Sex Differences in Opioid Prescribing Practices:

Do Differences Exist in Therapeutic Treatment Between Men and Women Presenting to the Emergency Department with Low Back Pain?

by

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Submitted in partial fulfilment of the requirements

for the degree of Master of Science

at

Dalhousie University

Halifax, Nova Scotia, Canada

July 2023

Dalhousie University is located in Mi'kma'ki, the ancestral and unceded territory of the Mi'kmaq.

We are all Treaty people.

DEDICATION

My thesis is dedicated to the friends, family, and mentors, without whom this thesis would not have been possible. Thank you to my friends who have been a constant support. Thank you to my encouraging and loving family. Thank you to my patient and helpful committee.

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ABSTRACT

Objectives

The primary objective of this study was to investigate sex/gender differences in the experiences of patients seeking pain management from the healthcare system through the comparison of their presentation, diagnosis, and treatment in and after a discharge from the Emergency Department (ED). The focus was patients experiencing low back pain, a frequently occurring condition, with a high likelihood of pain management treatment through opioids.

Methods

This study was a retrospective cohort design using health administrative data. I used data from two existing datasets. I considered sex and gender as the exposure variable, using the concept of entanglement. For my outcomes, I examined differences in the nature of the diagnosis and treatment in and after urgent care between men and women. I conducted descriptive statistics of demographic and clinical differences in men and women attending the ED. I then performed inferential analyses including logistic and linear regression modelling with clustering of patients.

Results

A total of 4 027 men and women attended the ED and data was available for 548 of these participants whether a prescription was administered in ED or was not. Women had a longer average stay than men, while men were more likely to be diagnosed with mechanical back pain. There were no significant differences in the odds of receiving opioids in ED between men and women. An adjusted logistic regression model found that men were more likely to fill a prescription than women (aOR for women: 0.72 [0.59,0.88]). There were no significant differences in doses or the nature of the prescription between men and women.

Discussion

This study provides information on sex differences in treatment of low back pain. While men were found to be more likely to fill prescriptions, this may be due to two potential explanations: men were more likely to fill a prescription at the pharmacy, or men were more likely to receive prescriptions in the ED. Understanding sex differences in what opioids men and women receive may lead to a better understanding of sex differences in the risk of developing problematic use of opioids. This research may help to inform policy when creating sex-specific prescribing practices for opioids in urgent care.

LIST OF ABBREVIATIONS

AIC – Akaike information criterion

BIC – Bayesian information criterion

CIMD – Canadian Index of Multiple Deprivation - Atlantic

CTAS – Canadian Triage and Acuity Scale

ED – Emergency Department

LBP – Low back pain

OR – Odds ratio

QEII – Queen Elizabeth II

QQ Plot – Quantile-Quantile plot

VIF – Variance Inflation Factor

CHAPTER I: INTRODUCTION

A person's identity influences all facets of their life. Although many characteristics comprise a person's identity, sex is one aspect that is foundational. Sex has long influenced how a person experiences the world, and in particular, the healthcare system.[1] Sex alters anatomy, hormones, physiology, and many other characteristics of a person. Differing from sex, gender also influences how a person experiences and interacts with the healthcare system, although this manifests in other ways, such as expectations of adherence to gender roles, help seeking, and treatment decisions by healthcare workers. Sex and gender have the power to alter how patients behave and are treated.

Gender and sex are understudied in certain areas of healthcare, although they influence how one navigates the world. One area where there have been calls to increase research is in the effect of gender and sex on substance use and abuse.[1–4] Differences have been observed in use and abuse between men and women, as well as biological differences in effects and likelihood of developing dependence between males and females (in my study, I will use male and female when discussing the impact of sex, and men and women when acknowledging gender as well).[4–6] Opioids are one substance where differences between men and women have been observed, ranging across factors such as the source of their opioids, to their likelihood of developing dependence, to the chances of experiencing an overdose.[7–9]

The ongoing opioid crisis in Canada has resulted in significant growth in research into opioid prescribing, use, and related consequences. A key feature of the opioid crisis has been the significant rise in opioid overdoses, particularly in the past decade, with further increases being observed during the COVID-19 pandemic.[10] Although most of these overdoses involve illegal opioids, notably fentanyl, it is important to note the contribution of prescribed opioids to the opioid crisis. Opioids are frequently prescribed for acute pain, as well as chronic non-cancer and cancer pain. Although opioids are not recommended as the first line of treatment for most conditions, they can be an effective second line of treatment if optimized non-opioid treatment is not providing appropriate pain relief.[11,12] Opioids have notable side effects such as vomiting, constipation, depression, adverse reactions, or coma.[7] There is also a risk of dependence or addiction with opioids, where the Canadian Guideline for Opioid Therapy and

Chronic Non-Cancer Pain reported a 5.5% chance of developing an addiction to opioids if treatment was longer than 90 days.[13]

Low back pain (LBP) is a health issue where opioids are frequently prescribed.[14–16] LBP refers to a musculoskeletal condition and is now considered the global leading cause of disability as listed by the Global Burden of Disease study.[17–19] Most LBP is described as 'non-specific LBP', where there is no diagnosed reason for the pain.[20] The majority of adults will experience an episode of LBP in their lifetime, and LBP was the fourth most common reason for presentation at the emergency department (ED) in Canada in 2019 and third most common reason in 2020.[21–23] Although other treatments are recommended before opioids, including other drugs such as acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDS), opioids are often prescribed to patients presenting to the ED with LBP.[20,24,25] These can range from weaker opioids, such as tramadol or codeine, to stronger opioids, such as morphine or hydromorphone.

As LBP is one of the most common reasons for presentations to the ED and one of the conditions where opioids are frequently prescribed, LBP is an appropriate avenue to investigate sex differences in opioid prescribing.[15,22] Differences between the sexes may exist navigating the healthcare system in an attempt to receive treatment for pain management. Men and women may present to the ED at different rates, either through a different prevalence of LBP or differences in the likelihood of help-seeking behaviours. There may be discrepancies in how physicians and other healthcare providers decide to treat men and women, including the choice of treatment (non-pharmaceutical or pharmaceutical treatments), the use of non-opioid based medicines or differences in opioid prescription regarding type of opioid, dose, or supply.

Chapter II of this thesis provides background about relevant subjects for this thesis. The first section explores the role of sex in health care, notably pain management and substance use. Next, I provide information on opioids, opioid harms, and prescribing practices. Then, I review evidence about the epidemiology and treatment of LBP. A background on emergency care is also supplied.

In Chapter III and IV, I describe the methods and results for my thesis, which aims to answer the question: do differences exist in therapeutic opioid treatment between men and women presenting to the ED with LBP? I used two health administrative datasets, which

contain information on ED presentations for LBP at the Queen Elizabeth II (QEII) Health Sciences Centre in Halifax, Nova Scotia during 2016-2020. To compare sex differences at presentation, I explore clinical and demographic differences in men and women that present to the ED. Second, I look at differences in the nature of the diagnoses received by men and women after seeking emergency care for LBP, such as the presence of non-specific vs. specific diagnoses. Third, I compare sex differences in treatment while in emergency care. Fourth, I examine sex differences in recommended treatment for LBP post emergency care. Last, I discuss the strengths, limitations, and importance of this study in Chapter V.

CHAPTER II: BACKGROUND

Identity, Sex and Gender

The Role of One's Identity in the Healthcare system

A person's identity, through factors such as sex, race, class, disability, influences all aspects of their life. In school, employment, life opportunities and other areas, identity plays a central role in how people experience the world. The healthcare system is no different. Identity plays a role in how people are treated within the healthcare system. Class is also social determinant of health, and this is frequently tied to education, wealth and poverty, where worse health can result through less access to resources, living in poorer and more dangerous environments, and worse working conditions.[26,27] Race also influences experiences within the Canadian healthcare system, where people of colour, notably those who are indigenous or African-Canadian, can receive poorer quality treatment as well as experiencing systemic racism or even outright bigotry from healthcare workers.[28–30] It can be difficult to assess differences in health and healthcare treatment due to a lack of race-based data in Canadian healthcare administrative data. Disability can also impact experiences, through inadequate access to care or discriminatory treatment within the system.[31] Sex and gender are also notable determinants of health and of health care.

The Role of Sex and Gender in Health Research

Sex and gender are two features of one's identity that can greatly influence a person's experiences within the healthcare system.[1] Sex refers to the biological characteristics of a person, such as hormones, physiology, genetics, or general anatomy.[32] Previously, most research has centred on the binary division of sex, where individuals with an XX chromosome are female and those with an XY chromosome are considered male.[32] This binary definition provides inadequate inclusion of individuals who are intersex, or who have alternate sex chromosomes, such as XXY, XYY, or XO (no second sex chromosome).[32] Depending on the definition of intersex used, estimates of the proportion of the population have fallen between 0.018 to 1.7% of the population, although this varies in whether those with chromosomal abnormalities are included in this statistic.[33] Sex affects health and subsequent healthcare on virtually every level. As frequently quoted, "every cell has a sex", which is used to emphasize that on the most fundamental biological level, there are sex differences in biological and

biochemical mechanisms.[34] Although differences in the reproductive system are thought of as the main difference between men and women, there are foundational differences in each cell due to the presence of the sex chromosomes, which lead to foundational differences even at the cellular level. It is imperative, then, to incorporate sex into studies on health.

In contrast, gender refers to the social and cultural identity of an individual rather than the biological identity.[2,35] This can include cultural expectations of behaviour and roles, as well as socializing of behaviours, thoughts, and opinions in individuals from infancy.[2,35] Gender roles, performance and expectations can also alter how people are perceived by others.[35] Gender affects health care in a different manner than sex: whereas sex affects health on a biological level, gender identity and gender roles can affect the behaviours and thoughts of those seeking health care and those providing it.[1,2,36–38]

In previous health research, the concepts of sex and gender have often been conflated.[32,39] They have been used synonymously, which is incorrect.[32] Separating the concepts entirely, however, also can cause issues.[39] For epidemiology, health administrative data frequently omits information on gender. This has led to sex being used as a variable in research, but not gender. But this does not mean that gender is not affecting differences between men and women. Springer et al. propose the concept of entanglement for sex and gender, where the two are distinct concepts, but are noticed to interact.[39] They further suggest that while sex is the predominantly studied variable, sex differences are often influenced by unmeasured aspects of gender.[39] Springer et al. give a useful example for understanding this concept.[39] They examined a difference historically attributed to sex, a difference in glucose metabolism in females and males that acts as a risk factor for cardiovascular disease and observed that difference in muscle mass has been found to explain differences in glucose metabolism more accurately than sex in previous studies. Then, they point to various social influences that affect men and women's difference in muscle mass – differential nutrition, aesthetic expectations and norms, type of employment, exercise habits – and state that these differences may contribute to differences in muscle mass, and so glucose metabolism is altered, which then becomes a risk factor for cardiovascular disease.[39] By using sex/gender as a variable, I can allow for the acknowledgment that many "sex differences" in health care may be attributed to both gender and sex. Unfortunately, transgendered and non-binary individuals can

not be accounted for using this concept. While non-binary and transgendered persons are important to acknowledge, they respectively comprise approximately 0.22% and 0.26% of the Nova Scotian population, which is difficult to study due to their small population size.[40]

One example of the intersection of sex and gender is in health care seeking behaviours. Women have been documented to access health care more frequently than men.[37] Several physical and cultural explanations have been offered as reasons for these differences. In terms of biology, women are more likely to experience chronic conditions, and chronic conditions significantly raise healthcare utilization.[37,41] When controlling for number of chronic conditions, however, women have reported better health than men.[42] Another study examining sex differences in healthcare expenditures found that although women had higher expenditures, 22% of women's healthcare expenditures were sex-based, such as pregnancy or childbirth, compared to only 3% of men's healthcare expenditures.[43] Women have also been observed to be more likely to be disabled, which is also associated with higher healthcare utilization.[37,44] Another proposed reason for women's higher rates of accessing health care is that women are more likely to engage in health care seeking behaviours than men due to gender roles and expectations. It has been previously reported that men feel that they are not supposed to complain or to report pain or issues that would be seen as a sign of weakness; whereas for women, help seeking is perceived as more acceptable.[38] Additionally, men have been documented to be more likely to leave against medical advice when seeking medical aid.[45] It is significant to mention, then, that issues of anatomy and physiology may intersect with gender roles and expectations to create sex/gender differences in health care, where it may not be easy to disentangle the two concepts. As such, moving forward, I will discuss sex, but this does not exclude the influence that gender may have.

The Role of Sex in Chronic Pain and Pain Management

One area of health care where sex can play an important role is in pain management, whether chronic or acute. Certain pain conditions are frequently more prevalent in one sex than the other: some conditions, such as migraines, LBP, or osteoarthritis, are more common in females, while conditions, such as duodenal ulcers, ankylosing spondylitis, or cluster headaches, are more common in males.[46,47] There are important biological differences between the sexes that impact how males and females feel pain, such as hormonal differences.

Hormonal differences in estrogen and testosterone have been reported to influence sex differences in experiences of pain, where testosterone may have a protective effect and changing levels in estrogen may impact females' pain levels.[48–50] Hormone cyclicity has been observed to also alter female reporting of pain, where depending on the point in their menstruation cycle, female patients may describe pain differently.[47] Other studies have reported higher pain sensitivity in females, as well as an increased risk for clinical pain and post operative pain.[50] Females have been observed to respond to pharmaceutical treatment differently than males, possibly due to hormonal fluctuations and or different receptivity of pain analgesic receptors, such as mu-opioid receptors, in the brain, which can affect treatment for pain.[46,50]

Gender can also alter how men and women report pain.[51] As previously mentioned, women have been documented to show more health-seeking behaviours. There is a cultural stereotype that women are more likely and willing to report pain than men, which has been supported by previous literature.[51,52] In a scoping literature review on gender bias in health care and gendered norms towards patients with chronic pain, men often reported that they avoided seeking health services, did not discuss pain or felt less masculine due to their chronic pain. Meanwhile, women were perceived as being more sensitive to pain, and women reported feeling mistrusted by health professionals.[38] One study in the United Kingdom found that health care providers were more likely to believe women were exaggerating their pain and believed that men had higher levels of pain.[53] That being said, women can also be perceived to have higher pain by physicians as they are more likely to report pain.[54,55] So, while women have been observed to report higher levels of pain, they may be susceptible to being perceived as dramatizing or overexaggerating.[55] Some researchers have also reported that women tend to catastrophize their pain.[56] Due to these psychosocial factors, gender may be affecting how men and women report their pain and may influence their willingness to seek help for pain management.

The sex and gender of the physician may also influence care in this area. One study in France found that of ED physicians, male physicians perceived women as being in less pain than men, compared to female physicians who perceived women and men similarly.[57] Men have been previously observed to be more hesitant to report symptoms to female physicians.[58]

Female physicians have been observed to spend more time with patients and to provide more follow up, although it has also been noted that they are more likely to treat women, who have more chronic conditions and tend to spend more time with physicians overall.[59,60] Male physicians were observed to spend more time on physical examinations and obtaining patient history during a visit.[59] Patients tend to prefer primary care physicians that are the same sex as themselves.[61] It has also been observed that gender concordant patient – doctor pairings are also more likely to have longer visits.[59,62,63]

The Role of Sex in Substance Misuse and Abuse

Substance use is an area of medicine that has been neglected for study and that calls for a sex analysis. Sex can alter how an individual experiences substance use, altering the quantity needed to be intoxicated or affected, and can also affect the likelihood of developing harmful or problem use.[4–6] In terms of the use of prescription medications, sex of the patient has also been observed to affect the likelihood of adherence to prescribing guidelines, as well as the likelihood of receiving a prescription that aligns with current guidelines.[64] Sex may also affect the quantity needed to damage the body or brain, or affect the chance of overdose.[2,65] There have been calls to increase the amount of research into the interaction of sex and gender with the use of substances and medications, and associated benefits and harms.[2,66]

Physician sex may also affect the substances available to patients and subsequent usage patterns. In a German study looking at prescriptions for congestive heart failure, male patients were equally likely to be prescribed medications and similar doses, regardless of physician sex, whereas female patients were prescribed medication less frequently and with lower doses when prescribed with a male physician, as compared to female patients treated by a female physician. The authors wrote that "A female patient was likely to receive the worst medical treatment from a male physician, whereas male patients were best treated by a female physician".[67] Female physicians have also been observed to be more conservative in prescribing practices, and more likely to prescribe lower than recommended dosages.[68] Female physicians are less likely to prescribe harmful or unnecessary treatments.[69] One previous study has found that female physicians are more likely to prescribe opioids as a first line treatment for LBP.[70] Male physicians, however, are more likely to discuss alcohol, cigarette and substance use than female physicians.[59]

Opioids

In this section, I will discuss opioids as one aspect where there are sex and gender differences in experiencing the healthcare system. This will include an overview of use, harms, prescribing practices, and previously observed sex differences in the literature.

Opioid Use in Canada

Pain management is a central feature of health care for patients due to acute injury, post-operative pain, chronic conditions such as LBP, or cancer. Opioids are a common analgesic prescribed to many Canadians to manage their pain. Opioids are usually categorized as either weak, such as codeine, tramadol, and buprenorphine, or strong, such as oxycodone, hydromorphone, morphine, or fentanyl.[11,71–73] The definition of strong and weak comes from comparing the opioid dosage to the equivalent in morphine by using the morphine milligram equivalent (MME), where the dosage of the opioid is multiplied by the morphine conversion factor for that specific opioid to convert the dosage of the given opioid to the dosage in MME.[12] This classification has been previously defined by examining whether the morphine conversion factor is 0.3 or less.[73] Appendix A presents the opioids recommended in the Canadian guideline for safe and effective use for chronic noncancer pain.[11] Opioids are typically prescribed to patients seeking pain management at age 15 and older.[74] Common reasons for opioid prescriptions include cancer pain, chronic noncancer pain, trauma, or surgery.[75] In a study using administrative health data in Ontario, Canada, 40% of patients with a recent cancer diagnosis had an opioid prescription that year, compared to 27% of patients without a cancer diagnosis.[76] A systematic review examining chronic non-cancer pain in various countries found a pooled estimate that approximately 31% of chronic non-cancer pain patients are prescribed opioids.[77] Trauma and surgery have been documented to have even higher rates of opioid prescription. In one study comparing opioid prescriptions after surgery in the United States, Sweden, and Canada, Canadian patients were the most likely to fill a prescription for opioids within 7 days of surgery with 79% of 84 653 patients filling an opioid prescription, although the dose in Canada was observed to be lower than the United States or in Sweden.[78] Another study examining opioid prescription after trauma in the United States military found that more than half of participants were prescribed opioids at discharge.[79] For the year ending June 2020, ‘all type’ opioid use prevalence in Canada was approximately 11.8%.[7] In the previous decade, Canada had the second highest level of prescription opioid use

globally, although this has been decreasing in recent years.[80,81] This prevalence varies by region; in Nova Scotia, use has been estimated to be 15% among adults.[82]

Opioid Harms in Canada

Unfortunately, potential complications can arise from opioid use. There are risks with short-term use, where opioids can cause vomiting and drowsiness at low doses, and can cause respiratory depression, adverse reactions, or coma at a higher doses.[7] Regular use of opioids during pregnancy increases the risk of premature birth and opioid withdrawal in the infant.[7] Other opioid harms include hospitalization for opioid use disorders.[71]

Prolonged opioid use has recently been identified as an important outcome in the study of opioid related harms, where patients are using opioids for a longer time than initially intended by the healthcare provider or by the patient. This is often difficult to capture in studies, however, as it is difficult and costly to monitor use, and prescription fills are often used as an indicator instead. Definitions may be based on patients receiving additional refills within a set time (e.g. 90 days) of the initial presentation to the health care provider.[83–85] Other investigators may use the length of prescription, for example, defined as longer than 90 or 120 days as sufficient for evidence of prolonged use.[86–90]

Due to their addictive risk, there is a high likelihood of developing problems when prolonged opioid use occurs. The Canadian Guideline for Opioid Therapy and Chronic Non-Cancer Pain found that there was a 5.5% chance of developing addiction or dependence to opioids with prolonged opioid therapy, if the treatment is longer than 90 days.[13] Martin and colleagues examined patients who were prescribed 90 days of opioids for non-cancer chronic pain, and they found that more than half were still taking opioids years later.[91] Another study in the United States of 478 981 opioid-naïve patients with newly diagnosed low back or lower extremity pain found that 4% of patients went on to have prolonged use.[92] Duration of opioid treatment is another factor that can affect likelihood of prolonged use leading to misuse. One study with 568 612 patients in a retrospective cohort study found that, after adjusting for covariates, each additional refill of opioids increased the average rate of misuse by 44% and each additional week of opioid use increased the average rate of misuse by 20%.[93]

There is a chance that treatment for an acute or chronic condition may result in prolonged opioid use, and this may also put a person at risk of developing opioid dependence or addiction.[94] Opioid dependence refers to the body becoming dependent on opioids to function normally, where stopping opioids may cause negative health outcomes. Dependence may also refer to behavioural, cognitive, or physiological issues that arise from their use.[7,95,96] It is important to note that physical dependence may not necessarily result in addiction, although dependence is usually a component of addiction. For some studies, a diagnosis of opioid dependence as listed on the ICD has been sufficient for a label of addiction for the patient.[97–99] This has resulted in some blending of the concepts in the literature where it can be difficult to distinguish the two.[95] In contrast to dependence, addiction refers to the behaviours and circumstances where one obtains and uses the opioid, which include misuse and abuse.[95] Misuse may refer to taking opioids not as prescribed, or obtaining opioids not prescribed to them. Misuse may also refer to taking more at a time than prescribed, or tampering with the opioids.[94] There is also description of misuse pertaining to opioids use via an alternate route of delivery, such as through inhalation.[100]

Although the terms addiction and dependence have been used historically, the new Diagnostic and Statistical Manual of Mental Disorders (DSM-V) has moved from using these terms and has now grouped them into a single disorder known as substance use disorder, with different levels of severity based on use patterns, effect on daily life, and issues with controlling their intake.[101] Opioid Use Disorder (OUD) is defined as "a problematic pattern of opioid use leading to clinically significant impairment or distress".[102] Diagnosing OUD is guided by multiple criteria, such as tolerance, withdrawal, and cravings of opioids, and the number of criteria exhibited by the patient aid in determining the severity of the disorder.[102]

Although many of these harms can be attributed to illicit opioids (including heroin and fentanyl), opioids prescribed by healthcare professionals are also responsible for a share of these harms. A study examining opioid related deaths in Ontario found that between 33% and 38% of people who died from opioid overdose had an active prescription for an opioid.[103] One study followed patients who had lumbar fusion operations and found that an opioid related overdose (whether alone or combined with other drugs) was the most common cause of death in the following three years after surgery.[104] During the pandemic, however, it has been

documented that although opioid related deaths are increasing, the proportion related to heroin and fentanyl has been increasing as compared to opioids related to pain management such as hydromorphone or morphine.[105] Jones et al. examined the defined daily doses of opioids dispensed per 1 000 people per day, and the opioid related hospitalization rates for each province, and found a correlation between opioid dispensing and opioid related hospitalizations; in Nova Scotia, the correlation was r=0.78.[106]

Prescribing Practices

There have been attempts in recent years to change prescription practices to safer supplies and doses. Overall, fewer people are being prescribed opioids, and opioids are being prescribed for shorter durations and in smaller doses.[71] Higher pain intensity is associated with a higher likelihood of being prescribed opioids, although prescription of opioids is associated with lower patient satisfaction and greater pain intensity reported later.[107,108] There are currently attempts to further decrease opioid prescribing, as well as attempts to change prescribing practices so that prescriptions align with a lower risk for prolonged use, addiction and subsequent negative consequences of opioids.[13,71,75]

One aspect of prescribing practices that has been changing in recent years is dose. Previously, there were few recommendations for opioid dose, and this was left to the discretion of the physician.[95] By lowering the dose of opioids, there can be a decrease in the risks for opioid misuse or overdose.[13,75,109] As morphine milligram equivalent (MME) increase, the likelihood of prolonged use also increases.[75,84,110] The Canadian Guideline for Opioid Therapy and Chronic Non-Cancer Pain and the Centre for Disease Control (CDC) both recommend avoiding doses above 90 milligram morphine equivalents (MME)/day, while the Canadian guideline further makes a further conservative suggestion to avoid doses above 50 milligram morphine equivalents (MME)/day.[12,13]

Another feature of opioid prescribing is the days' supply of the opioid. Days' supply refers to the number of days that the prescription is provided to the user; if the days' supply is 5, then 5 days worth of opioids has been provided. It has been previously found that as the days' supply of opioids increases, there is a lower likelihood of discontinuation of opioids, leading to unintentional long term use.[75] The CDC states that for acute pain, three days' supply is often sufficient, and seven days' supply should definitely be sufficient, as increasing days'

supply is associated with unnecessary prolonged use.[12] Opioid prescribing practices have been changing in Canada, where the days' supply has been decreasing. Overall, the average duration of supply for people starting opioids was shorter in 2017 (12.8 days) compared with 2013 (13.4 days), although this is still longer than research evidence and guidelines have recommended.[71] Decreasing days' supply of medication has previously been associated with higher transactional costs, and as such, higher pharmaceutical costs, and is, therefore, considered less cost effective.[111]

In adopting changes to prescribing practices, there is potential to avoid cases of prolonged use, and subsequently, opioid harms. Providing education and guidelines on opioid prescribing has been shown to be effective in lowering doses prescribed unnecessarily by doctors.[112] Opioid type, such as long acting or short acting, may also affect likelihood of discontinuation, where long acting opioids have also been observed to decrease chances of opioid discontinuation.[75,113] Changes such as these can prevent many of the harms that result due to misuse and abuse of opioids. Despite progress on some fronts, it is acknowledged, however, that women are more likely to receive prescriptions that do not align with prescribing guidelines.[64]

Differences in Opioid Use by Men and Women

In exploring the impact of opioid prescribing and potential harms, the role of patient sex has received limited attention. Differences have been documented in how men and women metabolize opioids, where sex has been observed to modify the likelihood of poor pain control and adverse reactions.[114] Findings on whether women need lower, higher, or similar doses to men have been inconsistent.[115] There may also be genetic and hormonal factors that result in sex-specific differences in males and females. Females may have different reactions to pain during their menstrual cycle, and this may be altered by oral contraceptive medications.[38]

There are estimates that women have higher rates of opioid use compared to men, where 14% of women in Canada reported using an opioid to treat pain compared to 11% of men.[7] Overall, women have been found to have lower daily use of opioids than men, and there is low quality evidence that women receive lower doses for their non-cancer pain.[116] Women are more likely to have chronic conditions, and thus to be prescribed opioids, and the greatest

risk for a woman to develop an opioid addiction is receiving a prescription for an opioid medication.[9]

Age is a predictor of opioid use and can intersect with sex. Increasing age has been associated with higher opioid use, and older women have been documented to have higher rates of long-term opioid therapy.[117] A study conducted in the United States examining prescribing to adults from 2008 to 2018 detected that adults aged 65 and older were more than 2.5 times more likely to have filled an opioid prescription and also found that women were more likely to have an opioid prescription filled at all ages than men.[118] Older women have been observed to engage in lower rates of misuse, despite a higher rate of usage.[117]

Evidence on opioid overdose deaths indicate that nearly three-quarters are suffered by men. Notable distinctions exist in how men and women obtain opioids. While most opioids are obtained via a physician's prescription, men are more likely to obtain prescription opioids via an illegitimate source.[8] Notably, men are also more likely to escalate to stronger opioids while on opioid therapy for noncancer pain, and stronger opioids raise the risk of dying due to opioid-related complications.[65]

Opioids and Emergency Care

Opioids may be prescribed in multiple settings, such as primary care or specialty clinics, but they are also commonly prescribed in the process of emergency care. There are varying definitions of emergency care, but emergency care is distinct in its acute care for patients who are suffering from acute conditions and who need care that has been not been scheduled.[119] One study examining administration of opioids in emergency care found that patients who received opioids while in emergency care were more likely to develop chronic use of opioids than patients who did not receive opioids while in emergency care.[120] A study conducted in the United States found that prescriptions written in the ED were more likely to follow guidelines recommended by the CDC compared to other clinical settings such as primary care.[121] The prescriptions were shorter, had fewer days' supply and were more likely to be short acting opioids.[121] In contrast, another study conducted in Ontario, Canada, found that emergency physicians were more likely to prescribe higher initial daily dosages, and patients were more likely to experience opioid toxicity compared to family physicians.[15] It is possible then, that opioid prescriptions in Canada's emergency care systems may not be following

prescribing guidelines. One Australian study documented that patients who arrived during working hours (between 8am and 5pm) were less likely to be prescribed opioids, and they also found that for each hour spent in the ED, the odds of being prescribed opioids increased by 1.39 (95% Confidence Interval: 1.31 to 1.48).[16]

Low Back Pain

In this section, I will discuss the potential for using the condition of LBP to explore the complexities of sex differences in opioid use and prescription.

LBP is a commonly occurring musculoskeletal condition. It has been defined as pain occurring between the 12th rib and the inferior gluteal folds.[122] Although there are many potential etiologies for LBP, approximately 90% of cases are labeled as 'non-specific' and 8% labelled as due to mechanical causes, such as stenosis or degenerative disc disease.[20,122] There are also nonmechanical causes, such as ankylosing spondylitis or cancer, or visceral disease, such as pelvic inflammatory disease or endometriosis.[20] According to a systematic review by Hoy and colleagues, there is a 39% lifetime prevalence of LBP globally, although this was much lower than expected by researchers and was attributed to much lower documented rates in countries such as China, Cuba, and Nepal.[123] In Canada, LBP has been estimated to have a one week prevalence of 34% and a lifetime prevalence estimate of 84% commonly cited.[21]. Chronic back disorders have been observed to be more prevalent in Nova Scotia than in other provinces.[124] The majority of cases of LBP resolve within four to eight weeks although recurrences are common.[20] Data collected through the Canadian Community Health Survey found that chronic back disorders are more common in women, older people, and people who live in rural communities.[124] LBP has been observed to become more prevalent with age, with a peak prevalence rate at a 85 years old, globally.[125]

Sex Differences in Low Back Pain

Previous research has found that women comprise a higher percentage of patients with LBP than men.[47,126] Functional capacity of women presenting with LBP has been observed to be lower than men.[126] Women have been observed to have more depressive symptoms than men when seeking treatment for LBP, however, which may affect their functional capacity.[126,127] Women were also more likely to have recurrent and chronic LBP [126]. In a systematic review of low back prognosis, Hayden et al. reported that review syntheses that

included nonsignificant results found insufficient evidence of sex differences, while review syntheses that excluded nonsignificant results reported that female sex was connected with worse prognosis[128].

Recommended Treatment of Low Back Pain

Treatment of LBP has evolved over the years. Treatments that were previously recommended in practice, such as bed rest, are being now discouraged since evidence emerged that it is not only ineffective, but harmful, with recommendations supported by research now being advised.[20,25] Treatments for LBP can include activity, physical therapy, muscle relaxants, or heat.[25] Education and reassurance are also important management strategies employed by healthcare providers.[129] As the majority of cases of LBP are non-specific, there is more focus on treating pain and the consequences of pain such as low physical activity and interference with employment.[129] A recent clinical practice guideline recommends non-pharmacological treatment, such as heat, massage or acupuncture, with potential for pharmacological treatment with NSAIDS or muscle relaxants as a first line of treatment.[130]

Opioid Treatment of Low Back Pain

If non-opioid treatment is optimized, but the patient is still experiencing pain, then guidelines typically recommend attempting opioid treatment.[25,130] Healthcare providers have attempted to reduce opioids as a first line of treatment, due to its addictive properties, as well as unpleasant side effects.[130] A systematic review of opioid prescribing for chronic LBP, found that patients who reported more disability, poorer functioning, greater suffering, more pain radiation and higher functional disability, were more likely to be prescribed opioids instead of NSAIDS or other treatments.[14] The review also found extreme variation in the proportion of patients prescribed opioids for chronic LBP, where between 3% and 66% were prescribed opioids, with primary care centers reporting smaller proportions than specialty care centers.[14] Another study in the United States found that opioids were prescribed to 42% of patients with LBP.[131] A more recent systematic review found that receipt of an opioid prescription was more likely in emergency care than from family practice, with a range of 17% to 61% of LBP patients receiving an opioid prescription in the ED.[132]

Prevalence of Low Back Pain in the Emergency Care System

LBP is a frequently occurring condition in the emergency care system. One systematic review pooled data from 21 studies in 12 countries and found that the pooled prevalence estimate was 4.39% (95% CI: 3.67-5.18) of emergency care presentations. LBP is a condition that is frequently treated by Canadian healthcare services and was even the fourth most common reason for presentation at the ED in 2019, accounting for over 200 000 visits.[22] Nova Scotia also has a high prevalence of LBP, with 12 914 visits constituting 3.2% of all ED visits between 2009-2015.[133] Non-specific and mechanical LBP made up the majority of all of these visits.[133]

Emergency Care in Nova Scotia

Previously, I have discussed the utility of LBP for studying opioid use and prescription. I have also discussed the ED as a setting for studying this relationship. In this section, I will briefly describe the location of my study, as well as its characteristics.

The Canadian Association of Emergency Physicians defines emergency medicine as "a field of medical practice comprised of a unique set of competencies required for the timely evaluation, diagnosis, treatment and disposition of all patients with injury, illness and/or behavioural disorders requiring expeditious care, 24/7/365 "[134(p508)]. Physicians who work in emergency care may have received training and certification in emergency medicine, or they may be physicians who are family doctors or have no other certification beyond being a medical doctor, or they may be a family physician who practices within the ED [134].

In Nova Scotia, since 2018, annual ED visits have ranged from a low of 496 492 to a high of 585 026.[135–137] There are 38 EDs in Nova Scotia, and 31 run on a 24 hours per day, seven days per week (24/7) schedule unless there are extenuating circumstances such as staff shortages.[138] Nova Scotia has tertiary care centers which provide higher level care, such as the Izaak Walton Killam Hospital for Children (IWK Health Centre) and QEII Health Sciences Centre, and several regional hospitals with EDs that provide coverage for the entire province.[138] The largest ED in Nova Scotia is located at the QEII Health Sciences Centre, which has the Charles V. Keating Emergency and Trauma Centre containing 36 emergency

medicine spaces.[139] This ED sees an average of 150 patients per day and 1.5 trauma patients per day.[139]

Opioids, Low Back Pain, and the Emergency Care System

Several studies have examined opioid prescriptions for LBP in the emergency care setting. In one study, LBP was one of the most common conditions for which opioids are prescribed.[15] Another study examining opioid use in emergency care found that patients with LBP were more likely to develop chronic use of opioids than those presenting with other conditions, such as migraines or gastroparesis.[120] Treatment within the ED has been documented to reflect treatment guidelines, where acetaminophen and NSAIDS are often prescribed as a first-line treatment for patients with LBP, although one study in Nova Scotia found that 35% of patients presenting to the ED were treated with opioids for their LBP, including hydromorphone, morphine and codeine.[24] While opioids are often given in emergency care, prescriptions are also frequently given to patients when they are discharged from the ED. Patients were slightly more likely to be prescribed opioids at discharge than administered in ED, with 39% prescribed opioids at discharge, including hydromorphone and codeine.[24] Another study noted that approximately 24% of first opioid prescriptions in 2016 did not follow guidelines for prescribing practices in emergency care.[140] Notably, patients who have been given early opioids for LBP while in the ED have been documented to have an increased likelihood of developing prolonged opioid use compared to those who did not, even after controlling for condition severity.[141]

Of the preceding studies of opioid use among LBP patients in the ED, none have focused on sex. One study examining prolonged use after opioid prescription in the ED for LBP found that female patients were more likely to have prolonged use, although differences between treatment for men and women was not highlighted.[140] One study on appendicitis and gallbladder removal found that there was no discrepancy between the sexes in opioid administration in emergency care.[142] Another study on patients undergoing an arthroscopy procedure found that female participants had an increased likelihood of developing prolonged opioid use after receiving an opioid prescription although opioid treatment was not compared between the sexes.[143] Overall, there has been a lack of research focussed on patient sex and gender when examining opioid prescribing in emergency care settings for LBP.

Need for Research

There are noteworthy gaps in the research literature outlined above. The opioid crisis in Canada has produced several harms to the population and has helped to propel an increase in opioid related research. Many factors associated with opioid prescribing have been studied; this includes important work on the association of opioid prescribing and the likelihood of prolonged use, and the role played by opioid dose, days' supply and other factors.[13,75,109] At the same time, examination of the role of sex and gender has been argued by multiple studies to be lacking.[2–4,66,144] While gender is lacking in research, this study examines sex due to limitations in health administrative data, where information about gender is not available. The concept of sex and gender entanglement is used so that the impact of gender on outcomes is not neglected. There are sex differences in where men and women receive opioid drugs, their likelihood of developing dependence, and their likelihood of overdose. There has been insufficient investigation of the reasons for these discrepancies. More importantly, there has been a lack of research that focus on sex differences in opioid prescriptions in the ED. Given that LBP is a common reason for presentation, for which opioids are frequently prescribed, this is an appropriate condition to examine to investigate sex differences in opioid prescriptions. As well, as the initial prescription of opioids influences likelihood of developing prolonged and problematic use of opioids, it is crucial to understand how sex influences prescriptions of opioids.[84,113]

STUDY OBJECTIVES

Objective of this Study

This study aimed to investigate sex/gender differences in the experiences of patients presenting to the ED with a pain complaint through the comparison of their presentation, diagnosis, and treatment in and after the ED. The focus was patients experiencing LBP, which is a frequently occurring condition, with a high likelihood of pain management treatment with analgesics, specifically opioids. This study considered sex and gender using the concept of entanglement, as information on gender was not collected in the datasets used in this project, but gender and sex are both likely to impact outcomes. As described above, the concept of entanglement acknowledges that sex and gender, while two different concepts, interact with each other and therefore it can be inaccurate to consider that they are not entwined. By using

sex/gender as a variable, I could acknowledgment that many "sex differences" in health care may be attributed to both gender and sex.

To address my objective, I asked the overall research question: Are there sex differences in men's and women's experiences with the healthcare system when attending the ED for LBP? I split this overall research question into four specific questions pertaining to: presentation, diagnosis, treatment in emergency care, and treatment post emergency care.

These four specific questions are:

Presentation

1. What are the demographic and clinical differences between men and women who present to the ED for low back pain?

Diagnosis

2. How is patient sex associated with low back pain diagnosis?

Treatment in Emergency Care

3. How is patient sex associated with receiving an opioid for the treatment of low back pain?

Treatment Post Emergency Care

4. How is patient sex associated with filling an opioid prescription?

CHAPTER III: METHODS

Data

For my thesis, I used study data drawn from two existing datasets that respectively include three and four administrative databases. The *first* of these datasets includes: (1) the Emergency Department Information System (EDIS) which contains information on ED visits and patients; (2) the Canadian Index of Multiple Deprivation: Atlantic region dataset which contains information on deprivation quintiles for each patient; and (3) the Nova Scotia Drug Information System (DIS) which contains information on prescriptions. The first dataset contained a sample of 4 027 presentations and includes all adults who attended the Queen Elizabeth II (QEII) Emergency Department in Halifax, Nova Scotia with non-specific LBP, between October 28th, 2016, and September 30, 2020. The *second* dataset included each of these databases and, in addition, contains the database of the BD Pyxis™ MedStation™ ES automated medication dispensing system (Pyxis), which has information on opioid administration in emergency care. The second dataset contained data for 548 presentations from April 9, 2020, to September 30, 2020. From here on, the first dataset will be referred to as the 'Non-Pyxis dataset' and second dataset will be referred to as the 'Pyxis dataset' to indicate that one dataset does not include Pyxis data. A previous study collected and used this data for a prior analysis[145] This dataset allowed for an assessment of potential inequalities between men and women in interactions with the emergency care system, diagnosis, and treatment, including opioid prescribing.

Population of Study

The population of this study included adult patients who presented to the QEII ED for LBP between October 28th, 2016, and September 30, 2020. This population included all presentations to the ED within this time frame. This means that some patients may have attended more than once. LBP was restricted to those who attended the ED with a chief complaint of back pain or traumatic back/spine injury and who were discharged with an International Classification of Diseases (ICD) code that corresponds to a back pain diagnosis. Appendix B presents the table of ICD codes used by the previous study.[145] This study excluded patients who were under the age of 18, who did not have a NS health card number, who died, who were admitted to the ED, or who had a scheduled ED visit.

Key Exposure

The exposure for this study was patient sex. While gender would be a relevant variable to include, this administrative data does not collect gender as a variable. For this reason, I used sex as the exposure variable, but I considered gender to be entangled with this sex in my interpretation of sex. As I have discussed in previous sections, Springer et al. proposed the concept of entanglement for sex and gender, where the two are acknowledged to interact with each other, although they are two different concepts.[39] Given that health administrative data usually does not include information on gender, this has led to sex being used more frequently as an exposure in health studies, rather than gender. But it is possible that gender may be influencing the thoughts and behaviours of patients and health care professionals, contributing to differences between men and women. By using sex/gender as a variable, I can allow for the acknowledgment that many "sex differences" in health care may be attributed to both gender and sex.

Key Outcomes

Differences in experiences with the healthcare system when seeking health care for LBP was the key outcome in this study. To operationalize differences in experiences of the healthcare system, I assessed key phases of the health care pathway for potential discrepancies and decided upon outcomes for each key phase: diagnosis, treatment in the ED, and treatment after the ED. I assessed differences in diagnosis by categorizing the discharge diagnosis as either mechanical or non-mechanical LBP. I also examined potential inequalities in recommended treatment modalities. For the primary outcome of treatment in emergency care, I used the receipt of an opioid in the ED, which was a binary variable. Secondary outcomes included the continuous variable, dose (in MMEs) and the binary outcomes of opioid type and guideline compliance if applicable. I defined guideline compliance as doses under 90 MME per day. To operationalize the primary outcome of treatment after emergency care, I assessed whether or not an opioid prescription from a pharmacy was filled, which was a binary variable. Secondary outcomes included the continuous variables, dose (in MMEs) and days' supply, and the binary variable, guideline compliance, if applicable. Appendix C describes these key outcome variables.

Covariates/Other Measures

From the databases, EDIS and Canadian Index of Multiple Deprivation: Atlantic dataset, I included other potentially confounding variables: age, primary care availability, discharge diagnosis (ICD codes) for each patient. Data derived through Statistics Canada had enabled the creation of deprivation quintiles based on postal code.[146] The Canadian Index of Multiple Deprivation (CIMD) uses geographic location to predict the level of deprivation of the area, using information on the area to predict residential instability, economic dependency, ethno-cultural composition and situation vulnerability.[147] Each of these four CIMD variables (residential instability, economic dependency, ethno-cultural composition and situation vulnerability) are ordinal variables. They are composed of three to five indicators each, which use data collected by Statistics Canada. Residential instability represents concepts such as the number of people who have moved from an area in the past five years, or the number of apartment buildings, where quintile five has the highest instability. Economic dependency includes concepts such as the ratio of employment to the population, the proportion of the population working, and the amount of people receiving governmental assistance where quintile five has the highest economic dependency. Ethnocultural composition refers to concepts such as the number of people self-identifying as a visible minority, or who do not speak either official language of Canada, or who are recent immigrants, where quintile five has the most diverse ethnocultural composition. Situational vulnerability includes concepts such as the proportion of people who do not have a high school diploma or the proportion of dwellings that need repair.[147]

I also used details of the ED visit as covariates, such as date, time, and length of the visit, which have been noted to influence the likelihood of receiving opioids.[16] I also included the pain intensity scale score, which allowed for controlling for the severity of the LBP. Another useful indication of disease severity is the Canadian Triage and Acuity Scale (CTAS) score. The CTAS score has five levels: 1 (Resuscitation), 2 (Emergent), 3 (Urgent), 4 (Less Urgent), 5 (Non-Urgent), which is used to assess a patient's need for medical attention and the urgency of the interventions needed.[148] Through controlling for these variables, confounding can be reduced in the statistical analysis. There are variables that were not available from

Health Data Nova Scotia which are discussed below in the Limitations section. Appendix C contains information on variables included in this study.

Missingness in the Data

Previous work in this area has reported a relatively low rate of missing data for most of the variables included (<5% of all variables), although the pain intensity score has previously had a higher chance of being missing (36%).[140] Missingness was very high (more than 30%) for pain intensity so a missing category was created for the pain intensity variable so that it could still be included in the analysis. The only other variable that had any missingness was CIMD values, which was likely due to a missing postal code, and given that it was such a small part of the sample, I used a complete case analysis, also known as listwise deletion. Appendix D shows missingness in both datasets for this study.

DATA ANALYSES

Presentation (Question 1)

What are the demographic and clinical differences between men and women who present to the ED for LBP*?*

To answer this question, I examined men and women's demographic and clinical characteristics in a descriptive analysis for the Non-Pyxis and Pyxis datasets separately. I also examined demographic characteristics, such as age, CIMD quintiles of deprivation and availability of a primary care provider. I also used clinical differences, including differences in presentation, such as time of day or whether presentation occurred on a weekend or weekday. I also included other clinical characteristics, such as the nature of the diagnosis (mechanical or non-mechanical LBP) and the pain intensity score. I reported and compared details on opioids administered in the ED between the sexes, including the filling of prescription (yes or no), the dose (morphine milligram equivalents (MME)/day) and the days' supply. Next, I used BD Pyxis™ MedStation™ ES information to investigate details of opioids delivered or dispensed in the ED. I also reported descriptive information for the Pyxis dataset using the same baseline and clinical characteristics, with the additional variables: receipt of an opioid in ED, dose of the opioid, and opioid type (strong or weak, oral, or parenteral). To investigate whether these differences were statistically significant, I ran chi-squared tests on categorical variables, and t-tests on continuous variables and proportion tests on binary variables.

Secondary Analyses

What are the demographic and clinical differences by mechanical pain diagnosis, opioid prescription in the ED, and opioid prescription after a visit to the ED?

To answer this question, I first found the most common diagnoses for men and women and conducted proportion tests to find any significant differences. I also described demographic and clinical characteristics on those who received a mechanical pain diagnosis and those who did not. I also described these characteristics for those who received an opioid and those who did not in the ED and for those who filled an opioid prescription from a pharmacy after attending the ED and those who did not.

Diagnosis (Question 2)

How is patient sex associated with LBP diagnosis?

Using the Non-Pyxis dataset, I examined the effect of sex on the odds of diagnosis (mechanical/non-mechanical) with an adjusted logistics regression for back pain conditions after controlling for covariates including patient characteristics (age, CIMD-A score, and availability of primary provider), visit characteristics (time of day, weekend/weekday, length of stay), and LBP characteristics (pain intensity, CTAS score) (see the Directed Acyclic Graph in Appendix E that describes diagnosis of LBP). For each logistic regression in my study, I ran an unadjusted model to investigate the role of sex alone. Then, I ran an adjusted model, controlling for: patient characteristics and visit characteristics. I calculated the odds ratios (OR) and 95% confidence intervals (CI). To investigate the significance of each of the covariate coefficients, I performed a Wald test. I checked assumptions by examining residuals. For all models, I have accounted for clustering of participants if they had repeated presentations. For the adjusted regression, two of four CIMD variables (situational vulnerability and residential instability) were dropped to prevent an underpowered regression. With my committee, we decided to keep economic dependency and ethnocultural composition, as they were the closest to what I was attempting to capture with this variable. To check the goodness-of-fit, I used the Pearson Goodness-of-fit test and pseudo R^2 and checked the area under the curve.

Treatment in Emergency Care (Question 3)

How is patient sex associated with receiving an opioid for the treatment of low back pain?

Using the Pyxis dataset, I conducted unadjusted and adjusted logistic regression analyses as described above to examine the effect of sex on whether opioids were administrated in the ED for LBP conditions (see the Directed Acyclic Graph in Appendix F that describes treatment in the ED). Given that the Pyxis dataset has a smaller sample size, fewer covariates could be used in the adjusted model than in the Non-Pyxis dataset. I considered variable selection with the help of my committee, and I sought to include variables with high confidence of accurate measurement and a high likelihood of confounding the results if not included. For this reason, I did not use pain intensity, CIMD scores or presentation times. CIMD scores were not collected at the individual level and pain intensity had a high degree of missingness so I did not use these variables. I also dropped variables related to presentation times as the literature indicated that they were less likely to confound the result than other variables.

Secondary Analyses

I also conducted a secondary analyses to investigate the dosage and opioid type delivered in the ED to further investigate if there were any differences between men and women in the nature of the opioid administered. Using the Pyxis dataset, I conducted linear regression analyses to examine the effect of sex on the opioid dosage (MME) administered in the ED. For a linear regression analysis, I conducted unadjusted and adjusted linear regression analyses to examine the effect of sex on the outcome. I calculated the coefficients 95% confidence intervals (CI). I checked assumptions and residuals to ensure the model was appropriate. For the adjusted regression, I dropped two of four CIMD variables (situational vulnerability and residential instability) to prevent an underpowered regression. With my committee, we decided to keep economic dependency and ethnocultural composition, as they were the closest to what I was attempting to capture with this variable. I checked multicollinearity by examining Variance Inflation Factor (VIF) values. I dropped variables that had multicollinearity. I checked heteroscedasticity by looking at a Quantile-Quantile plot (QQ plot) and conducting a Cook-Weisberg heteroscedasticity test. I attempted transformations to see if this would reduce the heteroscedasticity and improve the model. To examine goodness of fit, I used the adjusted R^2 and the AIC and BIC values.

I examined opioid type (oral or parenteral) to see if there was sufficient data to run an analysis. I then ran logistic regression analyses to see if any variables were statistically significant despite the small sample size and low power.

Treatment Post Emergency Care (Question 4)

How is patient sex associated with filling an opioid prescription?

I used the Non-Pyxis dataset to answer this question (see the Directed Acyclic Graph in Appendix G that describes factors affecting treatment after the ED). This data was available from the Drug Information System Database. I examined the odds of filling out an opioid script (yes/no) within one month of discharge and conducted logistic regression analyses as described above to see the effect of sex while controlling for potential confounders. I examined interaction terms through marginal effect plots.

Secondary Analyses

I conducted secondary analyses to investigate how the nature of the prescriptions might differ between men and women. These analyses included fewer observations, as it only included the presentations that had later filled a prescription. These analyses, therefore, also dropped pain score as a variable due to the large amount of missingness. I used linear regression analyses as described above to investigate the effect of sex on dose of the prescription after attending the ED. I also conducted linear regression analyses to examine the effect of sex on the opioid days' supply of the prescription filled at a pharmacy after attending the ED.

Sample Size and Power

The dataset was already collected, so I conducted power calculations prior to receiving the data to determine the potential scope of this project. There have been arguments for and against using power calculations for existing databases, where focusing on statistical significance could undermine the accumulation of evidence that would approximate an effect, but nonetheless I have conducted calculations so that I could estimate what statistically significant result could be detected by this study.[149,150]

The power calculations were based on previous estimated sample size. The Non-Pyxis dataset was estimated to contain 3 357 opioid naïve individuals, and the Pyxis dataset contains approximately 445 opioid naïve individuals when these calculations were done. Given that the data had already been extracted, I was able to use these numbers to calculate the potential power and potential effect size detected for this study. For this analysis, I am reporting based on Type I error rate (α) 95% confidence, with power (1-β) of 80%.

Diagnosis (Question 2)

How is patient sex associated with low back pain diagnosis?

Assuming a power of 80% and Type I error rate (α) 95% confidence, I calculated the odds ratio that could be viably calculated from this sample size. Deyo et al. found that only 15% of low back presentations to the ED receive a specific diagnosis. [151] With a sample of 3 357, it would have been possible to detect an Odds ratio of 1.3 or higher, if using the Kelsey method of calculation.[152]

For the use of other independent variables, researchers have previously used the idea of having a certain minimum number of events per variable, where for each additional predictor, there is sufficient statistical power for inclusion.[153] The formula for this calculation is: $n = 100 + xi$ where x represents the number of events per predictor and i represents the number of independent variables, and 100 is considered the minimum amount required for a logistic regression, and n is the total sample size. While some conservative estimates have recommended 10 events per predictor for x, a number of 50 has been found to calculate sizes with sufficient accuracy even for small effect sizes.[153] Using this formula, where eight independent variables were planned to be used, a sample size of 500 would have been sufficient for this analysis.

Treatment in Emergency Care (Question 3)

How is sex associated with receiving an opioid for the treatment of low back pain?

Assuming a power of 80% and Type I error rate (α) 95% confidence, I calculated the odds ratio that could be viably calculated from this sample size. Nunn et al. found that 35% of QEII ED patients were administered opioids in ED for LBP.[24] With a sample of 445, it would have been possible to detect an Odds ratio of 1.8 or higher, if using the Kelsey method of calculation .[152]

Given this smaller sample, there would be less statistical power if multiple independent variables were used. Using the formula above, there would have been sufficient statistical

power for six independent variables. It has been noted, however, that for medium and large effect sizes, samples under 500 are sufficient to support a logistic regression.[153]

Treatment Post Emergency Care (Question 4)

How is the sex of a patient associated with filling an opioid script?

Assuming a power of 80% and Type I error rate (α) 95% confidence, I calculated the odds ratio that could be viably detected from this sample size. As described above, if only 24% of the 3 357 sample fill a script, this leaves the sample at approximately 806. With a sample of 806, it would have been possible to detect an Odds ratio of 1.6 or higher, if using the Kelsey method of calculation.[152]

Using the formula for events per predictor as above, I found the number of independent variables supported by this sample.[153] For this section, if 12 independent variables were planned to be used, a sample size of 700 would be sufficient for this analysis.

Sensitivity Analyses

I only conducted sensitivity analyses for Question 4: "How is patient sex associated with filling an opioid prescription?" due to limitations in the Pyxis database. I conducted sensitivity analyses by changing the continuous opioid dosage variable to a binary variable reflecting on whether opioid dose follows Canadian Opioid Prescribing Guidelines or not. This was done first with the recommendation of less than 90 MME per day, and then the more conservative guideline of 50 MME per day. Similarly, I performed sensitivity analyses recoding days' supply by creating binary variables using the CDC guidelines, first with three days, and then seven days' supply.[12] I also conducted sensitivity analysis by modifying definitions of the prescriptions filled, where I grouped prescriptions into whether or not they aligned with prescribing guidelines, either defined by dose or days' supply to assess whether there are fundamental sex differences as seen in Hayden et al.[140] Finally, I conducted sensitivity analyses by modifying the population definition of opioid naivety. For my other models, opioid naivety was defined by any prescription in the previous 6 months, but for the sensitivity analysis, the effect of a prescription in the previous 6 months, 6 months – 1 year, or any record in the database, were considered to see if any record was associated with a recent record of opioid prescription. A sex-stratified analysis was conducted for any statistically significant findings to investigate any potential differences in the effects of the covariates.

CHAPTER IV: RESULTS

After initially linking the databases, the full dataset contained a total of 4 158 presentations. Figure 1 shows the patient flow chart and shows the number of presentations that were excluded due to the exclusion criteria outlined above, as well as exclusions due to removal of duplicated data from the linking process. After these exclusions, I included 4 027 unique ED presentations in this study. During the time that the Pyxis database was available, the QEII ED had 548 presentations for LBP.

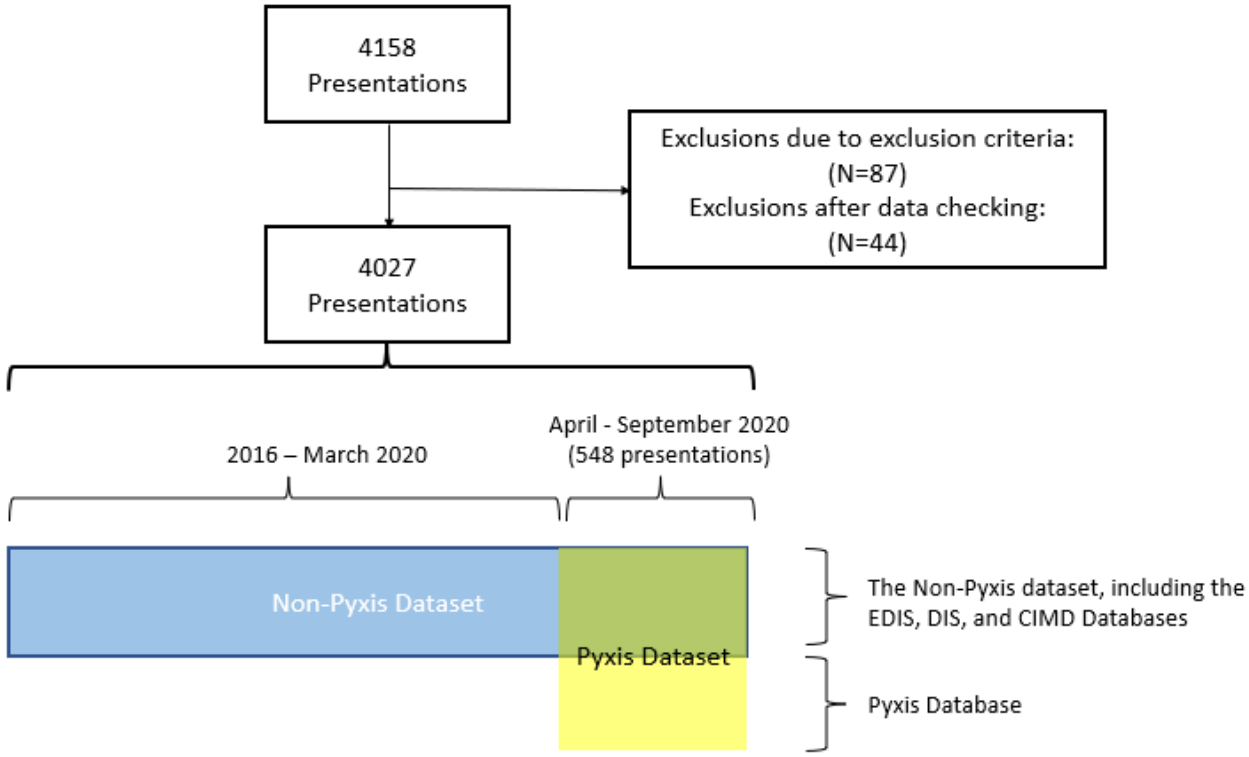

Figure 1. Patient flow chart showing exclusions due to study criteria and data checking. The figure shows the Non-Pyxis dataset as well as the Pyxis dataset, and their associated databases.

Data Analysis

Presentation (Question 1)

What are the demographic and clinical differences between men and women who present to the ED for LBP*?*

Table 1 presents demographic and clinical characteristics for all presentations in the Non-Pyxis dataset. 2048 ED presentations (50.9%) were from women, and the mean age of the entire dataset was 47.5 (SD=18.2) years old. I will now describe the demographic and clinical characteristics that differed significantly between men and women. There were statistically significantly greater proportions of women than men in areas with postal codes considered by the CIMD to be: an indicator of high levels of residential instability, economic dependency, situational vulnerability and to have higher levels of ethnocultural diversity, while a lower proportion of men had a primary care provider available. In terms of clinical characteristics, women had a significantly longer average length of stay, waiting 30 minutes more than men, and a higher percentage were assigned more urgent CTAS scores, and a significantly lower percentage received a mechanical pain diagnosis compared to men. When they did fill a prescription, women had a slightly longer days' supply on average than men. Other demographic and clinical characteristics did not differ significantly between the sexes. Appendix D presents information on missing information for variables in this study.

Table 1

Descriptive statistics (N, %, SD) for demographic and clinical differences between men and women who attended the QEII ED for LBP

Variable		Total	Men	Women	Significance
Presentation	N (%)	N = 4 027	N =1 979 (49.1%)	N = 2 048 (50.9%)	
Age	Mean years(SD)	47.5 (18.2)	47.1 (17.2)	48.0 (19.2)	P = 0.13
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	527 (13.0%) 492(12.2%) 326(8.1%) 513(12.7%) 2138(53.1%)	290 (14.7%) 236 (11.9%) 164 (8.3%) 266 (13.4%) 1010 (51.0%)	237 (11.6%) 256 (12.5%) 162 (7.9%) 247 (12.1%) 1128 (55.1%)	P = 0.02
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1845 (45.8%) 879 (21.8%) 623 (15.5%) 457 (11.4%) 192 (4.8%)	954 (48.2%) 421 (21.3%) 282 (14.3%) 221 (11.2%) 88 (4.5%)	891 (43.5%) 458 (22.4%) 341 (16.7%) 236 (11.5%) 104 (5.1%)	P = 0.04
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	82 (2.0%) 149 (3.7%) 331 (8.2%) 782 (19.4%) 2652 (65.9%)	55 (2.8%) 79 (4.0%) 169 (8.5%) 375 (19.0%) 1288 (65.1%)	27 (1.3%) 70 (3.4%) 162 (7.9%) 407 (19.9%) 1364 (66.6%)	P = 0.01
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1664 (41.3%) 877 (21.8%) 590 (14.7%) 394 (9.8%) 471 (11.7%)	823 (41.6%) 412 (20.8%) 329 (16.6%) 187 (9.5%) 215 (10.9%)	841 (41.1%) 465 (22.7%) 261 (12.7%) 207 (10.1%) 256 (12.5%)	P = 0.005
Availability of Primary Care Provider	No (%)	565 (14.0%)	365(18.4%)	200 (9.8%)	P <0.001
Opioid Naive	Not prescribed opioids in past 6 months (%)	3811 (94.6%)	1872 (94.6%)	1939 (94.7%)	P=0.91
		Clinical Characteristics			
Presentation Time of Day	Presentation during working hours of 9:00-17:00 (%)	2189 (54.4%)	1085 (54.8%)	1104 (53.9%)	P = 0.59
Presentation on day of week	Presentation on weekday (%)	2949 (73.2%)	1463 (73.9%)	1486 (72.6%)	P = 0.33
Pain intensity score	Mean (SD)	4.5 (3.4)	4.4 (3.4)	4.5 (3.3)	P = 0.34
Length of Stay	Mean number of hours (SD)	3.62 (3.05)	3.38 (2.82)	3.87 (3.24)	P <0.001
Canadian Triage and Acuity Scale	1 (Resuscitation) (%) 2 (Emergent) (%) 3 (Urgent) (%) 4 (Less Urgent) (%) 5 (Non-Urgent) (%)	0 (0%) 568 (14.1%) 2514 (62.4%) 905 (22.5%) 40 (1.0%)	0 (0%) 257 (13.0%) 1215 (61.4%) 490 (24.7%) 17 (0.9%)	0 (0%) 311 (15.2%) 1299 (63.4%) 415 (20.3%) 23 (1.1%)	P = 0.003
Mechanical Pain Diagnosis	Yes (%)	1372 (34.1%)	733 (37.0%)	639 (31.2%)	P <0.001
Received DIS Drug	Yes (%)	710 (17.6%)	372 (18.8%)	338 (16.5%)	P =0.06
Opioid Type	Hydromorphone Morphine Codeine Tramadol	414 (58.3%) 129 (18.2%) 118 (16.6%) 47 (6.6%)	222 (60.6%) 67 (18.0%) 63 (16.9%) 19 (5.1%)	192 (56.8%) 62 (18.3%) 55 (16.3%) 28 (8.3%)	P = 0.55
Opioid Type	Strong (%)	547 (76.8%)	291 (78.0%)	256 (75.5%)	P = 0.43
Dose	Measured as average MME/ Day (SD)	43.2 (28.6)	44.7 (26.0)	41.4 (31.2)	P = 0.13
Days' Supply	Measured in days Mean (SD)	5.7 (6.4)	5.2 (6.0)	6.2 (6.7)	P = 0.04
Against CDC Guidelines	Number over 90 MME per day	53 (7.5%)	32 (8.6%)	21 (6.2%)	P = 0.22

* Data displayed as Mean (SD) represents the mean plus or minus the standard deviation. Data displayed as Number(percentage) denotes the number in the sample and the percentage within that group. Groups under 5 were not reported. Chi square tests conducted to investigate differences between the categorical variables. A proportion test was done for binary variables. A t-test was conducted for continuous variables. The data was checked to ensure the distribution was approximately normal, the sample size was sufficient for the t-test, z-test, and the samples were assumed to be independently collected.

The Pyxis dataset included a total of 548 presentations. Table 2 displays the demographic and clinical features for the Pyxis dataset. 279 presentations (50.9%) were from women, and the mean age was 48.1 (SD=18.0) years old. Fewer characteristics had statistically significant differences between men and women in this data, but I will now discuss the statistically significant variables. A statistically significantly greater proportion of women came from postal codes considered by the CIMD to have higher levels of ethnocultural diversity. A smaller proportion of men had a primary care provider available. Women had a longer length of stay, waiting 46 minutes more on average than men. Table 3 presents more information on second and later doses of opioids. Men had a higher total MME dosage average for all combined opioids given in ED. The number of cases where the opioid dose was over 90 MME, and against CDC guidelines, was small and will not be reported due to privacy restrictions. Although not statistically significant, the time from presentation to receiving an opioid was 40 minutes longer for women than men on average in this sample.

Table 2

Descriptive statistics (N, %, SD) for demographic and clinical differences between men and women who attended the QEII ED for LBP in the Pyxis Set

Variable		Total	Men	Women	Significance
Presentation	N	N = 548	N =269 (49.1%)	N = 279 (50.9%)	
Age	Mean years (SD)	48.1 (18.0)	47.6 (17.2)	48.6 (18.7)	P = 0.50
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%)	56 (10.2%)	29 (10.8%)	27 (9.7%)	P = 0.15
	Quintile 2 (%)	68 (12.4%)	41 (15.2%)	27 (9.7%)	
	Quintile 3 (%)	43 (7.9%)	25 (9.3%)	18 (6.5%)	
	Quintile 4 (%)	76 (13.9%)	37 (13.8%)	39 (14.0%)	
	Quintile 5 (%)	303 (55.3%)	137 (50.9%)	166 (59.5%)	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%)	255 (46.5%)	120 (44.6%)	135 (48.4%)	P =0.55
	Quintile 2 (%)	128 (23.4%)	64 (23.8%)	64 (22.9%)	
	Quintile 3 (%)	79 (14.4%)	39 (14.5%)	40 (14.3%)	
	Quintile 4 (%)	56 (10.2%)	28 (10.4%)	28 (10.0%)	
	Quintile 5 (%)	28 (5.1%)	18 (6.7%)	10 (3.6%)	
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 or 2(%)	34 (6.2%)	25 (8.9%)	10 (3.6%)	P = 0.05
	Quintile 3 (%)	38 (6.9%)	21 (8.2%)	16 (5.7%)	
	Quintile 4 (%)	101 (18.4%)	49 (18.2%)	52 (18.6%)	
	Quintile 5 (%)	373 (68.1%)	177 (64.7%)	199 (71.3%)	
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%)	240 (43.8%)	117 (43.5%)	123 (44.1%)	P = 0.68
	Quintile 2 (%)	118 (21.5%)	56 (20.8%)	62 (22.2%)	
	Quintile 3 (%)	81 (14.8%)	46 (17.1%)	35 (12.5%)	
	Quintile 4 (%)	46 (8.4%)	22 (8.2%)	24 (8.6%)	
	Quintile 5 (%)	61 (11.1%)	28 (10.4%)	33 (11.8%)	
Availability of Primary Care Provider	No (%)	77 (14.1%)	49(18.2%)	28 (10.1%)	P =0.006
Presentation Time of Day	Presentation during working hours of 9:00-17:00 (%)	301 (54.9%)	146 (54.3%)	155 (55.6%)	P = 0.76
Opioid Naïve	Not Opioid Naïve (%)	31 (5.7%)	16 (6.0 %)	15 (5.3%)	P=0.77
		Clinical Characteristics			
Presentation on day of week	Presentation on weekday (%)	398 (72.6%)	192 (71.4%)	206 (73.8%)	P =0.52
Pain intensity score	Mean (SD)	4.6 (3.1)	4.4 (3.3)	5.0 (2.8)	P = 0.36
Length of Stay	Mean number of hours (SD)	4.00 (2.82)	3.61 (2.42)	4.37 (3.11)	P = 0.002
Canadian Triage and Acuity Scale	1 (Resuscitation) (%)	0	0	0	P = 0.40
	2 (Emergent) (%)	55 (10.0%)	24 (8.9%)	31 (11.1%)	
	3 (Urgent) (%)	386 (70.4%)	187 (69.5%)	199 71.3%)	
	4 or 5 (Less Urgent and Non-Urgent) (%)	107 (19.5%)	58 (21.6%)	49 (17.6%)	
Mechanical	Yes (%)	181 (33.0%)	93 (34.6%)	88 (31.5%)	P = 0.45
Received Pyxis Drug	Yes (%)	128 (23.4%)	55 (20.5%)	73 (26.2%)	P = 0.11
Opioid Type (1st Drug)	Hydromorphone	72 (56.3%)	36 (65.5%)	36 (49.3%)	P = 0.23
	Morphine	29 (22.7%)	10 (18.2%)	19 (26.0%)	
	Codeine	25 (19.5%)	9 (16.4%)	16 (21.9%)	
Opioid Type	Parenteral (%)	26 (20.3%)	13 (23.6%)	13 (17.8%)	P= 0.42
Opioid Type	Strong (%)	103 (80.5%)	46 (83.6%)	57 (78.1%)	P = 0.43
Dose	MME total for visit (SD)	21.9 (18.8)	25.9 (21.8)	18.8 (15.6)	P = 0.03
Time to opioid	Hours	3.02 (2.26)	2.64 (1.68)	3.30 (2.60)	P=0.09
Filled DIS Drug	Yes (%)	94 (17.2%)	44 (16.4%)	50 (17.9%)	P=0.69
Received an opioid in ED and an Rx	Neither	385 (70.3%)	197 (73.2 %)	188 (67.4%)	P=0.40
	ED Only	69 (12.6%)	28 (10.4%)	41 (14.7%)	
	Prescription only	35 (6.4%)	17 (6.3%)	18 (6.5%)	
	Both ED and Rx	59 (10.8%)	27 (10.0%)	32 (11.5%))	

* Data displayed as Mean (SD) represents the mean plus or minus the standard deviation. Data displayed as Number(percentage) denotes the number in the sample and the percentage within that group. Groups under 5 were not reported. Chi square tests conducted to investigate differences between the categorical variables. A proportion test was done for binary variables. A t-test was conducted for continuous variables. The data was checked to ensure the distribution was approximately normal, the sample size was sufficient for the t-test, z-test, and the samples were assumed to be independently collected.

Table 3

Drug information on patients receiving multiple drugs who attended the QEII ED for LBP

Variable			Pyxis Set
Number of Drugs received	0	N (%)	420 (76.64%)
	1		68 (12.41 %)
	2		46 (8.39%)
	3		7 (1.28%)
	4+		7 (1.28%)
1st Opioid Drug	Hydromorphone	N (%)	72 (56.3%)
	Morphine		29 (22.66%)
	Codeine		25 (19.53%)
Later Opioid Drug	Hydromorphone	N (%)	59 (65.6%)
	Morphine		15 (16.7%)
	Codeine		16 (17.8%)
MME for First Drug	MME	Mean (SD)	12.0 (12.0)
MME for Second Drug	MME		14.9 (11.2)
MME for Third Drug	MME		14.4 (11.2)

The discharge diagnoses were very similar between men and women (Table 4). Most diagnoses assigned were general and non-descriptive, making it difficult to draw conclusions with the ICD codes.

Table 4

Top five most common discharge diagnoses for men and women who attended the QEII ED for LBP between 2017 - 2020

Men		Women		P value
Diagnosis	Number of people with diagnosis (percentage)	Diagnosis	Number of people with diagnosis (percentage)	
Back Pain	927 (46.8%)	Back Pain	1032 (50.4%)	P = 0.02
Mechanical Low Back Pain	312 (15.8%)	Mechanical Low Back Pain	281 (13.7%)	P = 0.06
Pain – Back NYD	206 (10.4%)	Pain – Back NYD	244 (11.9%)	P = 0.13
Low Back Strain	186 (9.4%)	Low Back Strain	112 (5.5%)	P < 0.0001
Muscle Spasm Back	52 (2.6%)	Musculoskeletal pain	56 (2.7%)	

Secondary Analyses

What are the demographic and clinical differences by mechanical pain diagnosis, opioid prescription in the ED, and opioid prescription after a visit to the ED?

After examining the most common discharge diagnoses, I grouped all diagnoses into either a mechanical or non-mechanical category. Appendix H shows a comparison of demographic and clinical differences between people who received mechanical and non-mechanical diagnoses. People diagnosed with mechanical pain were younger on average and men comprised a higher proportion of mechanical pain diagnoses compared to those with non-mechanical pain diagnoses. A significantly lower percentage had a primary care provider available, and a higher proportion were opioid naïve. Clinically, they had a shorter stay on average and a greater proportion were assigned a higher (and less urgent) CTAS score. A lower percentage received an opioid, and a lower percentage of people with a mechanical pain diagnosis received a strong opioid.

Appendix I shows baseline characteristics from the Pyxis dataset of those who received an opioid in the ED and those who did not. A marginally higher percentage of those who received opioids were women than those who did not receive an opioid, though this difference was non-significant. Significantly higher proportions of patients who received an opioid from the ED came from a postal code determined to have less situational vulnerability, had an available primary care provider, stayed (64 minutes on average) longer in the ED, received a CTAS score of Emergent, and filled a prescription after leaving the ED, than those who did not receive an opioid in the ED. There was no statistically significant difference in patient reported pain score for those who received an opioid and those who did not.

Next, I compared the patients who filled an opioid prescription for LBP that they received after attending the ED, and those who did not (Appendix J). The average age of a patient filling a prescription was older (54.5 years), compared to those who did not (46.0 years). A lower proportion of women filled a prescription, although this result was marginally non-significant. A greater percentage of those who filled a prescription came from a postal code with low residential instability and situational vulnerability than those who did not fill a prescription. A greater proportion of patients who filled their prescription were also had an available primary care provider and presented during working hours. Clinically, they had a

longer stay on average, were given a higher urgency CTAS score, and a lower proportion received a diagnosis of mechanical pain. A greater proportion of those who filled a prescription were opioid naïve. There was no statistically significant difference in patient reported pain score for those who filled an opioid and those who did not.

Diagnosis (Question 2)

How is patient sex associated with LBP diagnosis?

Table 5 shows the results for unadjusted and adjusted logistic regressions of patient diagnosis of mechanical pain on patient sex and other covariates. To ensure sufficient statistical power analysis, I excluded two CIMD variables, situational vulnerability and residential instability as described in Chapter III. For unadjusted models, women had lower odds of receiving a diagnosis of mechanical pain, and this held true for the adjusted model as well. One influential outlier was found during assumption checking. After examination, it did not appear to be an error, and so remained in the model. I conducted the Pearson goodness of fit test, and this model was considered to have poor fit ($p = 0.03$), and the area under the ROC curve was also low, at 0.5768.

Table 5

Unadjusted and adjusted logistic regression (OR and 95% CI) of mechanical pain diagnosis on patient sex and other covariates among QEII ED LBP patients

Variable		Unadjusted Model	Adjusted Model
Sex	Men	1.0 (ref)	1.0 (ref)
	Women	0.77 [0.67, 0.87]***	0.79 [0.69, 0.91]***
Age	Years	0.99 [0.99, 0.99]***	0.993 [0.989, 0.997]***
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%)	1.0 (ref)	-
	Quintile 2 (%)	0.89 [0.69, 1.15]	
	Quintile 3 (%)	0.92 [0.69, 1.23]	
	Quintile 4 (%)	0.98 [0.76, 1.27]	
	Quintile 5 (%)	0.93 [0.76, 1.14]	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%)	1.0 (ref)	1.0 (ref)
	Quintile 2 (%)	0.98 [0.83, 1.17]	1.00 [0.84, 1.20]
	Quintile 3 (%)	1.06 [0.88, 1.28]	1.11 [0.91, 1.36]
	Quintile 4 (%)	1.06 [0.86, 1.32]	1.09 [0.87, 1.36]
	Quintile 5 (%)	0.86 [0.62, 1.19]	0.90 [0.64, 1.26]
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 (%)	1.0 (ref)	1.0 (ref)
	Quintile 2 (%)	0.97 [0.55, 1.71]	1.12 [0.63, 2.00]
	Quintile 3 (%)	0.95 [0.57, 1.59]	1.04 [0.62, 1.74]
	Quintile 4 (%)	1.00 [0.62, 1.62]	1.15 [0.70, 1.88]
	Quintile 5 (%)	0.86 [0.55, 1.38]	1.00 [0.62, 1.61]
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%)	1.0 (ref)	-
	Quintile 2 (%)	1.08 [0.91, 1.28]	
	Quintile 3 (%)	1.13 [0.93, 1.38]	
	Quintile 4 (%)	0.96 [0.76, 1.21]	
	Quintile 5 (%)	1.22 [0.99, 1.52]	
Availability of Primary Care Provider	Yes	0.78 [0.65, 0.93]**	0.94 [0.77, 1.15]
Presentation Time of Day	Presentation outisde of working hours	1.0 (ref)	1.0 (ref)
	Presentation during working hours of 9:00-17:00	1.05 [0.92, 1.20]	1.06 [0.93, 1.21]
Presentation on day of week	Presentation on weekday	1.0 (ref)	1.0 (ref)
	Presentation on weekend	0.90 [0.78, 1.05]	0.91 [0.78, 1.06]
Pain intensity score	0	1.0 (ref)	1.0 (ref)
	1	0.93 [0.37, 2.32]	1.00 [0.40, 2.52]
	2	0.69 [0.39, 1.20]	0.73 [0.42, 1.29]
	3	1.01 [0.57, 1.80]	1.04 [0.58, 1.85]
	4	1.42 [0.92, 2.22]	1.50 [0.96, 2.37]
	5	1.67 [1.13, 2.46]**	1.76 [1.18, 2.60]**
	6	1.06 [0.70, 1.61]	1.10 [0.72, 1.68]
	7	1.26 [0.87, 1.82]	1.34 [0.92, 1.95]
	8	1.17 [0.78, 1.74]	1.21 [0.80, 1.82]
	9	1.08 [0.63, 1.88]	1.11 [0.64, 1.93]
	10	1.15 [0.72, 1.82]	1.14 [0.71, 1.81]
	Missing	1.11[0.88, 1.40]	1.15 [0.91, 1.45]
Length of Stay	Number of hours	0.91 [0.88, 0.94]***	0.93 [0.90, 0.96]*
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	1.0 (ref)	1.0 (ref)
	3 (Urgent)	1.11 [0.92, 1.36]	1.11 [0.91, 1.36]
	4 (Less Urgent)	1.36 [1.09, 1.70]**	1.20 [0.95, 1.51]
	5 (Non-Urgent)	1.37 [0.70, 2.68]	1.27 [0.65, 2.51]

*denotes an odds ratio for which the p value is less than 0.05.** for 0.01 and ***for 0.001 Odds ratios are derived from the logistic regression. The 95% confidence intervals are expressed as [lower band, upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable.

Treatment in Emergency Care (Question 3)

How is patient sex associated with receiving an opioid for the treatment of LBP?

Table 6 displays the results for unadjusted and adjusted logistic regressions for receiving an opioid in the ED on respondent sex and other covariates. Due to the limited sample size, I, with the help of my committee, selected variables for the adjusted analysis with high confidence of accurate measurement and a high likelihood of confounding the results if not included. For this reason, I did not use pain intensity, CIMD scores and presentation times. Sex was not significantly associated with receiving an opioid in the ED, in either the unadjusted model or adjusted model. I examined model residuals and there were no notable influential outliers. The Pearson goodness of fit test indicated the adjusted model was statistically significant ($p = 0.42$) and the area under the curve was 0.66. The adjusted model had the lowest Akaike information criterion (AIC). The null model had the lowest Bayesian information criterion (BIC), even compared to the unadjusted model with the lowest BIC, which only included length of stay as an independent variable.

Table 6

Unadjusted and adjusted logistic regression (OR and 95% CI) of receiving opioid in ED on patient sex and other covariates among QEII ED LBP patients for Pyxis set

Variable		Unadjusted Model	Adjusted Model 1
Sex	Men	1.0 (ref)	1.0 (ref)
	Women	1.38[0.93, 2.05]	1.19 [0.77, 1.83]
Age	Years	1.01 [0.99, 1.02]	0.99 [0.98, 1.01]
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1	1.0 (ref)	-
	Quintile 2	0.71 [0.32, 1.57]	
	Quintile 3	0.52 [0.20, 1.36]	
	Quintile 4	0.71 [0.33, 1.55]	
	Quintile 5	0.68 [0.36, 1.27]	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1	1.0 (ref)	-
	Quintile 2	1.80 [1.10, 2.92]*	
	Quintile 3	1.30 [0.71, 2.37]	
	Quintile 4	1.24 [0.62, 2.48]	
	Quintile 5	1.37 [0.55, 3.39]	
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1	1.0 (ref)	-
	Quintile 2	1.43 [0.28, 7.26]	
	Quintile 3	0.90 [0.20, 4.08]	
	Quintile 4	1.32 [0.34, 5.04]	
	Quintile 5	1.24 [0.34, 4.48]	
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1	1.0 (ref)	-
	Quintile 2	0.96 [0.59, 1.57]	
	Quintile 3	0.41 [0.20, 0.81]*	
	Quintile 4	0.54 [0.24, 1.23]	
	Quintile 5	0.51 [0.24, 1.05]	
Presentation Time of Day	Presentation outside working hours	1.0 (ref)	-
	Presentation during working hours of 9:00-17:00	1.38 [0.92, 2.06]	
Presentation on day of week	Presentation on weekday	1.0 (ref)	-
	Presentation on weekend	0.90 [0.57, 1.41]	
Availability of Primary Care	No	1.0 (ref)	1.0 (ref)
	Yes	2.951.38, 6.31]**	2.55 [1.13, 5.76]*
Pain intensity score	0-10	0.97 [0.91, 1.04]	-
Length of Stay	Number of hours	1.13 [1.05, 1.21]***	1.11 [1.03, 1.19]**
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	1.0 (ref)	1.0 (ref)
	3 (Urgent)	0.45 [0.25, 0.81]**	0.53 [0.27, 1.02]
	4 (Less Urgent)	0.30 [0.14, 0.64]**	0.38 [0.14, 0.64]*
	5 (Non-Urgent)	-	-
Opioid Naivity	Opioid Naïve	1.0 (ref)	1.0 (ref)
	Not Opioid Naive	2.91[1.39, 6.09]**	2.20 [0.84, 5.79]

*denotes an odds ratio for which the p value is less than 0.05.** for 0.01 and ***for 0.001 Odds ratios are derived from the logistic regression. The 95% confidence intervals are expressed as [lower band, upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable.

Secondary Analyses

I conducted secondary analyses to investigate the effect of sex on the nature of the opioid received in the ED. Table 7 shows the results of a linear regression for the total opioid dose delivered in the ED, as measured in morphine milligram equivalents (MME) per day. As described above, I selected variables for the adjusted analyses with high confidence of accurate measurement and a high likelihood of confounding the results if not included. There were few variables here that remained signifcant in both the unadjusted and adjusted model. Being a woman was associated with receiving approximately 7 MME less opioid than men in the ED in the unadjusted model; however, this finding was attenuated in the adjusted model. Low VIF values indicated that multicollinearity was not an issue. After examining the QQ plot and conducting a Cook-Weisberg heteroscedasticity test, found that at very extreme values, there was slight heteroscedasticity, but overall, most of the model was acceptable. The adjusted R^2 value was 0.21, and while the adjusted model AIC was lower than the null model AIC, the adjusted model BIC was larger than the null model BIC. The smallest BIC value was found to be for the unadjusted model where only drug type was used to predict the total MME.

A logistic regression analysis was planned for examining the odds of receiving a parenteral prescription, but the sample was small and and any analyses would have been underpowered. The only covariate that approached significance was the CTAS, where less urgency was associated with lower odds of receiving a parenteral opioid dose. Compared to an emergent score, an urgent score had an 68% lower odds of receiving a parenteral dose [aOR 0.32 (95 CI%: 0.12, 0.87)] and a less urgent score had 91% lower odds [aOR 0.09 (95% CI: 0.01, 0.81)].

Table 7

Unadjusted and adjusted linear regression (Coefficient and 95% CI) of opioid dose (MME) on patient sex and other covariates among QEII ED LBP patients in Pyxis set

Variable		Unadjusted Model	Adjusted Model 1
Sex	Men	0.0 (ref)	0.0 (ref)
	Women	-7.06 [-13.60, -0.52]*	-4.24 [-10.59, 2.11]
Age	Years	-0.15 [-0.33, 0.03]	-0.08 [-0.23, 0.07]
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1	0.0 (ref)	-
	Quintile 2	8.58 [-4.34, 21.50]	
	Quintile 3	6.71 [-9.19, 22.61]	
	Quintile 4	9.93 [-2.61, 22.47]	
	Quintile 5	2.17 [-7.86, 12.22]	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1	0.0 ref	-
	Quintile 2	3.37 [-4.42, 11.16]	
	Quintile 3	10.59 [0.76, 21.35]*	
	Quintile 4	-3.50 [-14.86, 7.85]	
	Quintile 5	-9.26 [-23.98, 5.15]	
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1	0.0 (ref)	-
	Quintile 2	-2.80 [-28.82, 23.22]	
	Quintile 3	20.86 [-28.83, 45.44]	
	Quintile 4	-8.82 [-60.59, 12.95]	
	Quintile 5	-2.11 [-51.14, 18.81]	
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1	0.0 (ref)	-
	Quintile 2	3.35 [-4.55, 11.26]	
	Quintile 3	2.03 [-9.94, 14.01]	
	Quintile 4	-6.80 [-20.57, 6.97]	
	Quintile 5	13.16 [0.68, 25.64]*	
Presentation Time of Day	Presentation during working hours of 8:00-17:00	0.0 (ref)	-
	Presentation outside working hours	2.32 [-4.42, 9.06]	
Presentation on day of week	Presentation on weekday	0.0 (ref)	-
	Presentation on weekend	4.12 [-3.34, 11.65]	
Availability of Primary Care	No	0.0 (ref)	0.0 (ref)
	Yes	4.85 [-8.74, 18.43]	9.46 [-0.42, 19.35]
Pain intensity score	0 -10	-0.02 [-2.14, 2.09]	-
Length of Stay	Number of hours	-0.77 [-1.65, 0.12]	-0.56 [-1.24, 0.12]
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	0.0 (ref)	
	3 (Urgent)	1.11 [-7.76, 9.98]	
	4 (Less Urgent)	6.28 [-5.74, 18.30]	
	5 (Non-Urgent)	-	
Drug Type	Hydromorphone	0.0 (ref)	0.0 (ref)
	Morphine	-10.13 [-17.63, -2.62]**	-7.33 [-14.82, 0.16]
	Codeine	-19.43 [-27.35, -11.51]***	-19.13 [-25.04, -13.23]***
Opioid Naivity	Opioid Naïve	0.0 (ref)	0.0 (ref)
	Not Opioid Naive	12.15[1.82, 22.49]*	14.62 [1.37, 30.60]*

*denotes coefficients for which the p value is less than 0.05. Coefficients were derived from the linear regression. The 95% confidence intervals were expressed as [lower band, upper band]. The reference category was denoted as 1.00 (ref) for each categorical variable.

Treatment after Emergency Care (Question 4)

How is patient sex associated with filling an opioid prescription?

Table 8 displays the results for unadjusted and adjusted logistic regression models of filling an opioid prescription within one month from an ED visit on patient sex and other covariates. While sex bordered on statistical significance in the unadjusted model, the adjusted model found that women had lower odds of filling a prescription than men. Clinical characteristics, such as a longer length of stay and CTAS score, were associated with an increase in the odds of filling a prescription. In contrast, a patient's reported pain score was not significant. Filling a prescription in the past six months for opioids, or not being opioid naïve, demonstrated a robust association with filling a prescription after this ED visit [aOR: 16.78 (95%CI: 11.18, 25.17)]. The area under the ROC curve was found to be 0.7412 and pseudo R^2 was 0.1586. The Pearson goodness of fit test indicated that the model had a statistically significant fit (p=0.33). Alternative models were considered with fewer variables, removing pain score or CIMD measurements, and the AIC and BIC were not meaningfully smaller (3195 vs 3175 for AIC and 3390 vs 3301 for BIC). Given that there was not a meaningful difference between the AIC and BIC, I used the planned adjusted model.

Table 8

Unadjusted and adjusted logistic regression (OR and 95% CI) of filling an opioid prescription after attending the QEII ED for LBP on patient sex and other covariates

Variable		Unadjusted Model	Adjusted Model 1
Sex	Men	1.00 (ref)	1.00 (ref)
	Women	0.85 [0.73, 1.00]	0.72 [0.59, 0.88]***
Age	Years	1.02 [1.02, 1.03]***	1.02 [1.01, 1.02]***
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1	1.0 (ref)	-
	Quintile 2	0.71 [0.52,0.96]*	
	Quintile 3	0.55 [0.38, 0.80]**	
	Quintile 4	0.81 [0.60, 1.09]	
	Quintile 5	0.66 [0.52, 1.83]**	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1	1.0 (ref)	1.0 (ref)
	Quintile 2	0.99 [0.80, 1.22]	1.01 [0.78, 1.31]
	Quintile 3	1.00 [0.79, 1.27]	1.01 [0.76, 1.35]
	Quintile 4	0.85 [0.64, 1.13]	0.81 [0.57, 1.17]
	Quintile 5	1.21 [0.84, 1.76]	1.07 [0.67, 1.73]
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1	1.0 (ref)	1.0 (ref)
	Quintile 2	1.40 [0.61, 3.21]	1.34 [0.50, 3.62]
	Quintile 3	1.76 [0.83, 3.72]	1.66 [0.69, 3.98]
	Quintile 4	1.56 [0.76, 3.19]	1.41 [0.60, 3.28]
	Quintile 5	1.83 [0.91, 3.69]	1.62 [0.71, 3.70]
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1	1.0 (ref)	-
	Quintile 2	0.88 [0.71, 1.09]	
	Quintile 3	0.71 [0.55, 0.92]**	
	Quintile 4	0.65 [0.48, 0.89]**	
	Quintile 5	0.61 [0.46, 0.82]**	
Presentation Time of Day	Presentation outside working hours	1.0 (ref)	1.0 (ref)
	Presentation during working hours of 9:00-17:00	1.21 [1.02, 1.42]*	1.11 [0.92, 1.35]
Presentation on day of week	Presentation on weekday	1.0 (ref)	1.0 (ref)
	Presentation on weekend	1.06 [0.89, 1.27]	1.08 [0.87, 1.35]
Availability of Primary Care	No	1.0 (ref)	1.0 (ref)
	Yes	2.90 [2.09, 4.0]***	1.91 [1.32, 2.79]***
Pain intensity score	0	1.0 (ref)	1.0 (ref)
	1	0.80 [0.27, 2.43]	0.82 [0.26, 2.66]
	2	1.06 [0.59, 1.92]	0.89 [0.41, 1.92]
	3	0.82 [0.41, 1.65]	1.01 [0.47, 2.19]
	4	0.90 [0.52, 1.54]	0.94 [0.48, 1.84]
	5	0.89 [0.56, 1.44]	1.03 [0.57, 1.90]
	6	0.77 [0.46, 1.28]	0.82 [0.45, 1.49]
	7	0.87 [0.55, 1.35]	0.88 [0.50, 1.55]
	8	0.95 [0.58, 1.52]	1.12 [0.63, 1.99]
	9	0.97 [0.51, 1.83]	1.08 [0.51, 2.29]
	10	0.55 [0.29, 1.03]	0.73 [0.36, 1.50]
	Missing	0.77 [0.59, 1.01]	0.97 [0.69, 1.38]
Length of Stay	Number of hours	1.12 [1.08, 1.14]***	1.08 [1.03, 1.12]***
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	1.0 (ref)	1.0 (ref)
	3 (Urgent)	0.53 [0.43, 0.66]***	0.59 [0.45, 0.77]***
	4 (Less Urgent)	0.28 [0.21, 0.37]***	0.41 [0.30, 0.58]***
	5 (Non-Urgent)	0.06 [0.01, 0.46]**	0.07 [0.01, 0.74]*
Opioid Naivity	Yes	1.0 (ref)	1.0 (ref)
	No	21.1 [15.12, 29.46]***	16.78 [11.18, 25.17]***

*denotes an odds ratio for which the p value is less than 0.05.** for 0.01 and ***for 0.001 Odds ratios are derived from the logistic regression. The 95% confidence intervals are expressed as [lower band, upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable.

Secondary Analyses

I conducted secondary analyses for this question to examine how sex was associated with the nature of the prescription. To examine this outcome in more depth, I ran a linear regression to examine differences in opioid dose among those filling an opioid prescription within one month of their ED visit. Table 9 has further details on the unadjusted and adjusted models. Sex was not statistically significant in either the unadjusted or the adjusted model. Few variables showed statistical and meaningful differences. As per my analysis plan, economic dependency and ethnocultural composition were included in the adjusted model, but ethnocultural composition had to be dropped after it was found to have high multicollinearity. I plotted and examined Pearson and deviance residuals, and included influential outliers in the model as they did not appear to be errors. The outlying residuals were likely due to smaller lengths of stay than the majority of the sample. It is important to acknowledge, however, that this model was found to have heterscedascity. I examined the QQ plot of residuals and this indicated that residuals were acceptable for the majority of the model, with the exception of very high values. I attempted transformation of the data, but the transformation for this model resulted in a less favourable QQ residual plot. This model, therefore, is best suited to predicting the dose with no transformation, but caution is needed at very low or very high doses.

Table 9

Unadjusted and adjusted linear regression (Coefficient and 95% CI) of opioid dose from pharmacy on patient sex and other covariates among QEII ED LBP patients

Variable		Unadjusted Model	Adjusted Model 1
Sex	Men	0.0 (ref)	0.0 (ref)
	Women	-3.29 [-7.51, 0.92]	-0.70 [-5.70, 4.30]
Age	Years	-0.31 [-0.42, -0.19]***	-0.25 [-0.37, -0.13]***
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1	0.0 (ref)	-
	Quintile 2	-8.50 [-16.40, -0.59]*	
	Quintile 3	-4.03 [-13.75, 5.67]	
	Quintile 4	-1.19 [-8.76, 6.39]	
	Quintile 5	-7.66 [-13.57,-1.76]*	
Level of Deprivation: Economic dependency (5 is highest deprivation)	Quintile 1	0.0 (ref)	0.0 (ref)
	Quintile 2	-0.61 [-6.10, 4.87]	-1.19 [-6.76, 4.38]
	Quintile 3	-1.55 [-7.72, 4.63]	-1.50 [-8.56, 5.55]
	Quintile 4	-6.47 [-13.84, 0.89]	-1.73 [-8.40, 4.94]
	Quintile 5	3.31 [-6.12, 12.74]	5.18 [-5.03, 15.39]
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1	0.0 (ref)	-
	Quintile 2	26.14 [4.06, 48.23]*	
	Quintile 3	17.52 [-2.45, 37.49]	
	Quintile 4	13.73 [-5.53, 32.98]	
	Quintile 5	8.23 [-10.54, 27.00]	
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1	0.0 (ref)	-
	Quintile 2	4.99 [-0.41, 10.38]	
	Quintile 3	5.38 [-1.28, 12.05]	
	Quintile 4	7.33 [-0.78, 15.44]	
	Quintile 5	4.21 [-3.51, 11.92]	
Presentation Time of Day	Presentation outside working hours	0.0 (ref)	0.0 (ref)
	Presentation during working hours of 9:00-17:00	-2.91 [-7.18, 1.36]	-2.76 [-7.00, 1.49]
Presentation on day of week	Presentation on weekday	0.0 (ref)	0.0 (ref)
	Presentation on weekend	-1.94 [-6.65, 2.76]	-0.34 [-4.90, 4.23]
Availability of Primary Care	No	0.0 (ref)	0.0 (ref)
	Yes	-12.97 [-21.76, -4.18]**	-12.20 [-26.41, 2.00]
Pain intensity score	0	0.0 (ref)	-
	1	-22.50 [-51.23, 6.23]	
	2	-5.05 [-20.00, 9.90]	
	3	-11.12 [-29.13, 6.89]	
	4	-1.59 [-15.31, 12.12]	
	5	-1.60 [-13.24, 11.00]	
	6	9.21 [-4.02, 22.45]	
	7	-7.33 [-18.78, 4.11]	
	8	-2.55 [-14.68, 9.57]	
	9	13.03 [-3.19, 29.26]	
	10	-5.48 [-22.24, 11.26]	
	Missing	-1.73 [-8.49, 5.02]	
Length of Stay	Number of hours	-0.40 [-0.89, 0.08]	-0.24 [-0.72, 0.24]
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	0.0 (ref)	0.0 (ref)
	3 (Urgent)	-7.29 [-12.38, -2.20]**	-6.00 [-11.97, -0.36]*
	4 (Less Urgent)	-7.27 [-14.51, -0.04]*	-6.04 [-13.10, 1.07]
	5 (Non-Urgent)	-8.77 [-64.90, 47.35]	-15.78 [-23.14, -8.43]***
Opioid Type	Hydromorphone	0.0 (ref)	0.0 (ref)
	Morphine	-12.83 [-18.24, -7.42]***	-13.25 [-19.35, -7.14]***
	Codeine	-16.52 [-22.11, -10.93]***	-15.26 [-19.90, -10.61]***
	Tramadol	-27.03 [-35.28, -18.77]***	-27.80 [-32.71, -22.88]***
Opioid Naivity	Yes	0.0 (ref)	0.0 (ref)
	No	2.43 [-2.53, 7.39]	2.33 [-3.83, 8.48]

* denotes coefficients for which the p value is less than 0.05. Coefficients derived from the linear regression. The 95% confidence intervals are expressed as [lower band, upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable. An example is placed in the row for the variable of sex.

To examine if there was any difference in days supply, I ran a linear regression to assess the relationship between these variables and the number of days' supply. Table 10 shows the results for the unadjusted and adjusted models. Sex was associated with about one extra days' supply in the unadjusted model, but this was attenuated in the adjusted model. I checked multicollinearity and observed no issues. Residuals were distributed normally in this model. After examining the QQ plot and doing the Cook-Weisberg test, I found no heteroscedascity present in this model. I attempted transformation of the data, but heteroscedascity remained. The adjusted R^2 was found to be 0.17, and the AIC and BIC values were improved for the adjusted model over the null model and unadjusted models. Sensitivity analyses conducted with opioid naivety found that there was no signifcant difference between opioid naïve patients and patients who had been prescribed opioids between 6 and 12 months prior or longer than 12 months prior. I investigated interaction terms with marginal effect plots and found no significant interactions between sex and any of the variables.

Table 10

Unadjusted and adjusted linear regression (Coefficient and 95% CI) of days' supply from pharmacy on patient sex and other covariates among QEII ED LBP patients

Variable		Unadjusted Model	Adjusted Model 1
Sex	Men	0.0 (ref)	0.0 (ref)
	Women	0.96 [0.02, 1.89]*	0.58 [-0.46, 1.62]
Age	Years	0.07 [0.05, 0.10]***	0.05 [0.02, 0.08]***
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1	0.0 (ref)	-
	Quintile 2	1.44 [-0.33, 3.21]	
	Quintile 3	1.25 [-0.92, 3.43]	
	Quintile 4	-0.15 [-1.84, 1.55]	
	Quintile 5	1.03 [-0.29, 2.35]	
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1	0.0 (ref)	0.0 (ref)
	Quintile 2	0.27 [-0.95, 1.49]	-0.09 [-1.26, 1.08]
	Quintile 3	1.71 [0.34, 3.09]*	1.37 [-0.20, 2.95]
	Quintile 4	2.02 [0.38, 3.66]*	1.09 [-1.10, 3.29]
	Quintile 5	1.00 [-1.10, 3.09]	0.41 [-1.81, 3.78]
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1	0.0 (ref)	0.0 (ref)
	Quintile 2	-2.93 [-7.90, 2.05]	-3.62 [-7.27, 0.03]
	Quintile 3	-2.21 [-6.71, 2.29]	-3.66 [-7.27, -0.04]*
	Quintile 4	-1.97 [-6.30, 2.37]	-3.01 [-6.48, 0.45]
	Quintile 5	-1.17 [-5.40, 3.05]	-2.97 [-6.31, 0.38]
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1	0.0 (ref)	-
	Quintile 2	-1.66 [-2.87, -0.46]**	
	Quintile 3	-0.55 [-2.04, 0.94]	
	Quintile 4	-1.09 [-2.90, 0.72]	
	Quintile 5	0.07 [-1.65, 1.79]	
Presentation Time of Day	Presentation during working hours of 9:00-17:00	0.0 (ref)	0.0 (ref)
	Presentation outside working hours	-0.11 [-1.06, 0.85]	-0.23 [-0.47, 1.77]
Presentation on day of week	Presentation on weekday	0.0 (ref)	0(ref)
	Presentation on weekend	0.80 [-0.25, 1.85]	0.64 [-1.20, 0.74]
Availability of Primary Care	No	0.0 (ref)	0.0 (ref)
	Yes	1.49 [-0.48, 3.46]	1.13 [-0.52, 2.78]
Pain intensity score	0	0.0 (ref)	-
	1	16.30 [10.06, 22.55]***	
	2	7.22 [3.97, 10.47]***	
	3	1.90 [-2.02, 5.81]	
	4	1.18 [-1.79, 4.17]	
	5	2.39 [-0.24, 5.03]	
	6	0.11 [-2.77, 2.99]	
	7	2.62 [0.14, 5.11] *	
	8	1.05 [-1.59, 3.68]	
	9	4.59 [1.06, 8.11]	
	10	-0.43 [-4.39, 3.21]	
	Missing	1.28 [-0.19, 2.75]	
Length of Stay	Number of hours	0.11 [0.00, 0.22]*	0.04 [-0.09, 0.17]
Canadian Triage and Acuity Scale	1 (Resuscitation)	-	-
	2 (Emergent)	0.0 (ref)	0.0 (ref)
	3 (Urgent)	1.02 [-0.12, 2.16]	0.76 [-0.51, 2.03]
	4 (Less Urgent)	1.01 [-0.61, 2.63]	0.83 [-0.82, 2.48]
	5 (Non-Urgent)	-3.88 [-16.44, 8.68]	-2.44 [-4.13, -0.76]*
Opioid Type	Hydromorphone	0.0 (ref)	1.0 (ref)
	Morphine	-1.14 [-2.36, 0.07]	-1.35 [-2.36, 0.24]
	Codeine	2.55 [1.29, 3.82]***	2.64 [0.94, 4.34]**
	Tramadol	5.60 [3.74, 7.46]***	6.10 [3.46, 8.74]***
Opioid Naivity	Yes	0.0 (ref)	0.0 (ref)
	No	3.42 [2.34, 4.50]***	3.97 [2.40, 5.53]***

* denotes coefficients for which the p value is less than 0.05, and** for 0.01 and ***for 0.001. Coefficients are derived from the linear regression. 95% The confidence intervals are expressed as [lower band, upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable.

I conducted another planned analysis to examine sex differences in the odds of being given a prescription that did not adhere to CDC guidelines. This was a small proportion of the overall sample, where only 53 (7.5%) prescriptions had a dose over 90 MME per day, with 8.6 % of men and 6.2% of women receiving a prescription that did not follow CDC guidelines. After running a logistic regression, being a woman was not significantly associated with a dose that did not follow CDC guidelines in either the unadjusted regression [OR: 0.70 (95%CI: 0.40, 1.25)] or the adjusted regression [aOR: 0.77 (95%CI: 0.40, 1.48)]. The only variable significantly associated with being prescribed a dose that followed CDC guidelines was age, where for every ten years gained, a person was 17 percent more likely to be prescribed a dose that followed CDC guidelines [aOR of a dose that did not follow CDC guidelines: 0.982 (95%CI: 0.967, 0.998)].

Sensitivity Analyses

Originally, I had planned a logistic regression for determining if sex and gender were associated with filling a prescription above 90 MME, however, this definition only applied to small number of cases in the ED and an analysis was not possible. A sensitivity analysis was conducted with prescriptions above 50 MME instead. For treatment post ED, a total of 188 cases (26.5%) had prescriptions above 50 MME. A total of 77 women (22.8%) and 111 men (29.8%) were prescribed more than 50 MME per day. This analysis found that in an unadjusted model, a woman had 0.69 odds [95% CI: 0.49, 0.97] of being prescribed a prescription over 50 MME, but this did not remain significant in the adjusted model.

I conducted sensitivity analyses to see if sex and gender were associated with having a prescription of three or five days. A total of 324 (45.6%) of the people who filled prescriptions had more than three days supply, and 185 (26.1%) had prescriptions with longer than five days supply. A subset of 162 (47.9%) women had prescriptions longer than three days and 101 (29.9%) had prescriptions over five days. There were 162 (43.6%) men who also had prescriptions longer than three days and 84 (22.6%) had prescriptions over five days. Sex was not significant for predicting who filled a prescription over three days and was not significant in predicting filling more than five days' supply after adjusting for drug type prescribed. Sensitivity analysis conducted with opioid naivety found that being prescribed opioids within

the past 6 months was significantly associated with filling an opioid prescription, but that being prescribed opioid 6-12 months prior, or more than 12 months prior, were not significantly associated with filling a prescription in the adjusted model.

I also conducted a sex-stratified logistic regression to investigate the odds of filling a prescription. There were very few considerable differences between men and women in the analysis, where the same covariates were statistically significant for both models. After examining both models, the confidence intervals for each variable overlapped, indicating that estimates did not differ significantly between the men and women's models. Although not statistically significant, one potentially notable difference between the models was the opioid naivety of the patient. For men, not being opioid naïve had 24 times higher odds of a filling a prescription [aOR: 24.41 (95%CI: 13.92, 42.83)], compared to women where not being opioid naïve had 12 times higher odds [aOR: 12.34 (95%CI: 7.85, 19.39)].

Summary of Results

Table 11 shows a summary of each of the reported statistical analysis outcomes from the previous sections.

Table 11

Summary table of relevant outcomes for men and women from previous sections

Outcome	Analysis Type	Regression Type		Adjusted Model
How is patient sex associated with low back pain diagnosis? (Question 2)				
Odds of receiving a mechanical pain diagnosis [a]	Primary	Logistic	Men Women	1.00 (ref) 0.79 [0.69, 0.91]***
How is patient sex associated with receiving an opioid for the treatment of low back pain? (Question 3)				
Odds of receiving an opioid in ED [b]	Primary	Logistic	Men Women	1.00 (ref) 1.19 [0.77, 1.83]
Total dose received in ED [c]	Secondary	Linear	Men Women	0.00 (ref) -4.24 [-10.59, 2.11]
How is patient sex associated with filling an opioid prescription? (Question 4)				
Odds of filling an opioid prescription [a]	Primary	Logistic	Men Women	1.00 (ref) 0.72 [0.59, 0.88]***
Dose of the opioid prescription [d]	Secondary	Linear	Men Women	0.00 (ref) -0.70 [-5.70, 4.30]
Days' supply of the opioid prescription [e]	Secondary	Linear	Men Women	0.00 (ref) 0.58 [-0.46, 1.62]
Odds of a prescription against CDC guidelines [e]	Secondary	Logistic	Men Women	1.00 (ref) 0.77 [0.40, 1.48]

* denotes outcomes for which the p value is less than 0.05, and** for 0.01 and ***for 0.001. For logistic regressions, odds ratios are reported and men as the reference category are denoted as 1.00 (ref). For linear regressions, coefficients are reported and men as the reference category are denoted as 0.00 (ref). Confidence intervals are expressed as [lower band, upper band].

[a] adjusted for age, economic dependency, ethnocultural composition, availability of primary care provider, presentation time of day, presentation on weekend, pain intensity score, length of stay, CTAS score

[b] adjusted for age, availability of primary care provider, length of stay, CTAS score, opioid naiviety

[c] adjusted for age, availability of primary care provider, length of stay, CTAS score, opioid naiviety, drug type

[d] adjusted for age, economic dependency, availability of primary care provider, presentation time of day, presentation on weekend, length of stay, CTAS score

[e] adjusted for age, economic dependency, ethnocultural composition, availability of primary care provider, presentation time of day, presentation on weekend, length of stay, CTAS score

CHAPTER V: DISCUSSION

Statement of Principal Findings

When examining sex differences in the experience of attending the ED for LBP, the results of this study were mixed, possibly due to the limitations in sample size for the Pyxis database, hindering analysis of opioid administration in the ED. There appeared to be little difference in the proportion of men and women attending the ED for LBP; however, there were significant demographic and clinical differences between the men and women attending the ED. I found sex was associated with the odds of a mechanical pain diagnosis after adjustment for demographic and clinical characteristics, although the model had very poor overall fit. No effect of sex on opioid administration in the ED was detected, although it is likely that this dataset was too underpowered to detect a small effect. Indeed, for the larger dataset, I found that men were more likely to fill an opioid prescription after attending the ED, although there were no detected differences in the dose, days' supply, or odds of adhering to prescribing guidelines after adjustment for demographic and clinical characteristics.

Study Findings in Relation to Other studies

The similar proportion of men and women attending the ED in this study was comparable to other studies, which also found little difference in the number of men and women presenting to the ED for LBP. Waterman et al. found that men comprised 51.5% episodes of LBP presentations, while women accounted for 48.5% in the National Electronic Injury Surveillance System (NEISS) database, comprised of more than 52 000 United States ED visits between 2004 and 2008.[154] Another study, examining a single ED in Alberta from 2017 to 2018, found that 50.2% of LBP presentations were men.[155] Drazin et al. used the Nationwide Inpatient Sample (NIS) database to examine LBP admissions to hospitals between 1998 and 2007 in the United States, and found that 62.6% of presentations were women.[156] Another study in three Australian hospitals reported that 60% of patients admitted to the hospital after attending the ED were women, so it is possible that women are more likely to be admitted to the hospital after attending the ED for LBP, something that this study was unable to examine due to insufficient numbers.[157]

When examining treatment in the ED, this study found that 23.4% of LBP patients were given an opioid during presentation. Kamper et al. did a systematic review and reported finding

a range of 17% to 61% of patients receiving opioids in the ED for LBP, so variation in this area has already been documented.[132] One study conducted in Brazil with four EDs found that 22% of patients presenting to the ED between 2014 and 2016 with LBP were administered opioids.[158] Another study examining a single ED in the state of Utah found that 35.9% of patients were given opioids in the ED.[159] When examining the odds of receiving an opioid and the dose, there were no statistically significant differences between men and women. Lau et al. also found no differences in the odds of opioid administration for men and women for most reasons for attending the ED, and this was also the case for back pain.[160] Another study conducted in Colorado examining opioid naïve patients found that both 41% of men attending and 41% of women were administered opioids in the ED after a diagnosis of LBP.[161]

Opioid prescribing after presentation to the ED due to LBP has varied across studies. In our study, 18.8% of men and 16.5% of women filled a prescription after attendance to the ED. One study set also in Nova Scotia found that 24.4% of LBP patients from 2010 - 2017 filled an opioid prescription within 7 days of attending the ED, although it is important to acknowledge that this data may have had some overlap with my own, as it included 2016 and 2017.[140] One study examining opioid prescribing for acute LBP in a workers compensation database in the US found 12% of participants filled an opioid prescription, although they only looked at those who filled within 2 days, which may partly explain why this estimate is lower than the estimate in this study.[141]

After adjusting for potential confounders, our study found that men had 39% higher odds of filling a prescription [aOR of women filling a prescription: 0.72 (95% CI 0.59, 0.88)]. In contrast to my results, a study examining outpatient opioid prescription dispensing found that women had 1.5 higher odds of filling a prescription in 2018.[118] One study examining opioid initiation for pain management in Ontario in 2015-2016 found that women comprised a slightly higher proportion of opioid prescriptions filled for musculoskeletal pain than men (52% vs 48%).[162]

After assessing guideline compliance, a smaller proportion of cases than expected were found not to adhere to the CDC guidelines. Only 7.5% of prescriptions had daily MME values of over 90 MME per day, and only 26.5 % of prescriptions were over the softer guidelines of 50 MME per day. A study conducted in Ontario examining initiations of opioid prescriptions

found that 20.6% of opioid prescriptions in 2016 and 13.9% in 2019 for LBP were over 50 MME per day.[163] There were no detected differences in the odds of receiving a prescription against prescribing guidelines for men and women in this study after adjustment for confounding variables.

The CTAS score of a patient was consistently associated with the odds of receiving or filling an opioid prescription as well as opioid dose, days supply, and strength. Previous research that has found that a lower CTAS score, or more urgent score, is associated with a higher chance of receiving opioids.[160,164,165] CTAS scores have been previously documented to be highly associated with the odds of consultation, admission, length of stay, hospital costs, and the likelihood of dying.[166] Although women were slightly more likely to be assigned a lower CTAS score, this did not necessarily translate to an increase in the odds of receiving an opioid prescription. After further investigation, CTAS scores and sex did not appear to interact in this study.

While CTAS was strongly associated with opioid prescriptions in this study, patient reported pain scale did not have any consistent association with opioid prescription. Men and women had similar mean pain scores in this study, as did those who did and did not receive an opioid, either during attendance or after attending the ED. Interestingly, there appeared to be no association between a patient's reported pain score and receiving an opioid in ED or filling an opioid after attending the ED in this study. Other studies have found that higher pain scores are associated with a greater likelihood of receiving opioids.[167,168] Some past literature has found that patient and healthcare provider perceptions' of pain do not always align.[169–171] A large number of pain scale scores were missing in this data, which is associated with both a greater gap between health care provider and patient perception of pain, and also with a lower likelihood of analgesic administration in the ED.[168,171–173] There may be several potential reasons why patient pain was less associated with opioid prescription than CTAS score, although potentially the healthcare provider's perception of patients' pain may be more relevant to clinical decisions than patient's reported pain.

Other studies have examined sex with other factors such as race and socioeconomic status. This study used CIMD, which proved to be a variable with inconsistent trends when used in statistical analysis. As CIMD is not collected at the individual level, it is important to

consider other studies' findings. Previous studies have found that Non-Hispanic whites have been consistently more likely to receive opioids, compared to Black individuals and Hispanic individuals.[174–177] Lower socioeconomic status has also been found to be associated with a lower likelihood of opioid prescription.[177]

Another aspect of this study is that it included the beginning of the coronavirus pandemic 2019 (COVID-19), which became a national emergency. This may have impacted the results of this study, specifically for 2020. This would have been particularly relevant for the Pyxis dataset, which was only available during this time. During this period of COVID-19, ED visits declined significantly.[178,179] It is possible that the results for 2020, especially for the Pyxis dataset, may represent a sample not representative of non-pandemic times. Given that people were being advised to stay home, it is possible that the study sample is biased to more severe cases, as participants presented to the ED despite a pandemic. A study conducted in the United States found that women were less likely to attend the ED during a state declaration of emergency due to COVID-19 than men, where visits by men decreased by 30 percent from 2019 while visits by women decreased by 40%.[180] If women were less likely than men to attend the ED for low back pain during the pandemic, it is possible that only women with the more severe LBP attended the ED, where there may have been men that presented with less severe cases. This would have been more evident in the Pyxis dataset. While these differences between men and women were not statistically significantly different, women did report a slightly higher pain intensity score and were slightly less likely to be assigned the non-urgent or less urgent CTAS score than men. Despite this, there was no difference in the odds of being administered an opioid in the ED. If the Pyxis data had been available for a period not influenced by the pandemic, it is possible that we may have observed that men had slightly higher odds of being administered an opioid as was observed in the odds of filling a prescription.

Strengths and weaknesses of the study

This study has several strengths. Most importantly, it addressed a gap in the evidence on the role of sex in a patient's interaction with the healthcare system. Specifically, pain management and substance use were, and continue to be, two areas that require more study. An examination of sex differences on opioid prescribing allowed further insight on how sex can

influence one's interactions with the healthcare system, which may result in consequences on overall health. LBP was an effective condition for this research to examine, given its high prevalence in the population, as well as its high rate of opioid prescription, specifically for LBP and emergency care.

Another strength was in the study's capture of several years of administrative data. For the Non-Pyxis dataset for Question 1,2, and 4, I had sufficient statistical power to detect smaller clinical and demographic differences, as well as smaller effect sizes. Given that there were a high number of presentations to the QEII ED, and this study contained one dataset with nearly four years of data, there was a large sample size. Although there was high missingness for a patient's pain score, there was extremely low missingness for all other variables, so most patients had complete data

The use of entanglement was another strength in this study. By using entanglement, I could acknowledge that gender and sex are likely interacting. As I discuss below in my implications section, men had greater odds of filling a prescription than women after attending the ED. Because I have used the concept of entanglement, I could discuss the societal and cultural factors that may lead to these results, such as gender roles and expectations of men and women. If I were to only consider sex, I would be unable to consider how the patients' behaviour, and healthcare providers' perceptions of patients, may play a role in the association with the different outcomes measured in this study. This could lead to potentially erroneous conclusions, or perhaps missing some of the nuances of the implications of my findings. For example, if I had examined sex alone, I may have concluded that men are filling more prescriptions due to biology, perhaps because men's physiology leads to higher pain or that women have a higher pain tolerance than men. But while gender was absent from the administrative data, that does not mean it was absent in the study. It was important, therefore, to use the concept of entanglement for considering the implications of my results.

There are potential limitations to this study. Some of the key limitations are related to the sample size of the Pyxis dataset for Question 3, which investigated opioid administration in the ED, limitations in the scope of health administrative data collection, and the definitions of certain variables. Below, I discuss these limitations.

First, the data for BD Pyxis™ MedStation™ ES was only available for a section of the study. This limits the sample size for the investigation of opioid administration in the ED. This means that smaller effect sizes could not be detected with this sample. If the effect size was smaller than what was detectable, this study may have concluded that there was no evidence to support sex differences in opioid administration in the ED, even if there was a true sex difference. This study, therefore, was susceptible to Type II error.

Given that the data comes from administrative health data, there are limitations in the variables provided. Some variables that were not included in this dataset may affect the outcome in this study; for example, no other health history was collected for the patients. Substance use disorders have been observed as predictors of more frequent presentations to the ED.[181] Another variable not included was comorbidities such as depression, anxiety or other chronic pain conditions, which have been also documented to increase likelihood of presentation.[181] Given that women are more likely to have chronic conditions, as well as certain mental illnesses such as anxiety and depression, this may have acted as a confounding variable when examining sex and ED presentation.[37,182] Race has previously also been noted to influence likelihood of receiving opioids in the ED, where black patients are less likely to receive pain management.[177,183,184] Physician sex has also been observed to influence the likelihood of the patient receiving an opioid prescription as well as the nature of the prescription.[68–70] Education and income have also been documented to influence likelihood of receiving opioids, where high socioeconomic status patients are more likely to receive opioids and less educated patients are also more likely to receive opioids.[177,185] While the CIMD score was available, CIMD only estimated level of deprivation, and did not provide information on the individual.

The second potential limitation was the disconnect between data on who had filled prescriptions after attending the ED, and confirmation of what prescriptions were written in the ED. This caused two potential issues. The first is that I was unable to be certain that the prescription filled was written by a healthcare provider in the ED and had to assume that this prescription came from the ED. I attempted to mitigate this by limiting the time of the prescription to one month within an ED visit, but it is still possible that I may have included opioid prescriptions that were written for reasons that were unrelated to the ED presentation.

The second potential issue is that I was unable to determine if there were sex differences in the patient's odds of being written a prescription in the ED. So while I could observe who has filled the prescriptions, I could not be certain of what proportion of the people who were written a prescription by a healthcare provider then proceeded to go to a pharmacy and fill these prescriptions.

The third potential area of limitation was in the definition of opioid-naïve. Opioid-naïve was defined as no opioid prescriptions in the previous six months. Although sensitivity analyses found no difference between opioid naïve patients and those who had received an opioid more than six months prior, it is possible that there may have been an undetected effect. It is also possible that the participant had been consuming non-prescription opioids. Given that men are more likely to receive opioids from an illegitimate source, this may have affected the results in the study.[8] Additionally, some patients may have received opioids in ambulatory care, which may have impacted the likelihood of receiving opioids in the ED. In another study that used this data, this was found to apply to only a small proportion of patients.[145]

The fourth limitation in this study was the lack of capacity to incorporate gender fully into the analysis. While gender roles may play a role in behaviours and cultural expectations of clients, this study does not have measures for gender, and cannot create a gender index with the information given. I was unable to capture any transgender or non-binary individuals, as health administrative data does not record a patient's gender identity. For this reason, there is a limitation on our ability to interpret any differences for individuals whose gender identity does not align with their sex.

Meaning of the study: possible mechanisms and implications for clinicians or policymakers

One of the most meaningful study results was that men had 39% higher odds of filling a prescription at a pharmacy after attending the ED than women. There are two potential explanations for this result. First, men and women were equally as likely to receive a prescription from a health care provider at the ED, but men were more likely to fill this prescription. There is some evidence to support this conclusion. A study examining gender differences in analgesic prescribing for LBP in Israel found little difference in the proportion of men and women that received opioids (23% vs 22% respectively).[186] Studies examining other health conditions have found that men and women can be similarly likely to be given a

prescription for opioids.[160,187] If men and women were receiving opioid prescriptions at a similar rate for comparable back pain, then this would mean that these differences were not the result of differential treatment from healthcare providers, but rather that the sex differences in prescriptions filled were the result of differences in behaviour. If this is to be attributed to sex, it could be due sex differences in the experience of LBP, but previous evidence has found that there was no evidence of sex differences in LBP overall prognosis, or even that women with LBP tend to have worse functional capacity than men with LBP.[126,128] I would hypothesize that gendered behaviour, however, would be more likely. One potential explanation could be related to cost. One study examining cost-related adherence to prescription drugs found that women in Canada were more likely to forgo a prescription due to its cost than men, possibly due to having a lower socioeconomic status.[188] Given that the women included in this study were statistically more likely to come from postal codes that had higher levels of economic dependency, it is possible some women in this study did not fill prescriptions due to a lack of funds. Another possible explanation could be in the gender roles as related to occupation, as traditionally masculine occupations with heavy lifting or driving commercially, or with high levels of mechanical low back pain load, can lead to LBP.[189,190] If men's LBP is related to their occupation, they may feel more pressure to address the pain for a faster recovery and return to work, especially if they are the primary source of income for their family. This could lead to more willingness to fill their opioid prescriptions. Additionally, previous studies have indicated that women may feel stigma around using opioids, especially if they are mothers, as this deviates from traditional gender expectations of being responsible and suitable carers, which may have resulted in some women being less likely to fill their prescriptions.[191,192] Given that men and women had no statistically significant differences in the nature of their prescriptions, such as dose or days' supply, this provides potential evidence that there was not differential treatment from healthcare providers.

A second explanation could be that men and women filled prescriptions at the same rate, but men were more likely to receive an opioid prescription when attending the ED. There has been some previous evidence that there is no difference between men and women in the likelihood of filling an opioid prescription after ED discharge.[193] One study that examined receipt of an opioid and filling of an opioid after attendance to the ED contained data that showed that men and women were similarly likely to fill a prescription, where 71% of men and

73% of women filled a prescription if they received one.[194] There is evidence to support that men are more likely to receive opioid prescriptions than women for other non-cancer pain conditions.[176] If this is the case, and men are more likely to receive an opioid prescription than women, this may be the result of differential treatment from healthcare providers. A potential explanation could be related to both sex and gender; men have been historically observed to have a higher pain tolerance, possibly due to biological sex factors such as hormonal fluctuations or gendered factors such as being less willing to report pain.[38,195,196] Given that men historically have had the reputation of being less likely to report pain and to have higher pain tolerances, it is possible that health care providers may have believed that if a man was attending the ED for pain, he was in more pain than he may have indicated in his pain score, and therefore, the health care provider may have been more willing to write a prescription for opioids.

Although not a primary or secondary outcome of this study, it was interesting to see that women had longer lengths of stay than men in both the Pyxis and Non-Pyxis database, waiting 46 and 30 minutes longer respectively on average. Indeed, although marginally significant, they also waited longer for opioid analgesia in the Pyxis dataset. Women have been observed to have longer wait times in other health studies as well.[197,198] Previous studies have also observed longer wait times for women to be treated or to see a doctor.[199,200]. Given that women were observed to have longer wait times, it is possible that there may be differential treatment, although women were also more likely to be assigned lower (and more urgent) CTAS scores which could have also resulted in a longer visit.

This may be an area where future research could be focused. A future study would be useful to investigate whether men and women are receiving prescriptions at the same rate, and men are more likely to fill them, or if there is differential treatment from health care providers. Given that there were similar average pain intensity scores for men and women, and women were statistically more likely to be assigned to more urgent CTAS scores, one would expect that they would be either similarly likely to fill a prescription or women would be more likely to fill a prescription. Without recording both the receipt of a prescription and the filling of the prescription, it is difficult to be certain about the implications of this finding.

For future research, another useful addition would be to include variables that were not available in this study. If gender and sex were both collected, transgendered and non-binary individuals could be controlled for in the analysis. To further investigate how sex and gender influence experiences in the health care system, the physician's gender could also be analyzed. Gender may impact the behaviour of the patient, but it also impacts how they are perceived by others. It would be interesting to further investigate how physician gender and patient gender interact. Previous evidence has found that physician sex may impact the care of patients, and given that it may have impacted patient care in this study, it would be good to incorporate in future research.[68,70] Other variables discussed above, such as race, education level or income, could also be incorporated to further investigate how a person's identity influences their experiences in the healthcare system.

While this study reported that men were more likely to fill a prescription, I had insufficient power to make conclusions on the administration of opioids in the ED. For future research, a study with more statistical power could further advance the knowledge of sex differences in treatment within the ED. Data limitations in this study make conclusions about this area tentative.

This study makes several important contributions to the field and can attend to multiple gaps in the literature. To date, there has been a lack of research on how sex may influence one's experiences navigating the healthcare system. From this study, we can examine how interacting with the healthcare system can lead to different treatment for men and women. This study showed that even with a similar condition, men were filling more prescriptions than women after attending the ED, despite attending with a similar pain intensity and a less urgent CTAS score.

In addition, this research adds to the body of evidence examining how sex may impact how people are able to access health care, which can help further research in identifying inherent biases and potential structural inequalities in the healthcare system. It may act as the foundation for later research, which can build on whether men are more likely to receive analgesia, and pain management, than women who present with a similar condition.

This study may help to inform how sex impacts opioid prescriptions in ED, which has the potential to impact opioid harms. Future research may focus on how sex differences in opioid prescriptions and uptake may lead to sex differences in opioid harms. Understanding sex differences in prescribing patterns and uptake of opioids may lead to a better understanding of sex differences in the risk of developing prolonged and problematic use of opioids. Given the ongoing opioid crisis in Canada, it is crucial to understand any potential harmful consequences of prescribing in emergency care, which has been noted to influence later opioid habits. This research may contribute to policy when creating sex-specific prescribing practices for opioids in emergency care, leading to improved outcomes in clinical practice. Understanding sex differences in prescribing patterns and uptake of opioids may lead to a better understanding of sex differences in the risk of developing prolonged and problematic use of opioids.

CHAPTER VI : CONCLUSION

In this study, men were found to be more likely than women to fill opioid prescriptions after attending the ED for LBP. The nature of the prescription, including the dose and prescription, did not differ. This may have implications that either men are far more likely to fill a prescription than women are, or perhaps that healthcare providers are more likely to write prescriptions for men. For future steps, it will be essential to determine whether these differences are due to differences in patient behaviour or differential treatment from the health care system, and consequently, whether these differences contribute to opioid harms across Canada.

STATEMENT

Data Declaration

Portions of the data used in this report were made available by Health Data Nova Scotia of Dalhousie University. Although this research analysis is based on data obtained from the Nova Scotia Department of Health and Wellness, the observations and opinions expressed are those of the authors and do not represent those of either Health Data Nova Scotia or the Department of Health and Wellness.

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APPENDICES

Appendix A :Types of opioids as recommended in Canadian guideline for safe and effective use of opioids for chronic noncancer pain

Opioid Name	**Hydromorphone**	**Codeine**	**Morphine**	**Tramadol**	**Oxycodone**
Common names / brands	Dilaudid	Tylenol 3	Kadian®, M-Eslon®, MS-Contin®, Statex®	Ralivia®, Tridural®, Zytram®	OxyNeo®, Percocet®
Classification Weak/strong[12,73]	Strong	Weak	Strong	Weak	Strong
Addictiveness [11,201]	Higher	Lower	Medium	Lowest	Higher
Potency Relative to Morphine [12,13]	4-5	0.10	1.0	0.10 – 0.15	1.5

Appendix B : ICD Code classification taken from the previous study that collected this data

Step 1: QEII ED chief complaint of 'back pain' or 'traumatic back/spine injury' **Step 2:** ICD code indicating non-specific low back pain or mechanical/radicular low back pain at discharge		
Non-specific low back pain (previous published studies)		
724.2	Recurrent low back pain	ICD9
724.5	Back pain	ICD9
724.5	Chronic back pain	ICD9
724.5	Pain - back nyd	ICD9
724.6	Pain sacrum	ICD9
724.79	Pain coccyx	ICD9
724.8	Facet joint syndrome	ICD9
729.1	Musculoskeletal pain	ICD9
729.82	Muscle cramp	ICD9
729.9	Other msk	ICD9
Non-specific low back pain (consensus process)		
715.9	Osteoarthritis	ICD9
719.45	Pain - hip nyd	ICD9
719.49	Polyarthralgia	ICD9
720.2	Sacroiliitis	ICD9
721.3	Sacroiliac arthritis	ICD9
724	Unspecified back disorder	ICD9
724.6	Disorders of sacrum (ankylosis or instability of lumbosacral/ sacroiliac joint)	ICD9
724.6	Pain buttock	ICD9
724.7	Disorders of coccyx	ICD9
729	Other disorders of soft tissues	ICD9
729.9	Other msk	ICD9
780.9	Chronic pain (misc)	ICD9
843.8	Strain gluteal muscle	ICD9
843.9	Sprain hip	ICD9
844.8	Strain hamstring	ICD9
846.9	Unspecified	ICD9
847	Sprain/strain back	ICD9
847.2	Lumbar	ICD9
847.3	Sacrum	ICD9
847.4	Coccyx	ICD9
847.9	Unspecified	ICD9
848	Other and ill-defined sprains and strains	ICD9
848.8	Other sprain/strain trunk	ICD9
848.9	Unspecified site	ICD9
959	Injury, other and unspecified	ICD9
959.1	Trunk injury	ICD9
959.19	Other site on trunk	ICD9
959.8	Other specified sites, including multiple	ICD9
998.1	Bruising (po)	ICD9

M13.9	Arthritis, unspecified	ICD10
M25.5	Joint pain	ICD10
M54.5	Back pain	ICD10
M62.6	Muscle strain	ICD10
M79.1	Myalgia	ICD10
M81.9	Osteoporosis	ICD10
S30.8	Superficial inj low back/pelvis	ICD10
S31.0	Ow lower back/pelvis, uncomplicated	ICD10
V71.8	Normal exam	ICD10
Z71.9	Counselling/medical advice	ICD10
Mechanical/radicular low back pain (previous published studies)		
721.3	Spondylosis lumbar spine	ICD9
721.9	Arthritis back	ICD9
721.9	Osteoarthritis back	ICD9
722.1	Herniated lumbar disc	ICD9
722.2	Herniated disc (neuro)	ICD9
722.6	Degenerative disc disease	ICD9
724.2	Mechanical low back pain	ICD9
724.2	Recurrent low back pain	ICD9
724.3	Sciatica	ICD9
724.8	Muscle spasm back	ICD9
724.9	Ankylosis spine	ICD9
729.1	Musculoskeletal pain	ICD9
729.1	Myalgia	ICD9
729.2	Neuralgia	ICD9
729.2	Radiculopathy	ICD9
729.2	Radiculopathy leg	ICD9
846	Lumbosacral strain	ICD9
846.1	Sprain sacroiliac jnt/ligament	ICD9
847.2	Low back strain	ICD9
Mechanical/radicular low back pain (consensus process)		
722	Intervertebral disc disorder	ICD9
722.52	Degenerative disc disease	ICD9
722.93	Other and unspecified disc disorder (lumbar)	ICD9
724.0	Spinal stenosis	ICD9
728.9	Weakness leg	ICD9
733.13	Compression fracture, not due to trauma	ICD9
782.0	Paresthesia, nyd	ICD9
846.0	Lumbosacral joint or ligament	ICD9
846.2	Sacrospinatus (ligament)	ICD9
846.3	Sacrotuberous (ligament)	ICD9
846.8	Other specified sites of sacroiliac region	ICD9
M48.0	Spinal stenosis	ICD10
R20.8	Paresthesias - numbness	ICD10

Appendix C : Variables included in this study

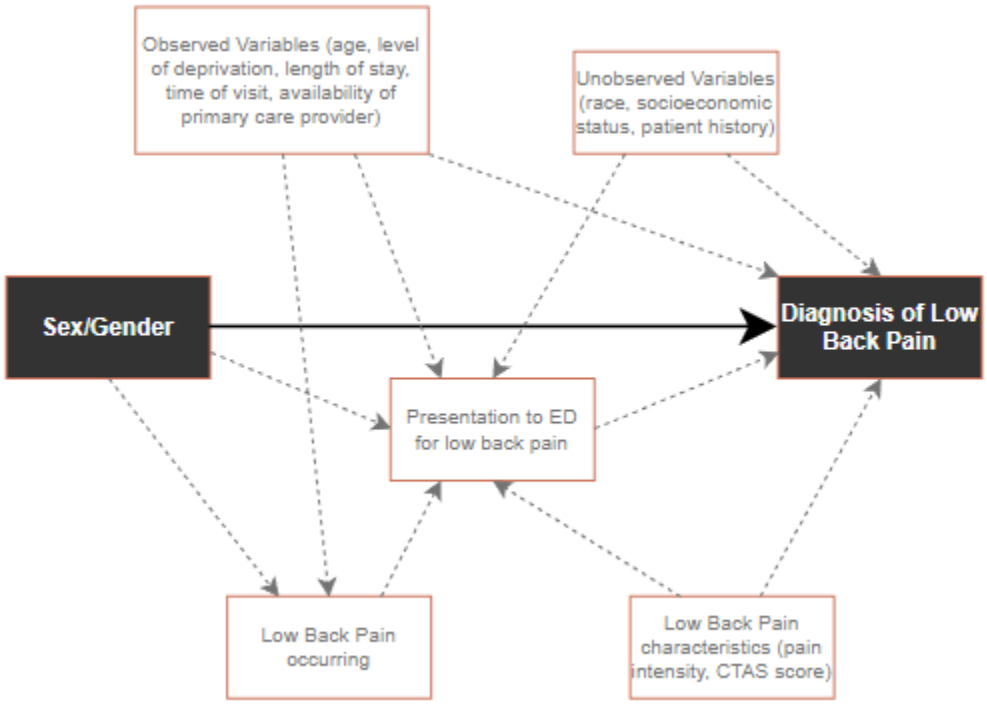
Source	Variable	Measurement Given	Variable Type
Visit characteristics			
EDIS	Time of presentation	Working or nonworking hours (8:00-17:00)	Binary
EDIS	Time of presentation	Weekend or Weekday	Binary
EDIS	Pain intensity score	Rating of 0-10 where 0 is no pain and 10 is severe pain	Ordinal
EDIS	Length of stay	Hours from triage to diagnosis code	Continuous
EDIS	Low back pain diagnosis	Non-specific or Radicular / Mechanical	Binary
EDIS	Canadian Triage and Acuity Scale Score	1 (Resuscitation) (%) 2 (Emergent) (%) 3 (Urgent) (%) 4 (Less Urgent) (%) 5 (Non-Urgent) (%)	Categorical
Patient Characteristics			
EDIS	Age	Measured in years from birth to visit	Continuous
EDIS	Sex	Male or Female	Binary
EDIS	Availability of primary care provider	Either has one or does not have	Binary
CIMD derived from Statistics Canada method	Economic Dependency	Rated as 1-5 where 1 is the least deprived and 5 is the most	Ordinal
CIMD derived from Statistics Canada method	Situational Vulnerability	Rated as 1-5 where 1 is the least deprived and 5 is the most	Ordinal
CIMD derived from Statistics Canada method	Ethnocultural Composition	Rated as 1-5 where 1 is the least deprived and 5 is the most	Ordinal
CIMD derived from Statistics Canada method	Residential Instability	Rated as 1-5 where 1 is the least deprived and 5 is the most	Ordinal
ED Dispensed Opioid Characteristics			
Pyxis	Opioid Type	Hydromorphone, Morphine, Codeine or Tramadol	Categorical
Pyxis	Dose	Measured in MME	Continuous
Pyxis	Delivery Method	Oral or Parenteral	Binary
Pyxis	Time to Opioid	Hours	Continuous
Pharmacy Dispensed Opioid Characteristics			

DIS	Opioid Type	Hydromorphone, Morphine, Codeine or Tramadol	Ordinal
DIS	Dose	Measured as average MME/ Day	Continuous
DIS	Days' Supply	Measured in days	Continuous

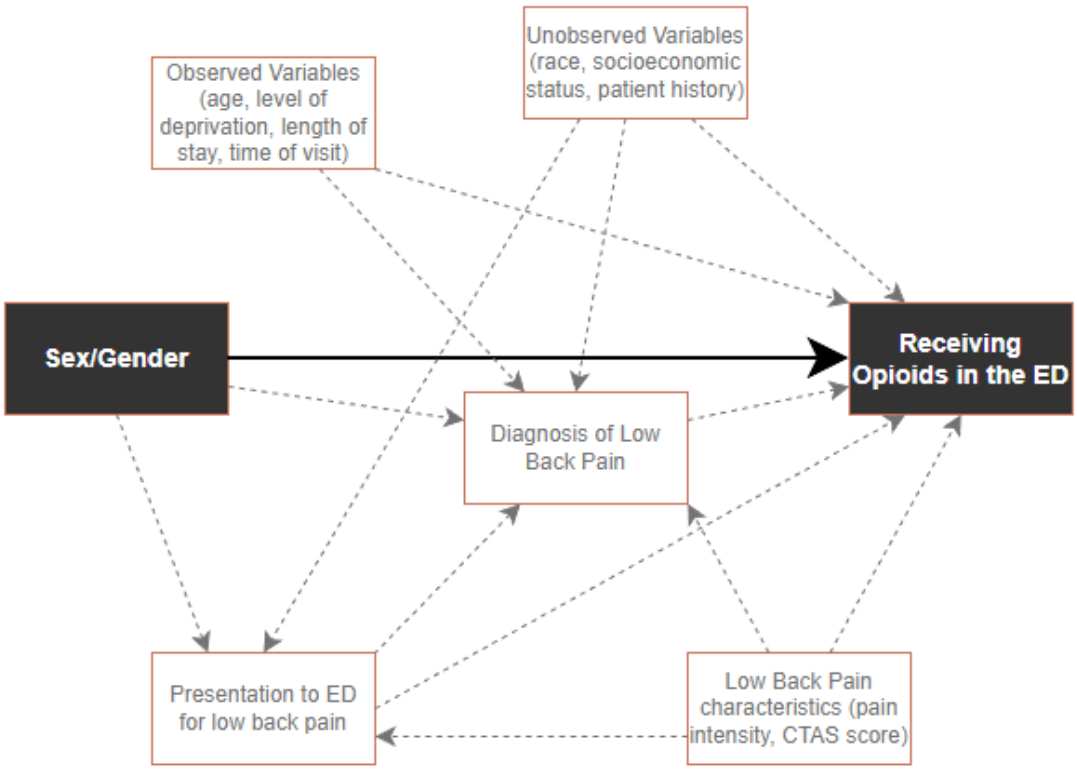
Apprendix D : Missingness in the both the full dataset and Pyxis dataset for QEII ED LBP patients attending from 2017-2020

Variable	Number Missing (%) Total	Number Missing (%) Pyxis
Pain Score	2568 (64%)	434 (79.2 %)
Level of Deprivation: Residential Instability (5 is highest instability)	31 (0.8%)	<5
Level of Deprivation: Economic Dependency (5 is highest deprivation)	31 (0.8%)	<5
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	31 (0.8%)	<5
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	31 (0.8%)	<5

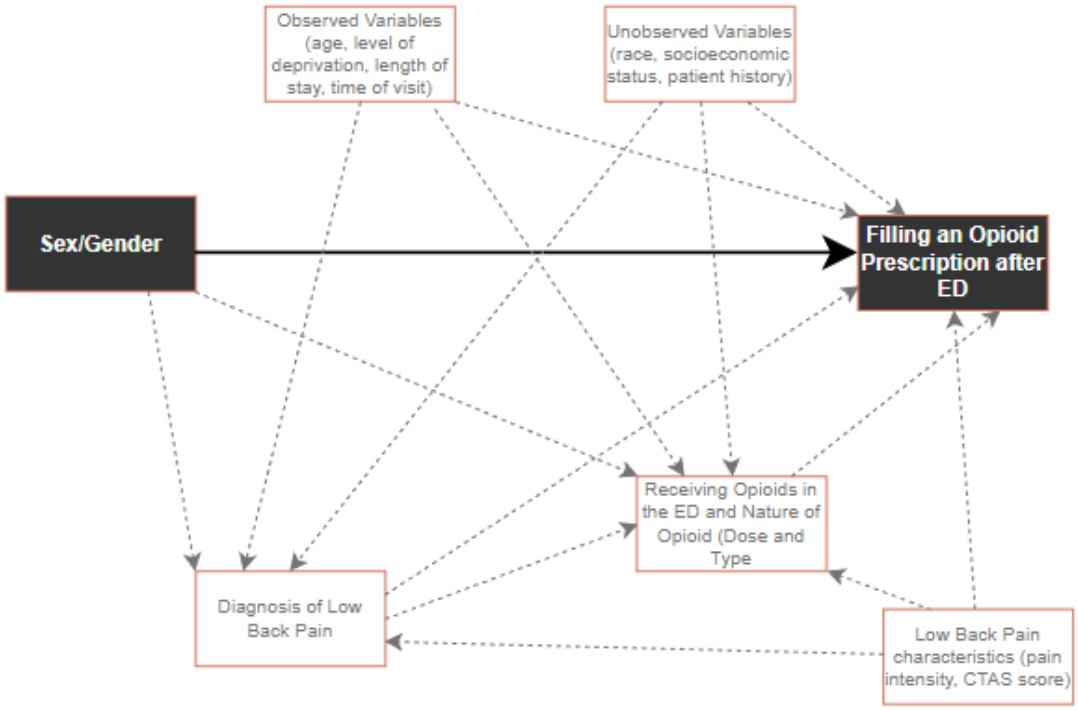
Appendix E : DAG showing previously conceptualized relationships between sex and diagnosis of low back pain, and other variables



Appendix F : DAG showing previously conceptualized relationships between sex and receiving an opioid in the ED, and other variables



Appendix G : DAG showing previously conceptualized relationships between sex and filling an opioid after attending the ED, and other variables



Appendix H : Descriptive statistics (N, %, SD) for demographic and clinical differences between people who received a diagnosis of mechanical pain vs non-mechanical pain

Predictor		Total	Mechanical	Non-Mechanical	Significance
Presentation	N (%)	N = 4 027	1 373 (34.1%)	2 651 (65.9%)	
Sex	Women (%)	2 048 (50.9%)	640 (46.6%)	1 408 (53.1%)	P <0.001
Age	Mean years (SD)	47.5 (18.2)	45.5 (17.1)	48.6 (18.7)	P<0.001
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	527 (13.0%) 492(12.2%) 326(8.1%) 513(12.7%) 2138(53.1%)	187 (13.6%) 162 (11.8%) 110 (8.0%) 179 (13.0%) 724 (52.7%)	340 (12.8%) 330 (12.5%) 215 (8.1%) 333 (12.6%) 1413 (53.3%)	P=0.91
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1845 (45.8%) 879 (21.8%) 623 (15.5%) 457 (11.4%) 192 (4.8%)	626 (45.6%) 297 (21.6%) 219 (16.0%) 161 (11.7%) 59 (4.3%)	1218 (45.9%) 580 (21.9%) 404 (15.2%) 296 (11.2%) 133 (5.0%)	P=0.81
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	82 (2.0%) 149 (3.7%) 331 (8.2%) 782 (19.4%) 2652 (65.9%)	29 (2.1%) 53 (3.9%) 116 (8.5%) 284 (20.7%) 880 (64.1%)	53 (2.0%) 96 (3.6%) 215 (8.1%) 497 (18.8%) 1770 (66.8%)	P=0.55
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1664 (41.3%) 877 (21.8%) 590 (14.7%) 394 (9.8%) 471 (11.7%)	548 (39.9%) 303 (22.1%) 209 (15.2%) 126 (9.2%) 176 (12.8%)	1116 (42.1%) 573 (21.6%) 380 (14.3%) 267 (10.1%) 295 (11.1%)	P=0.34
Availability of Primary Care Provider	No (%)	565 (14.0%)	220 (16.0%)	344 (13.0)	P=0.008
Opioid Naive	Not prescribed opioids in past 6 months (%)	3811 (94.6%)	1327 (96.7%)	2484 (93.6%)	P<0.001
		Clinical Characteristics			
Presentation Time of Day	Presentation during working hours of 9:00-17:00 (%)	2189 (54.4%)	756 (55.1%)	1431 (54.0%)	P=0.51
Presentation on day of week	Presentation on weekday (%)	2949 (73.2%)	350 (25.5%)	728 (27.4%)	P=0.19
Pain intensity score	Mean (SD)	4.5 (3.4)	4.6 (3.3)	4.4 (3.4)	P=0.17
Length of Stay	Mean number of hours (SD)	3.62 (3.05)	3.20 (2.37)	3.85 (3.32)	P<0.001
Canadian Triage and Acuity Scale	1 (Resuscitation) (%) 2 (Emergent) (%) 3 (Urgent) (%) 4 (Less Urgent) (%) 5 (Non-Urgent) (%)	0 (0%) 568 (14.1%) 2514 (62.4%) 905 (22.5%) 40 (1.0%)	0 (0%) 177 (12.9%) 840 (61.2%) 341 (24.8%) 15 (1.1%)	0 (0%) 391 (14.7%) 1674 (63.1%) 564 (21.3%) 25 (0.9%)	P=0.04
Filled DIS Drug	Yes (%)	710 (17.6%)	208 (15.2%)	502 (18.9%)	P=0.003
Opioid Type	Hydromorphone Morphine Codeine Tramadol	414 (58.3%) 129 (18.2%) 118 (16.6%) 47 (6.6%)	122 (58.7%) 24 (11.5%) 41 (19.7%) 20 (9.6%)	292 (58.2%) 105 (20.9%) 77 (15.3%) 27 (5.4%)	P=0.01
Opioid Type	Strong (%)	547 (76.8%)	148 (71.2%)	399 (79.2%)	P=0.02
Dose	Measured as average MME/ Day (SD)	43.2 (28.6)	43.3 (28.2)	42.8 (29.7)	P=0.83
Days' Supply	Measured in days Mean (SD)	5.7 (6.4)	5.4 (6.2)	5.8 (6.5)	P=0.50

*denotes an Odds Ratio for which the p value is less than 0.05.** for 0.01 and ***for 0.001 Odds ratios are derived from the Logistic Regression. 95% Confidence intervals are expressed as [lower band,upper band]. The reference category is denoted as 1.00 (ref) for each categorical variable.

Appendix I : Descriptive statistics (N, %, SD) for demographic and clinical differences between those who received an opioid in ED and those who did not who attended the QEII ED for LBP in the Pyxis Set

Predictor		Total	No Opioid	Opioid	Significance
Presentation	N	N = 548	420 (76.6%)	128 (23.4%)	
Sex	Women (%)	279 (50.9%)	206 (49.1%)	73 (57.0%)	P=0.11
Age	Mean years (SD)	48.1 (18.0)	47.7 (17.9)	49.6 (18.5)	P =0.32
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	56 (10.2%) 68 (12.4%) 43 (7.9%) 76 (13.9%) 303 (55.3%)	39 (9.3%) 52 (12.4%) 35 (8.3%) 58 (13.8%) 234 (55.7%)	17 (13.3%) 16 (12.5%) 8 (6.3%) 18 (14.1%) 69 (53.9%)	P = 0.71
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	255 (46.5%) 128 (23.4%) 79 (14.4%) 56 (10.2%) 28 (5.1%)	205 (48.8%) 89 (21.2%) 60 (14.3%) 43 (10.3%) 21 (5.0%)	50 (39.1%) 39 (30.5%) 19 (14.8%) 13 (10.2%) 7 (5.5%)	P =0.22
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 or 2(%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	34 (6.2%) 38 (6.9%) 101 (18.4%) 373 (68.1%)	26 (6.2%) 31 (7.4%) 76 (18.1%) 285 (67.9%)	8 (6.3%) 7 (5.5%) 25 (19.5%) 88 (68.8%)	P = 0.93
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	240 (43.8%) 118 (21.5%) 81 (14.8%) 46 (8.4%) 61 (11.1%)	173 (41.2%) 86 (20.5%) 70 (16.7%) 38 (9.1%) 51 (12.1%)	67 (52.3%) 32 (25.0%) 11 (8.6%) 8 (6.3%) 10 (7.8%)	P = 0.03
Availability of Primary Care Provider	No (%)	77 (14.1%)	69 (16.4%)	8 (6.3%)	P = 0.003
Opioid Naïve	Not Opioid Naïve (%)	31 (5.7%)	17 (4.1 %)	14 (10.9%)	P=0.003
Clinical Characteristics					
Presentation Time of Day	Presentation during working hours of 9:00-17:00 (%)	301 (54.9%)	223 (53.1%)	78 (60.9%)	P = 0.12
Presentation on day of week	Presentation on weekday (%)	398 (72.6%)	303 (72.1%)	95 (74.2%)	P = 0.64
Pain intensity score	Mean (SD)	4.6 (3.1)	4.5 (3.3)	5.1 (2.6)	P = 0.30
Length of Stay	Mean number of hours (SD)	4.00 (2.82)	3.75 (2.44)	4.82 (3.70)	P <0.001
Canadian Triage and Acuity Scale	1 (Resuscitation) (%) 2 (Emergent) (%) 3 (Urgent) (%) 4 or 5 (Less Urgent and Non-Urgent) (%)	0 55 (10.0%) 386 (70.4%) 107 (19.5%)	- 33 (7.9%) 297 (70.7%) 90 (21.4%)	- 22 (17.2%) 89 (69.5%) 17 (13.3%)	P = 0.005
Mechanical	Yes (%)	181 (33.0%)	141 (33.6%)	40 (31.3%)	P = 0.60
Filled DIS Drug	Yes (%)	94 (17.2%)	35 (8.3%)	59 (46.1%)	P < 0.001

* Data displayed as Mean (SD) represents the mean plus or minus the standard deviation. Data displayed as Number(percentage) denotes the number in the sample and the percentage within that group. Groups under 5 were not reported. Chi square tests conducted to investigate difference between the categorical variables. A proportion test was done for binary variables. A t-test was conducted for continuous variables. The data was checked to ensure the distribution was approximately normal, the sample size sufficient for the t-test, z-test, and the samples were assumed to be independently collected.

Appendix J : Descriptive statistics (N, %, SD) for demographic and clinical differences between those who filled a prescription after attending the QEII ED for LBP

Predictor		Total	No Prescription	Prescription	P-value
Presentation	N (%)	N = 4 027	N =3 317 (81.5%)	N = 710 (17.4%)	
Sex	Women (%)	N = 2 048	1 710 (51.6%)	338 (47.6%)	P = 0.06
Age	Mean years (SD)	47.5 (18.2)	46.0 (17.9)	54.5 (18.1)	P <0.001
Level of Deprivation: Residential Instability (5 is highest instability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	527 (13.0%) 492(12.2%) 326(8.1%) 513(12.7%) 2138(53.1%)	406 (12.2%) 406 (12.2%) 280 (8.4%) 413 (12.5%) 1786 (53.8%)	121 (17.0%) 86 (12.1%) 46 (6.5%) 100 (14.1%) 352 (49.6%)	P =0.03
Level of Deprivation: Economic Dependency (5 is highest deprivation)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1845 (45.8%) 879 (21.8%) 623 (15.5%) 457 (11.4%) 192 (4.8%)	1517 (45.7%) 724 (21.8%) 512 (15.4%) 386 (11.6%) 152 (4.6%)	328 (46.2%) 155 (21.8%) 111 (15.6%) 71 (10.0%) 40 (5.6%)	P=0.59
Level of Deprivation: Ethnocultural Composition (5 is highest diversity)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	82 (2.0%) 149 (3.7%) 331 (8.2%) 782 (19.4%) 2652 (65.9%)	73 (2.2%) 127 (3.8%) 272 (8.2%) 656 (19.8%) 2163 (65.2%)	9 (1.3%) 22 (3.1%) 59 (8.3%) 126 (17.8%) 489 (68.9%)	P =0.21
Level of Deprivation: Situational Vulnerability (5 is highest vulnerability)	Quintile 1 (%) Quintile 2 (%) Quintile 3 (%) Quintile 4 (%) Quintile 5 (%)	1664 (41.3%) 877 (21.8%) 590 (14.7%) 394 (9.8%) 471 (11.7%)	1328 (40.4%) 717 (21.6%) 500 (15.1%) 338 (10.2%) 408 (12.3%)	336 (47.3%) 160 (22.5%) 90 (12.7%) 56 (7.9%) 63 (8.9%)	P = 0.001
Availability of Primary Care Provider	No (%)	565 (14.0%)	522 (15.7%)	43 (6.1%)	P < 0.001
Presentation Time of Day	Presentation during working hours of 9:00-17:00 (%)	2189 (54.4%)	1776 (46.4%)	413 (58.2 %)	P = 0.02
Presentation on day of week	Presentation on weekday (%)	2949 (73.2%)	881 (26.6%)	197 (27.7%)	P = 0.51
Pain intensity score	Mean (SD)	4.5 (3.4)	4.5 (3.4)	4.2 (3.6)	P =0.17
Length of Stay	Mean number of hours (SD)	3.62 (3.05)	3.40 (2.65)	4.67 (4.33)	P < 0.001
Canadian Triage and Acuity Scale	1 (Resuscitation) (%) 2 (Emergent) (%) 3 (Urgent) (%) 4 or 5 (Less Urgent orNon-Urgent) (%)	0 (0%) 568 (14.1%) 2514 (62.4%) 945 (23.5%)	- 403 (12.2%) 2064 (62.2%) 850 (25.6%)	- 165 (23.2%) 450 (63.4%) 95 (13.4%)	P < 0.001
Mechanical Pain Diagnosis	Yes (%)	1372 (34.1%)	1164 (35.1%)	208 (29.3%)	P=002
Opioid Naive	Not prescribed opioids in past 6 months (%)	3811 (94.6%)	3269 (98.6%)	542 (76.3%)	P <0.001

* Data displayed as Mean (SD) represents the mean plus or minus the standard deviation. Data displayed as Number(percentage) denotes the number in the sample and the percentage within that group. Groups under 5 were not reported. Chi square tests conducted to investigate difference between the categorical variables. A proportion test was done for binary variables. A t-test was conducted for continuous variables. The data was checked to ensure the distribution was approximately normal, the sample size sufficient for the t-test, z-test, and the samples was assumed to be independently collected.

Appendix K : Knowledge Translation

The findings from this study will be submitted to a peer reviewed journal in the fields of epidemiology and health services research, and to a journal focusing on substance use or pain medicine. I will present my findings at the Canadian Biostatistics and Epidemiology Conference in June.

Appendix L : Funding

This study was funded by the Canadian Institute of Health Research graduate scholarship.