hospital. These results suggest that family members or friends of opiate users are likely to be present at the time of the overdose and need to be trained in overdose recognition, basic life support measures and EMS activation.

Opiate users impose a significant burden on the health care system. On arrival to the ED approximately half the patients in this study required emergent physician assessment (CTAS score 1 or 2). Patients with opioid overdoses tend to be sicker than the average ED patient, and potentially consume more resources. The median length of stay in the ED for discharged patients in this study was approximately three hours longer than the average length of stay for all patients arriving to these EDs (8.7 vs. 5.8 hours). Given that these patients are rarely admitted but do require lengthy periods of observation in the ED, they contribute to the overcrowding problem common in EDs in this jurisdiction and across North America (18, 19).

The high proportion of coingestants found in this study may have contributed to the severity of the initial presentation in these patients. For example, taking opioids, particularly in combination with other CNS depressants such as alcohol, has previously be shown to be a risk factor for opioid related overdose death (16, 20-23).

Despite requiring EMS transport and emergent physician assessment on arrival to the ED, less than 1% of patients died in the ED or while admitted to hospital. Indeed, the

vast majority (77%) were discharged from the ED after treatment and/or observation. This suggests that with appropriate pre-hospital and hospital care, the majority of opioid or poly-drug overdoses including an opioid need not be fatal.

To date, most of the research into the circumstances surrounding opioid overdoses has come from user self-reported data (5, 12, 16, 17, 24). While this information is important, due to the biases (e.g. selection, social desirability, recall, etc.) inherent in those users willing to complete surveys, it may not reflect the experience of opioid overdose victims in general. This study helps to fill this information gap by systematically examining all opioid overdoses that presented to an emergency department within one Canadian health region. It is also the first study to document the emergency department care and resources required by these patients.

3.5 Limitations

There are a number of limitations to this study that warrant comment. First, this data represents the experience of one urban Canadian centre over the period of one year. The circumstances surrounding opioid overdoses tend to change with drug supply and location (24, 25). Canada also has a universal health care system in which EMS and ED services can be accessed without financial barriers for the patient; this may affect when and how patients present to the ED compared to other jurisdictions.

Second, this study includes all patients for whom an ICD-10 code of "opioid overdose" was recorded on the chart by health records. It is possible that some opioid overdose patients were missed. For example, a cardiac arrest victim who died shortly after arrival in the hospital may have taken a lethal opioid overdose. It is also possible

that some patients who were not opioid overdose victims were included in the sample. For example, some ED patients were *presumed* opioid overdoses based on clinical findings or response to naloxone; however, ingestion of an opioid was not confirmed by serologic testing.

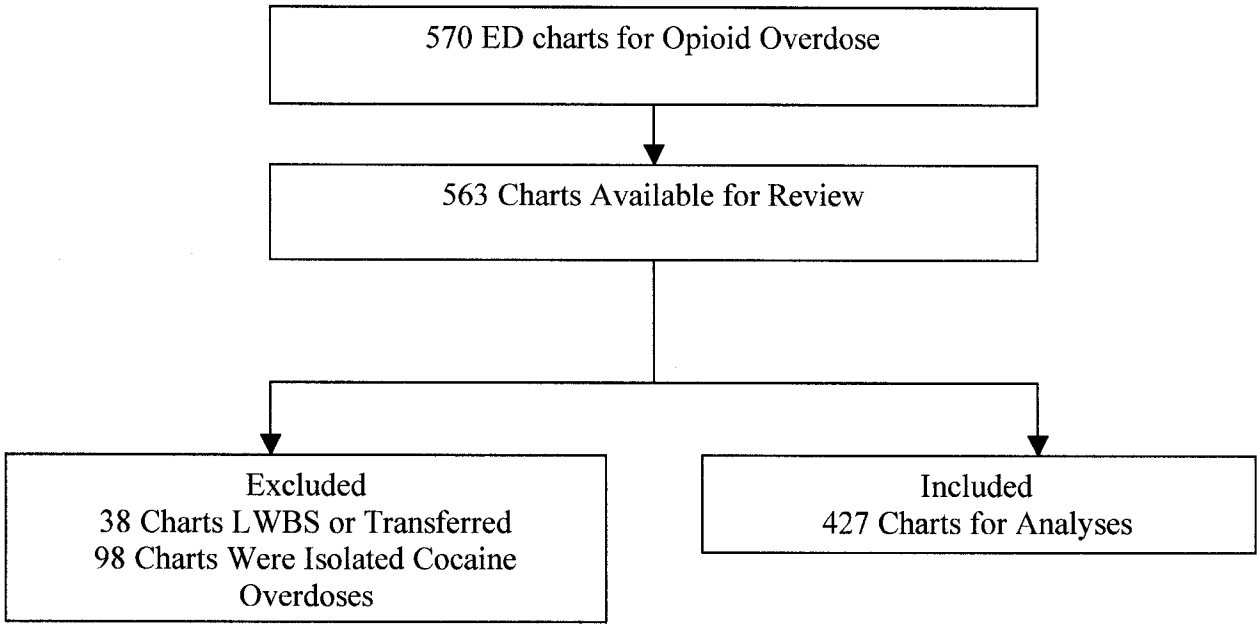
Third, the results of this study should not be interpreted to reflect only the experience of those chronic opioid users who sustain a non-fatal overdose. Some of the overdoses in this study occurred in non-regular opioid users as an intentional overdose attempt. Fourth, this study also has the limitations inherent to retrospective reviews including missing data; specifically not all questions of interest (such as witnessing of the overdose) were recorded or were legible on the ED charts. Finally, 1.2% of the charts were not available from medical records at the time of the review; however, it is unlikely that these additional charts would have altered the overall results reported.

3.6 Conclusions

Opioid overdoses presenting to the EDs in this urban Canadian centre occurred predominantly in young individuals in a private residence; most patients arrived via EMS and required emergent physician assessment on arrival to the ED. The average opioid overdose patient required a prolonged period of observation and/or treatment in the ED and contributed to ED overcrowding. The use of coingestants was high with 82% of patients having consumed at least one other drug in addition to an opioid. Despite the severity of the initial presentation in these patients, and the high rates of multi-drug overdose, less than 1% of patients died in the ED or while admitted to hospital.

These results suggest that with appropriate EMS activation, pre-hospital and hospital treatment, the majority of opioid or combination overdoses need not be fatal. Overdose prevention campaigns should target the friends and relatives of opioid users, teach overdose recognition and basic life support measures, and encourage early EMS activation. Community based naloxone programs in which users are trained to administer an intramuscular injection of naloxone to reverse the effects of opioid overdose have also been proposed (26).

Figure 3-1: Flow diagram of patients included in the NORE study



Note: LWBS = left without being seen by a physician.

Table 3-1: Baseline characteristics of patients with an opioid overdose presenting to an urban Canadian centre ED in 2004

Factor	Summary Results
Age	39.0 years (SD=15.5)
Gender:	
Female	238 (56%)
Male	189 (44%)
Time of Day:	
08:01 – 16:00	124 (29%)
16:01 – 24:00	184 (43%)
00:01 – 08:00	117 (28%)
Day of Week:	
Weekend (Saturday 00:00 – Sunday 23:59)	124 (29%)
Weekday (Monday 00:00 – Friday 23:29)	302 (71%)
Site:	
Royal Alexandra Hospital	212 (50%)
University of Alberta Hospital	71 (17%)
Grey Nuns Hospital	67 (16%)
Misericordia Hospital	50 (12%)
Sturgeon Hospital	27 (6%)
Pre-hospital:	
EMS Activation	305 (71%)
Naloxone administration	81 (19%)
Intubation	13 (3%)
ED care:	
Naloxone administration	85 (20%)
Naloxone infusion	22 (5%)
Intubation	17 (4%)
Outcome:	
Discharged from ED	330 (77%)
Admitted to Hospital	93 (22%)
Admitted to ICU	17 (4%)
Died in ED or while admitted	4 (< 1%)

Table 3-2: Number of coingestants found in patients with an opioid overdose presenting to an urban Canadian centre ED in 2004

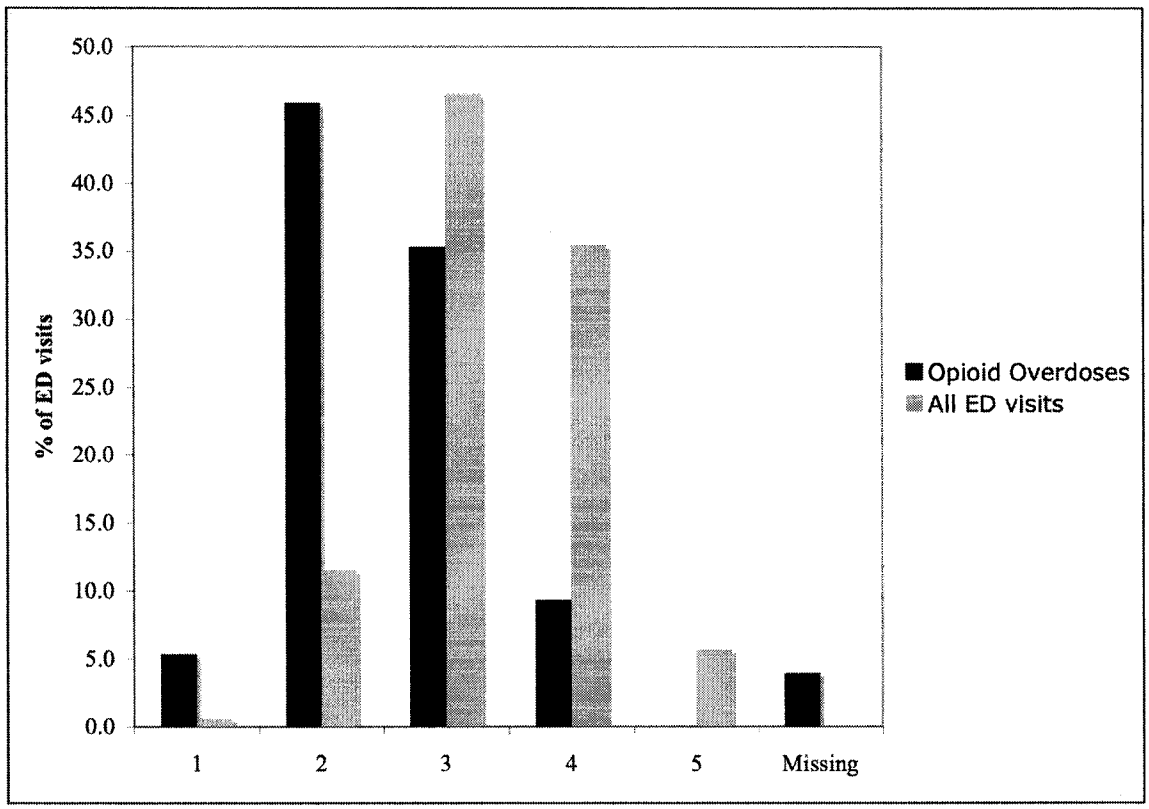
Number of Coingestants	Patients
0	79 (19%)
1	151 (35%)
2	124 (29%)
3	62 (15%)
4	9 (2%)
5	2 (<1%)

Table 3-3: Type of coingestants found in patients with an opioid overdose presenting to an urban Canadian centre ED in 2004

Coingestant	Patients
Acetaminophen	215 (50%)
Ethanol	116 (27%)
Benzodiazepine	90 (21%)
Cocaine	35 (8%)
Methamphetamine	8 (2%)
Other drug	147 (34%)

Note: Numbers total more than 427 and 100% due to multiple coingestants.

Figure 3-2: Canadian Triage and Acuity Scale (CTAS) Score of opioid overdoses on presentation to Canadian EDs in an urban centre compared to all ED patients in 2004



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Chapter 4

Surveying Opioid Users: Results from the Narcotic Overdose Respondent Intervention Survey (NORIS)

4.1 Introduction

Injection drug use is an important problem in Canada and the United States. Although it is difficult to obtain accurate information on rates and patterns of illicit drug use, conservative estimates suggest there are 50,000 to 90,000 injection drug users (IDUs) in Canada alone (1, 2). This translates into a rate of 2.5 – 4.6 Canadians who use injection drugs per 1,000 population aged 15-54 years (3). Because of the many health challenges faced by this population, IDUs are frequent users of the emergency department (ED); one study estimated rates of ED use 30% higher than demographically similar non-drug using controls (4). In a Vancouver study of a prospective cohort of IDUs, 60% had visited the emergency department in the preceding two years. The most common reasons for visiting the ED were abscesses or cellulitis, wounds or lacerations and substance use or overdose (5).

While many different drug classes can be used intravenously, intravenous opiate use is particularly important since it is associated with elevated morbidity and mortality. Respiratory depression, which may lead to respiratory arrest and death in opioid overdose, results from a direct effect of the drug on the brainstem respiratory centers, primarily mediated through a reduction in responsiveness to carbon dioxide (6). This central effect on respiration can be enhanced by the use of other drugs such as benzodiazepines and alcohol (7-9). One recent meta analysis has estimated the excess mortality ratio to be 13.2 (95% CI 12.3 - 14.1) for heroin users (10). In this study four

major causes of mortality were identified: accidental overdose, suicide (either by drug or another method), violence and accident/injury, and medical conditions (often related to drug use). Overdose was the cause of death in approximately 23-49% of cases (10). The morbidity associated with opioid addiction has not been as well studied; however, non-fatal overdoses appear to be particularly common among heroin users. For example, in Australia, 69% of heroin users admitted to ever overdosing, with a median of 3 overdoses per person (11). In Canada, 1 in 7 opioid users reported overdosing in a six month period prior to assessment and multiple overdoses were common (12). Many non-fatal overdoses are associated with complications, including physical injury (e.g. fractures, dislocations, lacerations and/or head injuries) sustained when falling. Over three-quarters (82%) of those who overdose experience at least one overdose-related health complications (11). Other, less common causes of morbidity in opioid overdose include pulmonary edema, cardiac arrhythmia, rhabdomyolysis and compartment syndrome (8).

In order to design effective prevention programs to reduce the morbidity and mortality associated with opioid overdose, it is important to understand the social context in which overdoses occur. Most overdoses appear to be witnessed (13), and death occurs over several hours (14), thus giving ample opportunity for those present to intervene. Previous surveys have indicated that other users will frequently try to reverse the overdose by injecting the victim with salt water, putting ice on the victim or taking them into a cold shower, injecting them with other drugs like cocaine, inflicting pain or walking the person around (15-17). Unfortunately, despite the best intent of these other interventions, low rates of bystander cardiopulmonary resuscitation (CPR) have been documented in this setting (14, 18). Even more alarming, formal medical assistance is

often not called or delayed; fear of police involvement, manslaughter charges, and distrust of medical institutions have all been cited as barriers to accessing emergency medical services (EMS) (13, 17, 19). These findings are supported by Canadian user surveys which suggest that between one quarter and one third of opioid overdoses do not receive any type of formal or informal medical assistance in response to this urgent health threat (12, 20).

Community based naloxone programs in which users are trained to administer naloxone to themselves or another acquaintance in the setting of an opioid overdose, are one proposed intervention to reduce the morbidity and mortality associated with overdose in this population (21). Preliminary user support for such programs has been documented (15, 22, 23) but support by health care personnel and community workers has been mixed (24-27). Concern that users will increase their drug use due to the ease of rescue (28) and the theoretical risk Hepatitis C transmission if unclean needles are used (29), have been cited as concerns.

The goals of this study were to: (1) characterize social contexts associated with overdoses among clients accessing harm reduction services; and (2) to compare social contexts of overdose reported by opioid users with those reported by non-opioid drug users (to our knowledge a direct comparison of this nature has not been previously conducted). The study methodology was designed to capture user-reported barriers to accessing formal medical assistance, and to assess common responses to overdose among users. This was also the first Canadian study to determine whether there was user support for community based naloxone programs, and to document users' beliefs about how such programs would affect their drug use.

4.2 Methods

Study Design: A convenience sample of clients presenting to the needle exchange program in a large Canadian centre were approached for participation in this study. Clients were excluded if they were under the age of 18 years, refused, were unable to provide informed consent, or if they had previously completed the survey during the data collection phase of the study. The original survey was pilot tested in the community by 11 individuals (7%) and then revised based on combined user feedback. The individuals involved in the pilot phase were paid $20 CDN for their participation. This study was approved by the Health Research Ethics Board at the University of Alberta.

Study Setting and Population: This study was conducted in the Capital Health region of Edmonton, Alberta, Canada. The Capital Health region provides services for approximately one million people and includes a large inner city teaching hospital. Edmonton has a large intravenous drug using population – the local needle exchange program, Streetworks, has approximately 400 unique users per month and due to group exchanges, exchanges 2000 needles per person per year (30). In addition to needle exchange services, Streetworks also runs several user support groups, provides basic nursing services to the community and disseminates information about vein care, first aid and overdose prevention.

Study Protocol: Clients presenting to the needle exchange program were asked by one of the program's staff members if they were interested in participating in a short survey on overdose. Those clients that expressed interest were then referred to an on-site research assistant. Informed consent was obtained by the research assistant and

witnessed by a member of the program staff. Clients were informed that their participation in the study would in no way affect their ability to obtain supplies from the needle exchange program and that they were free to terminate the survey at any time. Clients were given the option of completing the survey by writing in their own responses or by having the survey read to them by the research assistant who would then record their answers. A copy of the informed consent form and the survey can be found in Appendices 5 and 6, respectively. Data collection took place from July 2005 – July 2006.

Measures: This study collected information on client demographics, current drug use patterns, personal experience with overdose, EMS activation during an overdose, other actions taken at the time of an overdose and assessed support for a community based naloxone program. Study questions were generated after a thorough review of the controversies in the literature and included 6 general questions on demographics, 18 questions for opiate users and 17 questions for non-opiate users. Clients were considered current opiate users if they reported regularly using opioids (e.g. heroin, morphine, dilaudid, oxycodone or codeine) within the last 6 months. Opiate and non-opiate users were then compared on the basis of overdose experience, willingness to call EMS, response to an overdose and whether they thought community based naloxone programs would encourage increased drug use.

Sample size: With a sample size of 150, we could detect client opinions as rare as 10% with a relative standard error of 25% or less.

Data Analysis: Statistics were calculated using SPSS (SPSS Inc., Chicago, IL). Categorical variables are described with percentages, while continuous variables are described with means and standard deviations (SD) or medians and interquartile ranges

(IQR), where appropriate. When comparing groups, chi-square analyses were used for categorical variables and Mann-Whitney tests were used for continuous variables. In order to avoid inflated Type I error rates due to multiple statistical tests, a Bonferroni correction ($p < 0.01$) was used to determine significance when multiple comparisons were made across study groups.

4.3 Results

Sample: A total of 153 clients participated in the study. Although a formal refused, missed and other (RMO) registry was not kept, approximately 75% of clients were not interested in completing the survey when initially approached.

Demographics: Most participants were male (113; 74%) and the median age was 40 years (IQR 33.0, 46.0). Sixty participants (39%) self identified as white/British/Commonwealth, 36 (24%) as First Nations Status and 16 (11%) as First Nations non-status. More than half had completed all or part of a high school education (91, 59%); in addition, 30 (20%) had attended or completed college or university.

The most commonly used drugs within the last six months were marijuana (94, 61%), crack cocaine (89, 58%), alcohol (77, 50%) and morphine (76, 49%). Thirty clients (20%) were regular heroin users and only 9 respondents (6%) reported no regular drug use within the last six months. Please refer to Table 4-1 for a summary of demographic information.

Overdose Experience: The median number of overdoses ever experienced by the respondents was one (IQR: 0, 4). The median number of overdoses experienced by the respondents in the past year was zero (IQR: 0, 1). The median number of overdoses

observed by the respondents was two (IQR: 1, 10) and the median number of overdoses observed in the last year was 1 (IQR: 0, 3). Of note, when asked how many overdoses they had ever witnessed, eight participants wrote such phrases as "too many to count" or "more times than I can remember". Approximately half of the participants (78, 51%) had ever called an ambulance for someone else who had overdosed, and of those who had called the median number of times they had called EMS was two (IQR: 1, 6.5).

More than a third (56, 37%) of respondents reported that they avoided calling the ambulance all or some of the time when an overdose occurred. Fear of police involvement (42, 28%), thinking that they will be blamed for the overdose (27, 18%), or thinking that the person can recover on their own (20, 13%) were the most commonly cited reasons for not calling EMS. More than half of respondents (86, 56%) had tried to help an overdose victim by doing artificial respiration and/or chest compressions. Other common actions taken during an overdose were to put cold water or ice on the person (25, 16%); "keep the person alert and talking" (22, 14%); put the person in the recovery position or turn onto their side and open the airway (11, 7%); and, use naloxone or Narcan® (9, 6%).

Community based naloxone: Many respondents (105, 69%) had heard of naloxone or Narcan®; about 20% (33, 22%) had received it from paramedics or in the hospital. There was widespread support for studying a community based naloxone program (126, 83%). When asked if people would use more drugs if they knew that naloxone could bring them back 53 (34%) replied "No", 51 (33%) replied "Yes" and 39 (26%) were unsure. More than two-thirds of respondents (102, 67%) wanted more information on how to help people when they overdose.

Opiate vs. Non-opiate users: Over half the sample (94, 61%) had used opiates regularly within the last six months; most of these individuals were using opiates on a daily basis (64, 68%). There was no significant difference between current opiate and non-opiate users in terms of number of witnessed overdoses ever (median 3.0 vs. 2.0, U=1622.0, p=0.04). There was also no significant difference in avoiding calling EMS ("Yes" 26% vs. 13%; "No" 53% vs. 73%; "Sometimes" 21% vs.15%; $x^2(2)$=5.89, p=0.05). Opiate users were, however, significantly more likely to have experienced an overdose (median 2.0 vs. 0.0, U=1423.5, p<0.001) and more likely to assist an overdose victim with artificial respiration and/or CPR (70% vs. 43%, $x^2(1)$=10.84, p=0.001). There was no significant difference between the groups as to whether a community based naloxone program would promote increased drug use due to the possibility of easy rescue ("Yes" 36% vs. 36%; "No" 41% vs. 30%; "Unsure" 23% vs. 34%; $x^2(2)$=2.61, p=0.27).

4.4 Discussion

This study surveyed clients presenting to a needle exchange program in a large Canadian centre. Overall, the results support previous research suggesting that non-fatal overdoses are common among opiate users (11, 12). It is also clear from this research and other studies that drug users, both opiate and non-opiate users, regularly witness overdose incidents among other users (13). What has not been previously reported is that there appear to be certain members of the community who witness a disproportionate number of overdoses; thirteen people (8%) in this study reported witnessing over 100 overdoses, or more overdoses than they could count. While it is not possible to verify the

accuracy of these statements, if true, these individuals would be prime targets for overdose prevention campaigns, first aid and CPR training.

Other studies have hypothesized reasons for the low rates of EMS activation seen in this setting such as concern of police involvement, fear of manslaughter charges and distrust of medical institutions (13, 17, 19). In this study, fear of police involvement and/or concern that they would be blamed for the overdose were reported to be barriers to requesting formal medical assistance. Overall, 46% of respondents endorsed these concerns; this rate is not as high as that reported in the US and Australia, however, where 75-80% hesitate to call EMS for these reasons (13, 19). This suggests that in order for timely EMS activation to occur, it must be in a setting free from persecution and fear of arrest.

Most individuals in this study (56%) had previously tried to help an overdose victim with artificial respiration and/or chest compressions. This is much higher than the previously reported rates of CPR in this (14, 18) or other community settings (31). Not only does this suggest a willingness of other drug users to perform CPR on an overdose victim, it also suggests that CPR training and personal protective equipment (such as pocket masks) should be provided to this high-risk community.

Support for a community based naloxone program was widespread in this respondent group with over 80% thinking that a trial of such a program may be effective. This is similar to the previously reported rates of 70-90% found in other US and Australian settings (14, 22, 23). The users in our study demonstrated a mixed opinion as to whether such a program would result in increased drug use due to the possibility of easy rescue; approximately one third each believed that drug use would not change,

would increase or were unsure. Any jurisdiction implementing such a program should carefully monitor for increased rates of fatal and non-fatal overdose.

One clear finding that has emerged from this study is that users are concerned with their own safety, and that of others. Most people interviewed (67%) wanted more information on how to help others when they overdosed.

4.5 Limitations

There are a few limitations to this study that warrant comment. First, these data represent the experience of one community of users in one urban Canadian centre over the period of one year. The circumstances surrounding overdoses tend to change with drug supply and location (32, 33). Canada also has a universal health care system in which EMS and ED services can be accessed without immediate financial barriers for the patient; this may affect when and how patients access formal medical assistance.

As with any convenience sample, the results are limited due to selection bias. The users participating in this study were organized enough to present to a needle exchange program for clean supplies, did not appear intoxicated at the time of the survey, and were willing to take 15-20 minutes to talk to a research assistant. Consequently, they likely only represent a subset of the drug-using community. Due to the sensitive nature of the survey contents, a RMO registry was not maintained for this study, so it is difficult to determine the extent of this potential bias.

4.6 Conclusions

Overdoses are commonly experienced by regular opiate users and commonly witnessed by both regular opiate and non-opiate users. Thirty percent of respondents in this survey attempted to avoid calling EMS at least some of the time; the most common barriers to EMS activation were fear of police involvement and/or fear that they would be blamed for the overdose. At least 50% of respondents, particularly regular opiate users, had attempted artificial respiration and/or chest compressions at some point in order to revive an overdose victim. This respondent group demonstrated widespread support for a trial of a community based naloxone program and more than 60% of respondents wanted more information on what to do when an overdose occurs. Community based interventions should focus on overdose prevention campaigns as well as first aid and CPR training for this community; free provision of personal protective equipment (such as pocket masks) should also be considered. Future research should be designed to measure the incremental effects of overdose education, basic life support training and community based naloxone programs.

Table 4-1: Characteristics of clients presenting to a needle exchange program who participated in a survey on overdose

Factor	Summary Results
Age	39.3 years (SD 9.6)
Gender:	
Male	113 (74%)
Female	38 (25%)
Transgendered	1 (< 1%)
Race:	
White/British/Commonwealth	60 (39%)
First Nations Status	36 (24%)
First Nations Non-Status	16 (11%)
Other	41 (27%)
Education level:	
Elementary	1 (< 1%)
Junior High	28 (18%)
High School	91 (60%)
College/University	30 (20%)
Regular Opiate use in the last 6 months	
Yes	94 (61%)
No	59 (39%)
Drugs used regularly in last 6 months:	
Marijuana	94 (61%)
Crack cocaine	89 (58%)
Alcohol	77 (50%)
Morphine	76 (49%)
Cocaine	67 (44%)
Codeine	55 (36%)
Hydromorophone	51 (33%)
Benzodiazepines	45 (29%)
Oxycodone	44 (29%)
Methamphetamines	41 (27%)
Heroin	30 (20%)

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Chapter 5

General Discussion and Conclusions

5.1 Overview

Injection drug use (IDU) is an important health problem affecting the lives of approximately 50,00 – 90,000 Canadians (1). Illicit opiate use, in particular, can result in excessive mortality, mainly due to overdose, suicide, violence and other medical conditions related to drug use (2). This thesis reports on the results of three separate but linked projects involving overdoses from opioid agents. The first study -- the Narcotic Overdose Registry of Alberta (NORA) -- described opioid-related deaths in Alberta over a one year period. The second study -- the Narcotic Overdose Registry of Edmonton (NORE) -- reviewed all the opioid overdoses presenting to five hospitals within the Capital Health region of Alberta in the year 2004. The final study -- the Narcotic Overdose Respondent Intervention Survey (NORIS) -- examined overdose experiences of users encountered in a community based support clinic.

Data from NORA indicate that death from opioid overdose or ingestion claimed the life of approximately one Albertan per day in the year 2004 (352 deaths). More deaths occurred in males (60%), who were relatively young (median age of death 46 years), and took place at home or in another private residence (72%). Rates of coingestant use were high (83%). There were a total of 10,522 potential years of life lost (PYLL) in this province in 2004 at least partially attributable to opiate use; this represents 29.9 years per person. Rates of bystander cardiopulmonary resuscitation (CPR) were low (13%) in this setting.

In addition to extracting a high mortality toll, injection drug users also experience increased levels of morbidity related to their drug use. One study has estimated rates of emergency department (ED) use 30% higher than demographically similar non-drug using controls (3). Illicit opiate users also seem to be particularly vulnerable to non-fatal episodes of overdose. In a Canadian study, 1 in 7 opiate users reported overdosing in a six month period prior to assessment and multiple episodes of overdose were common (4).

The NORE data revealed that most overdoses presenting to an ED occurred in young adults (median age 37.0 years), and more often in females (56%). Similar to fatal overdoses, most overdoses (58%) took place at home or in another private residence. Most individuals (71%) were transported to hospital by emergency medical services (EMS) and approximately half (51%) required emergent physician assessment within 15 minutes of arriving at the hospital. On average, these patients stayed three hours longer in the ED than other ED patients (8.7 vs. 5.8 hours). The use of coingestants was also high in this population (82%). Despite needing emergent physician assessment on arrival to hospital and requiring prolonged observation in the ED, the majority of these patients (77%) were discharged in stable condition.

Many opiate overdoses, however, do not end in death or present to an ED for medical assistance. Most NORIS respondents reported experiencing at least one overdose in their lifetime, and the median number of overdoses witnessed was two. More than one third (37%) of respondents avoided calling EMS all or some of the time; fear of police involvement (28%), fear of being blamed for the overdose (18%), or thinking that the person could recover on their own (13%) were commonly cited barriers. More than

half of respondents (56%) had tried to help an overdose victim by doing artificial respiration and/or chest compressions. There was also widespread support (83%) for studying a community based naloxone program.

Taken together, findings from these three studies indicate that opioid overdoses are a significant cause of mortality and morbidity in Albertans, and likely contribute to ED overcrowding in this province. Most overdoses occur in a private setting and community members seem willing to provide whatever assistance they can; however, significant barriers to activating EMS and seeking formal medical assistance are reported. Interventions to reduce these figures are clearly warranted and have been effective in selected Canadian and international communities (5). Some of these interventions have included needle exchange programs, safe injection facilities, methadone programs, outreach education and prescription opioids.

5.2 Future Research Directions

From this research there are a number of directions for future research and advocacy. For example, community based naloxone programs have the potential to reduce the morbidity and mortality associated with opioid overdose and have the support of the drug using community in Canada, as we have shown in the NORIS study. In addition, addressing the barriers that exist to activating EMS, and the role of coingestants in the morbidity and mortality associated with overdose were identified as important issues during this thesis work.

Community based naloxone programs: Community based naloxone programs have been proposed as a method of reducing the morbidity and mortality associated with

opioid overdose (6). Two recent pilot studies have just been completed, one in New York City (7), and one in San Francisco (8). Our Edmonton-based research group is in the process of conducting a pilot study in Edmonton, the Naloxone Overdose Prevention in Edmonton (NOPE) study. In this and the published studies, drug users were recruited from the community, given information about overdose prevention in general, taught basic life support measures and trained how to administer intramuscular naloxone in the setting of opioid overdose.

While these types of pilot studies are very important, further work will need to be completed to determine the incremental benefits of overdose prevention education, basic life support training and naloxone administration; it could be that providing artificial respiration and/or CPR until EMS arrives will confer the same morbidity and mortality benefit as administering naloxone in the field. Since a randomized trial in one site would be difficult due to cross-contamination, a multi-centered trial in which each site is randomized to a different intervention would likely be the most methodologically sound approach.

There is also some concern from this work and other studies that community based naloxone programs may increase the amount of drug used due to the possibility of easy rescue (9). Moreover, similar concerns have been expressed by the political leaders who provide support for these interventions. While recent evidence suggests otherwise, close monitoring for increased rates of drug use and overdose will nonetheless need to be an integral part of any future work.

Barriers to EMS activation: Early EMS activation is important in any serious emergency medical condition; however, fear of reprisal appears high in the community

most likely to be bystanders at a drug overdose – other users. The NORIS study and other studies (10-12) demonstrate that multiple barriers to activating EMS exist in opiate-using communities; these include fear of police involvement, concern that they would be blamed for the overdose and distrust of medical institutions. Our work has demonstrated that in fatal overdoses, while EMS is activated 81% of the time, in 41% of deaths the individual was declared dead at the scene, suggesting that the call for medical assistance was made at a futile point in the overdose continuum. Further work needs to be done to characterize and deconstruct these barriers. This could include more in-depth qualitative survey data to explore in detail the social situations associated with EMS avoidance, as well as pre- and post-intervention trials measuring rates of EMS activation and opioid-related mortality. With timely formal medical assistance there is little reason that death from opioid overdose should exist.

Role of coingestants: Rates of coingestant use were high in this study in both fatal overdoses (83%) and those overdoses that presented to the ED (82%); these rates are higher than those previously reported in American and Australian studies (58-76%) (13, 14). The high rates of acetaminophen use found in both NORA and NORE data is likely due to the widespread use of acetaminophen plus codeine preparations found in this community. Further work needs to be completed to determine whether these coingestants increase the risk of overdose and death, and also to determine if rates of coingestant use are increasing or just vary by location.

5.3 Barriers to using administrative data sources in the drug using population

While more research is urgently needed to successfully reduce the morbidity and mortality burden found in the drug using community, significant limitations to using administrative data exist.

Lack of permanent housing and/or telephone: Survey data collected by going door-to-door or by telephone is likely to under-represent the drug using community since many individuals cannot afford housing or telephone services.

Illegal nature of their activities: Unfortunately, due to fear of discrimination or persecution, many individuals will not access mainstream resources (e.g. EMS, EDs), or if they do, they may not be truthful about the real circumstances surrounding their situation. This makes EMS records and medical records both unreliable as sources of information and also under-representative of the true extent of the problem.

Bias of existing administrative databases: Existing administrative databases are not designed to collect information related to drug use in a standardized fashion. This makes case identification for chart reviews extremely difficult, time consuming and potentially inaccurate. If more prospective data were routinely collected relating to drug and alcohol use, administrative databases could be used to more accurately characterize this population.

5.4 Barriers to community based research in the drug using population

Well-designed studies are urgently needed to reduce the morbidity and mortality burden found in this population; however, we found that there are multiple barriers that exist to performing rigorous studies in this setting.

Illegal nature of their activities: Users of illicit substances are frequently incarcerated or suffer from fear of incarceration. This reduces their ability to access mainstream resources, in particular formal medical assistance, as we have demonstrated. Individuals interested in studying this population are required to spend a considerable amount of time gaining the trust of the community before it is possible to gain access to research subjects and accurate information.

Transient nature of the population: Lack of stable housing, variable monetary assets and the possibility of imminent arrest all make prolonged follow up of these individuals difficult. Many individuals do not even own a telephone, making telephone follow up studies extremely difficult, if not impossible.

Priorities of participants: For those suffering from addiction, finding more drugs, food, and housing understandably represent higher priorities than participating in a research project. This makes recruitment of participants difficult.

Selection bias: For all of the above reasons, most studies performed in this population have the potential to suffer from important selection biases. In general, those users participating in research have more stable addictions, are less transient, and have their basic needs met to the degree that they have the time and inclination to participate in a research trial.

Many of the barriers that exist to collecting useful administrative data or community based data are a direct result of the criminalization associated with drug use in our society. Until addiction is treated more like a disease and less like a crime, it is unlikely that these barriers will disappear to a substantial degree. In the meantime, harm reduction approaches seem to offer the best way to deal with the mortality and morbidity

burdens associated with drug use (15); however, they should not be seen as a substitute for bringing addiction, its acceptance as a disease, and the urgent need for effective treatment modalities to the forefront of the mainstream consciousness.

5.4 Conclusions

Notwithstanding the above considerations, this program of research has offered new insight into the opiate using community. Opiate use in Alberta results in approximately 1 death per day and over 400 ED visits per year in the Edmonton area alone. Opioid overdoses presenting to the ED generally required emergent physician assistance and needed prolonged observation in the ED, contributing to ED overcrowding. Overdoses are commonly experienced and witnessed by the drug using community in the Edmonton area; however, significant barriers to calling EMS exist in the community. Most overdoses occur at home or in another private location suggesting that those most likely to be present at the time (i.e. other drug users and their acquaintances) should be trained in overdose prevention, overdose recognition and basic life support measures. There is widespread community support for more education about overdose prevention and also for a community based naloxone trial.

Future research is needed to determine the incremental efficacy of overdose prevention education, basic life support training and community based naloxone programs. Further exploration of the barriers that exist to seeking formal medical assistance, and the role of coingestants in both fatal and nonfatal overdoses needs to be done.

While substantial barriers exist to performing high quality studies in this population, there is no group more worthy of our time and energy. Generally speaking, these individuals are young with many potential years of productive life remaining; however, often through no fault of their own, they have become ensnarled in the downward spiral of addiction and persecution. Because of the illegal nature of their activities and mainstream discrimination, those in most dire need of urgent medical assistance are often left to fend for themselves. Further research in this area can result in access to basic medical care for all Canadians, an improved understanding of addictions in general, and hopefully a more tolerant and accepting society in which one person sleeping outside with a needle in their arm is one person too many.

5.5 References

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Appendices

Appendix 1: Search terms for the systematic review of the morbidity and mortality associated with opioid use in Canada

opiate$, opioid$, narcotic$, heroin, intravenous drug user$, heroin user$, opioid addiction, opiate addiction, addiction, drug addict$, mortality, overdose$, death$, morbidity, complication$, overdose$, overdose fatality, overdose fatalities, drug-related mortality, overdose death$, overdose mortality, heroin overdose, drug-related morbidity, overdose morbidity, Canada and Canadian

Appendix 2: Search terms for the systematic review on community based naloxone programs

opiate$, opioid$, narcotic$, opiate addiction, opioid addiction, opioid user$, heroin, heroin user$, addiction, drug addict$, IDU, IVDU, intravenous drug user$, drug abuse; overdose, OD, overdose prevention, opioid overdose prevention, overdose mortality, overdose death$, drug-related mortality, heroin overdose, overdose fatalities, overdose fatality; naloxone, narcan, opiate antagonist$, opioid antagonist$, drug program, take-home, take home, home based, home-based, naloxone distribution, narcan distribution, community, community based, out of hospital, non-clinical, peer-based, peer based, overdose management, opioid detoxification, opiate detoxification

NORA (Narcotic Overdose Registry of Alberta)
Data Collection Form

Study ID Number: _____

Patient Demographics:

Age: _____ years

Time Found or Time of Death: _____/____/____ _____:_____
yyyy mm dd hr min

Gender: ☐ Male ☐ Female ☐ Unknown

Race: ☐ Black ☐ Caucasian ☐ East Indian ☐ Inuit
☐ Métis ☐ Native ☐ Southeast Asian ☐ Other

Circumstances surrounding Death:

Location of death: ☐ Home
☐ Other private residence, specify _____
☐ Public location, specify _____
☐ Hospital
☐ Police Custody
☐ Other

Manner of death:
☐ Accidental ☐ Suicide ☐ Homicide ☐ Natural ☐ Undetermined
☐ Unclassified

Time of drug use: _____/____/____ _____:_____ ☐ Unclear
yyyy mm dd hr min

Was the drug use witnessed? ☐Yes ☐ No ☐ Unclear
If yes: Bystander BLS? ☐ CPR ☐ Airway support/Ventilations
Other Bystander treatments? _____
_____
_____

If no, time patient was found: _____/____/____ _____:_____
by bystander yyyy mm dd hr min

Was EMS activated? ☐ Yes ☐ No

If yes:

Time of EMS activation: _____/____/____ _____:_____
yyyy mm dd hr min

Time of EMS arrival: _____/____/____ _____:_____
yyyy mm dd hr min

Vitals on EMS arrival: _____ HR _____ RR _____ BP _____ O_2 Sat
_____ GCS _____ chemstrip

Which of the following treatments were provided?

☐ Declared dead at the scene, no treatments provided
☐ Airway management – ☐ Oxygen ☐ BVM ☐ Intubation
☐ IV access
☐ ACLS including CPR, epinephrine, atropine, pacing or other
☐ Naloxone – ☐ effective ☐ ineffective ☐ unclear
Route: ☐ IV ☐ sc ☐ IM
Dose: _____ mg
Any complications? ☐No
☐ Yes, specify _____

Other notes on EMS treatment: _____
_____

Drugs contributing to death:

				Quantification
Opioids:	☐ Heroin			_____
	☐ Morphine	☐ po	☐ IV	_____
	☐ Codeine	☐ po	☐ IV	_____
	☐ Hydromorphone	☐ po	☐ IV	_____
	☐ Oxycodone	☐ po	☐ IV	_____
	☐ Methadone	☐ po	☐ IV	_____
	☐ Fentanyl	☐ po	☐ IV	_____
	☐ Propoxyphene	☐ po	☐ IV	_____
	☐ Meperidine	☐ po	☐ IV	_____

Other drugs: ☐ Cocaine ☐ Ethanol ☐ Barbituates ☐ Benzodiazepines
☐ Acetaminophen ☐ Salicylates ☐ Amphetamines
☐ Other(s), specify, _____

Cause of Death:

Immediate cause of death: a) _____
b) _____
c) _____

Contributing factors but not immediately related to cause of death:
_____
_____

Signs of trauma? ☐ Yes ☐ No
If yes, explain: _____

Other contributing factors to death noted on autopsy? ☐ Yes (explain) ☐ No

_____

_____

Additional Notes:

_____

_____

_____

NORE (Narcotic Overdose Registry of Edmonton)
Data Collection Form

Study ID Number: _____

☐ RAH ☐ UAH ☐ Misericordia ☐ GNH ☐ SGH

Patient Demographics:

Age: _____ years

Gender: ☐ Male ☐ Female ☐ Trans-gendered

Race: ☐ Caucasian ☐ Native ☐ Asian ☐ Hispanic
☐ Other, specify _____ ☐ Unclear

Circumstances surrounding drug use:

Time Drug was taken: _____/____/____ (yyyy mm dd) _____:_____ (hr min) ☐ Unknown

Location:
☐ Home
☐ Other private residence, specify _____
☐ Public location, specify _____
☐ Other, specify _____
☐ N/A

Drugs taken:			Amount taken (if known)
☐ Heroin			_____
☐ Morphine	☐ po	☐ IV	_____
☐ Codeine	☐ po	☐ IV	_____
☐ Hydromorphone	☐ po	☐ IV	_____
☐ Oxycodone	☐ po	☐ IV	_____
☐ Methadone	☐ po	☐ IV	_____
☐ Propoxyphene	☐ po	☐ IV	_____

☐ Cocaine ☐ Ethanol ☐ Barbituates ☐ Benzodiazepines
☐ Tylenol ☐ ASA ☐ Methamphetamines
☐ Other(s) specify, _____

Was the drug taking witnessed? ☐ Yes ☐ No ☐ Unclear

Time patient was determined to need medical attention: _____/____/____ (yyyy mm dd) _____:_____ (hr min)

Bystander BLS? ☐ CPR ☐ Airway support/Ventilations ☐ None ☐ Unknown

Other Bystander treatments? _____

_____

_____

Pre-hospital treatment:

Was EMS activated? ☐ Yes ☐ No

If yes:

Time of EMS activation: _____/____/____ (yyyy mm dd) _____:_____ (hr min)

Time of EMS arrival: _____/____/____ (yyyy mm dd) _____:_____ (hr min)

Vitals on EMS arrival: _____ HR _____ RR _____ BP _____ O_2 Sat _____ GCS _____ chemstrip

Which of the following treatments were provided?

☐ Airway management – ☐ oxygen ☐ NIV ☐ Intubation

☐ IV access

☐ ACLS including CPR, epinephrine, atropine, pacing or other

☐ Naloxone – ☐ effective ☐ ineffective ☐ unclear

Route: ☐ IV ☐ sc ☐ IM

Dose: _____ mg

Any complications? ☐ No

☐ Yes, specify _____

Other notes on EMS treatment: _____

_____

If not transported by EMS, then transported by: ☐ Self ☐ family/friend ☐ other

Hospital treatment:

Time of arrival to ED: _____/____/____ (yyyy mm dd) _____:_____ (hr min)

CTAS Score: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5

Time of physician assessment: _____/____/____ (yyyy mm dd) _____:_____ (hr min)

History:
Previous history of overdose ☐ Yes ☐ No ☐ Unknown
Vomiting since ingestion ☐ Yes ☐ No ☐ Unknown
Seizure since ingestion ☐ Yes ☐ No ☐ Unknown

Initial vital signs in ED:
_____ HR
_____ RR or ☐ intubated
_____ BP
_____ O_2 saturation ☐ RA ☐ O_2 _____
_____ Temperature
_____ GCS
_____ chemstrip

Investigations:
☐ CBC
☐ Lytes
☐ BUN, Cr
☐ EtOH _____
☐ ASA _____
☐ Tylenol _____
☐ ABG pH _____
pCO_2 _____
pO_2 _____
HCO_3 _____
☐ EKG
☐ CXR
Evidence of pulmonary edema ☐ Yes ☐ No

Treatment:

Airway Management	☐ Oxygen	☐ BVM	☐ Intubation
IV access	☐ Yes	☐ No	
Cardiac monitor	☐ Yes	☐ No	
Nasogastric tube	☐ Yes	☐ No	
Foley catheter	☐ Yes	☐ No	
Inotropes	☐ Yes	☐ No	
Activated charcoal	☐ Yes	☐ No	

Naloxone ☐ Yes ☐ No
If yes: Dose _____ mg
☐ IV ☐ sc ☐ IM
Time given: _____:_____
hh mm
Effective: ☐ Yes ☐ No
More than one dose needed? ☐ Yes ☐ No
If yes, other doses given:
_____:_____ _____ mg ☐ IV ☐ sc ☐ IM
_____:_____ _____ mg ☐ IV ☐ sc ☐ IM

Naloxone infusion needed? ☐ Yes ☐ No
If yes, dose started: _____ mg/hr
Any side effects observed: ☐ Yes ☐ No
If yes, ☐ seizure
☐ pulmonary edema
☐ withdrawal symptoms
☐ other, specify _____

Outcome:

		# of days
☐ Admitted	☐ ICU	_____
	☐ Medical Ward	_____
	☐ Psychiatry	_____
	☐ Other, specify _____	_____

Date of discharge: _____/____/____ _____:_____
yyyy mm dd hr min

☐ Discharged from ED
Date of discharge: _____/____/____ _____:_____
yyyy mm dd hr min

☐ Died in ED or while admitted
Date of death: _____/____/____ _____:_____
yyyy mm dd hr min

ME case: ☐ Yes ☐ No

Final Diagnosis: _____

Additional Notes:

_____
_____
_____
_____
_____

The Epidemiology of Narcotic Overdose in Capital Health:
Narcotic Overdose Respondent Intervention Survey
Informed Consent Form

Contacts: If you have any questions about this study, you can contact Dr. Kathryn Dong or Dr. Brian Rowe at 407-6707 or Dr. Cam Wild at 492-6752.

Background: Each day in Alberta, one person dies from some kind of drug overdose. Many more people go to the emergency department sick from overdosing on drugs. Frequently, friends may see them use too much or too many drugs and then stop breathing and turn blue. Death doesn't happen right away. There is some time to stop death from occurring. In many places in the world, a drug called Narcan© or naloxone is given by ambulance workers or community support staff on the street. If they have overdosed on narcotics or heroin, this drug can help them start breathing again, and save their life.

Purpose: This study will help us figure out how often overdoses are happening. It will also help us see if Narcan© or naloxone is something that the community wants.

Study Procedures: You are being asked to participate in a survey. You can take the survey by talking to the study coordinator or by writing your answers down. The survey should take about twenty minutes of your time to complete.

Benefits: This study will let us take your opinions back to the medical community. It may help us prepare for a study on whether Narcan© or naloxone can save lives in Edmonton.

Risks: Sometimes people don't like talking about their own or their friend's overdose. If you start to feel upset let me know and we can stop anytime. We can help you find someone to talk to if you would like.

Confidentiality: All information will be held confidential (or private). The only time I have to tell someone what you have said is if you tell me you are going to hurt yourself or someone else. The information you provide will be kept for at least five years after the study is done. The information will be kept in a secure area (i.e. a locked filing cabinet). Your name or any other identifying information will not be attached to the information you gave. Your name will also never be used in any presentations or publications of the study results.

Emergency Medicine Research Group (EMeRG©)/Division of Emergency Medicine

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New Findings: Participating in this study does not waive any of your legal rights. If you have concerns about your treatment you can contact Capital Health Patient Concerns at 407-1040. If we get any new information that is important to share with you, we will pass it on.

Consent: You only have to participate in this study if you want to. If you have questions you can stop and ask them at any time. We can also stop at any time. Whether you participate or not in the study will not affect your ability to get supplies from Streetworks.

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CONSENT

Title of Project: The Epidemiology of Narcotic Overdose in Capital Health: Assessing the feasibility and acceptability of a community based naloxone trial.

Principal Investigator(s): Kathryn A. Dong MD, FRCP(C)

Co-Investigator(s): Dr. Cameron Wild, Associate Professor
Dr. Brian H. Rowe, Professor
Marliss Taylor, RN

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to refuse to participate or withdraw from the study at any time?	☐	☐
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records?	☐	☐
This study was explained to me by: _____		
I agree to take part in this study.	☐	☐

_____ _____

Signature of Participant **Witness**

_____ _____ _____

Printed Name Printed Name Date

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____ _____

Signature of Investigator or Designee Date

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH SUBJECT

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Telephone: (780) 407-7047 • Fax: (780) 407-3314 • E-mail: kathryni@ualberta.ca

Study Record Number: _____

NORIS (Narcotic Overdose Respondent Intervention Survey)

People in Canada come from many racial and/or cultural groups. You may belong to more than one group. Please list the single group **that most closely identifies** your racial and/or cultural background.

Are you:

- ☐ White/British/Commonwealth
- ☐ First Nations Status
- ☐ First Nations Non-Status
- ☐ Chinese
- ☐ Japanese
- ☐ Korean
- ☐ South Asian (e.g. Sri Lankan, East Indian etc.)
- ☐ Black
- ☐ Filipino
- ☐ Latin American
- ☐ Southeast Asian (e.g. Vietnamese, Cambodian, etc.)
- ☐ Arab/Middle Eastern
- ☐ West Asian (e.g. Iranian, Afghan, etc.)
- ☐ Scottish
- ☐ Ukranian
- ☐ Another group? Please specify _____

What sex are you? ☐ Male ☐ Female ☐ Trans-gendered

How old are you? _____ years

How far did you go in school?

☐ Elementary ☐ Junior High ☐ High school ☐ College/University

Which drugs have you regularly used in the last 6 months (please check all that apply)?

		Route		
Opiates:	☐ Heroin	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Morphine (pinks, greys)	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Hydromorphone (Dilaudid)	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Codeine	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Oxycodone (Percocet)	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Propoxyphene (Darvon)	☐ IV	☐ smoke/snort	☐ by mouth
Stimulants:	☐ Cocaine	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Crack	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Methamphetamines (Speed)	☐ IV	☐ smoke/snort	☐ by mouth
Others:	☐ Benzos (Valium, Ativan etc.)	☐ IV	☐ smoke/snort	☐ by mouth
	☐ Marijuana	☐ smoke	☐ by mouth	
	☐ Talwin & Ritalin (T's &R's)	☐ IV	☐ by mouth	

☐ Alcohol
☐ None

Do you currently use opiates (heroin, morphine, dilaudid, oxycodone or codeine) or have you used them in the past 6 months? ☐ Yes ☐ No

If No, go to page 4
If yes, continue below

Opiate users:

How often do you use opiates?

		# of times				
Current use:	☐ Daily	☐ 0-5	☐ 6-10	☐ 11-15	☐ 16-20	☐ > 20
	☐ Weekly	☐ 0-2	☐ 3-4	☐ 5-6		
	☐ Occasional					
	☐ Not currently using					

How many times have you ***ever*** overdosed (accidentally or intentionally)? _____
How may times have you overdosed ***in the past year***? _____

How many times have you ***ever*** seen someone else overdose (accidental or intentional)?

_____

How many times have you seen someone else overdose ***in the past year***? _____

Have you ever called the ambulance for an overdose for someone else?

☐ Yes ☐ No

If yes, how many times? _____

What stops you from calling the ambulance?

☐ Worried police will become involved
☐ Think person will recover on his or her own
☐ Think you'll be blamed for the overdose
☐ Other, _____

Do you try to avoid calling an ambulance?

☐ Yes ☐ No ☐ Sometimes

Have you ever tried to help the person with their breathing or done chest compressions?

☐ Yes ☐ No

What else do you do if someone overdoses?

_____
_____
_____

Have you ever heard of a medicine called naloxone or Narcan©?

☐ Yes ☐ No

To your knowledge, have you ever been given it by the paramedics or in hospital?
☐ Yes ☐ No ☐ Can't recall

We are trying to figure out if training people to give naloxone to themselves before they pass out from an overdose can save lives. Naloxone or Narcan© is a medicine used by doctors and paramedics to help reverse the effects of narcotics.

Do you think you would give it if you overdosed and you were trained how to use it?
☐ Yes ☐ No ☐ Unsure
If no or unsure, why?
_____

If we were to study something like this in Edmonton, do you think this would be a good idea?
☐ Yes ☐ No ☐ Unsure
If no or unsure, why?
_____

Do you think people would use more drugs if they thought naloxone might be able to bring them back?
☐ Yes ☐ No ☐ Unsure
Why? _____

Would you like more information on how to help people when they overdose?
☐ Yes ☐ No ☐ Unsure

What other things can you suggest to prevent people from OD'ing?
_____
_____
_____

Do you have any additional comments?
_____
_____
_____
_____

End of Survey for Opiate Users

Non-opiate users:

How many times have you ***ever*** overdosed (accidentally or intentionally)?

_____

How may times have you overdosed ***in the past year***?

_____

Are you ever around when other people are using heroin, morphine or other opiates?

☐ Yes ☐ No

How many times have you ***ever*** seen someone else overdose (accidental or intentional)?

_____

How many of these were due to narcotics? _____

How many times have you seen someone else overdose ***in the past year***? _____

How many of these were due to narcotics? _____

Have you ever called the ambulance for an overdose for someone else?

☐ Yes ☐ No

If yes, how many times? _____

What stops you from calling the ambulance?

☐ Worried police will become involved

☐ Think person will recover on his or her own

☐ Think you'll be blamed for the overdose

☐ Other, _____

Do you try to avoid calling an ambulance?

☐ Yes ☐ No ☐ Sometimes

Have you ever tried to help the person with their breathing or done chest compressions?

☐ Yes ☐ No

What else do you do if someone overdoses?

_____

_____

_____

Have you ever heard of a medicine called naloxone or Narcan©?

☐ Yes ☐ No

To your knowledge, have you ever been given it by the paramedics or in hospital?

☐ Yes ☐ No ☐ Can't recall

We are trying to figure out if training people to give naloxone to themselves before they pass out from an overdose can save lives. Naloxone or Narcan© is a medicine used by doctors and paramedics to help reverse the effects of narcotics.

If we were to study something like this in Edmonton, do you think this would be a good idea?

☐ Yes ☐ No ☐ Unsure

If no or unsure, why?

_____

Do you think people would use more drugs if they thought naloxone might be able to bring them back?

☐ Yes ☐ No ☐ Unsure

Why? _____

Would you like more information on how to help people when they overdose?

☐ Yes ☐ No ☐ Unsure

What other things can you suggest to prevent people from OD'ing?

_____

_____

_____

Do you have any additional comments?

_____

_____

_____

_____

End of Survey for Non-opiate users