

## The Michael G. DeGrootte Institute for Pain Research & Care



Toward the conquest of pain

# Vision

Using the conceptual model of persistent post-surgical pain, bring together behavioural, clinical and basic scientists to develop a new understanding of the origin, mechanisms and treatment of chronic pain.

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# A Generous Individual... A Pivotal Gift

## About Michael G. DeGroot and his gift

In 2003, businessman Michael G. DeGroot made history when he made the largest single donation ever to a Canadian university or institution. His donation of \$105 million has had a wide impact on health sciences research, education and care, and accelerated the pace of discovery at McMaster.

“With this gift, I know McMaster will be able to make new breakthroughs and make a real difference in more people’s lives.”

- Michael G. DeGroot, December 2003

McMaster’s Faculty of Health Sciences followed a “people first” guideline in allocating the \$105 million gift from Mr. DeGroot. Emphasis was placed on hiring international caliber experts in health education, research and care, particularly in the areas of pain, infectious diseases, stroke prevention and cancer. One of the key initiatives was the Michael G. DeGroot Institute for Pain Research and Care, which received a \$15 million endowment.

## Message from the Scientific Director



Once again Dr. Panju and I are excited to welcome you to the Sixth Annual Symposium and Scientific Advisory Board meeting for the Michael G. DeGroote Institute for Pain Research and Care. This has been an exciting year, and the symposium includes reports from a number of our supported students and investigators as well as excellent guests and members of our Scientific Advisory Board. We are pleased once again to welcome our Scientific Advisory Board members who represent a Who's Who of the National and International world of Pain Research and Care.

Our vision is to use the clinical problem of persistent post-surgical pain as an experimental model in which chronic pain, its causes, predisposing factors and treatments can be studied. We have now seen knowledge synthesis projects funded in the early stages of the IPRC turn into clinical trial protocols, and have supported basic science projects which have fascinating sex difference clinical implications leading to reanalysis of previous trials from McMaster University. The CIHR funded Chronic Pain Network (CPN) held its annual meeting in conjunction with the Canadian Pain Society annual meeting in April in Toronto, and we were witness to the announcement of the Federal Health Minister's Canadian Pain Task Force. Work from the CPN has included 'knowledge

into policy' presentations at several meetings which led to a meeting with the Federal Minister of Health and movement towards a Canadian Pain strategy. Our partnership with the Centre for Medical Cannabis Research has begun to bear fruit in the form of research protocols addressing the peri-operative use of cannabis products.

The Institute is linked through common membership with the clinical practice of pain care in Hamilton, both acute post-operative pain and chronic pain including interventional, pharmacologic and behavioural care, and is working to broaden its relationships across the country. One exciting collaboration which has arisen from the links to the DeGroote Pain Clinic at Hamilton Health Sciences is the recent announcement of a national Centre of Excellence for Veterans with Chronic Pain. This will be based at McMaster and closely linked with the IPRC, along with the DeGroote Pain Clinic, the Centre for Medicinal Cannabis Research and the Chronic Pain Network.

Our faculty members are supported by their home base departments which allows us to direct the Institute's resources towards infrastructure and training. Fully one-third of our budget is allocated to fellowships and graduate awards. In this way, we hope to support the future of pain research in Canada.

Thank you for your interest and support. We look forward to the future.

A handwritten signature in blue ink, appearing to read 'Norm Buckley'.

**Norm Buckley**, BA (Psych), MD, FRCPC  
Scientific Director  
Michael G. DeGroote Institute for Pain Research and Care  
McMaster University

# Institute for Pain Research & Care Fast Facts



Multidisciplinary research team made up of **21** research members from **9** health disciplines



**\$701,038** spent this year on research awards and projects



**325** publications by members last year



**10** research awards and projects funded every year



**9** full-time and part-time Institute staff members overseeing all operations and activities

## Milestones

**2004** The Institute for Pain Research and Care is founded, funded by a \$15 million endowment through the generosity of Michael G. DeGroote, and begins its work to understand the underlying mechanisms of chronic pain.

2004

**2014** The Institute for Pain Research and Care establishes Pain Postdoctoral Fellowships, Graduate Studentships and Seed Project Awards.

2014

**2016** The Institute for Pain Research and Care becomes the host institution and home of the coordinating centre for the Chronic Pain Network - one of five national networks addressing chronic disease funded through the Strategy for Patient Oriented Research.

2016

**2017** McMaster University and St. Joseph's Healthcare Hamilton launch the Michael G. DeGroote Centre for Medicinal Cannabis Research, which becomes a partner to the Institute in funding the Medicinal Cannabis Research for a total of \$1 million.

2017

**JAN** The Institute for Pain Research and Care and MIRA establish a Catalyst Grant for the January 2019 awards competition to support research on pain within the aging population.

2019

**FEB** The Institute for Pain Research and Care host its Inaugural Research Day, with focus on work-in-progress updates from Institute research projects and discussions about what's happening in pain research at McMaster.

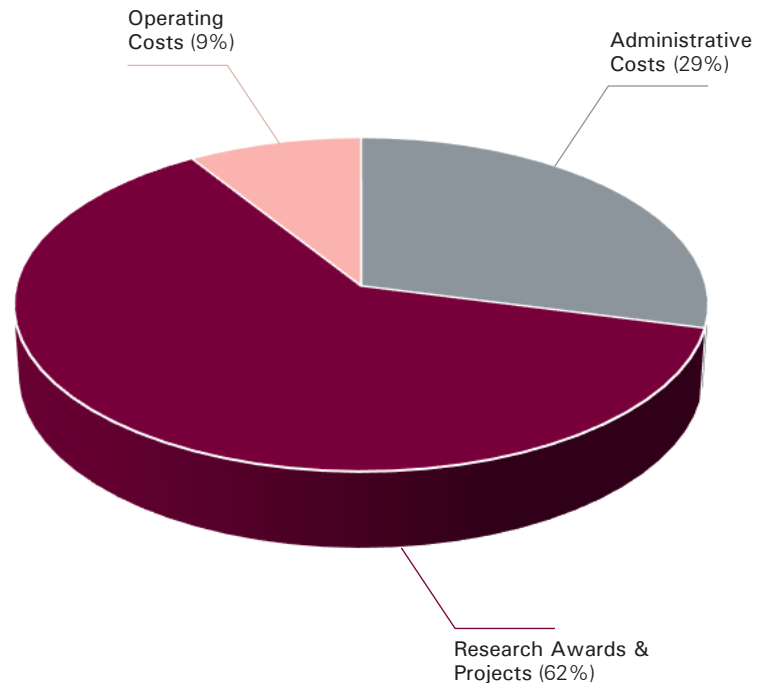
**APR** At the Canadian Pain Society's Annual Scientific Meeting, the Federal Minister of Health, the Honorable Ginette Petitpas-Taylor, announces the creation of the Canadian Pain Task Force and its External Advisory Panel, of which Dr. Norm Buckley is a member.

**JULY** Lawrence MacAulay, minister of Veterans Affairs, announces the establishment at McMaster University of the Chronic Pain Centre of Excellence for Canadian Veterans to develop innovative therapies to be shared with health professionals across the country.

# Institute for Pain Research & Care Budget 2018-2019

<b>Budget Categories</b>	<b>Percentage</b>	<b>Amount</b>
Administrative Costs	29%	\$334,924
Operating Costs	9%	\$105,937
Research Awards and Projects	62%	\$704,038
<b>TOTAL</b>	<b>100%</b>	<b>\$1,144,899</b>

Over 60% of our annual budget is spent directly on research awards (grad studentships and postdoctoral fellowships) and research projects (seed grants, IPRC/MIRA catalyst grant, other funded research projects). Annual administrative cost is 29% of the total budget, while the operating cost (including community engagement through the IPRC Symposium, Canadian Pain Care Forum meetings, Institute for Pain Research and Care Research Day) made up of 9% of the annual expenses.





# Institute for Pain Research & Care Graduate Studentships

Chad Brown, MSc  
PhD Candidate

**Project Title:** A Human Neuronal Model of Pain to Identify Novel Drug Therapies

**Supervisor:** Dr. Karun Singh

## Brief Overview and Progress to Date

This project seeks to tackle that how patients with Autism-spectrum disorder (ASD), more specifically genetic origins of ASD perceive and transduce pain signals. There are three main aims: investigate the effects of Cannabidiol (CBD) and Tetrahydrocannabinol (THC) on human iPSC-derived neurons; generate SCN9A mutant sensory neurons derived from human isogenic iPSC lines; and perform drug-screening of cannabinoid derivatives on SCN9A mutant sensory neurons to rescue cellular pain phenotypes.

We plan to investigate the family of voltage-gated sodium channels that are necessary and crucial for excitation within neurons and nerves within both the central nervous system and peripheral nervous system. The two genes of interest that encode the channels are SCN2A and SCN9A. Patients with SCN2A mutations can have clinical phenotypes ranging from epileptic encephalopathy to core ASD characteristics, while patients with SCN9A mutations express core ASD phenotypes with some also exhibiting erythromelalgia, paroxysmal extreme pain disorder or channelopathy-associated congenital indifference to pain.

Carley Ouellette, RN, BSc  
MSc Candidate

**Project Titles:** SMArTVIEW: In-Study Process of Monitoring Evaluation; and The SMArTVIEW Nurse: A Novel Nursing Approach to Pain Assessment and Postoperative Management Through Virtual Hospital-to-Home Recovery Support

**Supervisor:** Dr. Michael McGillion

## Brief Overview and Progress to Date

Postoperative pain is a leading driver of hospital readmission following surgery and is associated with poor sleep hygiene and fatigue anxiety and depressive disorders, poor perceived self-efficacy as well as poor self-rated health. In addition, unrelieved postoperative pain is associated with a number of complications. While effective pain assessment and management are key to optimal recovery, little is done to address unrelieved acute pain as a leading driver of readmission. To address this postoperative complication, among many other complications such as infection, fluid volume overload, and arrhythmia, our team set out to improve postoperative monitoring models both in hospital and at home for 30 days post discharge using digital health solutions.

SMArTVIEW is a 3-component intervention which combines A) remote automated radio-frequency enabled in-hospital monitoring, B) virtual, hospital-to-home nurse-guided recovery support, and C) self-management training. These components are supported by the Philips IntelliVue Guardian (IGS) remote automated monitoring system in hospital (component A), the Philips' electronic Transition to Ambulatory Care (eTrAC) system (component B), and SMArTVIEW Restore & Recover program, hosted on QoC Health's tablet-based patient engagement platform (component C), respectively. A sub-speciality team of nurses, known as SMArTVIEW Nurses, deliver the eTrAC intervention.

# Institute for Pain Research & Care Fellowships

Katja Linher-Melville, PhD  
Postdoctoral Fellow

**Project Title:** Evaluating the Efficacy of Cannabidiol to Manage Surgically Induced Neuropathic Pain in a Preclinical Rat Model: Do T-cells Play a Sexually Dimorphic Role?

**Supervisor:** Dr. Gurmit Singh

## Brief Overview and Progress to Date

After thymi and spleens, as well as DRGs from lumbar (L) 4 of immunocompetent male and female sciatic nerve cuff-implanted Sprague-Dawley rats orally gavaged with vehicle (medium-chain fatty acids) or CBD oil for 14 days beginning on the day of surgery, were isolated at experimental endpoint and cryopreserved. Thymic and splenic changes in the expression of a panel of experimentally validated markers associated with Th1, and Th2 cells were assessed at the mRNA level using quantitative (q)PCR, and compared to data collected from naïve age-matched male and female rats that were equally handled by research staff. Marker profiles were correlated with changes in nociceptive behaviour and changes in neural firing patterns. This work is currently in manuscript format, awaiting inclusion of the DRG data and will be submitted by the end of November 2019 to a suitable journal for publication.

The expression of markers associated with Th1 and Th2 cells in DRGs are currently being assessed by qPCR. This step required significant optimization, as the amount of total RNA extracted from a single DRG is very small resulting in the need for a second animal experiment. Three DRGs were pooled per animal for RNA extraction. In addition, contralateral DRGs were also collected for within-animal comparison. Importantly, three of these particular DRGs represent innervation from the sciatic nerve. This approach produced significantly enhanced yields of total RNA using an extraction protocol successfully set up in the lab, allowing for robust cDNA synthesis and qPCR analysis.

Cheryl Chow, MSc, PhD  
Postdoctoral Fellow

**Project Title:** Predictors and Trajectories of Pediatric Postsurgical Pain  
**Supervisor:** Dr. Louis Schmidt and Dr. Norm Buckley

## Brief Overview and Progress to Date

In support of the larger project of the study, a systematic review that examined association of temperament with preoperative anxiety in pediatric patients undergoing surgery has been published (Chow et al., 2019, JAMA Open Network). Moreover, another systematic review to identify research gaps in the existing literature and to examine risk factors (i.e., preoperative, intraoperative and postoperative factors) in predicting pediatric acute and persistent postsurgical pain is currently underway. To date, 7,303 titles and abstracts have been screened through six databases, identifying 98 articles for full-text screening. A total of 31 studies were deemed eligible for the review. Data extraction from all 31 studies has been completed and are now assessing the quality of these studies. A meta-analysis on eligible studies will also be conducted.

In order to generate pilot data to inform the project of the power and sample size required for the larger study, the project will be using data from 70 pediatric patients that were previously recruited for our pediatric anxiety study. Over the past few months, four undergraduate students have provided support to develop a computer program to process the collected EEG data and have extracted postoperative pain data from medical charts on all 70 pediatric patients. The next step will be to conduct preliminary analyses to examine the associations between brain activity, temperament and postsurgical pain.

In the next 7 months, the project goals include: i) completing the systematic review for publication, ii) securing funding (i.e., HAHSO AFP and/or CIHR) for the project, iii) conducting a pilot and feasibility study, and iv) to begin enrolling and recruiting pediatric patients for the study.

# Institute for Pain Research & Care Seed Grants

An Investigation into the Effectiveness of a New Transitional Pain Service (TPS) on Opioid Cessation After a Broad Range of Surgeries Done at Hamilton Health Sciences (HHS) and its Affiliated Hospitals

**Primary Investigator:** James Paul, MD, MSc, PhD

## Brief Overview and Progress to Date

The aim of this project is to examine the effectiveness of the TPS in getting patients off opioid analgesia at 12 months post-surgery compared to patients with usual pain care who are not referred to the HHS TPS. This project will also look at the effectiveness of the TPS in getting patients off opioid analgesia at 3 months post-surgery (Time point 3) compared to patients in a control group with usual pain care in a nearby surgical centre, as well as what are the number, percentage and characteristics of patients referred to the TPS at HHS and what factors are predictive of patients that won't be weaned off opioid analgesics at 12 months after surgery.

This study will be nested within the prospective cohort study that was also submitted, titled 'An investigation into the incidence of chronic post-surgical pain (CPSP) after a broad range of surgeries done at Hamilton Health Sciences (HHS) and its affiliated hospitals.' Cases and controls will be selected from patients within this established cohort study. The intent will be to use the TPS database to collect information about patients who will undergo a wide range of surgeries and then use the prospective data collected to help determine the effectiveness of the TPS in weaning patients off opioids post-surgery compared to patients with usual post-surgical pain care at HHS.

The project is currently undergoing HIREB ethics approval.

Feasibility of a Definitive Trial to Evaluate the Effect of Cannabinoid Oil, Versus Placebo, on PPSP and Functional Outcomes in Patients Undergoing Total Knee Arthroplasty

**Primary Investigator:** Jason Busse, DC, PhD

## Brief Overview and Progress to Date

The aim of this pilot trial is to assess the feasibility of a definitive trial to determine the effect of medicinal cannabis, versus placebo, on the proportion of patients experiencing PPSP following total knee arthroplasty (TKA).

Each year, up to 20% of Canadians undergoing knee replacement develop persistent post-surgical pain. A complaint that is associated with depression, anxiety, unemployment and reduced quality of life. A number of studies have found that greater pain just before and after knee replacement surgery is associated with the development of chronic pain, suggesting that reducing peri-operative pain may help prevent persistent post-surgical pain.

Cannabidiol has begun to emerge as a potential therapy for pain reduction and we plan to assess the feasibility of a definitive trial to explore whether adding CBD vs. placebo to usual care before and after surgery can reduce the rate of persistent post-surgical pain after total knee replacement.

Protocol has been submitted to the Hamilton Integrated Research Ethics Board and received provisional approval (pending a license from Health Canada). A CIHR grant for \$123,000 to support the pilot trial was awarded. A research license is being acquired and the clinical trial application for Medicinal cannabis with Health Canada is being completed.

Analgesic Effects of Cannabinoids in an Animal Model of Post-Surgical Chronic Pain: An Examination of Mechanism(s) for Sex Differences

**Primary Investigator:** Gurmit Singh, PhD,

## Brief Overview and Progress to Date

Post-surgical pain is influenced by sexual dimorphisms in neurally mediated nociceptive responses as well as immune cell function. Cannabinoids may elicit central and peripheral analgesic responses through interactions with nociceptors, microglia, T cells and gonadal hormone-producing cells. While the effects of THC on acute pain have been well-documented, there is a paucity of research on the anti-nociceptive effects of other cannabinoids, with an unmet need to assess effects in chronic pain models. In particular, the evaluation of sex differences that may affect the efficacy of non-psychotropic neuroimmune-modulators such as CBD are lacking.

Administration of each cannabinoid was beneficial in males, although CBD and the 1:1 combination of THC:CBD elicited sustained anti-nociceptive effects on tactile allodynia that were maintained until the 9 week endpoint. This outcome was not observed in females. An analysis of markers associated with CD4+ lymphocytes highlighted significant sex differences between vehicle- and cannabinoid-treated groups of rats, with specific cytokines up- or down-regulated in response to cannabinoids 7 weeks after the administration period.

# Institute for Pain Research & Care Seed Grants

## SMARVIEW

**Primary Investigator:** Michael McGillion, BScN, PhD

### **Brief Overview and Progress to Date**

The aim of this project is to determine the effect of the SMARVIEW intervention compared to standard care on the 45-day risk of a composite of hospital readmission, urgent care center and emergency department visits (not requiring hospital admission), in patients, aged 65 years or older, who undergo cardiac or major vascular surgery.

SMARVIEW is a two-phase monitoring program that follows patients throughout their surgical recovery journey. Initial monitoring starts on the surgical ward with the application of Philips' IntelliVue Guardian continual vital signs monitoring devices. These devices are paired with ThoughtWire's third party paging notification system, alerting nurses to any subtle signs of deterioration for their patient. Upon discharge, patients go home with Philip's eTrAC monitoring system. These devices are linked to an in-hospital nurse (the SMARVIEW nurse) who will review the patients' measurements and conduct virtual video assessments of each patient for 30 days. Patients are also directed to complete the SMARVIEW Restore and Recover Self-Management Program during these 30 days—a 5 week interactive, tablet-based recovery education program we have built for this study.

Preliminary findings suggest a high degree of compliance with the RAM and virtual hospital-to-home intervention protocol, and while SMARVIEW nurses are guiding recovery across all domains of care, further clarification of focused areas of nursing recovery support was required for full trial deployment.

## Tibial Shaft Fractures/SPOC Questionnaire

**Primary Investigator:** Jason Busse, DC, PhD, Sheila Sprague, PhD and Brad Petrisor, MD, MSc

### **Brief Overview and Progress to Date**

Our pilot trial aims to explore the feasibility of a definitive trial to determine if cognitive behavioural therapy (CBT) versus usual care reduces the prevalence of moderate-to-severe persistent post-surgical pain (PPSP) and moderate to severe pain interference at 12 months, post-fracture in participants with extremity fractures treated with internal fixation.

A multi-centre, pilot, randomized controlled trial (RCT) to evaluate the feasibility of a definitive trial to explore the effect of cognitive behavioural therapy (CBT) in patients with operatively managed extremity fractures. The primary objective of this pilot RCT is to determine: 1) our ability to set up the CBT intervention at each participating site; 2) our ability to recruit patients across clinical sites; 3) site investigators' adherence to the study protocol; and 4) our ability to follow patients to one year.

Our pilot trial successfully enrolled and randomized 78 patients to receive CBT or usual care, and we are currently following them for 1-year, and using the results to revise the protocol for our definitive trial (which we anticipate will launch in January 2020). We will write up the pilot trial for publication once our follow-up is complete.

## FORESITE-VISION

**Primary Investigator:** Michael McGillion, BScN, PhD and Jason Busse, DC, PhD

### **Brief Overview and Progress to Date**

The specific objectives of FORESITE VISION are to examine the influence of cognitive factors, namely, pain-related beliefs and gender-based pain expectations, on the following outcomes up to 1 year following cardiac surgery: the development of CPSP, functional status, and patient-level cost of illness. An additional aim is to determine the impact of CPSP on quality adjusted life years (QALY) borne by cardiac surgery, as well as the incremental cost for one additional QALY gained for patients, by virtue of cardiac surgery, among those who develop CPSP compared to those who do not. To meet these goals, we proposed a prospective cohort study of 1,250 in-patients who would undergo cardiac surgery, recruited over a 3-year period.

As of October 2019, 1,410 patients have been recruited. Seed funding from the Michael G. DeGroot Institute for Pain Research and Care, supported instillation of FORESITE results on CardiacPain.Net - our multimedia knowledge dissemination centre, built in partnership with Elsevier, which engages end users in 158 countries on 5 continents. The dedicated FORESITE section has been constructed, and guest editor filming (introduction of the study on the website) took place at the Elsevier studio, in New York (Fall 2016).

A prospective cohort sub-study involving potential perioperative risk factors is underway, with 645 in-patients undergoing cardiac surgery over a 2-year period.

## Institute for Pain Research & Care Seed Grants

Topicals for Osteoarthritis Pain in Knee Surgery (TOPIKS): A Pilot Randomized Controlled Trial

**Primary Investigator:** Harsha Shanthanna, MD, MSc, PhD  
(c), FRCPC and Anthony Adili, MD, FRCSC

### Brief Overview and Progress to Date

Since the funding application, and after subsequent discussions and suggestions by reviewers, we have updated our protocol. The study is presently designed as a four-arm factorial design trial with the following 4 arms; 1) Topical CBD plus Placebo; 2) Topical NSAID plus Placebo; 3) Topical CBD plus Topical NSAID; and 4) Topical placebo plus placebo. We have also included an embedded in vivo bioavailability study and collaborated with Dr. Joseph Macri from the Hamilton Regional Laboratory Medicine Program.

A license with Health Canada has been applied for. Discussion is also underway with two companies which have the potential to provide topical CBD preparations under GMP requirements, which have been tested in phase 1 and 2 studies.

PAIN STOP: Preventing pAin with Nmda Antagonists-Steroids in Thoracoscopic LOectomy Procedures

**Primary Investigator:** Harsha Shanthanna, MD, MSc, PhD  
(c), FRCPC and PJ Devereaux, MD, PhD, FRCPC

### Brief Overview and Progress to Date

Our target recruitment of 24 patients at St Joseph's Hospital, Hamilton was achieved in February 2018.

As there was a significant procedural delay involving the ethics board at the Cleveland Clinic site, USA, the recruitment was initiated in April 2018. The study drug "memantine/placebo" which was procured and packaged for use in February 2017, had an expiry month of April 2018. Further, the only company (pharmascience) that manufactured both 5 mg and 10 mg tablets and had a license for use in both Canada and the US, did not have any supply/stock of 5mg tables in April 2018.

In view of all these logistical challenges, the trial recruitment was stopped at the end of April 2018. In total there have been 28 patients (target was 48) recruited for the trial. We have completed all the patient follow ups, data cleaning and data verification for the statistical analysis.

The study came to a closure in April 2018. We are in the process of submitting the manuscript for publication in a peer reviewed journal.

## IPRC / CMCR Ongoing Research Fellowship

Vahid Ashoorion, MD, PhD

**Project Title:** Exploring Predictors Of Persistent Post-Surgical Pain Following Total Knee Arthroplasty

**Supervisor:** Dr. Jason Busse

### Brief Overview and Progress to Date

The focus of my post-doctoral work at IPRC and continuing at CMCR has been a systematic review of predictors for development of persistent post-surgical pain following total knee replacement (TKR) surgery.

The search has been updated by October 1, 2019, and it includes 25 studies for data extraction and meta-analysis. We found 164 predictors (4 supported by more than 10 studies, 14 supported by 4-8 studies, 17 supported by 2-3 studies, and 128 supported by one study).

The data for all predictors has been cleaned and meta-analysis conducted for all predictors endorsed by at least two studies. We explored four a priori hypotheses for subgroup analysis and reported the results if each subgroup contained two or more studies; we also explore subgroup effect with test of interaction.

We assessed the certainty of evidence by the GRADE approach to develop evidence profiles for each predictor and will optimize interpretation of significant predictors by co-presenting the absolute risk difference associated with development of persistent post-surgical pain.

# Institute for Pain Research & Care / McMaster Institute for Research on Aging Catalyst Grant

## A User-Centered Approach to Develop a Pre-Surgical Rehabilitation Program for Patients with Lumbar Spinal Stenosis

**Primary Investigator:** Luciana Macedo, BScPT, MSc, PhD

**Co-Investigator:** Lisa Carlesso

### **Brief Overview and Progress to Date**

The proposal had two primary aims: 1) investigate expectations, satisfaction and lived experiences of surgical patients with LSS using a qualitative approach, and; 2) Identify modifiable predictors of post-surgical outcomes in patients with LSS.

Lumbar Spinal Stenosis is associated with high levels of back and leg pain, decreased walking capacity and diminished health related quality of life. Surgery, an elective procedure is only offered to those with severe symptoms for whom conservative management has failed. However, there is evidence to suggest that although surgery may be more effective than conservative management in reducing associated disability, full recovery is not expected. Unfortunately, significant persistent pain, functional limitations, diminished HRQoL and narcotic use can affect up to one third of patient's post-surgery. Evidence from other orthopedic procedures (e.g. total knee replacement) suggest that a pre surgical rehabilitation (prehab) program may improve post-surgical outcomes such as pain, function and health related quality of life. Thus, our goal is to develop a prehab program for patients with lumbar spinal stenosis. The proposed project will be foundational for the identification of evidence-based and patient oriented components to be included into our program.

This is a mixed method study including two main components:

1. A descriptive case study design using qualitative interviews with patients about to undergo LSS surgery (25) and patients 1-year post surgery (25) to identify expectations, satisfaction and lived experiences.
2. A historical cohort study data from the Canadian Spine Outcomes Research Network (CSORN registry) to investigate predictors of outcomes 12 months post surgery with a focus on modifiable predictors. The CSORN database currently includes ~3000 patients with LSS. The novelty of this study is that we will use a multivariate Partial Least Square model in our analysis. This approach is superior to traditional linear regression as it results in more stable variable selection in addition to allowing for the inclusion of two outcomes at the same time. Due to the multiple response nature of the model, patient phenotypes can be identified by examining factors that uniquely relate to a combination of outcomes (i.e. high pain/high disability, poor pain/disability response, etc).

For Project One, we have received ethics approval for the project in Hamilton (September 2019) and we are on the last stages of ethics approval at UHN in Toronto. We have also started recruitment and have 1 patient included in the study. Recruitment is slower than expected, but we are in the process of reaching out to spine surgeons to continue with the development more effective recruitment strategies.

For Project Two, we have received ethics approval and this project is well under way. We have access to the data and have cleaned it and developed our analysis algorithms. We are now on the early stages of data analysis but will soon have our results.

# Institute for Pain Research & Care Supported Projects

## Management of Acute Musculoskeletal Pain: Two reviews from the Michael G. DeGroot National Pain Centre

**Primary Investigator:** Jason Busse, DC, PhD

### Brief Overview and Progress to Date

The Michael G. DeGroot National Pain Centre is assisting the American College of Physicians with two systematic reviews to inform a new guideline on the management of acute, non-low-back, musculoskeletal pain. Dr. Jason Busse, Associate Professor in the Department of Anesthesia, McMaster University, is leading these important reviews.

The first review examined the comparative effectiveness of drug (e.g. aspirin, opioids, muscle relaxants) and non-drug (e.g. education, advice, ice) treatments, tested in randomized controlled trials, that clinicians might consider offering patients for outpatient pain management. It found 181 studies that proved eligible include 30,360 participants and evaluated 45 therapies. Considering both magnitude of benefits and harms and certainty of evidence, topical non-steroidal anti-inflammatory agents (NSAIDs) proved to have the greatest net benefit followed by oral NSAIDs, and acetaminophen with or without diclofenac. Effects of these agents on pain were modest. Compared to placebo, tramadol provided no pain relief, and increased risk of gastrointestinal and/or neurologic harms (moderate quality evidence).

The second review included 9 studies with 12,231,617 participants. The overall prevalence of prolonged opioid use for low risk populations was 5%. Moderate certainty evidence showed increased odds of persistent opioid use with prescribing >7 days of opioids (absolute risk increase, greater co-morbidity, and older age). Low-certainty evidence suggested an association with past or current substance use disorder, positive smoking status, and co-morbid anxiety.

Avoiding prescribing opioids for acute musculoskeletal pain to patients with past or current substance use disorder and, when prescribed, restricting duration to  $\leq 7$  days are potentially high-yield targets to reduce rates of persistent opioid use.

## Medicinal Cannabis Research

**Primary Investigator:** Jason Busse, DC, PhD

### Brief Overview and Progress to Date

The aim of this initiative is to support research regarding the role of cannabis in the management of chronic pain. Multiple projects have been initiated or completed, with select initiatives listed below.

- Completed an analysis of the National Cannabis Survey (NCS) data, collected just prior to legalization of cannabis for non-medical use
- Currently pursuing analyses of both the post-legalization NCS data, and data from the Canadian Community Health Survey data to further inform patterns of cannabis use
- Completing a systematic review of cannabis for chronic pain
- Completing a review of cannabis as a substitution agent for opioids among chronic pain patients
- Completing a systematic review of cannabis for sleep
- Completing a qualitative study of chronic pain patients' experiences with therapeutic cannabis
- Completing a qualitative study of pain physicians' attitudes and beliefs towards medicinal cannabis
- Completed a cohort study of emerging adults and cannabis use
- Preparing to initiate pilot trials of cannabis for: (1) sleep disorder, (2) patients undergoing dialysis that experience uremic pruritus, (3) total knee replacement to prevent development of persistent pain

# Institute for Pain Research & Care Supported Projects

## PainPLUS CPN

### **Brief Overview and Progress to Date**

PAIN+ CPN assists researchers in keeping up-to-date and applying the latest research in clinical practice. To save researchers time, articles are pre-assessed for quality by research staff and for clinical relevance and interest by practicing clinicians. A wide range of publications from multiple disciplines are surveyed.

PAIN+ CPN is a “one-stop” access to current best evidence from research on pain management, PAIN+ CPN offers:

- A searchable database of the best evidence from care literature.
- An email alerting system.
- Links to selected evidence-based resources.
- Patient-focused lay summaries of evidence-based research

This service is customized for pain specialists through recruiting clinical raters for articles, including pain specialist physicians, nurses, occupational therapists, physiotherapists, and clinical psychologists. Criteria for critical appraisal of articles are explicit and posted at: [http://hiru.mcmaster.ca/hiru/HIRU\\_McMaster\\_PLUS\\_projects.aspx](http://hiru.mcmaster.ca/hiru/HIRU_McMaster_PLUS_projects.aspx). Rating scales are available at [http://hiru.mcmaster.ca/more/physicians/sample\\_rating\\_form.htm](http://hiru.mcmaster.ca/more/physicians/sample_rating_form.htm). The fidelity and effectiveness of this service for professional groups has been reported in several publications. This project is integrated into the PainHQ website.

PAIN+ CPN has recently launched patient-focused lay summaries of select research from the PAIN+ database. Articles selected for lay summaries have direct relevance to the CPN strategic priorities and to patient experiencing chronic pain. Users of PAIN+ CPN are encouraged to rate potential candidates for relevance using the Jury Rating feature. There are currently 34 Evidence Summaries on the PAIN+ CPN site.

PAIN+ CPN has 1084 registered users as of September 2019.

## DeGroote PainHQ

### **Brief Overview and Progress to Date**

In September of 2015, McMaster University announced the launch of DeGroote PainHQ, an online resource for individuals living with neuropathic pain. PainHQ provides access to a range of evidence-based resources, curated by the experts, rated by the public and supporting over two million Canadians living with neuropathy.

The range of resources provided is, in part, what makes PainHQ unique. Personal stories, e-learning videos, webinars and expert blogs make up part of the site's diverse offerings. The goal is to educate on neuropathic pain and to help make the condition more accessible to the general public. Building on McMaster's strengths in evidence-based medicine, health education and e-learning, PainHQ is an innovative and sustainable resource for patient-centred care.

In 2018/2019:

- The PainHQ main site had 5,471 new users in the last year, which represents 92.8% of the page's audience.
- Analytics indicate that users within the 25-34 age bracket continue to be the most active on the site, making up 26.99% of total web traffic, followed by 45-54 (18.83%). This is a change over last year which saw 35-44 age bracket ranked second. Those ages 65+ make up only 11.69% of users.
- Breakdown of users by gender remains the same as last year with women accounting for 59.14% of PainHQ users.
- Most traffic (69.78%) is driven to PainHQ via organic searches, with 20.15% from direct referrals.
- The PainHQ Twitter account now has approximately 1,420 followers and the Facebook account has 554 followers.



# Inaugural Institute for Pain Research & Care Research Day



Luciana Macedo, Assistant Professor at the School of Rehabilitation Sciences, discussed improving post-surgical outcomes in lumbar spinal stenosis at the Institute for Pain Research and Care's Inaugural Research Day.

On Feb 14th, 2019, the Michael G. DeGroot Institute for Pain Research and Care held its inaugural Research Day in the Farncombe Atrium at McMaster University. Participants included our institute research members, postdoc fellows and grad students.

The first half of the conference included work in progress updates of IPRC funded projects. Dr. Harsha Shanthanna talked about "NMDA Antagonists and Steroids for the Prevention of Persisting Post-Surgical Pain after Thoracoscopic Surgeries." Post-doc Research Fellow Vahid Ashoorion presented on "The effect of cannabidiol (CBD) vs. Placebo on persistent post-surgical pain following total knee arthroplasty: A multicenter, randomized pilot trial." Dr. Katja Linher-Melville, research scientist, reviewed "The connection between T-cells, chronic pain, and sex differences in analgesia." Dr. Jason Busse gave an update

on the "Characteristics of Canadian likely to try or increase cannabis use following legalization for recreation. A cross-sectional study."

After the break, we learned more about what's happening in pain at McMaster with presentations from Dr. James Khan (Persistent incisional pain after noncardiac surgery: Update on the VISION Pain Analysis), Dr. Gurmit Singh (The endocannabinoid system as an emerging target of pharmacotherapy) and Dr. Luciana Macedo (Improving post-surgical outcome in lumbar spinal stenosis).

# The Chronic Pain Network



Nader Ghasemlou discusses setting up his first human study of circadian pain variability at the Canadian Consensus Conference in Biomarkers in Pain Research, held at McMaster University in February 2019.

The Chronic Pain Network (CPN), funded through the Strategy for Patient Oriented Research (SPOR) and matching funds from Network partners, is one of five addressing chronic disease. Reporting for the award began January 2016 and will conclude March 2021.

Recent activities include the third annual Chronic Pain Network meeting, which took place on April 2, 2019 in Toronto and a strategic planning session, also held in Toronto, on September 25, 2018.

A joint effort between the Chronic Pain Network and the Institute for Pain Research and Care was the Canadian Consensus Conference in Biomarkers in Pain Research. Held in February 2019 at McMaster University, the meeting brought together pain researchers from across the country and even saw attendees from the United States.

Overviews were given of biomarkers in Pain Research, the Canadian Longitudinal Study of Aging; the Clinical Research Laboratory and Biobank; the importance of understanding chronic pain through genomics and transcriptomics; challenges, surprises and opportunities when setting up the first human study of circadian pain variability; imaging, QST biomarkers and ethical considerations; methylation markers; and the challenges and directions in developing and commercializing biomarkers in Chronic Pain. The conference featured well-known names in the field of pain research, including Luda Diatchenko, Nader Ghasemlou, Karen Davis and Laura Stone.

The Chronic Pain Network currently has 20 active patient perspective partners and caregiver representatives across Canada, including representatives from Indigenous communities. Patient perspective partners are engaged in the Network committees and contribute to the research priorities.

## Canadian Pain Care Forum

Approximately a decade ago, the US Pain Care Forum held its inaugural meeting to share information and coordinate responses to federal and state initiatives. Starting with handful of patient, medical and industry representatives, this group has grown to encompass 74 national and regional organizations that meet monthly and often attract key guest leaders/speakers from various agencies of the U.S. administration.

With the election of a new federal government in October 2015, there were early indications of a collaborative tone and direction to engaging with Stakeholders. It was felt that the timing was right to establish the Canadian Pain Care Forum in 2016. Many organizations in Canada are devoted in some capacity, directly or in-directly, to the relief of palliative, acute and/or chronic pain or policy efforts in this area. These organizations face similar challenges such as: putting “pain” on the public policy (national, provincial or local) radar to effect policy discussion(s) and positive policy/legislative/regulatory change; educating policy makers and the general public on the pervasiveness of “pain” in Canada and its inherent personal, healthcare and societal costs (estimated at \$60B annually); and balancing discussion (policy, media and societal) on major public health issues such as the crisis of prescription drug abuse, misuse and diversion in the context of the continuing need of access to the responsible treatment of pain across a breadth of diseases and health conditions.

These organizations include non-profit patient/consumer education and advocacy organizations, healthcare professional(s) associations, policy organizations, medical services organizations, academic health-science centres, law enforcement, addiction and treatment, and the pharmaceutical and medical products businesses.

Participation in the CPCF is open to all organizations who have a demonstrated interest in and desire to improve national and/or provincial pain care public policy –



Andrea Furlan discusses demonopolizing knowledge from pain experts to clinicians practicing in underserved, rural and remote areas using ECHO

respectful debate/differing positions welcome. The CPCF is committed to improving the understanding and knowledge of member organizations and to promote coordinated actions on common interest public policy issues.

Recent presenters at the CPCF include Katie Gasparelli, Senior leadership team of Six Nations Health Services; Fiona Campbell and Maria Hudspith, co-chairs of the Canadian Pain Task Force; Jason Busse, Associate Professor and co-director of the Institute for Medicinal Cannabis Research at McMaster University; and Andrea Furlan, associate professor in the Department of Medicine at the University of Toronto.

## Developing a National Pain Strategy for Canada

Building on the findings of a Deliberative Dialogue on developing a national pain strategy held by the McMaster Health Forum in 2017, members present at the April 2018 Canadian Pain Care Forum were asked to review the Proposal for a National Pain Strategy document, taking it back to their organization executives for discussion and returning with changes or indications of support.

Our target was to have a document that will outline a bold but achievable plan to improve the prevention and treatment of chronic pain in Canada and, in so doing, help to address the opioid crisis. We wanted a National Pain Strategy document that is ready to go on to Health Minister's agendas.

In June 2018, Owen Williamson, President of the Pain Medicine Physicians of BC Society, and Norm Buckley, Director of the National Pain Centre at McMaster University, met in Ottawa with Jean-Francois Leroux, then-Senior Policy Advisor / Opioid Response Team Health Canada. They presented our proposal and an "ask" - funding to establish and support a Canadian Pain Task Force to be led by Health Canada and facilitate discussions with all the other relevant federal government ministries.

In April 2019, the Federal Minister of Health, the Honourable Ginette Petitpas-Taylor, announced the formation of a Chronic Pain Task Force at the Canadian Pain Society 2019 Annual Scientific Meeting.

The eight-member Task Force includes advocates with lived chronic pain experience, as well as researchers and health providers who have experience preventing and managing pain.

In addition to the Task Force itself, an External Advisory Panel was formed to provide advice and information on certain elements of the Task Force's mandate. Four members of the Task Force and four members of the Advisory Panel also have ties to the Canadian Pain Care Forum and its continued work towards a National Pain Strategy. The Michael G. DeGroote Institute for Pain Research and Care's own scientific director, Dr. Norm Buckley, was asked and has accepted a position on the Panel.



The Honourable Ginette Petitpas-Taylor announcing the Canadian Pain Task Force at the Canadian Pain Society 2019 Annual Scientific Meeting

The Canadian Pain Task Force released its first report to the public in June 2019.

**Funding:** CPCF members are voluntary, and attend at their own expense. Meeting expenses are underwritten by the Michael G DeGroote Institute for Pain Research and Care and the National Pain Centre, at McMaster University, through the generous gift which Mr. DeGroote has given to support pain research and care in Canada.

## Centre of Excellence for Canadian Veterans with Chronic Pain



**On the left:** (from left to right) McMaster Faculty of Health Sciences Vice President Paul O'Byrne, Hamilton Mayor Fred Eisenberger, MP and Minister of Seniors Filomena Tassi, Veterans Affairs Minister Lawrence MacAulay, retired Corporal John Brown and Centre of Excellence on Chronic Pain medical director Ramesh Zacharias. **On the right:** (from left to right) Michael G. DeGroote with McMaster Faculty of Health Sciences Vice President Paul O'Byrne

"The research conducted by the new Centre of Excellence on Chronic Pain will allow the delivery of the best chronic pain treatments and supports for Canada's veterans,"

- Lawrence MacAulay, Minister of Veterans Affairs

On July 29th, 2019, Lawrence MacAulay, minister of Veterans Affairs, announced the establishment of a new research centre at McMaster University to specifically address the issue.

The Centre of Excellence for Veterans with Chronic Pain will focus on research on chronic pain of veterans, setting standards of care and ensuring that information is shared across the country and will receive \$20.1 million for its first five years, with \$4 million per year subsequently.

"The research conducted by the new Centre of Excellence on Chronic Pain will allow the delivery of the best chronic pain treatments and supports for Canada's veterans," he said.

Canadian Armed Forces members, veterans and their families face unique challenges due to the nature of military service. The department's survey on life after service in 2016 found chronic pain contributed significantly to various challenges for veterans. Veterans experience higher levels of physical and mental health challenges compared to the general Canadian population, including higher rates

of chronic pain, post-traumatic stress disorder and suicide.

Retired corporal John Brown spoke at the announcement, and said: "The biggest thing I've learned is that pain doesn't control you, you can learn how to control the pain. The work being done at this centre will help my fellow veterans across the country access better treatment and help them do the same."

McMaster is well positioned to host the Centre of Excellence on Chronic Pain, as it has the Michael G. DeGroote Institute for Pain Research and Care and the Michael G. DeGroote National Pain Centre. It also leads the Chronic Pain Network established by the Canadian Institutes of Health Research which is a unique partnership between patients, clinicians, researchers and policy-makers dedicated to advancing the management of chronic pain in Canada.

Michael G. DeGroote, who attended the announcement, said he was pleased that his philanthropy (which launched the pain institute, centre and clinic) has become a focus for cutting edge developments in pain treatments.

# Team

## Directors

### Norm Buckley

Scientific Director, Michael G. DeGroote Institute for Pain Research and Care; Director, Michael G. DeGroote National Pain Centre; Professor, Department of Anesthesia, McMaster University

### Akbar Panju

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## Scientific Advisory Board Members

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### Gurmit Singh

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# Mission

The mission of the Michael G. DeGroot Institute for Pain Research and Care is to become a cutting edge institute in the area of chronic pain and a magnet for researchers and trainees in the field.

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