The Krembil

November 2023

The Krembil is the official newsletter of the Krembil Research Institute, highlighting recent news and awards, innovative research and exciting events happening at Krembil. For more information, visit www.discoverkrembil.ca.

Stories in this month's issue:

Jaideep Bains, PhD
Director, Krembil Research Institute
University Health Network

News

Reaching Our North Star

The 2023 UHN Research Report focuses our ambition on Our North Star—creating A Healthier World.

The 2023 report features discoveries and achievements from across UHN's research institutes and foundations: (pictured clockwise) Drs. Michael LaFlamme and Stephanie Protze (Senior Scientist and Scientist, McEwen Stem Cell Institute), staff from project UHN Cares, two students from Dr. Tony Lam's lab (Senior Scientist, Toronto General Hospital Research Institute), Dr. Anastasia Tikhonova (Scientist, Princess Margaret Cancer Centre Research), Dr. Mojgan Hodaie (Senior Scientist, Krembil Research Institute), and Dr. Tatyana Mollayeva (Scientist, KITE).

November 10 marks the annual World Science Day for Peace and Development, a day to celebrate the importance and impact of science in our everyday lives. In recognition of this day, UHN is proud to announce the launch of the 2023 UHN Research Report, Reaching Our North Star.

This year's World Science Day theme, Building Trust in Science, highlights the impact of trust in shaping science perception and strengthening science-based policy. As the world continues to struggle with pressing healthcare challenges, more trust is put on the promise of science to deliver safe and transformative solutions.

Our North Star—Creating A Healthier World—is a vision that unifies TeamUHN by creating a common purpose, strengthening trust, collaboration and determination to empower researchers to push the boundaries of knowledge and take on some of the world's most complex challenges.

With the launch of our 2023 UHN Research Report, we showcase the transformative power of UHN's breakthroughs that echo worldwide. Through a dynamic multimedia website, this year's research report features research advancements, milestones, awards and other highlights from across UHN's research institutes, including the following:

● KITE researchers investigate the impact of traumatic brain injury on patients, caregivers and their relationships, emphasizing the importance of inclusive rehabilitation and gender-sensitive care for enhanced recovery outcomes.

● Artificial intelligence is helping Krembil Research Institute scientists unveil the connections between chronic pain conditions and accelerated brain aging.

● A McEwen Stem Cell Institute project was awarded $23.6M to transform the landscape of heart disease therapies.

● Cancer researchers from the Princess Margaret Cancer Centre explore critical factors in cancer development and treatment effectiveness.

● A Toronto General Hospital Research Institute team unlocks the key to weight loss and obesity therapies.

● Researchers at The Institute for Education Research launch a mental health support program, UHN CARES, in response to heightened stress and demanding conditions faced by healthcare workers during the COVID-19 pandemic.

The report also highlights how we have engaged tens of thousands of listeners through our award-winning, science-focused podcasts and recaps the generous support of our donor community, facilitated by the dedicated teams at UHN Foundation and The Princess Margaret Cancer Foundation.

All of these achievements would not have been possible without our partners at the University of Toronto, non-profit organizations, the private sector, the government and our foundations.

Join us as we reflect on a year of remarkable achievements and look ahead to forging a path to a boundless future.

Click here to read the full report. Previous reports can be found here.

A Royal Tour

UHN welcomes its Patron Her Royal Highness, The Duchess of Edinburgh, for a three-day tour.

(Clockwise from top-left) Her Royal Highness, The Duchess of Edinburgh in an intimate reception with UHN staff, visiting with frontline health care workers, visiting with patients, and touring Toronto General Hospital with UHN President & CEO Dr. Kevin Smith, UHN Foundation Chair Raj Kothari and The Honourable Elizabeth Dowdeswell, Lieutenant Governor.

On November 6–8, University Health Network had the privilege of hosting its Patron Her Royal Highness, The Duchess of Edinburgh, for a three-day tour of Toronto General Hospital, Toronto Western Hospital and Toronto Rehab.

Her Royal Highness met with frontline health care workers, researchers, staff and patients to learn about medical and scientific innovation across UHN. Discussions covered the latest advancements in emergency and social medicine, cardiovascular care and physical rehabilitation, and vision, arthritis and brain research.

On the first day of the royal tour, Her Royal Highness visited the Michael Lawrence Turk Emergency Rapid Assessment Centre, which has served more than 37,000 patients since its inception in 2022. She also visited the Peter Munk Cardiac Centre, a leading institute in cardiac and vascular care.

(Clockwise from left) Her Royal Highness, The Duchess of Edinburgh testing a virtual reality system at the Donald K. Johnson Eye Institute, touring the Krembil Discovery Tower with UHN Foundation Chair Raj Kothari and The Honourable Elizabeth Dowdeswell, Lieutenant Governor, and at a ribbon cutting for the Peter Gilgan Program in Neuroregeneration Research at the Krembil Research Institute.

On the second day, Her Royal Highness visited Toronto Western Hospital, where she toured the Donald K. Johnson Eye Institute's Clinical Research Unit.

There, she met with internationally recognized research teams that are shaping our understanding of the visual system and developing novel approaches to treat vision loss. She even tried on a virtual reality headset in Dr. Michael Reber's lab, while learning about his research into the use of virtual reality in rehabilitation for people living with low vision.

Her Royal Highness also shared her passion for medical innovation with research teams at the Schroeder Arthritis Institute, where she learned about the Psoriatic Arthritis Program and the impact of Dr. Dafna Gladman's work.

At the Krembil Brain Institute, she learned about stem cell research conducted in Dr. Michael Fehlings' lab and took part in a ribbon-cutting ceremony for the Peter Gilgan Program in Neuroregeneration Research.

Her Royal Highness also learned about the new 15-storey surgical tower under construction at Toronto Western Hospital. The tower will push boundaries in research

and clinical practice across UHN, with 20 operating rooms, and technology to incorporate real-time imaging and artificial intelligence into patient care and education.

(Clockwise from left) Her Royal Highness, The Duchess of Edinburgh testing DriverLab, getting a tour of KITE's state-of-the-art simulation research spaces and visiting with a patient at Toronto Rehab.

On the last day of her visit, Her Royal Highness visited Toronto Rehab and the KITE Research Institute. She toured the physiotherapy gym where she met patients and health care workers and witnessed various rehabilitation techniques. She also tried the reactive balance training frame and harness in the Movement Evaluation Laboratory—a system built to improve the control of movement and mobility, especially among people recovering from stroke and brain injury.

At KITE, Her Royal Highness learned about the multidisciplinary research teams that are developing products, practices and policies to improve the lives of people living with disability and illness, and support healthy aging.

She enjoyed guided tours of DriverLab—Canada's most advanced driving simulator—WinterLab and StreetLab, and took part in the ribbon-cutting for the Schroeder Pain Assessment and Rehabilitation Research Clinic.

"Having been Patron of Toronto General and Toronto Western hospitals since 2005, I've seen over many years how they are always moving health care forward while continuing to put communities first," said Her Royal Highness. "On this visit it was fascinating to

hear how they are using advancements in research and technology to enhance patient care and the exciting opportunities this offers for the future."

Throughout her visit, Her Royal Highness met with some of UHN's prominent donors and volunteers, whose generous philanthropy and support enhances research, care and education and helps us build *A Healthier World*.

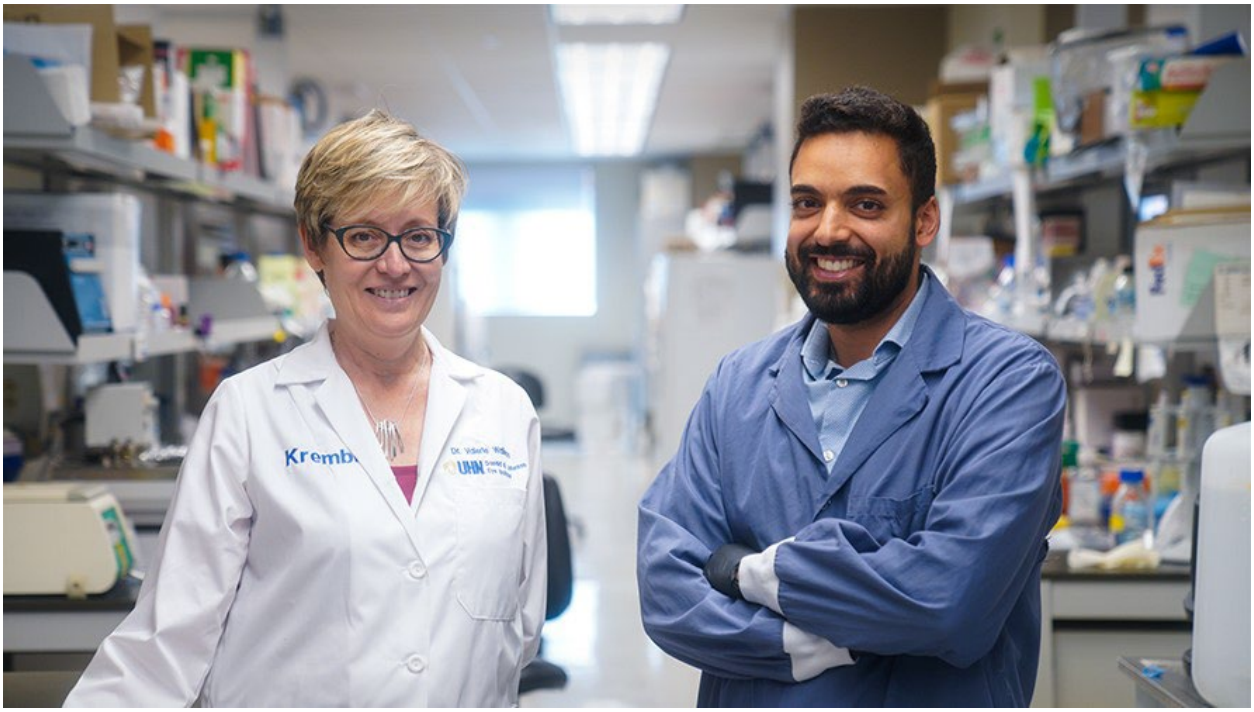
Addressing donors, she remarked with gratitude, "You are making things change for people. This is change for community. It's change for good."

UHN is grateful for Her Royal Highness' continued support and it was an honour to host her!

Research

Everything in Its Place

Study uncovers processes that govern the arrangement of light-sensitive cells in the retina.



(L-R) Dr. Valerie Wallace, Co-Director and Senior Scientist at the Donald K. Johnson Eye Institute, and Dr. Akshay Gurdita, a postdoctoral researcher in Dr. Wallace's lab.

Researchers at UHN's Donald K. Johnson Eye Institute (DKJEI) have identified key processes that guide the positioning of light-sensitive cells in the retina—the neural tissue that lines the back of the eye.

All brain functions, from thinking and feeling to controlling the body's movements, hinge on precise communication between neurons. To communicate effectively, neurons must migrate to particular positions and connect with nearby cells to form specialized circuits.

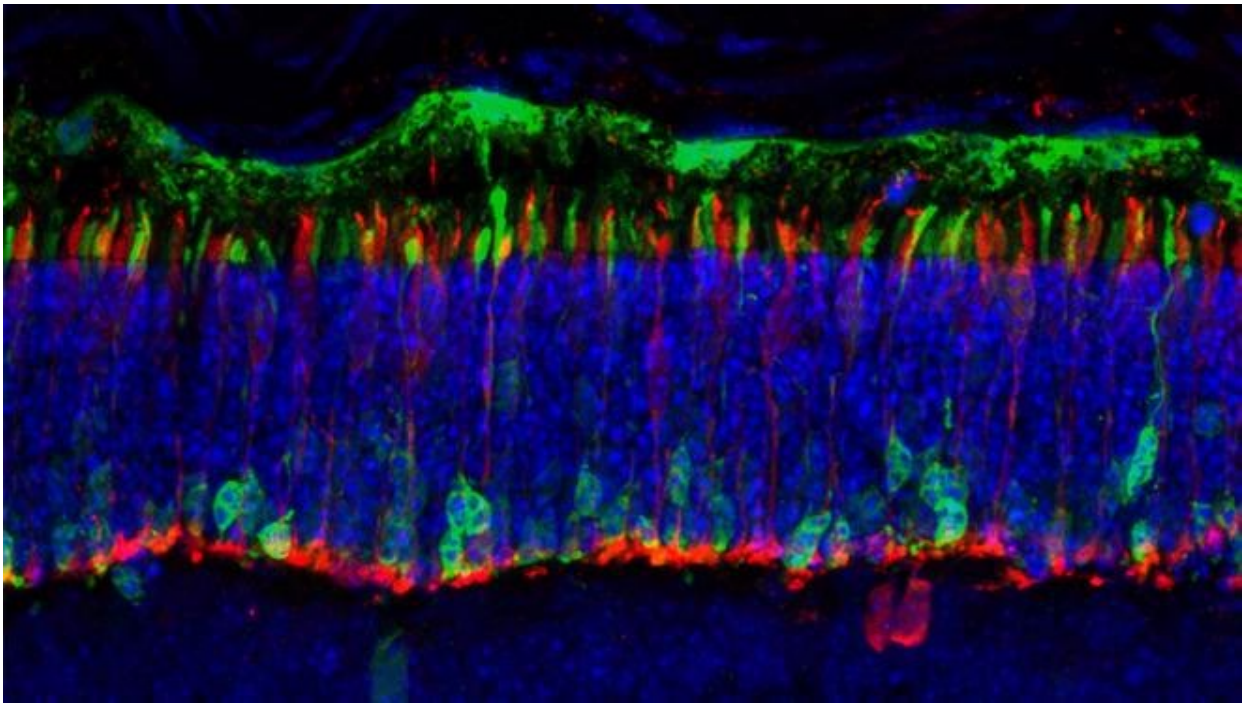
A fundamental question in neuroscience is how neurons find their place and form neural circuits—and how this process goes astray, leading to disease.

In a study published in *Proceedings of the National Academy of Sciences*, researchers led by DKJEI Co-Director and Senior Scientist Dr. Valerie Wallace explored the mechanisms underlying neural circuit formation in the retina.

“The human brain has billions of neurons, so it is extremely challenging to study, at the single-cell level, how circuits form and change over time,” explains Dr. Wallace. “The retina, an extension of the brain, has a much simpler structure, wherein different cell types reside in distinct layers. This arrangement makes it easy to pinpoint when cells are out of place.”

To clarify the factors that govern circuit formation, Dr. Wallace’s team studied how light-sensitive cells called photoreceptors migrate and connect with other cells during development. The team was particularly interested in rod photoreceptors—a type of neuron that responds to dim light.

The researchers used techniques that label individual cells to track the location and behaviour of rods in response to changes in the activity of genes that are involved in cell development and migration.



Looking at the photoreceptor layer of the retina under a microscope is like looking at a dense forest where it is difficult to pick out individual trees. The team used fluorescent markers to tag and study the location and behaviour of individual rods. Pictured: a microscopy image of the retina with tagged rod photoreceptors shown in green.

“When we started this project, we likened the photoreceptor layer to a cobblestone street—all the stones are identical, and you can assemble the street by adding stones

from any direction," says Dr. Akshay Gurdita, a postdoctoral researcher in Dr. Wallace's lab and the lead author of the study. "But we learned that this layer is more like a brick wall, with younger photoreceptors added on top of older ones."

The team also discovered that all rods start at the top of the layer and move downwards over time.

This movement is guided by two factors. Initially, younger cells push older cells downwards as they jostle for space. Then, each cell moves to its final position as it matures and connects with other cells. If either of these processes is disrupted, photoreceptors fail to position properly.

"Our findings highlight the importance of two factors for determining rod positioning: those that are inherent to the cell itself—namely, maturation and the process of wiring with other cells—and those that are external to the cell—namely the proliferation of new cells and resulting space constraints," explains Dr. Gurdita.

The team's findings have implications for developing cell-based therapies to treat neuron loss and restore vision.

Several research teams, including Dr. Wallace's group, are exploring photoreceptor transplantation as a treatment for retinal degeneration. Unfortunately, progress in this area has been limited by transplanted cells failing to integrate into the recipient retina.

"Our findings are very exciting because they point us to processes that we can target to coax donor cells to form functional connections with host cells," says Dr. Wallace. "If we transplant more mature cells that are ready to form connections or modify the cells and chemical signals that are present in the host retina, we might be able to improve cell integration and restore vision."

"Eventually, we might also be able to measure donor cell maturation and connectivity to predict the success of a cell transplantation, before vision changes occur," adds Dr. Gurdita.

This work was supported by the Canada First Research Excellent fund-Medicine by Design University of Toronto, the Natural Sciences and Engineering Research Council of Canada, the Government of Ontario, the UofT-UHN Vision Science Research Program, the Ontario Institute for Regenerative Medicine, Foundation Fighting Blindness Canada, the Krembil Research Institute, Krembil Foundation and UHN Foundation. Dr. Valerie Wallace is a Professor in the Department of Ophthalmology and Vision Sciences and holds a Tier I Canada Research Chair in Retina Regeneration at the University of Toronto.

Gurdita A, Pham Truong VQB, Dolati P, Juric M, Tachibana N, Liu ZC, Ortín-Martínez A, Ibrahimi M, Pokrajac NT, Comanita L, Pacal M, Huang M, Sugita S, Bremner R, Wallace VA. Progenitor division and cell autonomous neurosecretion are required for

rod photoreceptor sublaminar positioning. Proc Natl Acad Sci U S A. 2023 Oct 17;e2308204120. doi: 10.1073/pnas.2308204120. Epub 2023 Oct 9.

Dr. Akshay Gurdita working in the Wallace Laboratory.

Matters of the Brain

Study reveals potential link between structural brain changes and neuropsychiatric symptoms.

(L-R) Dr. Carmela Tartaglia, senior author of the study, and Miracle Ozzoude, first author of the study.

Researchers at the Krembil Brain Institute have uncovered links between structural changes in the brain and neuropsychiatric symptoms of various neurodegenerative diseases.

Neuropsychiatric symptoms, such as depression, anxiety and hallucinations, can pose a tremendous burden for people living with neurodegenerative diseases, as well as their families and care partners.

A research team led by Dr. Carmela Tartaglia, a Clinician Investigator and cognitive neurologist at the Krembil Brain Institute, set out to clarify the neural basis of these symptoms and how they differ across conditions, including Alzheimer disease and Parkinson disease.

The researchers analyzed brain imaging and clinical data from more than 510 adult men and women who participated in the Ontario Neurodegenerative Disease Research Initiative—a program focused on advancing our understanding of neurodegenerative diseases to improve diagnosis, treatment and health outcomes.

They found that neuropsychiatric symptoms were common across all conditions studied, with depression being the most prevalent. The highest symptom burden was seen in frontotemporal dementia—a group of disorders that primarily affect brain areas involved in cognition, memory, emotional control and other complex behaviours.

They also found that neurodegenerative conditions had distinct symptom profiles. For example, anxiety was more common among people with frontotemporal dementia, whereas symptoms of psychosis, such as hallucinations, were more common in people with Parkinson disease.

In parallel, the team examined how these symptoms relate to changes in brain structure.

Most studies of neurodegenerative diseases focus on the impact of brain shrinkage, but these conditions are also commonly linked to abnormalities in the brain's white matter—the bundles of nerve fibres that connect different brain regions.

"White matter changes warrant further investigation because they can indicate cerebrovascular disease—a condition that disrupts blood flow in the brain, such as stroke—which can play a role in neurodegeneration," explains Miracle Ozzoude, a former Research Analyst in Dr. Tartaglia's lab and the first author of the study.

Upon analyzing their imaging data, the researchers discovered a stronger link between symptom burden and brain shrinkage across all conditions studied. Additionally, the team identified subtle links to changes in white matter.

"This is an important development because it suggests that cerebrovascular disease might be a contributing factor to neuropsychiatric symptoms," says Mr. Ozzoude. "However, more research is needed to confirm the exact impact of white matter changes on these symptoms."

Given that cerebrovascular disease is preventable, this finding suggests that implementing lifestyle changes, such as diet, exercise and medications that improve blood flow, could help reduce symptom burden and enhance quality of life.

Due to their high prevalence across neurodegenerative diseases, Dr. Tartaglia stresses the importance of studying neuropsychiatric symptoms in future research. "These symptoms are often responsible for patient institutionalization and caregiver burnout. Learning more about their presence and severity can provide valuable insights into the disease processes occurring in the brain."

This work was supported by the Ontario Brain Institute, the Baycrest Foundation, the Bruyère Research Institute, the Centre for Addiction and Mental Health Foundation, the London Health Sciences Foundation, the Faculty of Health Sciences at McMaster University, the Brain and Mind Research Institute and the Faculty of Medicine at the University of Ottawa, the Faculty of Health Sciences at Queen's University, the Thunder

Bay Regional Health Sciences Centre, the Sunnybrook Health Sciences Centre, the Windsor-Essex County ALS Association, the Temerty Family Foundation and UHN Foundation. Dr. Carmela Tartaglia is the Marion and Gerald Soloway Chair in Brain Injury and Concussion Research, Director of the Memory Clinical Trials Unit and a Cognitive Neurologist at UHN. She is also an Associate Professor at the Tanz Centre for Research in Neurodegenerative Diseases at the University of Toronto. Miracle Ozzoude is a PhD student at the University of Edinburgh and a former Research Analyst in Dr. Tartaglia's lab.

Ozzoude M, Varriano B, Beaton D, Ramirez J, Adamo S, Holmes MF, Scott CJM, Gao F, Sunderland KM, McLaughlin P, Goubran M, Kwan D, Roberts A, Bartha R, Symons S, Tan B, Swartz RH, Abrahao A, Saposnik G, Masellis M, Lang AE , Marras C, Zinman L, Shoesmith C, Borrie M, Fischer CE, Frank A, Freedman M, Montero-Odasso M, Kumar S, Pasternak S, Strother SC, Pollock BG, Rajji TK, Seitz D, Tang-Wai DF, Turnbull J, Dowlatshahi D, Hassan A, Casaubon L, Mandzia J, Sahlas D, Breen DP, Grimes D, Jog M, Steeves TDL, Arnott SR, Black SE, Finger E, Rabin J, ONDRI Investigators, Tartaglia MC. White matter hyperintensities and smaller cortical thickness are associated with neuropsychiatric symptoms in neurodegenerative and cerebrovascular diseases. Alzheimers Res Ther. 2023 Jun 20. doi: 10.1186/s13195-023-01257-y.

Brain imaging techniques, such as magnetic resonance imaging (MRI), can reveal changes in the brain associated with neurodegenerative diseases.

Advancing Arthritis Research

Scientists facilitate osteoarthritis research with detailed analysis of patient data.

(L-R) Dr. James Young, a Postdoctoral Researcher in Integrated Arthritis Care at the Schroeder Arthritis Institute, and Dr. Michael Zywiel, a Clinician Investigator at the Schroeder Arthritis Institute and an Orthopedic Surgeon at Toronto Western Hospital.

Researchers at the Schroeder Arthritis Institute have compiled a comprehensive overview of people living with knee and hip osteoarthritis (OA), aiming to create a valuable resource for global research and clinical progress.

OA, the most prevalent form of arthritis, arises as joint cartilage deteriorates. There is currently no cure or treatment that can slow disease progression. Available interventions include medications and, in severe cases, surgery to alleviate symptoms, such as pain and inflammation.

“The key with treating OA is intervening early, and helping patients manage their symptoms before they become debilitating,” says Dr. Michael Zywiel, a Clinician Investigator at the Schroeder Arthritis Institute and senior author of the study. “Although education and exercise are important parts of non-surgical care of knee and hip OA, access to structured and evidence-based care has been a challenge, negatively impacting patient care and outcomes.”

Addressing this gap, the University of Southern Denmark introduced the Good Life with osteoArthritis in Denmark (GLA:D®) program in 2013, a treatment program that combines exercise and education.

The GLA:D® program is targeted to people with mild to severe hip and/or knee OA and is a safe, cost-effective approach to improving pain, walking function and quality of life. Based on the program's success in Denmark, it has been implemented by several other countries, including Austria, China, Switzerland and Canada.

With the help of researchers from the Schroeder Arthritis Institute, the GLA:D® Canada program was launched in 2017 by Bone and Joint Canada. GLA:D® Canada closely mirrors the Denmark program, including the development of a patient outcomes registry.

"Now that GLA:D® Canada has operated for over five years, we are in a good position to use this program and its outcomes to guide future OA research," says Dr. Zywiel, who is also a Primary Investigator for the GLA:D® Canada Registry. "However, an important first step is to provide the OA research community with a comprehensive description of the participants who pursue education and exercise-based treatment of hip and knee OA in Canada."

To analyze this data, Dr. Zywiel's team summarized the sociodemographics (e.g., age and body mass index), clinical profiles (e.g., medical conditions and physical activity levels) and health status (e.g., pain intensity and joint function) of approximately 10,000 participants with hip and knee OA. The team collected this information through surveys that participants completed before starting and during the GLA:D® program.

"We identified several common characteristics of people who participate in the program, which will be useful for researchers when designing studies and recruiting patients," says Dr. James Young, a Postdoctoral Researcher in Integrated Arthritis Care working with Dr. Zywiel, and the lead author of the study.

Their findings revealed that participants were predominantly female, averaging 66 years old and overweight or obese. Of these, two-thirds relied on pain medications and one-third considered joint surgery. Participants reported an average pain intensity of 5 out of 10 and activity levels averaged four days per week.

"Our results indicate that people who participate in the GLA:D® program in Canada are similar to those in Denmark and Australia," explains Dr. Young, who is also on the leadership team for the GLA:D® International Network. "This similarity opens avenues for bridging international datasets and comparing data from multiple GLA:D® registries."

These approaches will be important for studying program outcomes in a real-world setting, such as the effects of the program on health status, non-surgical outcomes and the need for joint replacement surgery, as well as barriers to therapy uptake.

“The Schroeder Arthritis Institute has been instrumental in implementing the GLA:D® program in Canada and we are excited for the potential to use the GLA:D® registry to tackle big questions in the field,” concludes Dr. Zywiel.

This work was supported by UHN Foundation. Dr. Michael Zywiel is an Assistant Professor of Surgery at the University of Toronto.

Dr. Michael Zywiel has been a paid consultant to Smith and Nephew, DePuy Synthes, Johnson & Johnson, ZimmerBiomet and OPEXC Inc. Co-author Dr. Christian Veilette has served as a paid consultant, board member or received research support from Zimmer Biomet, CODMAN Group, DePuy Synthes, Orthogate, Orthopaedic Web Links, OrthopaedicsOne, and Smith and Nephew. Co-author Dr. Rhona McGlasson is the National Director of GLA:D® Canada and Executive Director of Bone and Joint Canada.

Young JJ, Perruccio AV, Veillette CJH, McGlasson RA, Zywiel MG. The GLA:D® Canada program for knee and hip osteoarthritis: A comprehensive profile of program participants from 2017 to 2022. PLoS One. 2023 Aug 3. doi: 10.1371/journal.pone.0289645.

Common symptoms of knee and hip OA include pain while walking, joint stiffness and reduced flexibility.

Optimal Sleep, Faster Recovery

Habitual short sleepers may be at an increased risk of developing long COVID.

(L-R) Drs. Frances Chung, Krembil Clinician Investigator, and Linor Berezin, Anesthesiology Resident at the University of Toronto.

A recent study led by researchers at the Krembil Brain Institute suggests that short sleep duration may contribute to the development of persistent symptoms of COVID-19, particularly in people with pre-existing medical conditions.

Most people recover fully from COVID-19, but a significant percentage experience lasting symptoms, such as difficulty breathing, fatigue, sleep problems and brain fog. The persistence of these symptoms for more than two months after a person recovers from the acute illness is called post-COVID condition or long COVID.

“Despite nearly 40% of patients going on to experience long COVID, there are still a lot of unknowns about the condition, including what makes one person more susceptible than another,” says Dr. Frances Chung, a Clinician Investigator at the Krembil Brain Institute and ResMed Chair in Anesthesia, Sleep and Perioperative Medicine Research at UHN.

Preliminary evidence suggests that pre-existing medical conditions, including chronic obstructive pulmonary disease (COPD), heart disease and diabetes, increase one’s risk of developing long COVID.

This evidence, together with the known importance of sleep for immune system function, led Dr. Chung to explore whether the odds of developing long COVID are higher among people who have chronic health conditions and whether the impact of these conditions is influenced by sleep duration.

Using an online survey, Dr. Chung's team collected data from 13,461 adult men and women in 16 countries, 2,508 of whom reported having COVID-19. Of the 1,505 people who reported experiencing long COVID, 945 had at least one chronic medical condition before the pandemic.

The team found that, among people with pre-existing conditions, average sleepers (those who regularly slept for six to nine hours per night) had a 1.8-fold higher risk of developing long COVID; while habitual short sleepers (those who regularly slept for less than six hours per night) had a 3-fold higher risk compared to healthy average sleepers. Interestingly, despite having similar pre-existing conditions, habitual long sleepers (those who regularly slept for more than nine hours per night) did not have an increased risk of long COVID.

"Our findings suggest that not getting enough sleep may increase susceptibility to long COVID among people with pre-existing health conditions," explains Dr. Linor Berezin, an anesthesiology resident at the University of Toronto and the first author of the study. "This could be due to the detrimental effects of sleep loss on immune responses, such as impaired immunity against pathogens and increased release of inflammatory molecules."

"Although the proportions of people with pre-existing conditions were generally similar among short, average and long sleepers, we saw that heart conditions were most common among short sleepers," cautions Dr. Berezin. More research is needed to determine whether the higher prevalence of this condition among short sleepers underpins the team's observations.

Nonetheless, these findings have important implications for preventing long COVID. "Insufficient sleep is a risk factor that we can change," says Dr. Chung. "Encouraging at-risk individuals to regularly get a sufficient amount—ideally seven to nine hours— of nighttime sleep is an easy, cost-effective approach to reducing the prevalence of long COVID."

This work was supported by the Ontario Ministry of Health Innovation, the ResMed Foundation, the Wellcome Trust, the National Institute for Health and Care Research, and UHN Foundation.

Berezin L, Waseem R, Merikanto I, Benedict C, Holzinger B, De Gennaro L, Wing YK, Bjorvatn B, Korman M, Morin CM, Espie C, Landtblom AM, Penzel T, Matsui K, Hrubos-Strøm H, Mota-Rolim S, Nadorff MR, Plazzi G, Reis C, Chan RNY, Cunha AS, Yordanova J, Bjelajac AK, Inoue Y, Dauvilliers Y, Partinen M, Chung F. Habitual short

sleepers with pre-existing medical conditions are at higher risk of Long COVID.(link is external) *J Clin Sleep Med. 2023 Oct 3. doi: 10.5664/jcsm.10818*

Symptoms of long COVID include fatigue, persistent cough, muscle aches and cognitive dysfunction, among others. Getting an optimal amount of good-quality sleep may reduce one's risk of developing the condition.