Evaluation of a Patient-Centred, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy: A Preliminary Report

by

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A Thesis submitted to the Faculty of Graduate Studies of
The University of Manitoba
in partial fulfilment of the requirements of the degree of

MASTER OF SCIENCE

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Abstract

Background: Opioid tapering is highlighted as a priority action to combat the Opioid Crisis in many Canadian practice guidelines, but there is sparse evidence on clinically safe and effective tapering, with less still on practical implementation strategies. Directed by these gaps, an interdisciplinary team with chronic pain expertise collaboratively developed "Evaluation of a Patient-Centered, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy". With clinical utility at its core, outcomes and tools are developed to be meaningful to practice.

Methods: Half of study participants are randomized to participate in a one-day, interprofessional patient education workshop (PEW), which includes pain and opioid education and a novel application of Acceptance and Commitment Therapy (ACT). The workshop's impact is measured through pre- and post-questionnaires collecting data on opioid knowledge, tapering readiness, and feedback. Following the workshop, all participants begin a 12-month multidisciplinary opioid tapering program (MTP). Study pharmacists base each individualized program on starting dose, clinical picture, and participant goals, incorporating consistent and frequent follow-up and support. MTP impact is measured at weekly phone follow-ups and quarterly in-person visits. Opioid dose, pain, and health and wellbeing questionnaire scores are measured. This review summarizes results from the first 10 PEW participants and 16 patients to reach the MTP's 3-month mark.

Results:

MTP: Sixteen participants had a 21.9% opioid reduction by month 3 of the 12-month program ($p=0.007$), without changes to other scores. In fact, pain and pain disability show trend reductions.

PEW: PEW participants ($n=10$) demonstrated a 1.3-point improvement on the 6-point opioid knowledge quiz pre- and post-workshop ($p=0.031$). Tapering readiness improved among 40% of participants post-workshop, 30% remained "very ready" pre and post, 20% did not improve, and 10% decreased in readiness. 100% reported they'd use PEW teachings to manage pain, 78% felt the workshop provided value, and 50% were satisfied with the format.

Conclusion: The opioid crisis shows no sign of slowing down and patient-focused, evidence-based strategies are urgently needed. This preliminary review demonstrates the strength of the overall project's design, including interdisciplinary teams (pharmacists and psychologists) and close patient follow-up, as integral contributors in mitigating the opioid crisis.

Acknowledgements

My advisor, Dr. Dana Turcotte, and the rest of my advisory committee: Dr. Brigitte Sabourin (psychology) and Dr. Christine Leong (pharmacy), who are exemplary clinicians and researchers.

All the members of our study team: Dr. Turcotte and Dr. Sabourin, plus Dr. Gregg Tkachuk (psychologist), and Dr. Ryan Amadeo (anesthesiologist), as well as Brenden Dufault (biostatistician), Caroline Kehrer (research assistant), and Jenna Villarba (BSc pharmacy student). We are appreciative of the Internal Research Grant from the Department of Clinical Health Psychology at the University of Manitoba, which has provided the funding for this project.

The primary care teams at each of the four study sites: physicians, nurse practitioners, nurses, allied health, managers, admin, and of course the patients themselves, who collaborated (and continue to collaborate) with me on this project, especially my team at ACCESS Winnipeg West. As well, my PharmD students who worked with study participants and all the other students and residents that have been involved.

The Winnipeg Regional Health Authority's Pharmacy Program and the Canadian Society of Hospital Pharmacists: Manitoba Branch also provided support for my involvement in this trial and in the master's program.

Dedication

To all the powerful teams of women working in STEM research, including my advisory committee

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List of Abbreviations

2SLGBTQQIA+: 2 spirit, lesbian, gay, bisexual, trans, queer, questioning, intersex, asexual, +
ACT: Acceptance and Commitment Therapy
ADL: Activities of daily living
AFPC: Association of Faculties of Pharmacy of Canada
ARE: ACCESS River East
AWW: ACCESS Winnipeg West
BREB: Biomedical Research and Ethics Board
CBT: Cognitive behavioural therapy
CDC: Center for Disease Prevention and Control
CNCP: Chronic Non-Cancer Pain
CPAQ-8: Chronic Pain Acceptance Questionnaire 8
CPERC: Canadian Pharmacy Education and Research Conference
CPVI: Chronic Pain Values Inventory
CPA: Canadian psychology association
CPhA: Canadian Pharmaceutical Association
CPJ: Canadian Pharmacist's Journal
DSM-V: Diagnostic and Statistical Manual of Mental Disorders – 5th version
GAD-7: Generalized Anxiety Disorder 7 Item
HCP: health care provider or health care practitioner
HSC: Health Sciences Centre
LTOT: Long term opioid therapy
MD: Medical Doctor
MED: Morphine Equivalent Dose
mg: milligrams
MTP: Multidisciplinary Tapering Program
NNT: Number needed to treat
NP: Nurse Practitioner
NRS: Numeric Rating Scale
OIH: Opioid induced hyperalgesia
ORT: Opioid Risk Tool
OTC: over the counter
OUD: Opioid use disorder
PDI: Pain Disability Index
PEW: Patient Education Workshop
PHQ9: Patient Health Questionnaire 9
PROMIS Global-10: Patient-Reported Outcomes Measurement Information System Global-10
PTSD: Post-traumatic stress disorder
RCT: Randomized Controlled Trial
REDCap: Research Electronic Data Capture
SI: Suicidal ideation
SOAPP-R: Screener and Opioid Assessment for Patients with Pain-Revised
STEM: Science, Technology, Engineering, Medicine
TENS: transcutaneous electrical nerve stimulation
WHO: World Health Organization
WRHA: Winnipeg Regional Health Authority

Thesis Preface

The worldwide Opioid Crisis has reached an all-time high. After rates of overdose and death had been steadily worsening for years, it began to reach a plateau, and even slowly trend downwards in 2018-19, but the COVID-19 pandemic has since caused it to take a sharp upturn[1–5]. This crisis has and continues to negatively impact patients, communities, healthcare workers, and health systems profoundly[2].

Long-term opioid therapy (LTOT) in chronic non-cancer pain (CNCP) is associated with considerable risks that have been a factor in the above overdose and death rates but were not widely known until the late 2000s and into the 2010s[6]. This was partially due to a narrative influenced by some drug manufacturers, downplaying the addiction potential of specific prescription opioids[6]. Since that time, evidence and awareness has emerged that prescription opioid use is not benign and comes with risks such as misuse, dependence, and disordered use, increasing the risk of overdose and death[6,7]. In response, health organizations in Canada and around the world have recommendations to change their approach towards opioids to reduce risks in both prescription and illicit users[8–10].

In patients with CNCP that are already established on LTOT, it becomes a challenge to not only reduce their opioid intake (and hopefully risks), but also to adequately manage chronic pain. Currently, there are few studies that demonstrate methodology to successfully accomplish this in clinical practice[11,12].

In response, the randomized, prospective, ongoing clinical trial entitled "Evaluation of a Patient-Centred, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy," the overall project, was designed. This master's thesis is a preliminary review of the overall project that examines and analyzes preliminary data as well as participant feedback, which will then inform the project on optimization strategies to improve success and maximize clinical impact.

Chapter 1: Introduction and Background

1.1 Chronic Pain

Today, eight million Canadians are living with chronic pain[13,14], a chronic condition affecting physical and mental health that impacts a person's ability to work, play, and participate in successful relationships, often reducing overall quality of life[13]. Health Canada defines chronic pain as an "unpleasant sensory and (or) emotional experience... last[ing] longer than 3 months," adding that "chronic pain can occur without a known cause, after an injury has healed, [or] after a condition has been treated"[14]. As recognized by Health Canada and the World Health Organization (WHO), chronic pain is its own disease, not simply a symptom of another condition[14] - chronic pain is when pain persists past the typical timeframe for tissue healing[13].

Chronic pain is often further classified into chronic non-cancer pain (CNCP), to separate it from long lasting pain associated with a malignant source. Neuropathic pain, rheumatoid arthritis, low back pain, osteoarthritis, and fibromyalgia are a few examples of types of CNCP, but can be a range of many pain conditions, often coexisting[15,16].

In addition to experiencing pain, patients with CNCP are faced with challenges to their physical, emotional, and social health[13,14]. Chronic pain has been shown to have direct or indirect impacts on physical health measures; mental, emotional, and spiritual wellbeing; relationships and social interactions; sense of self; financial and job security; and ability to perform activities of daily living[13,14]. Canadian data suggests chronic pain has disproportionate impacts for people who live in poverty, have mental health conditions (especially those with a history of trauma), work in trades, are Indigenous or members of other racialized communities, identify as a woman or 2SLGBTQQIA+, have a disability, or are a person with a disability.

1.1.1 Stigma

Pain is often described as invisible because it is self-reported and subjective[14]. Those living with chronic pain often report that people they encounter in their lives do not believe or understand the impact that pain has on their life, or even that it exists. Along with stigma related to the validity of chronic pain, those using opioids to help manage their symptoms may experience further stigmatization[17]. A 2022 study

found that people who used higher doses of opioids, had a mental health condition, or were unemployed experienced greater stigma than those who didn't[17].

Stigma can come from a many different sources, including family, friends, employers, towards themselves, and most impactfully from health care providers (HCPs)[17]. This can lead to feelings of isolation and frustration, and may contribute to a reluctance to access or seek out health services, treatment, or support[14]. The presence of stigma related to chronic pain is associated with higher levels of depression, disability, and lower social support[17]. Particularly when health care providers and the health care system is the source of this stigma, it can increase patient health risks by increasing barriers to care[18]. Patients in pain, regardless of the cause or the manner in which it is being managed, deserve easy-to-access, stigma-free, treatment and support for their healthcare needs.

1.1.2 Treatments

Treatments for chronic pain work best when tailored to an individual patients' needs and goals, most often using a combination of different modalities[14,19,20]. Pharmacotherapy is rarely substantially effective for CNCP when used on its own, with relatively high numbers needed to treat (NNTs) for prescription medications across various CNCP conditions. Though the NNT ranges significantly depending on drug or drug class, an average NNT of near six for meaningful reductions in pain is commonly reported[19,21].

Some recommended treatments to combine or add to medications (over the counter and prescription) include psychological interventions (cognitive behavioural therapy or CBT, acceptance and commitment therapy or ACT, individual or group psychotherapy, and mindfulness-based interventions), physical and rehabilitation interventions (exercise, movement, physical activity, like yoga and Tai Chi), medical devices or interventional pain procedures (transcutaneous electrical nerve stimulation or TENS, nerve blocks, and steroid injections), practitioner administered or manual therapy (massage therapy, physical therapies), and self-management strategies (meditation, support groups, education sessions, relaxation / breathing exercises, and life skills / self-efficacy programs)[14,19]. While different treatments or interventions may have varied theoretical and clinical efficacy in different pain subtypes based on the etiology or pathophysiology of certain pain conditions, applying specific indication-based treatments to real world patients is difficult, as mixed pain types is common[22–24]. In fact, many chronic pain trials assessing treatments and/or opioid tapering do not separate pain subtypes when evaluating the intervention[25–32].

1.1.3 Treatment goals

Treatment goals for any of the above strategies look different for each patient, but often include improving physical function, mental health, cognitive health, sleep quality, and social function, instead of, or in addition to, reducing pain[14,33]. Two terms often used in evaluating chronic pain treatment are pain self-efficacy, the confidence a patient has in their ability to effectively function in their life while experiencing pain[34] and pain interference, a measure of how much pain interferes in one's everyday life – including to physical, cognitive, emotional, and social activities, sleep, and overall quality or enjoyment of life[33,35]. When the focus is redirected from pain reductions to these more functional goals, the patient is better able to concentrate on something more meaningful, as opposed to chasing a potentially unreachable pain reduction target. Remarkably, when focus is taken off pain, as in some psychological therapies, pain often improves, especially if other outcomes or targets are reached[36].

1.2 Opioid Medications

Opioids are a class of medications used by prescription to manage pain in many different settings, scenarios, and medical conditions[7]. The most common opioids used by prescription worldwide include codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, tramadol, and buprenorphine but may also come in different forms if from illicit sources[37].

Generally, opioids are recommended to be used at low doses, for short term, acute pain management (i.e., less than 12 weeks and therefore not CNCP)[38]. This indication is supported by evidence, including in randomized controlled trials (RCTs)[16]. In contrast, the evidence of benefit for opioid use in chronic pain conditions, is lacking[19,39,40]. Studies evaluating patients using opioids for longer periods of time have shown minimal change in the pain outcomes mentioned above, including quality of life[15,16].

Even when used short term and as prescribed, opioids are associated with frequently occurring negative side effects including drowsiness, headache, constipation, nausea, and vomiting, in addition to a myriad of more, less common side effects[41]. Prolonged opioid use can also be associated with cognitive dysfunction, liver damage, infertility, immune system changes, in addition to tolerance and dependence, which can result in withdrawal symptoms and even worsening pain, known as opioid-induced hyperalgesia[7,42,43]. Most concerningly, using opioids for long periods has been shown to increase the risk of serious adverse events, including overdose, addiction, and death [2,7,16,39].

Though lacking efficacy evidence, opioids remain a commonplace treatment for CNCP, increasing the risk of the long-term and serious side effects[7,39]. However, there are some individuals with CNCP for whom opioids remain among the best options for their pain management[14,19]. These patients are difficult to elucidate or define and would be considered amongst those that have tried and failed other treatment options. Considering this, Health Canada's current statement on opioid use in CNCP is that it is "best determined through shared decision-making between the patient and their health provider based on the unique needs of the individual"[14].

1.2.1 Complications of chronic opioid use

Among the most significant opioid-induced harms are the powerful and detrimental psychological and physical effects of dependence and disordered use[7]. Prolonged or chronic use of opioids is associated with an increase in these risks, whether they are from prescription or illicit sources and even if they are taken as prescribed and monitored appropriately.

Prolonged use, chronic use, or long-term opioid therapy (LTOT) are synonymously defined as opioid use for longer than would be required to treat acute or subacute pain, which is defined as approximately three months[7,14]. While many patients with CNCP on LTOT today were started on opioids prior to recommendations discouraging chronic use, there has been some more recent research into what risk factors predict short-term opioid users to continue them long term. These include using higher opioid doses[44], longer durations (e.g., one or more refills after the first opioid prescription)[44,45], and longer acting opioids[44], as well as non-opioid factors like younger age, lower household income, concurrent chronic diseases, and chronic use of other medications including benzodiazepines[46].

The most dangerous opioid outcomes more commonly occur in those with disordered use and when these drugs are misused and/or poorly managed[7,47], but can occur in any setting. Toxicity related to opioids results in a reduced respiratory rate, among many other adverse effects. This respiratory depression is the mechanism of death in a fatal opioid overdose[7]. The risk of mortality related to opioid overdose is higher in those using higher daily doses of opioid: patients taking more than 90-100mg morphine equivalent dose (MED) per day are at significantly higher risk of a fatal overdose than those on lower doses[48]. Fatalities related to opioid toxicity are also more common in those who are also using other drugs, in particular, benzodiazepines, muscle relaxants, and first-generation antihistamines, like diphenhydramine or Benadryl[7].

1.2.1.1 Opioid tolerance, dependence, and withdrawal

"All opioids that produce analgesia also can cause tolerance, addiction and withdrawal"[49]. Tolerance—a clinical phenomenon in which larger doses are needed to provide the same pain control as lower doses used previously—frequently occurs with prolonged opioid use[40,49] . The prevalence of tolerance is not clearly elucidated due, in part, to challenges with identifying and quantifying it. In clinical practice, it is often evidenced by higher and higher opioid doses being required by an individual over time, with some estimates citing an increase of ten times the original opioid dose as a common scenario[49]. Although the exact mechanism of tolerance is unclear, the development of tolerance to opioids occurs more frequently with consistent (as opposed to intermittent) use, higher doses, and extended duration[49].

Tolerance often happens concurrently with physical dependence: when physiological symptoms occur in the absence of the medication, whether that's in between doses or if doses are missed or lowered[19,40,49,50]. Like tolerance, it presents with increasing frequency the longer the duration of opioid use[49,51]. These uncomfortable symptoms are called withdrawal and can be widespread, causing physical, psychological, or other symptoms. Some common withdrawal symptoms include fever, chills, body or muscle aches, tachycardia, hypertension, diaphoresis, gastrointestinal symptoms (nausea, cramping, diarrhea), sleep disruptions (insomnia, fatigue, restlessness), mental health changes (irritability, anxiety or panic, depressed mood), and increased pain[49,51]. Physical withdrawal symptoms usually present within 24 hours, peak in the first three days, and last for one to two weeks, though this timeline will vary based on the opioid and formulation. Other symptoms, particularly psychological or emotional symptoms, can persist for months[49,51]. When compared to withdrawal from other harmful substances like alcohol or benzodiazepines, opioid withdrawal has often been touted as less imminently dangerous but can also be life threatening in some circumstances[52]. Presentation or severity of withdrawal can theoretically be different for different opioids, but clinically, patient-specific factors and opioid dose, duration, and pharmacokinetics are more important factors[49].

1.2.1.2 Opioid induced hyperalgesia

Opioid induced hyperalgesia (OIH) is a clinical complication that can also occur with prolonged opioid use[7,42,53]. Hyperalgesia is a state of *increased* pain, or increased sensitivity to stimuli, due to changes in the way the brain processes sensory input, with or without inappropriate sensitization at nociceptive nerve endings[54]. OIH then, is this hyperalgesic state that is caused paradoxically by exposure to chronic opioid therapy. Rather than improving pain, those on higher doses of LTOT may experience a worsening of pain,

often correlated with dose[53]. It may present as worsening of the original chronic pain syndrome, or as a different and diffuse, allodynia-type pain[53]. While there have been studies in different populations to estimate prevalence[55], without a clear diagnostic process, the rate of OIH in patients with chronic pain is not clear[53]. However, it is likely an important factor in the development of decreasing opioid efficacy that is seen in patients with prolonged use[42,53]. The treatment or reversal of OIH involves tapering off or reducing the dose of opioid[42,53]. Some clinicians find that hyperalgesia may not improve until a certain dose reduction has been reached[1].

1.2.1.3 Opioid use disorder

In contrast to these physical conditions, disordered use (previously termed as addiction or abuse) is a psychological dependence wherein cravings, psychological distress, or other feelings occur in the absence of the opioid after prolonged or chronic use[56]. Opioid use disorder (OUD) – previously referred to as opioid abuse, addiction, or dependence[57] – is summarized by the Center for Disease Prevention and Control (CDC) as a "problematic pattern of opioid use leading to clinically significant impairment or distress,"[57] and involves features of both physical and psychological dependence[47,56,58]. The DSM-V describes OUD as including uncontrollable opioid cravings (even when resulting in social or professional consequences), increased tolerance, and worsened withdrawal [56,58].

While anyone can develop OUD, there are many factors that increase patient's likelihood. A few of the risk factors associated with opioid use include details such as easy access to opioids (prescription or illicit); high opioid doses, especially for prolonged duration; and significant tolerance, especially if coupled with increasing doses and/or withdrawal symptoms[47]. These can all increase the likelihood that a patient will develop OUD[47,58]. There are also predisposing characteristics that make developing OUD more likely in certain patients who take opioids[58]. These include personal or family history of any substance use disorder; history of depression, post-traumatic stress disorder (PTSD), or anxiety; and childhood trauma or abuse, including pre-adolescent sexual abuse[47,58].

The reported prevalence of OUD varies significantly, but the literature reports consistently cite its occurrence as a significant percentage of individuals taking opioids. The National Institute of Drug Abuse reported in 2020 that 8-12% of people who received a prescription opioid develop OUD, while 21-29% misuse them[59]. A review of twenty-five reports describing the prevalence of OUD in patients with CNCP cited an OUD rate as high as 50%[43].

It is this opioid misuse, combined with complex physical dependence and disordered use mechanisms, that are linked to increased rates of drug overdoses and death[7].

1.3 The Opioid Crisis

The "Opioid Crisis" refers to the unprecedented increase in prescription and illicit opioid use and misuse beginning in the 1990s, that has since led to staggering rates of overdoses and death. In addition to mortality, significant additional consequences of the Opioid Crisis including medical, social, psychological, and economic, have had profound and detrimental impacts on society[59]. It has also been referred to as the "opioid epidemic", although as a worldwide issue, "pandemic" would be a more appropriate term. The United States has topped the charts with the highest per capita prescription opioid consumption rate for many years according to the International Narcotics Control Board[37,60]. Its most recent report on 2020 use statistics (that was released in 2022) has Canada ranked eighth, a significant fall from the second and third top spots in the late 2010s, despite Canada's consumption rates continuing to rise, indicative of an overall global increase in opioid use[37].

Health Canada reports that since they began tracking in 2016, over 30,000 Canadians have died due to opioids[2]. While concerted and multifaceted efforts did lead to a shift towards reduced consumption and death rates in 2018 and 2019, all gains were promptly reversed - and worsened - by the COVID-19 pandemic[2]. The Government of Canada describes multiple contributing factors: an increase in toxic drug supply, associated with border closures and restrictions and a decrease in overall mental health, related to pandemic stress, isolation, uncertainty, and other anxieties, which was coupled with reduced access to mental health services[2]. During the first two years of the pandemic (April 2020-March 2022) there was a reported 91% increase in opioid-related deaths and a 24% increase in opioid-related hospitalizations[2]. The first quarter of 2022 (January – March) saw approximately 21 deaths per day[2]. These unsettling statistics led the Government of Canada to declare the Opioid Crisis a public health emergency, calling for "a response that is comprehensive, collaborative, compassionate and evidence-based"[7].

Although multifactorial in its causes, the Opioid Crisis was triggered, in part, by a surge in opioid prescribing and subsequent prescription opioid use and misuse worldwide. A combination of the unknown - or underemphasized - risk of addiction and significant concern for untreated and undertreated chronic pain led to increased opioid prescribing between the 1980s to 2000s[61,62]. Over twenty years later, we now know that use of these prescription opioids has not been as benign as once touted. A timeline of

prescription opioids is below in **Figure 1**. This fact combined with the substantial opioid consumption in Canada, has made reducing overall opioid use a top national priority. Strategies to reduce opioid consumption are multifactorial, though many are focused on areas such as safer opioid prescribing, multidisciplinary pain management strategies, and opioid tapering[42,62]. And as such, professional organizations around the world have detailed new recommendations and guidelines regarding opioid prescribing in CNCP and managing patients on LTOT[8–10].

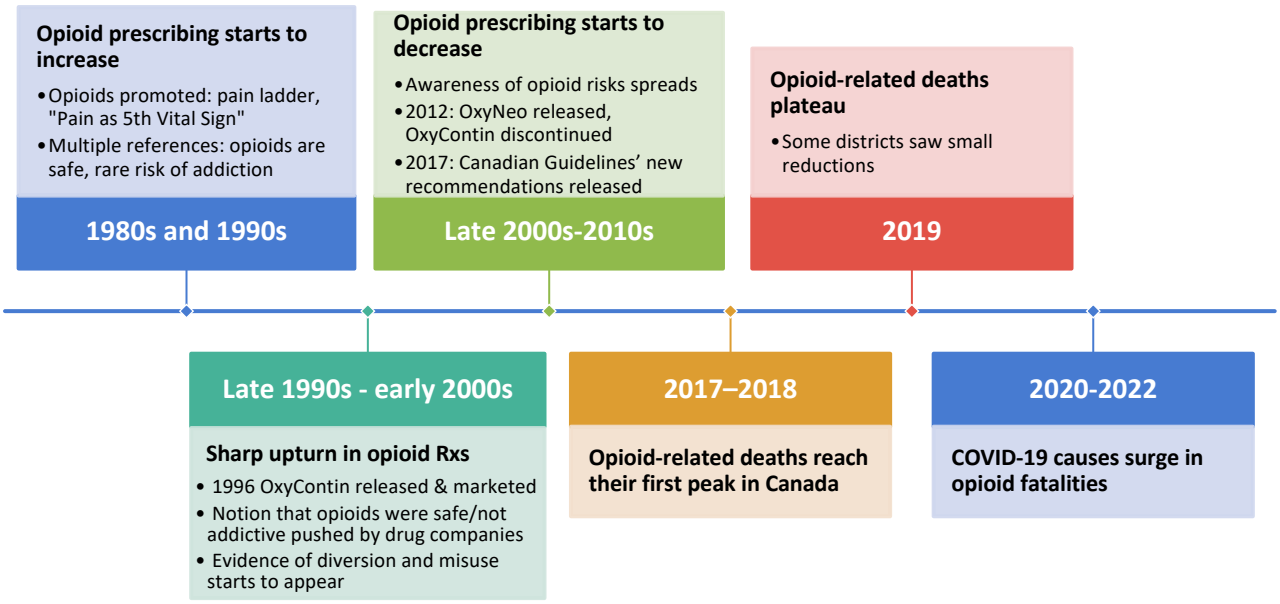

Figure 1: Timeline of prescription opioids: Important occurrences between 1980 and today that have affected opioid prescribing, use, and negative outcomes [2,6,10,61,63].

1.4 Mitigating the Opioid Crisis

In 2017, following the first peak of opioid-related deaths in Canada (see **Figure 1**), a large comprehensive team comprised of clinicians and researchers from multiple areas of applicable expertise, as well as patients with lived experience, collaboratively developed updated Canadian opioid prescribing guidelines, entitled "The 2017 Canadian Guidelines for Opioids for Chronic Non-Cancer Pain"[10]. These evidence-based guidelines introduced standards of care and recommendations on pain management that emphasized patient-centeredness and safer prescribing practices, including the reduction, discontinuation, and judicious use of opioids[10]. Similarly, the Royal College of Physicians and Surgeons of Canada released their Policy and Position Statement, entitled "Safer Opioids for All"[8], which highlighted safer, evidence-based opioid prescribing practice recommendations[8]. At the provincial level, the College of Physicians and Surgeons of Manitoba created their own opioid Standard of Practice in 2019 with explicit

recommendations on opioid prescribing and management, including specific recommendations for tapering[9].

1.4.1 Canadian guidelines for mitigating the Opioid Crisis

These guidelines have prescribed changes to clinical management of opioids that have made opioid prescribing much more limited than in the past, although clinical judgement and shared decision making remain a cornerstone of prescribing for chronic pain[14]. These changes align with principles of opioid stewardship, which can be described as "coordinated interventions designed to improve, monitor, and evaluate the use of opioids in order to support and protect human health"[64]. Within these guidelines, there are considerable restrictions on the allowable indications for opioids, as well as maximum doses and durations[9,10]. Whether starting new or continuing ongoing therapy in patients with CNCP, providers are now required to document that a thorough history has been taken, other treatment strategies haven been optimized, and that adequate screening for risks has been completed[9,10]. At higher doses and/or longer durations, trialing a taper is also included as a requirement[9,10]. If patients struggle with tapering, using a multidisciplinary team is recommended[9,10]. Many health organizations have recognized this need for the revitalization of patient care to educate, empower, and encourage individuals towards judicious and knowledgeable opioid use[10,12].

Multidisciplinary teams are explicitly recommended by these guidelines in the clinical management of inadequately controlled pain in those with CNCP, whether or not they are taking opioids[20]. Healthcare teams that provide interdisciplinary care are associated with increased healthcare capacity and improved care[65]. This comes at a time when good chronic pain care is needed more than ever; while these practice changes to opioid prescribing and tapering are likely contributing to overall improvements in patient care, it cannot go unrecognized that patients on LTOT often have untreated or undertreated chronic pain[66]. Poorly managed pain can significantly impact quality of life and lead to the risk of harms, including substance use disorders[14], and potentially impacting the success of a recommended opioid tapering program[11,12]. As healthcare professionals are being shifted from relying so heavily on opioids for CNCP, there is an urgent need not only for support with tapering opioids, but also additional tools and strategies to manage patients' pain safely and effectively [66].

In March of 2019, Health Canada formed the "Canadian Pain Task Force" to provide that support and released three reports in subsequent years, providing recommendations on chronic pain management[14].

These reports included gaps in care, best pain management practices, and ways to improve Canada's strategies, which highlighted multidisciplinary healthcare teams as a prioritized strategy going forward[14,65].

1.4.2 Multidisciplinary care

Multi- or interdisciplinary,[†] multimodal, and patient-centered pain management approaches are effective and essential practice strategies for managing complex chronic pain, including situations of refractory pain, polypharmacy, and those on LTOT[12,20]. Multidisciplinary teams utilize a collaborative approach amongst health professionals, patients, and families to develop holistic and individualized chronic pain treatment and tapering strategies[12,20]. They often include physicians (primary care or specialists), nurses, pharmacists, physical therapists, occupational therapists, psychiatrists, and/or psychologists[10]. Multidisciplinary care is multimodal and can look different in different settings. It can be a formal program or an informal collaboration between colleagues[10]. Different practitioners bring different knowledge bases and strategies; members of multidisciplinary teams often emphasize non-pharmacological approaches and target diverse outcomes[20], rather than focusing solely on prescribing a medication to reduce pain, for example. Given the inherent complexity of chronic pain management - which is often confounded by comorbidities such as mood, sleep and substance use disorders[14,65] - a multimodal approach is, unsurprisingly, the preferred approach to clinical management of chronic pain [12,20]. In fact, preliminary research has demonstrated that patients undergoing opioid tapers within interdisciplinary teams have higher overall success rates than expected with standard care [12,67].

As previously noted, many disciplines and practitioners can be involved in a beneficial multidisciplinary approach, notably those skilled in non-pharmacological interventions, which play a vital role in the effective management of CNCP [20]. For example, a trained healthcare worker like a nurse, counsellor, or mental health support worker could lead a meditation or mindfulness session, which have been shown to be effective in chronic pain[68]. An occupational therapist could optimize a patient's home or work environment to support function and quality of life[69,70]. Physiotherapists also provide many evidence-based strategies, including techniques such as manual therapy and transcutaneous electrical

[†] "Multidisciplinary" and "interdisciplinary" are often used interchangeably in the literature, and will be used similarly here for consistency; however, the terms do have subtle differences. While both describe multiple disciplines working on a team towards a common goal, these disciplines work within their respective scopes and often independently on multidisciplinary teams whereas interdisciplinary teams work collaboratively with roles often overlapping[165].

nerve stimulation (TENS)[71]. Further to these modalities, physiotherapists – among other disciplines – bring additional focus onto exercise training for chronic pain, which is important as there is substantial evidence to support a reduction in pain severity and improved physical function and quality of life with regular exercise and physical activity[71]. Despite knowing the impact these team members can have on chronic pain outcomes, research is limited in defining the best combination of clinicians and their roles on interdisciplinary teams, though pharmacists and mental health specialists are often included[12].

1.4.2.1 Pharmacists

Pharmacists have frequently been identified as the most accessible and trusted healthcare providers in Canada[72,73] and have deservedly been highlighted as important and influential team members to combat the Opioid Crisis[12,74]. The Canadian Pharmacists Association (CPhA) created the "Canadian Pharmacists Association Action Plan to Address Prescription Opioid Abuse" in 2016 that outlines the pharmacist's role in addressing the Opioid Crisis and preventing opioid misuse, abuse, and other harms[74], including a plan to "develop and promote interprofessional education programs on opioid abuse and misuse, including appropriate prescribing"[74].

There is considerable evidence demonstrating pharmacists' impact on improving chronic pain management and opioid tapering initiatives and outcomes[75–77]. Pharmacists are involved in many aspects of this care, including pain and opioid risk assessments, medication reviews, deprescribing and opioid tapering, optimizing drug and non-drug pain treatments, monitoring treatment interventions, managing adverse effects, patient and HCP education, and facilitating transitions of care[30,75–82]. When pharmacists are integrated into care teams, evidence shows that opioid doses and overall pain is reduced, among other positive outcomes[31,82–84]. For example, a retrospective study in Saskatoon, Saskatchewan found that patients living with CNCP who were referred to a pharmacist-led clinic had, on average, a 17% reduction in opioid dose with this pharmacist intervention (despite only 43% of pharmacists' recommendations getting implemented)[31]. Whereas when patients did not have pharmacist involvement – and changes were made independently by a physician – opioid dose reductions were negligible[31]. Similarly, the Opioid Safety Initiative in the USA had pharmacists involved in education, pain management, risk reduction, and addiction management and had in a 45% decrease in opioid prescriptions between 2013 and 2018[81,82].

As pharmacists are very clearly integral and impactful members of chronic pain and opioid stewardship teams, their inclusion in the design and implementation of this project was essential and

invaluable. Their comprehensive role in this project includes a significant portion of the prescribed patient education, as well as coordination and facilitation of the opioid tapering program.

1.4.2.2 Psychologists

Chronic pain and mental health symptoms frequently coexist and interact; and in some cases, this interaction contributes to opioid misuse and abuse[20,85]. In 2017, in collaboration with nine other healthcare organizations, the Canadian Psychological Association (CPA) created the Coalition for Safe and Effective Pain Management, which describes a role renewal for opioid use in chronic pain[86]. The CPA "call[s] for better access to interdisciplinary pain management services as a treatment alternative to opioids"[87]. Clinical psychologists offer their unique knowledge and skills to a variety of pain conditions to improve patient care[85].

Psychological therapies for chronic pain can include mindfulness-based interventions, in which patients are encouraged to experience the present moment (including thoughts, emotions, and physical sensations) in an open, non-defensive manner without trying to change their internal experiences[50]; cognitive behavioural therapy (CBT), that through cognitive restructuring, identifies and modifies problematic thought processes and behaviours to achieve specific goals[50]; and acceptance and commitment therapy (ACT), a "third wave" form of CBT wherein patients develop more flexible strategies for accepting or opening up to difficult internal experiences (i.e., thoughts, emotions, and physical sensations) and committing to values-based behaviour change[50]. These interventions all have substantial evidence for effective CNCP treatment[88].

Because of psychologists' broad and significant scope in chronic pain that is complementary to pharmacists working in the field, they also play important roles in this project. They were heavily involved in the design of the program, its materials, and evaluation methods in addition to leading the patient education and providing group therapy with their implementation of ACT.

1.4.3 Opioid prescribing requirements

Not only are multidisciplinary teams able to provide improved care and support patients with CNCP on LTOT, but they can also improve adherence to the prescribing guidelines, including opioid tapering[10]. "The Canadian Guideline for Opioids for Chronic Non-Cancer Pain" released in 2017 made

recommendations on when and how to prescribe opioids. The guideline splits clinical recommendations into two categories: initiating new opioid therapy and patients on existing opioid therapy[10].

In these prescribing guidelines, providers are required to ensure that opioid prescribing to those with CNCP who are not currently using opioids (often referred to as 'opioid naïve') is restricted to a small number of patients who have exhausted other options and who are low risk for opioid harms. These individuals need to have persistent and significant pain despite being optimized on non-pharmacological treatments and on non-opioid medications. They also need to be screened for current or past substance use disorders and active psychiatric conditions, as this may preclude them from opioid initiation, or they may be required to have better control over pre-existing conditions prior to being considered for opioid therapy. In these opioid naïve patients, prescribers are recommended to keep doses at less than 90mg of MED per day, and preferably under 50mg[10].

In patients already established on opioids for CNCP, there are slightly different recommendations that follow the same values previously noted. Firstly, for patients with either persistent pain or bothersome side effects on opioids, prescribers are recommended to rotate their opioid in hopes of improvements. Secondly, for patients on 90mg MED per day or more, an opioid taper is recommended - to lowest effective dose or completely off. For patients who are unable or struggling to taper their opioids, a multidisciplinary program is recommended. If a multidisciplinary program is not available or accessible to the patient, HCPs are recommended to collaborate with other healthcare disciplines, specifically recommending pharmacists and psychologists (among others), for support and/or involvement[10].

Manitoba released a Standard of Practice, requiring their members to adhere to their recommendations, which are more detailed, specific, and restrictive than the Canadian guideline[9]. Regardless of indication, dose, or duration, all opioid prescriptions in Manitoba must be written for no more than three months and cannot be dispensed more than one month at a time. The Standard is then broken down into three groups, from least to most restrictive: acute or post-operative pain management, CNCP: continuing opioid therapy, and CNCP: new opioid therapy. All groups require a comprehensive history, prior optimization on non-pharmacological treatments and non-opioid medications (which may include considering multidisciplinary teams), screening for risk of substance use disorder, misuse, and diversion (including urine screens), lowest effective dose prescribed with slow titration occurring only with regular follow up, and patient education on the risks. Dosing and duration vary for different

indications. Acute or post-surgical pain is recommended in most cases to continue for no longer than 7 days and if more than 30 days are required to get a second opinion. For patients already on LTOT for CNCP, opioid tapers are recommended if the daily dose is MED of 90mg or higher and if this is not possible, a second opinion is required. For patients with CNCP who are prescribed an opioid for the first time, the recommended dose limit is a MED of 50mg per day or lower. For any patient with CNCP on opioids longer than 90 days, a multidisciplinary team's involvement is recommended. If LTOT is required beyond that, prescribers must document clinical improvements in pain, function, and QOL that outweigh the risks of opioid therapy in that patient[9].

1.4.4 Opioid tapering

Although tapering is highlighted as a priority action in these documents, especially for those on high doses (MED of 90mg per day or higher) and for longer durations, there is sparse evidence on clinically safe and effective tapering approaches for LTOT for patients with CNCP[11,12,30,89,90]. The evidence that is available illustrates that opioid tapering can be a complicated and difficult intervention[12,27,90].

The Canadian Guideline does not give any detailed recommendations on tapering beyond utilizing a multidisciplinary team when patients have difficulty with tapering[10]. Without clearer evidence-based practice directions, clinicians that have been directed to reduce opioids in their practice are left unprepared and overwhelmed[30,77,91]. The resulting care approaches can be discouraging and anxiety-provoking for patients, who demonstrate high psychological distress and low self-efficacy[92].

1.4.4.1 Limitations of current evidence

Studies examining opioid tapering or reductions often have significant limitations such as small sample sizes, high drop-out rates, biases, and inconclusive or non-significant results[11,25,93,94]. In Kurita et al.'s randomized controlled trial, for example, over half of the participants dropped out before progressing to Phase 2, when structured tapering actually began[27]. Results similar to these are not in isolation and even occur when other supportive interventions are done in conjunction with tapering[32,95]. Data analysis with limitations like high attrition rates can be particularly challenging and difficult to interpret, and findings drawn from these studies need to be considered.

1.4.4.2 Findings from limited evidence

Despite the limited evidence, there are enough reviews and analyses of the available data that predict that most patients in opioid tapering programs do well. In fact, most patients tapering opioids experience

improved functional and quality of life outcomes without increasing (and often improving) pain[11,27,90,93,96], and even potential improvements in depression, anxiety, sleep, withdrawal symptoms, and opioid misuse scores[27,96]. Some proposed rationale for these improvements include, firstly, that adverse effects due to opioids are reduced or alleviated, resulting in possible improvements in symptoms such as fatigue and cognition deficits, and sexual dysfunction; secondly, reduction of opioid-induced hyperalgesia and/or between dose withdrawal pain may occur, resulting in pain reduction overall; and lastly, participants are often provided with alternative coping mechanisms for pain, augmenting further the benefits observed from opioid reduction[11,90,93].

As previously noted, data from tapering trials are mostly non-significant and, therefore, it can be difficult to draw clinically meaningful conclusions from them. However, we can use their strengths and limitations to reveal some of the potential facilitating factors and challenges that have arisen for patients and clinicians during opioid tapers, discontinuations, or even small reductions. For example, fears of experiencing withdrawal or worsening pain are often reported as barriers to patient buy-in to opioid tapering[97]; however, as stated above, most individuals are likely to be able taper opioid doses without significant pain increases[11,25,28]. Clinicians cite lack of trust as a barrier to tapering [91] and patients that have been successful often credit that to a trusting relationship with their HCP[97]. In addition, it has been demonstrated that when in a supportive environment with regular follow up, patients undergoing tapering regimes are more likely to have successful tapers and have larger improvements in pain self-efficacy and interference[11,12,25]. Considering and mitigating noted barriers to opioid tapering study success, while incorporating observed facilitating factors whenever possible at the study design phase is integral to improving the quality of opioid tapering evidence.

1.4.4.3 Filling the gap in evidence

With the above lessons learned, new trials and reviews can, and should, be designed with these successes and limitations in mind. Increasing and improving the available research on this subject will guide clinical practice. Higher quality research in this field is essential to improving clinical outcomes, with researchers and clinicians calling for studies focused on addressing the common limitations and challenges associated with tapering[91,94]. The mandated practice changes in the Canadian and Manitoba guidelines, while prudent, have left clinicians scrambling for evidence-based recommendations on how to best approach opioid tapers[91]. The importance lies too, with not only filling these evidence gaps, but filling them with clinically meaningful and applicable research. This is paramount to improving the lives of

patients with CNCP. This must incorporate strategies to improve study recruitment and retention, systematically evaluating differences between various tapering regimens, more active pain management strategies (like physical activity, psychological treatment, social connection, and nutrition), expanding knowledge on the potential harms of opioid tapering (including overdoses and suicide) and how to mitigate them, and evaluating the clinical feasibility of protocols. These are all essential in ensuring that research being done is actually meaningful and valuable to patient care[11,12,93,94,98–100].

1.5 Introduction to the Project

A multidisciplinary team of clinician researchers in Winnipeg, Manitoba identified the need to improve opioid tapering approaches in their pain management practices. The team - comprised of a clinical pharmacist/primary investigator (DT), anesthesiologist (RA), and two clinical psychologists (BS & GT) - conducted a literature review to inform the development of a new project, which has since been titled "Evaluation of a Patient-Centred, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy." The team utilized data from this search to identify common pitfalls and facilitators to opioid tapering research protocols, which were considered in the design of this project. This ongoing project (from here on, called the "overall project") is a randomized, prospective, clinical trial that implements up-to-date, evidence-based opioid reduction strategies, including considerable patient involvement and consistent and frequent clinical support strategies, combined with a structured opioid and pain education program with the aim of mitigating anticipated challenges during the opioid tapering process. As all members of the research team are also actively involved in direct patient care, it was integral that the project be as clinically relevant and applicable to practice as possible.

As the overall project is a large trial with a projected sample size of 131 participants, evaluating the implementation logistics, feasibility, and patient acceptance of numerous aspects of the project in a preliminary report was warranted. Further, it was decided that a preliminary report would be valuable in reporting initial data related to primary study outcomes such as opioid consumption and pain ratings, among other measures. The data compilation for and composition of this report has been the responsibility of study coordinator, KE (clinical pharmacist, master's student) and is presented here as a thesis to satisfy degree requirements. With this information, it is the aim of the thesis to inform the overall project with feedback from initial data, allowing for opportunities to optimize study procedures at the outset of the project. This master's thesis will from here on be referred to as the "master's project."

The overall project is comprised of two primary interventions. The first is a one-day Patient Education Workshop (PEW), to which 50% of participants are randomly assigned, with a focus on opioid and pain education and psychological interventions for chronic pain. The second intervention, to which all participants are assigned, is a one-year Multidisciplinary Tapering Program (MTP) aimed at providing optimal pain management and support for individuals undergoing opioid tapering. Both arms are evaluated in the overall and master's projects, to varying degrees. This thesis reports on the first ten participants who have completed the PEW and sixteen participants who have completed the first three months of the MTP.

1.5.1 Patient Education Workshop (PEW)

The overall project starts with randomized participants attending a one-day, group educational workshop. This multi-disciplinary workshop is delivered through multiple modalities, incorporating a mix of interactive, didactic, and activity-based learning focused on engagement and participant involvement. Due to the COVID-19 pandemic, the workshop design was pivoted to a virtual platform. In order to ensure transferability of evidence-based strategies employed in the PEW, a pilot virtual PEW was designed and took place in October of 2020. Based on survey responses from participants and clinician feedback from both the pilot and experience in their clinical practices, it was deemed a success and the PEW proceeded as a virtual workshop.

1.5.1.1 Chronic pain and opioid education

The workshop includes pharmacist-led education on chronic pain and opioids, which has been shown to be associated with reductions in opioid consumption[80]. This provides foundational knowledge on chronic pain, non-opioid (including non-pharmacological) chronic pain management strategies; opioid facts, myths, misinformation, and stigma; treatment goals and goal setting; and the basics of tapering and withdrawal. It is delivered in multiple modalities including visuals, group discussions, video, and interaction, in addition to didactic delivery. The pharmacist-led section comprises approximately 1 hour of the 6-hour workshop, with the remaining time focused on psychologist-led Acceptance and Commitment Therapy (ACT).

1.5.1.2 Acceptance and Commitment Therapy (ACT)

Acceptance and Commitment Therapy (ACT) is a relatively novel psychological intervention for chronic pain, especially when compared to CBT[101]. However, it has been used successfully for decades in a wide variety of medical conditions, both psychiatric and physical[102–104]. In contrast to traditional interventions

that focus on controlling pain and other symptoms, ACT aims to facilitate the development of psychological flexibility (i.e., the ability to notice interfering thoughts, emotions, and bodily sensations without acting on them in the service of living in accordance with chosen values)[101,105]. ACT integrates practices of acceptance and mindfulness with commitment and behaviour-change strategies to increase the psychological flexibility of individuals[103–105]. With this, it aims to shift patient goals from eliminating or avoiding unpleasant feelings (i.e., pain) towards more valued behaviors (even if in presence of pain)[105]. Valued behaviours are highly individualized, as they reflect what gives meaning to one's life. As an example, one individual may prioritize spending time being active in nature and observing wildlife, whereas another may consider regular meaningful discussions with certain family members to be among their governing principles. While assisting patients in identifying these valued behaviours that are personal motivators for them, as well as the barriers they may have from experiencing them, it helps patients reshape pain perception, accept internal experiences, and renew goals and values towards living a life that aligns with these valued behaviours[101,103,104].

During ACT for chronic pain, patients are led through reflections on their unique pain experience to analyze the relationships between their thoughts, behaviours, and feelings surrounding their chronic pain history[106] in order to identify past attempts to control or avoid pain and come to their own conclusions about how successful these have been over time. Attachment to an experientially avoidant change agenda can then be undermined, and we can propagate willingness to abandon unworkable attempts to control or avoid pain. Through this process, patients can consider alternative ways of responding to pain (and related emotional distress) to live more in accordance with their chosen values (i.e., psychological flexibility)[101,103,104].

The overall goal is to reconsider one’s perception of pain: allowing for the mindful acceptance of the internal experiences while setting values-based goals and committing to engage in valued behaviours, and shifting focus away from symptomatic pain relief, especially with pharmacological strategies[36,105,106]. **Figure 2** below depicts the ACT “hexaflex” – a commonly used infographic that portrays the six core principles of ACT, including aspects of psychological flexibility.

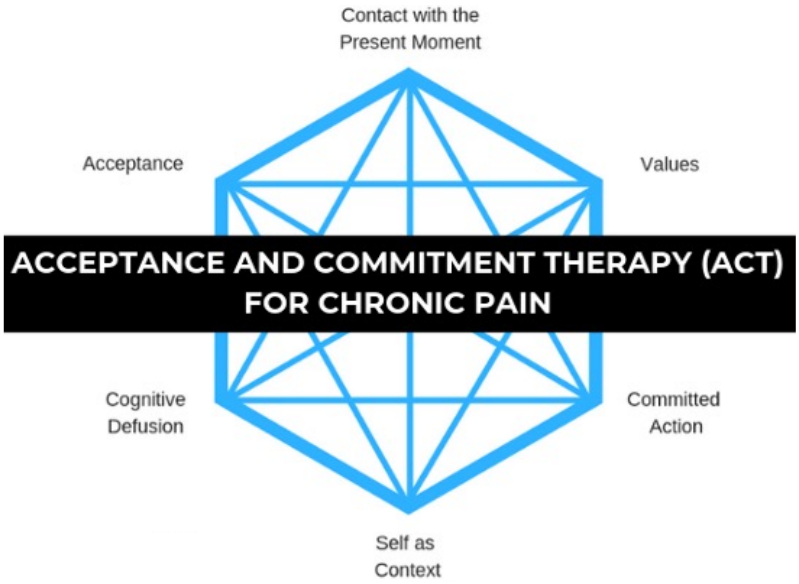

Figure 2: The ACT "Hexaflex", a commonly used ACT infographic to illustrate the six core principles of ACT. This infographic is copyrighted image and is used with written permission from the Integrative Pain Science Institute[106]

There is significant supporting evidence for ACT in multiple conditions, including CNCP[101] and substance use disorders, including OUD[107]. ACT has been found in RCTs to be clinically effective in chronic pain, observed as improvements on a range of outcomes including pain scores, disability, quality of life, pain interference, anxiety, and depression, with small to large effect sizes[102,103,108,109]. Larger reviews and meta-analyses in chronic pain confirm this data and report benefits in medium to large effect sizes when across numerous comparators including inactive controls (placebo or waitlist), treatment as usual, and active comparators such as CBT[102,103,107] showing improved quality of life and improved disease management[36,103]. In fact, several studies even demonstrate ACT's effectiveness in reducing opioid use as part of multidisciplinary programs[29,110–113]. As such, it has recently become accepted as effective and recommended treatment for CNCP pain, particularly for individuals on LTOT[101,103,104].

While ACT has been shown to have benefits in CNCP and those on LTOT, there are barriers to its utility in clinical practice. Traditionally, psychological or behavioural treatments like ACT are delivered in weekly group sessions, often over longer periods of time. Commonly, ACT is delivered to groups of 5-10 once weekly for twelve weeks and up to twenty-four weeks[104,114]. It has been shown that the effectiveness of interventions conducted over numerous sessions, such as traditional ACT, may be impeded due to dropout and adherence rates[114,115]. The implementation of effective abbreviated ACT workshops - in one or two sessions, for instance - has been reported for a wide variety of conditions including diabetes[116], multiple sclerosis[117], pain and stress in health care workers[118], migraines[119], vascular disease[104], preventing

chronic post-surgical pain[112], inflammatory bowel disease[120], chronic pain[36], shame associated with substance use[121] and obesity[122]. Results from these studies are encouraging, highlighting success across numerous outcomes such as improved quality of life, decreased emotional distress, and improved disease management[36,104,112,116–123]. There is not yet evidence to support abbreviated ACT for opioid tapering in patients with CNCP on LTOT. Resultantly, the PEW was developed to incorporate a one-day ACT workshop to evaluate in this patient population.

Much of the research on implementing one-day, or brief, ACT has been conducted by Lilian Dindo, Ph., a licenced clinical psychologist, investigator/researcher, and associate professor based in Houston, Texas, United States[124]. Her area of expertise is the design and research of psychotherapeutic interventions, like ACT, that are both innovative and pragmatic – to improve the lives of patients with chronic health conditions, including pain[124,125]. She has over 70 publications in the field of ACT in various conditions, including implementation and feasibility [125], many of which have been cited in this report. Her work heavily influenced and became a vital part of the design and implementation of this overall project. The project's educational workshop, in which ACT is used as a main intervention, was largely informed by Dindo's work, with her permission, and developed through a highly collaborative interprofessional process. The psychologists involved in this project use ACT to help participants independently navigate through their pain experience with increased awareness, motivation, and willingness to move forward. Based on Dindo's research, the workshop was developed and implemented as a one-day workshop to minimize barriers and improve access for participants that have chronic medical conditions that affect their daily activities of living. Dindo summarized in 2015 that "1-day group workshops in medical settings are more feasible, less stigmatizing, and more cost effective than weekly treatments"[104].

Therefore, the overall project's education workshop is a one-day workshop, with the majority being psychologist-led ACT. The ACT content is split into different exercises delivered in various ways: brainstorming sessions, videos, discussions, problem solving exercises, auditory listening exercises, and more, and is punctuated by breaks. These all work towards establishing psychological flexibility and identifying personal motivation for (and barriers to) opioid tapering, goal setting, pain self-management, and rethinking pain. Although ACT is administered by psychologists in this trial and others, it can be administered by other appropriately trained healthcare providers[120]. This is important for the applicability and accessibility of the trial's results into practice since access to ACT modalities for chronic pain is often significantly limited based on the availability of psychology services.

Again, based on Dindo's work, following the workshop, participants receive educational materials containing session-specific content and take-home activities for support and to continue the work during the opioid tapering portion of the project. Materials provided include exercises that were completed collaboratively by the participants during the PEW, audio files with ACT exercises, and workbooks that contain explanations of the theory explored during the workshop as well as other material, assignments, activities, and goal setting worksheets. Information on the chronic pain and opioid education portion of the PEW are also provided and include more detailed information as gone over in the workshop and links to other references and resources. All these materials are intended aid participants in their ongoing education and application of ACT, including how to change the nature of their relationship to pain as opioid doses are being reduced throughout the tapering program and provide access to ongoing psychological supports throughout study duration.

1.5.2 Multidisciplinary Tapering Program (MTP)

A commonly highlighted challenge to successful opioid tapering is lack of clinician time for appropriate assessment, planning, and follow-up[91,126]. This has the potential to lead to clinical challenges that cause patient harm, for example significant or poorly managed withdrawal effects, which may cause the taper to be unsuccessful[93]. Utilizing a multidisciplinary team can address some of the barriers to successful opioid tapering by providing increased support to the patient and by implementing pain management strategies that are multimodal and comprehensive[12,97]. These concepts are foundational to the development of the overall project's tapering program, named Multidisciplinary Tapering Program, or MTP, for that reason. Pharmacists act as the lead in this program, and work collaboratively with prescribers (physicians and nurse practitioners), other members of the healthcare team (nurses, allied health, and admin), and with the participants themselves to develop a tapering, monitoring, and follow-up plan that is individualized and patient-centered.

All study participants, including those who were randomized to and have completed the PEW, take part in the MTP, which lasts one year. It begins with extensive pharmacist-led medication reviews with collaboration with clinic providers when indicated. These reviews have led to medication optimizations such as new non-opioid pain treatments, other new therapies to optimize the management of other chronic conditions or comorbidities (e.g., mental health, insomnia, diabetes, hypertension, and asthma), deprescribing when indicated, and referrals to other allied health as appropriate (e.g., physiotherapy, occupational therapy, dietitian, amongst others).

Opioid tapering strategies in the MTP generally follow these initial optimizations and are goal focused, flexible, individualized, and patient-centered. There is significant patient involvement in the planning, goal setting, and follow up of the tapering process. Based on participant's starting opioid and opioid dose, unique clinical picture (including comorbidities and other medications), individual tapering goals, and clinician input and expertise, opioid doses during the trial can be reduced, kept them the same, or even increased. This flexible approach differs from opioid tapering recommendations and trials that took place prior to the design of this project. Taper directions were previously recommended to be unidirectional: patients in these studies were not permitted to increase the dose of an opioid after it had been reduced[127,128]. More recent trials, including this project, have pivoted away from this strategy in order to decrease anxieties and hesitancy towards tapering, facilitating a more patient-centered opioid tapering process[26,28]. Prescriptions for the management of withdrawal symptoms as well as for naloxone kits are also facilitated and provided during the MTP.

The MTP incorporates frequent and consistent interdisciplinary follow-up and support as foundational to the process. We have included this follow-up as well as the patient-focused and flexible tapering program with the goal of improving tapering outcomes. Increasing follow-up through phone visits ensures that any clinical concerns are identified early and managed promptly. In doing so, participants may also experience improved relationship building with their clinician and comfort as part of this tapering protocol versus standard of care, which would typically have substantially fewer contact points.

1.5.3 Summary

The overall project is multidisciplinary, patient-centered, and multifaceted, including pharmacological and non-pharmacological management in addition to psychological intervention. In its design, we aimed to address and mitigate many of the commonly reported barriers to opioid tapering. Further, we sought to empower patients with an enhanced understanding and control over their own pain experience and to play an important role in creating a targeted plan for opioid dose reductions. We predict that once complete, both the MTP and PEW components will contribute to improved tapering success and therapeutic outcomes measured across multiple domains. By doing a preliminary review (i.e., this master's project), we hope to optimize the methods and the materials produced, improve recruitment and attrition, and build awareness, interest, and discussion for the overall project, thereby increasing the likelihood of the overall project's success.

Chapter 2: Methods

2.1 Methodology

2.1.1 Overview

As described in the Background section, this thesis is a preliminary report to the overall project, "Evaluation of a Patient-Centered, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy". It evaluates the data from the first ten participants who have completed the PEW and sixteen participants who have completed the first three months of the MTP. The initial data collected and analyzed is related to study outcomes (e.g., opioid dose and pain ratings) while implementation logistics, feasibility, and patient acceptance of all aspects of the project are also evaluated.

This methodology section will go through the methods of the overall project: including ethics and site approvals, inclusion & exclusion criteria, recruitment, consent, and details on the PEW and MTP. Details specifically relevant to the master's project will be highlighted and described throughout.

The overall study consists of two components: the Multidisciplinary Tapering Program (MTP) and the Patient Education Workshop (PEW). All participants enrolled in the overall project take part in the MTP, an informed and targeted multidisciplinary opioid tapering program. Half of study participants are randomly assigned to also take part in a comprehensive opioid education and chronic pain workshop, the PEW, which precedes the tapering program.

A methodology flow diagram that includes the abbreviated details on participant progression through the study is shown in **Figure 3** on the following page.

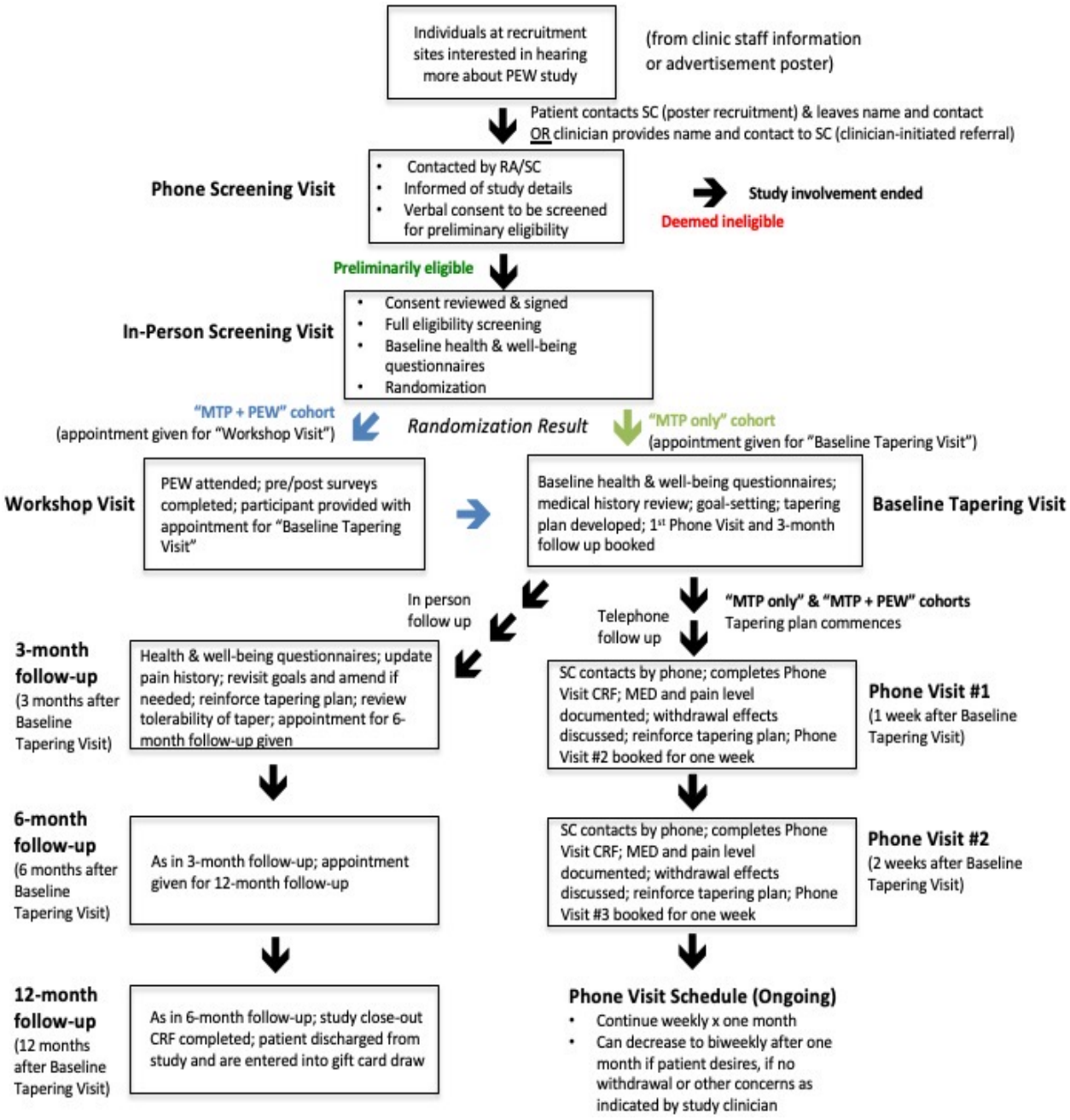

Figure 3: Study Flow Diagram: Flow diagram used by study clinicians to guide participants through each stage of the trial, from screening to study completion, including all in-person and telephone visits along the way.

2.1.2 Ethics and site approvals

The study protocol and related materials were submitted to the Biomedical Research and Ethics Board (BREB) of the University of Manitoba in Winnipeg, Manitoba, Canada, in April of 2020. The application was conditionally approved on May 25, 2020, with final approval on Sept. 2, 2020, stating it was found to

be acceptable on ethical grounds for research involving human participants. This study was registered with Clinicaltrials.gov (ID # NCT04902547).

Following Ethics approval, site approval applications were sent to the Winnipeg Regional Health Authority (WRHA) in October of 2020 for the first three sites: ACCESS Winnipeg West (AWW), ACCESS River East (ARE), and Pan Am Pain Management Clinic. The three initial sites were approved in December of 2020. An expansion of the project occurred to include the Pain Management Centre at Health Sciences Centre (HSC). HSC was approved as the fourth site in April of 2022.

Both the BREB and the WRHA required additional details and/or applications to ensure safety in the context of the COVID-19 pandemic, especially considering its in-person visits. Plans rationalizing the role of the study and its in-person contact as well as to mitigate risks to participants and study personnel were summarized and signed off on by pertinent parties. Final approvals were complete in March 2021.

2.1.3 Inclusion and exclusion criteria

Study inclusion and exclusion criteria were crafted to ensure that we capture those with chronic pain who were at higher risk of opioid-related harms, specifically, those on higher dose opioids, and exclude those for whom participation in opioid tapering in a study setting may not be safe. The inclusion criteria seek to include individuals who: have a confirmed diagnosis of CNCP, experienced on more than half the days in the previous 6 months; used opioids more than half the days in the previous 90 days; take a daily morphine equivalent dose (MED) greater than 50mg; have a minimum weekly average pain score of 3/10 on the numeric rating scale (NRS); are 18 years of age or older; and are cognitively able to understand questionnaires and participate in education sessions, which are conducted in English only.

Study exclusion criteria seek to exclude those who: have experience with ACT or CBT within 12 months of study recruitment (or are currently engaged in either); have known or suspected opioid misuse or abuse, and/or known or suspected opioid diversion; and who are experiencing significant and uncontrolled depression, with or without suicidal ideation. Risk for opioid misuse or abuse is screened for during the In-Person Screening Visit using the Opioid Risk Tool (ORT)[129,130] . Patients exceeding a pre-defined cut-off score on this assessment are deemed to be at high risk and are excluded from the trial. Further details on the ORT, including questions and scoring, can be found in Section 2.2: Data collection tools. Diversion can be more difficult to screen for and is therefore based on referring clinician report and

may or may not include urine drug screen results. Depression is also screened for at the In-Person Screening Visit utilizing the Patient Health Questionnaire (PHQ9), a commonly used depression screening, diagnostic, and severity measurement tool that has been validated in numerous settings, including in various pain diagnoses[131–134]. Anyone scoring above the defined threshold cutoff and/or those who screen positive for suicidality is referred to study psychologists for screening for safety and appropriateness prior to enrollment. No specific score results in absolute exclusion from the study; instead, psychologist assessment serves as the determinant for eligibility. Further details on the PHQ-9, including questions and scoring, can also be found in Section 2.2.

Table 1: Inclusion and Exclusion criteria

Inclusion Criteria:	Exclusion criteria:
Age ≥ 18	Experienced CBT or ACT in the last year
Chronic non-cancer pain Duration: ≥6 months Frequency: >50% of the time Weekly average pain score: ≥3/10 (NRS)	Currently enrolled in CBT or ACT
	Known or suspected opioid misuse or abuse*
	Known or suspected opioid diversion
Opioid use Duration ≥90 days Frequency: >3 days per week Dose: morphine equivalent ≥50mg/day	Significant uncontrolled depression (+/- SI) *
	Current psychosis
Cognitive ability to understand questionnaires	
Can participate in English-only education	
	*screened for on study questionnaires

NRS=numeric rating scale

2.1.4 Recruitment, consent, and enrollment

Recruitment for this project is being conducted at the sites within Winnipeg previously identified, including two primary care clinics inside WRHA ACCESS Centres (AWW and ARE) and two specialty pain clinics - Pan Am Pain Management Clinic and HSC Pain Management Centre. Project summary materials were sent out to non-study team members at these recruitment sites to guide discussions about the study with their patients, including a desk reference document, pre-written scripts and appointment notes they could use during patient encounters. These documents are included in **Appendix A-1** through **A-3**.

Patients at these sites using opioids for CNCP were either informed about the study by a non-study member of their health care team (physician, nurse practitioner, or nurse) or had their charts screened by study members and referred to non-study nursing staff to inform them about the study and get permission for further contact by the research team. In both scenarios, patients were notified of the study

and informed that the project was developed to support patients in making and meeting their opioid use goals. At this time, individuals were asked if they were willing to be contacted by a study team member to learn more about the project.

Recruitment advertisement posters with contact information were also displayed at recruitment sites. Interested patients were able to reach out by phone or email to the study team and have a study representative contact them. An example of a recruitment poster displayed at ACCESS Winnipeg West can also be found in **Appendix A-4**.

Individuals interested in additional information were referred to study pharmacists (Dana Turcotte and Karin Ens) who contacted them by phone ("Phone Screening Visit"). They provide additional study details, as well as ask preliminary screening questions (current opioid dose, current pain level, duration of pain and opioid use) to assess if the patient was eligible to move forward to further screening and consent. Responses to the Phone Screening Visit were collected and subsequently entered into University of Manitoba's secure online data repository used for this trial, Research Electronic Data Capture (REDCap) Survey Server. See **Appendix B-1** for the Telephone Screening Form that includes all data collected during the Phone Screening Visit.

Following preliminary phone screening, eligible individuals were asked if they would like to attend an in-person visit ("In-Person Screening Visit") to learn more about the study, have their questions answered, review and complete two consent forms, and participate in a more comprehensive screen for eligibility. This appointment for this visit is booked at the end of the Phone Screening Visit. Interested and eligible participants are booked at one of the study sites for the In-Person Screening Visit. When attending the appointment, they are brought into a confidential clinic room where the study coordinator provides the participant with paper copies of two consent forms: the detailed Research Participant Information and Consent and the COVID Information for Participants forms for review and to have any questions and concerns addressed. If a patient wishes to consent, they are asked to provide initials on the footer of each page of the form indicating that each page has been reviewed, as well as final signature indicating official consent to take part. Copies of both signed consent forms are offered to the participant. Signed consent forms are stored in a locked cabinet at each clinic. Consent forms are attached in **Appendix B-2**.

The In-Person Screening Visit continues once consent has been obtained, as individuals are then fully screened for eligibility. This comprehensive screening process includes the completion of multiple health and wellbeing questionnaires (Summary and full of questionnaires can be found in **Appendix C-1**; more detailed information about the questionnaires can be found in Section 2.1.6). Participants are given the option to complete these questionnaires directly into REDCap using an iPad or desktop computer or participants can fill out the questionnaires on paper. Responses on paper copies are subsequently entered by members of the study team into REDCap at a later time. If neither of those options are suitable, a participant can be read the questions aloud by the study clinician and answer verbally while the clinician enters the responses into REDCap.

Responses to the questionnaires are used to determine final eligibility (as detailed above in inclusion and exclusion criteria). Those who consent and meet the defined inclusion and exclusion criteria above are officially enrolled. Enrolled participants are interviewed for baseline and demographic information during this visit as well. See **Appendix B-3** for the In-Person Screening/Consent Form that includes all data collected during this visit.

Randomization also takes place during this visit, once enrolled. Participants are randomized 50/50 to one of two treatment arms: MTP-only or MTP + PEW. Participants are randomized using Blocked Randomization with randomly selected block sizes. Due to the overall project's projected sample size of 130, block sizes are factors of 130: either 5, 10, or 13.

2.1.5 Patient Education Workshop (PEW)

Participants assigned to MTP + PEW cohort are scheduled to attend the next PEW ("Workshop Visit"). In order to facilitate the delivery of an online workshop, participant email addresses are collected, with consent, during the In-Person Screening Visit, in addition to discussions about the accessibility and feasibility of a virtual workshop for each individual participant. Study iPads to be used with clinic Wi-Fi were offered to participants that did not have access to internet or a suitable device at home. In the upcoming days before a PEW, participants receive an email from "opioidsandpainstudy@gmail.com" (a private study email) containing the Pre-Workshop Questionnaire, which is to be completed and emailed back prior to attending the PEW. If not able to receive, complete, or email back the questionnaire, participants are offered the option to complete it in person or over the phone. Responses to the questionnaire are subsequently entered into REDCap. **Appendix C-2** contains the full Pre- and Post-

Workshop Questionnaires. The email also contains information about the workshop, including the link to the workshop, instructions on how to log on, and what to do if they experience trouble. The link to the virtual workshop opens 30 minutes prior to the start time. If a few minutes prior to starting, a participant is not yet logged in, they are contacted by phone. Zoom for HealthCare Professionals is used as the platform to protect privacy. Participants are informed about the potential risks of using the platform at the beginning of the workshop, in addition to other housekeeping items, including how to mute/unmute, use the chat box, use their video, see the shared screen, online meeting etiquette etc.

As detailed in Section 1.5.1, the PEW's main objective is to educate patients on chronic pain, risks associated with prolonged opioid use, effective alternatives to opioid therapy, and provide introductory ACT training. The PEW is primarily comprised of psychological content, including ACT, created and co-presented by Dr. Brigitte Sabourin and Dr. Gregg Tkachuk. This is broken up with multiple opportunities for questions, feedback, sharing, and breaks. Approximately halfway through the workshop, there is education on general pain and opioids (content created by Karin Ens, Jenna Villarba, Dr. Ryan Amadeo, and Dr. Dana Turcotte; and presented by Karin Ens). For more details on the content explored during the PEW, an example of a PEW agenda is included in **Appendix D-1.** Note that the agenda is used a general guideline during the workshop; times are flexed when participants find something particularly meaningful or have more input or questions. The slides presented during the Chronic Pain and Opioids section of the PEW are also included in **Appendix D-2.** While the content reflected in these slides is consistent, the presentation of them can vary significantly based on participant response and input.

Following the workshop, participants are sent the Post-Workshop Questionnaire in the same process as the Pre-Workshop Questionnaire. As already mentioned, it is also included in **Appendix C-2.** Post-workshop, participants are also distributed additional educational materials as detailed at the end of Section 1.5.2. These materials can be received as either electronic copies or printed / hard copies per participant preference. Electronic files are disseminated by email and hard copies can either be mailed or picked up by the participant in clinic. The ACT resources distributed in this project were created or collected and collated by psychologists Dr. Brigitte Sabourin and Dr. Gregg Tkachuk, with Jenna Villarba. The Chronic Pain and Opioid workbook was created by Karin Ens, Jenna Villarba, Dr. Ryan Amadeo, and Dr. Dana Turcotte, and has content that closely mirrors the presentation slides mentioned above. A list of these resources is attached in **Appendix D-3**.

2.1.6 Multidisciplinary Tapering Program (MTP)

After completing the PEW, participants are given a date and location for their initial taper planning visit ("Baseline Tapering Visit"), which begins the MTP. Participants not randomized to take part in the PEW (assigned to the MTP-only cohort) are given a date and location for this visit during the In-Person Screening Visit. All participants in this study participate in the MTP.

At the Baseline Tapering Visit, a significant amount of information is collected. The Baseline Tapering Visit Form is attached in **Appendix E-1** and contains all interview questions from this visit. As detailed in Section 1.5.2, this visit also includes a full medication review where medications for pain and other coexisting conditions are optimized and any pertinent referrals are made. Goal setting and planning for opioid tapering also takes place at the Baseline Tapering Visit, even if the participant is not ready to start a taper; the plan may include when to reassess readiness. The tapering plan is individualized by study pharmacist (KE and DT) for all participants. A general starting place for study taper planning, based on previous trials and guideline recommendations, is a 10% dose reduction every two weeks until one third of the original dose (or the tapering goal) has been met. Then if further tapering is planned, the tapering rate can be reduced to a 5% dose reduction every four weeks [25,90,128]. Taper planning also includes providing participants with prescriptions for treatments for withdrawal symptoms as indicated and naloxone kits to decrease the risk of a fatal overdose. Tapering goals are patient-focused in order to ensure that the opioid tapering plan is as patient-centered as possible in hopes of improved tapering retention and success. All of this information is inputted into REDCap by the study clinician (with the exception of the questionnaire responses, which follow the same process as in the In-Person Screening Visit), and into the participant's clinic chart where appropriate (e.g., prescriptions, referrals, chart notes).

Once the participant and pharmacist create a plan at the Baseline Tapering Visit, the study pharmacist (KE and DT) continues to follow the participant by phone ("Phone Visit") and in person ("3-, 6-, and 12-month follow-up") in order to implement, adjust, and manage the participant's plan, with regular updates provided to their health care team, including the primary care provider. During these follow-ups, tapering plans may be adjusted (slowed, increased, halted etc.) and allow for bidirectional dose changes, in consultation with participants and at the discretion of study clinicians.

Phone visits are conducted by the study pharmacists (KE and DT) and besides potentially adjusting the opioid tapering plan, they also assess various clinical parameters. These include pain, mood, withdrawal

symptoms, physical activity, function, sleep, opioid dose, and any other information that participant or clinician would like to bring up, including potential clinical improvements. As well, goal setting and planning for the next stage of the participant's tapering plan are also discussed. If there are any other medications that need adjustment, symptoms of withdrawal that need treatment, or other conditions requiring new or changed management, the pharmacist can facilitate these as needed. An important part of these follow-up visits is also reinforcing functional goals and positive endpoints. Initially, telephone follow-ups are scheduled weekly, and then, based on participant preference and clinician recommendation in response to tapering progress and other clinical details, frequency can be reduced. Data collected at these visits are entered directly into REDCap. Please refer to **Appendix E-2** for the detailed Ongoing Telephone Monitoring Form used.

In-person follow-up visits take place at months 3, 6, and 12. At these visits, participants complete the same questionnaires as at the In-Person Screening and Baseline Tapering Visits, as well as undergo a similar, but more detailed clinical assessments as at phone follow-ups. Opioid dose, pain, and withdrawal are assessed as well as any impact on mood, physical activity, and sleep. Further taper planning and reassessing and reframing goals are also discussed at these visits. Study pharmacists then input the assessments and plans directly into REDCap and responses to questionnaires are collected in the same way as at the In-Person Screening Visit. **Appendix E-3** and **E-4** show the data collection forms used for these visits.

After the 12-month visit is complete, participants are thanked for their participation and given the opportunity to share any questions, concerns, or other feedback with the study clinician that they like. Participants randomized to the MTP cohort are offered the opportunity to attend a subsequent PEW if they would like. Their primary care providers are contacted to ensure continuation of care and participants are officially unenrolled.

2.2 Data Collection Tools

2.2.1 Patient Education Workshop data

While the PEW includes time during and after the education segments for informal feedback and discussion, contributing to qualitative data, the workshop and its initial impact is also formally measured in several ways. Participants are distributed the Pre-Workshop Questionnaire as mentioned above. This tool includes questions on general opioid knowledge, attitudes and experience with chronic pain and

opioids, experiences and readiness for opioid tapering, as well as experience or pre-conceived opinions about ACT in order to assess baseline knowledge and beliefs. Following the workshop, participants are sent the Post-Workshop Questionnaire, which includes many of the same questions as the Pre-Workshop Questionnaire, in order to measure gained knowledge and/or any changes to attitudes or beliefs. The Post-Workshop Questionnaire also includes a brief feedback section that collects both qualitative (short answer) and quantitative (Likert scale) data.

2.2.2 Multidisciplinary Tapering Program data

Data for the MTP is collected and entered into REDCap at each study visit. Demographic information is collected during the In-Person Screening Visit through patient interview. The Baseline Tapering Visit and the 3-, 6-, and 12-month follow-ups are where data on opioid dose (measured in MED), pain scores (measured on the NRS), and responses to seven health and wellbeing questionnaires are collected. Phone visits also collect opioid dose and pain scores. All visits include interview questions where freeform data on other topics is also collected. This can include information about opioid taper planning, progress, barriers, participant goals, withdrawal or other symptoms, pain, physical activity, function, mental health, sleep, and any other information the clinician determines to be relevant.

Data on clinician experience and feedback is collected separately. Study pharmacists keep an individual logbook on various aspects of their experiences within the MTP and document it as it comes up, on topics such as the study protocol, experience with participants, findings or trends that arise, and informal feedback relayed to them from participants. This information is also shared among study pharmacists during meetings in person or over the phone and/or in a shared document where experiences and clinical pearls are shared, ensuring no patient information is revealed. The feedback from both pharmacists from these sources is subsequently combined and sorted.

2.2.2.1 Health and wellbeing questionnaires

Each questionnaire used in the study was chosen for its established validity, relevance, and comparability to other similar trials. Care was taken to include questionnaires that would assess not only pain, but the impact of pain on mental, physical, and social aspects as well (i.e., pain interference and self-efficacy). The questionnaires also serve to triage for characteristics that may contribute to an increased risk of harm as a result of study participation, including mental health concerns and problematic opioid use.

As referenced below in Section 2.4, Hypotheses 3 and 4 (overall project), one of the intents of the overall project is to improve pain disability, pain, depression, anxiety, quality of life, pain acceptance, and valued living. Assessing for these improvements will be done using participants' answers to these questionnaires throughout the study. Due to the study design including exemplary chronic pain care, significant support, and close follow-up from pharmacists during the MTP in addition to the impact of the PEW, including the role of ACT, these benefits are predicted. The master's project, however, is not predicted to show improvement in these scores at this stage, but to simply show no emergence of harm. New emerging evidence showing opioid tapering may have a negative impact on mental health[11,99,100,135] is an important consideration and needed to be evaluated for in this preliminary review of the overall project. Evaluating any change to mental health or other harms that could arise has been a recommendation of other opioid tapering trials[11,100].

All questionnaires with the exception of the ORT are completed by participants at each in-person study visit (In-Person Screening Visit, Baseline Tapering Visit, 3-, 6-, and 12-month follow-ups). These seven questionnaires are estimated to take between 20-40 minutes. Participants are likely to take less time with each visit completing them, as they become more familiar with the questions. Participants that require assistance with the questionnaires take longer (e.g., participants who require the questions be read aloud). A summary of these questionnaires is also included in **Appendix C-1**.

Opioid Risk Tool (ORT)[129]: Clinicians administer this questionnaire to participants during the In Person Screening Visit to establish eligibility for the overall study within inclusion and exclusion criteria, as previously mentioned. It is not repeated at subsequent in person visits. It is scored out of a possible score of 26, with scores split into three categories: less than 3 indicates low risk, 4-7 indicates moderate risk and scores 8 and above indicate high risk[129]. Participants with a score of 8 or higher are excluded from the trial. The ORT is a validated screening tool for the risk of problematic opioid use[129,130]:

Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R):[136,137] Primarily used a screening tool (during the In-Person Screening Visit), but it is also implemented at each in-person visit to track changes. SOAPP-R is a 24-item questionnaire used to determine patients with chronic pain that are high risk for problematic opioid use as well as to guide monitoring frequency for patients on LTOT[137]. A score of 18 or higher (out of 96 possible points) is a positive screen for high risk. SOAPP-R is a validated tool in this population for both screening and monitoring[136,137].

Pain Disability Index (PDI):[138–140] This questionnaire evaluates the impact pain has on a participant's physical, mental, and overall health[138]. There are a total seven questions and on each, participants rate the impact of pain from 0-10, with ten being the highest level of disability, on different realms. The PDI has been validated to assess pain's effect on family/home responsibilities, recreation, social activities, occupation, sexual behaviour, self-care, and life-support actions (otherwise known as activities of daily living, or ADLs)[138–140].

Patient-Reported Outcomes Measurement Information System Glocal-10 (PROMIS Global-10):[141] A 10-item questionnaire that assesses health status, both physical and mental[35,142]. Questions require participants to rate different aspects of their health (general health, quality of life, physical health, mental health, and both satisfaction and success with social health) as excellent (5), very good (4), good (3), fair (2), or poor (1); rate their average pain from the last week from 0-10 (NRS); and rate physical activities, emotional problems, and fatigue on 5-point scales[141]. The PROMIS Global-10 questionnaires supplies two scores: Global Physical Health score and Global Mental Health score[142]. Both are scored out of a possible 20 points, 20 being excellent health and 0 being poor. It has been validated numerous times, including in the context of chronic pain[141–143].

Patient Health Questionnaire (PHQ9):[132] Screens for and assesses the severity of depression. A 9-item questionnaire, participants are required to quantify the frequency they feel specific symptoms that relate to depression in the last two weeks: not at all (0), several days (1), more than half the days (2), or nearly every day (3). The last question assesses suicidality on the same scale. The scoring of the PHQ9 splits into five categories: 0-4/27: minimal depression, 5-9/27: mild, 10-14/27: moderate, 15-19/27: moderate-severe, and 20-27/27: severe depression[132]. Participants scoring a total of 20 points or higher, or answer the last question regarding suicidality as 2 or higher, are referred to study psychologists to screen for appropriateness and safety[132]. The PHQ9 is a validated questionnaire for screening and monitoring depression[131] and is a recommended tool to for use in patients with chronic pain[144].

Generalized Anxiety Disorder 7 Item (GAD-7):[145] Screens for and assesses the severity of anxiety[145]. GAD-7 is a 7-item questionnaire that requires participants to quantify the frequency of specific symptoms that relate to anxiety in the last two weeks: not at all/not sure (0), several days (1), over half the days (2), or nearly every day (3). GAD-7 scores are split into four categories: 0–4: minimal anxiety, 5–9: mild, 10–14: moderate, and 15–21: severe anxiety. An additional question at the end has participants assess how

difficult the symptoms have made various aspects of their lives as not at all, somewhat, very, or extremely difficult. It has been validated for both screening and monitoring anxiety[145] and has been used in chronic pain, including in opioid tapering studies[25,146].

Chronic Pain Acceptance Questionnaire 8 (CPAQ-8):[147,148] An 8-item questionnaire gauges participants attitudes and acceptance towards chronic pain. For each question, participants rank each statement, e.g. "I lead a full life even though I have chronic pain," on a 7-point scale from never true (0) to always true (6). Scores are tabulated (some in reverse) to give scores in pain willingness and activity engagement[149]. It has been validated in chronic pain to measure pain acceptance[147,148].

Chronic Pain Values Inventory (CPVI):[150–152] This questionnaire requires participants to determine first the values that are important to them and then how successful they are at following their values. Participants give a ranking of not at all important (0) to extremely important (5) and then not at all successful (0) to extremely successful (5) in each of six domains: family, intimate relations, friends, work, health, and growth and learning. The CPVI has been validated for analyzing chronic pain as well as being itself part of chronic pain treatments, as it helps individuals identify values-based actions and goals for their pain[150–152].

2.3 Objectives

Overall project:

1. Evaluate the impact of a patient-centered, multidisciplinary opioid tapering program on overall opioid consumption in individuals with chronic pain on long-term opioid therapy.
2. Implement opioid patient education workshops to be used in conjunction with the opioid tapering program and evaluate their preliminary feasibility and overall patient acceptance.

Master's project:

1. Evaluate the impact of a patient-centered, multidisciplinary opioid tapering program on overall opioid consumption in individuals with chronic pain on long-term opioid therapy after 3-months in the tapering program.
2. Implement opioid patient education workshops to be used in conjunction with the opioid tapering program and evaluate their preliminary feasibility and overall patient acceptance.
3. Inform the larger study with feedback from early PEW and 3-month MTP data in order to contribute to study procedure improvements and optimization.

2.4 Hypotheses

Overall project:

1. All participants who participate ("PEW + MTP" and "MTP only" cohorts), will demonstrate significant reductions in their opioid dosage at the end of their tapering program.
2. Participants who participate in both aspects of the project ("PEW + MTP" cohort) will experience significantly greater reductions in their opioid dosage than those who participate exclusively the tapering program ("MTP only" cohort).
3. Participants who participate in the education workshop ("PEW + MTP" cohort) will demonstrate significant improvements on self-report measures of pain disability, pain, depression, anxiety, quality of life, pain acceptance, and valued living after attending the workshop,
4. These improvements will be maintained at the follow-up intervals and will be significantly greater than for patients who do not participate in the education workshop ("MTP only" cohort).

Master's project:

1. Both cohorts ("PEW + MTP" and "MTP only") will demonstrate trend reductions in opioid consumption by the in-person 3-month follow-up.
2. PEWs will be feasible to implement in their current format and feedback from PEW participants will indicate an overall patient acceptance and value, defined as at least 80% responding with 'agree' or 'strongly agree' to acceptance and values questions of Post-Workshop Questionnaire feedback.
3. Feedback from PEWs and 3-month follow-up MTP data will inform changes that will be implemented in both the PEW and MTP protocols, ultimately resulting in subsequent improvements in future PEW and MTP feedback.

2.5 Outcomes Measured

1. **Opioid dose**: Opioid dose is documented in MED at all phone and in-person visits. A chart of conversion factors used to calculate MED can be found in **Appendix C-3**. The master's project measures the average difference in MED between the Baseline Tapering Visit and the 3-month follow-up. The overall project will use all collected values to determine average overall change in MED. A 30% reduction was considered clinically meaningful based on the work of Sullivan et al[25].
2. **Pain score**: Participants rate their average weekly pain on the NRS at each phone and in-person visit. The master's project measures an average difference in pain scores between the Baseline Tapering Visit and the 3-month follow-up. The overall project will use all pain score values to calculate an

average overall change in pain. A two to three point or 30% change on the NRS has been defined as clinically significant[153].

3. **Scores on health and wellbeing questionnaires**: Participants complete seven questionnaires (see above Section 2.2.2.1) at each in-person visit. The master's project measures the average difference in all but the CPVI and CPAQ-8 scores from the Baseline Tapering Visit to the 3-month follow-up. The overall project will use all measured scores to determine average change. The minimally important difference is listed for each score in **Appendix C-1**.
4. **Change in opioid knowledge and tapering readiness**: Participants complete a 6-point quiz on basic opioid knowledge and answer two questions that assess readiness to taper both pre- and post-workshop. The master's project compares pre- and post-workshop responses to measure the impact of the PEW. These will not be formally assessed for the overall project but will rather measure the impact of the PEW by comparing outcomes 1-3 in the cohort who attended the workshop (PEW+MTP) to the cohort that did not (MTP-only).
5. **Feedback**: Participant and clinician feedback is collected throughout the PEW and MTP. Participant feedback on the PEW, specifically, is measured pre- and post-workshop on Likert scale and freeform questions, which the master's project analyzes and reports.

2.6 Statistical Considerations

2.6.1 Sample sizes

The overall project has a calculated target total sample size of 131 subjects. We estimate that 131 subjects [105 / 0.8 = 131] are required to detect a 30% reduction in average MED usage in a one-year period (e.g., from 200mg at baseline to 140mg at the in-person 12-month follow-up), using a single-group paired t-test. This calculation allows for 20% dropout and assumes a standard deviation of 250 MED and 150 MED at baseline and end of trial, respectively, based on the published work of Sullivan et al[25]. We also assume a moderate within-subjects correlation of 0.5. This sample size will give 80% power at a type-1 error rate of 5%. This estimate is likely conservative (i.e., will lead to greater than 80% power) since it only uses two MED measurements (baseline & end of study), whereas our design will have up to approximately 60 measurements per person by study end.

The master's project sample size is ten participants for the PEW data and 16 participants for the 3-month MTP data. These numbers were determined during a March 2022 committee meeting based on

referrals at that time and anticipated referrals based on escalated recruitment efforts (see Sections 3.1.1 and 4.1.1.1 for details). The initial proposed sample size was 10-15 participants who had completed the PEW and 25 participants who had completed 3 months in the MTP.

2.6.2 Statistical analysis

The overall project will use multiple methods for statistical analysis. Participants in the "MTP only" and "MTP + PEW" groups will be compared descriptively at baseline with respect to demographic and outcome variables. To test for average change over time in our primary outcome of opioid use, measured in MED, we will use a linear mixed-effects model. Random (subject-specific) intercepts and slopes will be fit, allowing for possibility that rate of change is correlated with baseline MED. We will also explore the effects of baseline covariates by adding them to the model. Competing correlation structures for the within-subjects' measurements will be compared using the AIC information statistic. This modeling approach uses all measurements from each person, including ones that miss a visit or drop out, thereby maximizing statistical power and mitigating bias if the data are missing at random.

The master's project used linear mixed-effects models to evaluate changes from baseline to 3 months. The dependent variables included MED, pain scores, and scores from 5/7 of the measured health and wellbeing questionnaires. For each model, the predictors were treatment group (MTP-only versus MTP + PEW), time (baseline versus 3 months), and their interaction. These models provided tests of a differential intervention effect between the treatment groups, as indicated by different average slopes over time, and overall changes from baseline to 3 months, while adjusting for any baseline imbalances between group. The model error term was generalized to include statistical dependence between measurements made on the same subject, thereby correcting standard errors, and improving power for testing changes over time.

The master's project assessed PEW data using Wilcoxon Signed-Rank test to detect changes in opioid test scores pre- and post-workshop and the McNemar test was used to detect change in tapering readiness. Patient acceptance was measured on Likert scale questions on the Post-Workshop Questionnaire feedback form and used an 80% response rating as agree or strongly agree as the cut-off for defining patient acceptance and value. The Likert scale questions as well as free form questions that were used can be found in **Appendix C-2**.

Chapter 3: Results

3.1 Recruitment and Attrition

3.1.1 Recruitment

There are 25 patients enrolled and an overall recruitment rate of 49% based on pooled data from all three sites (current to January 2023). Detailed recruitment numbers and progression through the study are illustrated below in **Table 2** and **Figure 4**.

Table 2: Recruitment rates, at each site and pooled, as of January 2023

Site	# of participants eligible/referred	# of participants enrolled	Recruitment rate
AWW	27	13	48.15%
ARE	16	8	50.00%
PA	6	3	50.00%
HSC	2	1	50.00%
Total	**51**	**25**	**49.02%**

AWW=ACCESS Winnipeg West, ARE=ACCESS River East, PA=Pan Am Pain Management Clinic, HSC=Health Sciences Centre Pain Management Centre

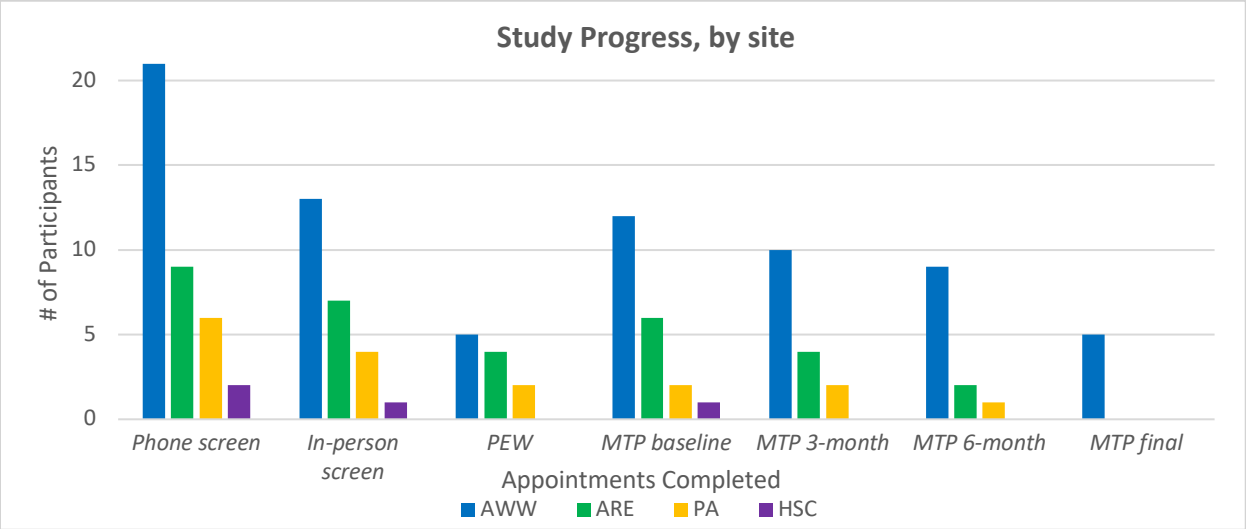

Figure 4: Participant progress through the study, by site: bar graph of participant numbers (from each site) that have completed each stage of the study (up to January 2023).
PEW=Patient Education Workshop, MTP=multidisciplinary tapering program, AWW=ACCESS Winnipeg, ARE=ACCESS River East, PA=Pan Am Pain Management Clinic, HSC=Health Sciences Centre Pain Management Centre

Recruitment began at AWW with slow numbers since it was during the heart of the COVID-19 pandemic. First recruitment efforts (March-July 2021) saw seven patients enroll out of 16 eligible referrals, a 44% recruitment rate. AWW then went through a second wave of recruitment in February 2022 with a different, more targeted recruitment strategy after lessons learned from the first wave and from

recruitment at the second site, ARE. This recruitment strategy captured an additional six patients, totaling 13 patients enrolled out of a total of 27 eligible at AWW (overall 48% recruitment rate). **Figure 5** shows the two waves of recruitment at AWW, before and after changes to recruitment strategies were made.

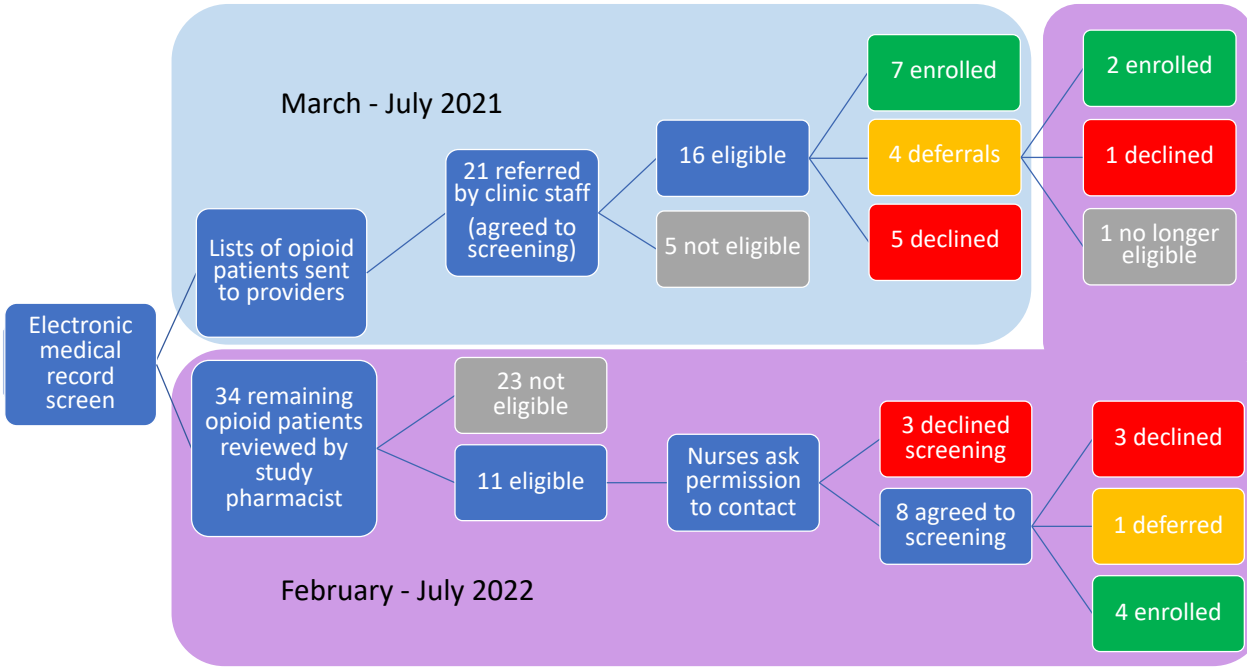

Figure 5: ACCESS Winnipeg West recruitment (in 2 waves) – flow diagram of the two different waves of recruitment at the first study site, showing adjusted recruitment strategies and resultant recruitment numbers.

ARE was the second site that started recruiting in fall 2021 and based on lessons learned and improved access had a slightly improved recruitment rate compared to that of AWW's first wave. Seven patients enrolled in late 2021-early 2022 out of 12 eligible referrals (58% recruitment). ARE has also recruited one additional patient since that time out of four new referrals, changing their total recruitment rate to eight enrolled out of 16 total referrals, or 50%.

Pan Am and HSC do not have study pharmacists on site, and therefore have a lower capacity for enrollment. Pan Am currently has three patients enrolled and HSC one, both with 50% recruitment rates.

3.1.2 Attrition

Based on high attrition rates in other opioid tapering studies results[27,94,95], a 20% drop out rate was predicted. As of January 2023, four participants were lost to attrition out of 25 enrolled, an attrition rate of 16%. Three of four participants lost to attrition provided reasons for dropping out. The first reported

stress and reduced mood that prevented them from committing as much as they wanted. The second was hospitalized during the trial period and was dealing with acute pain associated with that visit and subsequently did not think the study was appropriate at that time. That participant remains on a list to potentially re-enroll at a later date. The third participant requested to put study involvement on hold due to personal issues. At the time of attrition, the participant requested to be contacted again to re-enroll but upon re-connection was still not interested. This participant also remains on a list to potentially re-enroll. The last participant was lost to follow up after cancelling their first study visit due to viral illness. Following that, the study team (and the clinic staff) were no longer able to get a hold of them.

3.2 Demographics

Demographic information is extracted from data entered during the In-Person Screening Visit. **Table 3** below includes demographic details on 20 participants that were enrolled in the study from the beginning of study recruitment in March 2021 until data extraction for this project, which occurred in December 2022. The additional five participants recruited, as mentioned in the previous section, did not have data available for demographic analysis either because they were recruited after data extraction (since recruitment information above goes until January 2023) or were recruited prior to data extraction, but their information was not available for extraction in time for various reasons including participants requesting paper questionnaires that had not yet been entered into REDCap and In-Person Screening Visits going over time and requiring additional visits to complete all necessary interview questions and data collection.

Two of the four participants lost to attrition are included in **Table 3**, since they completed the In-Person Screening Visit when they were enrolled. The other two were not included because they did not have their data available for data extraction. The data sets in the following Results sections, Sections 3.3 and 3.4, on the results of the PEW and the MTP, do not contain data from all 20 participants in the table below. Only 10 of the 12 PEW participants were analyzed for their PEW data, since one withdrew from the study prior to attending the PEW and the other did not complete the post-workshop questionnaire. Only 16 of these 20 participants are analyzed in the MTP data because 4 of the enrolled participants had not made it to the 3-month follow-up visit by data extraction, including the two participants who withdrew.

Table 3: Demographics of study participants, up to December 2022 (n=20)

	MTP		PEW	
Site	Qty	%	Qty	%
AWW	7	54%	6	46%
ARE	1	20%	4	80%
Pan Am	0	0%	2	100%
HSC	0	0%	0	0%
Sex				
Male	2	25%	7	58%
Female	6	75%	5	42%
Other	0	0%	0	0%
Age				
18-29	0	0%	1	8%
30-49	1	13%	5	42%
50-64	7	88%	6	50%
65+	0	0%	0	0%

	MTP		PEW	
Opioid	Qty	%	Qty	%
Codeine	0	0%	1	8%
Tramadol	0	0%	0	0%
Morphine	1	13%	0	0%
Oxycodone	3	38%	5	42%
Hydromorphone	3	38%	5	42%
Fentanyl	1	13%	1	8%
Non-opioid pain medications				
Acetaminophen	5	63%	5	42%
NSAID (systemic)	1	13%	5	42%
NSAID (topical)	3	38%	0	0%
TCA	4	50%	2	17%
SNRI	3	38%	2	17%
Gabapentin/Pregabalin	2	25%	5	42%
Nabilone/Cannabis	1	13%	8	67%
Muscle relaxant	2	25%	2	17%
Pain Diagnoses				
Fibromyalgia	2	25%	3	25%
OA / RA	4	50%	3	25%
post MVA	1	13%	2	17%
Neuropathy	1	13%	0	0%
Migraine	0	0%	1	8%
IBS/IBD	1	13%	0	0%
Back Pain	0	0%	4	33%

	MTP		PEW	
Baseline MED	Qty	%	Qty	%
50-75	3	38%	6	50%
76-100	0	0%	2	17%
101-150	0	0%	1	8%
151-200	2	25%	2	17%
200+	3	38%	1	8%
Baseline Pain score				
3 - 4.9	0	0%	1	9%
5 - 6.9	1	13%	7	64%
7 - 8.9	4	50%	3	27%
9 - 10	3	38%	0	0%
Baseline PHQ9				
0-4	4	50%	3	27%
5-9	2	25%	2	18%
10-14	0	0%	3	27%
15-19	1	13%	2	18%
20-27	1	13%	1	9%

MTP=Multidisciplinary Tapering Program only cohort, PEW=Patient Education Workshop cohort, Qty=quantity, AWW=ACCESS Winnipeg West, ARE=ACCESS River East, Pan Am=Pan Am Pain Management Clinic, HSC=Health Sciences Centre Pain Management Centre, NSAID=non-steroidal anti-inflammatory drug, TCA=tricyclic antidepressant, SNRI=serotonin and norepinephrine reuptake inhibitors, OA=osteoarthritis, RA=rheumatoid arthritis, MVA=motor vehicle accident, IBS=irritable bowel syndrome, IBD=inflammatory bowel disease, MED=morphine equivalent dose, PHQ9=Patient Health Questionnaire score

Cohorts MTP and PEW are not equally distributed in most categories shown in **Table 3**, owing to small sample size and uneven distribution with block randomization. Most differences are unlikely to be relevant to the master's project analyses, but of note, the MTP group has more participants than the PEW group on the highest category of opioid dose and has a considerably higher opioid dose on average. The PEW group, in comparison, has the majority of its participants in the lowest category of opioid dose. This difference is expanded upon in Section 3.4.1 and further discussed in Section 4.1.3.1. Also of note, 67% of PEW participants use a cannabis product regularly (smoked, oral, or prescription nabilone) compared to only 13% of MTP participants. As this is a preliminary review, these differences will likely equal out with the full sample size of the overall project and any substantial baseline imbalances that exist between treatment groups at that time will be adjusted for in the final analysis, as necessary.

3.3 Patient Education Workshop (PEW)

Eleven participants from three sites attended six PEW workshops that took place May 28, July 27, and Oct. 27, 2021, and Feb. 16, Apr. 8, and Aug. 16, 2022. One participant (participant PEW 8) took part in the PEW on Feb. 16, but did not complete the post-workshop questionnaire, so no data was able to be collected from that participant. The data below is from the remaining ten PEW participants. Between one and three study participants were present at each PEW. In order to have a more suitable group size of at least five participants, patients from study sites with chronic pain outside of the study were invited to join the workshop. Although the maximum acceptable group size was set at 10-15, all PEWs had less than ten participants.

3.3.1 Opioid knowledge quiz scores

In this section we compare the scores on the opioid knowledge quiz from each participant's pre- and post-workshop questionnaire. This is defined as the sum of correct responses to questions one through six on the opioid knowledge quiz. These are paired data since each subject provides measurements under both conditions, meaning they are presumably not independent. This is to our advantage; a positive correlation between measurements within subjects would reduce variance and improve power to detect a change. One could use a paired t-test here. However, since the sample size is small and the change scores do not appear to have a Gaussian distribution, we use the Wilcoxon signed-rank text, a non-parametric alternative. It compares the signed sum of ranks to the null hypothesis that the data have a median of zero, indicating no change.

Results (n=10) are summarized below, in **Table 4**, beginning with basic descriptive statistics of the changes in scores (post minus pre). The positive average indicates an increase in knowledge scores. The p-value for the signed-rank test is 0.031, below our previously determined 0.05 cut-off, and hence we reject the null hypothesis of no change and conclude there was an increase in knowledge scores. The magnitude of this change is a mean improvement of 1.3 points (on a 6-point quiz) with a 1.418 standard deviation. No specific quiz question was associated with a significant improvement on its own.

Table 4: Opioid knowledge quiz score changes, pre- and post-workshop, basic statistical measures (n=10)

Basic Statistical Measures			
Mean	**1.300**	***Standard Deviation***	**1.418**
Median	1.000	*Variance*	2.011
		Range	4.000
		Interquartile Range	2.000

The average pre-workshop score was 3.84/6 (64%) and the average post-workshop score was 5.52/6 (92%). All post-workshop scores were 4/6 or higher (i.e., over 65%). The most improved questions were question 4: “Which of the following is NOT a side effect of opioid use?” with a multiple-choice answer and question 5: "Lowering the dose of an opioid (tapering) will cause pain levels to increase” true/false. Question 4 increased from 7/10 participants answering correctly pre-workshop to all 10/10 participants answering correctly post. Correct answers on question 5 increased from 4/10 participants answering correctly pre-workshop to 7/10 post. These are described descriptively in **Figure 6** and **Figure 7**, below.

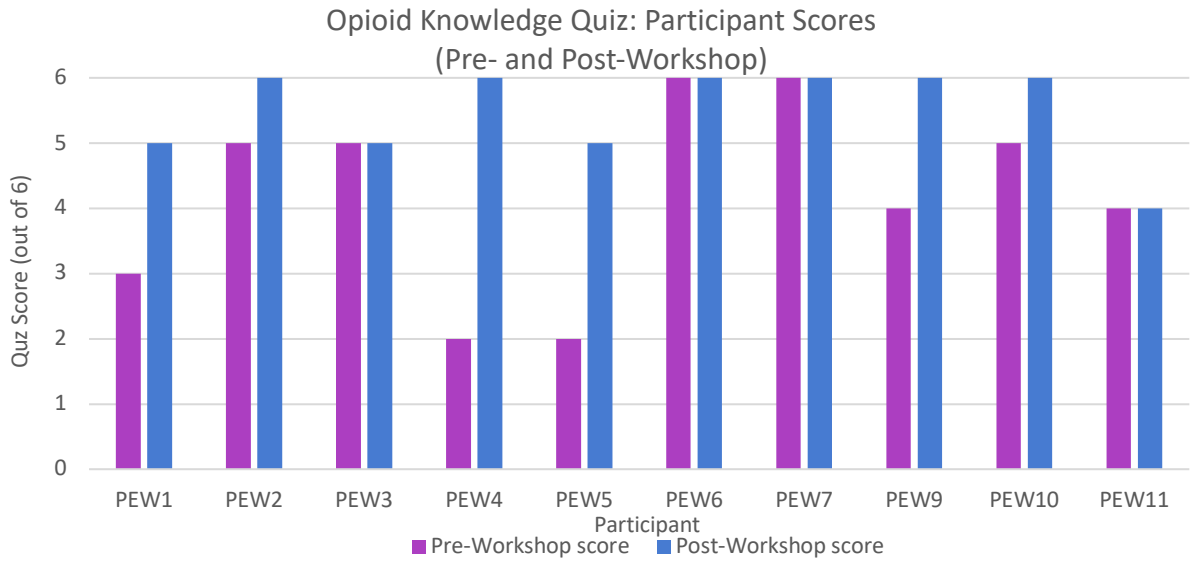

Figure 6: Opioid knowledge quiz bar graph: participant score changes (n=10): individual participant scores on the opioid knowledge quiz pre- and post- workshop

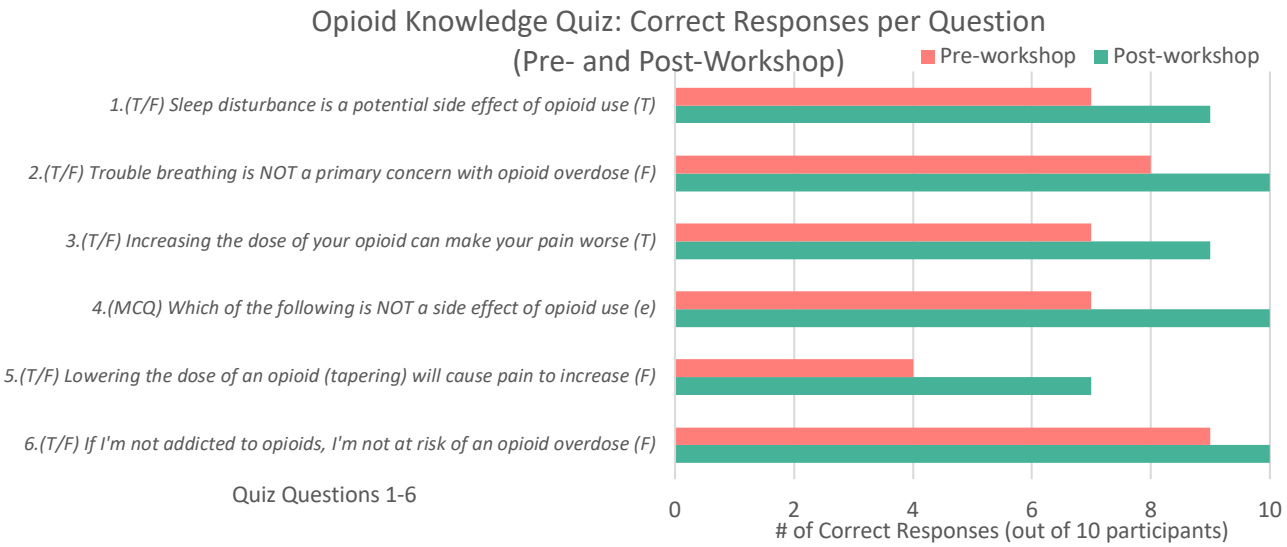

Figure 7: Opioid knowledge quiz bar graph: correct responses per question pre- and post-workshop (n=10): frequency of correct responses to each question on the opioid knowledge quiz, both pre- and post-workshop, out of 10 participants. T/F=True or False; MCQ=multiple choice question, e=e) all of the above

3.3.2 Tapering readiness

Tapering readiness was measured using a McNemar Test. These data are paired, nominal and binary, so in order to analyze them in one test, a McNemar grid was selected. The McNemar tests for a change in proportions while accounting for data being paired.

In total, 40% (n=4) of participants increased taper readiness. Two participants did not agree with the statement *"I would like to be able to reduce the amount of opioid that I currently take"* pre-workshop, but did agree post-workshop, and rated their readiness as either *"somewhat ready"* or *"not really ready"*. Two participants were *"not really ready"* pre-workshop and were *"somewhat ready"* post-workshop. Thirty percent of participants (n=3) were *"very ready"* pre- and post-workshop and could therefore not improve upon readiness. Further, 20% of participants (n=2) showed no improvement: 1 participant was *"somewhat ready"* pre- and post- and 1 was *"not really ready"* pre- and post. There was one participant (10% of total) whose tapering readiness decreased (*"somewhat ready"* to *"not really ready"*).

With a p-value of 0.970, these data are not significant of a change in taper readiness based on this preliminary sample. Of note, all participants responded positively to the first question about wanting to taper post-workshop. This data is presented below in **Table 5**.

Table 5: Change in taper readiness: pre- vs post workshop from the McNemar Test (n=10)

Tapering readiness (pre-workshop)	**Tapering readiness (post-workshop)**				
Frequency Row % Column %	Very ready	Somewhat ready	Not really ready	Not wanting to taper	**Total frequency**
Very ready	3 100.0 100.0	0 0.0 0.0	0 0.0 0.0	0 0.0 0.0	**3**
Somewhat ready	0 0.0 0.0	1 50.0 25.0	1 50.0 33.3	0 0.0 0.0	**2**
Not really ready	0 0.0 0.0	2 66.7 50.0	1 33.3 33.3	0 0.0 0.0	**3**
Not wanting to taper	0 0.0 0.0	1 50.0 25.0	1 50.0 33.3	0 0.0 0.0	**2**
Total frequency	**3**	**4**	**3**	**0**	**10**

3.3.3 Workshop feedback

Feedback on the workshops was collected both quantitatively and qualitatively on the post-workshop questionnaire. This questionnaire is included in **Appendix C-2.** Four Likert scale statements with a five-point response scale (strongly agree, agree, neutral, disagree, and strongly disagree) and two freeform questions were posed of participants in order to measure acceptance and value of the workshop's content and format.

3.3.3.1 Feedback on workshop content/value

The two Likert statements assessing workshop content were "This workshop provided value to my pain management" and "I will use what I learned in this workshop to help manage my pain" which scored 78% and 100% agree or strongly agree, respectively. There were no responses of "disagree" or "strongly disagree" on either question (one participant ranked question 1 as "neutral"). This data is detailed below in **Table 6.**

Table 6: Responses to Likert scale questions on Patient Education Workshop content/value (n=10): Two questions on the post-workshop questionnaire addressed participants' opinions on the content of the workshop and its value. Note that one participant left the first question blank, so there are only 9 responses.

Question 1: "The workshop provided value to my pain management"				
	Frequency	**Percent**	**Cumulative Frequency**	**Cumulative %**
Strongly Agree	3	33.33	7	77.78
Agree	4	44.44		
Neutral	2	22.22	2	22.22
Disagree	0	0	0	0
Strongly Disagree	0	0		
Frequency Missing = 1				
Question 2: "I will use what I learned in this workshop to help manage my pain"				
	Frequency	**Percent**	**Cumulative Frequency**	**Cumulative %**
Strongly Agree	7	70.00	10	100.00
Agree	3	30.00		
Neutral	0	0	0	0
Disagree	0	0	0	0
Strongly Disagree	0	0		

The freeform questions on the post-workshop questionnaire included: "What did you like about the workshop?" and "Do you have any suggestions for improving the workshop? (Please include comments on the workshop format and/or barriers you encountered from the previous two questions if applicable)."

While each of these questions capture feedback on both the content and the format of the workshop, responses specific to the workshop's content and value are presented in this section (format feedback can be found in Section 3.3.3.1). Nine out of ten participants included freeform comments about the workshop's content/value on one or both questions. All of these comments were positive – there were no constructive comments about the content or the value of the workshop. Participants commented on multiple topics, including the workshop's content, the delivery of the content, the presenters, and the group learning environment. These comments are below in **Table 7**.

Table 7: Participant freeform feedback on the Patient Education Workshop's content/value (n=9): Feedback collected from participants on the post-workshop questionnaire regarding the workshop's content and its value, grouped into four categories: Content, Delivery, Presenters, and Group Environment

<table>
<tr><th>Content</th><th>Delivery</th><th>Presenters</th><th>Group Environment</th></tr>
<tr><td>"I enjoyed how thorough and in-depth the workshop was. I also loved the metaphors that were used/taught... I think the metaphors will be tools that I will use for the rest of my life!" [PEW7]</td><td>"[I liked] the various modalities - technology (e.g. slide shows, videos and instructional techniques used within the workshop. This always kept us on our toes as participants and was an effective means of instruction as it kept us all engaged." [PEW6]</td><td>"The presenters were very well prepared, friendly, and knowledgeable" [PEW3]</td><td>"It feels good to be with friends who are going through the same problems" [PEW5]</td></tr>
<tr><td>"[I liked the] Pharmacist's presentation on drugs" [PEW4]</td><td>"I'm glad [the presenters] were able to walk us through all the exercises, instead of just giving us papers to read" [PEW7]</td><td rowspan="4">"I like how supportive everyone is and the advice" [PEW11]</td><td>"[I liked] Hearing other stories like my own" [PEW4]</td></tr>
<tr><td rowspan="3">"High quality of workshop content" [PEW10]</td><td>"I liked the high level of interaction between workshop participants and facilitators" [PEW6]</td><td rowspan="3">"[I liked] Hearing everyones stories and feeling less alone in my pain and what I'm experiencing" [PEW9]</td></tr>
<tr><td>"I enjoyed the practical exercises" [PEW10]</td></tr>
<tr><td>"[I liked that] Copies of resources such as the ACT workbook, audio files, Power Point were supplied... for future reference" [PEW6]</td></tr>
<tr><td colspan="4">"It was totally life changing for me" [PEW2]</td></tr>
</table>

PEW# indicates which participant submitted the feedback.

Participant acceptance and value of these workshops was pre-defined as 80% agreement rate on both content/value Likert questions, with agreement defined as "strongly agree" or "agree" responses. Although there was zero "disagree" or "strongly disagree" responses on these Likert scale questions and

the freeform feedback was exclusively positive, agreement rates were below the 80% criterion for one of the questions (78%). Despite this, early data trends towards overall participant acceptance and value.

3.3.3.2 Feedback on workshop format

The two Likert statements assessing workshop format were, "I found the format of the workshop (full day, online) worked well with my needs" and "I didn't have any barriers that affected my ability to attend this workshop significantly," which both scored 50% as agree or strongly agree. The specific answers to Likert scale questions are detailed in **Table 8** below.

Table 8: Responses to Likert scale questions on Patient Education Workshop's format (n=10). Two questions on the post-workshop questionnaire addressed participants' opinions on workshop format and acceptability.

Question 3: "I found the format of the workshop (full day, online) worked well with my needs"				
	Frequency	**Percent**	**Cumulative Frequency**	**Cumulative Percent**
Strongly Agree	1	10.00	5	50.00
Agree	4	40.00		
Neutral	3	30.00	3	30.00
Disagree	2	20.00	2	20.00
Strongly Disagree	0	0		
Question 4: "I didn't have any barriers that affected my ability to attend this workshop significantly"				
	Frequency	**Percent**	**Cumulative Frequency**	**Cumulative Percent**
Strongly Agree	3	30.00	5	50.00
Agree	2	20.00		
Neutral	4	40.00	4	40.00
Disagree	1	10.00	1	10.00
Strongly Disagree	0	0		

Seven out of ten participants included comments about the workshop's format on one or both of the questions: "What did you like about the workshop?" and "Do you have any suggestions for improving the workshop? (Please include comments on the workshop format and/or barriers you encountered from the previous two questions if applicable)." The responses are separated below into comments regarding the duration of the workshop (one full day as opposed to multiple days or shorter session) and comments about the online format using Zoom. Both categories included a mix of positive, neutral/constructive, and negative feedback. These feedback are included below in **Table 9**.

Table 9: Participant freeform feedback on the Patient Education Workshop's format (n=7): Feedback collected from participants on the post-workshop questionnaire regarding two format variables: the online delivery and one-day approach. Feedback is divided into three categories: "Positive", "Constructive/Neutral", and "Negative".

	One day	Online
Positive	"I found the format of this workshop (full day, online) worked well with my needs." [PEW1]	
	"I liked that the workshop was held in a one-day session rather than a couple hours one day a week for several weeks... I would have ended up missing multiple sessions [due to work]" [PEW6]	"[I liked] that I didn't have to activate my personal video [the whole time] and that messaging my input was acceptable" [PEW10]
Constructive/ Neutral	"My only suggestion would be going to a half day workshop, but a full day is not insurmountable" [PEW10]	
	"My only suggestion would be to arrange another workshop day (or even just a morning/afternoon) to all touch base again later in the study" [PEW6]	
Negative	"Make it not a whole day, eg. 2 half days, so it's not so much all at once. The full day workshop was a bit intense" [PEW2] "It felt long and could have been in 2 or 3 days to cover more" [PEW4]	"Technology is hard for me so it was confusing trying to get onto the Zoom and figure out how everyone can hear me" [PEW5]
	"[It was] hard for me to concentrate the whole time" [PEW5]	
	"It was tough to get a full day off of work to attend. If they could break it up or record some of the session that would help" [PEW9]	

PEW# indicates which participant submitted the feedback.

Participant acceptance of the workshop format was again pre-defined as 80% agreement rate (strongly agree" or "agree" responses). At 50% each, agreement rates on the workshop's format were below the 80% criterion for both questions.

3.4 Multidisciplinary Tapering Program (MTP)

Sixteen participants from three sites completed at least three months in the MTP, seven from the MTP-only cohort and nine from the PEW+MTP cohort. In this section, these cohorts are referred to as MTP (n=7) and PEW (n=9), respectively. Data from each participant's Baseline Tapering Visit is compared to their 3-month follow-up to evaluate study impact on various outcomes, including opioid dose, pain, and scores assessing quality of life and physical and mental health (measured on health and wellbeing questionnaires).

We use mixed-effects repeated measures models[154] to test whether there is an average difference in magnitude of each outcome between treatment groups (MTP vs PEW), time period (baseline vs 3-month), and lastly both treatment group and time period (i.e., whether the groups change in magnitude differently in the time period, a group-by-time interaction). A significant group-by-time interaction would imply that the two treatment groups perform differently over time and therefore would have different slopes. Mixed-effects models account for the fact that observations within subjects (baseline and 3-months) are correlated, which will aid power in detecting differences over time.

Residual diagnostic plots were used to evaluate the assumption of conditional normality. For each model, this assumption was satisfied. All models are fit with PROC MIXED of SAS version 9.4 (SAS Institute, Cary NC).

3.4.1 Opioid dose

The first outcome measured at two time points (Baseline Tapering Visit and 3-month follow-up) is opioid dose, measured in milligrams of morphine equivalents per day or MED, and is used to evaluate for significant opioid changes during this time. The 16 participants had a baseline mean opioid dose of 150.53 MED (243.57 MED for the MTP cohort and 78.17 MED for the PEW cohort). The data was analyzed by time, group, and group by time, as mentioned above. Since the overall sample size was small, pooled MED data (dose analyzed by time) is the primary outcome. The average MED reduction from both cohorts from baseline to the 3-month follow-up was 34.84mg/day (p=0.049; 95% CI 0.186 to 69.49). This pooled data is depicted graphically in **Figure 8a** below; the different cohort's data are highlighted in different colours for interests' sake. Trends are difficult to appreciate on this data subset due to wide range of baseline MED, from 50 to 900mg of morphine per day amongst the 16 subjects. Therefore, these data were transformed by taking the natural log (log base e) of the MED values at baseline and the 3-month follow-up. This facilitates calculating an average percent difference in opioid dose, which is more relevant clinically. The log-transformed data, then exponentiated, shows that baseline opioid doses are on average 28.09% larger than at the 3-month follow-up doses (95% CI 8.25% to 51.57%). This equates to participants on average having a 21.875% reduction in opioid dose in the first 3-month period in the study with a p-value of 0.007. This data is graphed in **Figure 8b** below; a variety of downward slopes can be appreciated in both cohorts.

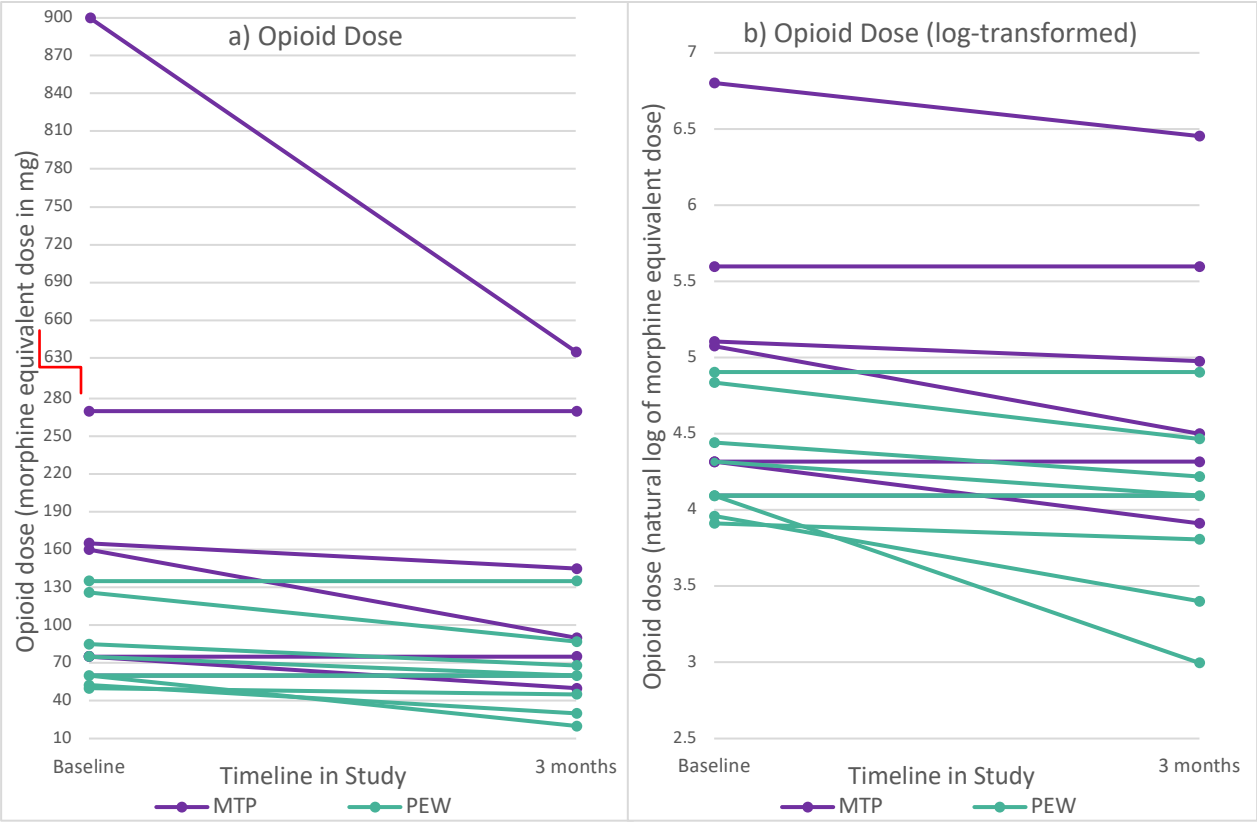

Figure 8: Opioid dose vs time side-by-side scatter plots (n=16)
a) Opioid dose vs time: morphine equivalent dose (MED) in mg from 0 to 3 months – scatter plot showing each participant's progress. An average 34.84mg reduction was observed (p=0.049), which is illustrated by lines mostly decreasing at 3 months with different slopes, but it is difficult to appreciate because the majority of the lines are compressed together in the bottom half of the graph (reason for the noted y-axis break at 280mg to 630mg)
b) Transformed opioid dose vs time: natural log of MED from 0 to 3 months – scatter plot showing the same data as in Figure 8a but transformed by natural log. An average 21.875% opioid dose reduction was observed (p=0.007). Again, lines trend downwards at different slopes, but more similarly and obviously.
MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

The MED data also reinforce that, on average, the MTP group has a higher MED overall than the PEW cohort as discussed in Section 3.2: Demographics. Pooled MED data from the baseline and 3-month visits confirm that the average MED is higher in the MTP group than in the PEW group. This group difference is not statistically significant in the first model, but the second, using the natural log of MED, it does show this to be a significant difference. The MTP group has average MED values which are 2.2 times larger than the PEW group (119.97% larger, 95% CI 4.5% to 362.9%). However, this difference in MED between groups is stable; it does not change significantly between months 0 and 3, meaning that there is no significant group-by-time interaction (p=0.249). In other words, there is no significant difference in opioid dose reduction between the two cohorts, MTP and PEW; their downward slopes are similar. **Table 10**, below,

shows the p-values for each analysis, with significant values highlighted in red. Additional data regarding the MED are displayed in detail in supplemental tables in **Appendix F-1.**

Table 10: Opioid dose modelled by time, group, and group-by-time using repeated measures model (n=16), significant p-values and their data points highlighted in red. This indicates an overall opioid dose reduction occurred.

Effect	Group	Time	Estimate	Standard error	Degrees of freedom	t-value	alpha	Confidence interval		Pr >|t| p-value
Morphine Equivalent Dose in mg/day										
Time (0 vs 3 months)	-	Baseline	34.8373	16.1563	14	2.16	0.05	0.1855	69.4891	0.0489
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	145.96	84.6371	14	1.72	0.05	-35.572	327.48	0.1066
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline& 3-month	-	-	14	-	0.05	-	-	0.2486
Log-transformed Morphine Equivalent Dose										
Time (0 vs 3 months)	-	Baseline	0.2475 *exponentiated:* 1.2809	0.07848	14	3.15	0.05	0.07923 1.0825	0.4159 1.5157	0.0070
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	0.7883 *exponentiated:* 2.1997	0.3469	14	2.27	0.05	0.04428 1.0453	1.5324 4.6292	0.0394
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline& 3-month	-	-	14	-	0.05	-	-	0.6257

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

3.4.2 Pain

The next outcome measured is pain, which is measured on the NRS, an 11-point scale from 0 to 10. The baseline score is compared to the score at three months, which evaluates for significant changes in pain over time. Studies have not shown opioid tapering to be associated with overall increases in pain[11,25], but opioid reductions can be associated with acutely or temporarily worsened pain[9,10]. This pooled data set shows trend improvements in pain despite a statistically significant drop in opioid dose. There was an average improvement of 0.968 points on the NRS, however, the p-value was just shy of significance at 0.059. These data are depicted in a scatter plot in **Figure 9** where a general downslope can be appreciated, although some lines do clearly increase. There was no significant difference in pain scores by group or group-by-time, indicating the cohorts PEW and MTP were not different at baseline or at three months. **Table 11**, below, shows the p-values for each analysis, with the p-value nearing significance and its

corresponding data point highlighted in yellow. Additional detailed data regarding pain scores are displayed in supplemental tables in **Appendix F-2**.

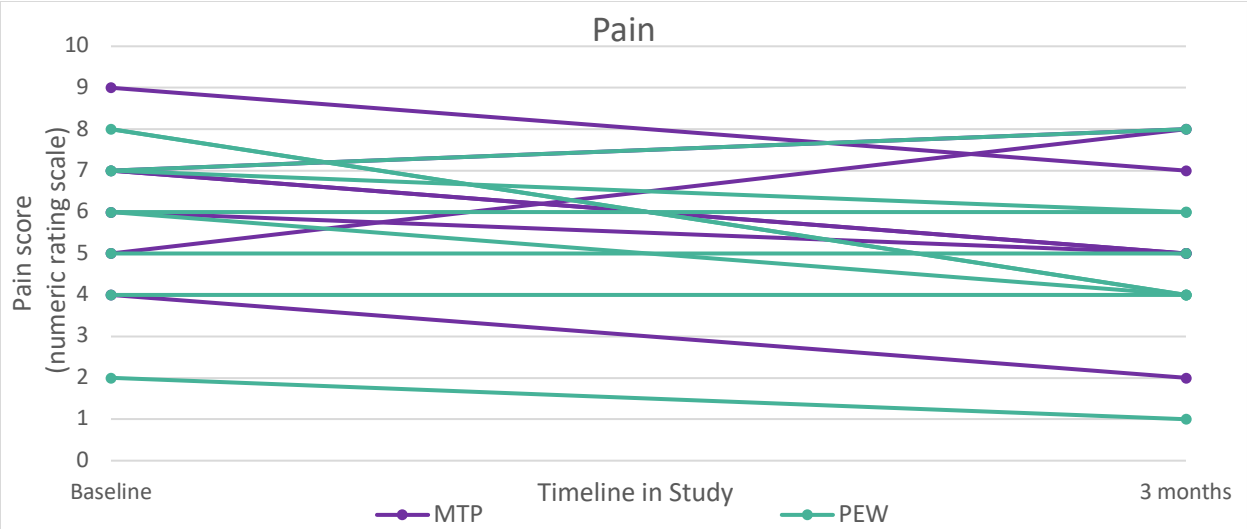

Figure 9: Pain vs time scatter plot (n=16): measured as an average weekly pain score on the numeric rating scale at 0 and 3 months – showing each participant's progression. An average 0.968-point (non-significant) reduction was observed (p=0.059). This reduction is visible as most lines slope downwards, but some increase.
MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort.

Table 11: Pain score modelled by time, group, and group-by-time (measured on numeric rating scale) using repeated measures model (n=16). Pain by time is close to significant, which indicates a trend toward improvement in pain. Near significant p-value and their data points highlighted in yellow

Effect	Group	Time	Estimate	Standard error	Degrees of freedom	t-value	alpha	Confidence interval		Pr >|t| p-value
Pain (numeric rating scale)										
Time (0 vs 3 months	-	Baseline	0.9683	0.4713	14	2.05	0.05	-0.04264	1.9792	0.0591
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	0.7937	0.8494	14	0.93	0.05	-1.0281	2.6154	0.3659
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0.5985

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

3.4.3 Health and wellbeing questionnaires

The results from five of the seven measured health and wellbeing questionnaires were compared from baseline to three months in this master's project in order to evaluate if decreased opioid dose coexisted with negative changes to health and wellbeing, measured on questionnaires evaluating physical health, mental health, quality of life, and risk of problematic opioid use. Recent opioid tapering trials have shown concerning worsening trends in mental health outcomes[11,99,100,135], so this was identified as a

priority for monitoring. None of these scores worsened in this time period; in fact, all point estimates are on the improvement side of zero and some scores even show trend improvements from baseline to three months. This indicates that no measurable harms have taken place. None of the health and wellbeing questionnaires have differences by group or group-by-time; all p-values were non-significant in these analyses. This indicates that the MTP and PEW cohorts had no difference overall, at baseline, or at three months.

The Pain Disability Index evaluates the impact of pain on various life functions, including family/home responsibilities, recreation, social activities, occupation, sexual behaviour, self-care, and ADLs [138]. At the 3-month mark, this score showed trend improvements, similar to pain scores. There was an average improvement of 5.325 points out of a total of 70 possible points on the PDI. This p-value did not achieve significance (p=0.064). These data are included in detail in a table in **Appendix F-3** with its p-value highlighted. **Appendix F-4** depicts this data in a scatter plot, where a general downtrend can be appreciated.

The GAD-7 screens for and measures anxiety severity[145]. The 16 participants in this study had trend improvements in GAD-7 scores at three months. There was an average improvement of 1.976 points out of a total possible of 21 points, from baseline to the 3-month visit (p=0.056). These data are presented in a scatter plot in **Appendix F-3** where again, a general downtrend can be appreciated. The complete data set table with its p-value highlighted is also in **Appendix F-4.**

The PHQ9 screens for and measures depression severity[132]. There were no significant differences or trends shown on this score. The scatter plot of this data shows just over half the lines slope down and the remaining have a weak upward slope. This graph and full data set with non-significant p-values are also found in **Appendix F-3** and **F-4.**

The PROMIS Global-10 provides two scores: the Global Physical Health score and the Global Mental Health score[141]. There were no significant differences or trends shown on either score, between baseline and three months. The table with complete data and non-significant p-values as well as scatter plots of both these scores can be found in **Appendix F-3** and **F-4** where no clear trends are visible. The Global Physical Score data go in different directions with varying magnitudes while the Global Mental Score has fairly flat slopes.

Lastly, the SOAPP-R screens for patients at high risk for opioid misuse and is intended to guide monitoring frequency for patients on LTOT[137]. SOAPP-R scores were measured during study recruitment, but also at baseline and three months to monitor for any changes. There were no significant differences shown on this score. The scatter plot of this data and a table of the complete data set with non-significant p-values are displayed in **Appendix F-3** and **F-4.**

3.4.4 Qualitative data

Study pharmacists have had over one hundred encounters (in person and over the phone) with study participants since the beginning of recruitment. They report their feedback and experiences with these encounters on the topics of study protocol, tools, results, participant experiences, and more. This qualitative data is summarized in the below **Figure 10,** and categorized into five fields: patient engagement, taper design, pain, withdrawal, other benefits (of tapering). This feedback will continue to inform changes to the overall project MTP protocol, with an aim of improving the MTP process and therefore better outcomes for participants.

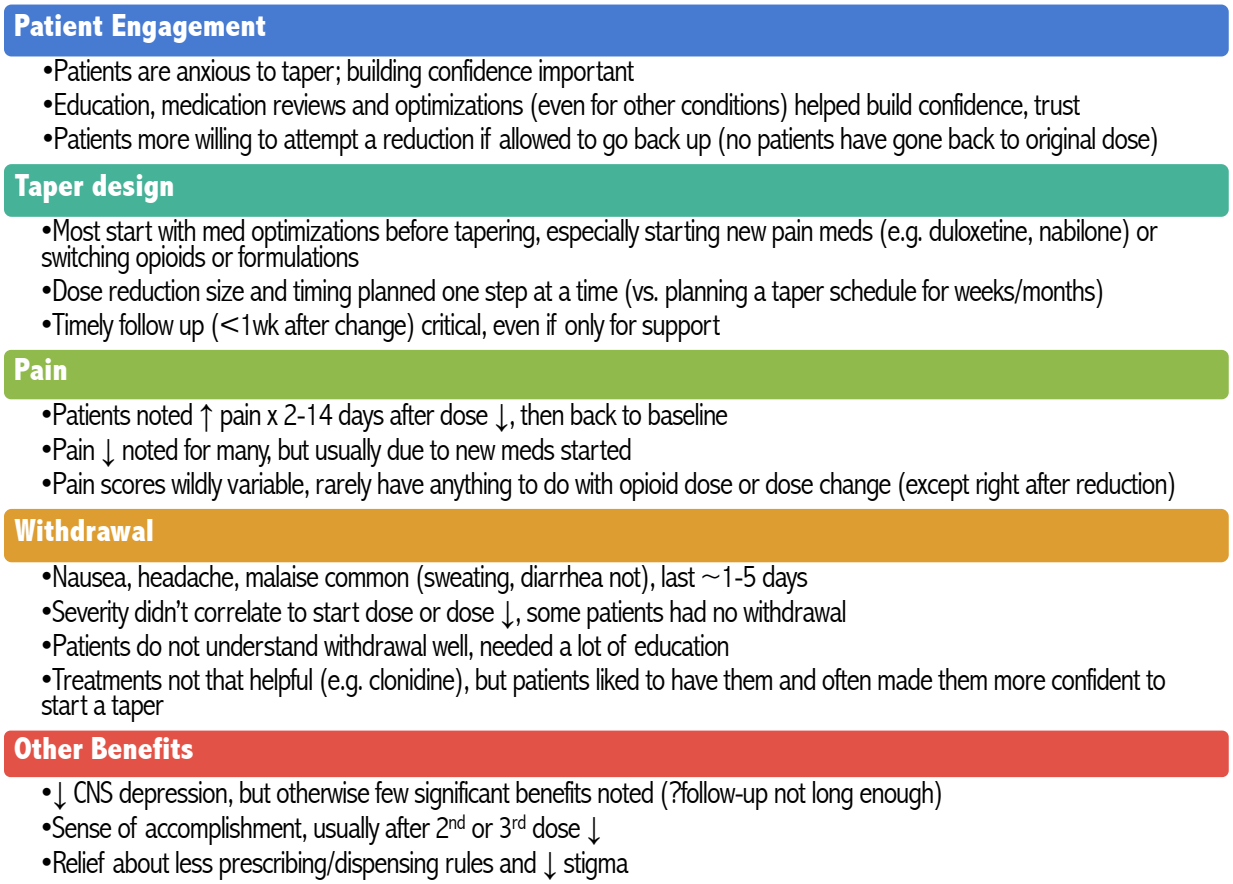

Figure 10: Qualitative feedback from study clinicians (pharmacists) on five aspects of the MTP: patient engagement, taper design, pain, withdrawal, and other benefits. CNS=Central Nervous System

3.4.5 Other data

This master's project was only intended to look at participants who had completed three months of the MTP, which has been presented above. However, at the time of data extraction for the master's project, five participants had completed all 12 months of the study. While their data has not been formally analyzed, their opioid doses at each in-person visit are highlighted for interest below in **Table 12**. Notably, all five participants experienced a reduction in opioid dose with an average decrease from baseline to 12 months of 44%.

Table 12: Preliminary 12-month opioid dose data: data from the first study participants to complete all 12 months of the study (n=5)

Participant (opioid)	**Morphine Equivalent Dose (mg/day)**				**% Change** (0 vs 12 months)
	Baseline	3 months	6 months	12 months	
MTP1 (hydromorphone)	75	50	38	0	**-100%**
MTP2 (morphine)	160	90	90	90	**-44%**
MTP3 (hydromorphone)	900	636	609	606	**-33%**
PEW1 (oxycodone)	60	60	45	53	**-13%**
PEW2 (fentanyl)	135	135	135	90	**-32%**
					-44% average

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

Chapter 4: Discussion

Recommendations from local, federal, and international guidelines include opioid tapering in patients with CNCP on LTOT in order to decrease the impact of the Opioid Crisis[8–10]. However, there is limited research on how best to taper, besides employing multidisciplinary teams[11,12,30,89,90]. The overall project seeks to develop strategies and tools to taper opioids in a successful, but also realistic and patient-friendly way. Based on existing research, and the gaps in that exist there, this project employs an interdisciplinary educational workshop (the PEW) focused on delivering ACT in an accessible way (one day, online) and a patient-centered, pharmacist-led tapering program (the MTP). All participants participate in the 12-month MTP while half are randomized to attend the PEW prior to starting the MTP. We anticipate these features will make tapering more successful due to increased patient involvement and buy in. The hypotheses of the overall project include significant reductions in opioid dose with improvements in pain, pain disability, depression, anxiety, quality of life, pain acceptance, and valued living in both cohorts, and that the PEW cohort will have larger improvements in both categories. The master's program aims to show that both the PEW and the MTP are successful at this preliminary stage as well as identify areas for improvement and optimization for the overall project in order to produce a ready-for-practice tapering strategy upon completion. The hypotheses of the master's project are similar, but due to smaller data sets (fewer participants and shorter duration), smaller effects are expected. They include 1) trend reductions in opioid dose, 2) that the PEW is feasible to implement and acceptable and valuable to participants, and 3) the data, including feedback on the MTP and PEW, will be used to implement study optimizations, resulting in overall study improvements. Section 2.3, 2.4 and 2.5 list the Objectives, Hypotheses, and Measured Outcomes in greater detail.

The data from the master's project - a preliminary review of the overall project - showed that while recruitment is slow, attrition rates are only 16%, slightly lower than the 20% that was predicted based on previous research[27,94,95]. As well, many changes to recruitment strategies have already been implemented based on this data and increased recruitment has been seen, therefore satisfying Hypothesis 3 (master's project). When evaluating PEW effects, it was found to have resulted in a statistically significant improvement in opioid knowledge but no significant change in tapering readiness. Feedback on the PEW content was strongly positive with a 78% overall acceptance rate on Likert scale and 100% positive in freeform feedback. Feedback on PEW format was more mixed at approximately half and half, showing additional accommodations would likely be welcome. This did not satisfy the second hypothesis of the master's project, as the threshold for acceptance was set as 80%. However, as detailed below in Section

4.1.2.3, the data do likely show an overall successful workshop. The PEW has also already implemented changes based on some this data to improve future PEWs, again satisfying the third hypothesis, and may predict success in the overall project. Of the master's project results, the most compelling is arguably that the MTP had a statistically significant reduction in opioid dose with an average reduction of 21.8% (p=0.007). Hypothesis 1 (master's project) anticipated only trend reductions and thus the data exceeded the prediction. As well, even with such a significant reduction, scores on pain, physical, and mental health did not worsen. In fact, pain, pain disability, and anxiety scores trended towards improvement, showing the MTP has more benefit beyond successful opioid tapering and may predict that the overall project will satisfy its hypothesis regarding improvement in these fields.

This section will go through each of the results mentioned in the previous chapter. With each result, the interpretation, including comparison from what occurred to the hypotheses mentioned as well as implications to the overall project will be discussed. If relevant, predictions for the outcomes in the overall project will be included as well. These results are also compared to any relevant existing literature with compelling differences highlighted. Strengths and limitations of the data and its interpretations are also discussed followed by recommendations for next steps.

4.1 Interpretation of Results

4.1.1 Recruitment and attrition

Previous opioid-tapering trials have inconclusive data sets[11,25,93], often at least partially associated with high drop-out rates[27,94,95]. Therefore, data on recruitment and attrition are important to report to inform the overall study and improve chances of participant and trial success.

4.1.1.1 Recruitment

Twenty-five participants have been recruited for the overall study with a 49% recruitment rate (current to January 2023). This is significantly fewer participants than anticipated coming up on the 2-year mark. However, it does closely match the recruitment rate of Sullivan et al, a similar study design[25.] Low recruitment also affected the sample size for the master's project, which was intended to provide early insights to the overall project with preliminary data.

Challenges to recruitment began with delayed start dates associated with delayed ethics approval due to in-person visits requiring a separate COVID-19 consent, and unanticipated delays to REDCap

establishment (as detailed in Section 2.1.2). Early referral numbers were also low; study promotion was difficult at primary care clinics because team members were segregated or working off site due to COVID-19 restrictions and team meetings were focused on pandemic planning. Recruitment at pain sites, without pharmacists on site, was even more delayed due to difficulty arranging meetings and also in part due to staff hesitancy to get involved during increased pandemic workload and short staffing. Patients themselves were also hesitant to join a trial that included medication changes during the pandemic as well as attend in person appointments (especially since AWW was a COVID-19 clinic, assessing and treating active COVID-19 patients). Appointment cancellations, no-shows, and reschedules were common. In-person visits were also a logistical difficulty – rules for the prioritization of non-COVID-19 patients as well as the procedures for in-person visits changed multiple times throughout study duration. Clinic room availability was impacted as well (as many rooms were reserved as symptomatic or COVID-19 treatment rooms), care for COVID-19 was prioritized over study visits, and clinicians were pulled to work on pandemic treatment as well as cover redeployed staff.

These challenges resulted in many lessons learned and, as a result, changes were made to recruitment processes. Although each site had its own nuanced recruitment process that was intended to facilitate recruitment at each location, it became clear that a more proactive approach was needed. This shift included frequent promotion of the study to clinic teams (reminder meetings, check ins, etc.) as well as increased efforts with study advertisement posters directly targeted to patients in more visible locations. There was also a change in direction from waiting for referrals to seeking out eligible patients. Instead of sending lists of patients on opioids to providers to determine eligibility and refer, study pharmacists reviewed lists and sent eligible patient files to clinic staff to contact for permission for the study team to connect with them. Patients that had already been referred were permitted to defer or hold enrollment (with frequent check-ins) and many of these patients subsequently enrolled in later months. **Figure 5** in Section 3.1.1 shows a flow chart of the effects these changes had on recruitment at AWW. The tools used for study promotion before and after changes were made to processes can be found in **Appendix A-1** through **A-3**. An additional site, HSC Pain Management Centre, was also added in response to low recruitment numbers, but as mentioned above, also presented difficulties and delays.

In-person visits continued despite the pandemic. Converting to virtual visits was considered, but due to the importance of relationship building and clinician-patient trust in the study, which is brought up as a barrier to tapering in previous literature[91], they were felt to be important enough to keep. Especially

since pivoting the In-Person Screening Visit to a virtual visit would have required a new process to sign consent and therefore a protocol amendment, which would have delayed recruitment further. In order to improve convenience and decrease in-person contact time, if participants were randomized to the MTP cohort during the In-Person Screening Visit (i.e., they did not have to be scheduled for the PEW), a back-to-back visit with the "Baseline Tapering Visit" (the first visit of the MTP) was facilitated.

Data on recruitment summarized in this master's project has been instrumental in improving the reach of this project in keeping with the master's project objective to contribute to study procedure improvements and optimization (Section 2.3, Objective 3, master's project). Referrals and enrollments have been steadily increasing since adjustments to recruitment strategies were made, while maintaining a fairly constant recruitment rate of approximately 50% throughout.

4.1.1.2 Sample size

These delays and adjustments were considered when deciding on the sample size for the master's project. In March of 2022, well into study recruitment and when recruitment optimization was beginning, 10-15 participants completing the PEW and 25 participants completing three months in the MTP was proposed, with contingencies if those numbers were not met in time. While 25 participants have now been recruited, by the necessary data extraction date (December 2022), there were only data from twenty participants available (see Section 3.2 Demographics). Participants exiting the study (attrition) prior to their 3-month visits; 3-month visit no-shows, cancellations, and/or rescheduling; delayed data collection; and slow processes signing on the fourth site (HSC) all contributed to not meeting the 25 person MTP goal. There were 11 participants that had completed the PEW by the deadline, with ten participants' data useable, which met the target. However, as seen in the results section, the collected data was able to show significant and meaningful results even with small numbers.

4.1.1.3 Attrition

Four participants were lost to attrition out of the twenty-five participants recruited in the study's progression up to January 2023. This is an attrition rate of 16%. An attrition rate of 20% was estimated for the overall project, based on rates in other opioid tapering studies[27,95].

Compared to other opioid tapering studies, the overall project has multiple different strategies to mitigate attrition, although a clear reduction to attrition rates was not observable with current data. As

discussed in detail in this project, the study design including ACT, high patient involvement, frequent and consistent follow up, and allowing a bilateral taper direction, aimed to mitigate attrition observed in previous tapering trials. Two other factors potentially influencing attrition include, first, that most participants are early on in data collection (less than 6 months of enrollment), which would underestimate attrition and second, attrition rates could be negatively affected because this study has taken place entirely during the COVID-19 pandemic.

One participant who left the trial cited increased stress and worsening mental health as the reason for withdrawing from the study. While they did not mention COVID-19 specifically, the pandemic has been shown to have negatively affected mental health across Canada[155]. Another attrited participant cited a hospitalization (unrelated to pain, but had a subsequent effect on pain) as the reason for dropping out. It is common for patients with CNCP to have comorbid conditions, and during COVID-19, these may have taken precedence over pain or opioid management. This may be especially true for common comorbidities in patients with CNCP like rheumatoid arthritis or diabetes, which increase the risk of severe outcomes with COVID-19. While not cited as a reason for attrition, multiple participants had difficulty with in-person visits: concerns about them being risky, inconvenient (due to screening, masking, or not being able to bring a support person) or not possible (in the case of symptoms or a positive COVID-19 test). Another participant no longer in the study cancelled their Baseline Tapering Visit due to a viral illness and was subsequently lost to follow-up. Potential participants also voiced concerns about making medication changes during a time of an overworked and under-supported healthcare system and how maintaining stability was a priority, which could also affect participants throughout the study. It is worth noting, though, that the COVID-19 pandemic may have had a positive effect on attrition for some people. For example, those working from home may have been more likely to be able to participate in workshop, though this was not specifically reported.

Considering three out of four participants lost to attrition have some link to the pandemic, COVID-19's effect on attrition may offset the potential under-estimation of attrition associated with being early on in data collection. And therefore, it is likely that the unique features of the overall project's study design as described above are playing a role in this lower than predicted attrition rate. Feedback from withdrawn participants and from patients at study sites that are struggling to enroll or stay enrolled during this master's project has helped and will continue to help with overall study procedure improvements and optimization, as listed as an objective (Section 2.3, Objective 3, master's project).

4.1.2 Patient Education Workshop (PEW)

A major aim of the master's project is to inform the overall study in order to contribute to procedure improvements and optimization (Section 2.3, Objective 3, master's project). Prior to data extraction and analysis, these optimizations were made to the PEW based on clinician experience and informal participant feedback.

One of the first optimizations made to the overall project was PEW group size. The first few PEWs in 2021 had small numbers of participants (three to four). It was determined by study clinicians during feedback discussions that an ideal group size would be larger (five to fifteen) to increase conversation and engagement between participants. This is similar to group sizes in other studies evaluating ACT workshops, where five to ten is commonly seen[114]. As such, patients at study sites that were not involved in the study (due to eligibility or other reasons) were invited to fill groups. Subsequent PEWs were larger, and a minimum group size was set to five participants. This required changes to scheduling based on referral numbers. More recent PEWs have longer times between each session in order to increase group sizes.

Optimizations to the virtual nature of the workshop have also been ongoing. Although the PEW was always presented virtually, it was originally planned as an in-person workshop. The COVID-19 pandemic required avoiding in-person group events, so the PEW was redesigned as a virtual workshop. Based on the recommendations from Dindo et al to tailor ACT to the intended populations, noting that ACT has been successfully delivered in many different formats, including online and telehealth[123], a pilot online PEW was planned and successfully completed. As virtual group education was a relatively new practice in the WRHA, optimizations to the virtual aspect of the workshop continued throughout the study duration, especially as everyone became more familiar and adept at the activity. As PEWs progressed, facilitators were able to share accommodations used by past participants to improve their comfort during the workshop. Some of these approaches included using their tools for pain during the workshop (e.g., heating pads, movements, specific positions or furniture), going off screen or turning off camera as needed (e.g., during pain flare or wave of fatigue), and taking extra breaks when needed. The schedule of the day has also been adjusted, placing different content and breaks at different times to establish the most cohesive day. An example of a PEW agenda from the most recent workshop is included in **Appendix D-1**. Facilitators have also been able to schedule PEWs with significant consideration to the preference of participants because of the online nature of the workshop; since all facilitators don't need to be on screen for the

entire workshop, it became easier to schedule around four clinician's busy schedules. While facilitators and participants have noted positive relationship building and learning experiences during the online PEWs, facilitators have noted more difficulty getting concepts across on a virtual platform and more frequent inappropriate participant behaviour (e.g., missing social cues, sharing inappropriate or irrelevant personal stories, or taking up significantly more time than other participants) than would be expected in an in-person workshop and have therefore had to develop and hone different mitigation strategies. Facilitators have been incorporating more frequent check-ins and sharing time with participants to give opportunities for questions or demonstrate what they've learned in order to catch misconceptions and build shared experiences among participants. As well, to help participants with behaviour and foster a safe environment, participants are warned about emotions that might come up and encouraged to leave and come back if they need.

While the ongoing PEWs and adjustments already made would indicate that these workshops are feasible to implement (Section 2.3, Objective 2, master's project), it is useful to use the additional data collected to affirm this further. With significant data collected from the PEWs, it is possible to evaluate the other primary objective: the PEW is preliminarily feasible and acceptable to participants (Section 2.3, Objective 2, master's project). Three categories of data were collected for the PEW: opioid knowledge quiz scores pre- and post-workshop, tapering readiness pre- and post-workshop, and participant feedback on the workshop.

4.1.2.1 Opioid knowledge quiz

There were no specific objectives or hypotheses regarding scores on the opioid knowledge quiz; however as previously mentioned, this data helps to strengthen the observation that the PEW was feasible and provided value (Section 2.3, Objective 2, master's project).

Opioid knowledge increased pre- to post-workshop as measured on the opioid knowledge quiz, the 6-question quiz on both the pre- and post-workshop questionnaires (found in **Appendix C-2**). A mean increase of 1.3 points was observed ($p=0.031$), indicating that participants increased their opioid knowledge. No specific question was associated with a significant improvement on its own, therefore it is likely that the workshop provided broad base of information and that participants started with different levels of knowledge on different subjects.

Pre-workshop scores were variable, ranging from 2/6 to 6/6, representing that participants are coming from different places of knowledge prior to study enrollment. Post-workshop, however, was much more consistent: all but one participant had five or six out of six questions correct, indicating that most participants had a good level of basic opioid knowledge leaving the workshop.

All questions had more correct answers post-workshop compared to pre-, but it is not surprising that the lowest score pre-workshop was also the lowest score post-workshop. The fifth question, "Lowering the dose of an opioid (tapering) will cause pain to increase," was the only question to have more than one participant answer it incorrectly post-workshop. It is a bit of a tricky question since tapering *may* cause pain levels to increase temporarily. This reinforces what is seen in many opioid tapering trials; patients with CNCP on LTOT are concerned about worsening pain associated with opioid tapering, despite these same trials showing patients are able taper without significant pain increases[11,25]. While this is an important point moving forward into the MTP, it is unlikely to be a concern as participants progressing to the MTP have one-on-one visits with the study pharmacist where they address any concerns regarding tapering and discuss tapering goals that participants feel comfortable with.

Based on the improvement in opioid knowledge, the workshop has been shown to be feasible and effective in educating participants on opioids, their risks, and tapering.

4.1.2.2 Tapering readiness

There were no hypothesis or objectives directly related to tapering readiness but would again contribute to PEW feasibility and value (Section 2.4, Objectives and Hypotheses 2 and 3, master's project).

Tapering readiness was measured on the pre- and post-workshop questionnaires, firstly by asking if participants were interested in reducing their opioid dose, and then if they were, rating their readiness to taper as "not really ready", "somewhat ready", and "very ready". Ultimately, this test showed that there was no change or improvement in taper readiness; the p-value of this test was not significant, but because it assessed for a change (and not establishing a certain level of readiness), it does not emphasize those that could not improve readiness because they were already at the highest level. It does show that a reduction in readiness did not occur.

Of the ten participants analyzed, 70% of them either increased in tapering readiness or were already "very ready" and stayed at that level. These participants are well positioned to proceed into the MTP, where tapering goals and next steps are discussed, based on these scores, even if a p-value overall is not significant. Of the remaining 30%, 20% did not change in readiness and 10% of participants decreased in readiness (from somewhat to not really ready) but continued to rate themselves as wanting to taper.

Notably, all participants rated themselves as wanting to be able to reduce their opioids post-workshop, which could be described as in the "Contemplation," "Preparation," or "Action" (but not "Pre-Contemplative") stage of change for opioid tapering[156]. This is the most important feature of this data, even though the change in readiness was more variable, because participants have 12 months in the MTP to develop an individualized tapering plan. Recommendations for patients on LTOT in these stages of change mirror much of what is done during the MTP, including support and goal setting[156]. The Baseline Tapering Visit in the MTP, which immediately follows the PEW, includes a medication review and adjustments to management strategies for their chronic pain and other conditions, which may also improve tapering readiness, but less likely to increase desire to taper. Based on participants wanting to taper post-workshop and having self-reflected on their readiness, the PEW has shown to be effective in preparation for the MTP and therefore feasible to implement.

4.1.2.3 Workshop feedback

Feedback on the workshop is gathered from participants on two topics - workshop content/value and format - using two types of questions, including Likert scale and freeform. Part of the second hypothesis for the master' project (Section 2.4 , Hypothesis 2, master's project) was that feedback from participants would indicate overall acceptance and value, pre-defined as at least 80% responding with 'agree' or 'strongly agree' on Likert scale questions on both topics.

All ten participants agreed or strongly agreed that they would use what they learned during the PEW to help manage their pain but only 78% agreed or strongly agreed that the PEW provided value to their pain management. Zero participants disagreed (or strongly disagreed) with either statement. Only one participant responded "neutral" to the values question and because one participant left that question blank, one neutral response was enough to decrease the overall acceptance rating below 80%. The average acceptance rating on the two questions is 89% and is well above the 80% cutoff. Freeform feedback on the content of the workshop validates this. Every comment collected on the content of the

workshop (14 comments from nine of the ten participants) was positive. There were no neutral, constructive, or negative comments. This clearly illustrates a valuable and accepted workshop from the perspective of the participants involved.

The acceptance of the format of the workshop is less clear. Half of all participants agreed or strongly agreed with both statements about the format. The first question on basic format (full day, online) had 30% respond as neutral and 20% disagree that they found it worked well with their needs. The second question about not having barriers had 40% respond neutral and 10% disagree. No one strongly disagreed to either question. The freeform data closely matches the Likert scale questions on this topic, indicating mixed acceptance of the format. Interestingly though, some of the feedback directly opposed other participants (e.g., one online day was easier to book off work vs a full day was difficult to get off work). This opposing feedback highlights how patients living with chronic pain have complex and unique challenges and barriers to care. Considering this, it is notable that all participants in the PEW group were able to attend and complete the workshop, although many did require accommodations, such as turning their camera off, taking unscheduled breaks, missing short sections, and cancelling and rescheduling to the next workshop. Other studies that have employed lengthier ACT interventions have up to 30% drop out rates with multiple participants not able to complete the workshop series and therefore limited and incomplete data[114]. Feedback from these PEWs as well as the accommodations used have and will continue to inform changes to the PEW and ultimately improve the overall project. As mentioned above, offering participants accommodations has already been employed and met with success. The team is always considering new changes, since one format for everyone does not seem to work well.

While only one of four Likert statements met the pre-defined patient acceptance rate of 80%, these data describe a widely accepted workshop in a group where delivery is difficult. Taking into account quantitative and qualitative data on content acceptance, it is clear that this first group of ten participants found the workshop added value to their lives. The format feedback is harder to interpret, but considering previous trials' difficulties, it is likely that this workshop is accessible enough, with room to accommodate participants further yet using the feedback gathered.

4.1.2.4 Summary

Based on clinician experience and feedback as well as significant data collected as part of this master's project, the PEW has been feasible to implement with success imparting knowledge on opioids and opioid

tapering and tapering readiness. Feedback from participants indicates an accepted and valuable workshop, with the caveat more optimizations and accommodations will be made in order to continue to improve the acceptance of the format.

4.1.3 Multidisciplinary Tapering Program

The master's project's objective for the MTP was to evaluate the impact of the PEW and the MTP on participants' opioid dose early on in the 12-month trial (Section 2.3, Objective 1, master's project) with anticipated trend reductions in opioid dose (Section 2.4, Hypothesis 1, master's project). Participants' baseline data from the Baseline Tapering Visit were compared to the 3-month follow-up data to assess for any changes or trends in MED, pain scores, and to responses to five of seven health and wellbeing questionnaires (**Appendix C-1**). While no specific hypothesis regarding other scores was made for the master's project, the overall project includes anticipated improvements in all categories: pain, pain disability, depression, anxiety, quality of life, pain acceptance, and valued living (Section 2.4, Objective 3, overall project). The master's project instead evaluated these scores as safety outcomes: to ensure no significant worsening in scores, which would indicate a preliminarily successful tapering program that doesn't cause harm. Assessing these scores is recommended in the literature in order to assess the full spectrum of the effects of a taper[94,99]. A recent systematic review of opioid tapering trials recommends "to successfully evaluate a reduction strategy, patient outcomes, such as pain severity and quality of life, should be assessed throughout the study to map the risks and benefits of opioid reduction strategies"[94] . Similarly to the PEW, the master's project also sought to use feedback from early on in the MTP process to inform the overall project, contributing to procedural improvements and optimization (Section 2.3, Objectives 1 and 3, master's project).

As with the PEW, alterations and optimizations have been made to the MTP prior to extraction and analysis of this data. Clinician feedback and experience, previously detailed in the Section 3.4.4, as well as feedback from participants has already impacted the MTP process, including individual clinician adjustments to hone communication strategies and other optimizations based on individual experience. One notable difference from the original study plan is that instead of preparing a full tapering schedule based on the study protocol and existing literature [26,28] from a starting point to their goal, clinicians and participants found more success planning one taper step at a time and then choosing the size and timing of the next step based on the tolerability or success of the previous step. Goal setting for end opioid dose is still an important feature of this plan, but the journey remains mostly unknown at the outset. Many

participants, under the guidance of the pharmacist, have made both short term and long-term tapering goals. So, while the overall project study protocol outlines an example tapering schedule based on previous trials and guidelines [26,28], most participants end up co-developing their own individualized tapering plan with the pharmacist that looks quite different than this recommended tapering template. Some have been faster and some slower, but most have had much more variable dosing changes with inconsistent intervals, plus breaks or pauses as needed. This is in line with newer opioid tapering trials that include more flexible tapering plans and patient input [26,28] and recommendations for more tailoring taper plans to individual patients[94]. It is also similar to the earlier mentioned retrospective study from Saskatchewan that compared patients on opioids with pharmacist involvement to those without and found that when pharmacists were involved and made recommendations for a tapering plan, tapering was more successful, regardless of the plan carried out[31]. Essentially, the taper planning was left to the pharmacist to apply to their specific patient, as has occurred here; however, this trial has significantly more patient involvement (since pharmacists were off site in the Saskatchewan trial[31]) and has a prospective design.

As mentioned in the interpretation of recruitment data, Section 4.1.1.1, in-person clinical visits were identified as valuable and integral to the patient-provider relationship, and were not converted to virtual, even during the COVID-19 pandemic. Study pharmacists reported that these in-person visits, especially at the beginning of the MTP (In-Person Screening Visit and Baseline Tapering Visit), made it easier to have good discussions and build trust. While undergoing the medication review portion of the Baseline Tapering Visit, patient-provider trust likely enhanced patient engagement in decision-making regarding therapy changes, especially preliminary changes to the opioid in preparation for a taper (e.g., switching formulations or drugs). As evidenced by approvals from both the BREB and the WRHA appropriate safety precautions were taken to ensure safety of both clinicians and participants.

Evaluating the success and the safety of the MTP is an important part of the master's project. This requires analysis of the data on opioid dose, pain score, and health and wellbeing questionnaires collected from the 3-month visit compared to baseline numbers in order to assess for improvements, stability, and if there is any worsening. Although these quantitative data only assess two visits with questionnaire scores to compare, there are also up to twelve weeks of data from the on-going telephone follow-up visits to draw qualitative data from and gauge preliminary risks or benefits to participants.

4.1.3.1 Opioid dose

The master's project hypothesis regarding opioid dose, measured in MED in mg, was that trend reductions in the overall group MED would be observed. At the 3-month mark, when participants still have 9 months left in the MTP to continue opioid tapering and meet their goals, large or statistically significant changes were not expected. Study pharmacists noted that many participants were not yet ready to taper at the beginning of MTP, but often were interested in starting after medication review changes were made, including optimization of non-opioid pain medications. This, in addition to a sample size smaller than expected (see explanation in Section 4.1.1.2), meant that significant changes as well as any perceptible differences between cohorts, PEW+MTP and MTP-only (referred to as PEW and MTP respectively), were not expected but all were tested for.

Opioid dose pooled data (MTP and PEW cohorts combined) was, however, significantly lower at 3 months compared to baseline doses. This was seen when compared by mg of morphine equivalent and by percent change (p-values 0.049 and 0.007 respectively). While the difference in mg of morphine was also significant, it is less relevant to clinical practice, especially considering such variable baseline MEDs (as mentioned in Section 3.2). A log transformation of MED data was chosen in order to calculate and compare percent differences and relate these to literature values. The magnitude of the percentage difference was 21.875% lower. Sullivan et al described clinically meaningful opioid reductions [25] and based on their work, a target 30% dose reduction was selected for the overall project. With the overall project powered to detect this MED reduction of 30%, it is of interest to note that the master's project data has already demonstrated a nearly 22% MED reduction in only the initial 3 months of data reviewed. This may be attributable to close participant to clinician relationship and trust as well as what has been mentioned about the differences in our study design compared to previous opioid tapering studies: pharmacist-led interdisciplinary program, close follow-up, allowed bilateral tapering directions, and the PEW. Previous studies have not been able to reach statistical significance, often due to incomplete data associated with low recruitment and high drop-out[25,94], so it is difficult to compare. However, some notable comparators include the previously mentioned Saskatchewan study, which showed a 17% reduction in opioid dose[31] and Sullivan et al, which showed a 43% reduction in 34 weeks, but was not significantly different than the comparator[25] . This 22% reduction in 3 months is strong data that predicts the overall project is very likely to achieve a clinically significant reduction with a larger sample size and longer duration.

We also compared pooled dose data among cohorts, PEW and MTP, to capture any significant differences. Using pooled data from both the 0- and 3-month visit, it confirmed what was observed in the demographics results, Section 3.2, that the MTP cohort is on higher opioid doses on average. While analyzing average overall MED in mg between groups was not statistically significant, percent differences were significant. Specifically, the MTP group has a 2.2 times larger average opioid dose than the PEW group, with a p-value of 0.039. Again, this anomaly is likely due to the small, uneven sample, which is why pooled data was used for the primary outcome of opioid dose by time. Block randomization could also be an important factor, since the sample size is small enough to be weighted by unequal blocks: this sample analyzes 7 participants from the MTP and 9 from PEW. This difference is unlikely to affect the validity of the data since pooled data (both cohorts) was always the intended analysis for the master's project. If there are any remaining substantial baseline imbalances at the time of the overall project's analysis, they will be adjusted for as necessary. This difference is likely to prevent the master's project from detecting a significant difference between groups by time for any outcome, which was observed.

This analysis of pooled opioid dose difference between cohorts was necessary to evaluate for any group-by-time differences, i.e., to capture if the two cohorts had different changes in opioid dose over time. This would assess if the PEW cohort was more effective at opioid tapering than the MTP group, as is predicted in the overall project. As mentioned above, due to the unequal and small samples and short duration, the master's was unlikely to be able to detect these differences and it ultimately did not: these values were not significantly different, as shown by large p-values (0.249 for mg of morphine equivalent change and 0.626 for percent change). This likely does not predict much for the overall project; it is possible the overall project with a larger sample size and longer duration will be able to detect a larger dose reduction in the PEW group than the MTP even though not shown in this data due to the limitations mentioned here. The metrics used to evaluate the PEW's effectiveness in the master's project, including improvements in opioid knowledge scores, tapering readiness changes, and feedback, may be a better predictor of PEW cohort performance in the overall project. The largely positive results on these metrics (detailed in Section 4.1.2) speaks to the value of the PEW and may predict that the PEW cohort will have a larger reduction in opioid dose than the MTP cohort in the overall project. The lack of difference between cohorts shown here in this preliminary MTP data is less important than it would be if these other metrics mentioned to measure the PEW did not show that it is a valuable addition to the protocol.

The data from the five participants who have completed all 12 months of the study showed further opioid dose reductions, or maintenance of established reductions, from month three to twelve. This strengthens the validity of the master's project's 3-month opioid dose reductions as a predictor of the overall project's success. Concerns about the study design including allowances for bilateral taper direction and the impact that may have on taper success can be at least partially assuaged. These five participants' continued success throughout the 12-month program suggests that the design is not associated with regression to baseline opioid doses or even overall increases between months 4 to 12. The 44% average opioid dose reduction observed in these five participants is comparable to the magnitude of the non-significant reduction shown in the trial by Sullivan et al[25] and exceeds the 30% target of the overall project. It also follows the trajectory of the 3-month data presented here, again reinforcing the validity of this project's data from the 16 participants at the 3-month mark.

4.1.3.2 Pain

The master's project did not include a hypothesis about pain scores, but their analysis was included to evaluate any early risks of opioid tapering that may be captured. Short-term worsening in pain is commonly seen in clinical practice and opioid tapering research (sometimes referred to as "rebound pain"), that typically resolves back to baseline in a number of weeks[9,10]. Generally opioid tapering has not been shown to increase overall pain scores[10,11] and there have been some trends showing improvements[11]. As previously mentioned, these improvements could have numerous rationale, which have been discussed in the literature. Firstly, reduced doses may result in reduced adverse effects due to opioids, potentially including symptoms such as fatigue and cognition deficits which can impact pain; secondly, reduction of OIH and/or between dose withdrawal pain may occur with lowered doses, resulting in pain reduction overall; and lastly, studies often provide participants with alternative or additional treatments or coping mechanisms for pain, augmenting further the benefits observed from opioid reduction[11,90,93].

The master's did not analyze the pain scores measured at weekly follow up visits (besides through clinician feedback), which would have captured any acute worsening in pain after opioid reductions. It was predicted that the 3-month mark may be at the start of the tapering process for some participants and therefore potentially capture periods of rebound pain and also too soon to see much improvement in OIH or opioid-related adverse effects. Any improvements to pain in the PEW cohort due to ACT would

likely also not show on the master's project since pooled data were analyzed. Therefore, pain scores were expected to remain stable or perhaps trend up.

However, despite a significant average reduction in opioid dose, meaning that the majority of participants were undergoing a taper by the 3-month mark and would be potentially experiencing that acute worsening of pain, trend reductions in pain scores were seen. An average of just under 1 point reduction on a 0-10 NRS was observed from pooled MTP and PEW data from baseline to 3 months (0.968-point decrease, p=0.059). This coincides with current literature showing that opioid tapering is not associated with worsening in pain overall[10,11], even this early on. In studies evaluating interventions to reduce pain, a clinically important reduction on the NRS is often defined as 2-3 points, or an approximate 30% reduction[153]. The 0.968-point improvement shown in this data did not reach the statistic or clinical threshold for significance and therefore suggest only that there is no worsening in pain. The qualitative data collected from study clinicians during phone visits summarized in **Figure 10** in Section 3.4.4 does report a subjective reduction in pain overall as a result of the MTP and that pain is not specifically correlated to opioid dose (except acute changes). This may add validity to the trend reductions seen. Unfortunately, current unanalyzed data from the 5 participants who have completed 12 months do not add much to the interpretation of this data. All 5 participants had quite variable pain scores throughout the study duration; some fluctuated by more than 4 points week to week or month to month. The overall project will evaluate the averages and slopes of pain scores in order to determine if there is any improvement overall. But, due to this variation, comparing only two data points (as was done with MED), especially in this small group, is not very descriptive or an accurate depiction of what occurred. For interest's sake, there was an average 0.8-point reduction from the week of the Baseline Tapering Visit to the score from the week of the 12-month visit in those five participants. This does not impact the interpretation of the pain scores changes or clinician feedback regarding pain in this preliminary review.

The features of the MTP, including medication reviews and optimizations, are the most likely contributor to these trend improvements in pain scores at 3 months. While it is possible that participants who tapered significantly by the 3-month mark may see some improvements to OIH[53], it is less likely. Medication reviews occur at the Baseline Tapering Visit and are followed by therapy optimization. At this visit, pharmacists often added non-opioid pain medications, improved control of chronic conditions that may be exacerbating chronic pain (e.g., treating uncontrolled mental health leading to improved sleep, which can have an impact on pain[157]), or deprescribed ineffective medications that may have been causing

side effects that worsen pain (e.g., constipating vitamins contributing to abdominal pain). They also gave advice about non-pharmacological methods to improve pain. Some of these details are summarized in the clinician feedback in Section 3.4.4, including in **Figure 10**, where it is reported that reduced pain scores correspond to new medications. This emphasizes the referenced value of pharmacists on multidisciplinary teams treating patients with CNCP, especially those on LTOT[31,75–77,82–84]. Pharmacists also facilitated referrals during the Baseline Tapering Visit, including to physiotherapy or other allied health, which could also contribute to improved pain, but these occurred in fewer participants (compared to all participants having a medication review), so is less likely to have as strong an effect. It does, again, emphasize the role of the multidisciplinary team, which is recommended for opioid tapering in the guidelines mentioned in Section 1.4.1[9,10].

A potential criticism of these improvements – which may be, at least in part, due to early medication reviews and optimizations – may be that pain reductions will plateau or not persist throughout the remaining 9 months of the study. If this is indeed a veritable phenomenon of this study, it is possible that the overall study won't succeed in reaching a clinically significant reduction in pain score at 12 months. However, most of these medication changes are likely to take time to reach full benefit, as many non-opioid medications that have been added throughout this study (e.g., duloxetine, pregabalin, nabilone) not only take time to titrate to target or effective doses, but may also have a slow onset time of up to 4-6 weeks to reach full effects[41]. Early reductions in pain from these changes may show continued improvements as they reach their full benefit. Most of these medications have average NNTs of around 6[21], making it likely that some participants will need to try more than one medication before experiencing a notable benefit. These participants may have later improvements in pain, contributing to additional average pain reductions in later months. In addition to non-opioid medications, other interventions and optimizations likely also take time and will continue offer improvements throughout the study duration. There is also anticipated improvements in OIH in some participants if they are successful at tapering their opioid significantly, which is more likely with a longer study duration.

The overall project includes a hypothesized reduction in pain in both cohorts, among other measures, by the 12-month visit (Section 2.4, Hypotheses 3 and 4, overall project). Based on trend improvements in this 3-month data, validated by clinician feedback, it is possible that the overall study could improve pain scores to clinically significant degree (i.e., at least 2 points or 30% reduction on the NRS [153]) by the end of the 12-month program, or, at the very least, not worsen pain. It is important to take note of this trend

towards improvement and the potential for the overall project to contribute to improvements in overall pain, not only because it strengthens the data that show opioid tapers are not associated with overall pain increases [11,25], but also because it is contrary to the concerns and beliefs of patients with CNCP on LTOT have, which can be a significant barrier to both patients and their health care providers to tapering and may influence prescribing and tapering attempts[11,25,97].

4.1.3.3 Health and wellbeing questionnaire scores

As with pain scores, there were no predictions regarding health and wellbeing questionnaire scores included in the master's project hypotheses. Instead, participants' baseline scores on five questionnaires, producing six different scores (**Appendix C-1**), were compared to the 3-month follow-up data to rule out any concerning effects of opioid tapering on other realms: mental health, physical health, quality of life, and risk of problematic opioid use. The master's project was anticipated to show no changes to health and wellbeing questionnaire scores, indicating no increased risk of harm to participants undergoing opioid tapering. The overall project predicts that participants will demonstrate improvements on these questionnaires, measuring pain disability, depression, anxiety, quality of life, pain acceptance, and valued living, by 12 months and that the PEW cohort will have significantly greater effects on these than the MTP cohort (Section 2.4, Hypotheses 3 and 4, overall project). Newer studies on opioid tapering have shown the emergence of some risks opioid tapering may present, particularly to mental health, including overdose and suicidality[11,99,100,135]. However, due to the MTP's unique features compared to other trials – including consistent follow-up and support, patient-centered design, allowed bilateral taper direction, and the roles of pharmacists and psychologists within multidisciplinary teams at each study site – it is predicted that participants will have fewer risks. In fact, at follow-up visits (telephone and in-person), in addition to data gathering, there is the opportunity to screen for mental health changes, adjust management strategies for pain or other conditions, treat and manage opioid withdrawal, and/or manage any other side effects symptoms that arise. For any mental health concerns, participants can be referred to study psychologists for assessments of safety continuing in the study or to non-study clinicians to receive standard mental health care they would otherwise have access to. In addition, the PEW, including significant ACT, is predicted to contribute to improvements in these realms as it has been shown in previous literature [102,103,108,109].

Again, in the master's project, differences between the cohorts, MTP and PEW, were not expected with the small sample size and short duration, but were measured for completeness, which is why pooled

data are reviewed primarily in this section. This is also the reason that two of the questionnaires used in the overall project are not assessed in the master's project. Questionnaires assessing attitudes towards pain – the CPAQ8 and CPVI, both previously described – were not analyzed because these questionnaires are intended to gauge the effect of the PEW on these attitudes, and not signal overall improvements or harm caused by the intervention. Since differences between cohorts were not anticipated, these scores were not expected to add value to a preliminary analysis and were not analyzed.

As expected, all scores showed no significant differences between 0 and 3 months, confirming no observable harms to participants were present. Notably, there were trend improvements in two scores: pain disability (p=0.064) and GAD-7 (p=0.056).

The GAD-7 was the only mental health score that showed a trend improvement. While this may hint at overall improvements as predicted in the overall project, it is less likely than if other mental health scores, PHQ-9 (which measures depression) and Global Mental Health (which measures overall mental health), had also trended towards improvements. However, the GAD-7 trend is quite strong with a high magnitude, 1.976-point reduction on a 21-point scale with a low p-value (0.056). A 3-point change is considered to be the minimally important difference for the GAD-7[158], which the confidence interval includes (-0.053 to 4.006). This could be interpreted – albeit very cautiously since the confidence interval also includes zero – that the MTP may have more of an effect on anxiety than other aspects of mental health. It is not unreasonable to deduce that a program with lots of support and follow-up regarding a potentially anxiety-provoking intervention (opioid tapering) may have more benefit to the anxiety surrounding that plan than any comorbid depression. The Global Mental Health score, which also assesses for anxiety, did not have a significant change at 0 and 3 months, but has more questions about depressive symptoms than anxiety and could miss an exclusively anxiety-related improvement. It is also possible that this trend in the GAD-7 is mostly driven by one participant who had an 11-point reduction and is not significant. Considering the confidence interval does include zero, it very well may indicate no effect. Based on this preliminary report it is not possible to predict strong improvements in mental health with the overall project, but certainly the data would indicate no harms or concerns towards mental health, which was the primary concern.

A trend showing improved pain disability score strengthens the conclusions previously made about the trend improvements in pain score in Section 4.1.3.2. Pain disability is measured on the PDI, which

measures the impact that pain has on a person's life in different areas: family/home responsibilities, recreation, social activity, occupation, sexual behaviour, self-care, and life-support activity. If pain scores trend towards improvement, it makes sense that the level of disability that pain imparts would also trend in that direction. However, the importance of trend pain disability improvements may overshadow importance of trends in pain score reductions. The ACT model emphasizes shifting patient goals from decreasing or avoiding pain towards more valued behaviors[105], including the functional realms that the PDI is validated to assess [138–140]. This assessment of function may better predict a participant's success at living a life that aligns with their valued behaviours. The overall magnitude of the improvement observed on the PDI was 5.325 points on a 70-point scale. The clinical significance of PDI reductions depends on baseline score, with larger scores (higher disability) requiring larger reductions to be minimally important[159]. The data for the 16 total participants had a mean baseline score of 30.56 points, indicating a necessary 15-point reduction to signify a minimal important change[159]. At one-third of the magnitude of a minimally important change only one-quarter through the entire duration of the study, it is feasible that the overall project may show improvements in pain disability, especially considering pain reductions may continue throughout the study as mentioned above in Section 4.1.3.2.

Comfortingly, the point estimates for all health and wellbeing score changes from 0 to 3 months were on the benefit side of zero. All but the PROMIS Global-10 scores have a positive baseline score compared to the 3-month score on the table in **Appendix F-3**, indicating worse outcomes at baseline compared to at 3 months. The PROMIS Global-10 scores are negative because they are interpreted in reverse compared to other scores – high numbers indicate better health instead of negative outcomes. Of course, with non-significant p-values and confidence intervals that cross zero in all cases, this can't be interpreted to signal improvements in these fields. However, it could strengthen the prediction that the MTP is not associated with harm, as it would be quite unlikely for all six scores (from five questionnaires) to fall on the benefit side when, in fact, a harm was present. The qualitative feedback supports this prediction, as it did not capture any increased harms during the study period. This observed lack of harm, and trends toward benefits in some areas, from the master's project further validates the overall project's study design.

None of the health and wellbeing scores had a significant difference in magnitude by group or change between cohorts, as was expected. This likely confirms what was predicted; that the sample size was too small and the duration in the study too short for a difference to occur and be measured.

4.1.3.4 Summary

Based on the 3-month quantitative data collected, in addition to clinician and participant feedback collected, the data from the master's project's analysis of the MTP met its Section 2.3, Objective 1, to evaluate the impact of the interventions on opioid dose and Objective 3, to inform the larger study to contribute to study optimizations. It outperformed predictions of only trend reductions in opioid dose with a statistically significant reduction of almost 22%, had no indicators of worsening safety outcomes in mental or physical health, and even showed trend improvements in pain and other scores. This contributes to the validity of the study design and predicts success of the overall program when complete.

4.2 Strengths and Limitations

Strengths:

As the primary focus of the overall project is to ensure the results are relevant to practice, outcomes have been designed to be clinically useful and applicable directly to patient care in this population. Our project is based on foundations of interdisciplinary care for pain management, which is strongly supported by existing literature emphasizing team-based care for CNCP [12,20]. The workshop that we have developed, with a primary focus on brief ACT administered by an interdisciplinary team is, to our knowledge, a novel approach to ACT in this patient population. Results from this evaluation may stimulate increased interest into this novel approach, including possible implementation in applicable practice settings and further, larger scale research studies. Our MTP protocol includes frequent and personalized patient follow-up as well as allowing for bi-directional opioid dosage changes which is in contrast to most existing opioid tapering trials. We anticipate that these details will result in reduced attrition rates, which are often significant in opioid tapering studies[93].

The master's project evaluates multiple completed sessions of the PEW and three months of MTP. Although quantitative data from the MTP is only collected at baseline and 3-month visits, it has collected qualitative feedback from participants and study clinicians as frequently as weekly. This is meaningful data that will be available to generate interest and discussion in the overall project and to contribute to ongoing design optimizations. In addition to these benefits, analyzing participant feedback collected frequently and early on in the overall project may also contribute to improved attrition rates through responsive protocol adaptations.

Limitations*:*

As with its strengths, the limitations of the overall project also relate to its goal of relevance and applicability to practice. The overall project follows an open-label, modifiable protocol approach with ongoing optimizations, therefore evaluating statistical significance of our outcomes is not the primary focus of this project and may limit conclusions that can be made as a result. Similarly, as this project's primary aim is to be applicable to practice and clinically relevant, patients with all types of CNCP can be included (as long as they meet the inclusion and exclusion criteria), leading to a potentially heterogenous group of participants. Different subtypes of pain (e.g., diabetic neuropathy, fibromyalgia, mechanical back pain, hip osteoarthritis, etc.) can be treated differently and may have modest differences in opioid tapering difficulties and successes, which will not be captured in this trial. However, mixing different pain subtypes together is commonly seen in existing trials in chronic pain and opioid tapering [10,25,147]. For this project, the primary outcomes are geared towards tapering efficacy more than specific outcomes related to pain subtypes. As with other opioid tapering projects, there is a significant time commitment required of participants in both cohorts. As obvious benefits to patients may not be observed for several months into the trial, there is a risk that patients will experience fatigue with their participation and choose to withdraw, ultimately impacting the quality of our final data.

The master's project's limitations are mostly related to its short duration (three of the overall project's 12 months) and small sample size (16 of the overall project's 130 projected MTP participants and 10 of the 65 PEW). And while these prevent strong conclusions from being made, it was designed in this way as a preliminary review, knowing these limitations, in order to catch early signals of benefit or harm and contribute to optimizations to the overall study. At this stage, only a few points can be confidently stated: 1) the PEW is associated with participants improving their knowledge about opioids, as measured on the study's quiz; 2) the PEW is associated with positive feedback on its content and value; 3) by the 3-month mark, the project is associated with opioid reductions that are statistically significant, but may not be clinically meaningful at this stage; 4) there are no observable preliminary signals that the trial's interventions are contributing to increased risk of harm, as measured on the selected health and wellbeing questionnaires.

By evaluating the MTP with so few participants, it was necessary to pool data between PEW+MTP and MTP-only groups and it was not possible to compare data between these cohorts. While this is a goal of the overall project, it was not identified as a priority for the master's because the master's project has

other assessment tools to assess the PEW: the opioid knowledge quiz, tapering readiness assessment, and participant feedback, instead of assessing the PEW's effect by measuring differences in outcomes between cohorts during the MTP. Further, these PEW assessment tools, though, have not been previously validated as they were created for this project. Validated questionnaires explicitly for this purpose do not exist, likely because the application of ACT used at the time of study design was novel. Drawing firm conclusions from this data, therefore, is not possible and even though a statistically significant improvement in opioid knowledge was observed, it is not possible to know if that translates to an important change in knowledge. Despite statistical significance, this data must be used only as guide for the overall project, and as mentioned in Section 4.1.3.2, is intended to gauge preliminary value and guide optimizations in order to present the best possible PEW in the overall project to achieve its objectives. The overall project will not assess the changes in these scores but will analyze the difference between the PEW cohort and the MTP-only cohort in opioid dose and on validated questionnaires in order to make conclusions about the PEW's effectiveness and potential role in clinical practice.

Pooling cohort data may impact the interpretation of the MTP data. Since it results in a heterogenous group, it is less likely to show significant changes, and therefore more difficult to draw conclusions, and may be less indicative of the larger group in the overall project. Because of block randomization, some early attrition, and incomplete or delayed data, the cohorts are not equal in number (intended 50-50 randomization), contributing to this early heterogeneity. There is data comparing the two groups with pooled time data that shows there is no difference between groups in measured outcomes, including opioid dose, pain scores, and health and wellbeing questionnaire scores, with the exception of the log-transformed opioid dose (see supplemental data tables in **Appendix F-1**). However, differences in baseline demographics (**Table 3**) of the two cohorts were not analyzed or adjusted for. While the groups were not compared officially in the master's project (since there was no significant differences), they were compared informally. Any observations made from comparing groups must be cautious and definitive conclusions should not be drawn.

Heterogeneity in the pooled sample size also exists because of site differences. Participants in the master's project analysis are heavily skewed towards patients from primary care (AWW and ARE), and not from the pain specialty clinics (Pan Am and HSC), where new referrals are mostly coming from. Specialty pain clinics follow the same study protocol and use the same study team, but study pharmacists are not on site as often which may result in less frequent communication with the team but would not affect

clinician-participant interactions. As well, study pharmacists may also have decreased access to a participant's primary care provider or primary care chart at these specialty clinics and could therefore have the potential to decrease the impact or breadth of medication reviews that occur at the Baseline Tapering Visit, which were identified as an impactful. However, these sites have more pain specialists on site and may have access to different treatments than primary care patients would. Participants at these clinics are likely to get similarly exemplary care, in accordance with study protocols, but the data from the master's project might not be as relevant or well suited to predict what will occur with all participants considering this difference. The goal of the overall project, though, is to inform practice and practice has the vast majority (over 95%[160]) of its patients in primary care[161], so while it may not be a perfect representation of the overall project's data to come, it is not an unrealistic distribution.

By evaluating the study's outcomes as early as 3 months in, there are only two data points to compare quantitative data (baseline and 3 months). It was predicted that no outcome would reach statistical or clinical significance. Non-significant data would have results with reduced validity and applicability. Data captured is also no exhaustive. While participants are required to complete a large number of validated questionnaires as part of the study design, it is not possible to assess for all potential risks. However, because qualitative data was taken at weekly phone visits, there are up to 12 additional data points per participant, which can strengthen and broaden results from the only two data points – both for predicted improvements and to assess for any risks present. Frequent one-on-one assessments should capture any risks that could be missed on the questionnaires and the repository of qualitative data did not mention any risks appreciated, reinforcing the questionnaire data showing no change to scores. The qualitative data also make trend improvements more meaningful if they reinforce the results, increasing their validity. For example, pain scores trended towards an improvement; coupled with qualitative data that also reported improved pain among participants, a more confident prediction about reduced pain in the overall project can be made. While only trends were expected, the most important outcome, opioid dose, showed a statistically significant reduction, measured both in mg of MED and in percent difference. This, while it may not be considered a clinically important difference, overcomes some of the predicted limitations of the master's project.

Overall, trends or no difference were anticipated based on the sample size and timeframe, the master's project's biggest limitations, but the results outperformed. It is less likely that the overall project

would underperform its predictions after this successful preliminary review, especially since feedback and data from the results have and will be used for improvements.

4.3 Recommendations

Most importantly, the results from this master's project support the ongoing overall project and predicts that it will demonstrate important reductions in opioid dose as well as likely improvements to other realms, without worsening pain or causing harm. Therefore, the primary recommendation is for the overall project to continue, with additions and improvements to optimize its success.

The master's project has already informed the overall project, as detailed in the discussion section, based on clinician and participant feedback. Now, with this newly analyzed quantitative data, further optimizations to the overall project will continue to be made. Using this data, the methods of the overall project can be optimized for effect, patient acceptance, and applicability, increasing its reach.

The master's project also served to generate interest in the overall project. The results of the master's project have and will be presented and disseminated prior to the overall study's completion and publication, in order to create increased awareness, interest, discussion, and potentially enhance recruitment and enrollment. Since the aim of the overall project is to ensure that data, developed tools, and program design are directly applicable to practice, attracting attention is crucial to the success of the overall study's objectives.

4.3.1 Knowledge translation

The targeted knowledge users, both for the overall and the master's project, are predominantly primary care practitioners who are engaged in the care of patients with CNCP (e.g., nurses, nurse practitioners, physicians, pharmacists, physiotherapists, and psychologists), as well as the patients themselves. Other knowledge users include University instructors of the different disciplines who educate on opioid use in CNCP, as well as those involved in the medical and political administrative structure who intersect with the areas of LTOT, CNCP and their consequences.

Throughout the study progression, updates to clinic providers and care teams have been ongoing in order to participate in collaborative care, but also for recruitment. Formal and informal presentations to each site have occurred on several occasions. An example of a study progress handout from November 2022 is included in **Appendix G-1**. Continued updates summarizing this master's project's results are

planned for after publication. This includes presenting at Anesthesia Grand Rounds in May 2023 to approximately 50-80 clinicians and other staff, including those from both Pan Am and HSC's pain clinics in order to increase recruitment to the overall study and share knowledge gleaned.

Students of various disciplines have been involved in the study, contributing to knowledge translation of the project. Pharmacy students and interns have been involved in study participants' care team, supervised by study pharmacists. They have shared about their experiences with their peers and teachers in addition to written reflections and evaluation of their experiences. Psychology and family medicine residents have also collaborated in the study and have learned about the study process as well as gleaned wisdom from the study team, including patients, by collaborating in workshop and taper processes.

After completion, the overall project will develop educational material, which will be available for consumption in addition to the study design beyond this project, with the knowledge users described. This will be undertaken at academic conferences and at administrative gatherings in academic and clinical settings. The protocol for the PEWs as well as the MTPs will be published in a relevant clinical journal, allowing for other clinicians and patients to benefit from the knowledge obtained and tools developed as a result of this project. Depending on final results of the PEWs, the group will look into running sessions to train various interested parties to give any/all sections of the PEW, including both the pain & opioid education and the ACT workshop portions ('train the trainer sessions') post publication.

With the master's project data, some of this has already been shared. Study design, recruitment details, and very preliminary results were submitted to the Association of Faculties of Pharmacy of Canada (AFPC) for their 2022 Canadian Pharmacy Education and Research Conference (CPERC) in St John's, Newfoundland and was accepted as a mini session where it was presented to Pharmacy faculty, students, and researchers. The abstract submitted was subsequently published in a November/December supplement of the Canadian Pharmacist's Journal (CPJ). A poster with similar data was presented virtually at University of Manitoba's College of Pharmacy research day in spring 2022 to faculty, staff, students, and researchers from multiple Rady Faculty of Health Sciences disciplines. These materials are included in **Appendix G-2** and **G-3**. In addition, a mini-session or poster presentation is planned for AFPC's CPERC in Winnipeg in 2023, if accepted, to share the master's project's results and recommendations. As well, portions of this dissertation will also be submitted for publication in relevant journals.

The results of the overall project will have a multipronged impact, not only on patients receiving LTOT for CNCP, but also on their health care providers. By using the information and tools from this study, health care providers will have clear guidance and support on how to translate the benefits gleaned by trial participants (predicted reduced opioid use and improved quality of life measured on health and wellbeing questionnaires) to their patients on LTOT in the community.

4.3.2 Recommendations for additional research

While the master's project itself presents great value to the opioid tapering and CNCP landscape, more data is needed to make definitive conclusions and provide practice directing results. The overall project requires more participants to reach its target sample size and participants will need to complete the 12-month study duration before a final analysis can occur. While preliminary results, lessons learned, and even study tools can already be shared, without the final data, it is less relevant.

Additional research into ACT in CNCP as well as other interdisciplinary education workshops is also warranted. This project presents a novel application of ACT in CNCP and, while promising, additional studies are necessary to replicate results and to expand the breadth of this strategy in CNCP. More one-day applications of ACT in different formats would also add value considering such diverse needs in the community of patients with CNCP. Comparing the feedback from this trial to one with in-person (or hybrid) ACT workshops would be valuable to determine the overall risks and benefits of both. With additional trials assessing these workshops, it would be possible to create validated assessment tools for such workshops and build the validity of the data gleaned.

While opioid tapering led by pharmacists is not novel, additional research into such programs is also needed in order to replicate and strengthen results, to study different methods of collaboration, evaluate what settings pharmacists are effective in (hospital vs primary care vs community practice), and to build a case for government funding of these positions.

Lastly, considering the lack of harm signals within this preliminary report and with emerging evidence of harm associated with opioid tapering in other designs[11,99,135], this study's design could be successful when applied to other areas. There may be a role for pharmacist-led, interdisciplinary, high support, and patient-centered benzodiazepine or z-drug tapering strategies as well.

4.4 Summary of Key Findings

Key findings from the master's project, the preliminary review of the overall project, "Evaluation of Evaluation of a Patient-Centered, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy" can be split into three categories: recruitment and attrition, PEW outcomes, and findings from the MTP. Each contributes its own data that relates to study objectives and hypotheses (see Section 2.3 and 2.4) and also contributes to improvements and predictions for the overall project as it continues recruitment and data collection.

4.4.1 Findings on recruitment and attrition

Slow recruitment mirrors similar studies done on opioid tapering in the past[25] but attrition rates are slightly lower than predicted based on previous research[27,95] at 16%. A major factor that contributed to both recruitment and attrition include running the trial in the heart of the COVID-19 pandemic, which was a potential factor in three of the four participants' attrition. Recruitment rates are already improving as the world comes out of the most pronounced effects of COVID-19 and likely attrition rates will hold fairly steady as well, even with progression towards the end of the 12-month program from early on in data collection.

4.4.2 Findings from the Patient Education Workshop

The PEW resulted in a significant improvement in opioid knowledge as measured on the quiz created for this study ($p=0.031$). Opioid knowledge quiz score changes revealed that, despite variable baseline knowledge, post-workshop scores were improved overall with most questions having all, or almost all, participants answering correctly. The least successful question post-workshop was about pain levels during tapering, which is a common patient misconception and will be addressed during the MTP when participants are one-on-one with the study pharmacist, discussing individualized tapering goals, including fears and barriers.

Tapering readiness data did not show significant changes or improvements. However, an average change score does not emphasize the 30% of participants who were already "very ready" to taper pre-workshop (and remained so after). Importantly, all participants rated themselves as wanting to reduce their opioid use post-workshop, albeit with varying readiness to taper. One can assess that post-workshop, all participants were in the "contemplation" stage of change or further, which predicts the MTP to be valuable in this population[156].

Feedback on the PEW, both scaled and freeform, was very valuable. Feedback on content and value had no negative responses with the majority of participants contributing; 9/10 participants answered both Likert scale questions, 9/10 contributed freeform responses. This indicates high level of acceptance of content and value, despite the not reaching the 80% threshold on both Likert scale questions (due to one neutral answer). Feedback on the format of the PEW was mixed at 50/50, revealing complex, and occasionally opposing, needs of participants. However, all participants were able to complete the PEW, which is in contrast to other ACT workshops in the literature[114]. Continued optimizations of the PEW for accessibility are warranted to create the best tool for practice possible.

In all, the PEW contributed value and prepared participants for the MTP phase of the protocol. While positive, it is unknown whether this data predicts the overall project to show significant benefit of PEW cohort over the MTP cohort in study outcomes like opioid dose and pain and quality of life measures.

4.4.3 Findings from the Multidisciplinary Tapering Program

The MTP showed compelling data, even at only three months into a 12-month program. A significant opioid dose reduction of 21.8% was shown (p=0.007) from baseline to three months, which exceeded the predicted trend reduction. This highlights the strength of the MTP's design, especially pharmacist involvement operating within an interdisciplinary team. This is reinforced by 12-month preliminary data showing that in five participants, the reduction rate was doubled, predicting continued reductions throughout the MTP.

Pain and other quality of life measures, as assessed on five health and wellbeing questionnaires, did not change at three months. This, despite the observed significant reduction in opioid dose, showed that while some newer studies on opioid tapering highlight concerns[11,100,135], this study has not resulted in those risks at this time. This may be attributable to the design that includes close follow up, significant patient support, flexible and patient-centered tapering strategies, and team-based care. These features are brought up in clinician feedback as successful, supporting to the validity of this assessment.

While none of these questionnaires' scores had statistically significant changes, three scores showed trend improvements: pain, pain disability, and anxiety. Both pain and pain disability had moderate magnitude improvements, but not enough for clinical significance (nearly one point on the NRS and just over five points on PDI), and non-significant p-values. However, this coordinated improvement in both

pain and pain disability and reports of reduced pain in clinician feedback strengthens a prediction that the overall project may contribute to improvements in pain, as seen as trends in some recent opioid tapering trials[11] . Anxiety measured on the GAD-7 had a fairly large magnitude improvement with the confidence interval crossing the threshold of clinical significance (but also crossing zero). Since other scores measuring mental health (Global Mental Health score and PHQ9) had high p-values, it is more difficult to make predictions about mental health, although it is feasible that anxiety would improve more than other mental health conditions.

These data strongly predict a successful overall project MTP with regards to meaningful and safe opioid dose reductions without increased risk of harm. The improvements in other fields that are present in the overall project's hypotheses are more difficult to predict at this time but are possible considering trend improvements.

Chapter 5: Conclusion

5.1 Summary

Opioid tapering is identified as a priority action in local, national, and international organizations to decrease the impact of the Opioid Crisis. However, previous research into how best to taper and what strategies to employ are incomplete, insignificant, or entirely absent[11,25,93] and recommendations from guidelines offer little direction or guidance beyond recommending multidisciplinary teams for those patients in whom tapering is difficult[8–10] . Patients and clinicians are struggling to successfully taper and reduce opioid-related risks[30,77,91].

In response, the overall project, a randomized, open label opioid tapering study designed for integration into clinical practice that emphasizes patient education, involvement, and support, was designed. It utilizes pharmacists and psychologists working within an interdisciplinary team to provide exemplary patient care not only for opioid tapering but also chronic pain management. The two components, a one-day, interactive, education workshop utilizing ACT in addition to chronic pain and opioid education (PEW) and a pharmacist-led opioid tapering program (MTP) that includes holistic management of CNCP, are anticipated to contribute not only successful opioid tapering, but also improve pain, pain disability, depression, anxiety, quality of life, pain acceptance, and valued living.

The master's project, acting as a preliminary review of the overall project, showed that the study design is effective at tapering opioids. At the 3-month mark, a 21.8% reduction in opioid dose was seen (p=0.007), predicting the overall project is likely to reach the previously determined 30% threshold to target a clinically meaningful effect[25]. While this project did not capture any significant improvements in other realms (such as physical or mental health), pain, pain disability, and anxiety scores did trend towards improvement (p-values=0.059, 0.064, and 0.056 respectively), which were corroborated by qualitative data. It also showed that the first subset of workshops was successful in improving opioid knowledge to participants (p=0.031) and providing education of good value (100% of PEW participants responded they would use what they learned, 78% of the 9/10 participants who responded agreed that the workshop was relevant and of value, and all left exclusively positive feedback). Accommodations could continue to be made to the format to suit more participants (50% agreed the format met needs and was barrier-free). While initial recruitment rates were slow due to the COVID-19 pandemic, adjustments to strategies have resulted in increased uptake, with a current overall recruitment rate of 49%. Attrition is slightly lower than

previous opioid tapering trials at 16%, and while there are likely multiple factors at play, it reinforces the study design incorporating high patient involvement and support.

5.2 Future Impact and Applications

The overall project will contribute direct benefits to its participants in both cohorts, likely through decreased opioid consumption and an overall improvement in wellbeing. Additionally, the project design (noting, especially, its interdisciplinary approach) and educational materials will be available for consumption by primary and tertiary care practitioners. Specifically, through the development and implementation of the PEWs, we will ultimately provide a novel multidisciplinary educational approach to encourage weaning opioid doses using psychology education sessions based on ACT, along with medical information sessions on LTOT. The evidence-based MTP design and implementation will inform safer opioid prescribing as well as tapering in CNCP. The knowledge created from this project will contribute to improved processes and better understanding of the care of individual patients and in the public health approach to long term opioid treatment and opioid weaning.

The master's project aimed to act as an optimization tool for the overall project and quantitative and qualitative data and feedback collected have already been implemented and will continue to be implemented to inform and optimize the overall project's design and tools for practice. It has contributed to the quality of overall project procedures and ultimately is anticipated to improve the final outcomes, extending its impact, but also to improve the tools and recommendations that come from it.

5.3 Contributions to the Field

When the harms of opioids began to come to light around the world, and guidelines and recommendations came from numerous sources to taper prescription opioids [8–10], the research into the practice of opioid tapering naturally increased. Multiple trials in the late 2010s evaluated different tapering strategies but came up short. Slow recruitment, high drop-out rates, and low patient buy-in mostly led to insignificant results and calls for more research[11,25,27,93–95]. This paltry literature did not match the need reported by primary care and specialty clinicians who sought to find a way to reduce their patients' opioid burden effectively and safely in order to decrease their risk of opioid-related harms. The overall project was designed to fill some of those gaps with a design intended to reduce attrition, increase patient involvement and engagement, and contribute significant results in both opioid tapering success and improvements to pain and wellbeing. The master's project shows that, in fact, these study design features have contributed to filling these gaps. Recruitment rates continue to improve, and attrition is at

or even slightly below predicted rates of other studies, despite the impact of COVID-19. Feedback from participants and clinicians reveal increased participant buy-in, which may be a factor in the preliminarily significant opioid tapering success. While only trends towards improvement in pain and wellbeing scores have been shown so far, this project discusses how this may lead to the overall project being successful in this area as well.

After recruitment began, newer tapering trials continued to come out and started to reveal potential risks of opioid tapering, including negative impacts to mental health and problematic opioid use[11,99,100,135]. Even though the project had already started as these were published, the design already screened for these concerns at baseline and allowed for continued monitoring. The master's project became a good opportunity to check in with participants to rule out these risks occurring as part of the overall project. And in fact, this was shown; harms of the project were not observable and trend towards improvements were seen.

Although this project may be contributing to filling these research gaps, some of the results are not entirely unexpected. Successful opioid dose reductions without increased pain, and improved pain in some, is in line with trends seen in previous studies scores[10,11]. As well, plenty of existing research shows the benefit of multidisciplinary teams in the treatment of CNCP [12,20], especially involving psychologists and ACT [101] [107] as well as pharmacist-led medication reviews [75–77]. Improvements associated with these features would confirm that they are effective, even during opioid tapering.

The master's and the overall projects contribute strategies, tools, and data that go towards filling critical research gaps in both chronic pain management and opioid tapering in the midst of the Opioid Crisis. Further, preliminary data is in line with predicted outcomes and validates previously available data.

5.4 Final Message

Opioid fatalities continue to increase across Canada – the Opioid Crisis shows no signs of slowing down[7] and there is no better time to create clinically relevant and practical strategies to taper opioids in primary care. This preliminary review of the overall project, "Evaluation of a Patient-Centered, Multidisciplinary Opioid Tapering Program for Individuals with Chronic Non-Cancer Pain on Long-Term Opioid Therapy", intended to contribute to the value of the overall project which aims to fill critical research gaps in opioid tapering.

The master's project has done just that. Its preliminary evidence outperformed predictions and likely predicts similar success in the overall project. It has, and will continue to, contribute additions and improvements to the overall trial, adding value to the disseminated information and tools, making them more effective, useful, and applicable to practice.

The combined data presented in this dissertation tell a story of a difficult intervention (opioid tapering) in a complex patient population (CNCP on LTOT) that needs individualized, well supported, and multidisciplinary care delivered in different modalities. In that environment, they can taper opioids successfully and are likely to have improved outcomes overall. If the overall project continues in the trajectory of this preliminary review, it will add much needed, clinically applicable, ready-for-practice data and tools, that will help taper the Opioid Crisis.

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Appendices

Appendix A: Recruitment Resources

A-1. Desk reference for clinic providers (physicians or nurse practitioners)

Provider Reference: Opioid tapering trial

Study title: *Evaluation of a Multidisciplinary Opioid Education and Tapering Program for Individuals with Chronic Non-Cancer Pain on Long Term Opioid Therapy*

Step I: Does your patient meet criteria?

Inclusion Criteria:	Exclusion criteria:
Chronic non-cancer pain Duration: ≥6 months Frequency: >50% of the time Pain score: ≥3/10	Significant uncontrolled depression (+/- SI) (if you're not sure, refer and our psychologists will screen carefully)
	Current psychosis
Opioid use Duration ≥90 days Frequency: >3 days per week Dose: morphine equivalent ≥50mg/day (T3x12, HM 8-10mg, Oxy 30mg /day)	Known or suspected opioid misuse/abuse
	Known or suspected opioid diversion
	Currently in CBT or ACT therapy
	Received CBT or ACT in the last year
Age≥18	
Cognitive ability to understand questionnaires	
Can participate in English only education	

Step II: Discuss with your patient

If your patient meets criteria, briefly explain the study to them by summarizing these points:

- Study goal: support patients in making and meeting goals for their opioid use
- All patients receive multi-disciplinary, evidence-based opioid tapering program:
  - Closely followed: weekly by phone, quarterly in person
  - Flexible tapering plan: dosing can go up or down as needed, patient directed
- Half the patients are randomized to also receive a one-day workshop facilitated by psychologists, pharmacists, and anesthesiologist (precedes tapering program)
- Study duration is 12 months, with optional drop out any time

Step III: Refer your patient

1. Ask if your patient is interested in participating in the study and would like more information
2. If yes, advise them that a study representative will contact them with more details and screening questions (note: enrollment is not guaranteed)
3. Document your interaction in EMR using the macro
4. Task your note to your clinical pharmacist (make sure there is an active phone number)

A-2. Chart note provided to clinic staff for study recruitment (first wave of recruitment)

Chart Note re: discussion about opioid tapering trial

1. Screen for eligibility:
   a. Patient meets all the inclusion criteria:
      - Chronic non-cancer pain ≥6 months ≥50% of the time with an avg weekly pain score ≥3/10
      - Opioid use for ≥90 days, >3 days per week, at a morphine equivalent of ≥50mg/day
      - Age ≥18
      - Cognitive ability to understand questionnaires
      - Can participate in English-only education
   b. and none of the exclusion criteria:
      - Significant uncontrolled depression
      - Current psychosis
      - Known/suspected opioid misuse/abuse
      - Known/suspected opioid diversion
      - Currently in CBT or ACT
      - Received CBT or ACT in the last year

[Yes, patient meets criteria|No the patient doesn't meet criteria and will not be referred]

2. Discuss the following with the patient:
   a. The goal of the study is to support patients in making and meeting goals for their opioid use
   b. All patients will receive a multidisciplinary, evidence-based opioid tapering program that is closely followed (weekly by phone, quarterly in person) with a flexible, patient directed tapering plan (dosing can go up or down as needed)
   c. Half of enrolled patients will receive a one-day online workshop (participants will be randomized). This workshop is led by psychologists, pharmacists, and an anesthesiologist
   d. The study duration is 12 months with optional drop out any time

[All points were discussed|These points were not all covered and will need to be discussed at another time]

[The patient is interested and would like more information|The patient is not interested]

3. Refer If the patient is eligible and interested:
   a. The patient has been informed that a study representative will contact them with more details and screening questions, since enrollment is not guaranteed [yes|no]
   b. The patient's phone number is in the chart [yes|no]
   c. This note tasked to the study representative [yes|no]

A-3. Script provided to clinic nurses for study recruitment (second wave of recruitment)

"You have been identified as someone who is eligible and might benefit from a chronic pain study that is going on at [clinic name]. The study's goal is to improve the quality of life of people with chronic pain who take opioid medication. It is run by pain specialists from the pain clinic and our clinic's pharmacist who would work together with you and your [doctor or nurse practitioner] here at [clinic name]. Some people may taper their opioid during the study while others won't – it's up to the patient. Would you be willing to accept a call from a study representative to get more information?"

A-4. Patient recruitment poster displayed at ACCESS Winnipeg West

Study Invite Poster #2
Version: April 22.2020

BREAKING FREE FROM CHRONIC PAIN AND RECLAIMING YOUR LIFE

Are you curious ABOUT YOUR OPIOID USE? Thinking you might want to make some changes, but not sure where to start?

YOU ARE INVITED TO PARTICIPATE IN A STUDY LOOKING AT SUPPORTING PATIENTS IN MAKING AND MEETING GOALS FOR THEIR OPIOID USE

You will work with a pain specialist to discuss your current opioid use and set your own personal goals regarding changes you would like to make. You will obtain weekly support to help you meet these goals

Half of study participants chosen randomly (by chance) will also participate in a workshop where you will:

- learn the benefits and risks of opioids for pain management
- change your relationship with chronic pain
- reconnect with what matters so you can live a more meaningful life, even with pain.

CONTACT

Karin Ens
Email: Karin.Ens@umanitoba.ca
Tel: 204-272-3170

Image sourced from Canva in alignment with their policies

Appendix B: Screening and Consent Forms

B-1. Telephone Screening Form - 3 pages

Telephone Screening Form

A. INTERVIEWER INFORMATION			
Date		**Time**	
Interviewer name			
B. PATIENT INFORMATION			
Patient name* *Patient name NOT entered into REDCap		**Ph. Number**	

C. INTRODUCTION

Hello, my name is (name) and I am a (position). May I speak with (patient, verify identity using 2 identifiers such as address or DOB)? I am calling today regarding a research study that you have recently expressed interest in.

This study is focused on the management of chronic pain and opioid use. As part of this study, we will be conducting workshops entitled, "Finding your path toward a meaningful life with chronic pain". Would you like to learn more about this and is now a good time for you?

- ☐ **Yes**
- ☐ **No**

Option 1: If participant interested and it's a good time, answer yes and continue to Section D
Option 2: If participant interested, but not a good time, answer no and arrange an appropriate callback date/time, fill it in, then complete the form at that time

Option 3: If participant not interested, answer no and proceed to Section G.

D. DESCRIPTION OF STUDY

You are being invited to be a participant in a research study about the management of chronic pain and safe and effective opioid use. This study is being done to look at the benefits of an opioid tapering program delivered by a team of different healthcare professionals including pharmacists, physicians, and psychologists.

This study is for people who have been experiencing chronic pain for 6 months or longer and have been on high-dose, long term opioid therapy. We aim to identify people who are interested in looking at other ways to manage chronic pain and how to reduce opioid use to a safer level.

We will also be conducting educational workshops on medical information and behavioural strategies based on acceptance and commitment therapy (ACT) to determine the effectiveness of this treatment approach. ACT is a type of behavioural intervention that has been shown to improve function and quality of life for people with chronic pain. Half of the participants will be randomly chosen by chance to attend this workshop while all participants will participate in a supervised and individualized tapering plan based on each participant's comfort level.

This research is being done because we are trying to find the most effective way to help people wishing to voluntarily reduce their opioid use, when it is advisable for them to do so. So far, only a few studies have examined this and there is no proven method as of yet. This is important because while opioid medication is very effective in reducing acute pain associated with injury or surgery, recent evidence suggests that it often becomes less effective, and sometimes harmful, for certain types of pain conditions, when used over a longer period.

Do you have any questions about this?

E. CONSENT

To ensure you are eligible for the study, we need to complete a short, preliminary screening questionnaire that will require about 5 minutes of your time. Your participation is completely voluntary and can be terminated at any time. Any answers you provide will remain private and confidential and will not be shared with any members outside of our study team. Do you consent to participating in this brief questionnaire by phone?

- ☐ **Yes** → Proceed to Section F. Screening Questions
- ☐ **No** → Skip to section G Ineligible Patients

F. SCREENING QUESTIONS

We will now begin the questionnaire. Please be sure to respond to each question as accurately and honestly as possible to facilitate your entry into the study

Q1: Are you currently experiencing chronic pain?

- ☐ If yes:
  - ❑ How long have you been experiencing chronic pain?
  - ❑ Can you estimate how many days in the last 6 months that you have experienced pain? Please check one of the following:
    - ◯ Every day
    - ◯ Every other day
    - ◯ Once a week
    - ◯ Other (patient to specify):
- ☐ If no, or ≤ half the days in the last 6 months, please refer to section G "Ineligible Patients" below.

Q2: On a scale of 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your average pain in the last week?

1 2 3 4 5 6 7 8 9 10

Note: If less than 3, please refer to section "Ineligible Patients" below.

Q3: Are you currently using opioids?

- ☐ If yes: What opioid medication(s) is/are being used?

Opioid	Dose/Sig*	Duration of Use

**Please clarify how the patient uses their medication at home in brackets if different from prescribed sig.*
***For as needed opioids, please clarify how frequently it is used on average. Example: Oxycodone 20 mg PO Q6-8H PRN (20 mg PO TID)*

For the opioids listed above, please calculate the total morphine equivalent dose (MED) using Appendix B-8.1 Oral Opioid Analgesic Conversion Table on the following link: click here.

Opioid	Total daily mg	Total daily MED
		TOTAL MED/DAY: _____

Eligibility:

- ☐ If using a morphine equivalent dose ≤ 50 mg/day: Please refer to section "Ineligible Patients" below.
- ☐ If using opioids ≤ half the days in the previous 90 days: Please refer to section "Ineligible Patients" below.

Q4: Have you had any experience with Acceptance and Commitment Therapy (ACT) or Cognitive Behavioural Therapy (CBT)? ( ) yes ( ) no

- ☐ If yes: When did you last participate in a session?
  If the individual participated in a session within the last 12 months: Please refer to section G. "Ineligible Patients" below.
- ☐ If no: Please continue on to section H. "Eligible Patients" below.

G. INELIGIBLE PATIENTS

Note: Please skip to Section H if not referred here from previous question
Thank you for your time. Based on (explain the reason the participant is ineligible), you won't be continuing further in the study. If you are interested, we are hoping to make these resources available to primary care clinics and other health care settings in the future. We are hopeful that these resources may be open to you at a different time when appropriate. If you would like to leave us your contact information, we can reach you when similar opportunities become available.
Contact: _____
Address: _____
Phone Number: _____

H. ELIGIBLE PATIENTS

Based on this pre-screening, you are invited to meet with one of your research team members to determine your full eligibility. During this second, in-person screening process, a team member will meet with you one-on-one to obtain a full history. This process will take roughly 60 minutes to complete. You will also be asked to review and sign a consent form if you are willing to participate in the study. More complete details about this will be provided to you at the next section.

I. QUESTIONS

Do you have any questions?

J. BOOKING IN-PERSON SCREENING

Date		**Time**	
Location			
Notes			

B-2. Participant consent forms: general consent (9 pages) and COVID-19 consent (2 pages)

College of Pharmacy
229-750 McDermot Avenue
Winnipeg, Manitoba
Canada R3E 0T5
T: 204 272-3170
Dana.Turcotte@umanitoba.ca

University of Manitoba | College of Pharmacy
Rady Faculty of Health Sciences

RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study: Evaluation of a Multidisciplinary Patient-Centred Tapering Program for Individuals with Chronic Non-Cancer Pain on Long Term Opioid Therapy.

Principal Investigator: *Dana Turcotte*, PhD, College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba. 229-750 McDermot Avenue, Winnipeg, MB R3E 0T5, 204-272-3170.

Co-Investigators: *Gregg Tkachuk*, PhD, CPsych, Department of Clinical Health Psychology Max Rady College of Medicine, Faculty of Health Sciences, University of Manitoba, Pan Am Pain Clinic, 75 Poseidon Bay, Winnipeg, MB R3E 1M7, 204-925-1568; *Brigitte Sabourin*, PhD, CPsych, Health Sciences Centre Pain Management Centre, MS261-820 Sherbrook Street, Winnipeg, MB R3A 1R9, 204-787-1506; *Ryan Amadeo*, MD, Health Sciences Centre Pain Management Centre, MS261-820 Sherbrook Street, Winnipeg, MB R3A 1R9, 204-787-1506

Study Coordinator: *Karin Ens*, BScPharm, EPPh, College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba, 750 McDermot Ave, Winnipeg MB, R3E 0T5; ACCESS Winnipeg West: 280 Booth Drive, Winnipeg MB R3J 3R7

Research Assistant: *Caroline Kehrer*, BSc Pyschology, Department of Clinical Health Psychology, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, 204-643-7907

Study Sponsor: Max Rady College of Medicine, Department of Clinical Health Psychology (Research Internal Grant Program), PZ350 771 Bannatyne Ave. Winnipeg, MB R3E 3N4

You are being asked to participate in a Clinical Trial (a human research study). Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand.

The study investigators are receiving professional fees and financial support to conduct this study.

Purpose of Study

This Clinical Trial is being conducted to study the potential benefits of a multidisciplinary opioid tapering program for people on long term opioid medication for the treatment of chronic pain. You are being asked to take part in this study because (1) you are an adult aged 18 years or older who has experienced chronic pain over the past 6 months or longer, (2) you have been prescribed high dose opioid therapy for the last 3 months or longer, and (3) you would like to learn more about how to reduce your opioid dosage, and participate in an opioid tapering program, with the assistance of a multidisciplinary health care team consisting of physicians, pharmacists, and psychologists. A total of 131 participants will participate in this study.

This research is being done because we are trying to find the most effective way to help people who would like to reduce their opioid use. So far, only a few studies have examined this and there is no proven method as yet. This is important because while opioid medication is very effective in reducing acute pain associated with injury or surgery, recent evidence suggests that it often becomes less effective, and sometimes harmful, for certain types of pain conditions, when used over a longer period. We will also be testing whether a one-time (5 hour) **online ("virtual")** education workshop consisting of medical information and behavioral strategies based on acceptance and commitment therapy (ACT) improves the effectiveness of this new treatment approach. Previous research has shown that ACT improves functioning and quality of life of people with chronic pain and helps people reduce their use of opioid medication when included as part of multidisciplinary programs.

Study procedures

In this study, you will be "randomized" into one of two study groups described below. "Randomized" means that you are put into a group by chance, like flipping a coin. You will have an equal chance of being placed in either the multidisciplinary tapering program only group or the multidisciplinary tapering program plus **virtual** education workshop group.

If you agree to participate in this study, you will be asked to:

Answer a series of questions to determine if you are eligible to participate in the study. If you meet the criteria to participate in the study, you will be randomly assigned to one of the two treatment conditions. You will also be asked to complete some questionnaires related to your

physical and emotional health and well-being, including your pain level and the impact of pain on your functioning. Depending on your preference, these questionnaires can either be completed digitally using a tablet to enter your responses, or on paper forms. If you are assigned to the group that receives the tapering program only, you will be scheduled for your initial tapering program visit. If you have been assigned to the group that receives the education workshop, you will be scheduled to attend one of the next available **virtual** workshops. After you attend the **online** workshop, you will be contacted to schedule your initial tapering program visit.

If you have been assigned to the group that receives the **virtual** education workshop, as part of the workshop you will receive one hour of medical information on the nature of chronic pain, risks of long-term opioid use, and effective alternatives to opioid therapy. You will also receive four hours of training in acceptance and commitment therapy strategies for learning how to change the nature of your relationship with pain and to live more in line with your chosen values. At this workshop you will be asked to complete a pre-workshop questionnaire that will ask basic questions on your knowledge of opioids and opioid tapering, as well as your own personal experience with opioid use, opioid tapering and acceptance and commitment therapy. As well, at the end of the workshop you will be asked to respond to similar pre-workshop questions, as well as provide feedback on the workshop itself. **In order to take part in the online workshop, you will require access to a computer (personal computer or laptop), a tablet (e.g. iPad) or a smartphone and have internet access. If you do not have a device to access the online workshop but would still like to take part, please let the researcher know as arrangements can be made to provide you with temporary access to a tablet. Please ask the research staff if you have any questions or concerns at all about the use of technology for this workshop.**

At your initial taper program visit (approximately 60 minutes) in clinic you will also be asked to complete the same set of questionnaires that you were asked to complete at your initial study visit. You will work with one of the study clinicians to establish your own specific tapering and functional goals. This will include letting the clinician know of your current medications and doses, any previous attempts to taper opioids, and any other medical concerns. Together with the clinician you will set a taper start date and determine if other medication changes would be recommended for the tapering. The study team will then develop a detailed taper plan that will include a taper summary, with dates of each taper step and the dose required at each time point, as well as a follow up schedule. This will be provided to you as soon as it is prepared.

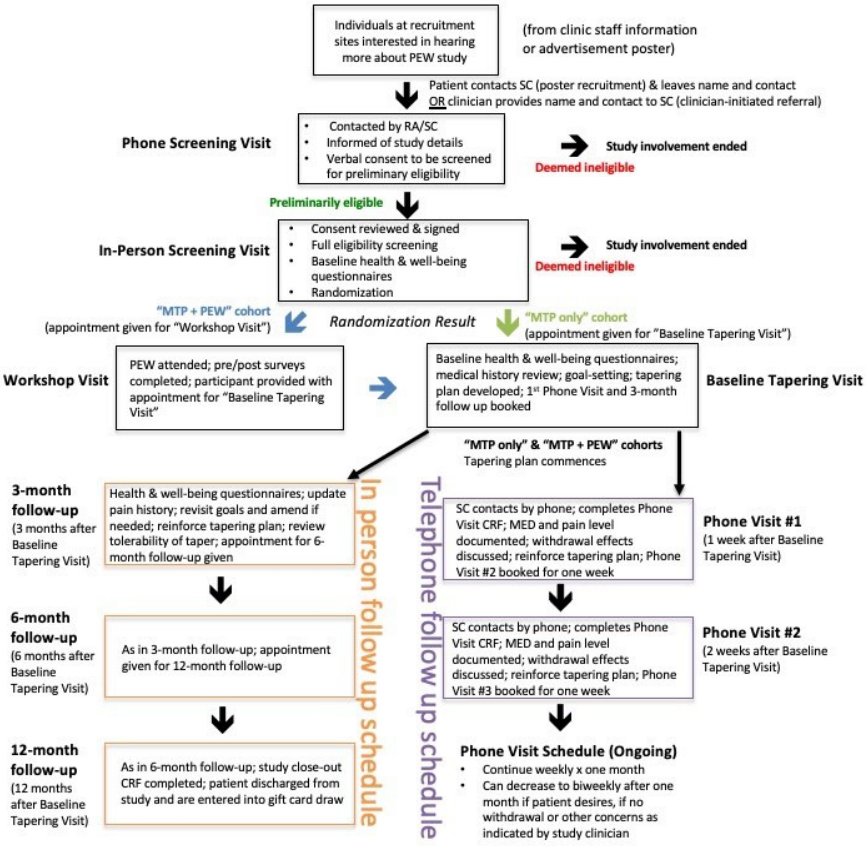
Note: *it is important to note that the taper schedule is designed to be extremely flexible and can be slowed or halted depending on how you respond. You are not expected to follow the schedule exactly as it is outlined at this initial visit. You will receive regular follow up to determine if the current tapering plan needs to be slowed, stalled or amended.*

You will be scheduled to receive follow-up telephone calls (approximately 15 minutes) from a member of the study team weekly and/or after each planned dosage reduction. During these telephone follow ups, your will discuss whether you are experiencing any withdrawal symptoms that require an adjustment to your taper rate or additional medication, what your current pain status is, and a general review of your overall health status. Based on your response to tapering after one month, these calls may be reduced to bi-weekly at the discretion of the study

clinicians.

In addition to the initial tapering visit and telephone follow ups, you will be asked to attend additional in-clinic visits (30-60 minutes) at 3-, 6-, and 12-months after your initial tapering visit to review your progress and obtain additional support. At these visits, you will again be asked to complete the same questionnaires that you were asked to complete at your initial study visit.

Participation in the study will be for a 12-month period (including in-person and telephone follow up appointments). Below is a figure outlining the steps of the study.



Abbreviations: PEW – Patient Education Workshops; SC – Study Coordinator; RA – Research Assistant; MTP – Multidisciplinary Tapering Program; CRF – Case Report Form; MED – morphine equivalent dos

The researchers may decide to take you off this study if it is in your medical best interest.

Situations where your participation in the study may be stopped include:

- Circumstances change such that you no longer meet study inclusion/exclusion criteria
- You experience significant and/or unmanageable withdrawal side effects
- Funding for the study is stopped or the study has ended

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study staff and your regular doctor first to ensure a safe transition of medical care.

Please take note: *You will be at serious risk of overdose if you increase your opioid dose to previous levels too soon after a period of being at a lower dose*.

Risks and Discomforts

Although the tapering of opioids will be done slowly and will be closely monitored, significantly reducing the risk of increased pain and/or symptoms of opioid withdrawal, there remains a risk of these occurring. While tapering your opioid, you may experience increased pain and/or symptoms of opioid withdrawal such as muscle aches, sweating, itchiness, diarrhea/loose stools, nausea and/or vomiting, yawning, & tremor, among others. You will be followed on a frequent basis by phone to assess for any of these symptoms and, if they are bothersome, you may be offered pharmacological treatment to help relieve them. You are also encouraged to contact Karin Ens or Dr. Turcotte (clinical pharmacists) if you experience any of these symptoms in between weekly phone follow-up. As well, it is possible that you may experience increased anxiety or lowered mood during the tapering process. If this should occur during the study, please contact a member of the study staff who can provide you with assistance and support, including putting you in touch with one of the study psychologists, Drs. Sabourin or Tkachuk, if needed. There is also a risk that you may experience some mild emotional discomfort related to the sensitive nature of some of the questions asked on the self-report questionnaires of health and well-being. If this becomes a concern, you may contact a member of the research team who can put you in touch with one of the study psychologists, if needed.

Your condition may not improve or may worsen while participating in this study.

If you are prescribed a drug to help manage withdrawal during the course of opioid tapering, it must only be taken by the person for whom it has been prescribed. All medication must be kept out of the reach of children and persons of limited capacity to read or understand.

Benefits

By participating in this study, you will be providing information to the study team that will show the effects of a new multidisciplinary tapering program for reducing opioid use in individuals with chronic pain. There may or may not be direct medical benefit to you from participating in

this study. We hope the information learned from this study will benefit other participants with chronic pain who would like to reduce their opioid use in the future.

Costs

All clinic and professional fees, diagnostic and laboratory tests which will be performed as part of this study are provided at no cost to you. There will be no cost for the study treatment that you will receive. You will be required to pay any parking expenses incurred during your in-person visits.

Payment for participation

By participating in this research study, you will be entered into a draw to receive one of four $250 grocery store gift cards. Your odds of winning one of these gift cards will be approximately 1 in 30. Under federal law, it is necessary that you answer a skill-testing question correctly in order to qualify for a chance to win the prize. If you wish to be considered for this prize, please answer the following question: (Write your answer in the blank space provided.) Skill testing question: (15 + 5) divided by 5 = .

Alternatives

Instead of being in this study, you may continue with standard medical treatment for your chronic pain condition through your primary care provider. If you are interested in tapering your opioid but do not want to take part in this study, please discuss this with your primary care provider. You do not have to participate in this study to receive treatment for your condition. Please talk to your regular provider about all your treatment options.

Notification of Study Participation

In order to ensure your family or primary care physician is up-to-date with your medical care, we will be notifying them of your participation in this study. They will be provided details of your clinical progress and will be made privy to your clinical details throughout the study. Please provide us with the necessary contact information of the physician you would like us to contact:

Your physician's name: _____

The name of your physician's clinic or practice: _____

Your physician's city and address (if known): _____

Your physician's phone number (if known): _____

Your signature authorizing us to contact your physician: _____

Clinical Trial Registration

As per regulation standards for all clinical research studies, this trial will be registered on the public database of clinical trials, ClinicalTrials.gov. This website provides information on federally and privately funded clinical research trials. A description of this clinical trial will be available on http://ClinicalTrials.gov. This registry does not include any information that can personally identify you. At most this site will include a description of the study and a brief summary of the results. You are free to search this registry at any time.

Confidentiality

Information gathered in this research study may be published or presented in public forums; however your name and other identifying information will not be used or revealed. Medical records that contain your identity will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law.

All study documents related to you will bear only your assigned patient code ("subject ID") so that all identifying information (e.g. name, date of birth) can be removed from individual data.

Despite our best efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. For example, your personal information may be disclosed if required by law; and The University of Manitoba Biomedical Research Ethics Board may review any records related to this study for quality assurance purposes. Medical records that contain your identity, such as the initial screening forms and the master list containing your name and your unique "subject ID", will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. All records will be kept on the Primary Investigator's computer that can only be accessed with a password known by the Primary Investigator and Study Coordinator. No information revealing any personal information such as your name, address or telephone number will leave the University of Manitoba.

As previously mentioned, your primary care provider (e.g. family physician, nurse practitioner, physician assistant) will be notified about your participation in this study. As well, your primary care provider will be notified if you are screened but not included in the study. If you are excluded from the study for reasons of safety (e.g. high levels of anxiety/depression, risk of opioid abuse/misuse etc.) your care provider will be notified of this for further clinical management.

Voluntary Participation/Withdrawal from the Study

Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect your other medical care at this site. If your study doctor feels that it is in your best interest to withdraw you from the study, your study doctor will remove you without your consent.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

Medical Care for Injury Related to the Study

You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) or the sponsor(s) from their legal and professional responsibilities.

Questions

You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study or if you have a research-related injury, contact the study doctor and the study staff: Dr. Dana Turcotte at 204-272-3170; Dr. Brigitte Sabourin at 204-787-1506; Karin Ens at 204-272-3170; Dr. Gregg Tkachuk at 204-925-1568.

For questions about your rights as a research participant, you may contact The University of Manitoba Biomedical Research Ethics Board at (204) 789-3389.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Statement of Consent

I have read this consent form. I have had the opportunity to discuss this research study with Dr. Turcotte and/or her study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statement or implied statements. Any relationship (such as employee, student or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my participation in this clinical trial is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that information regarding my personal identity will be kept confidential, but that confidentiality is not guaranteed. I authorize the inspection of my medical records by the University of Manitoba Biomedical Research Ethics Board.

By signing this consent form, I have not waived any of the legal rights that I have as a participant in a research study.

I agree to being contacted in relation to this study: Yes ( ) No ( )

Participant signature_____**Date** _____

Participant printed name: _____

This section is to be completed by the person obtaining consent:

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name:_____ **Date** _____

Signature: _____

Role in the study:_____[This must be done by an authorized/qualified member of the research team i.e. investigator, study nurse, etc.]

Relationship to study team members (if any):_____[eg. supervisor, teacher/professor or family

University of Manitoba | Research Ethics and Compliance

Research Ethics Bannatyne
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Winnipeg, MB R3E 0W3
T: 204 789 3255
F: 204 789 3414
bannreb@umanitoba.ca

Important Information about COVID-19 and Research Participation

At the University of Manitoba our primary responsibility related to research is to protect the safety of our research participants.

COVID-19 refers to the Coronavirus that is being spread across people in our communities. We need to provide you with important information about COVID-19, and to review ways in which your study participation might change because of COVID-19 related risk.
If you are considering joining a study at this time or are currently enrolled in a study, it is important that you consider the following information to determine if study participation is right for you at this time.

How is COVID-19 spread? COVID-19 is a respiratory virus spread by respiratory droplets, mainly from person-to-person. This can happen between people who are in close contact from one another (about 6 feet). It is also possible that a person can get COVID-19 by touching a surface or object that has the virus on it, then touching their mouth, nose or eyes.

Can COVID-19 be prevented? Current ways to minimize the risk of exposure to COVID-19 include "social distancing" which is a practice to decrease the potential for direct exposure to others who may have been exposed to COVID-19, for example by avoiding large gatherings or refraining from shaking hands with others. It is important to understand that since study participation may include increased travel outside of your home and increased exposure to others [within a clinical care environment] or research site it may increase your exposure to COVID-19. While there currently is no direct evidence that spending time in a health facility increases the risk of getting COVID-19, there might be a small increased risk.

What are the risks of COVID-19? For most people, the new coronavirus causes only mild or moderate symptoms, such as fever and cough. For some, especially older adults and people with existing health problems, it can cause more severe illness, including pneumonia. While we are still learning about this virus, the information we have right now suggests that the percentage of infected people who might die from the virus is about 3%.

Who is most at risk? Individuals over 60 and with chronic conditions such as cancer, diabetes and lung disease have the highest rates of severe disease from the infection.

Are there treatments available? At this time there is no vaccination or proven treatment for the COVID-19 infection.

How could your participation in this research change as a result of COVID-19? There are several ways we try to minimize your risk. If possible, we limit the number of times you have to come to a clinical care or research site. We ask every research participant if they have the symptoms of COVID-19 or have been in close contact with any cases. We reduce the time you are exposed to other people as much as possible. If you are suspected to be positive for COVID-19, there may be last minute changes to how research procedures are performed [such as a change from an in-person visit to a telephone call] or cancellations of research tests or procedures to ensure your safety.

The information related to risks of COVID-19 changes every day. The leaders at University of Manitoba are monitoring these risks and deciding how these risks should change our research. If you have questions about COVID-19 and your participation in research, please consult with the study team.

B-3. In-Person Screening/Consent Form - 3 pages

In-Person Screening/Consent Form

This form is to be used after preliminary eligibility has been confirmed on completion of a Telephone Screening Form. At this visit, patients will review consent forms and provide consent and will then be screened for full eligibility.

A. INTERVIEWER INFORMATION			
Date		Time	
Interviewer name			
B. PATIENT INFORMATION			
Patient name* *Patient name NOT entered into REDCap		Ph. Number	

C. CONSENT

To begin this next screening process, we will be providing you with two consent forms: a "Research Participant Information and Consent Form" and "COVID-19 Consent Appendix". The first consent form gives you a detailed review of the study including its purpose, procedures, risks, and benefits, etc. The second consent details the safety measures that are taken during the study to protect participants against COVID-19.

When these forms are given to you, you will be given as much time as you need to carefully read the contents and raise any questions or concerns that you may have. You are free to ask questions or clarify information at any point during this session and you may also ask the clinician to leave the room while you review it if you prefer.

Once you are satisfied with the information that has been provided, you will be asked to sign the consent forms to continue with the study. Your consent is completely voluntary and may be withdrawn at any time even if you have completed this portion of the session. Further details can be found in the consent form.

Option 1: Individual signs both consent forms:
Offer copies of signed forms and move on to Section D.

☐ Copy of signed consent form provided to the individual

Option 2: Individual refuses/withdraws consent:
Thank you for your time. If you are interested, we are hoping to make these resources available to primary care clinics and other health care settings in the future. We are hopeful that these resources may be open to you at a different time when appropriate. If you would like to leave us your contact information, we can reach you when similar opportunities become available.

Contact: _____

Address: _____

Phone Number: _____

D. BRIEF MEDICAL HISTORY

Q1: Do you have any medical conditions? (include condition and any clinical notes)

Q2: Do you have any allergies? (include allergy and reaction)

Q3: What is your age?

Q4: What is your sex (male/female/other)?

E. MEDICATIONS

Q1: Are you using any prescription medications? (include drug/dose/directions)

Q2: Are you using any non-prescription products like Tylenol, Advil, or Aspirin (include drug/dose/directions)

Q3: Are you using any vitamins, minerals, natural, herbal products, or supplements

Q4: Are you using any recreational drugs?

F. SCREENING TOOLS

We will now begin the screening process to help us determine your full eligibility in the study. This screening process is a series of questionnaires that will help to evaluate your pain, medical history, and opioid use. We will give these forms for you to fill out and you can take as much time as you need to answer the questions.

You have the option to complete the questionnaires electronically or on paper. Which option would you prefer?

- ☐ Electronic forms
- ☐ Paper forms

G. CONFIRMATION OF ELIGIBILITY CHECKLIST

Please ensure that the following boxes are checked if met:

- ☐ Age ≥ 18 years old
- ☐ Cognitively able to understand questionnaires and participate in education session education sessions (conducted in English only)
- ☐ CNCP more than half the days in the previous 6 months

Q2: Do you have any allergies? (include allergy and reaction)

Q3: What is your age?

Q4: What is your sex (male/female/other)?

E. MEDICATIONS

Q1: Are you using any prescription medications? (include drug/dose/directions)

Q2: Are you using any non-prescription products like Tylenol, Advil, or Aspirin (include drug/dose/directions)

Q3: Are you using any vitamins, minerals, natural, herbal products, or supplements

Q4: Are you using any recreational drugs?

F. SCREENING TOOLS

We will now begin the screening process to help us determine your full eligibility in the study. This screening process is a series of questionnaires that will help to evaluate your pain, medical history, and opioid use. We will give these forms for you to fill out and you can take as much time as you need to answer the questions.

You have the option to complete the questionnaires electronically or on paper. Which option would you prefer?

- ☐ Electronic forms
- ☐ Paper forms

G. CONFIRMATION OF ELIGIBILITY CHECKLIST

Please ensure that the following boxes are checked if met:

- ☐ Age ≥ 18 years old
- ☐ Cognitively able to understand questionnaires and participate in education session education sessions (conducted in English only)
- ☐ CNCP more than half the days in the previous 6 months

Appendix C: Data Collection Tools

C-1. Health and wellbeing questionnaires

The following seven questionnaires are completed at all in-person visits: In-Person Screening Visit, Baseline Tapering Visit, and again at 3-, 6-, and 12-month Follow-up Visits:

1. **Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)**[136]
   - Screens for risk of opioid misuse, guides monitoring frequency[137]
     - High risk: ≥18 (out of a max score of 96) [137]
2. **Pain Disability Index (PDI)**[138]
   - Measures pain's impact on family/home, recreation, social, occupation, sexual, self-care, and life-support [138]
     - Max score 70 (highest level of disability) [138]
   - Minimally important benefit depends on baseline score:[159]
     - Baseline score ≤27: a change of 7
     - Baseline score 28-42: a change 15
     - Baseline score ≥43: a change of 20
3. **Patient-Reported Outcomes Measurement Information System Global-10 (PROMIS Global-10)**[141]
   - Measures general health, generates 2 scores: Global Physical and Global Mental Health[142]
     - Max score 20 (excellent health) [141]
   - Minimally important benefit: a change of 4[162]
4. **Patient Health Questionnaire-9 (PHQ-9)** [132]
   - Depression score: screens for and assesses the severity of depression [132]
     - Max score 27 (highest severity of depression) [132]
       - minimal depression: 0-4
       - mild depression: 5-9
       - moderate depression: 10-14
       - moderate to severe depression: 15-19
       - severe depression: 20-27
   - Minimally important benefit: a change of 3[163]
5. **Generalized Anxiety Disorder-7 (GAD-7)** [145]
   - Anxiety score: screens for and assesses the severity of generalized anxiety disorder[145]
     - Max score 21 (highest severity of anxiety) [145]
       - minimal anxiety: 0-4
       - mild anxiety: 5-9
       - moderate anxiety: 10-14
       - severe anxiety: 15-21
   - Minimally important benefit: a change of 3[158,162]
6. **Chronic Pain Acceptance Quetionnaire-8 (CPAQ-8)**[147]
   - Assesses patient attitudes about pain, their indicators of quality of life, and target goals [147]
7. **Chronic Pain Values Inventory (CPVI)**[152]
   - Determines patient-specific values and evaluates success at following these values [152]

The Opioid Risk Tool (ORT)[129] is only completed at the In-Person Screening Visit to establish eligibility and is not repeated at subsequent visits.

- Screens for the risk of problematic opioid use
  - 0-3: low risk
  - 4-7: moderate risk
  - ≥8: high risk (excluded from trial)

C-2. Pre- and Post-Workshop Questionnaires

Pre-Workshop Questionnaire

Study ID#: _____ Date: _____

Opioid General Knowledge

Note: *opioids refer to a class of medications that on opioid receptors in our body and are commonly used to treat pain. Examples include morphine, codeine, hydromorphone & fentanyl*

Please select the most appropriate response:

1. Sleep disturbance is a potential side effect of opioid use.
   True False
2. Trouble breathing is NOT a primary concern with opioid overdose.
   True False
3. Increasing the dose of your opioid can make your pain worse.
   True False
4. Which of the following is NOT a side effect of opioid use?
   a) Constipation
   b) Dizziness
   c) Erectile Dysfunction
   d) Itchiness
   e) All of the above are possible side effects
5. Lowering the dose of an opioid (tapering) will cause pain levels to increase.
   True False
6. If I am not addicted to opioids, I am not at risk of experiencing an opioid overdose.
   True False

Personal Experience with Opioids

Please select the most appropriate response based on your experience with opioid use for pain:

1. Overall, how satisfied are you with your current opioid treatment?
   a) Very satisfied
   b) Somewhat satisfied
   c) Neither satisfied nor dissatisfied
   d) Somewhat dissatisfied
   e) Very dissatisfied
2. The opioids I take are effective at managing my pain.
   a) Strongly agree
   b) Agree
   c) Neither agree nor disagree
   d) Disagree
   e) Strongly disagree
3. How often do you experience side effects when you take your opioid dose?
   a) Most of the time
   b) Some of the time
   c) Seldom
   d) Never
4. How bothersome are the side effects that you experience due to opioid use?
   a) Very bothersome
   b) Bothersome
   c) A little bothersome
   d) No impact
5. Over the last 12 months, has your dose of opioid increased?
   a) No
   b) Yes
6. Over the last 12 months, has your dose of opioid decreased?
   a) No
   b) Yes

Opioid Tapering

1. I would like to be able to reduce the amount of opioid that I currently take.
   True False
   If you have been thinking about reducing your opioid dose, how ready are you to move forward with this?
   a) Very ready
   b) Somewhat ready
   c) Not really ready
2. Please list up to **three** things that you would be concerned about if you were to reduce/taper your opioid dose:
   i. _____
   ii. _____
   iii. _____
3. Have you tried to taper/reduce your opioid dose in the past?
   a) Yes
   b) No
   If yes, would you say your attempt was a success? Why or why not?
   _____
   _____
   _____

Acceptance and Commitment Therapy for Chronic Pain

1. Have you taken part in any Acceptance and Commitment Therapy and/or Cognitive Behavioural Therapy (CBT) in the past for your chronic pain?
   a) Yes
   b) No
   If yes, how beneficial did you find the experience in helping with the management of your chronic pain?
   i. Helped a lot
   ii. Helped a little
   iii. Didn't help at all
2. How helpful do you think this workshop will be in helping you to manage the impact that chronic pain has on your life?
   a) Very helpful
   b) Quite helpful
   c) Somewhat helpful
   d) A little bit helpful
   e) Not helpful at all

Post-Workshop Questionnaire

Study ID#: _____ Date: _____

Opioid General Knowledge

Please select the most appropriate response:

1. Sleep disturbance is a potential side effect of opioid use.
   True False
2. Trouble breathing is NOT a primary concern with opioid overdose.
   True False
3. Increasing the dose of your opioid can make your pain worse.
   True False
4. Which of the following is NOT a side effect of opioid use?
   a) Constipation
   b) Dizziness
   c) Erectile Dysfunction
   d) Itchiness
   e) All of the above are possible side effects
5. Lowering the dose of an opioid (tapering) will cause pain levels to increase.
   True False
6. If I am not addicted to opioids, I am not at risk of experiencing an opioid overdose.
   True False

Opioid Tapering

I would like to be able to reduce the amount of opioid that I currently take.
True False

If you have been thinking about reducing your opioid dose, how ready are you to move forward with this?
a) Very ready
b) Somewhat ready
c) Not really ready

Workshop Feedback

1. This workshop provided value to my pain management.
( )Strongly Agree ( )Agree ( )Neutral ( )Disagree ( )Strongly Disagree

2. I will use what I learned in this workshop to help manage my pain.
( )Strongly Agree ( )Agree ( )Neutral ( )Disagree ( )Strongly Disagree

3. What did you like about the workshop?

4. I found the format of this workshop (full day, online) worked well with my needs.
( )Strongly Agree ( )Agree ( )Neutral ( )Disagree ( )Strongly Disagree

5. I didn't have any barriers that affected my ability to attend this workshop significantly (eg. internet issues, time constraints, etc)
( )Strongly Agree ( )Agree ( )Neutral ( )Disagree ( )Strongly Disagree

6. Do you have any suggestions for improving the workshop?
(Please include comments on workshop format and/or any barriers you encountered from previous questions if applicable)

C-3. Opioid conversion table

Opioid conversion table: Conversion factors used to calculate Morphine Equivalent Dose (MED), which is used as a metric throughout the trial. This conversion is used for data collection / analysis only (NOT used for patient care, since opioid equivalence can be quite variable – especially fentanyl – and many factors must be taken into account for clinical interventions related to opioid dose equivalence, like opioid rotation). Modified from conversion factors recommended in the 2017 Canadian Guideline for opioid therapy and chronic noncancer pain[10].

Opioid*	Conversion factor**	Minimum daily dose for study enrollment
Morphine	1	50mg
Codeine	0.15	333mg
Fentanyl (transdermal)	150	25mcg/hr patch
Hydromorphone	5	10mg
Oxycodone	1.5	33mg
Tramadol	0.167	300mg

*Based on dose of oral opioid (except where explicitly noted)

**Does not reflect exact equivalence (simply the conversion factor used for data reporting in this trial)

Appendix D: Patient Education Workshop (PEW) Content

D-1. Example workshop agenda

Content (presenter)	Time	Hexaflex Theme
Housekeeping **(B)**	9:30-9:35 (5 min)	
Values-based intro (**G**)	9:35-9:45 (10 min)	Values
Your Life Path (**G**) (moving towards vs away, outside vs inside problem) *include opioid fear/withdrawal	9:45-10:15 (30 min)	Psychological Flexibility
Child in the Department Store **(B)**	10:15-10:25 (10 min)	Avoidance
Internal vs. External Events **(G)** "Find it and fix it" vs "If you don't want it, you've got it"	10:25-10:30 (5 min)	Creative Hopelessness/ Acceptance
Clean vs. Dirty Discomfort **(B)**	10:30-10:35 (5 min)	Acceptance
Tug of War with the Pain Monster **(B)**	10:35-10:50 (15 min)	Acceptance
Passengers on the Bus **(G)**	10:50-11:05 (15 min)	Cognitive Defusion/ Committed Action
BREAK	11:05-11:15 (10 min)	
Compassionate Hand **(B)**	11:15-11:20 (5 min)	Self-Compassion
Experiential Cognitive Defusion Exercises: a) Getting Off Your But's **(G)** b) Having a thought vs buying a thought **(B)**	11:20-11:40 (20 min)	Cognitive Defusion
Leaves on a Stream **(B)**	11:40-11:50 (10 min)	Cognitive Defusion
Values – Revisited **(G)** (Values vs. Goals video)	11:50-12:00 (10 min)	Values
90th Birthday **(B)**	12:00-12:15 (15 min)	Values
Unwelcome Party Guest video **(G)**	12:15-12:30 (15 min)	Willingness/ Committed Action
LUNCH BREAK	12:30-1:10 (40 min)	
Chronic Pain and Opioid Education **(K)**	1:10-2:10 (60 min)	
BREAK	2:10-2:20 (10 min)	
Urge Surfing **(G)** *include opioid craving	2:20-2:35 (15 min)	Mindfulness/ Willingness
Two Side of a Coin **(B)**	2:35-2:55 (20 min)	Willingness/ Committed Action
Complete Life Path Valued Actions **(G)** (Right side of matrix)	2:55-3:05 (10 min)	Willingness/ Committed Action
My valued action plan **(G)**	3:05-3:25 (20 min)	Willingness/ Committed Action
Path up the Mountain **(B)**	3:25-3:30 (5 min)	Mindfulness/ Self as Context
Wrap up/Questions	3:30-3:40 (10 min)	

D-2. Presentation slides (Chronic Pain & Opioid Education) - 10 pages

Images, including photos and clipart (except where otherwise specified), sourced from Canva and Microsoft Office in alignment with their policies.

CHRONIC PAIN & OPIOIDS

2021

PREPARED BY
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AGENDA

TREATMENTS
DRUG AND NON-DRUG OPTIONS FOR TREATING CHRONIC PAIN

CHRONIC PAIN
UNDERSTANDING PAIN

OPIOIDS
RETHINKING OPIOIDS FOR CHRONIC PAIN

What is Pain?

An uncomfortable, difficult experience that arises in many situations.

Often our body's response to danger, short-term (or acute) pain can protect us from harm.

Chronic Pain is pain lasting >12 weeks

No longer signals damage - it has no functional role or purpose

Involves complex pathways and factors that affect pain signals

TYPES OF PAIN

<u>*Neuropathic Pain:*</u>
Burning, pins & needles, shooting pain
Associated with the nervous system (nerves)

<u>*Nociceptive Pain:*</u>
Dull, sore, aching, sharp, throbbing pain
Associated with injured body tissues

<u>*Mixed Pain:*</u> A combination

Types of pain differ in symptoms and **how they are treated**

THE DEMEDICALIZATION OF PAIN

It is important to know that there is not always a disease causing your pain

Chronic pain is a disease process on its own

UNDERSTANDING PAIN

Understanding Pain in less than 5 minutes, and what to do about it!
By Pain Australia

VIDEO

HTTPS://WWW.YOUTUBE.COM/WATCH?V=RWMKUCUEJIS

Video sourced from www.youtube.com/watch?v=rwmkucuejis[164]

OUR **GOALS**

HOW MUCH CAN WE EXPECT OUR PAIN TO DECREASE BY?

Decreasing pain by 30% could be a reasonable goal

SHOULD THIS BE OUR ONLY GOAL?

What about day to day functioning and wellbeing?

If we only target pain reductions, it may come at the expense of our quality of life

HOW DO WE IMPROVE DAILY **FUNCTIONING**?

THIS IS DIFFERENT FOR EVERYONE, BUT COULD MEAN:

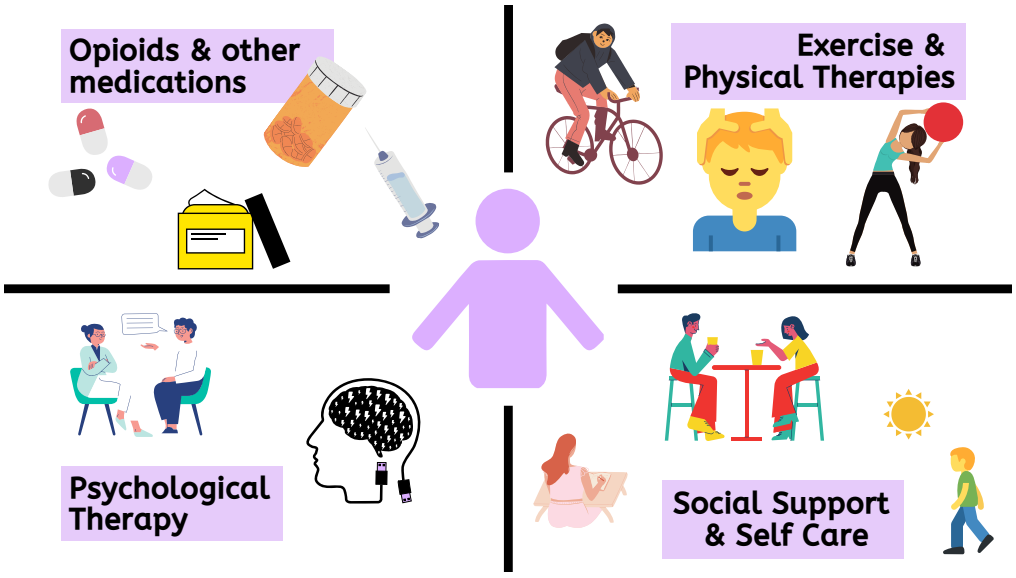
- Increasing mobility
- Ability to do exercise or activities
- Improving sleep quality
- Enhancing quality of life
- Improving mood
- Minimizing side effects
- Minimizing cost of treatment(s)
- Reducing pill burden

Treatments for Chronic Pain

Treating chronic pain extends beyond medications

Pain generally responds poorly to using pills alone (especially opioids)

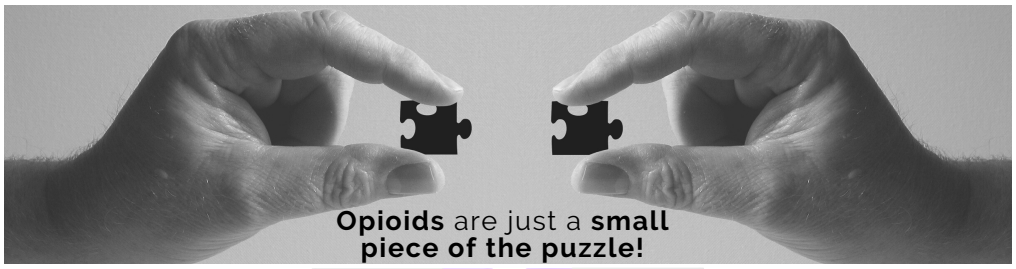
The best treatment strategies for chronic pain require approaches that are individualized and multi-faceted

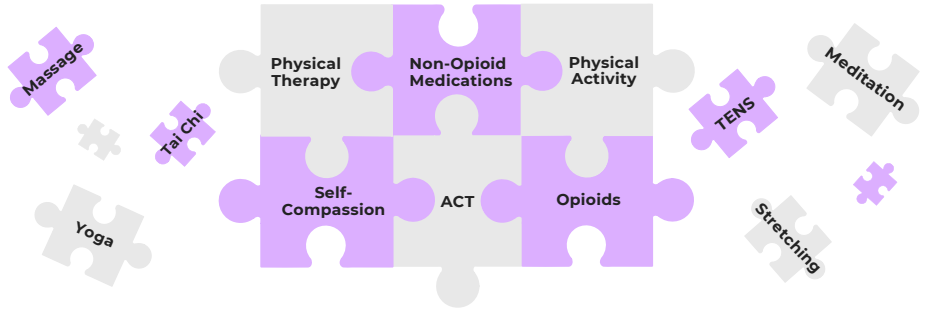


Treatments for Chronic Pain: **Non-Opioid Medications**

Pain management often requires multiple trials of different treatments to identify what works best for you

Drug	Examples	Role	How it Works	Pros and Cons
Acetaminophen	Tylenol	Musculoskeletal (muscle or tissue damage)	Increases pain threshold	- Cheap & relatively safe - Not very effective
NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)	Ibuprofen (Advil) Naproxen (Aleve) Celecoxib (Celebrex)	Swelling and musculoskeletal	Blocks inflammation and pain	- Very effective - Helps swelling - Lots of risks
Antidepressants	Duloxetine (Cymbalta) Venlafaxine (Effexor) Amitriptyline (Elavil)	Neuropathic pain, musculoskeletal	↑ brain chemicals that ↓ pain signaling	- Also helps with mood & sleep - Treats most pain - Take weeks to work
Anti-Seizure Drugs	Gabapentin Pregabalin (Lyrica) Valproic Acid	Neuropathic pain	↓ reactivity of brain receptors to ↓ pain signals	- Can be low cost - Causes drowsiness - Take weeks to work
Muscle Relaxants	Cyclobenzaprine (Flexeril) Methocarbamol (Robaxacet)	Muscle spasms, musculoskeletal	Relaxes the brain to ↓ muscle tension	- Short term only - Very sedating





WHAT ARE OPIOIDS?

Common examples:
Morphine
Oxycodone
Hydromorphone
Codeine
Fentanyl

Opioids are a class of medications that can be used to treat pain

- Acute pain
- Surgical pain
- Cancer pain
- Chronic pain

BENEFITS

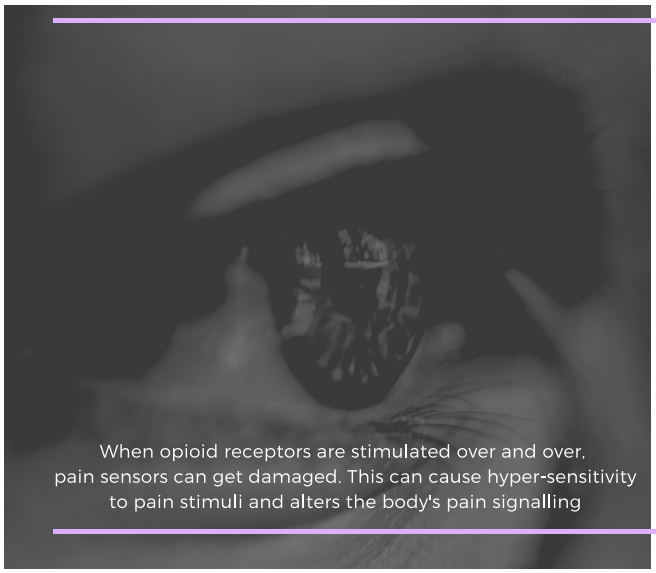
Opioids can improve pain over the short term
- Pain relief
- Improve function & quality of life

However, evidence for chronic pain has shown that opioids lose their benefit over time

HARMS

Even when taken as directed, opioids have bothersome side effects:
- Nausea & vomiting
- Constipation
- Dry mouth
- Sleepiness or dizziness
- Sweating
- Mood swings

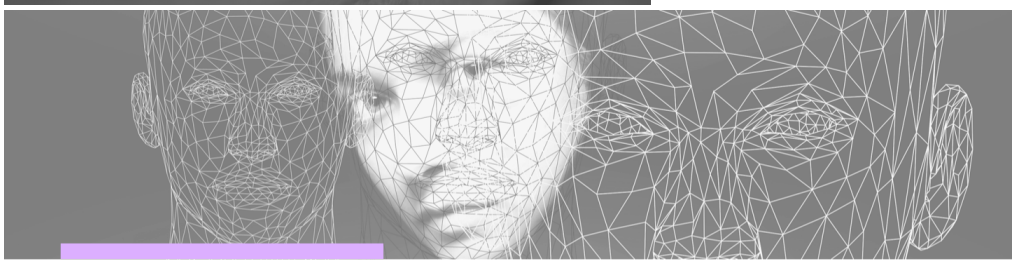
And risks that can become a concern:
- Heightened pain sensitivity
- Tolerance
- Dependence
- Addiction
- Overdose



When opioid receptors are stimulated over and over, pain sensors can get damaged. This can cause hyper-sensitivity to pain stimuli and alters the body's pain signalling

What is Hyperalgesia?

Increased sensitivity to pain associated with prolonged opioid use

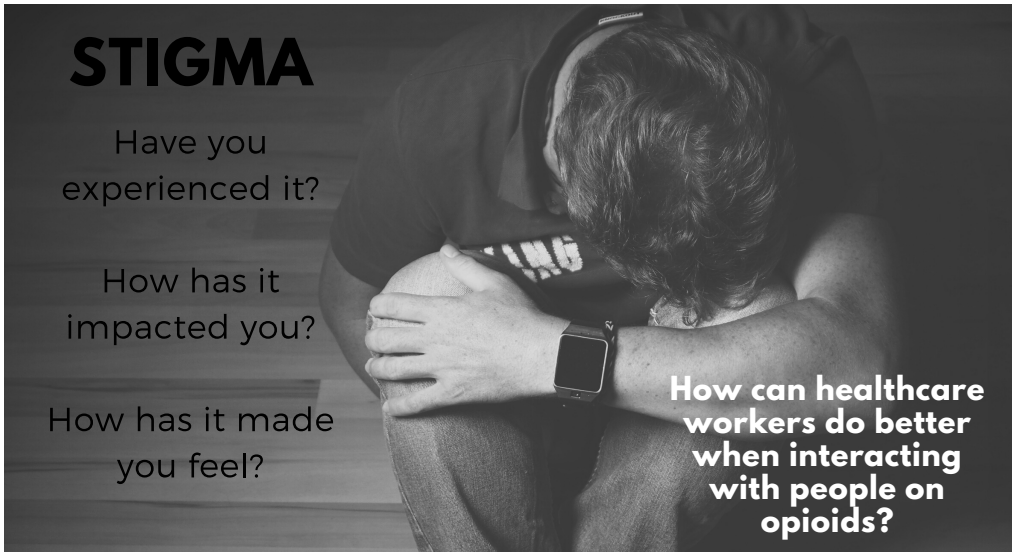


HOW LONG SHOULD YOU BE ON THEM?

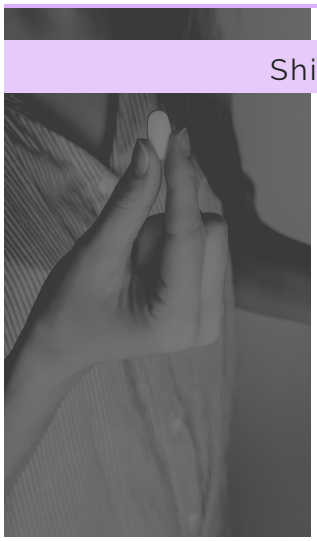
Opioids should be used at the lowest effective dose for shortest possible duration

DID THIS CHANGE?

According to the best and most recent evidence, opioids shouldn't be our 1st choice. We use them only when other treatments aren't working



Shifting the Focus on **Opioids**



"It is not an easy reality to face, but just as your chronic pain did not develop overnight, neither will the solution to finding relief develop in a day or two."

What to do Now: Tapering Opioids

The goal is to get you to safer doses while giving you alternative tools to help manage your chronic pain. In the long run, we are preventing the long-term side effects and harms that are associated with long-term opioid use.

What is **Tapering?**

THE DECISION TO TAPER YOUR OPIOIDS

What it is:

- Controlled dose reductions to safer levels
- Usually starts with 10% reductions every 2-4 weeks
- Regular check-ins with your healthcare team
- Adjusted based on your personal response and feedback

What it is NOT:

- Stopping completely
  - The goal is a reduction, not everyone will get to zero
- Terrible withdrawal or side effects
  - The taper is adjusted to minimize symptoms
- Pain increases
  - Studies show people do not experience more pain
  - Sometimes pain can increase after dose changes, but is temporary.

Dependence on Opioids

When taking opioids long term, the body becomes tolerant, which can affect the brain - causing physical and psychological dependence.

The body tries to adjust when it feels opioids missing by producing symptoms of withdrawal.

The level of dependency can be related to:

- dose
- duration of use
- which opioid
- other medical conditions, including mental health
- history of addiction
- previous trauma
- stressful environments

FREQUENTLY ASKED QUESTIONS

1. Why do I have to change my dose even if I'm doing fine?

Tapering is about getting to a **safer dose** to reduce the opioid's risks

Some people have side effects without knowing it. They don't realize until they've reduced their opioids and some minor problems like sweating or sleeping problems improve

FREQUENTLY ASKED QUESTIONS

2. Won't my pain get worse if I stop using my opioid?

Actually, studies that compare the differences in pain when opioid doses decrease show that pain increases only for a short-term after changing the dose and for some, pain does not increase at all.

In the end, there was no increase in pain after tapering the opioid dose.

FREQUENTLY ASKED QUESTIONS

3. What if nothing else works for my pain?

Since opioids are usually used when nothing else is working, it is common to fear having nothing else available for pain, but opioids are not are only option - there are other effective options out there.

Opioids are ok to use short term, but they start to lose their effect over time. They're not as effective as we used to think for chronic pain.

We're here to discuss the options and help you find what works best for you.

FREQUENTLY ASKED QUESTIONS

4. Do I need to worry about addiction?

The risk of addiction is low while being supervised, but can occur without warning. 1 in 4 people using long-term prescription opioids can struggle with addiction

The symptoms of addiction can include:

- cravings
- running out of your opioids early
- using opioids longer than planned
- giving up doing things that were once enjoyable to you as a result of opioid use

FREQUENTLY ASKED QUESTIONS

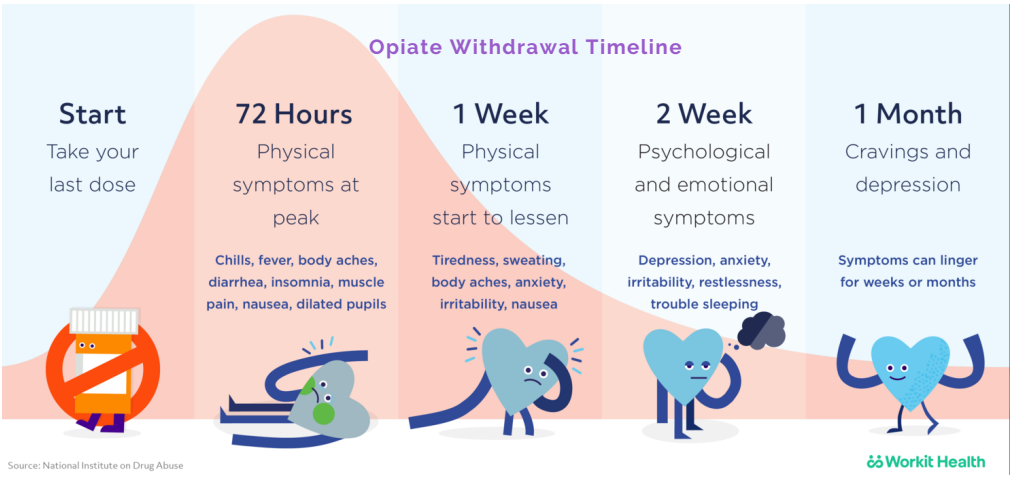
5. Does everyone get withdrawal?

Everyone is different - some people feel withdrawal symptoms quickly or severely while others have none at all.

When stopping opioids without a healthcare provider, withdrawal is intolerable for most and resuming opioid use is likely.

With a clinical team, withdrawal symptoms can be greatly reduced by:
- Beginning with a slow tapering plan
-Treating any symptoms with medications
- Slowing or pausing the taper

WITHDRAWAL:
WILL IT HAPPEN TO ME?



This infographic is a copyrighted image and is used with written permission from Workit Health [51]

questions?

D-3. Additional educational materials distributed post-workshop

- Workbooks
  - ACT workbook
  - Chronic Pain and Opioid workbook
- ACT exercises provided as audio files (corresponding ACT hexaflex theme in brackets)
  - “A compassionate hand” (self-compassion)
  - “Leaves on a stream” (cognitive defusion)
  - “Tug of War with the Pain Monster” (acceptance)
  - “Urge Surfing” (mindfulness/willingness)
- Exercises completed during the workshop (includes content developed collaborated by facilitators and participants)
  - Life Path matrix
  - Valued Action Plan

Appendix E: Multidisciplinary Tapering Program (MTP) Data Collection Forms

E-1. Baseline Taper Visit form - 7 pages

Baseline Taper Visit Form

This form is to be used after the patient has consented and has been successfully screened for eligibility. The purpose of this visit is to identify baseline information such as a full history and patient-specific goal setting. This information will be used to derive an individualized, initial tapering plan and follow-up schedule.

A. INTERVIEWER INFORMATION			
Date		Time	
Name			
B. PATIENT INFORMATION			
Study ID Number			
C. MEDICAL HISTORY			
Q1: Do you have any medical conditions?			
Condition		**Clinical Notes**	
Q2: Do you have any allergies?			
Allergy		**Reaction**	

E. MEDICATIONS
Q1: Are you using any prescription medications? (Include drug, dose, route, directions, eg. rosuvastatin 20mg po daily)
Q2: Are you using any non-prescription products like Tylenol, Advil, or Aspirin? (Include drug, dose, route, directions)
Q3: Are you using any vitamins, minerals, natural or herbal products or supplements?
Q4: Are you using any recreational drugs?
F. LIFESTYLE & SOCIAL HISTORY
Q1: Can you describe what your diet is like in a typical week?
Q2: On average, how often do you exercise in a week?

Q3: Are you currently employed? What is your occupation?
Q4: Have you ever smoked? How much do/did you smoke? When did you start (and quit)?
Q5: Do you drink alcohol? How much alcohol do you drink in a typical week?
G. PAIN HISTORY
Q1: Can you describe what your pain feels like (i.e. burning, needle-like, dull, aching)?
Q2: What is the location of your pain? Does it radiate?
Q3: When did you first begin experiencing pain? How has that changed from then to the present?
Q4: How long does your pain typically last?
Q5: Have you had any surgeries related to your pain?
Q6: Is there anything that makes your pain worse? Is there anything that makes your pain better?

H. TREATMENT HISTORY

Q1: What drug treatments have you tried in the past to manage your pain?

Drug	Duration	Notes (I.e. amount of relief, duration of relief)

Q2: What non-drug options have you tried in the past to manage your pain?

Therapy	Duration	Notes (i.e. amount of relief, duration of relief)

I. HEALTH/WELL-BEING QUESTIONNAIRES

This process includes a series of questionnaires that will help to evaluate your pain, medical history, and opioid use. These are the same questionnaires as during the in-person screening. We will give you as much time as you need to answer the questions. Typically, it takes about 15-30minutes to complete all the forms.

You have the option to complete the questionnaires electronically using a computer or tablet (that we provide) or using paper forms. Which option would you prefer?

- ☐ Electronic forms
- ☐ Paper forms

Please remember to answer each question as honestly and accurately as possible to help us better understand your condition.

Check to make sure all questionnaires are complete:

1. Patient Health Questionnaire 9 (PHQ9)
2. Patient Reported Outcomes Measurement Information System Global-10 (PROMIS Global-10)
3. Pain Disability Index (PDI)
4. Chronic Pain Acceptance Questionnaire 8 (CPAQ-8)
5. Chronic Pain Values Inventory (CPVI)
6. Generalized Anxiety Disorder 7 Item (GAD-7)
7. Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)

J. TAPER INITIATION PLAN

- ☐ Educate on the tapering process
  - ❑ Individualized process (may go as fast or as slow as needed)
  - ❑ Goal to maintain or decrease the opioid dose (but permitted to go up or down)
  - ❑ What to expect during the taper
- ☐ Discuss patient-specific goals and expectations (in terms of pain and function)
- ☐ Benefits and risks of opioid use (tolerance, opioid-induced hyperalgesia, overdose etc.)
- ☐ Benefits and risks of tapering (reduce opioid-related harms, improve QOL, etc.)
- ☐ Withdrawal: monitoring, symptoms, management
- ☐ Address misconceptions about tapering, e.g. "Pain will get worse" – emphasize that pain, mood, and sleep have been shown to improve
- ☐ Address patient fears/concerns about tapering
- ☐ Provide alternative methods of pain management as appropriate including self-management and non-pharmacological measures
- ☐ Discuss naloxone use and offer / prescribe naloxone kit
- ☐ Offer support
- ☐ Address patient questions and concerns

GOALS

Current medication			
Current Dose (in MED)			
Target Dose			
Start Date		Proposed End Date	
Description of Reduction Plan			

DETAILS OF TAPER

Including opioid, formulation, dose, and dosing interval	

K. TELEPHONE FOLLOW UP			
Verify Contact Information	☐ Yes ☐ No		
Date			
Time			
L. CLINIC VISIT FOLLOW UP			
Date			
Time			
Location			
M. PHARMACY INFORMATION			
Pharmacy Name		Address	
Phone Number		Fax Number	
Bubble Pack	☐ Yes ☐ No		
Drop-Off Method	☐ Patient to bring in prescription in-person ☐ Prescription to be faxed to named pharmacy		
Pick-Up Method	☐ Patient to pick up in-person ☐ Deliver to patient address		
Other Notes			

N. OTHER PRESCRIPTIONS (see sample Rx below)	
Prescription sent for naloxone kit	☐ Yes ☐ No
Prescription sent for withdrawal treatment	☐ Yes ☐ No
Other prescriptions sent:	

O. FINAL CHECKLIST

Please ensure that ALL of the following boxes are checked before ending the session:

- ☐ Review of medical history
- ☐ Review of medications
- ☐ Review lifestyle & social history
- ☐ Review pain history
- ☐ Review treatment history
- ☐ Completion of all health/well-being questionnaires
- ☐ Taper planning, including a taper schedule and withdrawal prescription (as applicable)
- ☐ Booking telephone follow-up
- ☐ Booking in-clinic visit
- ☐ Verify Pharmacy information

Prescription for Managing Opioid Withdrawal

Name: _____ Date: _____

Health Card: _____

℞

		check ☑	initial
acetaminophen 500 mg po qid prn for aches, pains, and flu-like symptoms.	x 100 tabs	☐	
ibuprofen 400 mg po qid prn for aches, pains, and flu-like symptoms.	x 100 tabs	☐	
cloNIDine 0.1 mg po bid prn for sweating and withdrawal pain.	x 30 tabs	☐	
dimenhyDRINATE 50 mg po qid prn for nausea or vomiting.	x 30 tabs	☐	
loperamide 2 mg po qid prn for diarrhea. Stop laxatives if loperamide started.	x 30 tabs	☐	
Use sleep hygiene for insomnia Pharmacist to please provide education.		☐	
***naloxone kit** for injection, 2 vials of 0.4 mg/mL in case patient restarts opioids at high dose.	x 1 kit	☐	
other: e.g. oxybutynin [for sweating], melatonin [for sleep], hydrOXYzine [for itchiness or anxiety], traZODone [for sleep], prochlorperazine [for nausea], hyoscine ...			

Refill _____ times

Physician name: _____

Physician signature: _____

E-2. Ongoing Telephone Monitoring Form - 2 pages

Ongoing Telephone Monitoring Form

This form is to be used for weekly follow-up.

A. INTERVIEWER INFORMATION			
Date		Time	
Name			
B. PATIENT INFORMATION			
Study ID Number		Visit #	
C. MONITORING			
Pain			
On a scale of 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your average pain in the last week? 1 2 3 4 5 6 7 8 9 10			
Other Updates on Pain			
Pain Management			
Mood			
Withdrawal			
Physical Activity			
Function			
Sleep			

Other Comments

D. GOALS	
Current medication	
Current dose (MED)	
Target Dose	
Other Comments (please refer to previous forms for current taper plan)	

E. ACTION

Please check and describe one of the following options if applicable:

- ☐ Continue current opioid dose:
- ☐ Opioid dose change (increase or decrease):
- ☐ Other opioid change:
- ☐ Other medications prescribed (e.g. other pain meds, meds for withdrawal, etc.):

F. TELEPHONE FOLLOW UP

We would like to schedule the next appointment to speak with you by phone like we have today. These phone conversations will happen regularly to follow your progress in the study.

Verify Contact Information	☐ Yes ☐ No
Date	
Time	

H. FINAL CHECKLIST

- ☐ Completion of mandatory monitoring questions
- ☐ Review of goals
- ☐ Determine following actions for taper and withdrawal
- ☐ Schedule future telephone follow-up

E-3. Ongoing In-Clinic Visit Form – 2 pages

Ongoing In-Clinic Visit Form

This form is to be used for the in-clinic visits at 3 and 6 months.

A. INTERVIEWER INFORMATION			
Date		Time	
Name			
B. PATIENT INFORMATION			
Study ID Number			
C. HEALTH/WELL-BEING QUESTIONNAIRES			
Check to make sure all questionnaires are complete: 1. Patient Health Questionnaire 9 (PHQ9) 2. Patient Reported Outcomes Measurement Information System Global-10 (PROMIS Global-10) 3. Pain Disability Index (PDI) 4. Chronic Pain Acceptance Questionnaire 8 (CPAQ-8) 5. Chronic Pain Values Inventory (CPVI) 6. Generalized Anxiety Disorder 7 Item (GAD-7) 7. Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)			
D. MONITORING			
Pain			
On a scale of 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your average pain in the last week? **1 2 3 4 5 6 7 8 9 10**			
Other Updates on Pain			
Pain Management			
Mood			
Withdrawal			
Physical Activity			

Function			
Sleep			
Other Comments			
E. GOALS			
Current medication			
Current dose (MED)			
Target Dose			
Start Date		Proposed End Date	
Description of Reduction Plan			
F. DETAILS OF TAPER			
Opioid Formulation Dose Dosing Interval			
G. CLINIC VISIT FOLLOW UP			
Date			
Time			
Location			
H. FINAL CHECKLIST			
▢ Completion of health/well-being questionnaires ▢ Completion of monitoring questions ▢ Review of goals ▢ Review details of taper ▢ Schedule following clinic visit			

E-4. Final In-Clinic Visit Form - 2 pages

Final In-Clinic Visit Form

This form is to be used for the last in-clinic visit at 12 months.

A. INTERVIEWER INFORMATION			
Date		Time	
Name			
B. PATIENT INFORMATION			
Study ID Number			
C. HEALTH/WELL-BEING QUESTIONNAIRES			
Check to make sure all questionnaires are complete: 1. Patient Health Questionnaire 9 (PHQ9) 2. Patient Reported Outcomes Measurement Information System Global-10 (PROMIS Global-10) 3. Pain Disability Index (PDI) 4. Chronic Pain Acceptance Questionnaire 8 (CPAQ-8) 5. Chronic Pain Values Inventory (CPVI) 6. Generalized Anxiety Disorder 7 Item (GAD-7) 7. Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)			
D. MONITORING			
Pain			
On a scale of 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your average pain in the last week? **1 2 3 4 5 6 7 8 9 10**			
Other Updates on Pain			
Pain Management			
Mood			
Withdrawal			
Physical Activity			

Function
Sleep
Other Comments

E. GOALS			
Current medication			
Current dose (MED)			
Target Dose			
Start Date		Proposed End Date	
Description of Reduction Plan			

F. DETAILS OF TAPER	
Opioid Formulation Dose Dosing Interval	

G. END OF STUDY FINAL CHECKLIST

- ☐ Completion of health/well-being questionnaires
- ☐ Completion of monitoring questions
- ☐ Review of goals
- ☐ Review details of taper
- ☐ Contact Primary Care Provider for continuation of care
- ☐ Discuss future study interest
- ☐ Offer PEWs for participants in the MTP alone group
- ☐ Thank individual for participation
- ☐ Address patient questions/concerns

Appendix F: Supplemental Data Tables and Scatter Plots

F-1. Opioid dose data tables

Opioid dose by time and cohort, basic statistical measures (n=16)

Time	Cohort	n	Minimum	Mean	Median	Maximum	Standard Deviation
Morphine Equivalent Dose in mg/day							
0 Months	MTP	7	60.00	243.57	160.00	900.00	298.69
	PEW	9	50.00	78.17	60.00	135.00	31.66
3 Months	MTP	7	50.00	189.29	90.00	635.00	210.62
	PEW	9	20.00	62.78	60.00	135.00	33.68
Log-transformed Morphine Equivalent Dose							
0 Months	MTP	7	4.09	5.04	5.08	6.80	0.95
	PEW	9	3.91	4.30	4.09	4.91	0.37
3 Months	MTP	7	3.91	4.84	4.50	6.45	0.91
	PEW	9	3.00	4.01	4.09	4.91	0.56

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

Significance table of p-values for Morphine Equivalent Dose (MED) difference by group, time, and group by time (n=16); showing MED by time is significant ($p<0.05$) in both models. Significant p-values are highlighted in blue. This indicates an overall opioid dose reduction occurred.

Effect	Numerator degrees of freedom	Denominator degrees of freedom	F Value	Pr>F (p-value)
Morphine Equivalent Dose in mg/day				
Group (MTP vs PEW)	1	14	2.97	0.1066
Time (0 vs 3 months)	1	14	4.65	0.0489
Group by Time	1	14	1.45	0.2486
Log-transformed Morphine Equivalent Dose				
Group (MTP vs PEW)	1	14	5.16	0.0394
Time (0 vs 3 months)	1	14	9.95	0.0070
Group by Time	1	14	0.25	0.6257

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

F-2. Pain data tables

Pain score by time and cohort, basic statistical measures (n=16)

Time	Cohort	n	Minimum	Mean	Median	Maximum	Standard Deviation
Pain score (numeric rating scale)							
0 Months	MTP	7	4.00	6.43	7.00	9.00	1.62
	PEW	9	2.00	5.89	6.00	8.00	1.96
3 Months	MTP	7	2.00	5.71	5.00	8.00	2.14
	PEW	9	1.00	4.67	4.00	8.00	1.94

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

Significance table of p-values for pain score (measured on numeric rating scale) difference by group, time, and group by time (n=16); showing pain by time is close to significant (p=0.059). This indicates a trend toward improvement in pain. Near significant p-values are highlighted in yellow.

Effect	Numerator degrees of freedom	Denominator degrees of freedom	F Value	Pr>F (p-value)
Pain score (measured on numeric rating scale)				
Time (0 vs 3 months)	1	14	4.22	0.0591
Group (MTP vs PEW)	1	14	0.87	0.3659
Group by Time	1	14	0.29	0.5985

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

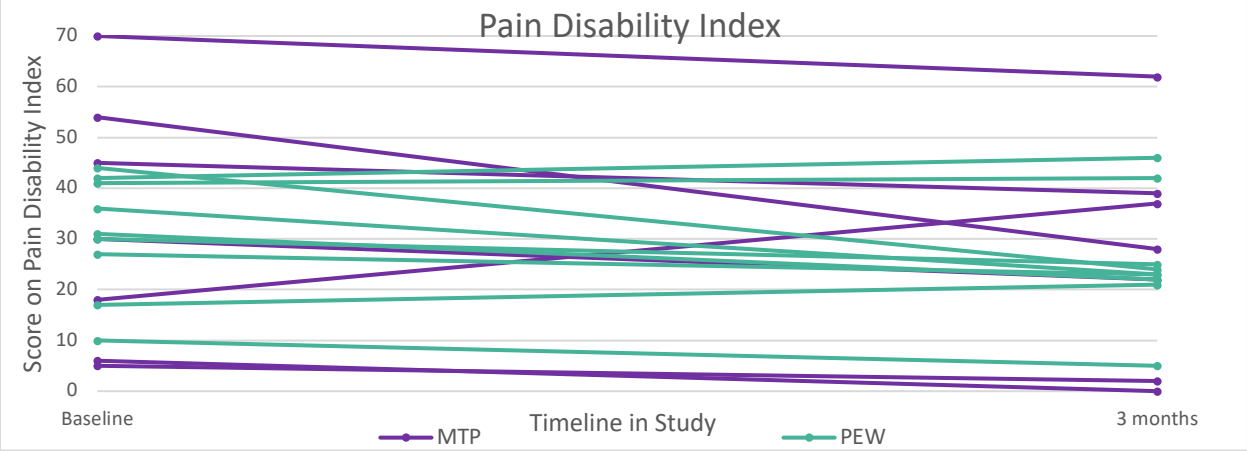
F-3. Health and wellbeing questionnaires: data table

Health and wellbeing questionnaire scores modelled by time, group, and group-by-time (n=14) using repeated measures model. P-values trending towards significance highlighted in yellow, along with their data points.

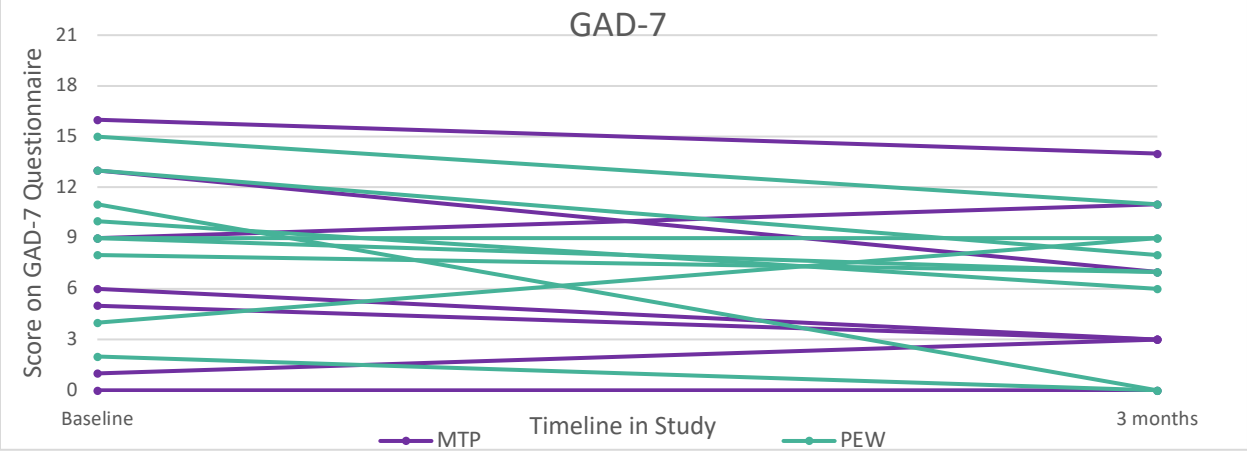
Effect	Group	Time	Estimate	Standard error	Degrees of freedom	t-value	alpha	Confidence interval		Pr >|t| p-value
Pain Disability Index (PDI) Questionnaire										
Time (0 vs 3 months)	-	Baseline	5.3254	2.6456	14	2.01	0.05	-0.3488	10.9995	0.0638
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	1.5794	8.5215	14	0.19	0.05	-16.6973	19.8561	0.8556
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0.9694
Generalized Anxiety Disorder (GAD-7) Questionnaire										
Time (0 vs 3 months)	-	Baseline	1.9762	0.9462	14	2.09	0.05	-0.05329	4.0057	0.0555
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	-1.1667	2.1655	14	-0.54	0.05	-5.8112	3.4778	0.5985
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0.4776
Patient Health Questionnaire-9 (PHQ-9)										
Time (0 vs 3 months)	-	Baseline	0.2778	1.0695	14	0.26	0.05	-2.0161	2.5717	0.7989
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	0.4841	2.3807	14	0.20	0.05	-4.6220	5.5902	0.8418
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0.5105
Patient-Reported Outcomes Measurement Information System (PROMIS) Global-10 Questionnaire: Global Physical Health score										
Time (0 vs 3 months)	-	Baseline	-0.3095	0.4922	14	-0.63	0.05	-1.3653	0.7462	0.5396
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	-0.5952	1.1446	14	-0.52	0.05	-3.0501	1.8596	0.6111
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0. 9621
PROMIS Global-10 Questionnaire: Global Mental Health score										
Time (0 vs 3 months)	-	Baseline	-0.6190	0.3671	14	-1.69	0.05	-1.4064	0.1683	0.1139
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	-0.5238	1.0333	14	-0.51	0.05	-2.7400	1.6924	0.6201
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	14	-	0.05	-	-	0.8986
Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) Questionnaire*										
Time (0 vs 3 months)	-	Baseline	1.2276	1.2764	12	0.96	0.05	-1.5534	4.0087	0.3551
		3-month	0	.	.	.	.	.	.	.
Group (MTP vs PEW)	MTP	-	1.9499	3.6161	12	0.54	0.05	-5.9290	9.8287	0.5996
	PEW		0	.	.	.	.	.	.	.
Group by Time	MTP & PEW	Baseline & 3-month	-	-	12	-	0.05	-	-	0.6436

*SOAPP-R has an n=12 because 2 participants did not complete this questionnaire at both visits
MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

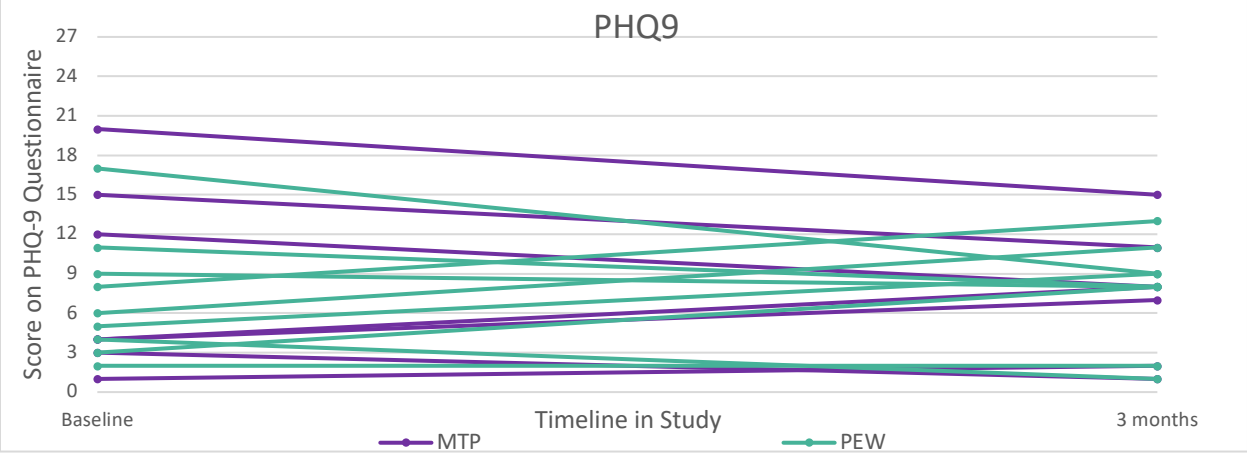
F-4. Health and wellbeing questionnaires: scatter plots – 2 pages



Graph of Pain Disability Index vs time (at 0 and 3 months, max score 70=highest level of disability) showing each participant's progress: most go downwards but some increase (mean 5.33-point decrease, p=0.064)



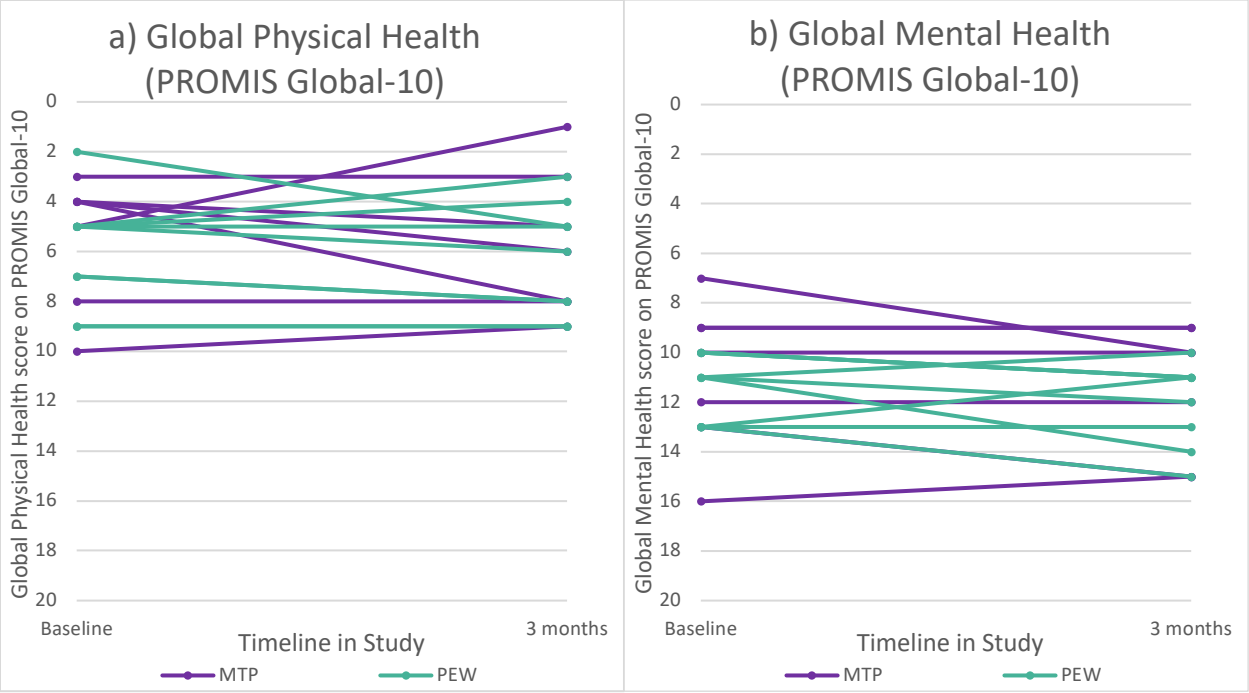
Graph of GAD-7 vs time (at 0 and 3 months, max score 21=severe anxiety) showing each participant's progress: lines mostly trend down, with one notable steep downward slope (mean 1.98-point decrease, p=0.056)



Graph of PHQ9 vs time (at 0 and 3 months, max score 27=severe depression) showing each participant's progress: lines go in both directions, no clear trend is seen (p=0.799)

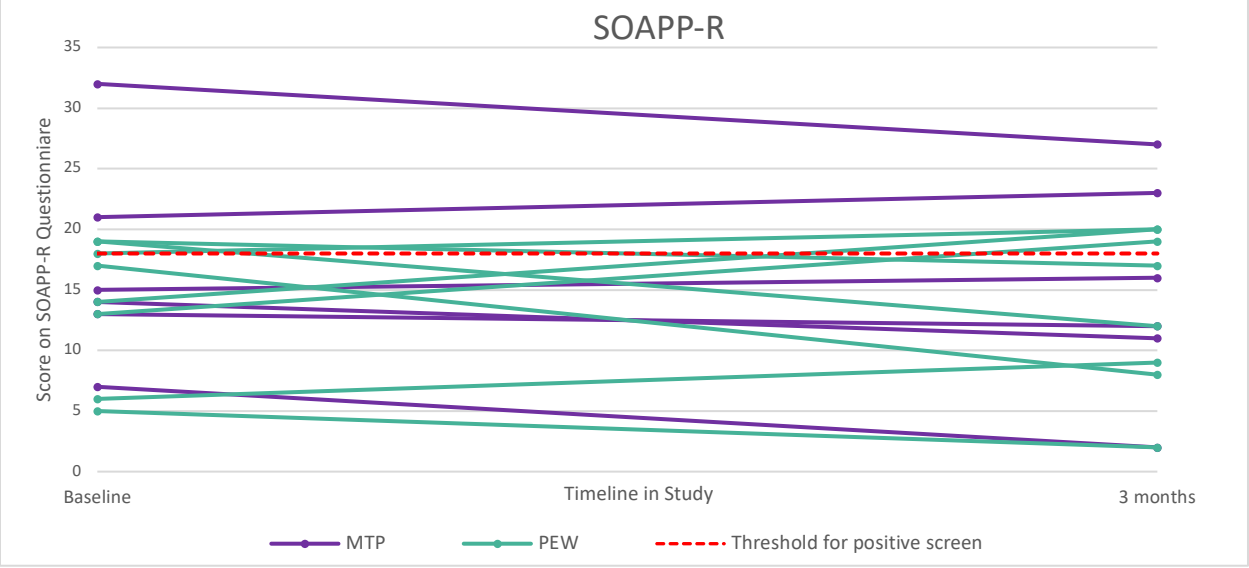
MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort

GAD7=Generalized Anxiety Disorder-7, PHQ9=Patient Health Questionnaire-9



a) Graph of Global Physical Health (on PROMIS Global-10) **vs time** (measured at 0 and 3 months, max score 20=excellent health) showing each participant's progress: no clear trend is seen - lines go in both directions with different magnitudes (p=0.540)

b) Graph of Global Mental score (on PROMIS Global-10) **vs time** (measured at 0 and 3 months, max score 20=excellent health) showing each participant's progress: no clear trend is seen - fairly flat slopes (p=0.114)



Graph of SOAPP-R score vs time (measured at 0 and 3 months, positive screen: ≥18, max score 96) showing each participant's progress: no clear trend is seen – mostly low-grade slopes (p=0.355)

MTP=Multidisciplinary Tapering Program-only cohort, PEW=Patient Education Workshop + MTP cohort
PROMIS=Patient-Reported Outcomes Measurement Information System Global -10
SOAPP-R=Screener and Opioid Assessment for Patients with Pain-Revised.

G-1. Study update provided to study sites (November 2022) - 2 pages

Opioid Tapering Trial: Progress Report

November 2022

Study Design

Randomized prospective trial

50% of participants	Patient Education Workshop
All participants	Multidisciplinary Tapering Program

Inclusion: Chronic non-cancer pain; Daily opioid use; VAS ≥3/10; MED ≥50mg/day

Exclusion: Recent ACT / CBT; Unsafe mental health; Opioid misuse, abuse, or diversion

Demographics

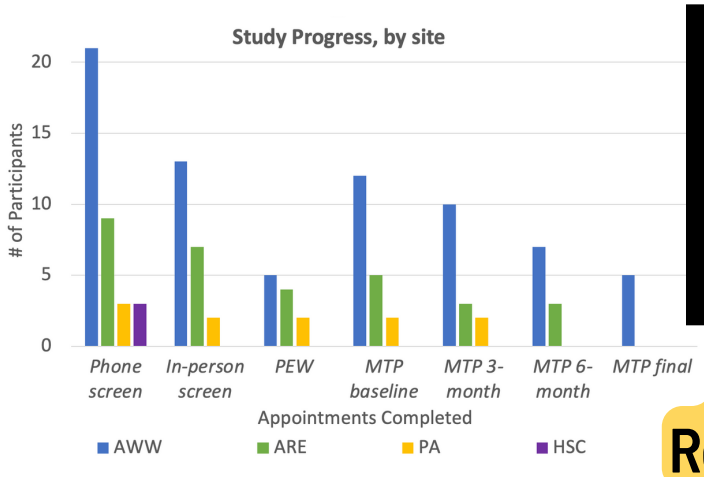
	MTP		PEW	
Site	Qty	%	Qty	%
AWW	7	54%	6	46%
ARE	1	20%	4	80%
Pan Am	0	0%	2	100%
HSC	0	0%	0	0%
Sex				
Male	2	25%	7	58%
Female	6	75%	5	42%
Other	0	0%	0	0%
Age				
18-29	0	0%	1	8%
30-49	1	13%	5	42%
50-64	7	88%	6	50%
65+	0	0%	0	0%

	MTP		PEW	
Opioid				
Codeine	0	0%	1	8%
Tramadol	0	0%	0	0%
Morphine	1	13%	0	0%
Oxycodone	3	38%	5	42%
Hydromorphone	3	38%	5	42%
Fentanyl	1	13%	1	8%
Non-opioid pain medications				
Acetaminophen	5	63%	5	42%
NSAID (systemic)	1	13%	5	42%
NSAID (topical)	3	38%	0	0%
TCA	4	50%	2	17%
SNRI	3	38%	2	17%
Gabapentin/Pregabalin	2	25%	5	42%
Nabilone / Cannabis	1	13%	8	67%
Muscle relaxant	2	25%	2	17%
Pain Diagnoses				
Fibromyalgia	2	25%	3	25%
OA / RA	4	50%	3	25%
post MVA	1	13%	2	17%
Neuropathy	1	13%	0	0%
Migraine	0	0%	1	8%
IBS/IBD	1	13%	0	0%
Back Pain	0	0%	4	33%

	MTP		PEW	
Baseline MED				
50-75	3	38%	6	35%
76-100	0	0%	2	12%
101-150	0	0%	1	6%
151-200	2	25%	4	24%
200+	3	38%	4	24%
Baseline Pain score				
3 - 4.9	0	0%	1	9%
5 - 6.9	1	13%	7	64%
7 - 8.9	4	50%	3	27%
9 - 10	3	38%	0	0%
Baseline PHQ9				
0-4	4	50%	3	27%
5-9	2	25%	2	18%
10-14	0	0%	3	27%
15-19	1	13%	2	18%
20-27	1	13%	1	9%

Lessons Learned

- Each site required its own unique process
- More pro-active approaches needed for recruitment during pandemic
- Patients permitted to defer or hold enrolment
- In-person visits continued despite pandemic, but facilitating back-to-back visits improved convenience



Total participants: 22

Recruitment ~50%

Attrition 18%

Active Sites:
ACCESS Winnipeg West
ACCESS River East
Pan Am Clinic
HSC Pain Clinic

Results: Recruitment

Results: Workshop

Lessons Learned

- Ideal group size is larger (5-10 vs 3-4)
  - Invited non-study patients to fill groups
- Pros of virtual:
  - Patients were relieved to not leave home
  - Patients had the option tune out/turn camera on/off as needed (e.g. during pain flare or wave of fatigue)
  - Facilitators flexible with scheduling (may not need to be present the entire day)
- Drawbacks of virtual:
  - Facilitators note more difficulty getting concepts across
  - Patients act inappropriately more often than in person
  - However: participation and relationship building between has still occurred

Participants are satisfied with content

100% agreed/strongly agreed with:
"I will use what I learned in this workshop to help manage my pain

78% agreed/strongly agreed with:
"This workshop provided value to my pain management"
(22% neutral)

Some participants are satisfied with format

50% agreed/strongly agreed with:
"I found the format of the workshop (full day, online) worked well with my needs"
(20% disagreed, 30% neutral)

50% agreed/strongly agreed with:
"I didn't have any barriers that affected my ability to attend this workshop significantly"
(10% disagreed, 40% neutral)

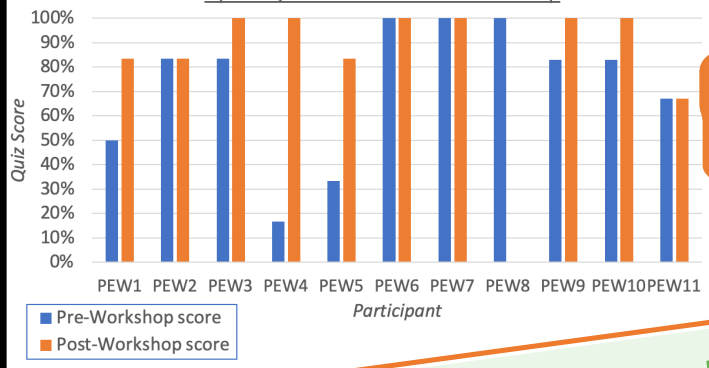
Some improvements to taper readiness

40% of participants had **+ve change**
20% not wanting ⇢ wanting to reduce
20% "Not really ready"⇢"somewhat ready"

50% of participants had **no change**
30% "very ready" pre & post
10% "somewhat ready" pre & post
10% "not really ready" pre & post

10% of participants had **-ve change**
"Somewhat ready" ⇢"not really ready"

Opioid Quiz Scores Pre- & Post-Workshop



Average score improved from **73%** pre-workshop, to **92%** post-workshop

Over half of participants improved their score

All participants scored >65% post-workshop

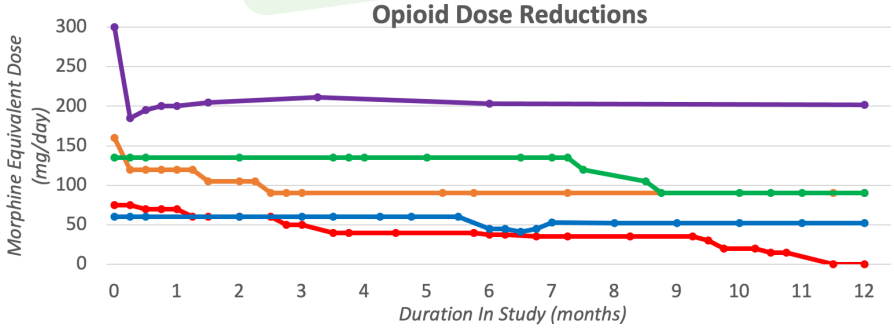
Results: Tapering Program

5 patients have completed 12 months in study:

100% ↓ (hydromorphone 15 to 0mg)
13% ↓ (Percocet x 8 tabs to 7 tabs)
44% ↓ (morphine 160 to 90mg)
32% ↓ (fentanyl 37 to 25mcg/hr)
33% ↓ (hydromorphone 180 to 120mg)

Average 44% dose reduction

Opioid Dose Reductions



Patient Engagement

- Patients anxious to taper; building confidence important
- Education, med reviews/optimizations (even for other conditions) helped build confidence, trust
- Patients more willing to attempt a reduction if allowed to go back up
  - No one has gone back to original dose

Taper design

- Most patients start with other optimizations before tapering, especially trialing other pain meds (duloxetine, nabilone) or switching opioid/formulation
- Timing and size of dose reduction decided one at a time (instead of planning multiple steps)
- Timely follow up (<1wk after dose reduced) has been critical, even if only for support (no changes)

Pain

- Patients noted increased pain for 1-2 weeks after dose ↓, then back to baseline
- Improvements in pain noted for many, but usually due to other new meds started
- Pain scores are wildly variable and rarely have anything to do with opioid dose or dose change (except the 1-2 weeks after a reduction)

Withdrawal

- Nausea, h/a, malaise common (sweating, diarrhea less), lasted <1 week
- Severity didn't always correlate to starting dose or size of dose ↓
  - Some patients had no w/d
- Patients have not understood withdrawal well, needed a lot of education
- Withdrawal treatments have not been that helpful (e.g. clonidine), but patients liked to have them

Other Benefits

- Reduced CNS depression, but otherwise little significant symptomatic benefits noted (?f/u not long enough)
- Patients note a sense of accomplishment, but usually after a 2nd or 3rd reduction
- Relief about less prescribing/dispensing rules and reduced stigma

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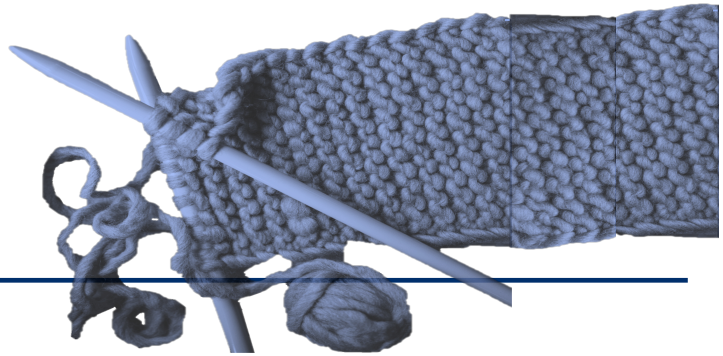

Unraveling Another Pandemic

Evidence-based strategies to taper the opioid crisis

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INTRODUCTION

Opioid dependence and addiction are linked to overdose and death. Canada has deemed the opioid crisis a public health emergency as the 3rd ranking country in per capita opioid consumption. A call was made for a "response that is comprehensive, collaborative, compassionate and evidence-based."[1] There have been few trials so far with clinically useful data on opioid tapering.

The COVID19 pandemic has had profoundly negative impact on the opioid crisis. The first year saw a 95% increase in deaths compared the year before and have not improved. Hospitalizations are still increasing.[1,2]

Conducting an opioid tapering trial during the pandemic has required flexibility in addition to on-the-go adjustments to study design and recruitment.

METHODS: in brief

This is an ongoing, multidisciplinary study evaluating two clinical interventions on opioid tapering patient outcomes. Participants with significant chronic non-cancer pain (CNCP) taking at least 50mg of morphine equivalents daily are currently being recruited at three clinical sites in Winnipeg.

Patient Education Workshop (PEW)

50% of patients are randomized to participate in this one-day workshop that aims to educate patients on chronic pain, risks of prolonged opioid use, and opioid tapering, in addition to providing Acceptance and Commitment Therapy (ACT). The workshop was developed collaboratively to be multidisciplinary, patient-centered, and applicable to various forms of CNCP. Its effectiveness and feasibility are measured in pre- and post-workshop questionnaires as well as data collected during the tapering program.

Multidisciplinary Tapering Program (MTP)

All patients participate in the MTP, an individualized program based on the patient's dose of opioid, clinical picture, and tapering goals. It is patient-directed, goal oriented, collaborative, and includes frequent follow up. Patients are permitted to slow, speed up, halt, or even reverse steps of their taper. Opioid reductions, pain scores, and health and wellbeing questionnaires are measured at in person visits at 0, 3, 6, and 12 months. Qualitative data (and pain scores) are collected weekly by phone.

RESULTS

Recruitment and Attrition

Access Winnipeg West (AWW) began recruiting in Mar. 2021. Using a referral-based approach, they had a recruitment rate of 38%. Access River East (ARE) starting recruiting in Sept. 2021 and combined a referral and proactive approach for a 66% recruitment rate. Based on this, AWW changed its strategy and now has an overall recruitment of 44%. Pan Am Clinic began recruiting in Dec. 2021 and is using a controlled process due to comparatively lower resources. It has a 50% rate. HSC begins recruitment in spring 2022. Only 1 participant has been lost to attrition so far (~6%). See **Figure 1** below for the status of screened and enrolled patients.

Recruitment Challenges:

- **Referral numbers**: Low promotion (working off site/ segregated); meetings dominated by pandemic; adding sites delayed for staff hesitancy (workload, short staffing)
- **Enrollment**: Patients cautious about changing meds; hesitant about in-person visits; high no show rates
- **In Person Visits**: Safe procedures changed; reduced room availability (COVID treatment); prioritized COVID care; staff pulled to work elsewhere/cover redeployed staff

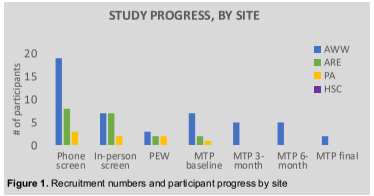

Figure 1. Recruitment numbers and participant progress by site

Preliminary Data from Patient Education Workshops

A pilot workshop preceded four PEWs conducted as part of the study. These have included a total of seven study patients to date. Data was collected from questionnaires that participants completed pre- and post-workshop. These questionnaires include an opioid knowledge quiz, tapering readiness assessment, and a feedback section. See complete results in **Figures 2, 3**, and **4**.

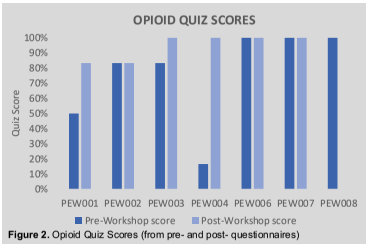

Figure 2. Opioid Quiz Scores (from pre- and post- questionnaires)

Figure 3. PEW Testimonials (from feedback section of post-PEW questionnaires)

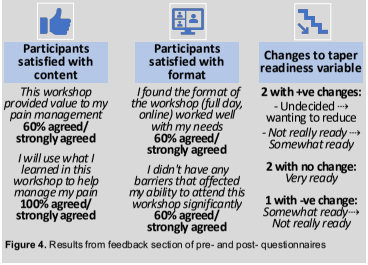

Figure 4. Results from feedback section of pre- and post- questionnaires

DISCUSSION

Changes to Recruitment

- **Promotion**: Posters added in clinic waiting rooms, patient rooms, staff areas; frequent reminder meetings with team
- **Referrals**: Change from referrals to seeking out eligible patients (no contact from study team without consent)
- **Deferrals**: allow patients to defer enrollment until ready, with regular check ins
- **Virtual**: Considering the importance of relationship building and clinician-patient trust, in-person visits were prioritized.

Changes to Patient Education Workshop

- **Virtual**: The entire workshop was pivoted to completely virtual after a successful pilot with good feedback
- **Schedule**: The one-day duration of the workshop was intentional and evidence-based[3], breaks were added after change to virtual
- **Group size**: Small (3-4) PEWs were changed to larger (5-15) by adding non-study participants in order to optimize conversation / engagement within participants.

NEXT STEPS

Changes to both recruitment and PEWs as above predict increased numbers and data.

However, in 3 months, the following strategies may be implemented if recruitment rate drops below 50%.

- Screening visit pivot to a virtual (requires protocol amendment and new process to sign consent)
- Additional sites considered
- Minimum opioid dose for inclusion lowered (MED≥30mg)
- Non-study participants attending PEW complete pre/post questionnaire

CONCLUSION

Opioid tapering research often faces notable recruitment and retention challenges outside of a pandemic setting. For this trial, COVID-19 effects have significantly impacted the predicted recruitment and have required thoughtful and flexible changes to study recruitment approaches to mitigate this challenge

ACKNOWLEDGEMENTS

MSc Committee: Dr. Brigitte Sabourin (psychology), Dr. Christine Leong (pharmacy)
Investigative team: Dr. Gregg Tkachuk (psychology), Dr. Ryan Amadeo (anaesthesiology), Caroline Kehrer
Clinic staff (MDs, NPS, nurses, admin) at ACCESS Winnipeg West, ACCESS River East, Pan Am Clinic

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G-3. Abstract submitted to Association of Faculties of Pharmacy of Canada (AFPC), presented as a mini session at the Canadian Pharmacy Education and Research Conference (CPERC), June 2022

Unraveling another pandemic: Evidence-based strategies to taper the opioid crisis

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Background: The opioid crisis has become a secondary pandemic, as we've witnessed its impact on morbidity and mortality multiply amidst COVID-19 restrictions and reduced access to care. Although tapering opioids is highlighted as a priority action to combat the crisis in many practice guidelines across Canada, there is sparse evidence on clinically safe and effective tapering approaches, with less still on practical implementation strategies.

Goals: This session will discuss an ongoing patient-centered, pharmacist-led, multidisciplinary opioid education and tapering initiative. Evidence behind the project's development along with potential impacts on clinical practice, pharmacy education, and patients will be highlighted. Challenges and lessons learned will also be shared as part of this session.

Description: This clinical trial focuses on the impact of a pharmacist-led tapering protocol and a one-day education workshop on opioid consumption and overall pain in individuals with chronic non-cancer pain on long-term opioid therapy. Half of all study participants are randomized to take part in a comprehensive, interactive one-day virtual workshop, which was developed through a highly collaborative process, resulting in a session that is multidisciplinary and patient-centered. The workshop includes pain and opioid education along with significant psychological content, specifically Acceptance and Commitment Therapy (ACT). Following the workshop, all patients participate in a targeted, pharmacist-led, multidisciplinary opioid tapering program based on evidence emphasizing high patient involvement, goal-setting, and significant clinician support. This clinical approach to tapering is individualized for all patients by the pharmacist clinician based on current dose of opioid, clinical picture, and individual tapering goals, with consistent and frequent follow-up and support being foundational to the process.

Relevance to Pharmacy Research/Education: The role of pharmacists in opioid stewardship initiatives is a growing priority of the profession. Recently, the AFPC collaborated with an interdisciplinary team to develop educational guidelines and materials on opioid use and opioid use disorder. Further, the Canadian Pharmacists Association established the Pharmacists' Opioid Stewardship Initiative, focused on providing evidence for pharmacist impact on opioid stewardship initiatives and advocating for advancing these roles across Canada. This project will provide Canadian data on the roles and impact of pharmacists in this clinical initiative.

Summary: Pharmacists are a key player in combatting the opioid crisis. This session will describe the supporting evidence and potential impacts of an ongoing randomized clinical trial evaluating the impact of a patient-centered, pharmacist-led, multidisciplinary opioid education and tapering initiative.