An Evaluation of the Effect of Primary Care Pharmacist Interventions on Patients with Chronic Pain

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT

Background: Chronic pain is a common condition that has significant impact on patients' physical and psychological well-being. Pharmacotherapeutic management of chronic pain differs on the basis of the cause pain. Pharmacists' expertise of pharmacological knowledge and patient care make them key players in managing chronic pain.

Methods: A three-month prospective pilot study was carried out at primary care settings including community pharmacies and family health teams. Patients were seen by pharmacists at the initial visit, 2-week follow-up, and 3-month follow-up visit. Pharmacists' interventions consisted of patient assessments, medication reviews, care plan recommendations, and patient education. Pain, quality of life, and medication adherence were measured with Brief Pain Inventory (BPI), Short Form-36, and Morisky Medication Adherence Scales-8, respectively.

Results: Thirteen patients were enrolled, one withdrew. There was no significant improvement in pain or quality of life at 3-month follow-up. However, trends toward improvement were found.

Conclusions: This study showed that interventions of primary care pharmacists had no significant effect on pain or quality of life of patients with chronic pain. However, positive trends towards reducing pain intensity and pain interference with patients' general activity, mood, normal work, and sleep were found. The reason for this could be due to small sample size, low implementation rate of pharmacist recommendations by physicians, low patient adherence, or extended study period.

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CHAPTER 1: INTRODUCTION

1.1 The nature of pain

1.1.1 Definition and classification

Pain is defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage”.[1] It is a natural feeling that every individual experiences at some point in their lifetime,[2] and is an important component of the body’s natural protection mechanism that alerts people to avoid or escape from potential danger or damage.[3] However, when pain persists, it can be harmful. IASP defines chronic pain as "pain that persists beyond normal tissue healing time, which is assumed to be three months".[1] Unlike acute pain, which is caused by identifiable trauma or injury, the causes of chronic pain are often unclear.[3] It “can be nociceptive, neuropathic, or both and may be caused by injury, malignant conditions, or a variety of non–life-threatening conditions such as arthritis, fibromyalgia, and neuropathy”.[3] Since the etiology of chronic pain is varied and not clearly known, the management of chronic pain is more challenging than acute pain.

1.1.2 Subjectivity of pain

The reality that pain is not only an indicator of body dysfunction but also an individualized emotional experience forms the subjectivity of pain. A noxious stimulus activates the nociceptors which as a result to this stimulus react by sending messages to neurons in the brain through nervous system; the brain then translates these messages into pain.[3] The nociceptive system is plastic and it enables the neurons in the brain to modify

their response to a stimulus in a specific environment so that different persons respond to a same level of stimulus differently.[3] In other words, stimulus alone cannot determine the pain level. Age, gender, cognitive level, previous pain experience, and relevant contextual and psychological factors also have significant impact.[4]

1.1.3 Psychological factors that influence the feeling of pain

As pain is a personal emotional experience, understanding psychological factors that are associated with pain is essential. Negative emotions including anger, depression, and anxiety have been proven to be associated with pain.[5] Negative thoughts predispose people to experience pain and in return, pain aggravates anger, depression, or anxiety. It is difficult to say which one comes first. In most cases, they are concomitant. When anger, anxiety, or depression is triggered by life events, the effect of medications becomes limited. In these scenarios, optimism and self-management have been shown to have beneficial effects.[6]

1.2 The prevalence of chronic pain

Chronic pain has become one of the most underestimated diseases affecting a large population all over the world. An estimated 17% of the Canadian population aged 15 years or older experienced chronic pain.[7] The estimates of the prevalence of chronic pain among Canadians are reported to range from 15.3% to 55% with a higher prevalence in females and the elderly.[7-11] The National Population Health Survey revealed that the prevalence of chronic pain among Canadians increased from 15.3% in 1996/1997 to 19.5% in 2004/2005.[8] These studies defined chronic pain either as pain that lasts longer than 3 months[11]or longer than 6 months,[9,10] or as usual pain.[7,8] In addition to the time

frame, age, and gender, other factors that contribute to the variation are socioeconomic status, educational level, employment status, and methodological differences. Such high prevalence causes detrimental consequences at both individual and societal levels.

1.3 Burden of chronic pain

There is evidence that patients who suffer from chronic pain experience limitations in social activities, an inability to work, and a poor quality of life.[12,13] According to a European survey, 79% of the respondents reported that pain had impacted their normal activities. Approximately 26% said that their employment status was impacted by chronic pain, and 21% had been diagnosed with depression.[14] Patients' inability to maintain an independent lifestyle also impacted family members of sufferers.[14,15] Since the duration of chronic pain is always protracted, usually more than two years, all these consequences place a heavy burden on patients and their families.[14]

Chronic pain also places a tremendous burden on the health system. The cost of chronic pain in Canada was reported to be $47 to 60 billion per year.[16] It was estimated that the total cost of pain in the United States ranged from US$560 to US$635 billion a year.[17] Moreover, evidence indicated that compared to patients without chronic pain, patients with chronic pain require health care resources more frequently.[14] The cost will likely continue to increase with the elevated prevalence rate.

1.4 Management of chronic pain in primary care

Managing chronic pain is challenging for healthcare providers. To determine the best treatment options, clinicians should consider pain intensity, type of pain, and pain quality.[18] Before implementing any care plans, a comprehensive pain assessment is

crucial. Although medications are considered as the core component in treating pain, patients will benefit from a more multidimensional management plan.

1.4.1 Assessing pain

Ideally, a comprehensive assessment of a new patient consists of pain history review, psychiatric comorbidity, psychosocial factors, risk of addiction, assessment of function, treatment goals, and physical examination.[6] In primary care, pain history reviews involving the evaluation of the onset of pain, palliative care, quality of pain, pain sites, pain intensity, duration, treatment history, and current treatments, plays a major role.

1.4.2 Pharmacological interventions

Chronic pain treatment mainly consists of pharmacological interventions and non-pharmacological interventions. The focus on one aspect is not sufficient to achieve appropriate pain relief.

Medications for chronic pain mainly consist of non-opioid analgesics and opioids. Non-opioid analgesics include topical agents, NSAIDS/acetaminophen, antidepressants, anticonvulsants, cannabinoids, NMDA inhibitors, and skeletal muscle relaxants.[18] Opioids that are recommended in the Canadian guideline for chronic non-cancer pain include codeine, tramadol, morphine, oxycodone/hydromorphone, fentanyl, and methadone, among others.[19]

There is variability across different medications in terms of targeting pain types and efficacy. For instance, tricyclic antidepressants (TCAs), serotonin and noradrenaline reuptake inhibitor (SNRI) antidepressants, and anticonvulsants (gabapentin or pregabalin) are the first line medications for neuropathic pain;[20] non-steroidal anti-inflammatory

drugs (NSAIDs), selective cyclooxygenase-2 (COX2) inhibitors, muscle relaxants, and tramadol are top options for non-specific lower back pain;[21] weak opioids (such as tramadol and codeine) are recommended for patients with neuropathic or somatic pain who have little response to first line treatments; stronger opioids (oxycodone, hydromorphone, and morphine) can be considered when patients have no response to weak opioids.[19]

A Cochrane systematic review of antidepressants for neuropathic pain which included 61 randomized controlled trials (RCT), revealed that TCAs were effective in treating neuropathic pain, with a numbers needed to treat of 3.6 (95% CI 3 to 4.5), and relative risk 2.1 (95% CI 1.8 to 2.5) to achieve at least moderate pain control. TCAs were proven to be effective in treating diabetic neuropathy and post herpetic neuralgia, while evidence of the effectiveness of the selective serotonin and norepinephrine reuptake inhibitors (SSRIs) was quite limited.[22] A systematic review which covered 6 RCTs and 2220 patients investigated the efficacy of duloxetine in treating painful neuropathy or chronic pain and found moderately strong evidence that duloxetine 60 mg and 120 mg daily were efficacious compared to placebo in treating painful diabetic peripheral neuropathy and fibromyalgia.[23]

There was moderate evidence that gabapentin at doses of 1200 mg or more daily was more effective than a placebo for people with painful diabetic neuropathy (38% versus 21%) and post-herpetic neuralgia (34% versus 21%). However, there were significantly more adverse effects with gabapentin than with placebo and caused side effects including, somnolence, peripheral oedema, dizziness, and gait disturbance.[24]

NSAIDs, as the most frequently used drugs on pain management, were slightly more effective in treating low back pain compared to a placebo but had significantly greater side effects such as gastrointestinal (GI) bleeding, hypertension, peptic ulcer disease, renal disease, and edema.[25,26]

Opioids showed no significant advantages over non-opioids for pain intensity, but were slightly worse than non-opioids for functional outcomes. In addition, compared to a placebo, opioids resulted in significantly higher reporting of constipation, nausea, dizziness or vertigo, somnolence or drowsiness, vomiting, and dry skin, itching or pruritus.[27]

1.4.3 Non-pharmacological interventions

Physical interventions and psychological interventions form the basis of non-pharmacological interventions. Physical interventions include massages, the avoidance of bed rest/staying active, physical exercise, therapeutic exercise/physiotherapy, acupuncture, ultrasound, electrical stimulation, traction, exercise, cryotherapy, and heat therapy.[28] Psychological interventions consist of biofeedback, relaxation training, hypnosis, and cognitive-behavioral therapy.[29] The effectiveness of the non-pharmacological interventions is unclear and varies from one individual to another.[29-33]

1.5 Problems in chronic pain management

The management of chronic pain remains suboptimal. It was reported by primary care providers from Canada that 60% of chronic non-cancer pain patients experienced improperly controlled pain,[34] which is comparable to a European survey (more than 50%).[14] According to this survey, 40% of Europeans who are suffering from chronic pain

demonstrated that they would be willing to spend all of their money on pain management if the treatments were effective, which indicated their despair in seeking good pain management.[14] In order to achieve pain relief, we ought to be clear of the obstacles in the way.

1.5.1 Treatment-related problems

The most significant problem in chronic pain management is the lack of effective medications. As mentioned above, despite certain types of drugs, the efficacy of pain medications remains unsatisfactory. In contrast, analgesics can lead to considerable side effects. This reality leaves a challenge to health professionals to carefully compare the benefits over the risks. What makes the situation even worse is that chronic pain is often accompanied with psychological disorders such as depression, anxiety, fatigue and sleep disturbances.[35] These multiple conditions always require poly-pharmacy, "the use of two or more medications",[36] which eventually increases the risk of side effects and drug interactions. As highlighted by physicians, side effects, low patient compliance, and concerns about the efficacy of available therapeutic options are three major barriers that prevent patients from obtaining optimal outcomes.[37]

1.5.2 Knowledge-related barriers

The importance of knowledge, attitudes and beliefs of patients and healthcare providers towards pain management has been well-documented.[37-43]

In the European survey, in which in-depth interviewes were conducted among 4839 chronic pain patients from 15 European countries and Israel,[14] when patients were asked about attitudes and beliefs about pain treatments, 63% of respondents indicated their

concerns with potential sides effects of pain, more than 50% commented that they would rather take medication for their illness than their pain, and 48% were concerned about addiction. This situation may reflect that patients failed to receive adequate education and information regarding pain therapies. This is compounded by the fact that about 30% patients are constantly receiving inaccurate information regarding their pain conditions from their caregivers.[14]

Although physicians and pharmacists are accepted as well-educated and trustworthy healthcare providers, they may be not knowledgeable enough or well prepared for pain management as evidenced by the European survey mentioned above.[14] When asked how their doctors evaluated their pain, 71% of the interviewers responded that evaluation was limited to verbal as self-reported, 52% were examined by their doctor, and less than 10% were assessed with a pain scale which is considered as the most reliable pain measure; furthermore, 43% of participants mentioned that they had a feeling of "my doctor would rather treat my illness than my pain", 40% indicated their pain was ignored by their doctors, and 30% said their doctor did not know how to treat their pain. A Canadian survey evaluating the knowledge, attitudes, and beliefs of pharmacists and physicians about chronic pain confirmed the situation, in which both physician and pharmacists received less than satisfactory performance in assessing pain, defining treatment goals and expectations, and developing treatment plans.[44] Additionally, more education on pain management is beneficial from healthcare providers' perspective.[44,45]

1.5.3 Satisfaction

In patient-focused care, patient satisfaction is considered an important indicator when evaluating the quality and effectiveness of healthcare services. Although

satisfaction may not solely reflect the effectiveness of treatments, dissatisfaction may lead to the break of the trust between patients and healthcare providers, which in return will worsen patients' psychological conditions and hence impact their pain. In the European survey,[14] 40% of respondents were dissatisfied with the treatment, 56% felt their medication somewhat effective or not effective at all, and 38% felt dissatisfied or only somewhat satisfied with their doctors.

1.6 Why and how can primary care pharmacists help in managing chronic pain

1.6.1 Education

Pharmacists receive comprehensive education in terms of pharmaceutical sciences, therapeutics, and communication skills at the undergraduate level. They are trained to develop individualized drug therapy plans, identify complex drug interactions, monitor side effects, and establish good relationships with patients and other health professionals. Apart from common pharmaceutical knowledge, pharmacy schools in Canada also offer mandatory pain-specific curricula. A survey investigating pain curricula in health science faculties in Canadian universities highlighted that the average hours for designated mandatory pain content in pharmacy were 13 hours with emphasis on pathophysiology of pain, etiology/prevalence, misbeliefs/barriers and challenges, assessment, pharmacological treatments (analgesics and adverse effects), non-pharmacological treatments, multidimensional nature of pain and management implications, and monitoring and policy/guidelines, while that in medicine and nursing school was 15

hours and 31 hours respectively.[46] Evidence showed pain education programs can significantly improve pain knowledge and beliefs of health professionals. [37,38,44]

1.6.2 Services provided by pharmacists in community pharmacies

Community pharmacists are the most accessible and frequently visited health professionals.[47] This advantage enables pharmacists to develop a close relationship with patients, which is fundamental to the achievement of pain relief. Pharmacists' role used to be restricted to dispensing medications and compounding. Following the trend of patient-focused care, Canada has continually expanded the scope of pharmacy practice in the last two decades.[48] As demonstrated in "Model Standards of Practice for Canadian Pharmacists", pharmacists' roles include patient care, drug information, drug distribution, management, and education.[49]

1.6.3 Services provided by pharmacists in multi-disciplinary teams

A pharmacist in a multi-disciplinary team acts as an information provider, as well as a bridge connecting doctors and patients. For instance, a pharmacist in a multi-disciplinary pain management team provides services such as patient assessment, consultation, care plan recommendations, and education. After these interactions with patients, pharmacists relay this information to physicians and also discuss patients' concerns regarding medications. This significantly improves the understanding between doctors and patients. [50]

1.6.4 Evidence

Evidence of the effectiveness of pharmacists' intervention is well-documented.[51,52] A systematic review and meta-analysis of 400 patients illustrated that educational interventions provided by pharmacists significantly decreased average pain intensity by 5%, reduced adverse effects by more than 50%, and improved patient satisfaction with treatment by approximately 10%.[52] Another systematic review/meta-analysis investigated the effectiveness of medication review provided by pharmacists from primary care in patients with chronic non-cancer pain. This review found an 8% and 5% pain intensity reduction at 3 and 6 months post-intervention respectively, a significant improvement in physical functioning at 3 months, and a significant improvement in patient satisfaction.[51]

CHAPTER 2: A Systematic Review of Primary Care Pharmacist Interventions in Chronic Pain

(This chapter will be submitted for publication at a future date)

2.1 Background

While acute pain is an important component of the body's normal protection mechanism by alerting it to danger or damage, chronic pain can be harmful or detrimental to a patient's health. [2,53] Between 15.3% to 55% of Canadians experience chronic pain, with a higher prevalence in females and the elderly.[7-10,54] Chronic pain limits social activities, ability to work, and quality of life,[13,55] and is associated with psychological disorders such as depression, anxiety, fatigue, and sleep disturbances.[35] Soaring medication costs drain patient resources,[8] and patients with chronic pain use clinic visits and inpatient care more frequently than those without chronic pain.[14] Thus, chronic pain has a negative impact on income, and, together with the high cost of pain treatment, places a significant economic burden on individuals and society.

The management of chronic pain remains suboptimal as demonstrated by the fact that 66% of chronic pain patients report that they experienced pain for more than five years.[14] Issues around medication use include lack of effective medications, inappropriate poly-pharmacy, numerous side-effects, and medications that decrease pain intensity but do not result in pain relief. Furthermore, the effectiveness of non-pharmacological interventions such as exercise and cognitive-behavioural programmes are inadequately investigated or reported and may be underutilized.[56,57]

Pharmacists use their expertise in identifying drug therapy problems to become key players in multi-disciplinary teams. Pharmacists can also monitor the efficacy and safety

of treatment and educate patients. Since appointments are generally not necessary, and pharmacies often have longer hours of peration than medical clinics, they are the most accessible health professionals. This provides numerous opportunities for patients to consult with pharmacists about medications and conditions.[14] The interactions between patients and pharmacists enhances patents' knowledge of pain and pain medications and can contribute to their confidence in their ability to manage pain.

Two recent systematic reviews evaluated the effectiveness of pharmacist-provided medication reviews and educational interventions, and supported the effectiveness of pharmacist intervention in reducing pain intensity and improving patient satisfaction.[52,58] As no systematic review has evaluated the effectiveness of various pharmacist interventions on ambulatory patients with chronic pain, a comprehensive literature review of all types of pharmacist interventions is necessary to determine a more fulsome understanding of the impact of pharmacist intervention on chronic pain. The intent of this systematic review is to investigate the process of delivering interventions by community-based pharmacists and the outcomes of the intervention in ambulatory patients with chronic pain.

2.2 Methods

We followed the 27-item PRISMA guidelines in conducting the present systematic review.[59]

2.2.1 Selection of studies

With the assistance of a medical librarian, comprehensive electronic searches of the PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL),

COCHRANE, Psych Info, EMBASE, and International Pharmaceutical Abstract (IPA) databases were conducted of English language publications up to July 2015 using the search terms presented in Table 1. Manual searches of bibliographies were performed and bibliographies of retrieved articles were examined for additional relevant articles, but grey literature was not included.

Inclusion criteria: All RCTs and all non-randomized studies (N-RS) that involved a pharmacist who directly dealt with managing chronic non-cancer pain were included. Team-based approaches to chronic non-cancer pain management were considered only if a pharmacist was included. Pharmacists working in primary care settings such as community pharmacies, primary care teams, pain specialty clinics, or general practices were included. Ambulatory patients with chronic non-cancer pain were included.

Exclusion criteria: Studies presented in abstract only, editorials, commentary, and reviews were excluded. Patients residing in long-term care facilities, retirement homes, and institutionalized settings, or with cancer pain were excluded. Studies that were not published in English were excluded.

Two reviewers (Mo Chen (MC) and Trupti Kulkarni (TK)) performed searches and screened the titles and abstracts independently. Full papers were retrieved if they appeared to meet the inclusion criteria and were reviewed independently by reviewers for inclusion. The corresponding authors of studies published as abstracts were contacted to determine whether a full-length paper had been published. Disagreements about inclusion between the any reviewers were resolved by a third reviewer (Feng Chang (FC) or Tejal Patel (TP)).

2.2.2 Data extraction and coding of outcome measures

The primary outcome measures were change in any measures of pain on scales for pain intensity or pain relief; change in quality of life measures of patients; and the pharmacist intervention processes. The secondary outcomes were changes in measures of anxiety, depression, and disability; changes in health resource usage (including patient referral to other healthcare professionals, cost, and number of clinic visits); changes in dosing or consumption of pain medications; reduction in adverse events; measures of patient satisfaction with interventions; and the acceptance of the interventions by the physicians. For convenience, we coded these outcomes as patient-reported improvement (Outcome 1), the acceptance of the intervention (Outcome 2), health resource usage (Outcome 3), and change of medication use (Outcome 4).

Two reviewers (MC, TK) independently extracted data using a pre-designed data extraction form. Disagreements were resolved by discussion with a third reviewer (FC or TP).

2.2.3 Risk of bias in included studies

We used the risk of bias tool of The Cochrane Collaboration to assess risk of bias in the RCT,[60] and A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-N-RSI), recently developed by the Cochrane Collaboration,[61] to assess the risk of bias on outcomes of each N-RS. Descriptive studies that only described how a health site worked but did not apply a study design were not subject to risk of bias assessment. Potential confounders affecting each of the outcomes of the N-RS were identified and are presented in Table 2.

Each of the included studies was assessed for bias independently by two investigators (MC, TK), then cross-checked and discussed by the two investigators. Disagreements were resolved by a third reviewer (FC or TP) or through group (FC, TP, MC, and TK) discussion.

2.3 Results

The initial search yielded 1077 records. After removing duplicates, 682 titles and abstracts were screened, resulting in the exclusion of 646 records, and leaving 36 full-text articles for full-text retrieval. After assessing the eligibility, seventeen articles met all of inclusion criteria and none of the exclusion criteria, describing the results of fourteen separate studies. Figure 1 illustrates the search and selection process.

2.3.1 Characteristics of the included studies

Of the 14 studies, seven were conducted in the United States,[62-68] five in the United Kingdom,[69-73] one in Belgium,[74] and one in Canada.[75] Three studies were RCT,[62,70,71] and eleven were observational studies including cohort studies, descriptive studies, and retrospective studies.[63-69,72-75] Three studies defined chronic pain as pain persisting longer than three months,[63,70,72] 1 defined it as longer than 6 months,[76] while the remaining studies did not provide a definition. The characteristics of each of the studies are summarized in Table 3. The risk of bias is summarized in Tables 4 and 5 for RCT and N-RS, respectively. The RCTs were judged to have lower risk of bias than the N-RS.

2.3.2 The delivery of pharmacist intervention

Five of the studies applied a pharmacist-only approach,[67,70-73] and nine involved pharmacists and other health professionals such as physicians and nurses.[62-66,74]

2.3.2.1 Pharmacists only approach

In the study conducted by Kroner *et al*.,[67] the pharmacist documented any medication conversion that was performed and assessed for serious adverse effects associated with medication conversion using the Naranjo Scale.[77] Medication conversions involved both inter-class and between-class ones, such as gabapentin converted to amitriptyline.

Bruhn *et al.* assigned participants to one of three arms.[70] Patients in the prescribing arm were requested to complete a pain diary before an in-person consultation with a pharmacist for pharmacist prescribing and medication review. Pharmacists then developed a therapeutic plan agreeable to both patient and pharmacist and followed up patients afterwards. On average, the paper-based medication review took thirty-five minutes, the consultation took thirty minutes, the care plan took ten minutes to formulate and the follow-up was ten minutes. The patients in the review arm received a paper-based medication review and a pharmaceutical care plan. The controls received standard care as usual.

The RCT conducted by Hay *et al.* also divided participants into three groups.[71] The intervention in the enhanced pharmacy review group involved three to six patient consultations over a 10-week period. During the medication reviews, the pharmacist made treatment recommendations based on a pre-defined algorithm in which proper medications were added step-by-step based on patients' pain control and provided

education and advice on medicines and relevant lifestyle factors. Community physiotherapy group received care from community physiotherapists. Participants in the control group received the same advice and information leaflet as the other groups but no interventions.

In the McDermott *et al.* study,[72] pharmacists reviewed patient prescribing records and identified 230 chronic pain patients who were sent a baseline questionnaire and a 6-month follow-up questionnaire. In-person interviews were conducted with 25% of randomly selected patients. During the interview, the pharmacist explored medication use, side effects experienced, and satisfaction with the medications, making recommendations if necessary. The results of the assessment and recommendations were sent to the appropriate physician.

In their study, Read *et al.* involved pharmacist-conducted structured interviews with rheumatoid arthritis patients to identify perceived side effects.[73] This resulted in the identification of twenty-eight patients with poor outcomes, leading to recommendations for a change of therapy for twenty-four of these patients that were subsequently discussed with the general practitioner. Advice from the pharmacist was given to improve efficacy, compliance, knowledge of medicine, and to minimize adverse effects.

2.3.2.2 Multi-Disciplinary Approach

The Bauters *et al.* study analyzed outpatient's medication data for nine months at Belgian Ghent University Hospital.[74] The clinical pharmacist performed 120 interventions for 93 patients that included clinical interventions (89.2%), providing medication information (10%), and provision of a specific product (0.8%). Clinical interventions were increasing therapeutic drug monitoring (35.5%), changing therapy

(20.6%), stopping a medication (19.6%), starting a medication (19.6%), and clarifying a prescription (4.7%). The majority of the stopped, started, or changed medications were related to analgesics and anti-depressants.

In the Gammaitoni *et al.* study,[62] the intervention contained two components; specialized prescription services offered by a palliative care pharmaceutical company to improve the delivery of medications, the other was a palliative-trained pharmacist's effort to monitor patients' medication use and outcomes, by asking patients a series of pre-defined questions during telephone or office visits. Pharmacists made forty-five calls (56% of total) to patients, averaging twelve minutes per call.

In the Dole *et al.* study,[63] an average of 18 patients per day were seen by a team of pharmacists, clinicians, and nurse practitioners. A clinical pharmacist with prescribing authority met with the patient for twenty minutes, with a ten-minute follow-up at an unspecified interval. At each visit, the patient was asked to fill a Visual Analogue Scale (VAS, a ten-point pain scale).[78] VAS scores were measured up to the tenth visit. A pharmacist-developed medication refill protocol to standardize the medication refill process was assessed by measuring the number of near-miss medication errors. Finally, a controlled substance monitoring program was initiated.

In the Chelminski *et al.* study,[64] pharmacists performed structured clinical assessments of the patients, followed by monthly follow-ups. During the assessment, patients were asked to sign pain contracts. Pharmacists also adjusted medication doses, recommended psychiatric consultation if deemed helpful, and monitored for substance abuse.

In the Suzuki *et al.* study,[65] the pharmacist, who had pain expertise, offered interventions including initial evaluation, buprenorphine inductions, and follow-up visits. Initially, patients were seen weekly, but after achieving clinical stability for at least four weeks, the visits decreased to bi-weekly, and then monthly.

In the study reported by Cunningham *et al.*,[66] the pharmacist was responsible for reviewing medications of patients and calculating the costs of the necessary medications at admission and again at discharge. Education was provided on medication use, efficacy, side effects, and any withdrawal effects.

Wiedemer *et al.* assessed an Opioid Renewal Clinic (ORC) managed by a pharmacist and a nurse practitioner to support primary care providers (PCPs) from a university-affiliated tertiary care center.[68] Initially, a pharmacist and a nurse practitioner met with a multidisciplinary pain management team biweekly to receive advice on treatment plans. Most cases were managed by PCPs and the pharmacist. Interventions included individualized treatment plans, monitoring, prescribing, pill counts, counseling, and education.

Briggs *et al.* evaluated a program run by a pharmacist and a nurse.[69] In the study, pharmacists conducted medication reviews and assessed pain scored on an eleven-point scale. The nurses and pharmacists then worked together on treatment plans, which were reviewed by physicians.

In the Turner *et al.* study,[75] community pharmacists displayed posters in the pharmacy requesting patients taking headache medications more than twice weekly to speak with their pharmacist. Pharmacists then provided education pamphlets to patients

who experienced medication induced headaches (MIH) and requested them to contact study nurses to log potential MIH patients.

2.3.3 Pain scores

While pain measures were reported in 10 of the 14 studies,[62-66,69-73] scales by which pain was measured varied. Suzuki *et al.* measured both pain intensity and pain interference using BPI.[79] Chelminski *et al.* applied the BPI to measure pain intensity and the Pain Disability Index (PDI) to measure pain disability.[80] McDermott *et al.* and Bruhn *et al.* reported pain intensity and pain disability using Chronic Pain Grades (CPG), which classify patients into five categories: grades zero (no pain) to four (high disability-severely limiting).[81] Cunningham *et al.* measured pain intensity and psychosocial functioning with the Multidimensional Pain Inventory (MPI).[82] Dole *et al.* and Read *et al.* reported pain intensity with a Visual Analogue Scale (VAS), which is a straight line where the start represents no pain and the end represents the worst pain.[78] Briggs *et al.* measured pain intensity according to a zero to ten on the Numerical Rating Scale (NRS), a scale where zero represents no pain and ten represents unimaginable pain.[83] Gammaitoni *et al.* assessed pain with the Pharmacotherapeutic Pain Inventory (PhPI), which was derived from the BPI and Health Background Questionnaire-Initial Patient Visit.[62] Hay *et al.* applied both NRS and the Pain and Physical Function subscale of the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) to measure pain.[84]

2.3.3.1 Pain intensity

Only 5 of the 10 studies reported significant reductions in pain intensity from baseline to follow-up,[63,64,66,69,70] 2 studies found significant reduction in pain intensity compared to controls at follow-ups.[70,71] Results from Suzuki *et al.*, McDermott *et al.*, and Read *et al.* studies also indicated improvement on pain intensity, but the significance of the improvement was not reported.[65,72,73] Hay *et al.* reported significant reduction of pain intensity in the pharmacy review arm using both the WOMAC pain intensity subscale and NRS compared with controls at three months, but not at six months or one year.[71] In the Bruhn *et al.* study, pain intensity reduced significantly within the prescribing arm at the six-month follow-up, but not in the review arm or control arm; compared to baseline, 47.7% (p=0.003) patients in the prescribing arm achieved improvement and 38.6% (p=0.001) in the review arm.[70] No significant pain intensity reduction was found in the Gammaitoni *et al.* study.[62]

2.3.3.2 Pain interference

Seven studies measured pain interference. Chelminski *et al.* reported significant improvement in pain disability with PDI at 3 months.[64] Bruhn *et al.* determined a significant reduction in pain disability in the prescribing arm at 6 months follow-up, pain disability was not reduced in the review or control arms,[70] no significant between-arm result was found. Suzuki *et al.* reported an improvement in pain disability without evaluating the significance.[65] Hay *et al.* did not find significant differences between the pharmacy review arm and the control arm at all the three time intervals in physical functioning.[71] Perceived life control and general activity level which were measured by MPI in Cunningham *et al.* study both showed significant improvement.[66] At the three-month follow-up of the Gammaitoni *et al.* study, the intervention group got significantly

better treatment relief than did the control group, but no significant results were found in pain interference with general activity, mood, walking, normal work, relationships, or enjoyment of life, despite significant improvement in physical and emotional problems interference with social life within the intervention group.[62] No significant improvement in pain interference was found in the intervention group when comparing baseline with the three-month follow-up.[62]

2.3.4 Quality of life

Only three of the fourteen studies reported on the quality of life of patients.[66,70,75] Turner *et al.* measured the quality of life of patients with The Henry Ford Hospital Headache Disability Inventory (HDI), a headache-specific instrument with emotional and functional domains,[85] and The Medical Outcome Study (MOS) short-form general health survey, a valid and reliable generic instrument.[86] Bruhn *et al.* reported quality of life with Short Form-12 and Health Utilities Index-3 (HUI-3), a generic preference-based health state utilities measure.[87,88] The Neilson *et al.* study, which was linked to the Bruhn *et al.* study, used the Short Form-6-Dimension questionnaire (SF-6D), which is a generic patient preference-scored instrument for measuring quality of life.[89] Cunningham *et al.* assessed quality of life using the Short Form-36, a generic instrument with 36 items.[90]

Turner *et al.* found a consistent, but not statistically significant trend toward improvement.[75] In the Bruhn *et al.* trial, only the control group showed statistically significant improvement in the physical component score of the SF-12, but a significant decrease in mental component score; no significant improvement was found in both prescribing arm and review arm. Neilson *et al.* reported that the SF-6D health utility scores were similar in all three arms at all three time points, and a slight improvement in

follow-ups compared to baseline.[91] The health perception and physical functioning subscales of SF-36 improved significantly from admission to six-month follow-up in the Cunningham *et al.* study.[66]

2.3.5. Other outcomes

2.3.5.1 Depression and anxiety

Depression was reported in three studies using either the Hospital Anxiety and Depression Scale (HADS) or the Centre for Epidemiologic Studies Depression Scale (CES-D).[92,93] One study measured anxiety with HADS.[93] CES-D is a self-reported depression scale with scores ranging from 0 to 60 with higher score indicating increasing severity in depression status.[92] HADS is a 14-item screening tool with 7 items detecting anxiety and 7 items detecting depression; each subscale scored from 0 (not present) to 21 (highly present).[93]

All of the three studies showed significant depression score reduction compared to baseline in patients who received pharmacist intervention. In Bruhn *et al.* study, only pharmacist prescribing arm reported significant improvement in depression and anxiety.[70]

2.3.5.2 Satisfaction and acceptance

Pharmacist interventions were highly accepted by physicians and patients. Bauters *et al.* and McDermott *et al.* reported that 95.3% and 77% of the recommendations made were accepted by physicians respectively.[72,74] Of the primary care providers in the Wiedemer *et al.* study, 84% were satisfied with the service.[68] The recommended treatment was accepted by 95.6% of patients in the Suzuki *et al.* study and 55% remained enrolled at the six-month follow-up.[65] In the Hay *et al.* study, 67%, 57%, and 52%

patients were satisfied with the treatment at three months, six months, and one year post-randomization, respectively.[71] Briggs *et al.* reported that 92% of patients were satisfied,[69] while in the Kroner *et al.* study, 24 of 47 patients persisted with the new medication after a year.[67]

2.3.5.3 Cost

In addition, the twenty-four patients who remained in treatment in the Kroner *et al.* study avoided $50,000 in medication costs.[67] The pain clinic described by Dole *et al.* generated $107,550 of actual revenues and saved health plans $450,000.[63] Cunningham *et al.* also achieved significant savings in medication costs admission to discharge.[66] However, Neilson *et al.* concluded that pharmacist interventions were more costly, but provided similar health benefits as controls.[91]

2.3.5.4 Medication usage

Both the Cunningham and Turner studies reported a decrease in medication use.[66,75] Self-reported use of non-steroidal anti-inflammatory drugs in the pharmacy review group was significantly lower than in control group, while the use of analgesics was higher in the Hay *et al.* study.[71] Contrarily, 48% of the patients in the Chelminski *et al.* study increased their opioid dose over three months, and the mean opioid equivalent increased from 53 mg to 105 mg per day.[64]

2.3.5.5 Health resource usage

Briggs *et al.* reported reduced need for secondary referral at 6-month follow-up, while Wiedemer *et al.* found a decreased number of ER visits following pharmacist intervention.[68,69]

2.4 Discussion

In this systematic review, seventeen published reports were reviewed and appraised to determine effects of pharmacist intervention on ambulatory patients with chronic pain. In the majority of published reports, pharmacists worked in multi-disciplinary pain management teams. The most frequently used pharmacist interventions was consultation that involved medication reviews, recommendations, follow-ups, and patient education. While there was variation in the scales used to measure pain and other outcomes, most showed positive results.

Medication is an important component in managing chronic pain and pharmacists, as trusted health professionals, contribute their pharmaceutical expertise in identifying drug therapy problems to improve the management of pain. Consultations with patients enable pharmacists to address patient concerns about their medications and pain problems, and to educate patients about chronic pain. Since pharmacist interventions involved in included studies were not single-itemed but a combination of different interventions, it is not practical to determine which part of the intervention was most or more effective. For example, Bruhn *et al.* found that 47.7% of patients in the prescribing arm and 38.6% of those in the review arm reported significantly improved CPG scores, but those in the control arm did not,[70] suggesting that prescribing is more effective than medication review, and that medication review is more effective than usual care. However, the SF-12 physical component score only showed a significant improvement in the control arm, but not in the prescribing or review arms, making it difficult to draw a conclusion.

We included studies from four different countries where the scope of pharmacist practice varied. For instance, in UK pharmacists can prescribe independently within their competence,[94] certain areas of the USA permit protocol-based prescribing by pharmacists while pharmacists in most parts of Canada cannot independently prescribe medications. In addition, pharmacists practiced in different settings, some pharmacists worked in multi-disciplinary teams, some saw patients independently. The variety of settings and scope of pharmacist practice impacts pharmacists' ability to independently make changes to patients' drug therapy.

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) identified pain intensity and physical and emotional functioning as the leading two core outcome measures for their chronic pain trial, [95] which is accordant with the primary outcomes in this review. The reduction in pain intensity of patients who received pharmacist intervention ranged from 1.5%-35%, of which some reductions were significant, some were not, and three months post-intervention showed preferable outcomes compared to six months post-intervention. Additionally, the clinical significance of the improvement of pain interference needs to be investigated. A 30% reduction on an eleven-point pain intensity rating scale is considered clinically significant.[96] The only study that achieved pain intensity reduction of 35% did not generate statistical significance due to small sample size and high rate of patients lost to follow-up.[65] Bruhn *et al.* found significant improvement in pain scores in both pharmacist intervention groups but no significant improvement in quality of life in either group, in which the intervention consisted of prescribing and medication review.[70] Only one study from Cunningham *et al.* where pharmacist did a detailed interview with patient at

admission and discharge demonstrated significant pain score reduction of 25% as well as significantly improved health perception and physical functioning in SF-36 ($p<0.001$). However, the variety of pain measures used in these studies, together with the subjectiveness of rating pain, which is affected by baseline pain characteristics and patient demographics, suggest that even a small reduction in pain may present a significant improvement for some patients.

2.5 Limitations

There are several limitations in this review. Firstly, most of the included studies were observational studies without control groups, making the data subjective. As the risk of bias of assessment showed, the majority of the included studies had serious or critical risk of bias. Secondly, most of the studies were conducted at a single site and had small sample sizes, thus decreasing the generalizability of the findings and power of the results. Furthermore, some of the outcomes being evaluated were patient-reported, which are usually influenced by the baseline characteristics such as demographics. With the exception of the Suzuki *et al.* study, the N-RS fails to adjust for these baseline characteristics which might have confounded the results, so the precision of the results is unclear. Aside from the limitations in study designs, the limitations of this review reside in the inability to include potentially relevant articles due to availability of inadequate data as they were published as abstracts only. Attempts to contact authors did not yield additional information. Lastly, articles published in non-English languages that might have been relevant to our review were excluded.

2.6 Conclusions

This systematic review demonstrates that pharmacist-provided interventions were effective in decreasing pain intensity, improving quality of life, and reducing cost and side effects in patients with chronic pain. However, results are limited by the quality of studies involved.

Table 1: Key terms

Pain	Location	Personnel	Intervention	Efficacy
Chronic pain-MESH	Community pharmacy	Pharmacists	Health services-MESH	Effectiveness of intervention
Widespread pain- MESH	Community-dwelling patients	Outpatient pharmacist	Effects of pharmacists	Effectiveness of treatment
Recurrent pain	Outpatient health	Healthcare professional	Treatment of chronic pain	Evaluation of intervention
Lasting pain	Clinic visit	Health personnel	Intervention	Efficacy
	Ambulatory care –MESH		Management of chronic pain	
	Clinical pharmacy		Patient care	
	Pharmacy		Therapy	
			Educational intervention	

Search terms within each column were combined using “OR” and “AND”.

Table 2:Potential confounders of each outcome

Outcomes	1. Patient-reported improvement	2. Acceptance of intervention	3. Health resource usage	4. Change of medication use
Confounders	Age	Complexity of the intervention	Age	Age
	Comorbidities	Expectations of patients and doctors	Comorbidities	Comorbidities
	Socioeconomic status		Socioeconomic status	Socioeconomic status
	Baseline scores		Baseline pain	Baseline pain
	Gender			
	Duration of pain			

Table 3:The Characteristics of the included studies

Study	Population mean age (SD)	Pain type	Study duration, site	Study design	Sample size	Who is involved	Interventions	Pain scores	Quality of life	Other results
Bauters (2008)	_	Chronic non-malignant pain	9 months; outpatient pain center	Retrospective study	93	Multidisciplinary pain team	Pharmacist provision of information, clinical intervention, and provision of a specific product			95.3% of pharmacist clinical interventions were accepted by physicians
Turner (1999)	_	Medication-induced headache	18 weeks; community pharmacies	Prospective cohort	11	Community pharmacists, study nurse	Pharmacists posted flyers in the community pharmacy to recruit patients. Asked them to complete questionnaires		Short Form Health Survey and Henry Ford Hospital Headache Disability Inventory: a consistent but not statistically significant trend toward improvement	1. Statistical reduction in headache frequency. 2. Reduction in daily consumption of analgesics. 3. Reduction in the frequency of medication use

Suzuki (2014)	44.3 (11,7); 57.8% male	Chronic pain	6 months at a urban academic primary care clinic	Prospective cohort	33	Psychiatrist, pharmacist, health coaches	Initial evaluations, buprenorphine inductions, follow-up visits	BPI-decreased from 5.1 (SD =3.7) at baseline to 3.3 (SD=3.3) at 3 months and 4.5 (SD=3.7) at 6 months; Pain disability: reduced from 5.5 (SD =3.8) at baseline to 2.7 (SD=2.9) at 3 months and 4.4 (SD=3.5) at 6 months		1. 95.6% patients accepted the treatment and 55% remained in the treatment at 6 months.
Kroner (2008)	61.6 (14.20); 45.1% male	Chronic pain	1 year in a not-for-profit, integrated health system	Retrospective cohort	47	Primary care clinical pharmacist, physicians, nurse practitioners, physician assistants	Used PharmDoc tool to project Medication Cost Avoidance (MCA). Converted medications for patients and assessed for subesquent adverse events			1. 24 of 47 patients persisted with new medication. 2. Achieved $50,000 medication cost avoidance for 24 persistent patients.
Hay (2006)	67.9 (8.2); 27% male	Knee pain	1 year at 15 general practices	RCT	325	Community pharmacist, community physiotherapists,	Intervention groups: enhanced pharmaceutical review or community physiotherapy control	WOMAC—Baseline to 3 months: pain scores reduction of 0.41 (SD=3.7) for control, and 1.59 (3.2) for pharmacy; Intervention		1. 67%, 57%, and 52% patients satisfied with the treatment at 3 months, 6 months, and 12 months post-

						nurse	group: advice leaflet reinforced by telephone call	vs control at 3 months: mean adjusted differences were 1.18 (0.3-2.0, p=0.006) for pain NRS-pharmacy review group: baseline to 3 months: 1.34 (SD=2.5) decrease; intervention vs controls: 0.72 (0.1-1.4, p=0.04)		randomization respectively. 2. Self-reported use of non-steroidal anti-inflammatory drugs in the pharmacy review group were lower than in control group, while the use of analgesics was higher (p=0.02).
Bruhn (2013)	65.6 (12.6) 62.2% female	Chronic pain	10 months in 6 general practices	RCT	196	pharmacists	Prescribing arm: medication review, prescribing, consultation, care plan recommendations, follow up; Review arm: medication review, care plan recommendations; Control arm:	CPG—Within prescribing arm: a 8.0 (SD =16.3, p=0.002, effect size r=0.45) mean pain intensity decrease and a 8.3 (0.0;23.3, p=0.003, effect size r=0.43) median pain disability decrease at 6 months; within controls: a median decrease of 3.3 in pain Disability (p=0.05, effect size r=0.26);	Short Form-12--only control group showed statistically significant improvement in physical component.	HADS scores improved in within the prescribing arm for both depression and anxiety(p=0.007), and between arms(p=0.022 and 0.045, respectively)

							treatment as usual	compared to baseline, 47.7% (p=0.003) patients in the prescribing arm got improvement and 38.6% (p=0.001) in the review arm		
Cunningham (2009)	46.4 (14.1) 81.2% female;	Chronic non-malignant pain	3 week program and 6 months outpatient at a rehabilitation center	Prospective cohort	186	Multidisciplinary team	Detailed pharmacist interview, review of medication bottles, educate on medication use, calculate medication cost and monitor for withdrawal	MPI—Pain intensity: admission to 6 months: 46.45 (SD=9.68) decreased to 35.05 (SD=12.43) (p<0.001); the perceived life control and general activity level also improved significantly (p<0.001).	Short Form-36-- Admission to 6 months: health perception: 42.67 (SD=22.25) increased to 60.82(SD =21.89); physical functioning: 42.57 (SD =23.43) improved to 69.37(SD =21.24) (p<0.001)	1. Significant medication cost saving of $9.31 from admission to discharge. 2. Maintained medication cost reduction at 6 months. 3. Decreased OTC use. 4. CES-D scores decreased from 27.97 (SD=13) at admission to 14.46 (SD=10.62) at dismissal (p<0.001).

Dole (2007)	60	Chronic non-cancer pain	1 year at the pain management ambulatory clinic	Descriptive study	1890	Pharmacist clinicians , physicians, nurse practitioners	Pharmacist clinician patient visits, follow-ups. write prescriptions, also developed medication-refill protocol	VAS--Significant reduction in pain intensity ($p<0.0001$) during the first 10 visits		1. Increased consistency of the authorization of medication refill process 2. Generated $107,550 of actual revenues and saved health plans by over $450,000
Wiedemer 2007	_	Chronic non-cancer pain	2 years at a primary care clinic at an urban academic Veterans hospital	Naturalistic prospective outcome study	335	Nurse practitioner and clinical pharmacist	Pharmacist run an Opioid Renewal Clinic (ORC)			1. Number of urine drug testing, opioid treatment agreement increased after ORC implementation. 2. Decline in ER visits from 72.7% to 59.6%. 3. 84% of PCP satisfied with service. 4. Met pharmacy budget goals.

Briggs (2008)	57 (15), range 27-86 years	Chronic pain	1 year at a primary care trust	A pilot study	120	Community pharmacist, nurse	Medication review, make treatment plan	NRS--over a 6-month period, pain intensity on referral were 8 (mean and median) and on discharge 6.3 (mean) and 6 (median) ($p<0.0001$)		1. Reduced need for secondary referral. 2. 92% of patient satisfied with the clinic
McDermott (2006)	51.4% aged 29-64, 48.6% aged 65-94; 62.1% female	Chronic pain	6 months at one general practice	Prospective cohort	140	Pharmacist	Paper-based medical record review, make recommendations, documentation; interviews among 25% of the population	CPG--19 progressed to a more severe CPG, 25 to milder CPG, 31 stayed the same grade.		77% of recommendations were implemented
Gammaitoni (2000)	21.6% aged ≤35, 75.7% aged 36-64; 58.1% female	Chronic pain	3 months; at a university pain clinic	RCT	74	PainRxperts, pharmacist, a nurse research coordinator	Monitor, counselling, documentation	PhPI--Physical and emotional problems interference with social activities showed a significant improvement in intervention group compared to baseline		At baseline, participants in control group were more satisfied with psychological assessment and treatment than intervention group ($p<0.05$); at 3

										months, participants in intervention group significantly more satisfied with pharmacist-related services than controls (p≤0.013).
Read (1998)	60.4, range 29-84; 71% female	Chronic pain	15 months at 3 medical practices	Prospective cohort	96	Pharmacists	Structured interview, recommend a change of therapy, give advice	VAS--out of the 14 patients available for follow up: 85 to 80 for pain relief, 80 to 70 for worst pain, 65 to 50 for average pain and 50 to 40 for pain now		
Chelminski (2005)	51, ranged 27-76 years; 40% female	Chronic non-cancer pain	3 months at a primary care pain management program	Prospective cohort	85	A primary care physician, a clinical pharmacist, a program assistant, a psychiatrist, a nurse	Structured clinical assessment, monthly follow-up, pain contracts, medication titration, monitor for substance abuse	BPI—Baseline to 3 months: pain intensity significantly improved by 12% to 15% PDI—Baseline to 3 months: pain disability scores improved from 47.0 to 39.3 (p<0.001)		1. Mean CESD reduced from 24 to 18, 79% to 54% of patients being depressed. 3. 48% of the patients increased their opioid dose over 3 months, and the mean opioid

										equivalent increased from 53 mg to 105 mg per day.
Neilson (2015)	65.6 (SD=12.6)	Chronic pain	10 months in 6 general practices	Regression analysis of cost and effects	125	Pharmacists	Prescribing arm: medication review, prescribing, consultation, plan, follow up; Review arm: same except prescribing; Control arm		Short Form-6-Dimension (SF-6D): prescribing arm showed slight and higher improvement than two other arms; review arm and control arm also improved compared to baseline	1. The mean of adjusted difference in total cost VS TAU from the baseline to 6 months was: 77.5 (−81.7 to 236.7) prescribing arm, 54.4 (−103.3 to 212.1) review arm (p=0.0000). 2. The mean of adjusted difference in total QALYs vs TAU were: 0.0069 (−0.0091 to 0.0229) prescribing arm, 0.0097 (−0.0054 to 0.0248) review arm

Table 4: Risk of bias in randomized controlled trials

Study	Hay et al. (2006)		Bruhn et al. (2013)		Gammaitoni et al. (2000)	
Bias	Risk	Support for judgement	Risk	Support for judgement	Risk	Support for judgement
Random sequence generation (selection bias)	*	Used a computerised random number generator	*	telephone randomisation service with a random number allocation	*	Used excel spreadsheet randomly assign participants
Allocation concealment (selection bias)	*	Used a sealed opaque envelope	*	telephone randomisation with a random number allocation, questionnaires posted to participants	*	randomization applied
Blinding of participants	**	Blinding of participants is not possible due to the nature of the intervention	**	Blinding of participants is not possible due to the nature of the intervention	**	Blinding of participants is not possible due to the nature of the intervention
Blinding of outcome	*	Participants reported,	**	No blinding	**	No blinding

assessment		independent data imputed, statistical analysis				
Incomplete outcome data	*	Analysis was by intention to treat	*	Analysis was conducted on intention-to-treat basis	*	More than half of the data were missing
Selective reporting	~	Not stated	~	Not stated	~	Not stated

Key ~ Unclear

*Low risk

**High risk

Table 5: Risk of bias in non-randomized studies

Study	Chelminski (2005)		Turner (1999)		Cunningham (2009)			Suzuki (2014)		Kroner (2008)	
Outcome # / **Bias**	**1**	**4**	**1**	**4**	**1**	**3**	**4**	**1**	**2**	**2**	**3**
Confounding	***	***	***	***	***	***	***	**	***	***	***
Selection of participants	*	***	**	**	**	*	*	*	*	~	~
Measurement of interventions	*	*	*	*	*	*	*	***	***	*	*
Departure from intended interventions	~	~	~	~	~	~	~	~	~	~	~
Missing data	***	***	****	****	**	*	*	****	**	*	***
Measurement of outcomes	***	**	***	***	***	*	*	***	**	*	**
Selection of the reported result	**	**	**	**	**	**	**	**	**	**	**
Overall bias	***	***	****	****	***	***	***	****	***	***	***

Study	Briggs (2008)			Wiedemer (2007)		McDermott (2006)		Read (1998)
Outcome # / **Bias**	**1**	**2**	**3**	**2**	**3**	**1**	**2**	**1**
Confounding	***	***	***	***	***	***	***	***
Selection of participants	~	~	~	~	~	**	**	**
Measurement of interventions	**	**	**	**	**	*	*	**
Departure from intended interventions	~	~	~	~	~	~	~	~
Missing data	**	**	**	**	**	***	***	****
Measurement of outcomes	***	***	**	**	**	***	**	***
Selection of the reported result	**	**	**	**	**	**	**	**
Overall bias	***	***	***	***	***	***	***	****

Key: ~ no information available

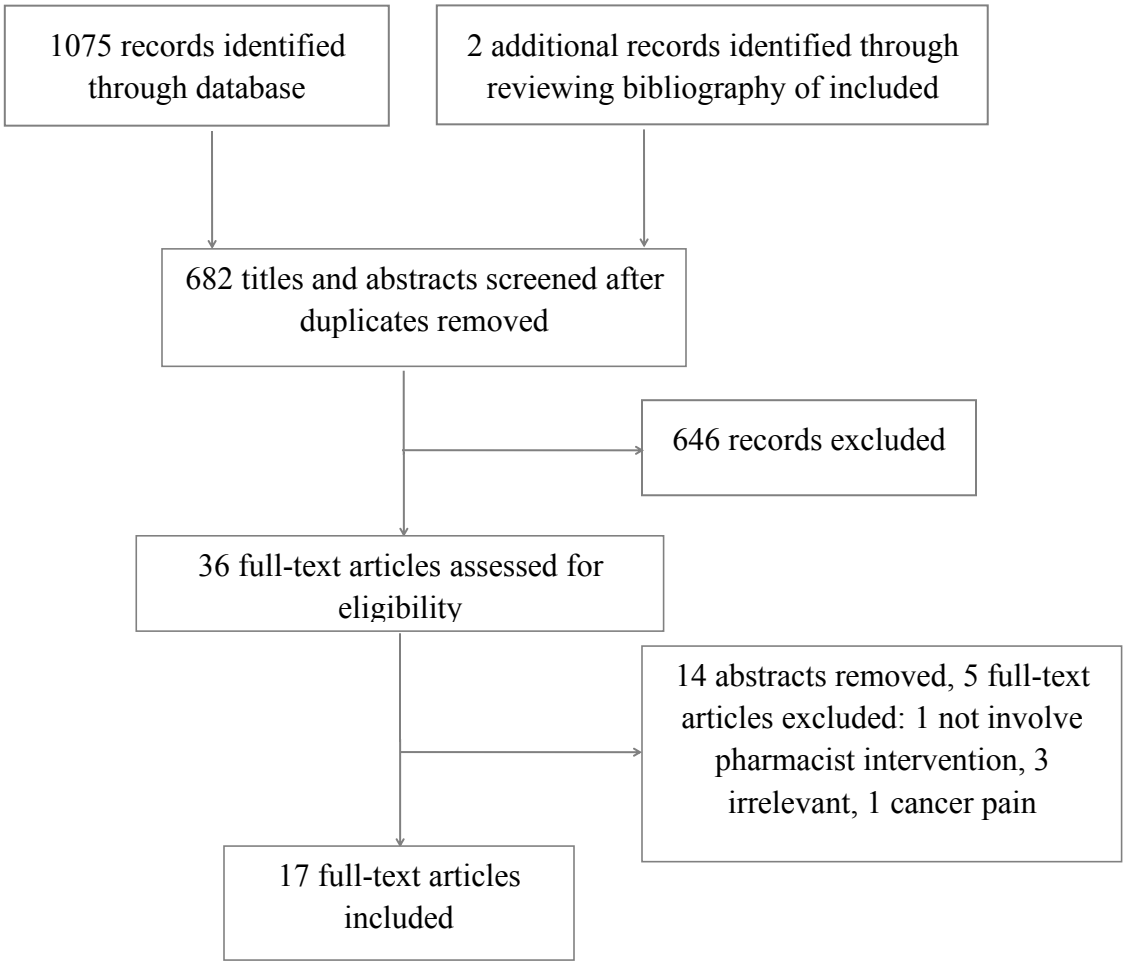
*Low risk

**Moderate risk

***Serious risk

****Critical risk

Figure 1: Systematic review flow chart



CHAPTER 3: RATIONALE, OBJECTIVES AND HYPOTHESIS

3.1 Rationale: Why care?

As previously discussed, chronic pain has been persistently impacting people's physical and psychological functioning in all ages. Given the multi-dimensional pathophysiology of pain, health professionals from diverse disciplines ought to be involved. The effective use of resources to address chronic pain management remains a major objective of health providers and policy makers. Primary care pharmacists, especially community pharmacists with extended working hours, are the most broadly distributed health professionals. They are located in nearly every community from cities to rural area. Following the trend of patient-focused care, Canadian pharmacists' scope of practice has continued to expand in the last two decades. In Ontario, these roles include the ability to initiate smoking/tobacco cessation, change drug dosage/formulation/regimen, renew/extend prescription, and administer travel and influenza vaccines.[97] However, the awareness and acceptance of the expanded roles have been low among the public.[98] Little research has been done to investigate the effectiveness of Canadian pharmacists' new roles.

As demonstrated in the systematic review, primary care pharmacists working independently or in multi-disciplinary teams offered patients interventions such as medication review, consultation, care plan recommendation, patient education, information provision, and follow-ups. The majority of the articles discussed in this paper investigated the effect of these interventions on pain intensity and found positive results

in reducing pain intensity. While some results were significant, others were not. Few studies have addressed the effect of pharmacist interventions on quality of life. Only one study generated significant improvement in physical functioning. Given the limited evidence, more investigation needs to be done. It is also noted that most of these studies were conducted either in the U.K. or in the U.S. There is still a lack of Canadian data on primary care pharmacists' effect on pain relief, particularly on quality of life in patients with chronic pain.

Therefore, the intent of this study is to evaluate the effect of primary care pharmacist interventions on pain scores as well as quality of life in patients with chronic pain in Canada.

3.2 Objectives

3.2.1 Primary objective

The primary objective of this study is to examine the effectiveness of a primary care pharmacist-driven chronic pain intervention on pain intensity of ambulatory patients with chronic non-cancer pain.

3.2.2 Secondary objectives

The secondary objectives of this study are:

1) To evaluate the effectiveness of the intervention on pain interference.

2) To determine the effect of the intervention on the quality of life.

3.3 Hypothesis

We hypothesize that community pharmacist interventions can reduce pain intensity scores by 30% using the Brief Pain Inventory pain intensity subscale.[79] A reduction of 30% in pain intensity is considered a clinically important difference.[96] Since chronic pain is multi-dimensional, to extensively measure the effect of the interventions, we also hypothesize that a 2-point reduction will appear in interference subscale of BPI and a 0.2 effect size in each of the 8 subscales of Short Form-36 will be accomplished, both of which are considered as the minimum clinical important difference.[99] Effect size is defined as the difference between the means of two groups divided by the standard deviation, which provides the magnitude of an effect.[100]

CHAPTER 4: METHODS

4.1 Study design

Before the commencement of the study, ethics clearance was obtained through the Office of Research Ethics at the University of Waterloo (ORE #21092).

This is a prospective, pre post, pilot cohort study to be conducted in patients with chronic pain, which is defined as pain that lasts beyond 3 months. To accomplish the primary and secondary objectives of the study, three phrases will be designed and completed during three months (Figure 2).

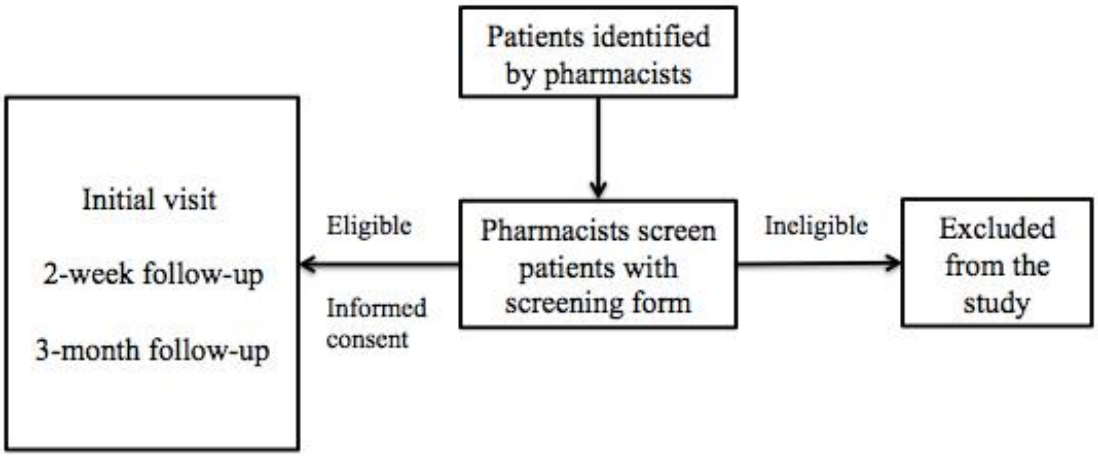


Figure 2: Study design

4.2 Population

4.2.1 Patient sample size estimation

The calculation of the sample size based on the primary research objective hypothesis. Considering it is a two-sided hypothesis, the following formula was applied to estimate sample size:

$$n = \frac{(Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \sigma_d^2}{(\mu_b - \mu_a)^2}$$

Where

A: Type I error: If α=0.05 then $Z_{\frac{\alpha}{2}}$ =1.96

B: Type II error: If β=0.2 then Z_{β}=0.834

μ_b: Before intervention pain intensity score

μ_a: After intervention pain intensity score

σ_d^2: Variance of difference. Since this was not available, it was estimated based on the available data from Farrar et al. study [96] using the formula Var(Xb-Xa)=Var(Xb)+ Var(Xa)-2*Cov(Xa Xb) where:

Xa: After intervention pain intensity score in Farrar et al. study

Xb: Before intervention pain intensity score in Farrar et al. study

Var: Variance

Cov: Covariance

In the calculation, reduction in pain intensity by 30% between baseline pain intensity scores and three-month visit pain intensity scores using the BPI pain intensity subscale and a 15% withdrawal rate was assumed. The sample size was calculated with 80% power and 95% confidence intervals. The estimated minimum sample size was 16.

4.2.2 Recruitment

Pharmacists from an existing professional network were contacted by the researcher through an invitation email and followed up through a telephone call or an in-person visit as needed. The network consists of pharmacists who are affiliated with the University of Waterloo School of Pharmacy and have indicated an interest in participating in research projects, as well as pharmacists with an interest in chronic pain and have previously provided consent to be contacted for pain-related research projects. For those who were interested, a member of the research team met with the pharmacists to explain the information letter and assess for eligibility. Informed consent was obtained from pharmacists who met the inclusion criteria and agreed to participate. After obtaining consent, the researcher trained the pharmacist in procedures relevant to the study and completed a demographic survey (Appendix 3).

Inclusion Criteria for pharmacists:

- Ontario pharmacists who are registered under Part A in the Ontario College of Pharmacists
- Practicing in community pharmacies, family health teams, or community health centers.

Inclusion criteria for patient participants:

- Aged 18 or older
- Baseline pain intensity using BPI is 6 or higher
- Ambulatory patients
- Diagnosis of pain lasting 3 months or longer

Exclusion criteria for patient participants:

- Patients with malignant or cancer pain
- Patients who are unable to communicate in English
- Unable to give informed consent

Patients were identified through two strategies:

1. Regular workflow. Patients who meet the eligibility criteria and seek help about pain-related problems were identified by participating pharmacists.

2. Pharmacy review. Potential eligible patients were identified by the participating pharmacists through their electronic records such as patients monitoring system or disease registries.

Pharmacists identified patients through routine care, either in refilling pain-related medications or providing education on pain-related conditions or medications. Patients were approached by the pharmacist and were briefly introduced to the study. Pharmacists then screened interested patients with a screening form (Appendix 4) and informed members of the research team. A member of the research team contacted eligible patients, provided a copy of the information letter, and explained the study in detail over the telephone, in person, or by email. For those who agreed to participate, informed consent was obtained. The researcher then informed pharmacists of the participation of patients. Pharmacists assigned each patient an identification number that was blinded to the research team and arranged visits with patients. Each pharmacist received $100 (in the form of cash or credit card) as appreciation for their participation in the study. There was no enrollment target for pharmacists and there was no impact on remuneration related to enrollment targets.

4.3 Study procedures

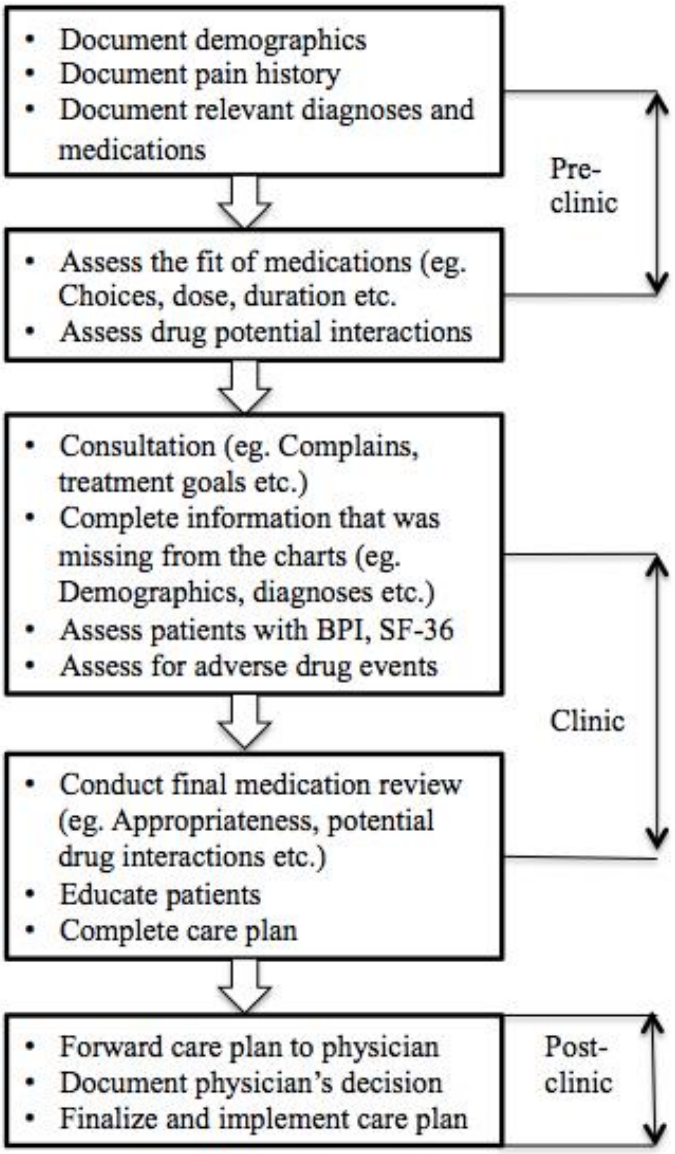
4.3.1 Initial visit (Figure 3)

Before the visit, pharmacists reviewed the patients' charts to collect available information on demographics, chronic pain & treatment history, current pain medications, other relevant medical conditions and medications. Pharmacists then assessed the appropriateness of pain-related medications and potential drug interactions.

During the visit, pharmacists met with patients in private sections of pharmacies or family health teams. Pharmacists asked patients questions in regard to their complaints and concerns on their medications and goals they wanted to achieve. Information that was missing would be completed during the course of consultation. Pharmacists then assessed pain score, quality of life, and adherence by administering the brief pain inventory (BPI) (Appendix 5), and short form 36 (SF-36) (Appendix 6), respectively. Scales were either self-administered or verbally administered by pharmacists. After obtaining above information, pharmacists and participants reviewed the medications and discussed the medications that were currently taken by the participants with regard to safety and efficacy based on their conditions. During the course, patients were educated in terms of understanding their pain and medications, potential side effects of medications, how to respond when side effects appear, self-management, and adherence. Following the discussion, pharmacists recommended a care plan with patients' agreement.

After the visit, pharmacists from community pharmacies forwarded the care plan to patients' physicians, and discussed patients' conditions with physicians in detail. Pharmacists from the family health team met with the whole team (including physician and nurses) to discuss the treatment plan. The finalized plan would then be implemented.

Figure 3: Pharmacists' initial visit with patients

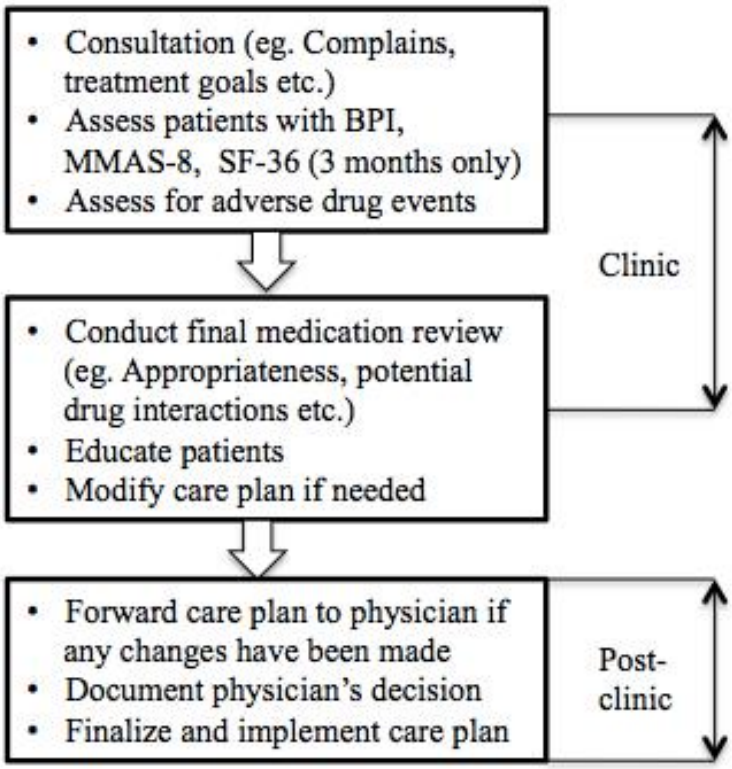


4.3.2 Follow-up visits (Figure 4)

Patients were followed up by pharmacists approximately 2 weeks and 3 months after the initial visit (in person or through telephone). Follow-up time frames were flexible considering the busyness of different study sites.

At the 2-week follow-up visit, when participants came back for reassessment of the safety and efficacy of the therapy, the following information was documented: BPI, MMAS-8 (Appendix 7). Changes in the therapies would be made if the current medications were not effective or serious side effects occurred. There were slight differences between different settings at 3-month follow-up. At community pharmacies, pharmacists would follow up with patients alone, while at family health team, pharmacists met with patients together with the whole team and came up with finalized plan through discussion.

Figure 4: Pharmacists' follow-up visits with patients



4.4 Data collection

A data collection matrix was designed and developed for collecting data (Appendix 8). The following data were included in the matrix:

1) Demographics:

- Age, gender, educational level, income, employment status, medication coverage

2) Chronic pain and treatment history:

- Type of pain, duration
- Past medications for chronic pain, non-pharmacological treatment currently using

3) Current medications for pain

4) Other medical conditions

5) Other medications in current use

6) History of substance use

7) Brief pain inventory

8) Short form 36

9) 8-item Morisky medication adherence scale

10) Care plan recommendations

11) Recommendation acceptance

12) Pain treatment changes

- Pharmacological treatments
- Non-pharmacological treatments

4.5 Outcome variables

- Demographics of pharmacists

  --Age, gender, years in practice, educational level, practice settings, working regime.

- Demographics of patients

  --Age, gender, marital status, educational level, employment status, income, medication coverage, type of chronic pain, pain duration.

- Pain treatment

  --Past pain medications, current pain medications, current conditions other than pain, current other medications, non-pharm interventions in current use.

- Pain score changes

  --Pain score was measured using brief pain inventory.[79] Pain score changes were calculated as BPI score at follow-ups minus BPI score at baseline.

- Quality of life changes

  --Quality of life was measured with short form-36.[101] Quality of life changes were calculated as SF-36 score at follow-up minus SF-36 score at baseline.

4.6 Analysis

Analysis was carried out using IBM's Statistical Package for Social Sciences (SPSS) (version 22.0.0.0) for the Macintosh operating system. Descriptive statistics were used to describe patients' baseline characteristics and interventions provided by pharmacists. Continuous data were reported as means and standard deviations and categorical data were reported as counts, percentages, and ranges. A paired t-test was conducted to detect

the changes of patients' pain scores between baseline and 3-month follow-up. One-way repeated analysis of variance (ANOVA) was conducted to compare the effect of time on the pain scores at baseline visit, 2-week follow-up visit, and 3-month follow-up visit. Non-parametric paired-t test (Wilcoxon Signed Rank test) was conducted to compare patients' quality of life between baseline and 3-month follow-up. Subgroup analyses were also conducted. Independent sample t-test was conducted to compare the changes in pain scores observed based on study period (from baseline to 3-month follow-up), gender, and adherence.

CHAPTER 5: RESULTS

5.1. Results

5.1.1 Study participants

5.1.1.1 Pharmacist participants

Between February 2016 and June 2016, 6 pharmacists agreed to participate in the study. Table 6 presents the demographics of pharmacist participants. The mean age of pharmacist participants was 43.50 years, all were full-time working females and had a BSc in Pharmacy degree, 83.3% had been practicing for more than 10 years, and 83.3% were currently practicing in community pharmacies.

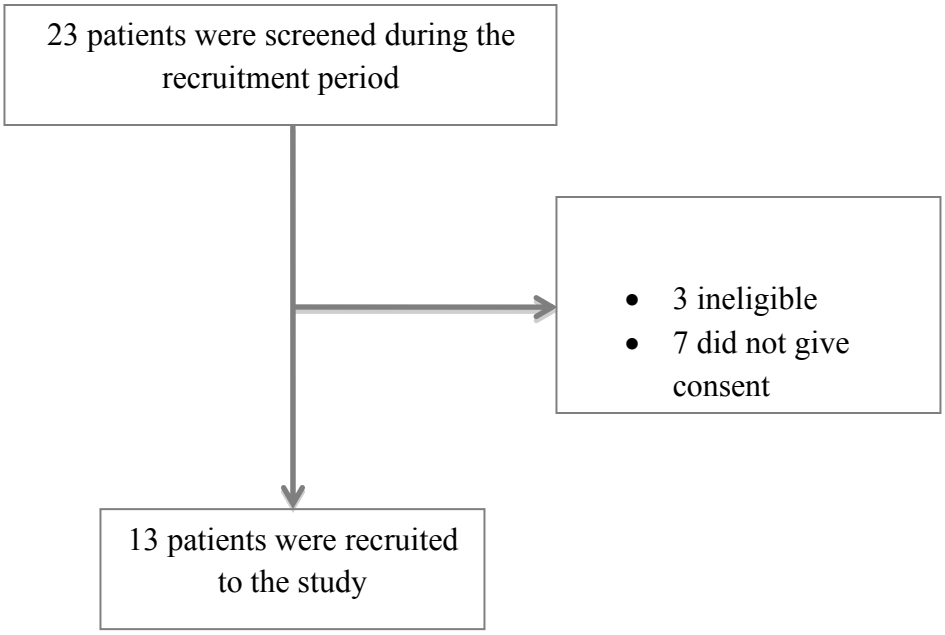
Table 6: Demographics of pharmacist participants (N=6)

Demographics	N (%, where applicable)
Age (years)	
Mean (SD)	43.50 (9.27)
Range	28-55
Gender	
Female (%)	6 (100%)
Practice experience (years)	
<5	1 (16.7%)
5-10	0 (0%)
11-15	1 (16.7%)
16-20	2 (33.3%)
>20	2 (33.3%)
Highest degree of education	
BSc (Pharmacy)	6 (100%)
Primary practice settings	
Family health team	1 (16.7%)
Community pharmacy	5 (83.3%)
Working regime	
Full-time	6 (100%)

5.1.1.2 Patient participants

In total, 23 patients were screened for inclusion from March 2016 to August 2016. Of these, 13 patients were recruited. Of the 10 who were not recruited, 3 were not eligible, and 7 did not give consent.

Figure 5: Recruitment flow chart



Of the 13 patients, 1 did not attend any visits, 12 completed the baseline visit, 10 finished the 2-week follow-up visit, and 12 completed the 3-month follow-up visit. The average times to 2-week follow-up and 3-month follow-up were approximately 20 days (range 14-35 days) and 122 days (range 84-155 days) respectively.

5.1.1.2.1 Demographics of patient participants

The average age was of 52.17 (SD=9.07) years, 75.0% were female, 33.3% married or had a stable relationship and the rest were either single, widowed or divorced. Only 25.0% attended post-secondary schools and 1 had missing education data, 16.7% were currently employed, 41.7% were unemployed and 33.3% were retired; 58.3% had an

after-tax income less than $20,000 and 16.7% were missing this information; more than half (58.3%) were covered by Ontario Drug Benefit (ODB); the types of chronic pain were various and the majority (91.7%) had been experiencing pain for more than 5 years.

Table 7: Baseline characteristics of patient participants (N=12)

Characteristics	N (%, where applicable)
Age (years)	
Mean (SD)	52.17 (9.70)
Range	41-70
Gender	
Female	9 (75.0%)
Male	3 (25.0%)
Marital status	
Married/Stable relationship	4 (33.3%)
Single	5 (41.7%)
Widowed	2 (16.7%)
Divorced	1 (8.3%)
Highest level of education	
Elementary school	5 (41.7%)
High school	3 (25.0%)
Technical/College/University	2 (16.7%)
Graduate/Professional education	1 (8.3%)
Missing	1 (8.3%)
Employment status	
Employed	2 (16.7%)
Unemployed	5 (41.7%)
Retired	4 (33.3%)
Missing	1 (8.3%)
After tax income	
<$20,000	7 (58.3%)
$20,000-$80,000	3 (25.0%)
Missing	2 (16.7%)
Medication coverage	
Private/Employment drug plan	4 (33.3%)
ODB	7 (58.3%)
Self-pay	3 (25.0%)
Types of chronic pain	
Nociceptive	2 (16.7%)
Neuropathic	2 (16.7%)
Mixed	7 (58.3%)

Unclear	1 (8.3%)
Duration of pain (years)	
<5	1 (8.3%)
5-10	4 (33.3%)
10-20	1 (8.3%)
>20	6 (50.0%)
Numbers of other medical conditions	
Mean	3.58 (1.93)
Range	0-6

5.1.1.2.2 Pain treatment history

Table 8 shows the pain medications that had been tried in the past by patient participants. The mean number of pain medications that had been tried was 3.17 (SD=1.99) ranging from 0 to 7. Opioids and NSAIDs were the most commonly tried pain medications, 28.2% and 23% of the total number of medications, respectively, followed by antidepressants and anticonvulsants (17.9% and 10.3%, respectively). Alpha2-andrenergic agonists and over-the-counter (OTC) medications were the least tried medications (only 2.6%).

Table 8: Past medications for pain (N=12)

Number of past pain medications	**N (%, where applicable)**
Mean	3.17 (1.99)
Range	0-7
Past pain medications	
Opioid	11 (28.2%)
NSAIDs	9 (23.0%)
Antidepressant	7 (17.9%)
Anticonvulsant	4 (10.3%)
Antiemetic	3 (7.7%)
Muscle relaxant	3 (7.7%)
OTC	1 (2.6%)
Alpha2-andrenergic agonist	1 (2.6%)

Table 9 shows medications in current use. Similar to past pain medications, the most common pain medications that in current use were NSAIDs and opioid, both of which accounted for 22.0% of the total number of medications currently being used. The mean of number of pain medications that patient participants were currently taking was 4.08 (SD=2.23) with a range from 1 to 8, while the mean of number of total medications in current use was 11.09 (SD=2.95).

Table 9: Medications in current use (N=12)

Pain medications in current use	
NSAID	11 (22.0%)
Opioid	11 (22.0%)
Antidepressant	7 (14.0%)
Anticonvulsant	6 (12.0%)
OTC (Codeine-contain product)	4 (8.0%)
OTC	2 (4.0%)
Acetaminophen	2 (4.0%)
Muscle relaxant	2 (4.0%)
Antiemetic	2 (4.0%)
Electrolyte supplement	1 (2.0%)
Alpha2-andrenergic agonist	1 (2.0%)
Opioid antagonist	1 (2.0%)
Number of pain medications in current use	
Mean	4.08 (2.23)
Range	1-8
Number of total medications in current use	
Mean	11.09 (2.95)
Range	3-17

Table 10 provides information on non-pharm interventions that patients were currently taking. The average of number of non-pharm interventions that patient participants were undergoing was 3.50 (SD=2.24) (range 0-7). There were variations across the non-pharm interventions; the most frequently used non-pharm interventions included exercise (66.7%), physiotherapy (53.8%), relaxation therapy (50.0%), and chiropractor manipulations (41.7%).

Table 10: Non-pharmacological interventions in current use (N=12)

Non-pharm in current use	Number of patient in current use
Exercise	8 (66.7%)
Physiotherapy	7 (58.3%)
Relaxation therapy	6 (50.0%)
Chiropractor	5 (41.7%)
Acupuncture	4 (33.3%)
Heating therapy	2 (16.7%)
Surgery	2 (16.7%)
Massage	1 (8.3%)
Epsom salt bath	1 (8.3%)
Number of non-pharm in current use	
Mean	3.50 (2.24)
Range	0-7

5.1.1.2.3 Recommendations provided by pharmacists

Table 11 presents information on recommendations provided by community pharmacists at the three study visits. Thirty-seven recommendations were made by community pharmacists for 10 patients; 54% of the recommendations were medication-related and patient acceptance rate was high (range from 75% to 100%) for these. The acceptance rate of medication-related recommendations by physician was 56.2%. Fifty percent (50%) of the medication-related recommendations were implemented, while none of the non-pharm interventions were implemented.

Table 11: Recommendations provided by community pharmacists at each visit (N = 10)

		1st visit	2nd visit	3rd visit	Patient acceptance	Physician acceptance	Implement
Medication-related	Add medication	6	2	1			
	Stop medication	0	0	0			
	Change medication	0	0	0	90%	56.2%	50%
	Increase dose	6	1	1			
	Decrease dose	3	0	0			

Referral	0	0	1	0%	N/A	N/A
Education	6	1	4	100%	N/A	N/A
Non-pharm	6	2	3	75%	N/A	0%

Note: Implement rate was calculated based on the first visit and second visit; physician acceptance rate was calculated based on prescription medications.

Table 12 shows the recommendations provided by pharmacists from family health team at the first and second visit. The pharmacist from family health team made 17 recommendations for 2 patients at the first visit. All of the recommendations were accepted by patients, and 44.4% were accepted and implemented by the team (including the pharmacist).

Table 12: Recommendations provided by pharmacists from family health team at the first and second visit (N = 2)

		1st visit	**2nd visit**	**Patient acceptance**	**Team-based acceptance**	**Implement**
Medication-related	Add medication	5	0			
	Stop medication	1	0			
	Change medication	2	0	100%	44.4%	44.4%
	Increase dose	0	0			
	Decrease dose	1	0			
Referral		1	0	100%	100%	100%
Education		6	0	100%	N/A	N/A
Non-pharm		1	0	100%	N/A	100%

5.1.1.2.4 Patient adherence

MMAS-8 scores of 8 patients were available (Table 13). Five out of 8 patients were highly adherent to the medications.

Table 13: Number (%) of people whose MMAS score were high adherence, medium adherence, or low adherence at the third visit.

	3rd visit (n = 8)
High adherence (scoring 0)	5 (62.5%)
Medium adherence (scoring 1-2)	0 (0%)
Low adherence (scoring 3-8)	3 (37.5%)

5.1.1.2.5 Pain score

The average pain score of patient participants was 5.83 (SD=1.34) when admitted to the study, which was concordant with our inclusion criteria.

5.1.1.2.5.1 The effect of time on pain score across the three visits

A one-way repeated measures ANOVA was conducted to compare the effect of time on the pain score changes across the three visits. Tables 14 and 15 show the results from repeated measures ANOVA. There was significant change in normal work scores across the three visits (p = 0.022). There were no significant changes across the three visits in terms of overall pain, worst pain in the last week, least pain in the last week, pain on average, pain right now, and overall pain interference, general activity, mood, walking ability, relations with other people, sleep, and enjoyment of life.

Table 14: Multivariate test (N = 10)

	Wilks' Lambda	F-value	p-value
Overall pain	0.715	1.596	0.261
Worst pain in the last week	0.844	0.740	0.507
Least pain in the last week	0.722	1.543	0.271
Pain on average	0.742	1.390	0.303
Pain right now	0.769	1.198	0.351
Overall pain interference	0.730	1.477	0.285
General activity	0.699	1.726	0.283
Mood	0.897	0.462	0.646
Walking ability	0.574	2.966	0.109
Normal work	0.385	6.389	**0.022**

Relations with other people	0.931	0.297	0.751
Sleep	0.872	0.585	0.579
Enjoyment of life	0.903	0.430	0.665

Three paired samples t-test were used to make post hoc comparisons between groups. There were significant differences between the first visit and second visit, and the first visit and third visit in normal work (p=0.49, 0.30 respectively).

Table 15: Pairwise comparison in mean (SD) BPI score at the first, second, and third visits (N = 10)

	1st visit	2nd visit	3rd visit	P_1	P_2	P_3
Overall pain	6.15 (1.61)	5.53 (1.83)	5.25 (1.89)	0.789	1.000	0.289
Worst pain in the last week	8.10 (1.79)	7.20 (1.87)	7.50 (2.22)	0.786	1.000	1.000
Least pain in the last week	4.70 (2.16)	3.70 (2.17)	3.40 (2.17)	0.663	1.000	0.308
Pain on average	5.90 (1.29)	5.60 (1.89)	5.20 (1.75)	1.000	1.000	0.397
Pain right now	5.90 (1.97)	5.60 (2.91)	4.90 (2.51)	1.000	0.879	0.710
Overall pain interference	6.10 (1.59)	5.64 (2.24)	5.35 (1.80)	1.000	1.000	0.447
General activity	6.50 (1.78)	5.10 (2.42)	5.50 (2.42)	0.299	1.000	0.777
Mood	5.70 (3.09)	4.80 (3.22)	5.00 (2.54)	1.000	1.000	1.000
Walking ability	6.50 (2.46)	5.70 (2.75)	5.40 (2.41)	0.411	1.000	0.307
Normal work	7.40 (1.35)	6.00 (2.26)	5.40 (2.32)	**0.049**	1.000	**0.030**
Relationships with other people	4.50 (2.12)	5.20 (3.05)	4.50 (2.88)	1.000	1.000	1.000
Sleep	7.00 (1.49)	6.90 (1.66)	6.50 (2.07)	1.000	1.000	1.000
Enjoyment of life	5.10 (2.51)	5.80 (2.78)	5.15 (2.21)	1.000	1.000	1.000

Note: p_1 refers to the p-value between the first and second visit; p_2 refers to the p-value between the second and third visit; p_3 refers to the p-value between the first and third visit.

5.1.1.2.5.2 Comparison between the first and third visit on pain score

A paired t-test was used to compare the difference in BPI scores between the first and third visits. There were trends toward improvement in overall pain, worst pain in the last week, least pain in the last week, pain on average, pain right now, overall pain interference, general activity, mood, walking ability, normal work, and sleep when

comparing baseline with 3-month follow-up, but none of the improvements were significant.

Table 16: Mean (SD) BPI score at the first and third visit, and the improvement (N = 12)

	1st visit	3rd visit	Improvement	P-value
Overall pain	5.99 (1.52)	5.48 (1.96)	8.51%	0.383
Worst pain in the last week	8.17 (1.64)	7.83 (2.17)	4.16%	0.570
Least pain in the last week	4.25 (2.22)	3.67 (2.23)	13.65%	0.482
Pain on average	5.83 (1.34)	5.42 (1.78)	7.03%	0.459
Pain right now	5.67 (1.87)	5.17 (2.44)	8.82%	0.477
Overall pain interference	6.07 (1.48)	5.84 (1.99)	3.79%	0.685
General activity	6.55 (1.69)	5.91 (2.66)	9.77%	0.463
Mood	5.67 (2.87)	5.42 (2.50)	4.41%	0.718
Walking ability	6.00 (2.34)	6.00 (2.63)	0%	1.000
Normal work	7.17 (1.85)	6.00 (2.56)	16.32%	0.171
Relations with other people	4.17 (2.08)	4.67 (3.26)	-11.99%	0.563
Sleep	7.00 (1.41)	6.75 (2.01)	3.57%	0.633
Enjoyment of life	5.50 (2.47)	5.96 (2.75)	-8.36%	0.605

5.1.1.2.5.3 Subgroup analysis

5.1.1.2.5.3.1 Comparison between different study periods at the third visit

Independent sample t-test was conducted to compare the differences on pain score changes at the third visit between groups who finished study within 4 months and beyond 4 months. The analysis showed that there were significant differences on general activity and enjoyment of life between the two groups (p=0.048 and 0.048, respectively). No significant results were found in other aspects of BPI score.

Table 17: Mean of BPI score changes (1st VS 3rd) (SD) in groups of study period<4 months and study period>4 months (N = 12)

	Study period<4 (n = 5)	Study period >4 (n = 7)	p-value
Overall pain	-1.17 (1.74)	-0.04 (2.06)	0.341
Worst pain in the last	-0.60 (1.52)	-0.14 (2.34)	0.711

week			
Least pain in the last week	-0.60 (1.14)	-0.57 (3.64)	0.987
Pain on average	-1.60 (1.52)	0.43 (1.72)	**0.061**
Pain right now	-1.40 (2.70)	0.14 (2.04)	0.284
Overall pain interference	-0.76 (2.57)	0.16 (1.21)	0.417
General activity	-2.75 (3.10)	0.57 (1.81)	**0.048**
Mood	-0.80 (2.49)	0.14 (2.34)	0.518
Walking ability	-1.20 (3.27)	0.86 (2.73)	0.263
Normal work	-0.80 (3.56)	0.00 (2.08)	0.716
Relations with other people	1.20 (3.96)	0.00 (2.08)	0.507
Sleep	-0.40 (1.82)	-0.14 (1.86)	0.817
Enjoyment of life	-1.50 (2.65)	1.85 (2.48)	**0.048**

5.1.1.2.5.3.2 Comparison between females and males at the third visit

Independent sample t-test was conducted to compare the differences on pain score changes at the third visit between female patients and male patients. The analysis showed that female patients had significant higher normal work score reduction than male patients (p=0.032). No significant results were found in other aspects of BPI scores.

Table 18: Mean of BPI score changes (1st VS 3rd) (SD) in female and male (N = 12)

	Female (N=9)	**Male (N=3)**	**p-value**
Overall pain	-1.04 (1.73)	1.08 (1.89)	0.102
Worst pain in the last week	-0.67 (2.18)	0.67 (0.58)	0.333
Least pain in the last week	-1.33 (2.40)	1.67 (3.06)	0.107
Pain on average	-0.89 (1.27)	1.00 (3.00)	0.138
Pain right now	-1.00 (2.35)	1.00 (2.00)	0.218
Overall pain interference	-0.64 (1.54)	1.02 (2.49)	0.191
General activity	-0.89 (2.76)	0.50 (3.53)	0.549
Mood	-0.22 (1.79)	-0.33 (4.16)	0.947
Walking ability	-0.78 (3.03)	2.33 (1.53)	0.126
Normal work	-2.11 (2.03)	1.67 (3.05)	**0.032**
Relations with other people	0.22 (1.72)	1.33 (5.77)	0.591
Sleep	-0.22 (1.39)	-0.33 (3.05)	0.930
Enjoyment of life	0.06 (3.30)	1.67 (1.53)	0.444

5.1.1.2.5.3.3 Comparison between high adherence group and low adherence group at the third visit

Independent sample t-test was conducted to compare the differences on pain score changes at the third visit between high adherence and low adherence groups. Results showed there was no significant difference between the two groups.

Table 19: Mean of BPI score changes (1st VS 3rd) (SD) in high adherence group and low adherence group (N = 8)

	High adherence (n = 5)	Low adherence (n = 3)	P-value
Overall pain	-1.00 (1.70)	-1.20 (2.52)	0.896
Worst pain in the last week	-1.60 (2.19)	0.33 (2.08)	0.265
Least pain in the last week	-1.20 (3.35)	-0.67 (1.53)	0.808
Pain on average	-0.80 (0.84)	-1.67 (2.08)	0.424
Pain right now	-0.40 (1.95)	-2.00 (3.46)	0.424
Overall pain interference	0.24 (2.05))	-1.57 (1.96)	0.267
General activity	-0.50 (2.08)	-2.67 (3.79)	0.371
Mood	0.60 (1.82)	-1.33 (2.52)	0.249
Walking ability	-0.40 (2.88)	-2.33 (2.08)	0.355
Normal work	-1.00 (3.67)	-3.33 (1.53)	0.346
Relations with other people	1.20 (3.96)	1.00 (2.64)	0.941
Sleep	0.20 (1.30)	-1.00 (1.73)	0.304
Enjoyment of life	1.20 (3.77)	-1.50 (3.12)	0.340

5.1.1.2.6 Quality of life

The Wilcoxon signed-ranks test indicated there was no significant difference in SF-36 score when comparing baseline with 3-month follow-up.

Table 20: Mean (SD) SF-36 at the first and third visit (N = 11)

	1st visit	3rd visit	P-value
Physical functioning	42.07 (20.26)	39.14 (22.27)	0.440
Role limitations due to physical health	18.94 (20.10)	46.22 (45.85)	**0.057**
Role limitations due to emotional problems	44.70 (43.19)	42.42 (39.69)	0.833
Energy/fatigue	35.00 (21.91)	32.73 (17.08)	0.721
Emotional well-being	61.09 (24.07)	62.91 (23.87)	0.878
Social functioning	54.55 (21.85)	63.64 (28.20)	0.380
Pain	31.36 (13.48)	35.45 (15.84)	0.206
General health	43.98 (15.94)	45.00 (16.73)	0.725

CHAPTER 6: OVERALL DISCUSSIONS AND CONCLUSIONS

6.1 Discussions

6.1.1 Summary of results

This three-month prospective pilot study investigated the effectiveness of interventions offered by pharmacists from primary care settings on pain intensity, pain interference and quality of life among patients with chronic pain. Interventions included patient assessments, medication reviews, care plan recommendations, and patient education. Findings at the 3 months follow-up indicated that pharmacists' interventions had no significant effect on pain or quality of life scores in patients suffering from chronic pain, except for the significant difference detected on the pain interference with normal work from baseline and 2 weeks follow-up. The research hypothesis of a 30% reduction in pain intensity was not proven. Nevertheless, there were trends toward improvement in many aspects of BPI scale except for pain interference with walking ability, relations with other people, and enjoyment of life.

6.1.2 Pain score

Although it has been established that pain is a multi-faceted disorder, pain intensity is still considered as the main outcome in pain management. Our study reported an improvement in pain intensity of 4.16% to 13.65% (including overall pain, worst pain in the last week, least pain in the last week, pain on average, and pain right now). Our results from BPI pain interference subscale found improvements on overall pain

interference, pain interference with general activity, mood, normal work, and sleep, but worse on pain interference with relations with other people and enjoyment of life. These findings are consistent with previous studies that investigated the effect of pharmacist interventions on larger population of chronic pain patients. For instance, one study reported a significant reduction of 21.25% in pain intensity at 6-month post-intervention.[76] Another study found a reduction of 12.0% to 15.0% ($p<0.05$) in pain intensity using BPI, and improvements of 16% and 37.0% ($p<0.05$) in pain disability using PDI and depression using CESD respectively. [64]

Although this study failed to detect any significant improvement in pain scores at the three-months follow-up, time factor was found to have a positive significant effect on pain that interferes with normal work, including housework and outdoor activities.

Several factors could have contributed to the lack of any significant data in our study. One of the major factors could be the small sample size of participants enrolled in this study. Small sample size usually affects the ability to generate enough power to detect any differences, if one exists. Several studies that detected significant effect on pharmacists' intervention in chronic pain management were conducted on a larger population.[64,66,69,70] According to our earlier sample size calculation, a total of 13 participants were required to complete the study at three time intervals (baseline, two-weeks, and three months). However, we were only able to include a total of 12 participants in the analysis.

The lack in detecting a noteworthy improvement could also be related to the extended follow-up period. We presumed that if patients spent shorter time employing pharmacists' recommendations, more meaningful effects could be detected. In an attempt

to verify this perception, we assessed the impact of study period on BPI scores at the 3 months' follow-up. We recorded that patients who completed their 3 months follow up on time achieved better outcome in pain interference with their general activity and enjoyment of life compared to those who did not complete their 3 months follow up on time. Overall, the average score of change in "pain on average" scores at 3 months' follow-up was about -1.60. This change in the average pain score is close to -1.74 which considered a clinically significant change on a 0-10 rating scale according to Farrar et al.[96]

The presumption related to the duration of follow-up is also consistent with findings from a British study conducted by Hay et al. who examined the effectiveness of medication review by community pharmacists on patients with chronic knee pain. Hay and colleagues detected a significant reduction in pain scores at 3-month interval, however this effect was not sustainable at both 6 and 12-month intervals. The reason behind the unsustainable effectiveness of pharmacist intervention is still unclear, but Hay et al. suggested that in order to obtain a sustainable effect, pharmacists' input in pain management should be maintained over a long-term period.[71]

This could also be due to the paucity of standardized collaboration model between physician and pharmacist, especially in chronic pain management. Physicians seem to be reluctant in accepting and implementing pharmacists' recommendations, which may fade the effect across time. In our study, only a little more than half of physicians (56.2%) accepted the medication-related recommendations provided by community pharmacists and only half of these recommendations were employed. This could considerably affect the impact of pharmacists' intervention.

Another explanation could be related to the low medication adherence. Medication adherence is an important predictor of effectiveness of medication-related treatments especially in managing chronic conditions. Only 8 patients' MMAS-8 were available at 3 months. Of those only 62.5% showed adherence to recommended medications. This indicates that our modest outcome could have been affected by low adherence.

Evidence shows that reaction to pain is subjective and can be influenced by psychological factors. Pharmacists participating in our study reported that patients with declined pain control had enduring family problems, while those who showed better pain control were unperturbed. However, it is not possible to examine this variable with our small sample size.

It was surprising to find that female participants were significantly more likely to report a reduction in the pain that interferes with standard work compared to males. Although studies showed that women are more sensitive to pain than men, no consistent findings regarding the impact of gender on responses to pharmacological and non-pharmacological treatment have been documented.[102]

6.1.3 Quality of life

Although the quality of life scale is one of the important indicators in pain management, it still hasn't been adequately investigated. Inconsistent results on quality of life, when investigated, were also found in previous studies. For example, Cunningham *et al.* evaluated pain in a multidisciplinary rehabilitation program which involved 178 patients and found significant improvement in health perception and physical functioning of SF-36 at 6-month post-treatment.[66] A British study done by Bruhn *et al.* did not find any significant results in SF-12 in both pharmacist prescribing arm or pharmacist review

arm with about 45 patients in each arm.[70] Turner *et al.* found a consistent but not significant improvement at follow-up in 10 patients.[75]

Our study couldn't identify any significant results for both BPI and SF-36 scores. However, we detected some discrepancies between pain interference scores between both scales. For example, we reported an improvement in pain control that interferes with the general activity by 9.77% and normal work by 16.32 % in BPI at three months' follow-up. On the other hand, a decline in physical functioning scores was detected by the SF-36 scale. Also, pain that interferes with a relationship with other individuals showed a reduction of 12.0% with the BPI whereas social functioning assessed by SF-36 showed improvement of 16.7%. The reason behind this contrariety could be due to the different ways each scale is interpreted by the patient when completing it.

6.1.4 Recommendations provided by pharmacists

The primary care pharmacists included in our study were from different settings. Pharmacists were either working at a community pharmacy, or at a Family Health Team. This likely influenced their practice approach. For example, the pharmacist working at a community pharmacy usually arranged for a one-on-one meeting with patients, then forward their treatment plan to physicians with no direct face-to-face contact with the physician. However, at the family health centre, pharmacist usually met with patients to perform a comprehensive assessment of their condition before coming up with a care plan. They then met with the inter-disciplinary team to discuss the plan. Therefore, the acceptance rate was expected to considerably differ between both settings. Additionally, the management plan is a team-based decision, which makes it difficult to assess the acceptance rate of the pharmacist interventions by physician at the family health team.

This might justify the low acceptance rate in our study, however it is still inconsistent with findings from other studies. For example, Bauters *et al.* reported an acceptance rate of 95.3% for medication management plan provided by pharmacists in a multidisciplinary pain management program. In addition, one British study reported a 100% acceptance rate of the pharmacists' pain intervention plan by physicians and an 84.4% acceptance rate in another. However, these high acceptance rates may depend on the ability of the British pharmacists to prescribe. Having the authority to implement recommendations may have influenced the acceptance and implementation rates found in these studies.

It is noteworthy that the role of Canadian pharmacists in most part of Canada is still limited with no prescribing authority. Although pharmacists' extended care in medication management had been established for decades, the awareness of pharmacists' extended role continues to be limited by both physicians' and pharmacists. Pharmacological treatment of pain is complex and sometimes problematic given the different dimensions of its pathophysiology and etiology. Therefore, the multidisciplinary collaboration and shared decisions are strongly needed for better pain management.

6.1.5 Clinical implications and future directions

This pilot study shed some light on the important role of primary care pharmacists in chronic pain management. Pharmacists can effectively contribute to pain management. Although, our results were not significant but promising, it is difficult to generalize our findings due to our small sample size. Further studies with larger sample size are needed to comprehensively investigate the effectiveness of pharmacists' contribution to pain management as well as cost-effectiveness aspect of the contribution.

6.1.6 Strengths

To our knowledge, this is the first study to assess the effectiveness of interventions provided by pharmacists in pain management in Canada. The study is the first in covering different primary care. Our study presented real-life practice skills with no previous training offered to pharmacists.

6.1.7 Limitations

Like all studies, our study had some limitations. The main limitation is the small sample size. It affected our conclusions from pain and quality of life scales. In addition, we were not able to adjust for patients' characteristics, which might have confounded some of the results, especially those related to subgroup analyses. It was our aim to investigate the impact of involving pharmacists from different primary care settings on patients' health outcomes, but this study was not powerful enough to explore this impact. Although our intention was to mimic real-life practice skills, enrolling pharmacists with diverse level of knowledge and experience might have affected the impact of the intervention.

6.2. CONCLUSIONS

Primary care pharmacists are widely allocated and readily accessible, which gives them a natural advantage in patients' care.

This study showed that interventions of primary care pharmacists had no significant effect on pain or quality of life in patients with chronic pain. However, positive trends towards reducing pain intensity and pain interference with patients' general activity,

mood, normal work, and sleep were observed. Reasons for why pharmacist interventions did not significantly improve patient outcomes could be attributed to small sample size, low implementation rate of pharmacist recommendations by physicians, low patient adherence, or extended study period.

Pharmacists' intervention in pain management is an effective use of resources for better health outcomes. However, for pharmacists' intervention plan to work effectively, collaboration between physicians and pharmacists based on mutual trust and shared decision-making is required.

REFERENCES

1. Merskey HE. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. *Pain Suppl*. 1986;3: S1-226. http://psycnet.apa.org/psycinfo/1987-31773-001. Accessed June 5, 2016.

2. Babos MB, Grady B, Wisnoff W, McGhee C. Pathophysiology of pain. *DisiMon*. 2013;59(10):330-358. doi: http://dx.doi.org/10.1016/j.disamonth.2013.05.003.

3. Katz WA, Rothenberg R. Section 3: The nature of pain: pathophysiology. *J Clin Rheumatol*. 2005;11(2): S11-S15. doi: 10.1097/01.rhu.0000158686.43637.af.

4. McGrath PA. Psychological aspects of pain perception. *Arch Oral Biol*. 1994;39:S55-S62. http://dx.doi.org/10.1016/0003-9969(94)90189-9. Accessed June 5, 2016.

5. Riley III JL. Chapter 5: The role of emotion in pain. In: Robert JG, Dennis CT, eds. *Psychosocial factors in pain: Critical perspectives*. New York, NY. DC: The Guilford Press; 1999. https://books.google.ca/books?hl=en&lr=&id=UtKfjjvohYYC&oi=fnd&pg=PA74&dq=The+role+of+emotion+in+pain&ots=hlTsk3Vlzi&sig=y4DyjRA-LkCSn2Gb7f9Ms2txXpc#v=onepage&q=The%20role%20of%20emotion%20in%20pain&f=false. Accessed June 6, 2016.

6. Fishman SM, eds. *Bonica's management of pain.4th ed.* Philadelphia, US. MO: Wolters Kluwer; 2009.

7. Millar WJ. Chronic pain. *Health reports*. 1996;7(4):47-53, 51-8. http://www.statcan.gc.ca/pub/82-003-x/1995004/article/2819-eng.pdf. Accessed June 6, 2016.

8. Reitsma M, Tranmer JE, Buchanan DM, VanDenKerkhof EG. The epidemiology of chronic pain in Canadian men and women between 1994 and 2007: longitudinal results of the national population health survey. *Pain Res Manag*. 2012;17(3):166-172. http://dx.doi.org/10.1155/2012/875924. Accessed June 6, 2016.

9. Moulin DE, Clark AJ, Speechley M, Morley-Forster P. Chronic pain in Canada--prevalence, treatment, impact and the role of opioid analgesia. *Pain Res Manag*. 2002;7(4):179-184. http://dx.doi.org/10.1155/2002/323085. Accessed June 6, 2016.

10. Schopflocher D, PhD, Taenzer P, PhD, Jovey R, MD. The prevalence of chronic pain in Canada. *Pain Res Manag*. 2011;16(6):445-50. http://dx.doi.org/10.1155/2011/876306. Accessed June 6, 2016.

11. Andersson HI, Ejlertsson G, Leden I, Rosenberg C, Centre BH, BromÃ¶lla,. Chronic pain in a geographically defined general population: studies of differences in age, gender, social class, and pain localization. *Clin J Pain*. 1993;9(3):147-82. http://journals.lww.com/clinicalpain/Abstract/1993/09000/Chronic_Pain_in_a_Geographically_Defined_General.4.aspx. Accessed June 6, 2016.

12. Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: results of an internet-based survey. *Clin J Pain*. 2010;11(11):1230-1239. doi:10.1016/j.jpain.2010.07.002. Accessed June 6, 2016.

13. Blyth FM, March LM, Brnabic AJM, Cousins MJ. Chronic pain and frequent use of health care. *Pain*. 2004;111(1–2):51-58. doi:10.1016/j. Accessed June 6, 2016.

14. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in europe: prevalence, impact on daily life, and treatment. *Eur J Pain*. 2006;10(4):287-333. doi: 10.1016/j.ejpain.2005.06.009. Accessed October 4, 2015.

15. Goddard JM. Chronic pain in children and young people. *Curr Opin Support Palliat Care*. 2011;5(2):158-163. doi: 10.1097/SPC.0b013e328345832d. Accessed June 7, 2016.

16. University Health Network. Chronic pain costs high to Ontario healthcare system and individual patients. http://www.uhn.ca/corporate/News/PressReleases/Pages/chronic_pain_costs_high_Ontario_healthcare.aspx. Published July 6, 2016. Accessed January 12, 2017.

17. Simon LS. Relieving pain in America: a blueprint for transforming prevention, care, education, and research. *J Pain Palliat Care Pharmacother*. 2012;26(2):197-198. doi: 10.3109/15360288.2012.678473. Accessed Jun 7, 2016.

18. Coulston B. Pain therapeutics part I. Presented as part of Pharm 321; February 24, 2015. Kitchener, CA.

19. Kahan M, Mailis-Gagnon A, Wilson L, Srivastava A, National Opioid Use Guideline Group. Canadian guideline for safe and effective use of opioids for chronic noncancer pain: clinical summary for family physicians. Part 1: general population. *Can Fam Physician*. 2011;57(11):1257-66.

https://divisionsbc.ca/CMSMedia/Divisions/DivisionCatalog-nanaimo/Documents/Resources/Kahan%20et%20al%20CFP%20clinical%20summary%20for%20family%20physicians.pdf. Accessed June 10, 2016.

20. Finnerup NB, Sindrup SH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. *Pain*. 2010;150(3):573-581. doi:10.1016/j.pain.2010.06.019. Accessed June 12, 2016.

21. Koes BW, van Tulder M, Lin CC, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J*. 2010;19(12):2075-2094. doi:10.1007/s00586-010-1502-y. Accessed June 12, 2016.

22. Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. *Cochrane Libr*. 2007; (4). doi: 10.1002/14651858.CD005454.pub2. Accessed June 12, 2016.

23. Lunn Michael PT, Hughes Richard AC, Wiffen Philip J. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database Syst Rev*. 2014; (1). doi: 10.1002/14651858.CD007115.pub3. Accessed June 12, 2016.

24. Moore RA, Wiffen PJ, Derry S, McQuay HJ. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Libr*. 2011;(3). doi: 10.1002/14651858.CD007938.pub2. Accessed June 12, 2016.

25. Roelofs P, Deyo RA, Koes BW, Scholten R, Van Tulder MW. Non-steroidal anti-inflammatory drugs for low back pain. *Cochrane Database Syst Rev*. 2008;(1). doi: 10.1002/14651858.CD000396.pub3.Accessed June 12, 2016.

26. Chou R, Helfand M, Peterson K, Dana T, Roberts C. Drug class review on cyclo-oxygenase (COX)-2 inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs). https://ohsucancer.com/xd/research/centers-institutes/evidence-based-practice-center/drug-effectiveness-review-project/upload/NSAID_final_report_update-3_NOV_06.pdf. Updated May 2004. Accessed June 12, 2016.

27. Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: A meta-analysis of effectiveness and side effects. *CMAJ*. 2006;174(11):1589-1594. http://www.cmaj.ca/content/174/11/1589.full.pdf+html. Accessed June 12, 2016.

28. Turk DC, McCarberg B. Non-pharmacological treatments for chronic pain: a disease management context. *Dis Manag Health Out*. 2005;13(1):19-30. doi: 10.2165/00115677-200513010-00003. Accessed June 12, 2016.

29. Turner JA, Chapman CR. Psychological interventions for chronic pain: a critical review. II operant conditioning, hypnosis, and cognitive-behavioral therapy. *Pain*. 1982;12(1):23-46. http://dx.doi.org/10.1016/0304-3959(82)90168-3. Accessed June 12, 2016.

30. Hilde G, Hagen KB, Jamtvedt G, Winnem M. Advice to stay active as a single treatment for low-back pain and sciatica. *Cochrane Libr*. 2002; (2). doi:10.1002/14651858.CD003632. Accessed June 12, 2016.

31. Hayden J, Van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non‐specific low back pain. *Cochrane Libr*. 2005; (3). doi: 10.1002/14651858.CD000335.pub2. Accessed June 12, 2016.

32. Koes BW, Bouter LM, Beckerman H, van der Heijden GJ, Knipschild PG. Physiotherapy exercises and back pain: a blinded review. *BMJ*. 1991;302(6792):1572-1576. doi: http://dx.doi.org/10.1136/bmj.302.6792.1572. Accessed June 12, 2016.

33. Ezzo J, Berman B, Hadhazy VA, Jadad AR, Lao L, Singh BB. Is acupuncture effective for the treatment of chronic pain? A systematic review. *Pain*. 2000;86(3):217-225. http://dx.doi.org/10.1016/S0304-3959(99)00304-8. Accessed June 12, 2016.

34. Boulanger A, Clark AJ, Squire P, Cui E, Horbay G. Chronic pain in canada: have we improved our management of chronic noncancer pain? *Pain Res Manag*. 2007;12(1):39-47. http://dx.doi.org/10.1155/2007/762180. Accessed June 15, 2016.

35. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012;13(8):715-724. doi:10.1016/j.jpain.2012.03.009. Accessed June 15, 2016.

36. Munger MA. Polypharmacy and combination therapy in the management of hypertension in elderly patients with co-morbid diabetes mellitus. *Drugs Aging*. 2010;27(11):871-883. doi:10.2165/11538650-000000000-00000. Accessed June 15, 2016.

37. Stannard C, Johnson M. Chronic pain management-can we do better? An interview-based survey in primary care. *Curr Med Res Opin*. 2003;19(8):703-706. doi: 10.1185/030079903125002478. Accessed June 15, 2016.

38. Silcock J, Moffett JK, Edmondson H, Waddell G, Burton AK. Do community pharmacists have the attitudes and knowledge to support evidence based self-management of low back pain? *BMC Musculoskelet Disord*. 2007;8(1):1. doi: 10.1186/1471-2474-8-10. Accessed June 15, 2016.

39. Dahan R, Reis S, Borkan J, et al. Is knowledge a barrier to implementing low back pain guidelines? Assessing the knowledge of israeli family doctors. *J Eval Clin Pract*. 2008;14(5):785-791. doi:10.1111/j.1365-2753.2007.00847.x. Accessed June 15, 2016.

40. Harris Jr JM, Fulginiti JV, Gordon PR, et al. KnowPain-50: A tool for assessing physician pain management education. *Pain Med*. 2008;9(5):542-554. doi: 10.1111/j.1526-4637.2007.00398.x. Accessed June 15, 2016.

41. Virginia W. Attitudes and knowledge about pain: an assessment of west virginia family physicians. *Fam Med*. 2005;37(7):477-480. http://67.199.94.58/fmhub/fm2005/July/Charles477.pdf. Accssed June 15, 2016.

42. Ponte CD, Johnson-Tribino J. Attitudes and knowledge about pain among west Virginia pharmacists. *J Am Pharm Assoc (Wash)*. 2007;47(3):379-382. http://dx.doi.org/10.1331/JAPhA.2007.06087. Accseed June 15, 2016.

43. Main CJ, Foster N, Buchbinder R. How important are back pain beliefs and expectations for satisfactory recovery from back pain? *Best Pract Res Clin Rheumatol*. 2010;24(2):205-217. doi:10.1016/j.berh.2009.12.012. Accessed June 15, 2016.

44. Lalonde L, Leroux-Lapointe V, Choinière M, et al. Knowledge, attitudes and beliefs about chronic noncancer pain in primary care: a Canadian survey of physicians and pharmacists. *Pain Res Manag* 2014;19(5):241-250. http://dx.doi.org/10.1155/2014/760145. Accessed June 15, 2016.

45. Kulkamp IC, Barbosa CG, Bianchini KC. The perception of health professionals about pain management and opioid use: a qualitative study. *Ciência & Saúde Coletiva*. 2008;13:721-731. http://dx.doi.org/10.1590/S1413-81232008000700022. Accessed June 15, 2016.

46. Watt-Watson J, McGillion M, Hunter J, et al. A survey of prelicensure pain curricula in health science faculties in Canadian universities. *Pain Res Manag*. 2009;14(6):439-444. http://dx.doi.org/10.1155/2009/307932. Accessed June 15, 2016.

47. Nola KM, Gourley DR, Portner TS, et al. Clinical and humanistic outcomes of a lipid management program in the community pharmacy setting. *J Am Pharm Assoc (Wash)*. 2000;40(2):166-173. http://dx.doi.org/10.1016/S1086-5802(16)31060-9. Accessed June 15, 2016.

48. Al-Sukhni M, Ballantyne P. Pharmaceutical-related strategies for health care reform in canada: Federal party principles, priorities, and actions 2004–2006. *Can Pharm J (Ott)*. 2007;140(1):38-45. http://journals.sagepub.com/doi/pdf/10.1177/171516350714000124. Accessed June 16, 2016.

49. National Association of Pharmacy Regulatory Authorities. *Model standards of practice for canadian pharmacists*.

http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf. Published March 2009. Accessed September 12, 2016.

50. Ratka A. The role of a pharmacist in ambulatory cancer pain management. *Curr Pain Headache Rep*. 2002;6(3):191-196. doi:10.1007/s11916-002-0034-5. Accessed September 12, 2016.

51. Hadi, Alldred DP, Briggs M, Munyombwe T, Closs SJ. Effectiveness of pharmacist-led medication review in chronic pain management systematic review and meta-analysis. *Clin J Pain*. 2014;30(11):1006-1014. doi: 10.1097/AJP.0000000000000063. Accessed June 12, 2016.

52. Bennett MI, Bagnall AM, Raine G, et al. Educational interventions by pharmacists to patients with chronic pain: Systematic review and meta-analysis. *Clin J Pain*. 2011;27(7):623-630. doi: 10.1097/AJP.0b013e31821b6be4. Accessed June 12, 2016.

53. Katz WA, Rothenberg R. Section 3: The nature of pain: Pathophysiology. *J Clin Rheumatol.* 2005;11(2):S11-S15. doi: 10.1097/01.rhu.0000158686.43637.af. Accessed May 12, 2016.

54. Andersson HI, Ejlertsson G, Leden I, Rosenberg C, Centre BH, BromÃ¶lla,. Chronic pain in a geographically defined general population: studies of differences in age, gender, social class, and pain localization. *Clin J Pain*. 1993;9(3). http://journals.lww.com/clinicalpain/Abstract/1993/09000/Chronic_Pain_in_a_Geographically_Defined_General.4.aspx. Accessed June 12, 2016.

55. Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in united states adults: results of an internet-based survey. *J Pain.* 2010;11(11):1230-1239. doi:10.1016/j.jpain.2010.07.002. Accessed June 12, 2016.

56. Boldt I, Eriks-Hoogland I, Brinkhof Martin WG, de Bie R, Joggi D, von Elm E. Non-pharmacological interventions for chronic pain in people with spinal cord injury. *Cochrane Database Syst Rev*. 2014;(11). doi: 10.1002/14651858.CD009177.pub2. Accessed June 12, 2016.

57. Hassett AL, Williams DA. Non-pharmacological treatment of chronic widespread musculoskeletal pain. *Best Pract Res Clin Rheumatol*. 2011;25(2):299-309. doi:10.1016/j.berh.2011.01.005. Accessed June 12, 2016.

58. Hadi MA, Alldred DP, Briggs M, Munyombwe T, Closs SJ. Effectiveness of pharmacist-led medication review in chronic pain management: systematic review and meta-analysis. *Clin J Pain*. 2014;30(11):1006-1014. doi: 10.1097/AJP.0000000000000063. Accessed June 12, 2016.

59. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA StatementThe PRISMA statement. *Ann Intern Med*. 2009;151(4):264-269. doi: 10.7326/0003-4819-151-4-200908180-00135. Accessed May 11, 2015.

60. Higgins J, Green S. *Cochrane handbook for systematic reviews of interventions.* Version 5.1.0 ed. Chichester, UK: The Cochrane Collaboration; Updated March 2011. www.cochrane-handbook.org. Accessed May 11, 2015.

61. Sterne J, Higgins J, Reeves B, eds. *A cochrane risk of bias assessment tool: For non-randomized studies of interventions (ACROBAT NRSI).* Version 1.0.0. ed. The Cochrane Collaboration. http://www. riskofbias.info. Published September 2014. Accessed May 11, 2015.

62. Gammaitoni AR, Gallagher RM, Welz M, Gracely EJ, Knowlton CH, Voltis-Thomas O. Palliative pharmaceutical care: a randomized, prospective study of telephone-based prescription and medication counseling services for treating chronic pain. *Pain Med*. 2000;1(4):317-331. doi: http://dx.doi.org/10.1046/j.1526-4637.2000.00043.x. Accessed March 12,2015.

63. Dole EJ, Murawski MM, Adolphe AB, Aragon FD, Hochstadt B. Provision of pain management by a pharmacist with prescribing authority. *Am J Health Syst Pharm*. 2007;64(1):85-89. doi:10.2146/ajhp060056. March 12, 2015.

64. Chelminski PR, Ives TJ, Felix KM, et al. A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. *BMC Health Serv Res*. 2005;5(3):1. doi: 10.1186/1472-6963-5-3. Accessed March 12, 2015.

65. Suzuki J, Matthews ML, Brick D, et al. Implementation of a collaborative care management program with buprenorphine in primary care: a comparison between opioid-dependent patients and patients with chronic pain using opioids nonmedically. *J Opioid Manag*. 2014;10(3):159-168. doi: 10.5055/jom.2014.0204. Accessed March 12, 2015.

66. Cunningham JL, Rome JD, Kerkvliet JL, Townsend CO. Reduction in medication costs for patients with chronic nonmalignant pain completing a pain rehabilitation program: a prospective analysis of admission, discharge, and 6-month follow-up medication costs. *Pain med*. 2009;10(5):787-796. doi: 10.1111/j.1526-4637.2009.00582.x. Accessed March 12, 2015.

67. Kroner BA, Billups SJ, Garrison KM, Lyman AE, Delate T. Actual versus projected cost avoidance for clinical pharmacy specialist-initiated medication conversions in a primary care setting in an integrated health system. *J Manag Care Pharm*. 2008;14(2):155-163. doi: http://dx.doi.org/10.18553/jmcp.2008.14.2.155. Accessed March 12, 2015.

68. Wiedemer NL, Harden PS, Arndt IO, Gallagher RM. The opioid renewal clinic: a primary care, managed approach to opioid therapy in chronic pain patients at risk for substance abuse. *Pain Med*. 2007;8(7):573-584. doi: 10.1111/j.1526-4637.2006.00254.x. Accessed March 12, 2015.

69. Briggs M, Closs SJ, Marczewski K, Barratt J. A feasibility study of a combined nurse/pharmacist-led chronic pain clinic in primary care. *Qual Prim Care.* 2008;16(2):91-94. http://primarycare.imedpub.com/a-feasibility-study-of-a-combined-nurse-pharmacistled-chronic-pain-clinic-in-primary-care.pdf. Accessed March 12, 2015.

70. Bruhn H, Bond CM, Elliott AM, et al. Pharmacist-led management of chronic pain in primary care: Results from a randomised controlled exploratory trial. *BMJ Open*. 2013;3 (4). doi:10.1136/bmjopen-2012-002361. Accessed March 12, 2015.

71. Hay EM, Foster NE, Thomas E, et al. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial. *BMJ*. 2006;333(7576):995. doi:10.1136/bmj.38977.590752. Accessed March 12, 2015.

72. McDermott ME, Smith BH, Elliott AM, Bond CM, Hannaford PC, Chambers WA. The use of medication for chronic pain in primary care, and the potential for intervention by a practice-based pharmacist. *Fam Pract*. 2006;23(1):46-52. doi:10.1093/fampra/cmi068. Accessed March 12, 2015.

73. Read RW, Krska J. Targeted medication review: patients in the community with chronic pain. *Int J Pharm Pract*. 1998;6(4):216-222. doi: 10.1111/j.2042-7174.1998.tb00940.x. Accessed March 12, 2015.

74. Bauters TG, Devulder J, Robays H. Clinical pharmacy in a multidisciplinar team for chronic pain in adults. *Acta Clin Belg*. 2008;63(4):247-250. http://dx.doi.org/10.1179/acb.2008.045. Accessed March 12, 2015.

75. Turner CJ, Pryse-Phillips W. Pilot study to improve health outcomes for medication-induced headache sufferers. *Can J Clin Pharmacol*. 1999;6(2):113-117. http://europepmc.org/abstract/med/10519737. Accessed March 12, 2015.

76. Briggs M, Closs SJ, Marczewski K, Barratt J. A feasibility study of a combined nurse/pharmacist-led chronic pain clinic in primary care. *Qual Prim Care*. 2008;16(2):91-94. http://primarycare.imedpub.com/a-feasibility-study-of-a-combined-nurse-pharmacistled-chronic-pain-clinic-in-primary-care.pdf. Access March 12, 2015.

77. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-245. doi: 10.1038/clpt.1981.154. Accessed April 11, 2015.

78. Carlsson AM. Assessment of chronic pain. I. aspects of the reliability and validity of the visual analogue scale. *Pain*. 1983;16(1):87-101. http://dx.doi.org/10.1016/0304-3959(83)90088-X. Accessed April 11, 2015.

79. Cleeland CS, Ryan KM. Pain assessment: Global use of the brief pain inventory. *Ann Acad Med Singapore*. 1994;23(2):129-138. http://www.health.utah.gov/prescription/pdf/guidelines/BPIglobaluseof.pdf. Accessed April 11,2015.

80. Pollard CA. Preliminary validity study of the pain disability index. *Percept Mot Skills*. 1984;59(3):974. doi:10.2466/pms.1984.59.3.974. Accessed April 11, 2015.

81. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain*. 1992;50(2):133-149. http://www.orofacialpain.org.uk/downloads/Orofacial%20pain%20assessment/Graded_chronic_pain_scale_Von_Korff.pdf. Accessed April 11, 2015.

82. Kerns RD, Turk DC, Rudy TE. The west haven-yale multidimensional pain inventory (WHYMPI). *Pain*. 1985;23(4):345-356. http://dx.doi.org/10.1016/0304-3959(85)90004-1. Accessed April 11, 2015.

83. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. *Ann Rheum Dis*. 1978;37(4):378-381. doi:10.1136/ard.37.4.378. Accessed April 11, 2015.

84. Bellamy N. *WOMAC osteoarthritis index: User guide IX*. Ontario, CA. http://www.womac.org/. Updated 2008. Accessed April 12, 2015.

85. Jacobson GP, Ramadan NM, Aggarwal SK, Newman CW. The henry ford hospital headache disability inventory (HDI). *Neurology*. 1994;44(5):837-842. doi: http:/ / dx. doi. org/ 10. 1212/ WNL. 44. 5. 837. Accessed April 12, 2015.

86. Tarlov AR, Ware JE, Greenfield S, Nelson EC, Perrin E, Zubkoff M. The medical outcomes study: an application of methods for monitoring the results of medical care. *JAMA*. 1989;262(7):925-930. doi:10.1001/jama.1989.03430070073033. Accessed April 12, 2015.

87. Ware Jr JE, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-233. http://ovidsp.tx.ovid.com/sp-3.23.1b/ovidweb.cgi. Accessed April 12, 2015.

88. Feeny D, Furlong W, Torrance GW, et al. Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. *Med Care*. 2002;40(2):113-128. http://www.jstor.org/stable/3767552?seq=1#page_scan_tab_contents. Accessed Aprila 12, 2015.

89. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. 2002;21(2):271-292. http://dx.doi.org/10.1016/S0167-6296(01)00130-8. Accessed April 15,2015.

90. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: Normative data for adults of working age. *BMJ*. 1993;306(6890):1437-1440. doi: http://dx.doi.org/10.1136/bmj.306.6890.1437. Accessed April 15, 2015.

91. Neilson AR, Bruhn H, Bond CM, et al. Pharmacist-led management of chronic pain in primary care: costs and benefits in a pilot randomised controlled trial. *BMJ Open*. 2015;5(4):e006874-2014-006874. doi: 10.1136/bmjopen-2014-006874. Accessed January 11, 2015.

92. Radloff LS. The CES-D scale a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385-401. http://journals.sagepub.com/doi/pdf/10.1177/014662167700100306. Accessed April 15, 2015.

93. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370. doi: 10.1111/j.1600-0447.1983.tb09716.x. Accessed April 15, 2015.

94. Law MR, Ma T, Fisher J, Sketris IS. Independent pharmacist prescribing in Canada. *Can Pharm J (Ott)*. 2012;145(1):17-23. http://journals.sagepub.com/doi/pdf/10.3821/1913-701X-145.1.17. Accessed April 15, 2015.

95. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2005;113(1-2):9-19. doi:10.1016/j.pain.2004.09.012. Accessed April 15, 2015.

96. Farrar JT, Young JP, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94(2):149-158. http://dx.doi.org/10.1016/S0304-3959(01)00349-9. Accessed April 15, 2015.

97. Canadian Pharmacists Association. Pharmacists' expanded scope of practice. Ontario, CA. http://www.pharmacists.ca/pharmacy-in-canada/scope-of-practice-canada/. Updated 2016. Accessed September 13, 2016.

98. Bishop AC, Boyle TA, Morrison B, et al. Public perceptions of pharmacist expanded scope of practice services in nova scotia. *Can Pharm J (Ott)*. 2015;148(5). doi: 10.1177/1715163515596757. Accessed September 10, 2016.

99. Mease PJ, Spaeth M, Clauw DJ, et al. Estimation of minimum clinically important difference for pain in fibromyalgia. *Arthritis Care Res (Hoboken)*. 2011;63(6):821-826. doi: 10.1002/acr.20449. Accessed September 10, 2015.

100. Kazis LE, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. *Med Care*. 1989;27(3):S178-S189. http://www.jstor.org/stable/pdf/3765663.pdf. Accessed April 12, 2015.

101. Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. conceptual framework and item selection. *Med Care*. 1992;30(6):473-483. http://www.jstor.org/stable/pdf/3765916.pdf. Accessed April 12, 2015.

102. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, and pain: a review of recent clinical and experimental findings. *J Pain*. 2009;10(5):447-485. doi:10.1016/j.jpain.2008.12.001. September 12, 2016.

APPENDICIES

APPENDIX 1: Information letter and consent form (pharmacists)

Title of the Project: An Evaluation of the Effect of Community-based Pharmacist Intervention on Patients with Chronic Pain

PHARMACIST INFORMATION/CONSENT LETTER

Faculty supervisors:

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School of Pharmacy
Phone: 1-519 888 4567 ext 21321
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Student researcher:

Mo Chen, B.Sc., M.Sc. candidate
University of Waterloo
School of Pharmacy
Phone: 1-226 978 5465
Email: m243chen@uwaterloo.ca

Purpose of the research: To evaluate the effect of pharmacist-provided interventions on patients with chronic pain. This pilot study, conducted as Mo Chen's Master's thesis project, will be conducted in local community pharmacies, family health team facilities, and community health centres.

Procedures: Pharmacists from community pharmacies, family health teams, or community health centers will be invited to join this project.

If you agree to participate, you will be trained in study-relevant procedures and asked to complete a demographic survey. You will be asked to recruit patients aged 18 and older and whose pain has lasted at least 3 months and whose average pain intensity scores are 6 or higher as determined by the Brief Pain Inventory (BPI). Patients who are unable to communicate in English or who suffer malignant or cancer pain or are unable to give informed consent will not be eligible to participate. Eligible patients can be identified through regular workflow or by reviewing patient records.

When a suitable patient is on-site, you will approach them and briefly introduce the study, specifying that the services offered are within the scope of usual care. If they are interested, you will ask their permission to be screened for eligibility by helping them to determine their average pain score using the BPI. If ineligible, you will thank the patient and provide the usual care. If eligible and interested, you will ask their permission to be contacted by a member of the research team. If they agree, a member of the research team will contact them to explain the study in detail, obtain consent and arrange for an initial visit with you. At the initial visit, you will collect patient demographic data, administer a baseline assessment and medication review, design and implement a customized patient care plan, and provide any education as needed. You will share documentation with the patient's physician. You will do the assessment in a patient counseling room or a private examination room in your practicing site. Follow-up visits will be scheduled two weeks and three months after the initial visit. The exact timing, duration and type of follow-up visit (clinic visit or telephone visit) will be determined by you and patient care needs. You will be asked to complete patient-related study data at each of these visits. A member of our research team will collect the data from you. The following provides additional detail.

Initial visit (approximately 1 one hour)

- You will ask each patient questions about their demographics (i.e. age), their chronic pain and treatment history, their pain medication use, other medical conditions and medications, and their substance use history.
- You will assess patients' general health and functioning, experience of pain, concerns about their medications, and medication adherence using standardized tools.
- You may then make recommendations to help improve their therapy, and discuss these with the patient and their doctor, as needed, to decide on an agreed upon plan.

Reaching the stage where a plan has been agreed upon and implemented may take some days, depending on the availability of the patient and the doctor. You will follow-up with the patient as needed according to the plan. For the purposes of this study, we ask that you meet with the patient two weeks and three months after the initial visit for formal follow-up and documentation.

Second visit—at two weeks (approximately 30 minutes)

- You will ask the patient questions about their medication use and any changes in their treatments since the last visit.
- You will assess patients' general health and functioning, experience of pain, concerns about their medications, and medication adherence with standardized tools as above.

Final visit—at three months (approximately 1 hour)

- You will again ask the patient questions about their medication use and any changes in their medical treatments since the last visit.
- You will assess their general health and functioning, experience of pain, concerns about their medications, and medication adherence with standardized tools as above.

Possible risks or discomfort: There are no anticipated increased risks to you in implementing the clinical service since it is within your scope of practice. The study is intended to provide structure to this service to collect data on its value.

Safeguards: As per usual care, patients are given detailed education during the session with you and their understanding is assessed. However, in the event they misunderstand, patients will be informed that you are available during business hours for them to call or come in to see. Outside of these hours, patients will be advised to go to an after-hours clinic or to an emergency room, if urgent.

Possible benefits: There is no direct benefit to you to participate in this study. Generally, you will be helping to demonstrate the potential value of pharmacists to patients with chronic pain in community settings.

Remuneration: You will receive $100 (in the form of cash credit card) as appreciation for your participation in the study. The amount received is taxable. It is your responsibility to report this amount for income tax purposes.

Confidentiality: All information obtained in the study will be kept confidential. No information identifying you or your practice/pharmacy will be associated with the data collection forms. All pharmacist participants will be assigned a study number that will replace their names. All files will be maintained on a secure server and password protected laptop encrypted with SecureDoc Enterprise by WinMagic in the School of Pharmacy, University of Waterloo. Access to all records will be limited to authorized individuals on the research team. University of Waterloo policies for use of restricted information are being followed. Once analysis is completed, all records of study will be stored for 3 years, then they will be destroyed, or erased. If under any circumstance the data is shared, only the anonymized dataset will be shared. The results of the study may be published for scientific purposes but will not include your name or any identifying information. The security plan for patients is explained in the patient letter, please refer to the patient information letter.

Voluntary participation in the study: Participation in this study is voluntary. You may decline to answer any question. You can withdraw your participation at any time with no penalty by

notifying Mo Chen at the email address and phone number below. The study is voluntary for patients as well, and they can withdraw at any time with no penalty by notifying Mo Chen at the email address and phone number below.

Since this study is taking place in your practice setting, in the event that you wish to participate, we request that your manager or supervisor acknowledge your participation by signing at the end of this form as well.

Questions and Contacts: Should you have any questions about the study, please contact Mo Chen at m243chen@uwaterloo.ca or 1 226 978 5465.

This project has been reviewed by, and received ethics clearance, through a University of Waterloo Research Ethics Committee. I was informed that if I have any comments or concerns resulting from my participation in this study, I may contact Dr. Maureen Nummelin, Director Ethics Officer, at 519-888-4567, ext. 36005 or maureen.nummelin@uwaterloo.ca.

UNIVERSITY OF WATERLOO

CONSENT FORM

By signing this consent form, you are not waiving your legal rights, or releasing the investigator(s), or involved institutions from their legal and professional responsibilities.

I have read the information presented in the information letter about a study being conducted by Feng Chang, PharmD, Tejal Patel, PharmD, and M.Sc. candidate Mo Chen, School of Pharmacy, at the University of Waterloo. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted. I am aware that I may withdraw from the study without penalty at any time by advising there searchers of this decision.

I have been given a copy of this informed consent and information sheet to keep for my own records. If I have any further questions I understand that I can contact a student Principal Investigator Mo Chen at m243chen@uwaterloo.ca or 1 226 978 5465.

With full knowledge of all foregoing, I agree, of my own free will, to participate in this study.

Print name: _____

Signature: **Date:**

Witness: **Date:**

Practice Manager/Supervisor Acknowledgment:

Print name: **Position:**

Signature: **Date:**

APPENDIX 2: Information letter and consent form (patients)

Title of the Project: An Evaluation of the Effect of Community-based Pharmacist Intervention on Patients with Chronic Pain

PATIENT INFORMATION /CONSENT LETTER

Faculty supervisors:

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School of Pharmacy
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Student researcher:

Mo Chen, B.Sc., M.Sc. candidate
University of Waterloo
School of Pharmacy
Phone: 1-226 978 5465
Email: m243chen@uwaterloo.ca

Purpose of the research: To evaluate the effect of pharmacist-provided interventions on patients with chronic pain. This pilot study, conducted as Mo Chen's Master's thesis project, will be conducted in local community pharmacies, family health team facilities, and community health centres.

Procedures: Pharmacists from community pharmacies, family health teams, or community health centres will be invited to participate in this project. They will assist with recruiting consenting patients 18 years of age, or older whose pain has lasted 3 months or more and whose average pain intensity scores are 6 or higher using the Brief Pain Inventory (BPI) to participate in this study with the aim to improve their pain management.

Patients will be approached by the pharmacist, briefly introduced to the study, and assured that the interventions employed in the study are within usual care guidelines. If interested, patients will be screened for eligibility by the pharmacist, who will help them determine their pain scores using one question from the BPI. Based on our inclusion criteria, pain scores less than 6 will make the individual ineligible for inclusion in the study, but the normal standard of care will continue.

If the score is 6 or higher, your pharmacist will reaffirm your interest in the study and obtain permission for research staff to contact you directly. Participation is voluntary and declining the invitation will not affect current or future care by the pharmacist. After you have enrolled in the study, the pharmacist will administer a comprehensive medication review and assessment using standardized tools, during which your treatment goals will be set up. These goals are set based on joint discussion between the pharmacist and you and will be communicated to the physician via the consultative letter. Based on the information obtained from the medication review and assessment, the pharmacist may have specific suggestions. The assessment will be conducted in a patient counseling room or a private examination room on-site at your pharmacy. Your documentation (the results of the assessment and medication review) will be shared with your physician. Your pharmacist will then plan to follow up with you to monitor progress in achieving your goals for pain control. Follow-up visits will be scheduled at 2 weeks and 3 months after the initial visit. At each visit, you will be asked questions about your health and medications. Any information collected by your pharmacist will be labelled with an ID instead of your name. Your information will not be shared outside of the research team.

Initial visit (approximately 1 one hour)

- Your pharmacist will ask you questions about your age, sex, education, chronic pain and treatment history, pain medication use, other medical conditions and medications, substance use history, and medication adherence.
- Your pharmacist will assess your general health and functioning, your experience of pain, your concerns about your medications, and medication adherence with standardized tools.
- Your pharmacist may make some recommendations to help improve your therapy. The recommendations will be discussed with you and your doctor to design an agreeable plan.

Reaching the stage where a plan has been agreed upon and implemented may take some days, depending on the availability of you and your doctor. Your pharmacist will follow-up with you as

needed to help you with the plan. As part of this study, we ask that you meet with the pharmacist two weeks and three months after the initial visit for formal follow-up and documentation.

Second visit—at two weeks (approximately 30 minutes)

- Your pharmacist will ask you questions about your medication use and any changes in your treatments since the last visit.
- Your pharmacist will assess your general health and functioning, your experience of pain, your concerns about your medications, medication adherence with standardized tools.

Final visit—at three months (approximately 1 hour)

- Your pharmacist will again ask you questions about your medication use and any changes in your medical treatments since the last visit.
- Your pharmacist will assess your general health and functioning, your experience of pain, your concerns about your medications, medication adherence with standardized tools.

Possible risks or discomfort: There are no known or anticipated risks associated with participation in this study. The care provided is within the scope of practice for pharmacists. More generally, contemplating changes to your pain treatment might cause you some anxiety, or discomfort. To help prevent or reduce this, your pharmacist will provide support as you make these decisions. Your pharmacist will be available during business hours for you to call or come in to see. Outside of these hours, you will be advised to go to an after-hours clinic or to an emergency room, if urgent.

Possible benefits: There are no direct benefits to you by participating in this study. There is the possibility that you may have improvements associated with your chronic pain management.

Confidentiality: There are always concerns about privacy when you provide information about yourself, your pain, and pain medications. Information obtained in the study will be kept confidential. You will be assigned a code number that will be used to label all information, in place of your name. The research team at the University of Waterloo will not have access any of your identifiable information. Data collected for the purposes of this study will be maintained in a secured locked cabinet and/or password protected laptop encrypted with SecureDoc Enterprise by WinMagic at the School of Pharmacy, University of Waterloo. Access to all records will be limited to authorized individuals on the research team. University of Waterloo policies for use of restricted information are being followed. Once analysis is completed, all records kept by University of Waterloo researchers will be stored for 3 years, then they will be destroyed, or erased. All of the data will be summarized and no individual could be identified from these summarized results. If under any circumstance the data is shared, only the anonymized dataset will be shared. The results of the study may be published for scientific purposes but will include group information and will not give your name or include information that will identify you.

Voluntary participation in the study: Participation in this study is voluntary. You may decline to answer any question you do not want to respond to and you can withdraw your participation at any time by notifying Mo Chen at the email address and phone number below. If you choose not to participate or you decide to withdraw at any time, your care will not be affected. The

pharmacist will not be upset if you choose not to participate. Regardless of your participation, your pharmacist will provide care as usual.

Questions and Contacts: Should you have any questions about the study, or would like additional information to assist you in reaching a decision about participation, please contact Mo Chen at m243chen@uwaterloo.ca or 1 226 978 5465.

This project has been reviewed by, and received ethics clearance, through a University of Waterloo Research Ethics Committee. I was informed that if I have any comments or concerns resulting from my participation in this study, I may contact Dr. Maureen Nummelin, Director Ethics Officer, at 519-888-4567, ext. 36005 or maureen.nummelin@uwaterloo.ca.

UNIVERSITY OF WATERLOO

CONSENT FORM

By signing this consent form, you are not waiving your legal rights, or releasing the investigator(s), or involved institutions from their legal and professional responsibilities.

I have read the information presented in the information letter about a study being conducted by Feng Chang, PharmD, Tejal Patel, PharmD and M.Sc. candidate Mo Chen, of the School of Pharmacy, at the University of Waterloo. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted. I am aware that I may withdraw from the study without penalty at any time by advising the researchers of this decision.

I have been given a copy of this informed consent and information sheet to keep for my own records. If I have any further questions I understand that I can contact the student Mo Chen at m243chen@uwaterloo.ca or 12269785465.

With full knowledge of all foregoing, I agree, of my own free will, to participate in the study including the screening part of this study.

Print name: _____

Signature: **Date:**

Witness: **Date:**

APPENDIX 3: Pharmacist demographic survey

Pharmacist and Pharmacy Characteristics

Participant ID:_____ Date:_____/_____/_____

Age (in years):_____ Gender (specify): _____

Practice experience (in years)

1. ≤5 2. 5-10 3. 11-15 4. 16-20 5. >20

Highest degree of education:

1. BSc (Pharmacy) 2. MSc 3. PharmD 4. Other (specify): _____

Primary practice setting:

1. Family health team 2. Community pharmacy 3. Community health centre

Working regime:

1. Full-time 2. Part-time 3. Other (specify): _____

APPENDIX 4: Patient screening form

☐ Aged 18 years or older

☐ Average pain intensity score out of BPI is 6 or higher

☐ Ambulatory

☐ Pain lasting 3 months or longer

☐ Diagnosed with malignant or cancer pain

☐ English speaking

☐ Unable to give informed consent

APPENDIX 5: Brief Pain Inventory

Hunter Integrated Pain Service

Brief Pain Inventory

Dec 2006

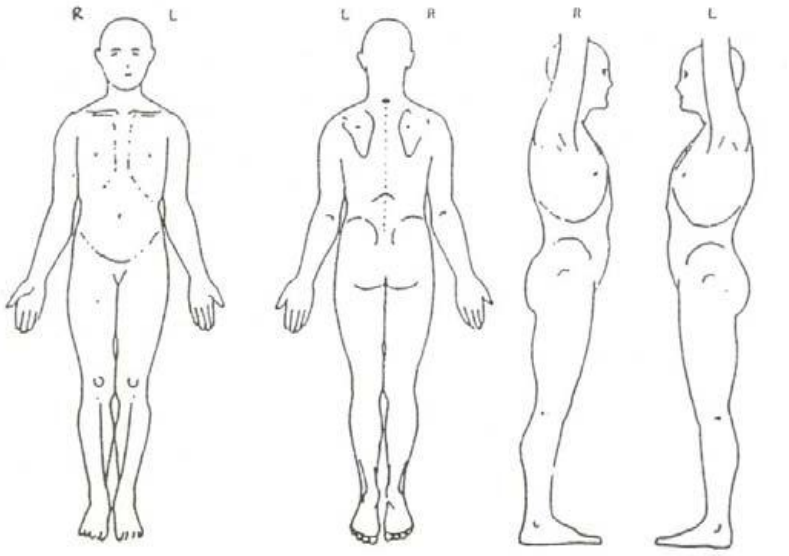
Reproduced with acknowledgement of the Pain Research Group

The University of Texas MD Anderson Cancer Center, USA

Participant ID#: _____

Date: _____

1. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts most.



2. Please rate your pain by circling the one number that best describes your pain at its worst in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

3. Please rate your pain by circling the one number that best describes your pain at its least in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain on average.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

5. Please rate your pain by circling the one number that tells how much pain you have right now.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

6. What treatments or medications are you receiving for your pain?

_____

_____

7. In the last week, how much relief have pain treatments or medications provided? Please circle the one percentage that

best shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

No relief Complete relief

8. Circle the one number that describes how, during the past week, pain has interfered with your:

a. General activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

b. Mood

0 1 2 3 4 5 6 7 8 9 10

c. Walking ability

0 1 2 3 4 5 6 7 8 9 10

d. Normal work (includes both outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10

e. Relations with other people

0 1 2 3 4 5 6 7 8 9 10

f. Sleep

0 1 2 3 4 5 6 7 8 9 10

g. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere *Completely interferes*

Brief Pain Inventory Scoring Instructions

1. Pain Severity Score

This is calculated by adding the scores for questions 2, 3, 4 and 5 and then dividing by 4. This gives a severity score out of 10.

2. Pain Interference Score

This is calculated by adding the scores for questions 8a, b, c, d, e, f and g and then dividing by 7. This gives an interference score out of 10.

APPENDIX 6: Short Form-36

Participant ID# :_____ Ref. Dr :_____ Data:_____

Age: _____ Gender: M / F

Please answer the 36 questions of the **Health Survey** completely, honestly, and without interruptions.

GENERAL HEALTH:

In general, would you say your health is:

☐Excellent ☐Very Good ☐Good ☐Fair ☐Poor

Compared to one year ago, how would you rate your health in general now?

☐Much better now than one year ago

☐Somewhat better now than one year ago

☐About the same

☐Somewhat worse now than one year ago

☐Much worse than one year ago

LIMITATIONS OF ACTIVITIES:

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Lifting or carrying groceries

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Climbing several flights of stairs

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Climbing one flight of stairs

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Bending, kneeling, or stooping

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Walking more than a mile

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Walking several blocks

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Walking one block

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

Bathing or dressing yourself

☐Yes, Limited a lot ☐Yes, Limited a Little ☐No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down the amount of time you spent on work or other activities

☐Yes ☐No

Accomplished less than you would like

☐Yes ☐No

Were limited in the kind of work or other activities

☐Yes ☐No

Had difficulty performing the work or other activities (for example, it took extra effort)

☐Yes ☐No

EMOTIONAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down the amount of time you spent on work or other activities

☐Yes ☐No

Accomplished less than you would like

☐Yes ☐No

Didn't do work or other activities as carefully as usual

☐Yes ☐No

SOCIAL ACTIVITIES:

Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

☐Not at all ☐Slightly ☐Moderately ☐Severe ☐Very Severe

PAIN:

How much bodily pain have you had during the past 4 weeks?

☐None ☐Very Mild ☐Mild ☐Moderate ☐Severe ☐Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

☐Not at all ☐A little bit ☐Moderately ☐Quite a bit ☐Extremely

ENERGY AND EMOTIONS:

These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Have you been a very nervous person?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Have you felt so down in the dumps that nothing could cheer you up?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Have you felt calm and peaceful?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Did you have a lot of energy?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Have you felt downhearted and blue?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Did you feel worn out?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Have you been a happy person?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

Did you feel tired?

☐All of the time

☐Most of the time

☐A good Bit of the Time

☐Some of the time

☐A little bit of the time

☐None of the Time

SOCIAL ACTIVITIES:

During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

☐All of the time

☐Most of the time

☐Some of the time

☐A little bit of the time

☐None of the Time

GENERAL HEALTH:

How true or false is each of the following statements for you?

I seem to get sick a little easier than other people

☐Definitely true ☐Mostly true ☐Don't know ☐Mostly false ☐Definitely false

I am as healthy as anybody I know

☐Definitely true ☐Mostly true ☐Don't know ☐Mostly false ☐Definitely false

I expect my health to get worse

☐Definitely true ☐Mostly true ☐Don't know ☐Mostly false ☐Definitely false

My health is excellent

☐Definitely true ☐Mostly true ☐Don't know ☐Mostly false ☐Definitely false

APPENDIX 7: Morisky Medication Adherence Scales - 8

Participant ID: _____ Date: _____

1) Do you sometimes forget to take your pills?

2) People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?

3) Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?

4) When you travel or leave home, do you sometimes forget to bring along your medicine?

5) Did you take all your medicine yesterday?

6) When you feel like your symptoms are under control, do you sometimes stop taking your medicine?

7) Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?

8) How often do you have difficulty remembering to take all your medicine?

___A. Never/rarely
___B. Once in a while
___C. Sometimes
___D. Usually
___E. All the time

Adherence	MMAS-8 Score
High Adherence	**0**
Medium Adherence	**1-2**
Low Adherence	**3-8**

APPENDIX 8: Data Collection Matrix

To be completed by Pharmacist Participants for each Patient Participant at their site.

Measure	Visit 1 Baseline assessment	Visit 2 2-week Follow-up	Visit 3 3-month Follow-up
Patient demographics	√		
Chronic Pain & Treatment History	√		
Current pain medications	√		
Other Medical Conditions	√		
Current Other Medications	√		
Substance Use History	√		
SF-36	√		√
BPI	√	√	√
MMAS-8	√	√	√
Care Plan Recommendations	√	√	√
Recommendations acceptance rates – patients, prescribers		√	√
Pain treatment changes		√	√

Other data collection from pharmacist participants:

Pharmacist & pharmacy characteristics (start of study).

Data Collection Item Detail

Pharmacist data for each patient (sections completed at times indicated in matrix)

Participant ID: _____ Date: _____/_____/_____

Patient Demographics

Age: _____ Sex (specify): _____

Marital status:

1. Married/Stable relationship2. Single3. Widowed4. Divorced

Highest level of education completed:

1. None 2. Elementary school 3. High School

4. Technical/college/university 5. Graduate/professional education

Employment status:

1. Employed 2. Unemployed 3. Retired 4. Other (specify)

After tax Income

1. <$20,000 2. $20,000-$80,000 3. >$80,000

Medication coverage (all that apply)

1. Private/employment drug plan 2. ODB 3. Self-pay

Chronic Pain and Treatment History

Types of chronic pain:

1. Nociceptive 2. Neuropathic 3. Mixed 4. Unclear 5. Other

How long has patient suffered chronic pain (in years)? _____

Specify Diagnosis: 1._____ 2. Unclear/unknown

Past medications for chronic pain:

Name or type of each _____

Reason for stopping (REPEAT x 5 medications)

1. Ineffective 2. Too expensive 3. Side-effects 4. Other

Non-pharmacologic treatments in current use:

1. Physiotherapy 2. Exercise 3. Acupuncture 4. Surgery 5. Relaxation therapy
6. Chiropractor 7. Other

Indicate the effectiveness of each non-pharmacological treatment in current use:

1. Effective 2. Minimally effective 3. Ineffective 4. Harmful 5. Other

Current Medications for Pain

List name, daily dose, schedule (regular/prn):

Other Medical Conditions

List:

Other Medications in Current Use

List:

History of Substance Use

For each substance listed below:

1. Ever used (tried even once): yes/no
2. Current use: yes/no
3. Use ever a problem for patient: yes/no
4. Current problem for patient: yes/no
5. Pharmacist comments: yes/no

Nicotine, alcohol, cannabis, heroin, other non-prescribed opioids, cocaine, hallucinogens, inhalants, non- prescribed amphetamines, non-prescribed methylphenidate, non-prescribed sedatives, other (specify)

Brief Pain Inventory (BPI)

Standard measure

Short Form-36 (SF-36)

Standard measure

8-Item Morisky Medication Adherence Scale (MMAS-8)

Standard measure

Care Plan Recommendations

Provide free text description for each recommendation

Categorize each recommendation:

1. Medication-related 2. Referral 3. Education 4. Other

For each medication-related recommendation indicate:

1. Dose increase
2. Dose decrease
3. Schedule change
4. Reduced quantities
5. Observed dosing
6. Drug change
7. Drug discontinuation
8. Other

Recommendations Acceptance

For each recommendation indicate:

Patient acceptance/rejection Physician acceptance/rejection

Still under consideration Modified recommendation – describe

Pain Treatment Changes

For each pain-related medication change since the last visit, indicate all that apply and specify:
Medication involved: _____ Time since change made: _____

1. Dose increase 2. Dose decrease 3. Schedule change 4. Reduced quantities
5. Observed dosing 6. Drug discontinuation 7. Other

For each new pain-related medication, complete the following:
New medication: _____ Time since started (days): _____
Total daily dose: _____ Schedule: _____
type (regular/prn): _____

New medication: _____ Time since started (days): _____
Total daily dose: _____ Schedule: _____
type (regular/prn): _____

New medication: _____ Time since started (days): _____
Total daily dose: _____ Schedule: _____
type (regular/prn): _____

New medication: _____ Time since started (days): _____
Total daily dose: _____ Schedule: _____
type (regular/prn): _____

New medication: _____ Time since started (days): _____
Total daily dose: _____ Schedule: _____
type (regular/prn): _____

For the changes of each non-pharmacological treatment, indicate all that apply:

Type of treatment:_________________ Time since started (days): _________________

1. Started – effective	2. Started - effectiveness unclear
3. Changed regimen – effective	4. Changed regimen - effectiveness unclear
5. Stopped – ineffective	6. Stopped – too expensive
7. Stopped – side effects	8. Other

Type of treatment:_________________ Time since started (days): _________________

1. Started – effective	2. Started - effectiveness unclear
3. Changed regimen – effective	4. Changed regimen - effectiveness unclear
5. Stopped – ineffective	6. Stopped – too expensive
7. Stopped – side effects	8. Other

Type of treatment:_________________ Time since started (days): _________________

1. Started – effective	2. Started - effectiveness unclear
3. Changed regimen – effective	4. Changed regimen - effectiveness unclear
5. Stopped – ineffective	6. Stopped – too expensive
7. Stopped – side effects	8. Other

Type of treatment:_________________ Time since started (days): _________________

1. Started – effective	2. Started - effectiveness unclear
3. Changed regimen – effective	4. Changed regimen - effectiveness unclear
5. Stopped – ineffective	6. Stopped – too expensive
7. Stopped – side effects	8. Other

Type of treatment:_________________ Time since started (days): _________________

1. Started – effective	2. Started - effectiveness unclear
3. Changed regimen – effective	4. Changed regimen - effectiveness unclear
5. Stopped – ineffective	6. Stopped – too expensive
7. Stopped – side effects	8. Other