Annual Report ▪ 2021

The Michael G. DeGroote Institute for Pain Research & Care

Toward the conquest of pain

Michael G. DeGroote
INSTITUTE FOR PAIN RESEARCH AND CARE

McMaster University

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. DeGroote and his gift

In 2003, businessman Michael G. DeGroote 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. DeGroote, December 2003

McMaster's Faculty of Health Sciences followed a "people first" guideline in allocating the $105 million gift from Mr. DeGroote. 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. DeGroote 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 Scientific Advisory Board meeting for the Michael G DeGroote Institute for Pain Research and Care. This has been a productive year, and the report includes updates on our supported students and investigators as well an overview of our work to engage the research community on the topic of chronic pain. We are pleased 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 Chronic Pain Network, one of five networks addressing chronic disease funded through the Canadian Institutes of Health Research's Strategy for Patient Oriented Research, is now in its sixth and final year of initial funding. The Network has held strategic planning sessions to discuss its future and what legacy items it would like to see continue forward. In August CIHR announced a competition for the SPOR chronic disease networks to establish Knowledge Mobilization-Implementation Science focused networks extending and applying the knowledge generated during the inaugural Network activity. In addition, the Canadian Pain Task force submitted its national pain strategy Action plan in March 2021, with recommendations for the Chronic Pain Network.

Our partnership with the Centre for Medical Cannabis Research is continuing to support research protocols addressing the peri-operative use of cannabis products.

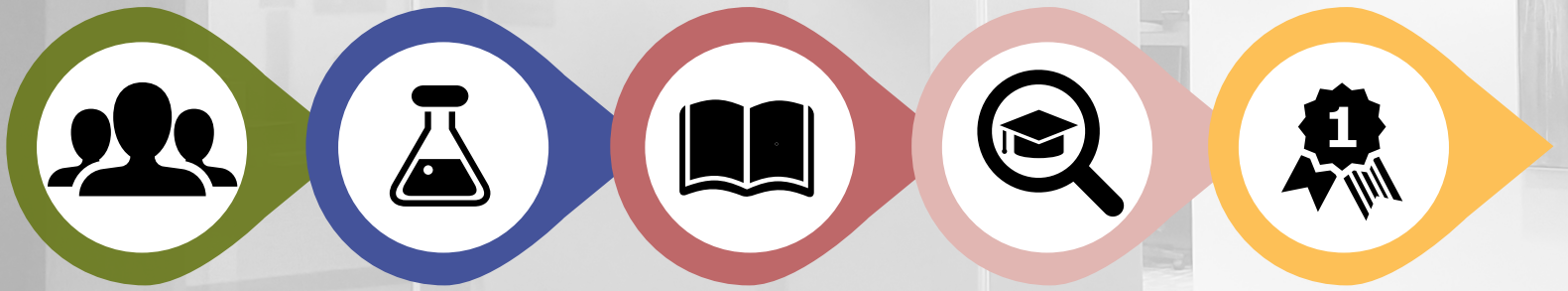
The Institute is linked through common membership with the clinical practice of pain care in Hamilton, both acute post-operative pain and chronic pain including interventional, pharmacologic and behavioural care, and is working to broaden its relationships across the country. The Chronic Pain Centre of Excellence for Canadian Veterans, announced last July and launched on April 1, 2020 as an independent 'not for profit entity,' has McMaster and Hamilton Health Sciences as its key stakeholders. It is rapidly establishing a national and international presence.

Our aim is to direct the Institute's resources towards infrastructure and training. Fully one-third of our research 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.

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



7
full-time and part-time Institute staff members overseeing all operations and activities

10
research awards and projects funded every year

65
publications on the topic of pain by our members last year

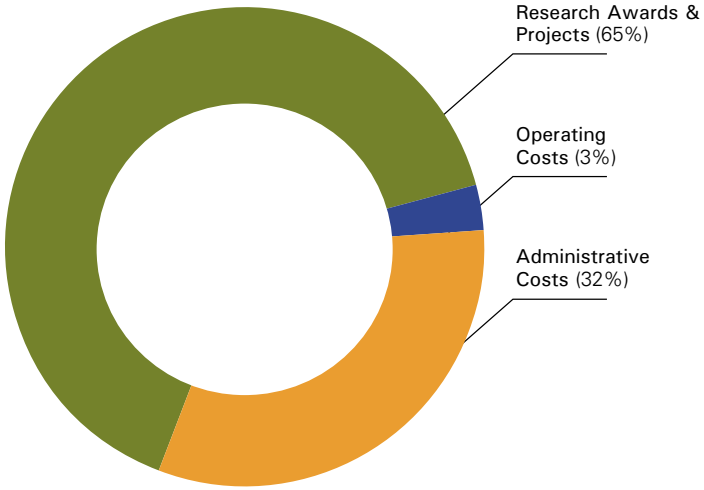
19
multidisciplinary research team members from nine health disciplines

$639,257
spent this year on research awards and projects

Institute for Pain Research & Care Budget 2020-2021

Budget Categories	Percentage	Amount
Administrative Costs	32%	$317,608
Operating Costs	3%	$27,953
Research Awards and Projects	65%	$639,257
TOTAL	**100%**	**$984,818**

Sixty-five percent of our annual budget is spent directly on research awards (grad studentships and postdoctoral fellowships) and research projects (seed grants, IPRC/MIRA catalyst grant, and other funded research projects). Annual administrative cost is 32% of the total budget, while operating costs (including community engagement through our IPRC Symposium, Canadian Pain Care Forum meetings, National Faculty meetings) made up of 3% of the annual expenses.



In addition to the research and operational activities within the Institute, our IPRC research and operational team administers 18 projects funded by various sponsors:

Sponsor	Amount	Number of projects
Canadian Institutes for Health Research	$4,058,241	4
Chronic Pain Centre of Excellence	$1,106,250	1
Canada Research Chair Program	$600,000	1
Michael G. DeGroote Institute for Pain Research & Care	$560,000	3
Centre for Medicinal Cannabis Research	$500,000	1
Other	$294,423	2
McMaster University	$185,658	6
TOTAL	**$7,304,572**	**18**

Institute for Pain Research & Care Graduate Studentships

Nora Bakaa, BSc, DC, MSc
PhD Candidate

Project Title: Development and Feasibility Testing of a Pre-Surgical Rehabilitation (Prehab) Program for Patients with Lumbar Spinal Stenosis
Supervisor: Dr. Luciana Macedo, PT, PhD

Brief Overview and Progress to Date

The proposed study will use an explanatory sequential mixed methods design, consisting of two phases. Phase one of this study will be a two-armed, pilot, randomized controlled trial of an eight-week virtual prehabilitation intervention. Participants will be randomized (1:1) to either the prehabilitation or usual care arms. The prehabilitation program will be delivered online using synchronous and asynchronous sessions delivered by an experienced clinician, with a booster session at six-weeks post-op. This will consist of exercises, as well as educational material. Participants in the control group will receive usual care as per surgeons' current practice style.

At this stage, we have finalized all study documents (i.e. consent forms, interview guide, timelines, standard operating procedures, etc.). We have also developed the intervention program consisting of educational videos, and an exercise intervention based on principals of graded activity. We have completed and submitted the ethics application for this study and have been given provisional approval. We expect full approval by mid-August 2021. The trial is in the process of being submitted for registration on clinicaltrial.gov. We have recruited various surgeons (Calgary, Edmonton, Toronto and Hamilton) to help with recruitment of participants and data collection. Recruitment and data collection for this study are expected to occur starting early-to-mid September 2021. Recruitment for this study is expected to take place over four to five months, and since we have a follow-up time of 12 months, data collection is expected to be completed January of 2022.

Carley Ouellette, RN, BSc
PhD Candidate

Project Titles: enVISION No Pain After Surgery
Supervisor: Dr. Michael McGillion, RN, PhD

Brief Overview and Progress to Date

Since the COVID-19 global pandemic, this research project and focus has shifted to examine virtual care and remote patient monitoring. Problem: Patients' physiologic status (i.e., vitals signs) following surgery is a promising yet understudied area of chronic post-surgical pain (CPSP) research. Due to technical and practical limitations, the available data have largely been generated in lab-based studies or in healthy subjects. The relationship between patients' physiologic status and the development of CPSP remains unknown. Dr. McGillion, will soon commence "VISION-2", a large-scale continuous biometric observational study of 20,000 patients following surgery. In VISION 2, we will apply a novel technology, the Vitaliti™ continuous vital signs monitor by Cloud DX, to patients who will wear the device for the first 30 days following their surgical procedure. Vitaliti™ is an unprecedented, wearable monitor that can measure continuously five-lead electrocardiogram, heart rate, respiration rate, temperature, SpO2, continuous non-invasive blood pressure, and pulse wave velocity. The objective of VISION-2 is to determine the pattern and frequency of physiological precursors, i.e., biometric 'signals' of major postoperative adverse events (e.g., major bleeding, infection) and build predictive models from these biometric signals through machine learning. As Dr. McGillion's trainee, my objective is to execute "enVISION no pain after surgery"— a sub-study of VISION-2 that will examine the relationship between biometric (vital signs) status and the development of CPSP in 1,000 patients.

Chad Brown, BSc, DC, MSc
PhD Candidate

Project Title: A Human Neuronal Model of Pain to Identify Novel Drug Therapies
Supervisor: Dr. Karun Singh, PhD

Brief Overview and Progress to Date

This project stemmed from pilot investigations of SCN2A, a high confidence Autism-associated risk gene. Patients with ASD are often found to be enriched for de novo mutations, with SCN2A representing one of the top three genes. However, since the homology between the voltage-gated sodium channels are similar other paralogs like SCN9A have been reported to be associated with ASD. Understudied are the comorbidities, pain represents one of the largest comorbidities with voltage-gated sodium channelopathy and ASD. Additionally, as Cannabidiol (CBD) and Tetrahydrocannabinol (THC) treatment are being used to manage pain we wanted to investigate the effects in an ASD-pain comorbidity manner. We have now characterized the neuronal function of two patient SCN2A de novo mutations and an SCN2A isogenic knockout using induced pluripotent stem cells (iPSC)-derived neurons. Characterizations were performed using patch-clamp and multielectrode array, where we were able to capture single neuron and network activity. Also, we now have captured biological pathways that are enriched using proteomics to infer targetable mechanisms which have not been investigated to date. Mitochondrial function represents one pathway identified in one patient mutation, we followed up this hit with a mitochondrial respiration assay and validated this enriched pathway. This work will be submitted in September 2021 with a target journal of Cell Reports or Stem Cell Reports. We have acknowledged the IPRC in the manuscript. Our next goal is to investigate THC and CBD effects in one of the patient lines, as one patient presents with ASD and seizures.

Related Publication

Brown, O. C, Uy, J, & Singh, K. K. (2020). A mini-review: Bridging the gap between autism spectrum disorder and pain comorbidities. Canadian Journal of Pain, 4(4), 37-44. DOI: 10.1080/24740527.2020.1775486

Related Working Manuscript

Disruption of the Autism-associated gene SCN2A in patient iPSC-glutamatergic neurons alters synaptic development and neuronal signaling. Chad O. Brown, Jarryll Uy, Nadeem Murtaza, Elyse Rosa, Alexandria Alfonso, Sansi Xing, Biren M. Dave, Savannah Kilpatrick, Annie Cheng, Sean H. White, Stephen W. Scherer, Yu Lu and Karun K. Singh

"This award has allowed me to expand my project from just a patient mutation characterization investigation of neuronal function to an interdisciplinary project that uses neuroscience and biochemistry. This award will directly contribute to an improved mechanistic understanding of voltage-gated sodium channels in ASD and its comorbidities."

- Chad Brown

Institute for Pain Research & Care Fellowships

Xiaoqin Wang, MD
Postdoctoral Fellow

Project Title: Interventional Treatments For Chronic, Local or Radicular, Non-Cancer, Spinal Pain: A Protocol for a Systematic Review and Network Meta-Analysis of Randomised Trials
Supervisor: Dr. Jason Busse, DC, PhD

Brief Overview and Progress to Date

Interventional procedures (e.g., nerve blocks, epidural steroid injections, radiofrequency nerve ablation) are commonly and increasingly used for chronic back and neck pain; however, the benefits and harms of these procedures are uncertain. We propose to conduct a comprehensive systematic review and network meta-analysis of interventional procedures for local and referred chronic spine pain that addresses the limitations of previous reviews and supports a clinical practice guideline.

We have published our review protocol and plan to finish the systematic review in December 2021. A separate review is also underway to establish the long-term and infrequent harms associated with interventional procedures by exploring observational studies.

An international panel of clinical experts, methodologists, and patient partners have been assembled that will review the evidence syntheses to make clinical practice recommendations. The British Medical Journal has indicated interest in publishing this research. We anticipate our findings will impact policy in Canada, as the effectiveness of interventional procedures (or lack thereof) has become a priority topic for Health Canada.

Related Publications

Wang X, Martin G, Sadeghirad B, et al. Interventional treatments for chronic, axial or radicular, non-cancer, spinal pain: a protocol for a systematic review and network meta-analysis of randomised trials; BMJ Open 2021;11:e046025. doi: 10.1136/bmjopen-2020-046025

Cheryl Chow, MSc, PhD
Postdoctoral Fellow

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

Brief Overview and Progress to Date

Due to the pandemic, we had to put the project on hold since March 15th, 2020. Over the past 12 months, we have been working on entering data for the 31 patients that were recruited for the CIHR-funded RCT in examining the effects of a table-based intervention in reducing pediatric anxiety and pain. We also completed coding all the videos that we captured in the OR and will begin to extract postoperative pain and other relevant clinical data from medical charts on these recruited patients.

In terms of re-starting the RCT study, we have submitted a revised protocol for ethics approval to recruit and follow-up with patients over the phone and to collect data electronically.

In support of the larger project of the study, I have presented our published review that examined the role of anxiety and its related in pediatric postsurgical pain (Chow et al., 2020, Can J of Pain) at the Canadian Pain Society Annual Scientific Meeting in April 2021. Moreover, I am completing on the manuscript write-up on 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. We are aiming to submit it JAMA Pediatrics by September 2021.

In addition to working under the supervision of Dr. Buckley from the Department of Anesthesia and Dr. Schmidt from the Department of Psychology, Neuroscience and Behaviour, I have been able to establish national collaborations with experts across a wide range of clinical and research skills. This multi-national collaboration allows me to learn from experts with different research backgrounds and to gain more in-depth knowledge about pediatric pain. This allows me to establish the methodology by which this work could be extended to multiple sites through the infrastructure created in the CPN and the influence of both the CPN, and the CPAS.

Related Publication

Cheryl H. T. Chow, Louis A. Schmidt & D. Norman Buckley (2020) The role of anxiety and related states in pediatric postsurgical pain, Canadian Journal of Pain, 4:4, 26-36, DOI: 10.1080/24740527.2020.1847600

Institute for Pain Research & Care Seed Grants

A Temporal Evaluation of Cannabidiolic Acid-Methyl Ester Administration: Can Post-Surgically Induced Neuropathic Pain be Blunted by Early Intervention in a Preclinical Rat Model?

Primary Investigator: Gurmit Singh, PhD
Start Date: 2020

Brief Overview and Progress to Date

CBDA is a precursor to CBD. However, it is very unstable, so its stability is enhanced by synthetic addition of a methy ester (ME) group to produce CBDA-ME. It is orders of degree more potent and efficacious compared to CBD. The primary goal of our project is to evaluate whether anti-nociceptive responses elicited by CBDA-ME are enhanced by an early pre-surgical treatment regimen in both males and females. An important point to consider in using CBDA-ME to therapeutically manage neuropathic pain is the timeline of treatment initiation. Initiating treatment at an early stage post-nerve injury has been shown to limit the development of hyperalgesia in a rat model of peripheral neuropathic pain. Investigations into whether anti-nociception imparted by early (i.e. shortly after an insult that initiates persistent neuropathic pain, such as a surgery) cannabinoid administration is sustained weeks after treatment cessation are lacking. Nociceptors may initially be sensitized by inflammation that arises in response to nerve damage, and peripheral nerve fibers consequently develop patterns of ectopic neuronal discharge. Therefore, initiating cannabinoid treatment at an early stage post-insult to limit the development of chronic hypersensitivity may be a promising means to block the propagation of peripheral ectopic impulses into the CNS, curbing pain chronification. Importantly, CBDA inhibits aspects of the initial inflammatory process. It is possible that CBDA-ME, by modulating specific immune cell responses, could dampen inflammation or promote a more rapid resolution of this process in a sexually dimorphic manner.

Related Publications

An evaluation of the anti-hyperanalgesic effects of CBDA-ME in a preclinical model of peripheral neuropathic pain. British Journal of Pharmacology. (2020) 177:2712-2725

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

Primary Investigator: Gurmit Singh, PhD
Start Date: 2019

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.

Related Publications

Evaluation of the preclinical analgesic efficacy of naturally derived orally administered oil form of THC, CBD and their 1:1 combination. PLOS ONE (2020) 15 (6): e 0234176

Sex Differences in Neuro (auto) immunity and chronic Sciatic nerve pain. Biology of Sex Differences (2020) 11: 62

"This seed funding enabled us to describe sex differences in analgesia using cannabinoids and to consider chronic pain being potentially an autoimmune disease. This also enabled us to develop a full CIHR project grant application to be submitted in Fall 2021."

- Dr. Gurmit Singh

Institute for Pain Research & Care Seed Grants

Who is Susceptible to Developing CPSP? A High-Throughput Clinical Proteomics-Based Approach for the Prediction of Susceptibility

Primary Investigator: Fei Geng, PhD
Start Date: 2021

Brief Overview and Progress to Date

Michael G. DeGroote Institute for Pain Research and Care has funded this project in July 2021. We have recruited McMaster Engineering Research Experience Award recipient Alexandra Wu and Vikash Nanthakumar for this project. The progress in the last month is: (1) Our research assistant Alexandra Wu has completed the literature review on the biomarker discovery for pain diagnosis; (2) Vikash Nanthakumar started working on supervised classification development for proteomic profiling; (3) Alexandra Wu has given a talk on this pain research at the Faculty's Annual Summer Research Poster Showcase on August 11, 2021.

This grant has allowed our research group to explore a most exciting and challenging area which is the identification and validation of pain signatures. This research development will generate a research program that creates powerful synergies between engineering and pain study.

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

Primary Investigator: James Paul, MD, MSc, FRCPC
Start Date: 2019

Brief Overview and Progress to Date

At hospitals affiliated with Hamilton Health Sciences (HHS), we have since adopted the Transitional Pain Service model. The proposed retrospective chart review will collect data from the APS, TPS, and chronic pain clinic, elucidate risk factors associated with the development of CPSP and long-term opioid use, and evaluate the efficacy of our Transitional Pain Service in reducing the opioid burden in the Hamilton-Niagara Region.

Although many studies have looked at the incidence of and risk factors for developing CPSP very few have actually taken a comprehensive large-scale approach in assessing whether a TPS is more effective at getting patients off opioid analgesia, in comparison to patients in a control group with usual pain care. This study will provide additional evidence for a Transitional Pain Service as a standard of care for managing CPSP, decreasing opioid burden in the Hamilton-Niagara Region, and give insight into a pain clinician's increasing role in Ontario's opioid crisis.

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, PhD, FRCPC
Start Date: 2019

Brief Overview and Progress to Date

The study is designed as a four-arm factorial design trial with the following four arms on patients having knee arthroplasty; (1) Topical CBD plus Placebo; (2) Topical NSAID plus Placebo; (3) Topical CBD plus Topical NSAID; and (4) Topical placebo plus placebo. It is relevant to note that this study is part of a broader program of cannabis studies, including an oral cannabis trial, on patients having knee arthroplasty and being coordinated from the Arthroplasty Research group at St. Joe's Hospital, Hamilton. The regulatory hurdles associated with acquiring approval from Health Canada to launch clinical trials of medical cannabis have proven extremely difficult to meet. The summary of requirements to begin a cannabis trial include: Trial registration; Local ethics approval; Agreement with a licensed producer to provide good manufacturing practice (GMP) certified product; Health Canada approval; and Cannabis research license.

After meeting with more than a dozen cannabis producing companies, we were able to identify MediPharm, a company with GMP certification that is ready to collaborate with our team on both the oral and topical cannabis trials. As of June 2021, some of the requirements for preclinical data have been relaxed. We must submit 6+ months of safety data from recreational cannabis sales in Canada in lieu of a full program of preclinical data, which we were able to do for the oral product and have successfully receive a Health Canada No Objection Latter. For the topical products, this was not possible because they had not been on the market until August 2021. We are presently waiting for six months of safety data and will submit to Health Canada for an NOL after this period. Presently, this process is ongoing, and we are hopeful that Health Canada will provide a No Objection Letter for the oral cannabis trial. After we receive a Health Canada NOL, we will then proceed to the license application, ethics approval, and then trial recruitment.

Pilot Study of Association of BIOmarkers and Neuropathic Pain with Intercostobrachial Nerves Sparing in breast surgery to improve Persistent post-surgical pain - an International RandomizEd controlled trial (BIO-INSPIRE)

Primary Investigator: Harsha Shanthanna, MD, PhD, FRCPC
Start Date: 2021

Brief Overview and Progress to Date

The primary study, (INSPIRE trial) is being conducted at two Canadian sites (Hamilton and Toronto) and two Indian sites (Narayan Hrudayalaya (NH)-Bangalore, and JIPMER-Pondicherry). Out of the required 50 patients, 40 patients were enrolled with 39 being randomized. From the 39 patients, 29 patients have been effectively included within the BIOINSPIRE trial and provided both preoperative and postoperative blood samples. Four patients from the Toronto site (Mount Sinai Hospital) could not be included because they had challenges with manpower/ lab resources; one patient with human immunodeficiency virus was excluded from the NH site as part of their hospital policy and four patients from JIPMER could not provide their blood samples in time during the COVID pandemic. All the patients have completed their appropriate follow ups.

The INSPIRE study has been affected by the COVID pandemic with the recruitment being slower than expected. However, we are hopeful that we can recruit the remaining participants in the coming months and include all of them within the BIOINSPIRE trial.

Institute for Pain Research & Care Seed Grants

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

Primary Investigator: Jason Busse, DC, PhD
Start Date: 2017

Brief Overview and Progress to Date

Each year, approximately 67,000 Canadians undergo knee replacement surgery, and up to 20% develop persistent post-surgical pain. A complaint that is associated with depression, anxiety, unemployment and reduced quality of life. Moreover, chronic pain after surgery is often managed with opioid therapy, which typically provides only modest benefits and is associated with rare but serious adverse events, such as overdose and death. Several 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. We will randomize 40 patients to receive either CBD or placebo and follow them for six months to confirm our ability to recruit patients, adhere to protocol, and capture full outcome data for at least 90% of patients.

Our pilot trial of cannabidiol to prevent persistent pain after knee replacement surgery was delayed by red tape at Health Canada (as were all RCTs) for two years. After an aggressive campaign (e.g. https://www.thespec.com/opinion/contributors/2021/05/20/medical-cannabis-easy-access-for-patients-but-not-for-researchers.html) we were successful in affecting changes to trial regulations. We have now acquired our letter of no objection from Health Canada, submitted our clinical trials license application which came back with very minimal requests that we have made and re-submitted, and we have engaged with an industry partner (MediPharm) for all required trial product. We anticipate being able to begin our trial enrollment in 2021.

A Persistent Post-Surgical Pain Survey

Primary Investigator: Jason Busse, DC, PhD
Start Date: 2020

Brief Overview and Progress to Date

An influential survey of 5,130 patients attending 10 outpatient chronic pain clinics found that 23% attributed their complaints to a surgical procedure. According to Google Scholar, this survey has been cited over 350 times; however, there are limitations with this report. The sample was restricted to patients in North Britain, there are no details reported regarding the response rate, and the data was acquired between 1989 and 1992. These issues suggest that generalizability to the current Canadian context is uncertain. Our group plans to conduct a survey of patients attending 17 tertiary chronic pain clinics across Canada to establish perceptions regarding causal attributions for their chronic pain, as well as demographic information and management strategies they have pursued. Our findings will inform the proportion of chronic pain outpatients in Canada that attribute their condition to a surgical procedure and explore patterns of healthcare seeking.

COVID disrupted in-person visits for the past one and a half years, but in-person visits are now resuming. As such, we have begun to pilot our survey among patients. When finalized, we will translate into French and seek ethics approval to administer with our partner clinics.

Institute for Pain Research & Care / McMaster Institute for Research on Aging Catalyst Grants

A Feasibility Study to Assess the Added Value of Integrated Musculoskeletal BiofFeedback Device (IMBED) Combined with Neuromuscular Exercise and Education (GLA-Dtm) to Decrease Chronic Pain in Older Adults with Osteoarthritis

Primary Investigator: Pasqualina Santaguida, PhD, PT, Stuart Phillips, PhD, MSc, BSc and Qiyin Fang, BSc, MSc, PhD, LEL
Start Year: 2020

Brief Overview and Progress to Date

This project will evaluate the feasibility and added value of a new technology called Integrated Musculoskeletal BiofFeedback Device (IMBED). We are using the neuromuscular exercise and education program called Good Living with Arthritis in Denmark (GLA:D™) as the test case for evaluating the benefit of this technology. Our study officially started on April 2021, and we have been working on Phase One to develop a new integrated device that adapts and combines three well-established technologies: digital mapping of chronic pain app (i.e. phone and iPad type screens), biofeedback surface EMG (sEMG) and body motion sensors (accelerometers).

To date, we have worked on the following: (1) selection of the sEMG device as we had to assess several different commercially available models by arranging meetings and sharing of information with manufacturers; we have selected the best model for our purposes; (2) we have a working prototype of the app (for smartphone or tablet) for identifying pain location and intensity; the anatomical figures displayed are gender specific, and we are working on improving the three-dimensional aspect; (3) The coding to integrate all three devices has been completed.

What remains for completing Phase One is: (1) finalizing best display modes for participants and clinicians on phone or tablet; (2) development of a calibration protocol and best placement on lower extremity for consistent data signal; (3) additional input from our patient collaborator; (4) user testing using with potential participants and clinicians (n=10).

For Phase II, we have received ethics approval to conduct the GLAD program at the PACE centre. We have arranged an MOU for the PI to go into the physiotherapy clinic to complete screening assessments for participants. What remains for completing Phase One includes: (1) awaiting university approval to enroll participants; (2) amending REB for the use of the IMBED device while conducting GLAD; (3) piloting GLAD exercise with IMBED at PACE; (4) recruitment of participants.

Persistent Post-Surgical Pain, Postoperative Cognitive Dysfunction, and Resilience in Older People Undergoing Elective Knee Surgery: A Mixed Method Project to Explore Associations and Underlying Mechanisms

Primary Investigator: Maura Marcucci, MD, MSc
Start Date: 2021

Brief Overview and Progress to Date

The project is a mixed methods study exploring the association between chronic post-surgical pain and cognitive decline in patients 55 year or older who are undergoing total knee arthroplasty (TKA). The quantitative part is a cohort study, nested into a main study where patients are longitudinally followed after surgery and assessed upon their pain, and adds to the main study a longitudinal assessment of cognitive function and biomarkers evaluation. For the qualitative part, a sample of study participants will be interviewed either before or after surgery upon their expectations and lived experience with surgery. The quantitative part of the study obtained provisional approval from HiREB; we submitted the required changes/clarifications, and we are awaiting for the full approval to launch the study at the SJH and Juravinski hospital. In the meantime, we are working on finalizing the protocol for the qualitative part.

We are still at the planning phase of the project, about to start the recruitment of participants. So far, the project has been a great opportunity of collaboration with the different co-investigators involved who have given important input to the finalization of the study protocol bringing in their own expertise. This collaboration has included sharing supervision of students involved in different aspects of the project. The project will inform future research and has been intended as a starting point for an expanding collaboration among the involved investigators and trainees.

Institute for Pain Research & Care / McMaster Institute for Research on Aging Catalyst Grants

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

Primary Investigator: Luciana Macedo, PhD
Co-Investigator: Lisa Carlesso, PhD
Start Date: 2019

Brief Overview and Progress to Date

The two primary aims of this project were to (1) investigate expectations, satisfaction and lived experiences of surgical patients with lumbar spine (LSS) surgery using a qualitative approach, and; (2) Identify modifiable predictors of post-surgical outcomes in patients with LSS.

Data collection has been completed for Aim One of this project. We have conducted 40 interviews (18 pre-op and 22 post op). We have completed coding all interviews and grouped results into themes. Given the richness of data provided to date, we expected a report and at least four manuscripts arising from the interviews (two to be completed by the fall). Concerning Aim Two, we are on the last steps of data analysis. We have completed traditional statistical analysis and now we are in the process of preparing for the least square means analysis (as one of our investigators responsible for this was unavailable due to the pandemic). We have published the study protocol and are preparing a manuscript for publication.

Related Publication

Rowe E, Hassan E, Carlesso L, Wilson JA, Gross DP, Fisher C, Hall H, Manson N, Thomas K, McIntosh G, Drew B, Rampersaud R, Macedo LG. Predicting recovery after lumbar spinal stenosis surgery: a protocol for a historical cohort study using data from the Canadian Spine Outcomes Research Network (CSORN), Canadian Journal of Pain 2020: epub ahead of print; doi: 10.1080/24740527.2020.1734918

"As an early career research this grant was crucial to kick start my research program. As part of this grant, I was able to develop new collaborations within and beyond the university. This includes collaborations with spine surgeons, health care administrators, community organization such as the YMCA, physiotherapists, psychologists and beyond."

- Dr. Luciana Macedo

Institute for Pain Research & Care Supported Projects

FORESITE-VISION: 'Further Observation for Chronic Pain and Poor Functional Recovery Risk Factor Examination at Selected SITEs (FORESITE), A Study in Partnership with The Vascular Events In Surgery patIents cOhort evaluatioN – Cardiac Surgery (VISION Cardiac Surgery)

Primary Investigator: Michael McGillion, RN, PhD and Jason Busse, DC, PhD
Start Date: 2015

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 one year following cardiac surgery: the development of Chronic Post-Surgical Pain (CPSP), functional status, and patient-level cost of illness. With a view to comprehensive examination of the impact of CPSP on patients, an additional aim is to determine the impact of CPSP on quality adjusted life years (QALY) borne by cardiac surgery (a measure of disease burden, including the quality and quantity of life lived), 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 from the Hamilton Health Sciences over a three-year period.

1,410 patients have been recruited. Seed funding from the Michael G. DeGroote Institute for Pain Research and Care, supported the architecture to install FORESITE results on our multimedia knowledge dissemination centre, "Reducing Global Perioperative Risk", a multimedia resource centre we built in partnership with Elsevier. Linked to Elsevier's worldwide readership, this resource centre is designed for global-scale knowledge 'push' and uses opt-in email blasts for mass knowledge dissemination. We have thus far engaged over 27 thousand unique end users across 176 countries and five continents, who have viewed and downloaded the knowledge product tools of our group's work (e.g. clinical practice guidelines, multimedia education programs), 58,834 and 15,868 times, respectively, to date.

FORESITE Update: Enrollment: 1,410 enrolled and one year follow up is complete.

Completed: Recruitment closed at UCL Site (US), HGH, Kingston (Canada) and Prince of Wales Hospital (China) and follow up data collection is completed at these sites. All data from these sites have been cleaned; 46,000 database queries have been addressed. Data analyses are presently underway.

There was also a sub study stemming from this project, titled Examination of Nurse-Modifiable Risk Factors for Chronic Post-Surgical Pain following Cardiac Surgery, led by S. Henry, (PhD Thesis Student), Michael McGillion, BScN, PhD which is now completed. The purpose of the study was to explore the association between preoperative moderate to severe anxiety and depressive symptoms; moderate to severe acute postoperative pain; and cumulative opioid dose consumption with the development of CPSP at six months and 12 months after cardiac surgery using a prospective observational cohort study design. This sub study is now complete.

Institute for Pain Research & Care Supported Projects

SMArTVIEW - TecHnology-Enabled remote monitoring and Self-MAnagemenT—VIsion for patient EmpoWerment following Cardiac and VasculaR surgery. (THE SMArTVIEW, CoVeRed)

Primary Investigator: Michael McGillion, RN, PhD
Start Date: 2015

Brief Overview and Progress to Date

The aim of this project is to determine the effect of the SMArTVIEW 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.

Approach: SMArTVIEW is a Two-Phase Study, conducted in Canada (Hamilton Health Sciences [HGH]) and the United Kingdom (Liverpool Heart and Chest Hospital [LHCH]). Phase One includes usability testing and Phase Two includes a randomized controlled trial (RCT) (n= 800), as well as economic and qualitative substudies of the impact of SMArTVIEW on cost of recovery and patient recovery experience, respectively.

Progress to date: For Phase One, usability Testing (n= 26 nurses; 11 patients), was completed last year in both Canada and the UK. Video and audio data were scored and transcribed for analyses. For Phase Two, user testing results shaped optimal clinical workflow and training requirements and a manuscript has been resubmitted to the Journal of Medical Internet Research following favourable reviews and minor comments. The RCT protocol was published in 2017 as in the Journal of Medical Internet Research. A state of the science paper on remote monitoring, including the SMArTVIEW approach was published in the Canadian Journal of Cardiology in 2018. The SMArTVIEW trial ended active recruitment in April of 2021 due to COVID-19 pandemic re-allocation of nursing staff. Total recruitment of patients was 573 of a targeted 800, with 496 and 76 participants from the Hamilton General Hospital, CA, and Liverpool Heart and Chest Hospital, UK, respectively.

We are now undertaking study close out procedures. At present, 100% of the data have been received from both sites and 97% of these data are clean. All follow-up visits have been completed successfully with a lost to follow up rate of zero. There are approximately 780 clinical events of interest documented in the database. Quality checks and corrections of the remaining 3% of data are underway and statistical analysis of primary data items has begun.

Related Publications

McGillion MH, Parlow J, Borges FK, et al; on behalf of the PVC-RAM Investigators. Post discharge after surgery Virtual Care with Remote Automated Monitoring technology (PVC-RAM): protocol for a randomized controlled trial. CMAJ Open, March 2, 2021. 9(1):e142-e148"

McGillion MH, Parlow J, Borges FK, and the PVC RAM -1 Investigators. Effect of Post discharge after surgery Virtual Care with Remote Automated Monitoring technology versus standard care: The PVC-RAM randomised controlled trial. BMJ (Accepted)

Institute for Pain Research & Care Supported Projects

PAIN+ PREMIUM LITERATURE SERVICES

CPN | RDC CHRONIC PAIN NETWORK | RÉSEAU DE DOULEUR CHRONIQUE

McMaster PLUS

Primary Investigator: Alfonso Iorio, MD, PhD, FRCPC and Brian Haynes, MD, PhD, FRCPC
Start Date: 2016

Brief Overview and Progress to Date

The objective of this project is to develop and maintain an evidence-based information service for health care practitioners engaged in the management of acute and chronic pain, in collaboration with the PainHQ website. In addition to including original and systematic review articles of relevance to all aspects of clinical pain care, the service provides dedicated streaming of neuropathic and post-stroke central neuropathic pain data. This service will provide a continuously updated, quality assessed, clinician rated on-line service, based on the McMaster PLUS Health Knowledge Refinery. Over 120 top clinical journals including leading pain journals are included in the assessment process (http://hiru.mcmaster.ca/hiru/journalslist.asp).

PAIN+ CPN also includes 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 article candidates for relevance using the Jury Rating feature. There are currently 36 Evidence Summaries on the PAIN+ CPN site.

The summaries can be accessed without registering at: https://www.painpluscpn.ca/Articles/EvidenceSummaries.

Main field of activity of the CPN KT committee have been:

1. Updating the KT platform strategic plan document
2. Approving the KT component reporting form for the CPN SPOR research projects
3. Collating a list of resources and guidance to support implementation of the KT components of ongoing research projects.
4. Summary of activities undertaken:
    - Writing and publishing of evidence summaries. Forty-nine Evidence Summaries have been published to date (https://www.painpluscpn.ca/Articles/EvidenceSummaries)
    - Articles selected for PAIN+ as relevant to Chronic pain. Total to March 31, 2021: 5,870

DeGroote PainHQ

Start Date: 2015

Brief Overview and Progress to Date

The PainHQ main site had 4,959 new unique visitors in the last year. Analytics indicate that users within the 25-34 age bracket continue to be the most active on the site.

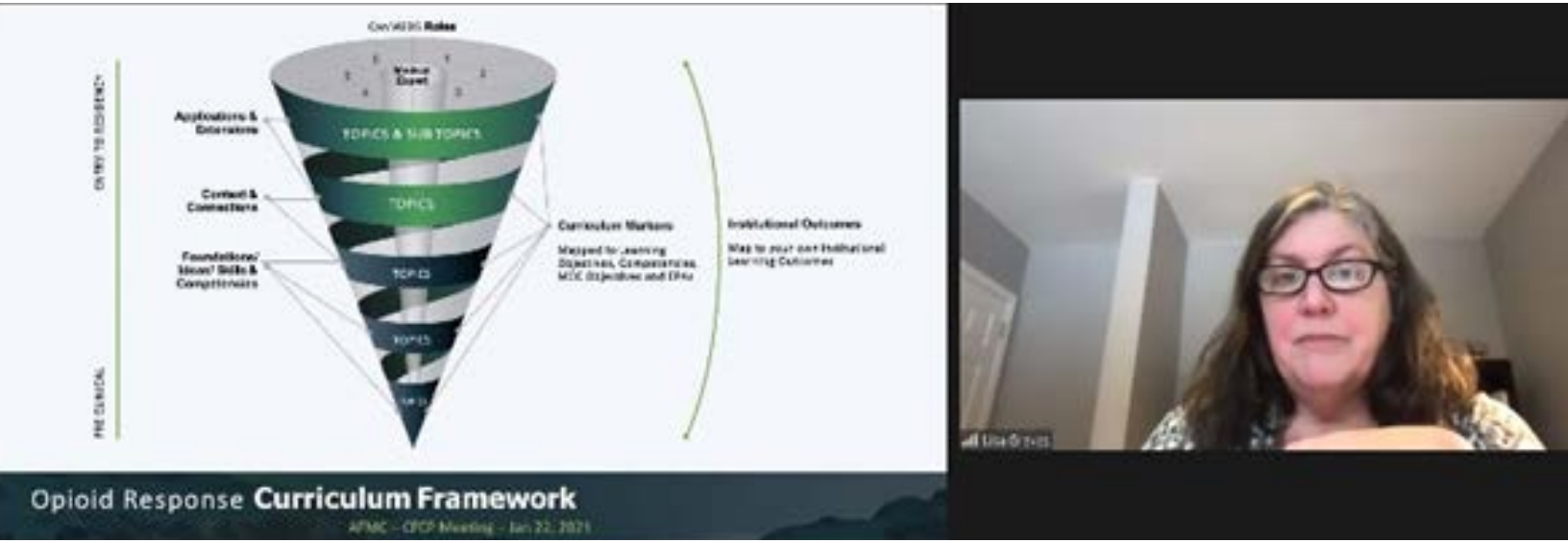
PainHQ currently has 1,430 Twitter followers and 538 followers with 535 likes on Facebook.

DeGroote PainHQ was launched in In September of 2015 by McMaster University and serves as an online resource for individuals living with neuropathic pain. Access is provided 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.

Engagement

Canadian Pain Care Forum



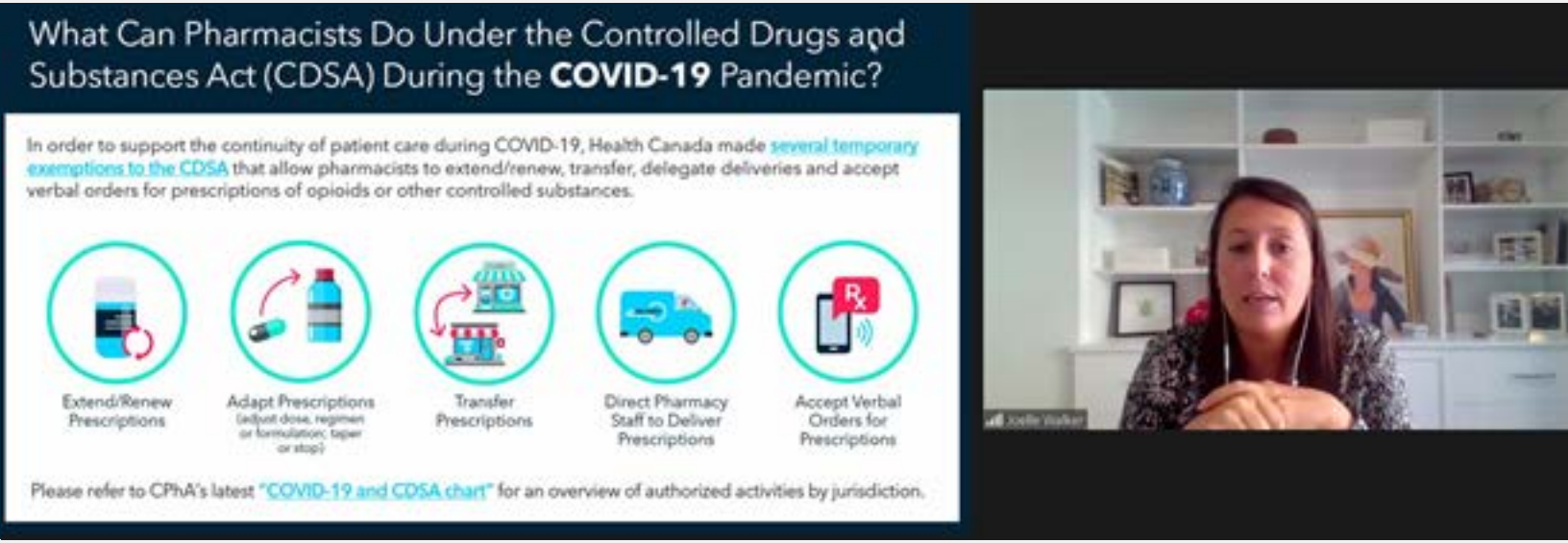
Above: Dr. Lisa Graves (AFMC) presenting at the January 2021 Meeting.

Established in 2016, the Canadian Pain Care Forum (CPCF) brings stakeholders from across the country together to consider current issues and policy affecting how pain is addressed in Canada. The Canadian Pain Care Forum meets quarterly, with in-person meetings held in the Greater Hamilton Area, and virtual options for those at distance. Virtual connection has become the norm during COVID. Organizations currently affiliated with the Canadian Pain Care Forum 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 treatment, and pharmaceutical and medical products businesses. Participation is open to all organizations who have demonstrated interest in and desire to improve national and/or provincial pain care public policy. Respectful debate and differing opinions are welcome.

Members of the Canadian Pain Care Forum were able to meet virtually during 2021 in order to adhere to restrictions enacted in response to COVID-19.

This year's meetings were focused on understanding current pain education and curriculum standards and future reforms for various health professions in Canada.

At the January meeting, we had Dr. Lisa Graves and Fran Kirby speak about the Association of Faculties of Medicine of Canada (AFMC) update on Canadian Medical Schools Response to the Opioid Crisis: Best Evidence Training for the Next Generation of Canadian Physicians on Pain Management, Opioid Stewardship & Substance Use Disorder. Dr. Dave Walton, from Western University, then spoke about Initiatives related to broad-based curriculum reform in Physiotherapy programs across Canada, and Western University's new competency-based Masters degree program in interprofessional pain management.



Above: Dr. Joelle Walker presenting on behalf of Dr. Phil Emberley at the October 2021 Meeting.

In April, we continued with understanding the health professional pain education landscape in the country. Dr. Karen Cohen, CEO of the Canadian Psychological Association and Alida Bowman, Assistant Professor at McMaster's School of Nursing, presented on the Psychology Graduate Training in Pain Care and Education, and Training Standards in Pain Care for Nurses, respectively.

In October, we had Dr. Phil Emberley's team present on the Canadian Pharmacists Association's role in interdisciplinary pain care and the pharmacy curriculum on pain. Then, Dr. Hillel Finestone presented on Chronic pain management: Learnings from a nurse-led program in primary care.

Our membership continues to grow. We are now at over 127 members, representing 89 organizations, and we are always looking for new members to represent our various stakeholders. We are especially excited to see our membership grow to include more people with lived and living experience of chronic pain.

Our next meeting is planned for January 2022.

Funding: CPCF membership is voluntary, and members 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.

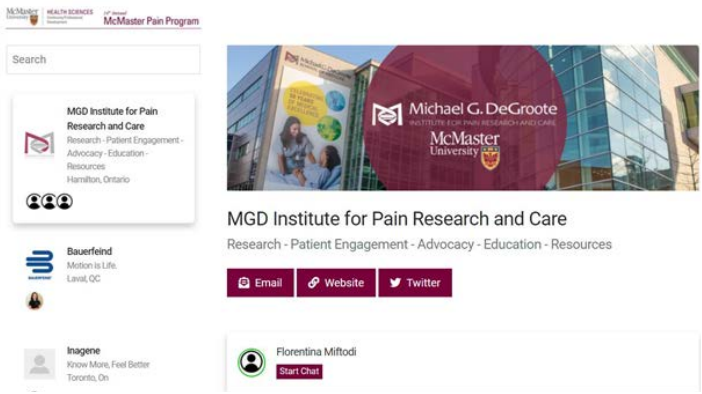
Engagement

Institute for Pain Research & Care Participation with Virtual Booth at Canadian Pain Society (CPS) 2021 Annual Scientific Meeting and McMaster Annual Pain Program

As a sponsor, the MGD IPRC had virtual booths showcasing the work it has done over the past year and the MGD IPRC team was on hand to answer any questions. We also had representation from our research members where they presented posters and engaged in meeting discussions.

The Canadian Pain Society's 2021 Annual Scientific meeting took place virtually on April 28-30, 2021. Dr. Karen Davis, CPS President and CPN Principal Applicant, welcomed all attendees to the meeting. The momentum continued with updates from Dr. Fiona Campbell and Maria Hudspith, co-chairs of the Canadian Pain Task Force, as well as a message from the Federal Minister of Health, The Honourable Patty Hajdu. It was announced that the 2022 CPS Annual Scientific Meeting will take place in Montreal.

At the McMaster Annual Pain Program held on September 22, 2021, Dr. Lydia Hatcher delivered two case presentations with the objective to identify and effectively utilize a variety of non-pharmacological therapies to improve pain and/or function.



The Michael G. DeGroote Institute for Pain Research & Care once again supported the 2021 McMaster Pain Program held September 22, 2021.

Engagement

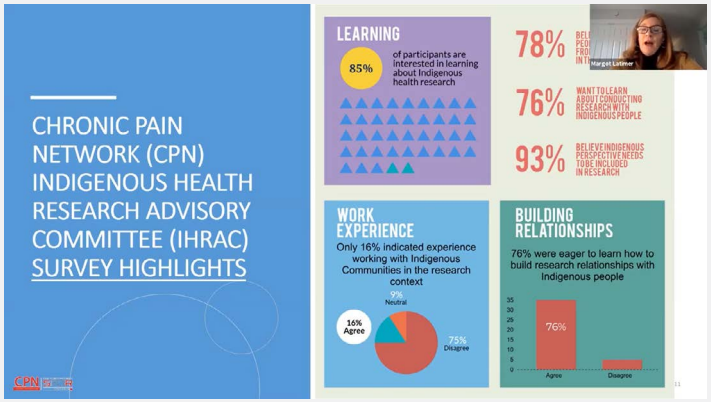
The Chronic Pain Network

In the summer of 2021, the Canadian Institutes for Health Research announced a new grant opportunity for the five chronic disease networks funded through the Strategy for Patient Oriented Research initiative, of which the Chronic Pain Network (CPN) is a part. This new funding seeks to support knowledge mobilization and implementation science, specifically focusing on knowledge generated through the initial funding provided during phase one of the networks. The announcement of funding decisions are tentatively schedule to be made in March of 2022, with a start date for phase two of the networks in April of 2022.

In addition to preparing the application for this new grant, the Network has seen a flurry of activity in recent months. The Clinical Research Network has now grown to 16 sites, with the addition of three locations in Quebec and one in Ontario.

The Network's Patient Engagement, Knowledge Translation and Training and Mentoring committees also came together this past year to offer a series of webinars that focused on patient engagement in research. Highlights from the webinars include talks from the Canadian Pain Task Force; Margot Latimer and John R. Sylliboy, of the Aboriginal Children's Hurt and Healing initiative; as well as the Solutions for Kids in Pain Centre of Excellence.

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.



Margot Latimer, of the Aboriginal Children's Hurt and Healing Initiative and co-chair of the Chronic Pain Network's Indigenous Health Research Advisory committee, delivered a webinar as part of the Network's series focusing on patient engagement. The webinar discussed protocols and considerations when conducting research in partnership with Indigenous communities.

Engagement

Centre of Excellence for Canadian Veterans with Chronic Pain

Creating a national community of care for Veterans & families.

The Chronic Pain Centre of Excellence was announced in July 2019 and launched in April 2020 at McMaster University.

The Chronic Pain Centre of Excellence for Canadian Veterans (CPCoE) launched on April 1, 2020. It is established as a Not for Profit entity, with the support of McMaster University and Hamiltion Health Sciences Corporation.

Funded by Veterans' Affairs Canada (VAC), the Centre's Vision is to improve the well-being of military veterans suffering from chronic pain and their families. The Mission includes fostering a national network of interdisciplinary pain management centers using research and evidence-based strategies to care for military veterans and their families.

The Centre of Excellence drew heavily on the experience of the Chronic Pain Network (CPN) in establishing its goals, objectives, relationships and operations. It has now completed 18 months of operations, conducting research to improve our understanding of pain in veterans and improve our ability to treat pain with evidence-based recommendations for clinicians treating veterans.

Since its launch, the CPCoE has collaborated directly with veterans living with chronic pain, and their families, to establish its research priorities, applying the model of Patient Engagement described by the CIHR and implemented in the CPN-veteran engagement from identification of priorities for research through conduct of the research itself. Under the direction of Dr. Jason Busse, a qualitative review was conducted to determine what research was important to Canadian veterans. One-on-one interviews were conducted with Veterans across five provinces, who reported pain that began during their service. Results showed the following research priorities:

- Pain care in the military
- Post-operative care in the military
- Coordination of services through VAC
- Military to civilian transition
- Primary care provider access outside the military
- Knowledge of pain among civilian healthcare providers
- Holistic care and patient knowledge
- Effective strategies for chronic pain management

A cross-sectional review of more than 700 veterans was

How we're here for you

KEEPING HOPE ALIVE

The Chronic Pain Centre of Excellence partners with veterans and their families to lead a national community of care and shape the future of veteran-first chronic pain management. At the Centre of Excellence, we put veterans at the heart of everything we do: from setting the research agenda, to developing evidence-based practices, and helping veterans access care closer to home.

also completed to establish the relative ranking of these established priorities. In conjunction, the CPCoE meets annually with its Advisory Council of Veterans to discuss their goals for research. Based on their responses, the CPCoE built its annual research plan.

The Center has reached out to researchers across the country, initiating studies with the families of Veterans experiencing chronic pain (Dr. Melanie Noel, Associate Professor of Clinical Psychology, University of Calgary), identifying the impact of sex and gender on pain and its experience (Dr. Joy MacDermid, Associate Professor, Western University) and developing a Veteran-specific registry to observe the impact of medical cannabis use.

The Centre's activities and objectives in the longer-term will be informed by its engagement with veterans, advisory boards, Board of Directors, ongoing research, and engaging with the clinics delivering care to fine-tune the research learnings that are most applicable in practice. These activities can include initiating clinical trials to further develop new therapies for managing pain, building the network of pain clinics and researchers across Canada, and continuously measuring the metrics associated with timely access to care and quality of life for veterans and their families.

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Mission

The mission of the Michael G. DeGroote 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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