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Dear Friends,

The Psoriatic Arthritis (PsA) Program at Women’s College Hospital in Toronto, Canada, is a clinical research program that was founded in 2016. The program includes a specialty PsA Clinic for individuals with PsA that integrates research through standardized collection of clinical information and biological samples. The aim of the research program is to improve the lives of men and women with PsA by discovering innovative, equitable and efficient ways to facilitate early diagnosis and thus early intervention to prevent morbidity from PsA. With funding from a number of national and international granting agencies (CIHR, Canada Research Chairs Program, Arthritis Society Canada, National Psoriasis Foundation, and GRAPPA), our team is currently undertaking research studies in the fields of clinical epidemiology and translational research in PsA.

I am excited to share our program’s first annual newsletter, which summarizes ongoing projects and collaborations, highlights the accomplishments of our staff and trainees, and provides important study updates from the past year. The newsletter is organized into four sections, representing the interdisciplinary nature of our program, supported by four main pillars:

- Psoriasis and Psoriatic Arthritis: Disease Outcomes
- Co-morbidities: Cardio-Rheumatology
- Health inequities: Sex- and Gender-related Disparities
- Imaging: Musculoskeletal Ultrasound

With the goal of early detection and equitable delivery of care for all individuals to improve health outcomes, our team is focused on understanding the risk factors for developing PsA among men and women with psoriasis. With earlier detection and improved care delivery, individuals living with psoriatic disease can benefit from receiving earlier treatment and possibly even future prevention of the disease. Thank you for your continued support and contribution to the PsA Research Program.

Sincerely,

Lihi Eder, MD PhD
Director, Psoriatic Arthritis Program
Canada Research Chair in Inflammatory Rheumatic Diseases (Tier 2)
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What is Psoriasis and Psoriatic Arthritis?

Psoriasis

Psoriasis is a chronic, inflammatory skin disease that is associated with multiple co-morbid conditions. It impacts individuals’ quality of life, partly due to negative effects of the skin disease on their psychosocial wellbeing and stress levels. A greater impact occurs among individuals with more extensive skin involvement, occurring in areas such as the face, palms and genitalia. As a result, individuals with psoriasis are more likely to have depression (up to 20%) and exhibit suicidal ideations compared to those without the disease.

Psoriasis is a common skin disorder, with a prevalence of about 2-3% in Europe and North America. Its prevalence is unequally distributed across regions of the world, being highest in more economically-developed countries and more common in individuals of European ancestry. Psoriasis occurs equally in both men and women, with an average age of onset of 33 years.

Psoriatic Arthritis (PsA)

Psoriatic Arthritis (PsA) is a chronic, inflammatory musculoskeletal disease associated with psoriasis. Its unique characteristics distinguish it from other types of inflammatory arthritis. PsA develops in up to 30% of individuals with psoriasis and is known for its diverse clinical presentation, often resulting in delayed diagnosis. Without timely intervention, PsA can lead to significant joint damage and disability.

While the disease is common among patients with psoriasis, PsA has a relatively low prevalence in the general population, with prevalence estimates of up to 0.25% in North America. PsA equally affects males and females and is more common in individuals of European ancestry.

Psoriatic Disease

Collectively, psoriasis and PsA are referred to as Psoriatic Disease. Individuals with psoriatic disease encounter substantial barriers in managing their conditions, which often present simultaneously with other co-morbidities or complications, such as cardiovascular diseases. While psoriatic disease tends to be equally distributed among males and females, it affects patients of the different sexes in unique ways. Females tend to respond less favourably to treatments and may experience delays in specialty care and diagnosis.
Current Research:

Disease Outcomes in Psoriasis and Psoriatic Arthritis

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Projects

1. Prognostic and Genetic Studies in Psoriasis and Psoriatic Arthritis

IPART is an international network of dermatologists and rheumatologists that focus on psoriasis and PsA, as well as other multi-disciplinary collaborators, including geneticists, epidemiologists and biostatisticians. The program focuses on the biological basis of psoriatic disease with an emphasis on predicting the onset and severity of PsA using clinical and genetic variables, and identification of disease biomarkers.

IPART consists of several psoriatic disease cohorts across Canada, USA and Israel. These cohorts are followed over time and consist of detailed clinical, laboratory, imaging and genetic data. There are currently over 5000 patients with psoriasis and PsA patients enrolled in IPART, making it one of the richest sources of research data in the world for studying various aspects of psoriatic disease. Our collaboration with IPART led to discoveries in the fields of genetics, imaging and co-morbidities in PsA.
Can we prevent the development of PsA in people with psoriasis?

2. Prediction of Psoriatic Arthritis Tool (PRESTO)

This study, funded by the PSI foundation, uses the IPART cohort to develop a new prediction tool that identifies individuals with psoriasis who are at risk of developing PsA. The study is conducted in collaboration with IPART investigators from Toronto Western Hospital. The first part of the study that included the development of a new prediction tool for PsA (PRESTO) has been completed. Our team is currently working on validation of the newly developed tool in other cohorts.

Since psoriasis typically precedes the onset of PsA, individuals with psoriasis are an ideal group to study interventions that may prevent PsA. The purpose of PRESTO was to develop a new tool that can accurately estimate the risk of a person with psoriasis developing PsA within the next one to five years.

We analyzed information collected from 635 individuals with psoriasis that have been followed for over a decade. We identified participant characteristics (such as male sex, back stiffness, use of biologic medications) that accurately predict the risk of developing PsA – these characteristics can be easily assessed during a clinic visit either through interviews or physical exams. Physicians can enter information about their patient, then the calculator provides the estimated risk or probability of developing PsA. The tool can help dermatologists and rheumatologists identify these high-risk patients, providing an opportunity for early interventions that may prevent the development of PsA. In a future study, we aim to validate the prediction model in other cohorts of psoriasis patients in Toronto, Canada and Rochester, New York.

PRESTO: New Prediction Tool for Psoriatic Arthritis in Psoriasis patients

Access the PRESTO-PsA Tool
Read the Manuscript

WCH Scientists Develop Tool Predicting Risk of Psoriatic Arthritis – A Global First
PRESTO Successfully Predicts Future PsA in Patients With Psoriasis
Tool Predicts PsA Progression From Psoriasis, No Fancy Biomarkers Needed
Study validates use of new psoriatic arthritis prediction tool
3. Preventing Arthritis In A Multi-Center Psoriasis At-Risk Cohort (PAMPA)

**Summary**
The study, led by researchers at New York University, was launched in 2022 as a prevention trial for PsA among patients with psoriasis. We are one of two Canadian sites that are participating in this first ever prevention trial in psoriasis. The study aims to recruit a total of 350 participants across multiple sites in North America.

Approximately one-third of people with psoriasis ultimately develop PsA. Early recognition, diagnosis and treatment of PsA are extremely important and may help prevent or limit further joint damage, pain and disability.

The PAMPA Study is a multi-centre, longitudinal study that will study to what extent we can slow or prevent the development of PsA in high-risk patients with psoriasis. The purpose of this study is to evaluate whether a biologic drug, guselkumab, that is approved for the treatment of psoriasis and PsA, is effective in reducing the chances of conversion to PsA in high-risk psoriasis patients. Participants will take part in medical exams and surveys over the course of a two-year period. The PAMPA study will help us determine whether we can use existing medications to prevent PsA from developing altogether.

**In-Depth**

**In this webinar**, rheumatologist Dr. Lihi Eder and registered dietitian Arlaina Waisman provide valuable knowledge and insights related to nutrition and arthritis.
Current Research:

Sex and Gender-based Disparities in PsA
SAGE-PsA aims to study how sex/gender influence response to advanced therapies in PsA. Our team leads the study that was launched in March 2023, with expected completion in 2026. The study is funded by grants from CIHR and GRAPPA and involves 36 sites worldwide.

The expansion of advanced targeted therapies has changed the way patients with PsA are treated. However, despite the effectiveness of these therapies, many patients do not achieve optimal response to these therapies. Sex and gender are important factors that influence treatment response in PsA. Women with PsA are less likely to achieve remission, are more likely to experience side effects and tend to stop treatments earlier than men.

The aim of the study is to understand how sex and gender influence response to advanced therapies in PsA. We hope to discover biological and socio-cultural mechanisms that explain the differences in treatment response between men and women with PsA. The results of this study will improve our understanding of the impact of sex and gender on PsA which will contribute to more personalized approaches to care of people living with PsA.

**Study population and procedures:**

The study will enroll 540 men and women with active PsA from several countries across North and South America, Europe and Asia.

All participants will be starting treatment with 4 classes of targeted advanced therapies for peripheral musculoskeletal manifestations of PsA. Participants will be followed for a period of 1 year and will complete the following procedures:

- Patient Questionnaires
- Physical examination by a Physician
- Laboratory tests
Inflammatory arthritis, such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis, are long-standing diseases of the joints. Without early diagnosis and treatment, they can cause joint damage and disability. Therefore, ensuring early diagnosis through timely access to the healthcare system is crucial. We studied 56,000 patients with inflammatory arthritis in Ontario to investigate and compare pattern of healthcare use between men and women.

Our study found that women tend to visit physicians more than men, both before and after diagnosis. Men, on the other hand, tend to visit the emergency departments more than women, before diagnosis. Women also tend to get more X-rays and laboratory tests before diagnosis than men. In particular, older women tend to visit physicians and get more X-rays before diagnosis compared to older men. When considering dispensation of medications, women with rheumatoid arthritis were more likely to be prescribed pain control medications than men. These sex-related differences in healthcare use may stem from biological differences in disease or from socio-cultural differences in patient behaviour or interaction with care providers.
Axial Spondylarthritis (axSpA) is an inflammatory disease characterized by arthritis in the lower back, hips, and shoulders. AxSpA affects males and females differently, as female patients with axSpA experience higher disease activity scores and a worse health-related quality of life. Advanced therapies have significantly improved patient outcomes. However, observational data suggests that female patients have lower treatment responses. Angel's project was a systematic literature search and meta-analysis on sex-related differences in randomized clinical trials (RCTs) on advanced therapies in axSpA.

After searching various databases, we included 103 records for our analysis. Our preliminary results show that females patients are less likely to respond to biologic therapies used to manage their disease. These findings are similar to results reported in observational studies and emphasize existing gaps in therapy and highlight the need for further studies to understand the mechanisms underlying these differences.

Women with PsA suffer from more pain, have lower quality of life and worse physical function, while men tend to develop more joint damage. Importantly, biologic treatments for PsA are less effective for women than men. It remains unclear if these differences are due to biological variations in immune response between males and females.

Steven’s Masters project aims to identify biological pathways that explain these differences between males and females living with PsA using advanced proteomics technology. We will identify differences in levels of immune and inflammatory proteins between male and female patients with PsA and healthy controls. We will assess the relevance of these differences by incorporating clinical and imaging data on PsA. Ultimately, we will determine biological pathways that explain the differences in disease course between men and women with PsA, which will support the development of precise, sex-specific diagnosis, monitoring and treatment selection for all people living with PsA.
The Cardio-Rheumatology Network

The Cardio-Rheumatology Network is a collaboration among clinicians and scientists within the Temerty Faculty of Medicine, University of Toronto. Established in 2017 by Dr. Lihi Eder and Dr. Paula Harvey, the Cardio-Rheum Network aims to improve the primary prevention of cardiovascular events in rheumatic patients by developing novel approaches to risk stratification using traditional risk factors, laboratory biomarkers and cardiovascular imaging.

The Program holds an annual symposium for health care providers and researchers that helps to disseminate the results of our research in the general medical community. For more information, visit our website: www.cardiorheum.org

Cardio-Rheumatology Clinic at Women's College Hospital

- The Cardio-Rheumatology Clinic at Women's College Hospital was established to help those with inflammatory rheumatic conditions manage their heart disease risk
- Patients undergo a thorough assessment by a cardiologist, and are evaluated for abnormal heart function using a variety of advanced imaging and laboratory tests
- In addition, our team is searching for better ways to assess heart risk in patients with PsA, rheumatoid arthritis and ankylosing spondylitis through its research program

Did you know?

Cardiovascular diseases remain a major cause of morbidity and mortality in individuals with established rheumatic diseases, including PsA. Individuals with chronic rheumatic diseases, such as rheumatoid arthritis, lupus and ankylosing spondylitis, have an increased risk (up to 50%) of developing cardiovascular events, such as heart attack and stroke. Cardiovascular risk factors are often undertreated in this population and there is uncertainty about the best approach for treatment in these patients.
The IMPACT study is investigating mechanisms leading to the development of cardiovascular disease, and assess the effectiveness of a dedicated Cardio-Rheumatology Clinic in patients with chronic rheumatic diseases. Recruitment is active across two sites in Toronto, with 530 participants with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis enrolled as of October 2023.

In 2017, we launched a collaborative Cardio-Rheumatology Clinic and Research Program at Women's College Hospital, the first of its kind in Canada. The Program includes a dedicated primary prevention clinic run by an expert cardiologist, Dr. Shadi Akhtari. Patients enrolled in the program are first evaluated by their rheumatologist and subsequently undergo a comprehensive cardiology assessment, which uses advanced imaging and laboratory markers to improve the detection of high-risk patients and improve the control of their cardiovascular risk factors. The study population includes patients with one of the following chronic rheumatic diseases: rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.

The IMPACT study has two aims:
1. Investigate the underlying mechanisms leading to development of cardiovascular disease in patients with chronic rheumatic diseases.

To assess the impact of this program, we monitor patients over time and collect information at 1 year, 5 years, or more frequently if necessary.

Summary
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In-Depth
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1. Investigate the underlying mechanisms leading to development of cardiovascular disease in patients with chronic rheumatic diseases.

To assess the impact of this program, we monitor patients over time and collect information at 1 year, 5 years, or more frequently if necessary.
Latest findings from the IMPACT Study:

Use of cholesterol-lowering medication is lower than expected in individuals with inflammatory arthritis

In this cross-sectional study of patients with inflammatory arthritis in the Cardio-Rheum Clinic, half of the cohort was eligible for statin (lipid-lowering) therapy. Factors most strongly associated with the need for statin therapy were male sex, high blood pressure, higher levels of apolipoprotein-B (an indicator of bad cholesterol and fats in the blood), and a coronary artery calcium score greater than zero (which indicates the thickness of calcium build-up in the arteries of the heart). Despite a high number of patients eligible to receive statin therapy, the use of this type of lipid-lowering therapy was lower than expected.

The study emphasizes the need to optimize clinical decision making for this higher-risk population and identify and treat those most likely to benefit. The creation of interdisciplinary models of care, such as our program, has offered specialized care that is needed in long-term management of patients with inflammatory arthritis.

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Jeannie has been working towards completing an interim analysis of the effectiveness of the Cardio-Rheum program, where the participants’ cardiovascular risk factor profile, treatment compliance, and treatment target achievement after one year will be compared to their initial visit. Jeannie’s summer work mainly consisted of quality assurance of the study database. By cross-referencing participant charts using an electronic medical record system, she was able to ensure accuracy of the blood test and imaging data for the first 348 participants. Jeannie will continue working on the project over the coming months.

The aim of this project was to assess the effectiveness of the Cardio-Rheum program after one year, by describing:

- CV risk factor profile
- Treatment recommendations and compliance
- Achievement of treatment targets
The 5th Cardio-Rheum Symposium was held on June 16, 2023 and featured more than 10 speakers, with this year’s theme being “Multidisciplinary Approaches to the Management of Rheumatic Conditions”. The plenary session included clinical, behavioural and pharmacological approaches to obesity management, co-presented by a rheumatologist, clinical psychologist, dietitian and bariatric medicine clinician. This was followed by a session on exercise, co-presented by a rheumatologist and advanced practice physiotherapist. The event concluded with international perspectives and lessons learned from Cardio-Rheumatology clinics in Norway and the USA.

To join our mailing list, learn about future events and watch past recordings, visit our website: www.cardiorheum.org
Musculoskeletal Ultrasound
Musculoskeletal Ultrasound

The PsA Program studies the application of musculoskeletal (MSK) ultrasound as the point of care for the management of PsA. The program has been involved in dissemination of musculoskeletal ultrasound among rheumatologists by offering one of the only fellowship programs in point-of-care MSK (rheumatology) ultrasound in Canada. We extensively use ultrasound to investigate clinical outcomes in PsA and developed sonographic outcome measures.

Dr. Lihi Eder is a recognized expert in musculoskeletal ultrasound, as she serves as President of the Canadian Rheumatology Ultrasound Society (CRUS) and leads an international initiative through GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) to develop sonographic scoring systems in PsA.

Dr. Sahil Koppikar completed a fellowship in MSK ultrasound and additional advanced level training in ultrasound. He is Co-Director of the CRUS national basic ultrasound course and leads several medical education initiatives in the area of MSK ultrasound.

Why is ultrasound useful?

In individuals with inflammatory arthritis, the use of ultrasound is important for several reasons:

- It is a safe and cost-effective method
- It allows for the evaluation of several joints at the same time
- It can detect important clues which could otherwise be missed in physical examinations
- It can visualize inflammation and other changes occurring in joints and surrounding structures, such as the bones and tendons
- It can detect early disease, which is becoming increasingly important in the diagnosis and management of PsA
Projects

1. The Diagnostic Ultrasound Enthesitis Tool (DUET) Study: Development of a Sonographic Enthesitis Score for Early Diagnosis of Psoriatic Arthritis

**Summary**

DUET aims to develop a new sonographic scoring method to help with early diagnosis of PsA. The study, funded by GRAPPA, was launched in 2021 and we reached our enrollment target of 400 participants from 17 sites worldwide. The data is currently being analyzed.

**In-Depth**

The objective of the DUET study is to create a reliable sonographic enthesitis tool to distinguish PsA from other non-inflammatory conditions in order to improve early diagnosis of PsA. DUET is conducted by an established ultrasound working group within GRAPPA as an international multicenter study. The study includes a comprehensive sonographic assessment of 16 enthesal sites as well as clinical assessment of the joints and entheses and collection of patient-reported outcomes. We will identify the optimal combination of enthesal sites and sonographic lesions that distinguish PsA from controls, and integrate these results to create a novel sonographic instrument for the diagnosis of PsA (DUET score). Such a scoring system that reliably identifies PsA at early stages will be an important step in optimizing early diagnosis and facilitating timely interventions which will ultimately improve long-term outcomes of PsA.

**Learn More**

**What is an enthesis?**

Bones and muscles are held together with tissues called tendons and ligaments, which allow them to work together and help with all types of movement. The site where a tendon or ligament inserts into a bone is called an **enthesis**. Physical stress can be concentrated at the enthesis, as well as repetitive biomechanical impact. Research has shown that, when stress is concentrated in these areas, it can result in inflammation in the surrounding structures.

**Enthesitis** (inflammation of the enthesis) is a key feature in PsA and may be the initial site of musculoskeletal inflammation. Ultrasound optimizes the detection of enthesitis, however the lack of a validated sonographic enthesitis scoring system for PsA limits the ability to conduct ultrasound-based studies exploring approaches to improve early diagnosis of PsA.
The study is led by investigators from the University of Ottawa, and aims to assess the accuracy of a handheld ultrasound device compared to a stationary ultrasound machine. We expect to recruit 30 participants across three sites in North America.

Ultrasound holds significant promise as an imaging tool in rheumatology. In the future, handheld ultrasound, which is relatively low-cost, could be used at the bedside to provide diagnostic information, as well as guide both systemic and local treatment decisions and applications.

The purpose of this study is to test whether the Clarius handheld ultrasonogram scanners are as accurate as the currently used high-quality ultrasonogram scanners to detect characteristic features of healthy and rheumatic joints. Handheld ultrasound also has the potential to accelerate the patient journey to diagnosis and optimized therapy by circumventing the long waiting lists associated with MRI imaging that plague the Canadian healthcare system. For PsA, a diagnostic delay of more than 6 months is associated to irreversible joint damage and poor functional outcomes.

Imaging phenotypes in PsA:
Can ultrasound help us individualize care?

For this project, Dr. Gutierrez studied 135 patients with active PsA who were about to start treatment. Information from the physical exam, such as swollen or tender joints and the presence of enthesitis and dactylitis, was collected. Inflammatory markers from the blood were measured along with patient-reported outcomes. We performed a comprehensive ultrasound evaluation of multiple joints and tendons to accurately assess the location and severity of inflammation.

The study found a disagreement between patients’ clinical manifestations and ultrasound findings of inflammation. The most consistent agreement with ultrasound findings were swollen joints and the presence of synovitis (inflammation of the synovium lining the joint) and peritenonitis (inflammation of a tendon and its sheath). The least consistent agreement were with patients’ reported pain levels with all ultrasound features. The results of this study indicate that disagreement between clinical features and ultrasound domains in PsA exists. Ultrasound can improve the accuracy of estimation of disease activity in PsA.
Dr. Lihi Eder
- Emerging Investigator Award 2023, Canadian Rheumatology Association
- Invited member of Task Force - EULAR Treatment Recommendations 2023
- Appointed as President of the Canadian Rheumatology Ultrasound Society (2022)
- Institute of Medical Science Faculty Recognition Award for Strong Citizenship, University of Toronto

Dr. Sahil Koppikar
Early Career Rheumatologist Award, Ontario Rheumatology Association
Young Clinician Award, Department of Medicine, Women's College Hospital

Dr. Jessica Gutierrez Manjarrez
Best Poster Award, 2023 GRAPPA Annual Meeting and Trainee Symposium

Steven Dang, MSc Student
2023 Pilot Research Grant Recipient, GRAPPA (Mentor: Dr. Lihi Eder)
Best Project, Joint Oxford & Toronto Symposium in Musculoskeletal Sciences

Podium Presentation:


Ignite Poster:

Posters:


77th Annual Meeting of the Canadian Rheumatology Association
Quebec City, Quebec, Canada, February 8–11, 2023


Podium Presentation:

Posters:
Colaco et al. Sex-Related Measures of Inequity in Randomized Controlled Trials in Psoriatic Arthritis: A Systematic Literature Review and Meta-analysis.

Podium Presentation:
Eder et al. Sex differences in perceptions of psoriatic arthritis disease impact, management and physician interactions: Results from a global patient survey.

Posters:


Eder et al. Sex-Related Measures of Inequity in Randomized Controlled Trials in Psoriatic Arthritis: A Systematic Literature Review and Meta-analysis.
Publications (2022-2023)


Thank you for standing with us on this important cause.
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