**Research Statement**

As a clinician, I have observed several gaps between common practice patterns and research evidence. I also observed that new interventions were often introduced and taken up with great enthusiasm, but with little clarity on the mechanisms, or rigorous trials to show effectiveness. This motivated my interest in high quality research design and analytical methods to rigorously evaluate mobility and activity interventions and outcomes to address important research questions in healthcare. I selected a training pathway to provide the skills and experiences to achieve this goal. My clinical experience is in the field of musculoskeletal health, with a focus on exercise, activity modification and complex multimodal interventions that improve physical and mental health. More recently, my focus has shifted to include pandemic public health issues. Crosscutting methodological themes in my work include evidence synthesis, design and conduct of clinical trials, clinical measurement methods and the use of regression models to assess prognosis and treatment effectiveness.

During my Ph.D. training I gained valuable experience in patient engagement and learned numerous scientific techniques including advanced evidence synthesis, trial/cohort design, and advanced analytical techniques. I have developed collaborations and strong partnerships in Australia, Canada, USA, and Europe with researchers from different fields. I will leverage and expand these collaborations if I am successful in achieving a faculty position at Western University. The strategic priorities of the Faculty of Health Sciences at Western University are highly aligned with my future research interests. An important aspect of my research program will be graduate supervision, and I have experience in including junior trainees in my work (14 publications with junior trainees).

My research themes are:

1. Development and evaluation of mobility and activity interventions

2. Clinical measurement methods and innovations

3. Identification of best practices using evidence synthesis

I have used a longitudinal contributions approach to explain my design experience and career trajectory and future plans.

**Contribution 1 - Bachelor of Science Thesis (Randomized controlled trial):** I designed, conducted and analyzed a superiority, 3-arm, randomized clinical trial (RCT) that evaluated three different therapeutic exercise interventions for the management of chronic neck pain. I was the first person in my school to design and publish a randomized trial as an undergraduate student. This trial established that neck muscle flexor training was effective in alleviating neck pain and disability by a clinical important amount. This resulted in a primary publication on the trial outcome, 2 secondary manuscripts on prognostic factors that affect outcome, and 3 conference presentations. Research on neck pain remains a theme in my program, and I have contributed to international efforts in establishing core outcome measures.

**Contribution 2 - Master Thesis (Prognosis cohort designs):** I chose to investigate the factors that affect hand dexterity after a wrist fracture to address a substantial gap in knowledge on this important aspect of hand function. My studies indicated that hand dexterity improved rapidly between 3 and 6 months when people would be engaging in physical therapy, and then worsened by 1-year. Hand dexterity did not recover to the state of the uninjured hand even by 1 year. This suggests that future rehabilitation programs need to include dexterity assessment and training. This project resulted in 3 published manuscripts, and 2 presentations; and informed my PhD thesis. This work informed a current project developing online interventions for patients with these injuries.

**Contribution 3 – PhD Comprehensive Project (Overview design):** For my comprehensive process, I worked with experienced evidence synthesis scientists at McMaster and Western University to gain experiential training on literature appraisal and synthesis. This overview (umbrella review) required synthesis of over 20 systematic reviews to establish the current state of knowledge on psychometric properties of outcome measures for patients with neck pain disorders. This work was particularly challenging as the methods for overviews were evolving, and I had to adapt to changing standards. This overview was published in Journal of Orthopaedic and Sports Physical Therapy (JOSPT), which is a high impact journal in the rehab field. One of my main findings suggested that very few patient-reported outcome measures have sufficient research on responsiveness. I have since published 3 overviews and have 4 in progress. Given the relative recent evolution of overview methodology, I would expect to share my expertise in this area with colleagues and trainees.

**Contribution 4 - PhD studies (Evidence synthesis and patient preference)**: My PhD work reflects my commitment to rigorous development of new interventions. Joint protection is critical to preserving joint function in people with arthritis. However, the evidence is weak, and programs are outdated. My PhD research focused on the development and evaluation of novel patient-centered joint protection programs (JPP) in combination with hand exercises in people with hand osteoarthritis. I worked with engineers, patients and evidence to inform my creation of a new JPP. I published 6 manuscripts that reported: A scoping and a systematic review with meta-analysis on JPP, the evaluation of content validity of patient-reported outcomes for patients with hand osteoarthritis and the investigation of the barriers, facilitators, expectations, preferences and patient priorities on JPP. This work will lead to a single center, investigator-blinded, randomized, 12-month, parallel-group, superiority trial on the fully developed program that I will conduct as a future faculty member. The development work was funded by The Arthritis Society, and they will be the target for a future grant application for the RCT. Novel aspects of my collaboration with engineers included evaluation of a new wearable fingernail sensors to empirically evaluate hand forces during functional activity. Joint protection and other aspects of safe joint preserving patient education will be an ongoing theme in my program of research. Currently no such programs have been developed for lower limb arthritis or following joint replacements – which are major gaps in the field.

**Other Contributions**

**Contribution 4 – Cochrane Systematic Reviews:** Evidence synthesis, has been, and will continue to be, a theme within my research program. I am a member in 2 Cochrane groups, The Cochrane Neck and Back Group and The Musculoskeletal group. I am currently involved in many Cochrane systematic reviews that cross other areas of musculoskeletal pain and disability. Currently, I am leading a Cochrane Review which evaluates the efficacy of cervical traction for patients with or without neck pain radiculopathy and co-authored another review on the efficacy of viscosupplementation for patients with knee osteoarthritis. I have substantial experience in the Cochrane methods and their evolving standards, as well as across different types of evidence synthesis. Cochrane represents the highest standards in evidence synthesis, and I have developed multiple productive evidence synthesis collaborations.

**Contribution 5 – Postdoctoral and supplementary projects using Network meta-analyses:** My post-doctoral work (funded by the Arthritis Society) extends my methods expertise and my contributions to advancing the management of OA. This is an important focus since OA is a leading cause of disability in adults in Canada and internationally. My experience with this trial will inform future RCTs on different interventions including different physical and mental health programs, fracture rehabilitation and mobility interventions. Bayesian methods have potential to improve the efficiency of trials and it will be an approach that I will share with colleagues and trainees**.** My post-doc project is a network meta-analysis (NMA) to determine which intra-articular treatments in knee osteoarthritis (OA) appear to have the greatest impact to treat knee OA. Intra-articular treatments are frequently used to allow patients to reduce pain and participate in rehab/mobility without the adverse effects usually caused by systemic treatment with oral intake of non-steroidal anti-inflammatory drugs, opioids or acetaminophen. However, there is controversy surrounding their effectiveness and safety. The historical data from the NMA will be used to design a Bayesian RCT allowing for a more precise estimation of the true effect of the intra-articular interventions for knee OA that will be focus on the 1st of the 5 years of my faculty position.

This RCT will investigate the safety and the efficacy of most promising intra-articular therapies identified in the NMA, with robust priors incorporating historical data from the NMA. I expect this work will be funded first by a pilot grant application to Canadian Musculoskeletal Rehab Research Network, with a plan for a full RCT application within 3 years.

**Contribution 6 - Operating Grant: Knowledge Synthesis: COVID-19 in Mental Health & Substance Use:** I was a co-Principal Investigator on a CIHR one-year grant where I led the network meta-analysis on a complex body of literature examining online versus face-to-face interventions that included both physical and mental health treatments for facilitating better mental and physical health in people living with chronic pain. This study involved screening of more than 15,000 papers to find those that uniquely addressed our research question. The network meta-analysis was challenging given the complexity of the intervention and outcomes and required the use of evolving methodologies. The summary was published by CIHR and the article is currently under review.

**Knowledge Translation (KT)**: I have been highly committed to knowledge translation as an integrated part of my research. Patients were included in the design of the grant for The Arthritis Society and inform development of future interventions. Throughout my program I have been actively involved in Arthritis Society initiatives. I actively engage in social media to disseminate research findings having taken on responsibility for this for periods of time for The Bone and Joint Institute at Western University, The Clinical Research Lab at HULC, University of Toronto Centre for the Study of Pain and The Pain Science Division of the Canadian Physiotherapy Association. My experience on the Ontario COVID-19 Science Table has allowed me to develop awareness and skills in policy-related KT.

**Musculoskeletal Health research plan in Activity and Mobility**

**Five-year research plan:** My research programs has both clinical and methodological areas of focus. In terms of clinical impact, I intend to focus on musculoskeletal health in activity and mobility in people with osteoarthritis. A major focus in my five-year research plan is to enable personalized osteoarthritis (OA) care by investigating the effectiveness of exercise and activity modification in patients with OA, and the identification of subgroups of patients who are more likely to respond to these treatments, understand physical inactivity behaviours and identify outcome measures that can be used in multi-cultural and diverse population in Canada. In terms of methodological expertise, I intend to focus on emerging network meta-analysis methods, application of Bayesian methods, enhancing methods around patient preference and improving how regression modelling is used to assess mechanisms and theoretical constructs in health research.

**Year 1 – Project 1:** The identification of the best exercise treatments to target OA pain, disability and physical inactivity behaviour will be conducted through a Bayesian component network meta-analysis to rank all the treatments in terms of their effectiveness and safety, and to identify subgroups of people that are more likely to respond to each treatment. This novel analysis will test and rank the effectiveness of all the exercise interventions based on probability to reach the minimum important between group difference in pain outcomes. My novel analysis also will examine the additive effects of the different exercise components which have not been considered in evidence synthesis yet. The next step will be to conduct an individual patient data (IPD) meta-analysis to allow proper investigation of subgroup effects. This subgroup analysis will identify patients that are more likely to benefit from these different treatments. Therefore, I will target CIHR early young investigator grants or Western University internal grants to support early work; and will leverage this success to future CIHR grants.

Expected outputs/publications will include:

1. A component network meta-analysis to evaluate the efficacy and safety of all the available exercise interventions for patients with osteoarthritis.

2. An individual patient data meta-analysis and meta-regression analysis to identify sub-group of patients with osteoarthritis that will respond to exercise interventions.

**Year 2 – Project 2:** The goal of Project 2 is to evaluate the accuracy of gathering contextual information on physical inactivity and mobility and sedentary behaviour using an ecological momentary assessment design in people with osteoarthritis. Ecological momentary assessment is a tool that can collect data on health behaviors and outcomes in real-time from participants as they experience their daily lives. To understand the consequences of daily physical inactivity and mobility behaviour we need to gather data about social and environmental contexts. To collect this information, we will use digital accelerometers and repeated contextual assessment through mobile smart mobile applications. The accelerometer recordings will analyze and collect data about body position (e.g. prone positioning) in a pre-specified timeframe and will trigger notifications for a contextual assessment through a patient-reported outcome measure. To assess the accuracy, we will calculate a percentage score of all triggered notifications in relation to the total number of all possible triggered prompts. We will examine also if demographics and social determinants of health will influence the accuracy of the score. This project will help to develop more effective intervention in the future with the aim of changing mobility and activity behaviour patterns in people with osteoarthritis that we have never considered before. This line of research will be optimized in collaboration with scientists from the Fowler Kennedy Sports Medicine Clinic and with bioengineers at Western University. An early young investigator grant will be submitted to CIHR to seek funding.

Expected outputs/publications will include:

1. Identification of e-Health technology platforms for ecological momentary assessment in physical activity and mobility research for people with osteoarthritis

2. Barriers, facilitators, and accessibility options of using e-Heath technology platforms

3. Accuracy, development and feasibility of physical inactivity and mobility behaviour with ecological momentary assessment

**Year 3 – Project 3:** The goal of Project 3 is to conduct an evidence synthesis to map all the diagnostic mental health outcomes in people with osteoarthritis. Canada has a growing multinational immigrant population which many commonly mental health tools have known cultural biases and therefore, are difficult to be used in diverse populations. A synthesis will be conducted to map all the available tools for mental health assessment commonly used in Canada and identify if they have been reproduced in digital platforms and cross-cultural validated in diverse populations. The next phase of this project is to determine how the most frequent mental health outcome measure compares with a current gold standard in a Bayesian meta-analytic framework. Data extraction will be done in duplicate and based on the reference standard sensitivity, specificity, and correlations of the outcomes of interest will be collected. Quality assessment will be done with Quality Assessment of Diagnostic Accuracy Studies (QUADAS) and the meta-analysis of pooled estimates of sensitivity and specificity, positive and negative likelihood ratios will be conducted with R package mada.

Expected outputs/publications will include:

1. Identification of mental health outcomes in Canada with people with lower limb osteoarthritis

2. Accuracy, sensitivity, and specificity in mental health outcome measures in diverse populations with osteoarthritis

**Year 4 – Project 4: The findings from Years 1-3 will inform specific projects.** The planned focus of project 4 will be to determine the effectiveness and safety of the most promising exercise interventions with additive components of these interventions (identified in project 1) that will target osteoarthritis symptoms, physical inactivity and mobility behaviours (project 2) and mental health (project 3) in a Bayesian randomized trial (RCT). This RCT will investigate the safety and the efficacy of most effective and safest treatments identified in the network meta-analysis (NMA), with robust priors incorporating historical data from the NMA. The approach will dramatically increase the power of the trial, while the use of robust priors will efficiently control the type I error rate by downweighting the contribution of historical information from the NMA. With this approach I anticipate that the random allocation of 80 to 100 patients per arm will provide more than 90% power to detect a minimally important between-group difference of 0.37 standard deviation units on global OA pain at an alpha of 0.005. This alpha will be chosen to avoid false positive conclusions. Central randomization will be performed using a web-based system to ensure adequate concealment of allocation, with stratification according to center and prognostically important clinical criteria (presence of malalignment or pain at baseline). Safety outcomes will be the number of patients experiencing any adverse events, the number of patients experiencing serious adverse events, and the number of patients dropping out of the trial. A team grant application to CIHR will be submitted to support the full RCT in collaboration with Lawson Health Research Institute.

Expected outputs/publications will include:

1. A Bayesian randomized trial to determine the effectiveness and safety of the best multimodal exercise interventions

**Post COVID-19 syndrome Research Plan**

**Five-year research plan:** The major aims in my second theme of my five-year research plan is to develop and test physical activity and mobility rehabilitation protocols to improve pulmonary function and disability status in post COVID-19 patients. Currently, all the countries around the world are trying to implement public health measures and vaccine policies to contain the spread of coronavirus. As of February 2022, more than 3.4 million Canadians had COVID-19 which leaves an important room for future research on post COVID-19 syndrome. Several modelling projections exist, and their forecasts and timelines may vary, but most of the scientists agree that COVID-19 is here to stay, and the future depends on a lot of unknowns, including great uncertainty in pathology of people who have previously been infected. In this frame, the role of post-covid syndrome research will be increased, and it will be pivotal to understand the relationship of physical activity and mobility with post-covid symptoms.

**Year 1 – Project 1:** The first objective of year 1 – project will be to conduct two large reviews to map all the available rehabilitation interventions for COVID-19 patients. Interventions and outcomes will be mapped and categorized based on acute COVID-19 (mild symptoms, hospitalized, high/flow oxygen, mechanically ventilated) and on post COVID-19 syndrome. This will be the first step to understand what interventions and outcomes are being used and what are the major gaps. This scoping study will be conducted by following the PRISMA extension reporting guidelines for scoping reviews. Article screening, data extraction will be done with artificial intelligence system. The second step is to conduct a systematic review and meta-analysis to quantify the effects of mobility and physical activity interventions that target pulmonary function outcomes such as the Barthel Index (BI), modified Medical Research Council (mMRC) Dyspnoea Scale, and 6-Minute Walking Test) in post-covid patients. This work will require minimal funding (primarily trainee support).

Expected outputs will include:

1. A scoping review of rehabilitation interventions and outcomes for patients with COVID-19 and post-covid syndrome

2. The efficacy of mobility and physical activity interventions on pulmonary function outcomes in patients with COVID-19 and post-covid syndrome. A systematic review with meta-analysis.

**Year 2 – project 2:** In year 2 the identification of prevalence and incidence of post-covid symptoms during physical activity in Ontario is crucial to quantify the burden of associated musculoskeletal disability from post COVID-19 syndrome across Ontario. This will be prospective cohort study that will collect data on demographics, clinical characteristics, social determinants of health and outcome measures (not limited to these) such as Barthel Index (BI), modified Medical Research Council (mMRC) Dyspnoea Scale, Health Anxiety and Depression Scale (HADS), health-related Quality of Life and disability. Ethics will be granted from Western University research ethics board and the study questions will be hosted in a digital platform (Qualtrics). Study questions will be developed, calibrated and pilot tested in collaboration with knowledge users such as patients and clinicians from affiliated Western University hospitals. Data analysis will include a logistic regression of experiencing post-covid symptoms with adjusted predictions on sex and gender. We will analyze the predicted probability on physical activity status plotted against the empirical Bayes post-COVID-19 symptom scores. I will seek funding support from the from the CIHR to support this project and doctoral support for my trainees.

Expected outputs will include:

1. Understanding the incidence and prevalence of post covid-19 symptoms during physical activity and mobility in Ontario. The Burden of post-covid syndrome in musculoskeletal health.

2. Predicted probability of experiencing post-covid symptoms after physical activity

**Year 3 – project 3:** The main goal of project 3 is to conduct a cross-sectional survey to identify barriers, facilitators, and expectations of physical activity and mobility interventions for post-covid syndrome. Understanding patient perspectives and which patients in Ontario have access to these treatments will be the next step to mitigate the post-covid symptoms but also to identify marginalized and minority groups that often do not have access in these treatments and are often underrepresented in research projects. Demographics will be analyzed with descriptive statistics and answers will be presented in frequencies. A grant application will be submitted to CIHR.

Expected outputs will include:

1. Barriers, facilitators and expectations of physical activity interventions for post-covid syndrome

**Year 4 – project 4:** Projects 1 – 3 will inform the main objective of project 4. In year 4, I will conduct a single arm observational study to investigate the usability and feasibility of the most promising physical activity and mobility interventions (project 1) to target the most prevalent post COVID-19 symptoms (project 2) on a longitudinal follow-up. Pulmonary function, physical activity and disability outcomes will be determined from project 1. Patients will be recruited from London, Ontario area in collaboration with affiliated university hospitals. This project will be a stepping stone to conduct an RCT in the future to further validate the results from the observational study. Funding will be sought mainly from CIHR.

Expected outputs will include:

1. Feasibility and usability of physical activity and mobility interventions to mitigate long-covid symptoms

*I expect to continue my collaboration with clinicians and scientists on various research projects where I can provide methodologic or content expertise to support colleagues doing research that shares goals of improving mobility, activity and participation.*

*Pavlos Bobos PT PhD*