PULMONARY HYPERTENSION ASSOCIATION OF CANADA
L'ASSOCIATION D'HYPERTENSION PULMONAIRE DU CANADA

CONNECTIONS

The Official Magazine of the Canadian PH Community

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Special Issue: Zooming In on PH Research in Canada

PULMONARY HYPERTENSION ASSOCIATION OF CANADA
L'ASSOCIATION D'HYPERTENSION PULMONAIRE DU CANADA

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Unless otherwise noted, all of the photographs in this issue were contributed by authors or by PHA Canada.

In this Issue:

Message from the Chair:
Tragedies and Advances in Pulmonary Hypertension

PH was first described medically more than 100 years ago. Since its first appearance in medical textbooks, PH has always been characterized as a serious illness, often incapacitating, usually progressively worse, and, unfortunately, fatal in many of the patients affected.

As many of you already know, the global medical PH community has made tremendous progress in the field, especially over the past 40 years. First, early advances in PH stemmed from extensive basic science research into the lungs and cells of people and animals with the disease. This work gave us a better understanding of what is wrong in the pulmonary arteries (blood vessels that carry blood to and through the lungs) in PH patients. Second, research has focused on why PH patients develop weakness and failure of the right-side of the heart, specifically of the right ventricle (RV). This RV failure is one of the most important clinical features of PH, as the degree of RV failure in each PH patient determines how sick that patient is and how long they are likely to survive. Finally, over the past 25 years, clinical research has directly studied the potential benefits of many new PH-targeted medications. Clearly, all types of research have been, and are still, crucial in order to make progress in a disease like PH.

Perhaps most importantly to PH patients and their caregivers, this research has led to the evaluation, development, and Health Canada-approval of 10 different PH medications. Canadian PH patients have benefitted greatly from these advances; they are now living better lives, experiencing fewer symptoms, and enjoying a greater ability to be active socially and recreationally. Progress made in the treatment of PH has a direct impact on patients' everyday lives and their interactions with their family, friends, and communities. Although a diagnosis of PH is still devastating, today Canadian patients have a better quality of life and are living much longer than ever before. Average survival has improved for the most severe types of PH, going from an average of two years to more than 10 years in some patients.

Unfortunately, despite the wonderful advances in the diagnosis and treatment of PH, many patients remain very ill, are limited in their everyday lives, and will eventually die of right ventricular failure or other consequences of the disease. As such, there is often still much sadness in our community. This sadness and grief has recently devastated PHA Canada, as two of our own Board members, Lynn-Marie Cox and Harry Kingston, lost their personal battles with PH. Despite the sadness, we choose to focus on the amazing lives they lived and their contributions to PHA Canada and the Canadian PH community. We celebrate the incredible 20 years that Lynn-Marie lived with PH, as well as her and Harry's dedication to fostering PHA Canada's mission!

We want all PH patients to benefit from such long, phenomenal lives, and one day perhaps even have access to a cure. As such, we clearly need ongoing research into PH. This is why PHA Canada is proud to have made a strong commitment to support PH research in Canada by awarding three Paroian Family PH Research Scholarships and an initial Mohammed Family PH Research Scholarship over the past two years.

In this issue of *Connections*, you will learn much more about exciting PH research in Canada, past and present, and its promises for the future. The goals of PH research are clear: better understand why patients develop PH; find new, better treatments to improve the lives of patients; and maybe one day, even find a cure.

Sanjay Mehta, MD, FRCPC, FCCP
Director, Southwest Ontario PH Clinic
LHSC—Victoria Hospital, London, ON
Chair, Board of Directors, PHA Canada

Message from the Executive Director:
Commited to Keeping You Informed and Connected

A diagnosis of pulmonary hypertension is a gateway to a whole new world of specialized information and knowledge. Along with learning a bunch of new medical jargon—or trying to figure out how treatments are approved and funded—it can feel impossible to "keep up" with what's happening in PH research.

We understand that having access to clear, accurate information about research advancements is important to PH patients and their loved ones. Therefore, we are very pleased to share with you this special issue of *Connections*, with a focus on Canada's rapidly evolving PH treatment landscape (pages 16-26). Later this year, we look forward to also sharing new resources on our website to help the community stay informed about research activities taking please in the country, including updates from PHA Canada's own research scholarship recipients.

The opportunity to share research and treatment updates with the PH community is one of the things that makes *Connections* magazine so important. It provides a valuable space for us to inform, support, and celebrate one another, and PHA Canada is committed to making this high-quality publication widely available to the whole community. To help make it easier for community members to receive *Connections*—and thus stay engaged with PHA Canada—membership will no longer be required in order to have the magazine sent to you directly. Instead, we have eliminated individual and family membership dues and PH patients/primary caregivers will now be eligible for a free lifetime subscription to *Connections*. To sign up for your free or paid subscription, complete the form included in your magazine or visit us online at: www.phacanada.ca/connections.

At the heart of *Connections* are your stories of strength, determination, and love. I find it fitting that in the same issue that we celebrate the hope offered by new research, we also celebrate many inspiring PHighters whose contributions also fill us with optimism for the future. We begin by commending the hard work and dedication of our community fundraisers (pages 6–8), who have raised almost $50,000 in support of PHA Canada's programs, services, and research scholarships so far this year! Next we pay tribute to two important community leaders retiring this year: Pediatric Cardiologist, Dr. Ian Adatia, and PHA Canada Pediatrics Committee Chair, Sarah Platnar (page 9). Finally, we remember three dear PHriends and colleagues recently lost to PH and honour the important role they played as members of PHA Canada's Board of Directors (pages 32–33).

We hope you will enjoy this newest issue of *Connections* and that it prompts you to send us your new subscription without delay! If you were looking forward to renewing your membership in order to ensure delivery of next year's magazine, I invite you to instead consider making a tax-deductible donation to PHA Canada at www.phacanada.ca/donate. As a registered charity—accredited by Imagine Canada since 2015—we rely on the generosity of our supporters to develop and deliver our programs and services, including *Connections* magazine. Your gift helps us ensure that everyone affected by PH in Canada is able to stay connected to an empowered and united PH community.

Jamie Myrah
Executive Director, PHA Canada

A New Look for *Connections*!

Connections is one of PHA Canada's most important publications. Over the years, we have worked to expand the scope and quality of the magazine's content to better inform our community, represent its diversity, and take an in-depth look at the issues affecting its members. As part of our efforts to continually improve upon our resources, we are excited to share a brand new look for *Connections*.

Led by our Communications and Engagement Manager, Mariane Bourcheix-Laporte, with support from our Summer Communications Assistant, Emily Johnston, the magazine has been completely redesigned. Taking into account our community's input, they have given *Connections* a fresh, clean, and contemporary new look. It is now easier to navigate through the magazine's content and engage with its feature stories and articles. We hope you enjoy this new reading experience!

For Every Season There Is an Event:

Winter, Spring, and Summer Community PHun

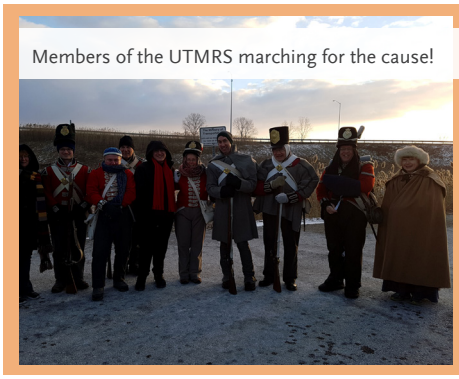
Every season is filled with special moments to enjoy: magical snowstorms in winter, gardening sessions in spring, and long sun-filled afternoons in summer. Each season also brings new events to the PH community's calendar, presenting various opportunities for PHighters to raise awareness and come together to celebrate the progress being made with every passing day.

In the last months, the Canadian PHamily's calendar has been filled with awareness and fundraising activities! Here's an overview of community events that took place between March and September 2017. Thank you to all the organizers, participants, volunteers, donors, and sponsors who contributed to making each event a PHantastic success!

10- and 20-Mile March in Honour of Everleigh Pierce

(March 4th, Mosa Township, ON)

Winter was still going strong when members of the Upper Thames Military Re-enactment Society (UTMRS) put on their walking boots and tall hats to walk 10 or 20 miles in honour of PHighter Everleigh Pierce. Organized annually by the UTMRS, this event commemorates the 20-mile march conducted by the Royal Scots and 89th Light Companies on March 4, 1814 from Delaware to Battle Hill, Ontario, at the Battle of Longwoods. Thank you to the marchers who braved the cold to raise funds to support our cause!

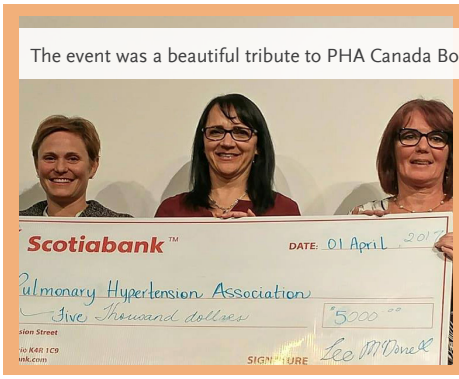


Members of the UTMRS marching for the cause!

PH Awareness Dinner

(April 01st, Russell, ON)

Over 240 supporters from the Ottawa region enjoyed a delicious dinner in Russell, Ontario on April 1st in support of the local PH community. Organized by a passionate group of residents, this benefit dinner and silent auction raised over $31,000 in support of Dr. Duncan J. Stewart's stem cell research at the University of Ottawa Heart Institute, PHA Canada, and local patients! This event was not only a PHantastic fundraiser; it also served as a great occasion to raise PH awareness and honour Harry Kingston's dedication to improving the lives of his fellow PHighters.

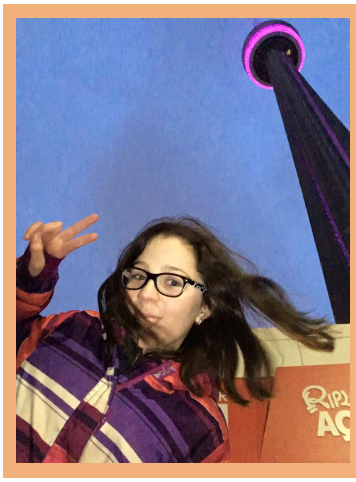


The event was a beautiful tribute to PHA Canada Board Member, Harry Kingston (far right).

The Berdan Family challenges our community to take the *Fear the Pie for PH* challenge!

World PH Day
(May 5th, throughout Canada and internationally)

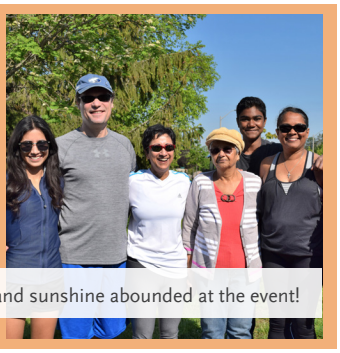
Every spring, the global PH community comes together to celebrate the strength and resiliency of the PH community, as well as developments in the areas of PH research and treatment. In Canada, the 6th Annual World PH Day was marked with the illumination of 11 Canadian monuments for our *Paint Canada Purple for World PH Day* campaign, a special celebration jointly organized by PHA Canada and the Ottawa PH Clinic at the University of Ottawa Heart Institute, and a flurry of periwinkle power demonstrations on social media! Our community also organized a number of fundraisers to mark the day—thank you to the Berdan Family whose *Fear the Pie for PH* challenge was a huge hit, the Castrillon Family who organized a special workout and PH awareness challenge, and Lorna Mulrooney who held a clothing sale in support of our programs and services.



World PH Day was a real demonstration of periwinkle-power!

Fourth Annual Run/Walk for PH Research
(June 10th, Ajax, ON)

On June 10th, 132 supporters came together in Ajax, Ontario to run, walk, or cheer on participants in support of the PH community. This year's event broke its own fundraising record; with upwards of $18,000 raised, the Fourth Annual Run/Walk for PH Research was a PHantastic success! We are grateful to event organizers Renae, Joseph, Judy, and Kam Mohammed for their ongoing support and thank everyone who contributed to the event, including participants, donors, volunteers, and sponsors!



Smiles and sunshine abounded at the event!

GolPH for PH is organized in honour of PHighter Brooke Paulin (far right).

Third Annual GolPH for PH Tournament
(July 13th, Brampton, ON)

The Third Annual GolPH for PH Tournament was a great success! It was a rainy day when golPHers took to the greens in support of the PH community, but that didn't stop participants from having a PHabulous time. Moreover, this year's event raised over $19,000, 50% of which will support our Research Scholarship Program!

Congratulations and thank you to the Paulin Family for organizing this important hole-in-one fundraiser in support of our programs and services. We are also grateful to Unither Biotech Inc., Actelion, and Bayer, for their generous sponsorship of the event.

PHun times on the golf course!

Volleyball Tournament in Memory of Brenden Brinkworth
(September 9th, Long Sault, ON)

This year again, volleyball enthusiasts had the opportunity to gather around a net in support of the Canadian PHamily. Organized by the Brinkworth Family in memory of PHighter Brenden, this year's benefit volleyball tournament was another smashing success, raising $1,600 for the cause!

Thank you to event organizer, Shawna Brinkworth, and the Brinkworth Family for their ongoing support. We are honoured that you pay tribute to Brenden by supporting other PHighters through PHA Canada.

We join the Brinkworths in honouring Brenden's memory.

Tribute to Pediatric PH Pioneers

In the last months, two pediatric PH community leaders have retired from their functions, leaving behind big shoes to fill. In this issue of *Connections*, we take the opportunity to recognize the contributions of Sarah Platnar, outgoing Chair of PHA Canada's Pediatrics Committee, and Dr. Ian Adatia, outgoing Pediatric Cardiologist at the Stollery Children's Hospital Pediatric PH Program (Edmonton, AB). On behalf of the Canadian PH community, thank you for all you have done to better the lives of children living with PH and their families!

Sarah Platnar

For the past three years, I have had the opportunity to work alongside some very talented, committed, and hardworking women in my role as the Chair of the Pediatrics Committee. As a team, we have accomplished much by creating new resources for families of children living with PH, such as the *School Package* and *Tips for Staying Active and Preventing Fatigue*, as well as providing input for the development of other kid-friendly materials. In 2013 and 2015, the Pediatrics Committee also ran programming for families at both the Ottawa and Montreal National Conferences. Most recently, the Committee has developed a video project to further empower and support young people living with PH across Canada by providing them with a platform to share their stories and create awareness.

It has been a real pleasure serving the Committee as Chair and I look forward to continuing my volunteer work as one of its members. On behalf of all the families, I would like to thank the members of the Pediatrics Committee for their tireless work and commitment to supporting children and families living with PH across Canada.

Contributed by: Sarah Platnar, Pediatrics Committee member and mother of a child with PH, Pickering, ON

Dr. Ian Adatia

In 1994, Dr. Ian Adatia established the first pediatric PH clinic in Canada at The Hospital for Sick Children (SickKids) in Toronto. I had the privilege of working with him at the clinic in the early 2000s; he shared his knowledge of PH with me and supported me in my role as a Pediatric PH Nurse Practitioner. In the three years that we worked together, I got to know a brilliant and compassionate person whose mind was always thinking of innovative ways to enhance the care of his patients. For example, he developed a research study that evaluated the effects of an oral therapy in children at a time when the only approved PH medication was intravenous Flolan®. Most importantly, Dr. Adatia always made time for his patients and their families; he listened to them and thoroughly addressed their concerns. Patients and families adored him. After pursuing professional opportunities in San Francisco between 2003 and 2008, Dr. Adatia returned to Canada where he continued to make an impact in the world of PH locally and internationally. He began a pediatric PH clinic at the Stollery Children's Hospital in Edmonton, conducted research, published abundantly, and co-chaired all Neonatal & Childhood Pulmonary Vascular Disease Conferences. Looking ahead, Dr. Adatia will be missed… but looking back, I can speak on behalf of the whole PH community and say: "Thank you, Dr. Adatia, for all that you have done for children with PH and their families. Congratulations and all the best with your retirement!"

Contributed by: Janette Reyes, Pediatrics Committee member and Nurse Practitioner, PH Service, SickKids, Toronto, ON

"Sarah has been an inspirational leader in the PH community for the past several years and her dedication to PHA Canada's Pediatrics Committee is one I have admired. I have been fortunate to get to work with Sarah through the Committee as well as meet her in person at past conferences. I have to say, she is everything in person that I was led to believe just connecting with her on the phone. We are not only Committee colleagues but PHriends, and I look forward to keeping in contact with her as she moves on to tackle new challenges. I have no doubt that wherever Sarah commits her heart to in the future, those she encounters will come to love and admire her as well. Wishing you all the best Sarah!"

—Stephanie Ricci, Pediatrics Committee member and mother of a child with PH, Edmonton, AB

"The love and care we have received from Dr. Adatia since the beginning has made this fearful journey a little less scary. We are very fortunate to have had Dr. Adatia and his team work so hard at making life better for Talitha. Even though I wish we weren't on this journey, I am so grateful it all began with someone as caring and passionate as Dr. Adatia. I would like to thank him for making pediatric PH care his life's work, for never giving up, and for inspiring me to do the same. Dr. Adatia, thank you for sharing your exceptional gift as a doctor, as a mentor, and most importantly as a caring, sincere man. And most of all, THANK YOU from the bottom of our hearts for providing care and treatment to our daughter while gracefully guiding our family through a difficult time. All our love,"

—The Decker Family, Fort McMurray, AB

"I first met Sarah in 2005, the year her daughter, Isabelle, was born. Weathering the medical challenges that her daughter has faced, Sarah has always maintained her composure and a positive, yet realistic, attitude. In 2012, when Dr. Adatia asked me to recommend a parent to be part of PHA Canada's new Pediatrics Committee, I immediately thought of Sarah. She understood her daughter's PH diagnosis and, rather than focus on what Isabelle could not do, Sarah did all she could to help her live each day to the fullest and as normally as possible. Since joining the Pediatrics Committee, Sarah has gone far beyond in her role. I am so proud of her and of her accomplishments in the pediatric PH community over the years; PHA Canada's Pediatrics Committee would not be where it is today if it weren't for Sarah's commitment and dedication. Our relationship has been multifaceted (I am her daughter's healthcare provider, her colleague, and her PHriend) and full of pleasantry—Sarah is kind, thoughtful, patient, and professional. I cannot thank Sarah enough for all the work that she has done to help children with PH and their families."

—Janette Reyes, Pediatrics Committee member and Nurse Practitioner, PH Service, The Hospital for Sick Children, Toronto, ON

Exceptional PHighters

The Canadian PH community is made up of many exceptional PHighters: patients, caregivers, healthcare providers, researchers, and supporters who, individually and collectively, refuse to give up in the face of the many challenges brought on by the disease. Every individual in the PH community has a unique story to tell and can help make a difference in the lives of Canadians affected by PH. We are inspired on a daily basis by our community's generosity, resiliency, creative ideas to raise awareness, novel fundraising initiatives, and passion for finding a cure. We are happy to feature the stories of a few exceptional PHighters whose unwavering commitment to the cause, unique journeys, or remarkable accomplishments deserve the spotlight.

Going the Distance:

Sam Bowker's Story

Sam Bowker has not let PH get in the way of achieving her goal of staying active. Less than two years post-diagnosis, she was able to reignite her love of physical activity by completing a 10-km walk as part of the Oak Bay Half-Marathon (Victoria, BC) and seized the opportunity to raise money in support of PHA Canada!

Sam, after completing her 10 km-walk!

I was diagnosed with PH in November 2015. Prior to receiving my diagnosis, I had visited my family doctor a number of times complaining of chest pain. Finally, after a few visits, he referred me to a cardiologist. I passed all the first tests they did with flying colours, but I kept insisting that something was very wrong so I was referred on to do a stress echocardiogram (stress echo). As soon as the tech doing the stress echo touched the ultrasound wand to my chest, she knew what it was. She told me I had pulmonary hypertension and left the room to ask the on-call cardiologist if she could continue the test. When I left the echo, I was told not to google PH. I did, of course, and was terrified by what I read on the Internet. Thankfully, it didn't take long before I met with the Vancouver PH clinic's medical team, which gave me hope.

I was very active before my diagnosis; I went to the gym almost every day and frequently trained for and ran races. I now find it difficult to be as active as I was because I tire quite easily and often have leg pain from my medications. Obviously, running is no longer an option for me, but I try to focus my attention and energy on what I can do. I can't run but I can walk. I haven't been able to go to the gym as much as I would like, but I have developed a yoga practice—I recently finished my yoga teacher training! I try to celebrate my body as much as I can and be grateful that I am still able to do so much.

I wanted to give back to PHA Canada because the conferences I have attended, *Connections* Magazine, and the organization's Facebook page have helped me feel connected with others and know that I am not alone in my PHight. When I used to race, I would run or walk half-marathons and other events in support of a number of different causes. In the spring, when I was able to participate in a race for the first time since receiving my diagnosis, it made sense for me to use this opportunity to raise funds for PHA Canada.

Walking 10 km at the Oak Bay Half-Marathon on May 28, 2017 was a much bigger challenge than raising money in support of the PH community! I easily created a personal fundraising page through PHA Canada's website and shared the link with my network. People were able to donate online, which was very convenient. I was surprised by how much support I received; my original goal was to raise $500 and I quickly doubled that amount! Amazing!

From now on, I plan on continuing to celebrate my health and what I am able to do every day. I hope that my story inspires others to keep moving forward, reach their goals, and never stop PHighting.

Contributed by: Sam Bowker, PAH patient, Victoria, BC

Where the Purple Saxifrage Blooms:

My Arctic Shoreline Encounters with PH

While every PHighter's journey is unique, certain patients' stories stand out as particularly exceptional. Living in Kugluktuk, Nunavut, an Inuit community of 1,500 bordering the Arctic Ocean, Millie Kuliktana has overcome many challenges that accompany life with PH in one of Canada's most northern communities.

Before the appearance of my PH symptoms, I was the Executive Director of Kitikmeot School Operations, managing a staff of 200+ and overseeing the education of 1,800 students spread-out in eight schools located in five different communities. Flying from school to school, my workdays were filled with travel, children, language, and culture in the beautiful Kitikmeot region, where Inuit people thrive in between two worlds. However, everything came to a halt in March of 2010 when I froze in my shoes—my legs cramped and I was unable to step forward or sit down. I had to be flown out on a medevac airplane to Yellowknife Stanton Hospital, where I was diagnosed with heart failure.

Several months later, I was still on medical leave without knowing the underlying cause of my heart problems. Thankfully, a flesh-and-bone guardian angel was placed on my path. The Nurse Practioner serving my region's communities, Monique, attended a health conference in Toronto where she learned of PH. She described my symptoms to the specialist who had given the talk and was advised to contact Dr. Dale Lien at the Edmonton PH Clinic. Shortly after Monique had returned to Nunavut, I was back in ICU in Yellowknife with kidney failure and other life-threatening symptoms. Monique informed Dr. Lien of my situation and I was immediately transferred to the University of Alberta Hospital to be seen by PH specialists. I will forever be grateful that Monique cared enough to seek more information regarding my symptoms.

I spent several weeks in recovery under the care of the Edmonton Clinic's PH medical team. I was put on oral medications and encouraged to consider intravenous treatment. However, because of the many complications associated with IV therapy, being put on Flolan® would have meant having to move to Edmonton and leaving behind my arctic community and family. I couldn't do it! I couldn't give up my hometown and leave my children and grandchildren. I couldn't live in a city. Not me! I decided against this treatment option and returned home. My life followed the phases of the purple saxifrage that blooms and fades each summer season; every three months, I flew from Kugluktuk to Edmonton via Yellowknife to see my medical team. On oral meds, my symptoms and quality of life remained stable, but without more aggressive treatment, I knew that I had limited time. I found myself attempting to make memories in a condensed timeframe and convinced myself that I had accepted my fate.

"My life followed the phases of the purple saxifrage that blooms and fades each summer season; every three months, I flew from Kugluktuk to Edmonton via Yellowknife to see my medical team. On oral meds, my symptoms and quality of life remained stable, but without more aggressive treatment, I knew that I had limited time."

Watching my family grow and my grandchildren get older, I changed my mind about moving to Edmonton to be put on IV therapy—I realized it was selfish of me not to do everything I could to stay alive. My husband and I moved to Edmonton in November of 2013. Before leaving to begin our new life, we were treated to a night of celebration by our community, who recognized how our involvement had contributed to the development of Kugluktuk and its people. This heartfelt departure gave us hope for good health and a happy new life.

I spent a month in the hospital adjusting to my new treatment and learning to mix my medication and deal with its side effects. When I came out, my husband and I stayed in an Inuit-owned home for northern patients. There, we formed a new family with other artic region lodgers; I was able to speak in Inuinnaqtun, my Inuit language, and share country foods when cravings of caribou and arctic char were strong.

Eventually, we moved into our own apartment. We adjusted to our new city life and became involved with PHA Canada's Northern Alberta Chapter. Fortunately, I was allowed to go back home twice a year for one-week visits, provided I was stable for travel. Life was so good during each visit home; I enjoyed fresh arctic air, frozen snow to walk on, fresh country food, familiar faces, and most of all my grandchildren's hugs and kisses. I remained stable and, with a new season of blooming purple saxifrages, my husband and I were granted our wish to move back home. The people of Kugluktuk greeted us with open hearts and community members were eager to help me carry groceries, offer me rides, and deliver me freshly caught bounties of berries gathered from the land.

I've been back in Kugluktuk for two and a half years now and thankfully have only had to deal with one emergency when my chest IV line came loose. Self-care is a must when your closest PH specialists are two air flights away from your home. Support from my family and community is also essential and helps me emotionally, physically, and spiritually. My door is never locked; friends and family come and go as they please to check in on me.

At the moment, I see my medical team every six weeks through Telehealth and only have to travel to Edmonton for certain tests. However, I know that when I'm ready for transplant, I'll have to move back to the city to wait for new lungs. Meanwhile I plan on enjoying the beauty of the arctic shoreline and the love of my family. I am happy to be with my community as we fight to thrive as healthy Inuit people in a fast-changing world.

Contributed by: Millie Kuliktana, PAH patient, Kugluktuk, NU

My New Life as a PH Patient

Across the country, PH patients and caregivers are raising awareness of the importance of ensuring publicly funded access to all Health Canada-approved treatments. James Altimas and Donna Downes, along with other Ottawa region PHighters, have been actively advocating for the needs of the PH community by meeting with Members of Provincial Parliament (MPPs) and sharing their story in local media.

There are key dates in a person's life: birthday, wedding day and birth of a first child. For me, one of those days was September 18, 2015 when I was diagnosed with idiopathic pulmonary arterial hypertension (IPAH) at the University of Ottawa Heart Institute PH Clinic. Although this date made it official that I was a PHighter, the journey that got me to this point began much earlier. In 2013, I became aware that something was changing in my body. It began with being a little out of breath going up stairs and progressed to being out of breath on walks. Eventually, regular activities around the house became difficult. As time went on, my wife Donna noticed more specific changes like my weight loss, my pale and grey skin tone, and my total lack of energy and desire to be physically active. She was very concerned, but I did not want to admit that something could be seriously wrong. In August 2013, we travelled to the Alberta Rockies and, attempting to climb up Mount Edith Cavell, I found myself gasping for breath. I could no longer deny that something was really wrong so I consulted my family physician, but he did not seem concerned with my symptoms. It was only in June 2015, when Donna and I went to a new family doctor, Dr. Nasim Bahramifarid, that our concerns were heard and I was sent to do a barrage of tests. Results of my echocardiogram showed that there was a serious problem and I was referred to the Heart Institute where I met Dr. George Chandy on that decisive September day.

PAH has impacted my life in so many ways. I have always enjoyed being active and involved in sports: downhill skiing in the Quebec Laurentians, completing numerous 10-km runs, and running three marathons, I am proud to say, all under four hours. Now, I can no longer join Donna for a bike ride on the Ottawa parkway. I am also unable to travel by plane due to the elevated pressure, which puts a damper on our retirement travel plans. However, the hardest part is not always being able to breathe freely. PAH has taken away the ease of doing everyday activities that I took for granted. Thankfully, I am a very positive person and I try to look at each day as another day to enjoy. I am appreciative of all Donna does to keep me balanced and moving ahead on my new life path.

My PH journey has also brought a number of positive elements. I am under the care of a wonderful medical team at the Ottawa PH clinic: Dr. Chandy, Advanced Practice Nurse Carolyn Pugliese, and Clinical Research Nurse Rosemary Dunne. I am so grateful to these professionals who work hard to keep me as healthy as possible and enjoying the best quality of life I can have. Moreover, Donna and I are members of the Ottawa PH Support Group and we feel a strong bond with everyone there. We receive valuable information at meetings and find it helpful to share our experiences with people who are able to truly understand our situation.

Recently, Donna and I became involved in PH advocacy. In May we sent a number of letters to local MPPs to invite them to PHA Canada's World PH Day celebration at the University of Ottawa Heart Institute on May 5th. At the event, we welcomed the opportunity to speak to politicians about how they can help ensure that no PAH patient is denied access to treatment. Shortly after, on May 8th, Donna and I were interviewed on a local TV information show, Daytime Ottawa, to raise awareness of issues affecting the PH community. We spoke about PAH and our experience living with the disease, focusing on the importance of publicly funded access to all Health Canada-approved PAH medications. We feel that these kinds of awareness-raising activities are important because PH specialists need to be able to prescribe the best treatment option for their patients. At present, we feel the government is more concerned with saving money than saving lives. This is why we have joined our fellow PH support group members at meetings with local MPPs to advocate for public funding for the newest approved PAH drug, selexipag (Uptravi®). Donna and I have learned that you can't always rely on someone else to fight for your cause. With the support and guidance of PHA Canada, we feel we have the tools to be efficient and effective advocates, both for ourselves and for other PH patients and their families.

We hope that in the imminent future, all PH drugs become publicly funded. We trust that researchers will find a cure for this disease. Personally, I am optimistic that my drugs will continue to keep me healthy, as Donna and I anticipate sharing many more years together.

Contributed by: James Altimas, PAH patient, and Donna Downes, wife and caregiver, Ottawa, Ontario.

James and MPP John Fraser at our Ottawa World PH Day Celebration.

Facing the Illness Together:

Lyne Ducharme's Story

PAH Patient Forum participants.

On June 3rd, PHighter Lyne Ducharme organized a Pulmonary Arterial Hypertension (PAH) Patient Forum at the Institut de cardiologie et de pneumologie de Québec (Quebec City, QC). The event enabled 30 patients and caregivers to come together, network, and learn more about PAH thanks to presentations given by specialists. PHA Canada is pleased to have supported this educational event through our Seed Grant program.

Lyne (centre) being thanked for her work.

I received my pulmonary arterial hypertension (PAH) diagnosis in 2004, but I had been suffering from shortness of breath since 2000, which developed after I underwent hip surgery. After the surgery, I was so out of breath that I could no longer speak or walk. It took four years for doctors to diagnose me with PAH after unsuccessfully treating me for anxiety and asthma. It is only after I had fainted for the sixth time that my local hospital decided to dig deeper and found the cause of my health issues.

The biggest impact that PAH has had on my life is making me unable to work, and I miss it very much. I am also unable to go out for dinner with friends or join them in different outings. At the end of the day, I'm so tired that I'm in bed by 6:30 p.m. Nevertheless, I manage to live well with PAH and I have learned to listen to my body. Because I have more energy earlier in the day, I schedule my most important activities in the morning or in the afternoon. So for example, instead of having dinner at the restaurant, I go out for brunch.

I have been involved in the Quebec pulmonary hypertension community for a number of years. When I was diagnosed, I remember feeling alone and having no one to turn to who could understand my situation. Back then, I didn't know anyone else on Flolan® and felt quite isolated. Living though these challenges made me stronger, but I wished for no one else to have to go through the same thing so I decided to get involved. As soon as I was able to, I organized a gathering of patients. I like to be able to connect and share with others and I wanted to tell fellow PHighters: "You are not alone, I am here for you."

I am in charge of Fondation hypertension artérielle pulmonaire Québec's (Fondation HTAPQ) Facebook page and, before organizing the June 3rd forum, people had been asking me if a patient meeting would take place soon. The demand was there and, given that I like to see PHighters come together to share their experiences, I decided to plan an event.

I'm glad I did because the forum was very interesting! The presentation given by Registered Nutritionist Marie-Christine Fortin was memorable; participants were quite surprised to learn about the amount of sodium contained in different foods (for example, she compared the sodium content in different types of cheeses). Marie-Eve Pouliot, Registered Nurse affiliated with the Quebec City PH Clinic, shared useful information on the basics of PH and PH management. Two other interesting presentations completed the day: Dr. Steeve Provencher shared insight from his point of view as a PH specialist and Art-Therapist Marie-Claude Fortier led an inspiring workshop on craft-based relaxation.

In preparation for the event, I put together comprehensive files for participants, filled with resources and information on the management of PAH. For example, I included educational documents on medication and oxygen use, low sodium recipes, stress management resources, tips on managing symptoms, and a list of additional online resources. Each participant was also given a colouring book and a set of crayons for the art-therapy workshop. Patients who attended the forum were very impressed by the resources they were given and told me they thought the event was PHantastic!

The one thing I would say to other patients, and particularly to newly diagnosed patients, is that you don't have to face the illness alone. If you are scared, I invite you to reach out to me by email at line.ducharme@gmail.com. I'll be happy to help you demystify the illness and learn how to live well with pulmonary arterial hypertension. We may be sick, but it doesn't mean that we can't spend some quality time with the ones we love. It just takes a bit of rest to get back on your feet after an outing! My advice is to listen to your doctor and nurse. I've been living with PAH for 17 years, I've always listened to my medical team, and I'm still here!

Of course, I am hopeful that a cure will one day be found, but I know that we're not there yet. For the time being, I have high hopes that patients will continue to get together and help one another. It doesn't need to be complicated; the essential thing is not to be alone!

Contributed by: Lyne Ducharme,
PAH patient, Trois-Rivières, QC

What does PHA Canada Mean to You?

PHA Canada's mission is to empower the Canadian pulmonary hypertension community through support, education, advocacy, awareness, and research. To fulfill this mission and achieve our vision of a better life for all Canadians affected by PH, we offer a variety of programs and services to the PH community. Acting as a resource hub, our organization empowers community members to become educated about PH, as well as to support one another and advocate on behalf of the PH community.

In 2018, PHA Canada will celebrate its tenth anniversary. In preparation for this milestone, we asked our community how our organization has impacted their lives. Here's a selection of quotes from members of the Canadian PHamily reflecting on what PHA Canada means to them.

"PHA Canada's community transpires hope, solidarity, and support. From my perspective, this community is united through the PHight of each of its members and through PHA Canada. PH patients and their loved ones are lucky to have access to support groups and other community-driven resources.

I am honoured to have received a PHA Canada PH Research Scholarship; this achievement motivates me to work even harder."

—Virginie F. Tanguay, researcher, Quebec City, QC

"I learn something from every PHA Canada social media post and can relate. I don't have to explain how I feel, or what I am going through. PH patients are very similar; our stories and our diagnoses are the outcome of a series of similar events. We look fine to everyone who is not affected by PH… The Canadian PHamily is the only family that understands us."

—Dennis Guiotto, PAH patient, Langley, BC

"PHA Canada has been invaluable to me in providing up-to-date pharmaceutical information and ongoing support through The Pulse, Connections, and Facebook. PHA Canada's effective communication has given hope to those of us dealing with a rare disease."

—Barb Heal, PAH patient, Burlington, ON

PHA Canada means support! Amazing and caring individuals help bring us all together.

—Heather Zloty, parent of a child living with PH, Langdon, AB

The most valuable service PHA Canada offers is being there for support when we need it most. They have really helped us in our endeavor to raise awareness of this disease so that one day, hopefully, there will be a cure and nobody else will need to adapt to their "new normal" because of PH.

— Pat Paulin, caregiver, advocate, and fundraiser, Mississauga, ON

Thanks to PHA Canada, I was able to meet other people with PH shortly after my diagnosis. These encounters gave me hope when I needed it most.

—Judith Moatti, PAH patient, Sainte-Clotilde-de-Châteauguay, QC

Hope… There is an organization fighting for us and our health interests!

—Susan Cosenzo, PH patient, Ottawa, ON

Zooming In on PH Research

An In-Depth Look at the Past, Present, and Future of PH Research in Canada

In the world of pulmonary hypertension, the word "research" is filled with hope, potential, and excitement. For the scientific community, research holds the key to better understanding of the disease, leading to the development of novel therapies, robust treatments, and overall more sophisticated tools to care for patients. For those directly affected by PH, research holds the promise of a better quality of life, increased life expectancy, efficient management of symptoms, and ultimately a cure. Research is at the heart of the Canadian PHamily's hope for the future, but it has also played an essential role in defining key milestones in our community's history. In the last 30 years, research advances have had a huge impact on the lives of PH patients and their loved ones. Discoveries in the fundamental mechanisms that cause PH have led to the development of new treatments, while increased treatment options have allowed PHighters to live longer and healthier lives. Better knowledge of the management of PH has also enabled a pan-Canadian network of specialized treatment centres to flourish. Throughout this evolution, the Canadian PHamily has grown stronger, more resilient, and more connected. Without a doubt, research developments, past, present, and future, breathe life into the PH community.

In this issue of *Connections*, we zoom in on PH research in Canada, starting with an in-depth look at the evolution of PH treatment and the many steps involved in making newly developed drugs available to patients. Next we share insight about participation in clinical trials, from both medical professional and patient perspectives. Finally, we present research into the emotional and social impacts of the disease on patients, an area in which much work has yet to be done. We are also happy to continue to highlight PH research throughout the issue by featuring an interview with Dr. Duncan J. Stewart about his pioneering research into stem-cell therapies for pulmonary arterial hypertension, a new *Research Corner* article focusing on the future of PH therapies, and an update on PHA Canada's Research Scholarships. We also take the opportunity to thank Arjun Pandey, who has volunteered his time and research skills to help us develop content featured in this issue and other new research-focused resources.

Evolution of PH Treatment in Canada

The landscape of PH treatment in Canada has evolved greatly over the last 30 years, with the result that patients have access to more treatment options and better care than ever before. Since the founding of the first PH clinic in Montreal, Quebec in 1986, our community has witnessed the expansion of a network of specialized treatment centres from coast to coast and the development of 10 new PH-specific drugs. While being diagnosed with PH today is still scary, life-changing news, patients and their families can take comfort in the fact that, thanks to the progress made in the last decades, PHighters are living longer and healthier lives.

Evolution of PH-Specific Drugs and Treatment Pathways

There are currently 10 PH-specific treatments approved in Canada. Taken individually (mono-therapy) or in combination (combination therapy), these drugs help alleviate symptoms and slow disease progression, allowing PHighters to live as normally as possible. If PH specialists are now well-equipped to provide their patients with optimal treatment, it was not the case 20 years ago, before Health Canada approved the first drug for the treatment of pulmonary arterial hypertension (PAH). Available therapies in Canada are now administered orally, intravenously, or subcutaneously, and target three different biological functions that play a role in pulmonary hypertension (therapeutic pathways).

Development of Drugs Targeting the Prostacyclin Pathway

After clinical trials were conducted in Canada on intravenous epoprostenol (Flolan®), Health Canada approved this drug for the treatment of PAH in 1997. This therapy delivers prostacyclin through a molecule called epoprostenol, which leads to the relaxation of the pulmonary arteries. The approval of Flolan® radically changed the landscape of PH care in the country as it gave patients access to a specialized drug to manage their symptoms. This treatment, however, had its drawbacks, as it needed to be delivered intravenously 24/7 through a permanent chest line and its temperature needed to be controlled in order to be effective. It was only in 2013, with the approval of room-temperature-stable epoprostenol (Caripul®), that IV epoprostenol therapy became much

easier to manage. Caripul® allowed patients to pre-mix medication and carry their pump without worrying about keeping it cool. Meanwhile, Health Canada approved another treatment targeting the prostacyclin pathway for the management of PAH: Remodulin®. Unlike Flolan® and Caripul®, this medication delivers synthetic prostacyclin through a molecule called treprostinil to help dilate blood vessels. This therapy can be administered subcutaneously or intravenously through a portable infusion pump. More recently, Health Canada approved the first oral therapy targeting the prostacyclin pathway: selexipag (Uptravi®). This drug, which is classified as a prostacyclin receptor agonist, works differently than others targeting the prostacyclin pathway. Uptravi® stimulates the IP prostacyclin receptor in the pulmonary arteries to cause vasodilation (relaxation of the blood vessels) as opposed to delivering pure or synthetic prostacyclin.

Development of Drugs Targeting the Endothelin Pathway

The first oral medication for the treatment of PAH, bosentan (Tracleer®), was approved by Health Canada in 2001. Classified as an endothelin receptor antagonist (ERA), this medication helps prevent blood vessels from narrowing by blocking the reception of endothelin-1, a protein that causes vasoconstriction (tightening of blood vessels) in the pulmonary arteries. The approval of bosentan (Tracleer®) represented breakthroughs in terms of both medication delivery and therapeutic pathways; with the arrival of this new drug, patients gained access to increased options to manage their disease. Two other oral drugs, which are also classified as endothelin receptor antagonists (ERAs), have since been approved for the treatment of PAH: ambrisentan (Volibris®) and macitentan (Opsumit®).

Development of Drugs Targeting the Nitric Oxyde Pathway

In 2006, the approval of sildenafil (Revatio®, Viagra®) added another tool to PH physicians' toolboxes as this new drug provided the option to target a third therapeutic pathway. Classified as a phosphodiesteras inhibitor (PDE-5 inhibitor), this oral medication prevents PDE-5 enzymes from degrading nitric oxide in the pulmonary arteries, which helps dilate the blood vessels. A similar drug, tadalafil (AdCirca®, Cialis®), came on the market in 2010. In 2013, an important breakthrough was made for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH) when Health Canada approved riociguat (Adempas®), the first (and currently only) medication for the treatment of non-operative or residual CTEPH. Unlike other drugs targeting the nitric oxide pathway, this medication is classified as a soluble guanylate cyclase stimulator (sCG stimulator) and helps increase sensitivity to nitric oxide in order to stimulate dilation of the pulmonary arteries. In 2014, Adempas® was also approved for the treatment of pulmonary arterial hypertension (PAH).

Current Research Into PH Therapies

PH clinics across the country are involved in multiple research trials with the goal of developing new therapies, assessing the efficacy of existing drugs, and testing the use of approved treatments in patients with different types of PH or in children with PH. Currently, new molecules are being tested for the treatment of PAH, which could lead to the approval of treatments targeting new therapeutic pathways. Innovative research is also being done on the use of stem cell therapies for the treatment of PAH (see our interview with Dr. Duncan J. Stewart on pages 27–28 for more information). A number of research trials are also monitoring the efficacy of the long-term use of treatments and evaluating their action in combination with other therapies (combination therapies). Research is also being accomplished in the treatment of pediatric pulmonary hypertension, which is vital given that the drugs currently available in Canada have only been approved for use in adults. Trials are ongoing to study the use of tadalafil (AdCirca®, Cialis®) in children with PAH and sildenafil (Revatio®, Viagra®) in newborns. Observational studies are also in progress to track outcomes and practice in pediatric PH. Recently, the U.S. Food and Drug Administration approved bosentan (Tracleer®) for use in pediatric patients, which makes us hopeful to see PH treatments approved for pediatric use in Canada in the near future.

Looking back at the last 20 years, our community has witnessed PHenomenal progress in the evolution of the PH treatment landscape in Canada. The development of 10 new drugs and three therapeutic pathways is progress worth celebrating, as these advances have had tangible impacts on the lives of patients and their families across the country. It is also worth noting that a strong network of Canadian PH clinics has evolved in parallel to the development of PH treatments. In the last three decades, a total of 21 specialized PH treatment centres have opened across the country, two of which offer specialized care for CTEPH and four of which provide treatment to children living with PH. We look forward to seeing the materialization of new treatment innovations in the years to come, as the scientific community works towards improving therapeutic options for the management of PH, and the discovery of a cure for the disease.

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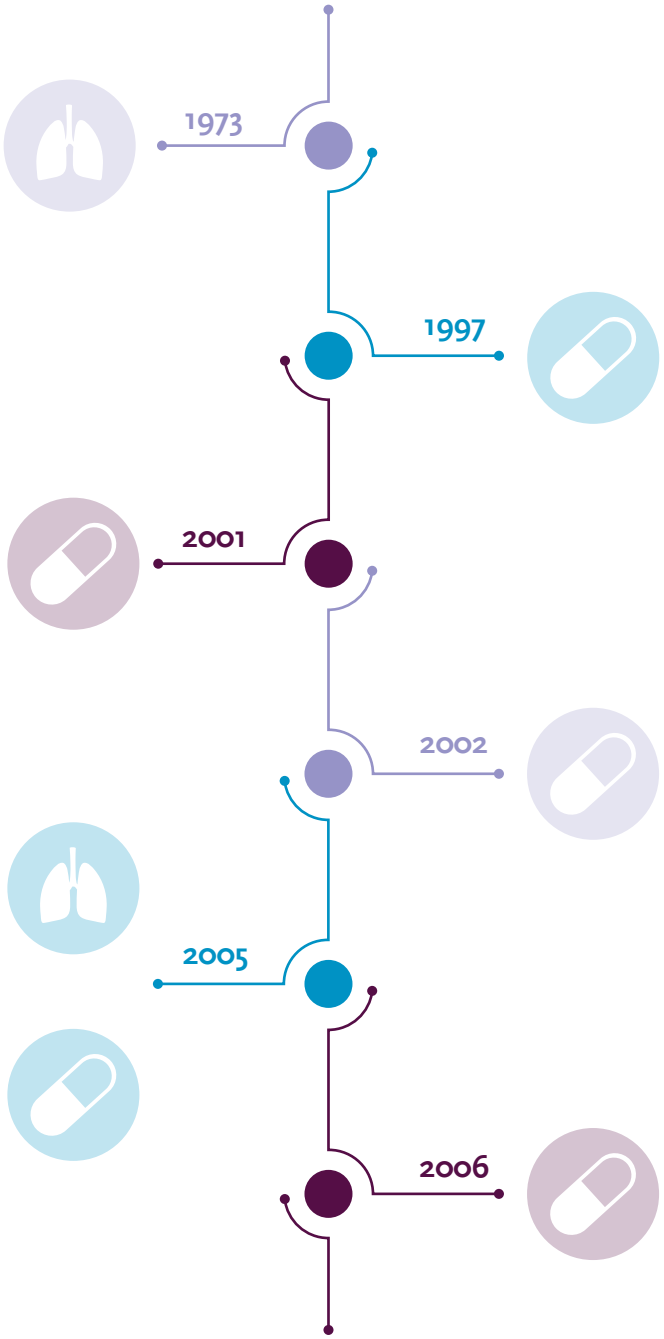
Timeline of PH Treatment in Canada

PH is a relatively new disease on the global medical community's radar, but in the last few decades, research has produced great strides in the development of novel therapies and innovative clinical practice. In Canada, the last twenty years of developments in PH research have been marked by the approval of 10 PH-specific treatments. Below is a timeline highlighting key developments that have impacted the treatment of PH in Canada. Looking back on the progress made, we have every reason to hope for a bright PHuture!



1973

The World Health Organization holds the first World Symposium on PH in Geneva, Switzerland.

1997

Health Canada approves the first PAH-specific treatment: intravenous epoprostenol (Flolan®). This new drug, which targets the prostacyclin pathway, spurs a revolution in the treatment of PH in Canada; for the first time PAH patients are offered a targeted therapeutic option to manage their symptoms.

2001

Health Canada approves the first oral medication for the treatment of PAH: bosentan (Tracleer®). Administered orally, this new medication has a huge impact on patients' quality of life and broadens therapeutic options for the management of PAH by targeting a new pathway.

2002

Health Canada approves subcutaneous treprostinil (Remodulin®) for the treatment of PAH. Targeting the prostacyclin pathway, this therapy is delivered under the skin through a portable infusion pump.

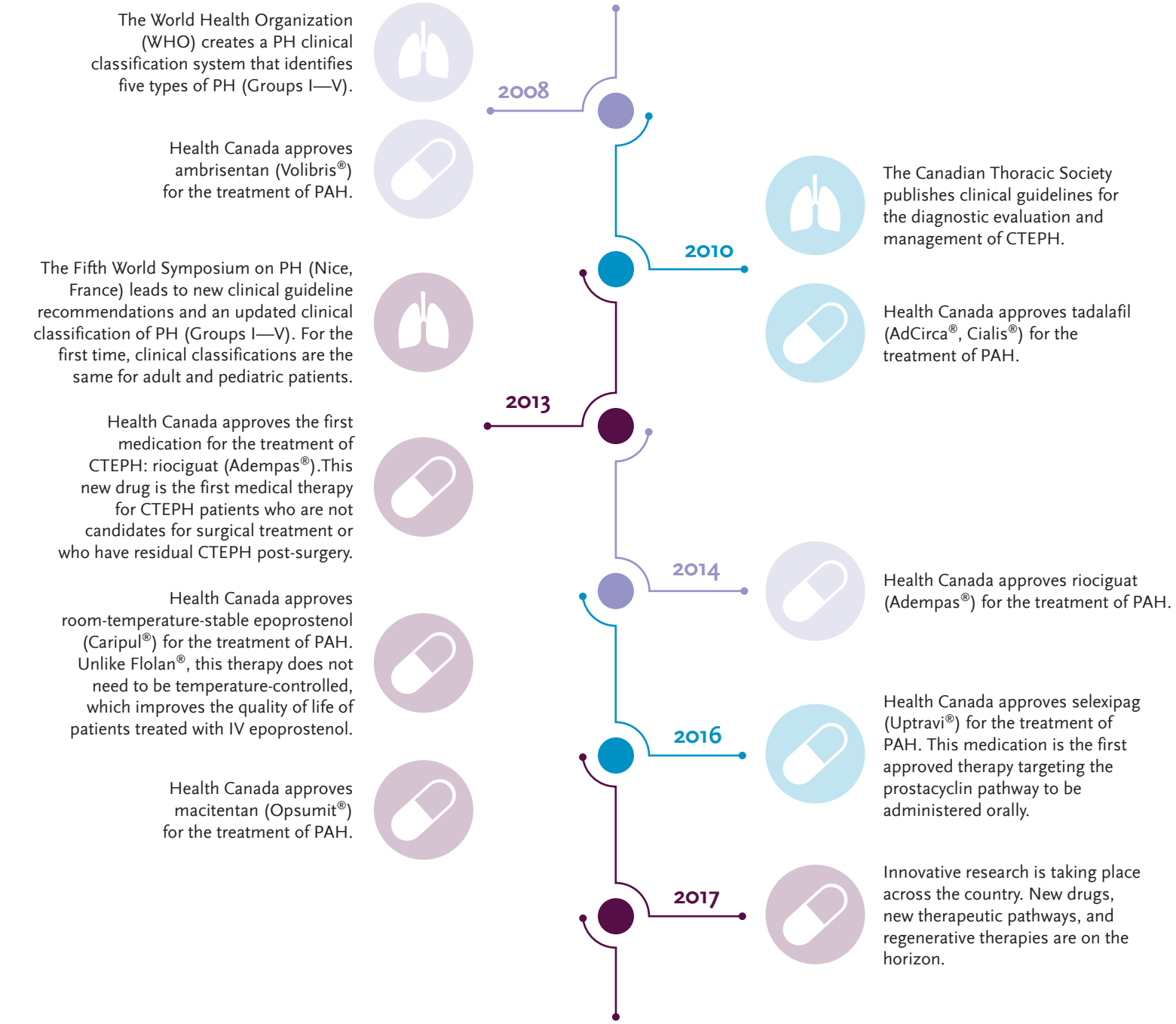
2005

The Canadian Cardiovascular Society and the Canadian Thoracic Society publish a joint position statement on PAH, providing clinicians with a comprehensive resource on management of the disease in Canada.

Health Canada approves intravenous treprostinil (Remodulin®) for the treatment of PAH.

2006

Health Canada approves sildenafil (Revatio®, Viagra®) for the treatment of PAH. Administered orally, this medication targets a new treatment pathway—nitric oxide—to alleviate PH symptoms.



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Bench-To-Bedside Flow Chart

How New Drugs Go from Being Developed to Being Administered to Patients

Innovative research is being done around the world to develop new therapies to better manage PH. However, it can take years before patients gain access to a newly developed drug. The journey from the research bench—where ideas for new drugs originate and are initially tested—to the patient's bedside—where treatments reach those in need—is long and complex. In Canada, all new treatments go through a rigorous approval process to ensure that available drugs are safe and effective. Once a treatment is marketed, patient access depends on multiple factors, including whether or not the drug is approved for public funding. The flow chart below illustrates the many steps involved in making new treatments accessible to patients. Start from the "Drawing Board" and follow the arrows to learn about the "bench-to-bedside" journey of new treatments.

RESEARCH BENCH

START

Drawing Board

Sky's the limit! Scientists worldwide are coming up with innovative ideas to treat PH and other rare diseases.

If pre-clinical studies/ Phase I show that the treatment is not safe

If the idea holds potential

Pre-Clinical Studies

Before a new treatment is tested on humans, initial research is conducted to determine potential safety concerns. Pre-clinical studies are typically done in a lab and involve testing on cells, tissue samples, and/or animals.

If pre-clinical studies show that the treatment is safe and has potential

CLINICAL STUDIES

Once pre-clinical studies have shown that a treatment is not dangerous, it is tested on humans in clinical studies (also know as clinical trials). Clinical studies allow researchers to determine the treatment's efficacy and potential for use in the general population. Clinical studies are accomplished over many years in multiple phases:

Phase I

Goal: To determine the treatment's safety when used on humans

Participants: Between 20-80 typically healthy participants

Duration: Several months

If Phase I is conclusive

Phase II

Goal: To measure the treatment's efficacy as a therapeutic option for a given condition and to continue to evaluate its safety

Participants: Generally between 100-300 people affected by the targeted condition

Duration: Up to two years

If Phase II is conclusive

Phase III

Goal: To evaluate the treatment's efficacy compared to standard of care (available existing treatments) and/or a placebo-control (inactive substance that looks identical to a drug but has no effect on the body)

Participants: May include up to thousands of people affected by the targeted condition

Duration: Up to four years

If Phase III is conclusive

BEDSIDE

Select patient access through Health Canada's Special Access Program

REGULATORY REVIEW

Health Canada Approval

In order for a new treatment to be sold in Canada, manufacturers must make a submission to Health Canada for a safety, efficacy, and quality review.

If the treatment complies with Canadian Food and Drug Regulations, Health Canada will provide a Notice of Compliance

If the treatment does not comply with Canadian Food and Drug Regulations, Health Canada will not provide a Notice of Compliance

The treatment can then be sold in Canada

The treatment cannot be sold in Canada

BEDSIDE

Patients can access it by paying out-of-pocket or through their private insurance coverage

PUBLIC FUNDING APPROVAL PROCESS

CDR/INESSS Review

In order to determine if a treatment should be funded through public drug plans, it is assessed by the Common Drug Review (CDR) at the Canadian Agency for Drugs and Technologies in Health. In Quebec, this assessment is done by the Institut national d'excellence en santé et services sociaux (INESSS).

If the treatment is determined to not be cost-effective in comparison to current therapies

If the treatment is determined to be cost-effective in comparison to current therapies

No recommendation for public reimbursement

Recommendation for public reimbursement

The treatment will likely not be accessible through public funding

Government Negotiations with Manufacturer

Governments negotiate with drug companies to establish the cost and criteria under which the treatment will be covered through public drug plans. Governments may negotiate individually or as a group through the pan-Canadian Pharmaceutical Alliance (pCPA), in an effort to reduce drug costs.

If negotiations are not successful

If negotiations are successful

The treatment will likely not be accessible through public funding

BEDSIDE

The treatment will be available for reimbursement through the patient's government drug plan

Ask a Research Coordinator

Interview with Scott Fulton

Scott (left) at work. Photo ©Capital Health Nova Scotia.

Most PH treatment centres in Canada are involved both in clinical care and research. As a result, patients may be offered the opportunity to participate in a clinical trial as part of, or in complement to, their treatment plan. To answer some of the questions patients may have about what it means to participate in a clinical trial, we've asked Scott Fulton, Research Coordinator at the Halifax Infirmary, Division of Respirology. Scott, who is affiliated with the Halifax Pulmonary Arterial Hypertension Program and accompanies patients every step of the way when they enroll in a PH study. We are happy to share his insight into the role of clinical trials, their potential impact on participants' lives and course of treatment, and the ethical considerations involved in these types of studies.

PHA Canada: Can you tell us about your background and how you became involved in the field of PH research?

Scott Fulton: Shortly after I began working as a Respiratory Therapist in 1999, a research opportunity presented itself and I haven't looked back. I enjoy working with patients and their families and seeing advancements in the treatment of various respiratory diseases.

PHA Canada: What is your role as a Research Coordinator?

Scott Fulton: I have a few different responsibilities. Initially, I help set up studies and ensure that we have approval from our hospital's Ethics Board. After a study is up and running, my job is to recruit participants and see them at their study visits. Given my background, I'm able to complete the majority of the required testing on my own. Throughout the studies, I get to know the participants and their families quite well.

PHA Canada: What are the types of research projects that PH patients might be asked to participate in?

Scott Fulton: There are several types of research projects that may be ongoing at any given time at a PH clinic. Some studies simply involve registries that help keep track of patient populations, the treatments they may be receiving, and the collection of other health information. Other studies may be of a more observational nature to see how a disease may progress and what factors may speed up/slow down this progression. However, clinical trials comprise the majority of my work and a number of these studies can be taking place at the same time. Clinical trials are the process new medications go through to determine their safety and effectiveness as new pharmaceutical treatments. Prior to being approved by Health Canada or the FDA (in the U.S.), clinical trials are undertaken to demonstrate that the benefits of new medications outweigh any potential risks.

PHA Canada: Why is it important that PH patients in Canada participate in clinical trials?

Scott Fulton: Participation in clinical trials, for PH and other diseases, is very important because this research helps broaden our knowledge of the disease, which can lead to the development of new treatments. Ideally, a clinical study will benefit the PH community in general, as well as the individual participants. In some studies, participants may have additional tests done, which would not typically be performed as part of their clinical care, or have access to a medication before it is available anywhere else.

PHA Canada: What is done to ensure participants' safety and confidentiality?

Scott Fulton: All studies conducted at our hospital have to first be approved by our Ethics Board to ensure potential patients' wellbeing and that the study is properly designed/conducted. Research studies may not benefit all participants, so it is important for the doctor conducting the research to thoroughly explain the study and any potential risks prior to enrolling a person. Regarding confidentiality, the research team is required to view a participant's health information in order to conduct the study and obtain the required data to test the study's hypothesis. However, participants are typically assigned a code number to ensure their health information remains as confidential as possible.

PHA Canada: From a patient's perspective, what are the important aspects to consider before enrolling in a clinical trial?

Scott Fulton: The decision to participate in a research trial is a big one and patients should carefully review their options prior to enrolment. Before taking part in a study, you should review the study's consent form, which will provide information on why a study is being conducted, what drug/procedure is being tested, potential risks, and the time required to participate in the study. You should also be aware of what other treatments may be available and if being in a study will impact whether you can receive these treatments or not.

PHA Canada: What is the typical duration of a clinical trial?

Scott Fulton: A trial can last for one day or several years depending on the type of research and what phase it may be in. In some of my studies, it took as long as eight years before the medication was approved and available in Canada.

PHA Canada: What processes and procedures should patients typically expect to go through after they enroll in a research study?

Scott Fulton: The first step in any research study is a discussion with your doctor to ensure you understand why the research is being conducted and what your participation will involve. After you've made the decision to participate, you will typically attend a screening visit to ensure that you meet the criteria to participate in the study. Procedures for this visit may be as simple as confirming your diagnosis or as complex as having certain medical tests performed (i.e. CT scan, echocardiogram). Depending on the study, results from your previous tests may be used so procedures may not have to be performed again. After it is confirmed you are eligible to take part in a study, you will attend pre-scheduled clinic visits for the duration of the study. A typical clinic visit might require you to answer questionnaires, perform breathing tests, perform a six-minute-walk test, and have blood samples drawn. At the study start, you will be informed of what will take place at each visit.

PHA Canada: Some clinical trials involve a placebo-control group of patients who are not given the medication being tested in order to measure its efficacy. Participants will normally be randomly assigned either to the test group or to the placebo-control group. What are the implications for patients who are assigned to the placebo-control group; will they be able to access the medication once the trial is over?

Scott Fulton: Placebo-controlled trials are the most effective at demonstrating whether a treatment works or not, but it may not always be feasible to conduct these types of studies. If an effective treatment is available, this should be the first option for patients. Prior to starting a research study, the study doctor should discuss all treatment options and explain the possibility that a person might be in a placebo-control group. In regard to accessing the medication when a trial is completed, this varies from study to study but should be discussed prior to enrolment. Some studies have open-label extensions where all participants receive the medication after the trial, but this is not always the case.

PHA Canada: What happens if a participant decides, part way through, that they no longer want to participate in the study?

Scott Fulton: It is important for patients to know that the research is voluntary and that they can stop at any time or for any reason without it impacting their regular healthcare. When stopping your participation in a study, you may be asked to come in for a final visit to ensure your wellbeing, but you are not obligated to attend this visit.

Contributed by: Scott Fulton, RT, Research Coordinator, Halifax Infirmary, Division of Respirology, Halifax, NS

Going Through the Trials and Errors of Clinical Trials

A Patient's Perspective on Participating in Research

I developed PH symptoms after the birth of my son in 2004, but I didn't get diagnosed until after my daughter was born, four years later, in July of 2008. She came 6 weeks early and I knew something was wrong afterwards. My legs blew up and I could barely walk. I was very scared because I had a 4-year-old and a week-old baby so I went to a walk-in clinic and was sent to emergency. The doctor who examined me in the ER was not very helpful and sent me home after telling me that fluid retention was "part of motherhood" and that I should just deal with it. I still remember leaving the hospital crying and, when my husband picked me up, I told him I didn't care what the doctor had said; I knew something wasn't right. So I met with my family doctor who referred me to an internist. For a week, he had me run one test after another. I didn't realize at the time what was going on but I knew it wasn't good. Finally, the internist let us know that he thought I had something known as pulmonary hypertension, but that I would have to go to a cardiologist to have it confirmed. Soon after, we saw a cardiologist who confirmed the diagnosis. However, he must have not been up to speed on the disease because I was told that in order to live, I would need a lung transplant within two years. It was devastating news. Thankfully, I saw the light at the end of the tunnel when I met Dr. John Granton at the Toronto PH Clinic about a week later.

My diagnosis completely changed my life but it also changed my husband's and my kids' lives; we were thrown a curve ball. My first year post-diagnosis was very rough. At first I cried myself to sleep and didn't think I could cope with the salt and fluid restrictions. I had trouble mov-

ing around and chronic fatigue made it so I needed to sleep a lot. The best way to explain how I felt is to compare it to losing someone and going through denial, anger, and acceptance. I had to mourn the life I had lost before I could start to mend and accept my "new normal." This took a long time. I had help from a very supportive family, joined a local support group, and found that the best way for me to cope was to talk willingly about my situation. Two and a half years later, I was finally stable enough to go back to work part-time, which was the start of finding my true "new normal."

I would do anything that could help me or others, and so I have always said yes to Dr. Granton whenever he has presented me with opportunities to participate in research. The first time was back in 2010 or 2011 when I participated in a project that tried to determine how PH affects patients' muscles given their limited ability to be active. Then in 2015, I participated in the second phase of a clinical trial testing a new oral medication. Dr. Granton told me that I was a perfect candidate because this was a national study and they needed stable patients to test the drug. Participating would mean taking the new drug on top of my current medications. I said yes immediately when asked if I was interested in contributing to this project. I was optimistic and knew that I wouldn't have to be taken off my regular meds and that I could drop out at any time.

Once my participation was confirmed, I had an initial appointment at the clinic and went through a number of tests (six-minute-walk test, blood work, echocardiogram, right-heart catheter, etc.) to record my starting stats. Then, I was given a 30-day supply of the drug being studied and was scheduled to return to the clinic for follow-up tests every three weeks. At every appointment, I would return any remaining meds, go through new tests to record the evolution of my stats, fill out a questionnaire about side effects, and be given my next 30-day drug supply. The process was easy and the only issue I had involved having to travel to Toronto every three weeks.

However, in the end, the experience was not what I expected. The trial was a blind study, meaning that participants didn't know whether they had been put on the actual drug or on placebo for the first six months, and then vice versa for the next six months of the trial. I thought I had been put on the drug from the start because I had signs of improvement and felt the best I had ever felt since being diagnosed. I still had restrictions but I felt like I could do a little more before my usual symptoms kicked in. Results from my right-heart catheter also showed improvements and my family and I were very excited. I felt like I had won the lottery. When the second part of the trial began, I found no change in my symptoms so I figured that I had been kept on the drug; I felt fantastic. However, a few months later, I got a call from my nurse asking to move my next appointment ahead. She asked me to bring all my remaining medication with me and explained that the study was being cancelled. I didn't understand why if the drug was helping. The nurse told me that they were not getting the results they needed or expected so the trial was to end early. I couldn't help feeling like the rug was pulled out from under me.

I was scared of going back to where I was before the study. I wasn't ready. I loved how I was feeling and didn't want it to stop. This really affected me; I was down and couldn't get my positivity back. I remember saying to Dr. Granton that it was like he had given me candy, and I really liked the candy, but then he'd taken it away. It took me a few months to readjust and I still don't feel as good as I did on the study drug, but I am stable. I learned that you really need to prepare yourself emotionally if you say yes to being involved in a drug study.

I totally believe in the need for PH patients to participate in clinical studies, both for ourselves and for others. So even though participating in this study was an emotional roller coaster ride for me, I would definitely do it again. I would also recommend it to other PH patients, but tell them that they need to be prepared and understand the pros and cons. I think anyone being asked to participate in a drug study should be given a short list of questions to consider. What happens if the study is cancelled? How will this study affect you emotionally? Are you strong enough to handle the emotional aspect of being involved in this study? Thinking through these questions ahead of time would have made a big difference for me. It would not have stopped me from saying yes to participating, but it would have prepared me for hearing the words "the study is being cancelled."

Throughout my journey, I lost hope, gained hope, had it stomped on, and found it again. I am still hopeful for a day when I can say "hey kids, lets go for a hike," because doctors will have found a cure for PH or medications that work so well I'll be able to do all the things I can't right now. Until that day comes, with strength and love, I will continue to PHight.

Contributed by: Carol Doyle Ploughman, PAH patient, Georgetown, ON

Taking One Step at a Time:

Understanding Pulmonary Hypertension Through the Voices of the Patients

PH is a disease that affects every aspect of patients' and caregivers' lives. While PHighters understand first hand the emotional, social, and financial implications of life with PH, little work has been done in Canada to map out the impacts of the disease beyond physiological changes and symptoms on those who are directly affected by it. Yet, a patient-centred approach to understanding the disease, from both clinical and psychosocial perspectives, can lead to better overall care and heightened quality of life for patients and their families.

In 2014, PHA Canada published *The Impact of Pulmonary Hypertension on Canadians*, a report outlining key statistics about the burden of illness for patients and caregivers. In this issue of *Connections*, we are happy to provide further insight into the psychosocial impacts of PH by featuring a summary of Renae Mohammed's Master's thesis, which she completed in 2016 as part of her graduate sociology studies. The daughter of PHighter Judy Mohammed and organizer of one of PHA Canada's most important yearly community fundraisers, the Run/Walk for PH Research, Renae is well positioned to understand the ramifications of a serious yet little known illness like PH and to use her research to bring visibility to the realities of those affected by this invisible disease.

This research presents and discusses the findings of a qualitative thematic analysis of interviews with eight pulmonary hypertension (PH) patients who discussed their experiences in relation to the illness. This is an important topic to focus on because PH is a rare, invisible, and potentially terminal illness about which little substantive research in the social scientific field has been done. Because of its invisible and rare nature, PH is a disease that is severely under-researched, both medically and sociologically. However, it is important that it, like all other rare chronic illnesses, receives the same attention that is given to more common illnesses.

Research Methodology

While gathering quantitative data (statistics) about how PH affects the people living with it is important, it is equally important to understand how the patients themselves describe, from a qualitative perspective, their unique experiences. This approach allows for greater understanding of the disease and its impacts and can lead to improved awareness of PH and advocacy for the needs of the community, which was important to all of the participants in this research. This is why I chose to conduct in-depth, semi-structured interviews with patients to gather information on their diagnosis experience, day-to-day life, and resilience and coping mechanisms. Because no patient's experience of PH is like another's, semi-structured interviews allowed the participants to elaborate on topics they felt strongly about. This format also provided interviewees with the opportunity to answer questions on their own terms and from the perspectives of their individual situations. This methodology enabled interviewed patients to recount their unique experiences with the disease, which is important because there are multiple PH realities.

Research Findings

Through this study, I was able to uncover a lot of information about the illness experiences of people with PH. First off, my conversations with patients made it apparent that there is much more to a person than meets the eye—invisible illnesses can affect anyone. Many of the participants appeared to be healthy on the outside despite being chronically and seriously ill. Further, through my analysis of the interviews, I realized that participants had been able to maintain a positive approach to life throughout their illness experiences, overcoming the hardships they faced and the challenges brought upon by PH.

Research findings are structured around three broad themes that reflect participants' experiences: the diagnosis experience, day-to-day life, and resilience and coping. These themes focus on the process of receiving a correct diagnosis, how the participants' lives have changed as a result of their illness, and how they have adjusted their lives to cope positively with having a rare, chronic, and sometimes terminal illness.

> **"I thought I was overweight. I was experiencing asthma issues and allergy issues—the asthma issues I had since I was a child—but I didn't go to a doctor. I was overweight, I was out of shape."**

The Diagnosis Experience

This section of the study explores the impact of downplaying PH symptoms, often by the patients themselves, and the trial-and-error nature of the diagnostic process. As one participant stated: "I thought I was overweight. I was experiencing asthma issues and allergy issues—the asthma issues I had since I was a child—but I didn't go to a doctor. I was overweight, I was out of shape."

Several study participants experienced delays to diagnosis due to the dismissal of symptoms they felt. One patient recounted that: "I would phone the doctor and say I'm even worse today than I was yesterday, and because of the type of person I am, I would have a shower and get ready, and look half decent going to his office. So he would just look at me and say 'hey, well you look good,' and he would just pat my leg."

Being told of one's life expectancy was also a gruesome, yet common, aspect of participants' diagnoses stories. Interviewees shared that seeing their lives be given an expiration date due to the severity

of their condition was, to say the least, difficult to process. On this note, one participant said: "I kind of had a situational depression at the time, like it wasn't going to get any better, feeling pretty discouraged and down... it was pretty depressing. You know, it's just that the proverbial rug was pulled out from under me."

Day-to-Day Life

This section of the study looks at the changes that participants experienced in their daily lives because of their illness. Loss was identified as a major area of change; energy, independence, and work are the three main areas in which participants expressed having lost control in their lives. Most interviewees also saw their personal relationships undergo changes, specifically in the case of relationships with extended family members, friends, and spouses. Participants shared stories demonstrating both negative and positive aspects to these changes. One patient said: "I didn't want to be incapacitated, I didn't like being dependent and not being able to basically care for myself, so that was the hardest part for me." Another recounted that: "There were people that I didn't realize cared about me so much and kind of came out of the wood work and were very supportive and kind. It was lovely to get that support."

A third factor impacting day-to-day life, and perhaps the most important, is the invisibility of PH, which many of the interviewees noted affects them. Several of the participants shared that they have been judged, criticized, and ridiculed for taking necessary precautions, simply because they do not look like they are sick.

Resilience and Coping

This final section looks at how the interviewees have coped with, and simultaneously fought against, PH. Participants' attitudes towards the 6-minute walk tests demonstrate their resilient mindsets and are a testament to their determination. As one participant explained: "I get very, very out of breath because I always try to beat my last record, but that's just a personal thing… I want to be able to walk as far as I can and maybe that's just like a personal message to myself that I can do it." Traveling is another area in which interviewed patients have shown true resilience. Numerous participants mentioned having found ways to travel the world despite their doctors' recommendations to avoid travel or the obstacles associated with traveling with PH.

Finally, the study has shown that, for PH patients, it is very important to generate awareness and support, and develop research and advocacy. Many interviewees decided to dedicate their time and resources in order to assist other PH patients in coping with their illness. Participants also mentioned taking a proactive approach by spreading the word about PH to the general public and medical professionals. The initiatives that participants have taken to improve their quality of life demonstrate their true strength and willingness to fight against this dreadful disease.

> **"I get very, very out of breath because I always try to beat my last record, but that's just a personal thing... I want to be able to walk as far as I can and maybe that's just like a personal message to myself that I can do it."**

Positive Attitudes

Some of the most notable findings from this research are the positive attitudes and coping skills that participants demonstrated. All eight patients who participated in this study have experienced changes in their self-understanding, social roles, and social interactions. Despite these hardships, all have found ways to turn the negativity of illness into positivity and hope. On this note, it is understood that positive attitudes contribute to the patient's capacity to cope with illness and to achieve a better overall appreciation for life.

It is important that pulmonary hypertension continues to be explored in academia. The more scholarly studies acknowledge PH illness experiences, the more healthcare professionals and the general public will want to understand the disease. Broader awareness is crucial because PH patients are a marginalized group due to the rarity and invisibility of their illness.

Contributed by: Renae Mohammed, caregiver, fundraiser, and social researcher, Ajax, ON

Kam, Renae, Judy, and Joseph Mohammed.

Meet Your Medical Professional:

Dr. Duncan J. Stewart

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Dr. Duncan J. Stewart is CEO and Scientific Director at the Ottawa Hospital Research Institute and occupies the position of Research Director at the University of Ottawa Heart Institute's PH Clinic. The research he has accomplished over the years has played an important role in advancing scientific knowledge of pulmonary hypertension (PH) and developing novel treatments for the disease. Recently, his research into regenerative therapies led to the first clinical trial in the world of a genetically enhanced stem-cell therapy for pulmonary arterial hypertension (PAH). We had the pleasure of interviewing this important figure of the Canadian PH research world. We are happy to introduce his work and share insignt into what drew him towards developing innovative treatments for PAH.

PHA Canada: Where did you begin your medical career, and in what field?

Dr. Stewart: I began at McGill University in Montreal and trained in internal medicine before going into cardiology. At that time, McGill was very different from other places since the respirology and cardiology divisions were very closely aligned. So even though I did cardiology, I was exposed to a lot of information about respirology and to a lot of important diseases that respirologists looked after. Obviously, one disease in which both cardiology and respirology are involved, because there are two parts to the problem, is pulmonary hypertension.

PHA Canada: So this is where you were you first introduced to PH?

Dr. Stewart: Yes, that was during my residency training. After my research training in vascular biology, I started talking with another colleague and good friend of mine, Dr. David Langleben, who had done research training in PH. This was around the time that endothelin, a protein that causes blood vessels to tighten, had been discovered. In fact, I remember reading an initial paper on endothelin and thinking that it could be very important in vascular diseases involving vasoconstriction (tightening of blood vessels). At that time, we thought vasoconstriction was a problem in PH and there was a search for the unknown constrictor factor. So Dr. Langleben and I thought: "Gee, what if endothelin was involved in PH?" This was only months after its discovery and we did the very first studies looking at endothelin levels in the blood of patients with various diseases. We discovered that endothelin levels were sky-high in PH patients, which led to our publication of a number of articles in scientific journals in the late 1980s and early 1990s. This work really established the role that endothelin plays in PH.

PHA Canada: So that was the beginning of your career as a researcher in the field of PH?

Dr. Stewart: That's right. This research was very topical and novel at the time. As it turned out, the work that Dr. Langleben and I did was very important because it opened the door for the first endothelin receptor antagonist (ERA), bosentan, to be used in PH.

PHA Canada: You are active both as a clinician and researcher. How do these two aspects of your practice influence one another?

Dr. Stewart: It's fair to say that when I began my career, my interests were into fundamental research, like molecular and physiological approaches. At the beginning it seemed like there was a big gulf between what I did in my lab and what I did in the clinic, but I was always striving to bring the two together. I think that the success we had in identifying endothelin as an important therapeutic candidate in PH is an example of that. So I've always thought that it was very important for me to continue doing clinical work because that's really where you see the problems and the needs, and that very much informs the direction and focus in the lab.

PHA Canada: Your current research into stem-cell therapy for pulmonary arterial hypertension (PAH) has generated a lot of interest in the community. Can you briefly explain this project?

Dr. Stewart: This research came out of a slightly different view I have, because I am a cardiologist, and other aspects of my research involve growing new blood vessels and repairing the heart. Doing this type of research, we were learning about the factors that control the repair and growth of blood vessels and the stem cells that are involved in developing the vascular system. It occurred to me that the problem in PH is really a problem of damage in the smallest and most delicate blood vessels in the lung. We think of the lungs as bags of air that we use to breathe in and breathe out with, but they are also the organs that have the most blood vessels in the body, which makes sense because their job is to oxygenate the blood. The problem in PH is that you loose the vasculature; there are not enough blood vessels left to efficiently provide blood with access to gas exchange airways.

We did a lot of work to see if we could repair or regrow blood vessels in the lungs, much like we can in other organs. And the answer is that we can. The lung actually has a very good capacity to regenerate and repair blood vessels. This research paved the way to asking the question: "If the problem in PH is the loss of functional blood vessels, maybe we can regenerate these vessels?"

PHA Canada: What phase is your research in now and what do you hope to achieve in the coming years?

Dr. Stewart: Some years ago, we completed a Phase I trial using genetically engineered progenitor cells and we are now positioned to begin a very large efficacy (Phase II) trial. We are trying to determine if this works in patients with severe PAH and if we can establish a more normal pulmonary circulation with a gene and cell therapy approach. To determine efficacy we'll be trying to see how much benefit we can get if we push the treatment as far as we can. We'll be giving at least four doses of cells to patients, but one group of participants will receive up to eight doses.

PHA Canada: What is the long-term goal for this research?

Dr. Stewart: We are hoping that this will be transformative. Right now we have a lot of drugs that basically do the same thing; they act on different areas to improve endothelial function (the inner lining of the blood vessels). The endothelin, prostacyclin, and nitric oxide therapeutic pathways are very important in regulating the functions that thicken blood vessels, but they are not themselves transformative. With our current research, we hope that we'll be able to make patients a lot better by restoring blood vessel function, which would lead to important improvement in pressures in the pulmonary arteries.

PHA Canada: Do you have a sense of when you would be able to achieve this?

Dr. Stewart: We are working very hard to start the Phase II trial in the summer of 2017. In Ottawa we are hoping to enrol our first patient in August or September. We have eight centres across Canada that we want to bring on board and hope that they will all be enrolling patients by 2018.

PHA Canada: Can you tell us about other research projects you are currently involved with in the field of PH?

Dr. Stewart: We are still trying to better understand what are the underlying problems in PH because these can give us hints as to how we can treat the disease better. The big dilemma is around what is the major cause of abnormalities in the pulmonary circulation. Is it damage that leads to loss of blood vessels or is it the growth of abnormal cells that leads to blood vessel remodelling and blockage? The treatments that address these two dynamics are quite different. In the lab, we are asking the question: "What is the primary problem that needs to be addressed and which of these is most likely to be the one we need to develop therapies for?" So we are doing a bunch of studies using different models and technologies. It's going to take us a year or so before we bring this to a conclusion, but I am hoping that it will give us definitive information as to the mechanisms that cause fundamental abnormalities in PH.

PHA Canada: The landscape for the treatment of PH in Canada has hugely evolved over the last twenty years. In your opinion, what have been some of the biggest achievements that have been made?

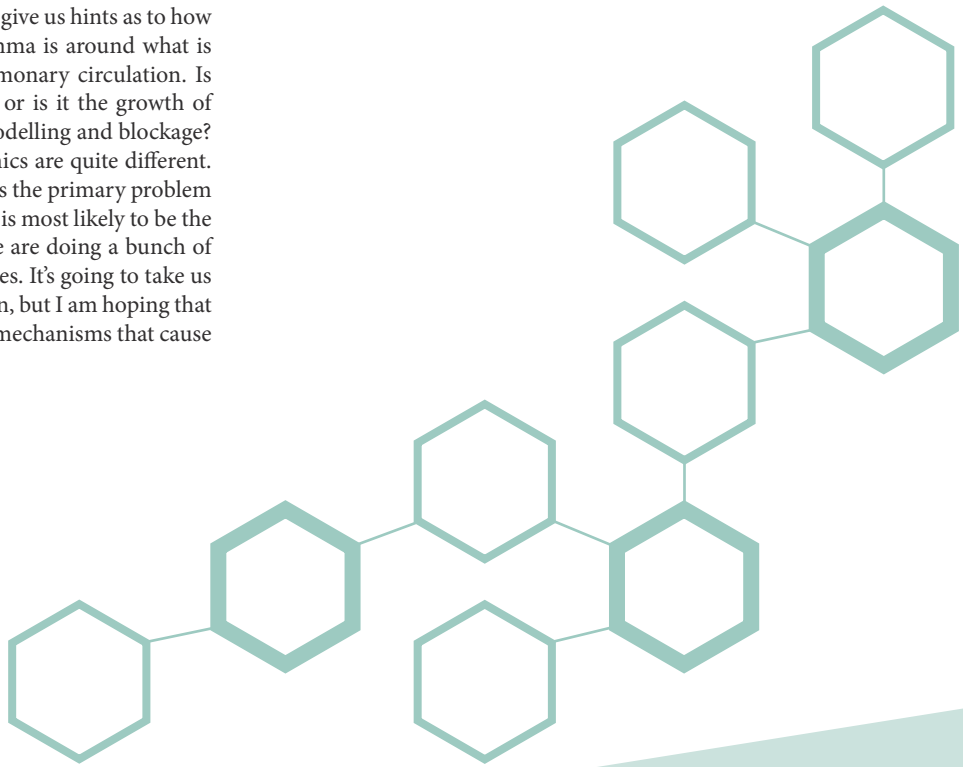
Dr. Stewart: I think there have been important advances in genetics. Even though we still don't understand how the gene mutations that cause PH actually cause the disease, research has opened a huge window in terms of trying to understand this. A number of mutations have been identified, which is an important advance.

It's also important to recognize that PH is complicated and that there are a lot of other systems involved, particularly the immune system. There's a lot of potential with advances that have been made in immunology with cancer and other immune diseases. We are only beginning to understand how these advances may help us treat patients with PH.

PHA Canada: What can the PH community look forward to in the near future?

Dr. Stewart: I am very confident that in the next few years we are going to see important developments; I think this will be the decade where we actually make real progress. I tend to be an optimist by nature, but I think PH is going to be a solvable disease. We just don't understand it well enough, and the therapies we have now are good but they are not curative. Looking forward to the next decade, I am confident that we'll have much more effective therapies. I even like to think that we'll have curative approaches. There's a lot of hope for the future.

Contributed by: Dr. Duncan J. Stewart, CEO and Scientific Director, Ottawa Hospital Research Institute and Research Director, University of Ottawa Heart Institute Pulmonary Hypertension Clinic



Research Corner:

From Fundamental PH Research to the Development of Novel Regenerative Therapies (Stem-Cell Therapies)

For the last few years, Mohamad Taha has regularly contributed articles that help demystify the science behind PH research and treatment, but he hasn't discussed the work he accomplishes as a PH researcher. For this issue of *Connections*, we've asked him to give us a backstage tour of the research lab he is affiliated with. Here's an overview of different types of behind-the-scenes PH research.

In this issue of *Research Corner*, we will discuss some of the scientific work performed in the laboratory of Dr. Duncan J. Stewart, at the Ottawa Hospital Research Institute, Ottawa, Ontario, in order to better understand and treat pulmonary hypertension (PH)

Understanding PH with the Help of our Amazing PHighters

Research on samples donated by PHighters helps us better understand PH and identify new therapeutic targets. As an example, we extensively study blood samples from PH patients, which we compare to blood samples from healthy donors. Using this method, we have been able to identify several components that are released in the blood, which can serve as future targets for therapy or function as markers of disease severity[1]. We can also grow cells from the donated blood on plates in the lab to study them. This allows us to better understand the changes happening inside the cells in PH and identify potential therapeutic targets[2]. We study these cells to better understand their metabolic ability (their ability to process chemical reactions and produce energy), which is an indication of how healthy they are. This type of research allows better understanding of PH pathology (nature of the disease) and may lead to the identification of potential therapy targets.

Understanding PH with the Help of Animal Models

Animal models of PH (research done on animals) allow us to better understand the disease on the level of a whole organism, not just on the cellular level. Projects in our lab focus on identifying genetic targets that may lead to the development of PH[3]. We also use these models to develop novel lung imaging techniques and study the role of enzymes in PH. Most importantly, we use these models to test newly developed therapies and monitor their efficacy in lowering pulmonary pressures and reversing changes in the lungs in PH.

Development of PH Therapies

Current PH therapies are "target specific," which means that each drug works on a specific biological function (target) that is involved in PH. Some therapies aim to increase targets that are usually reduced in PH like vasodilators, which open up blood vessels. For example, PDE-5 inhibitors (e.g. sildenafil) work on increasing nitric oxide signaling to help relax blood vessels (vasodilation). Other therapies aim to inhibit targets that are too abundant in PH, like vasoconstrictors, which close blood vessels. For example, endothelin-1 receptor antagonists (e.g. bosentan) work to inhibit endothelin-1 signaling to help reduce blood vessel tightening (vasoconstriction). In our lab, we test some target-specific therapies, but our focus is on the development of regenerative therapies (stem-cell therapies).

Stem-cells are best described as early cells that haven't completely committed to becoming a particular type of cell. Some subtypes of these cells circulate within the blood and play a role in replacing and repairing any damaged blood vessels. The advantage of stem cell therapy, compared to drugs, rests in the potential to deliver whole cells that can produce several therapeutic substances on their own and replace damaged cells. Our lab utilized these cells as a therapy for PAH by enhancing them so they would produce more vasodilators (nitric oxide). We completed a novel clinical trial showing the safety of these cells[4]. Currently, our lab and several others are working on a second phase of this research with a clinical trial that will assess the efficacy of stem cells as a therapy for PAH. You can find more information on this trial by searching for "NCT03001414" on www.clinicaltrials.gov.

Overall, PH research is happening here in Canada and novel therapies are being developed and tested, with the help of PHighters, making a path for a cure.

Contributed by: Mohamad Taha, PhD Candidate under the supervision of Dr. Duncan J. Stewart, Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa

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PHA Canada PH Research Scholarships

New Scholarship Recipients

One of the ways PHA Canada promotes Canadian research in the field of PH is by offering scholarships of up to $10,000 to outstanding trainees in support of their research. Through our research program, we provide a financial stipend to emerging PH researchers whose projects will contribute to the better understanding or treatment of PH. We currently support up-and-coming Canadian researchers pursuing scientific investigations that will help better the lives of Canadians living with PH through two PH research scholarships: the Paroian Family PH Research Scholarship and the Mohammed Family PH Research Scholarship.

In 2016, we were pleased to award our two first Paroian Family PH Research Scholarships to Sylvia Rinaldi of the University of Western Ontario (London, ON), and Virginie F. Tanguay from Laval University (Quebec City, QC). This year, thanks to the PHenomenal fundraising efforts of our community, we have awarded two new full research scholarships. We are happy to recognize the incredible support of the Mohammed Family, who have organized annual Run/Walk for PH Research fundraisers in Ajax, Ontario since 2014, by awarding the first Mohammed Family PH Research Scholarship to Alice Bourgeois, who is completing a Master's in Molecular Medicine at Laval University. We are also pleased to support further stages of Sylvia Rinaldi's research by awarding her a second Paroian Family PH Research Scholarship. We are excited to introduce Alice and Sylvia to the Canadian PHamily and share summaries of their projects in this research-focused issue of *Connections*.

Mohammed Family PH Research Scholarship Recipient

Alice Bourgeois
Laval University, Department of Medicine, Quebec City, QC

Under the supervision of:
Dr. Olivier Boucherat, Researcher and Assistant Professor
Laval University, Department of Medicine, IUCPQ Research Centre

Alice Bourgeois began her Master's in Molecular Medicine in January 2017 at Laval University, where she recently completed a Bachelor's Degree in Biology. She has always had a strong interest in understanding the fundamental mechanisms that cause disease, which is why she chose to pursue her graduate studies in this field. For the last two years, Alice has worked as a summer student for the Pulmonary Arterial Hypertension Research Group at Quebec City's Cardiology and Respirology Institute's Research Centre (Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec). This experience gave her insight into the broad field of health sciences research and consolidated her interest in pursuing a career in the field. She is pleased to remain involved with the PAH Research Group for her graduate studies, which will focus on understanding the molecular mechanisms leading to the development of PAH and investigating new therapeutic treatments. She feels privileged to have the opportunity to contribute to scientific knowledge.

Alice's Project: Role of FOXM1 in DNA Damage Response and Cell Cycle Progression in Pulmonary Arterial Hypertension

Pulmonary arterial hypertension (PAH) is a lung disease characterized by elevated blood pressure in the pulmonary arteries due to remodeling of the blood vessel walls. This increased pressure in the lungs can lead to right heart failure and premature death. The underlying cause of PAH remains unknown. Treatments are available, but they are limited, expensive, and often associated with undesirable side effects. Therefore there is an urgent need to identify new therapeutic targets and develop new treatments. The main goal of this project is to study the implication of Forkhead box protein M1 (FoxM1) in PAH. Previous promising studies in the field of cancer research have shown that FoxM1 is produced in abnormally large amounts and that it could be a potential therapeutic target. Considering characteristics shared by cancer cells and pulmonary arterial smooth muscle cells in PAH, the project proposes that FoxM1 may be involved in causing PAH. This research will investigate the

possible role of FoxM1 in the development of PAH using two different approaches. Firstly, PAH cell lines will be tested to see if it is possible to correct the hyper-proliferation of pulmonary arterial smooth muscle cells and resistance to cell death. Secondly, working with rodents, the researchers will evaluate whether inhibiting FoxM1 prevents or reverses PAH characteristics. This study opens new avenues to PAH treatment and will provide a better understanding of the disease at a molecular level.

Contributed by: Alice Bourgeois, Master's in Molecular Medicine student, Laval University, Department of Medicine, Quebec City, QC

Paroian Family PH Research Scholarship Recipient

Sylvia Rinaldi
The University of Western Ontario, Department of Health & Rehabilitation Sciences, London, ON

Under the supervision of:
Dr. Janet Madill RD, Researcher and Assistant Professor
Brescia University College, London, ON

Sylvia Rinaldi is a Registered Dietitian and PhD candidate in the Department of Health and Rehabilitation Sciences at the University of Western Ontario with a focus on health and aging. Sylvia earned her Bachelor's in Biochemistry at the University of Windsor and a Bachelor's and Master's in Foods and Nutrition at Brescia University College. She developed a passion for respiratory health while completing her Master's project, which focused on the nutritional status of individuals with interstitial lung disease. She has since expanded her research interests to exploring the nutritional concerns of people with pulmonary hypertension (PH). As a Registered Dietitian, Sylvia values evidence-based and research-driven clinical practice. These values guide her scientific investigations into the links between nutrition and disease and her research into how improvements in nutrition may lead to better disease outcomes and quality of life for patients.

Sylvia's Project: Nutritional Status of Patients with Pulmonary Hypertension

Research team: Dr. Janet Madill, Brescia University College (London, ON), Dr. Sanjay Mehta, London Health Sciences Centre (London, ON), and Sylvia Rinaldi, University of Western Ontario (London, ON)

Pulmonary hypertension (PH) is a serious lung disorder resulting from the narrowing of the pulmonary arteries, which carry blood from the heart to the lungs. Although it is known that being either underweight or overweight can hinder one's ability to breathe, there exists limited literature investigating the nutritional concerns of PH patients. The goal of the study is to determine the nutrition profile of PH patients through a comprehensive dietetic assessment conducted across disease subtypes and severity, as well as over time. Since minimal information is available in scientific literature focusing on the nutritional status of PH patients, this research will first seek to identify potential nutritional concerns in this patient population. The dietetic assessment will also involve measuring patients' body compositions (such as muscle mass, body fat, and body water) and functional status (such as muscle strength, weight history, and nutrient intake).

This project has the potential to improve the lives and outcomes of PH patients through inter-professional collaboration in the management of the disease. Given that there is limited information on PH patients' specific nutritional needs, it is anticipated that knowledge gained from this research will be used to guide health professionals involved in the care of PH patients to proactively manage patients' nutritional concerns.

Contributed by: Sylvia Rinaldi, PhD candidate, Department of Health and Rehabilitation Sciences, University of Western Ontario, London, ON

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Tribute to Remarkable PHighters

Celebrating the Lives of PHA Canada Directors

While progress continues to be made each year in the areas of research and access to care and treatment, PH continues to take loved ones away from us. In 2017, we were sad to share news of the passing of Rita Hébert, Lynn-Marie Cox, and Harry Kingston, who all have served the Canadian PHamily as members of our Board of Directors. We take this opportunity to celebrate the lives of these remarkable PHighters and pay tribute to their contributions to the PH community. In an effort to keep their memory alive, we have asked current PHA Canada Directors to reminisce on the relationships they built with their departed colleagues, friends, and fellow PHighters.

Tribute to Rita Hébert

PHA Canada Director, 2011–2013

Rita, a long-term survivor, was a very respected and involved member of the Canadian PHamily. After serving as a PHA Canada Director, she remained closely involved with the organization and played an important role in the Quebec PH community by ensuring that other patients could find support in the Montreal area. We pay tribute to Rita, whose resilience and strength will continue to inspire others battling PH.

As a founding member of PHA Canada I have been involved for many years in the PH community and, throughout this time, have had the opportunity to meet many wonderful people connected to PH in a variety of ways. One of the true shining stars I had the pleasure of knowing due to our mutual connection to PH was Rita Hébert. A PH patient living in Quebec, Rita was truly dedicated to providing support to patients in the province in both French and English—she worked to ensure that both groups felt equally supported. Through her connections at both the Jewish General Hospital and the Montreal Heart Institute, Rita organized many patient support group meetings and information sessions to support the local PH community. I had the pleasure of traveling to Montreal to attend one of her first sessions in my role as PHA Canada Regional Coordinator in the organization's early days. Rita's energy and passion for helping others was obvious in all that she did. Despite living with PH due to a congenital heart issue she had been dealing with her entire life, Rita always had a smile and never let illness keep her down. She was involved not only as a Board member with PHA Canada, but also acted as a support group leader in Montreal for several years. She sat on our National Conference Planning Committee when the event was held in her region and participated in various other groups and sub-committees as the French-speaking liaison for our Board. I feel truly blessed to have known Rita and to have had the opportunity to work with her for numerous years. She was not only a fellow Board member but also a friend. She will be deeply missed but always remembered.

Contributed by: Jennifer Gendron, PHA Canada Founding Board Member, Hampton, NB

Roberta Massender and Rita Hébert at our 2015 National Conference.

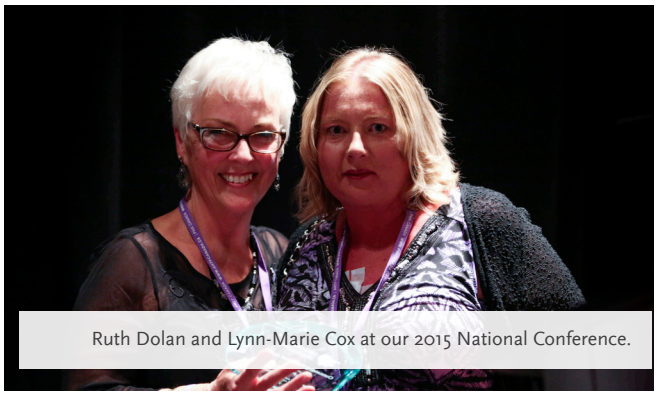
Tribute to Lynn-Marie Cox

PHA Canada Director, 2011–2017

Lynn was instrumental in creating a network of support for patients across the country. She touched the lives of many Canadians affected by PH through her work with PHA Canada and the support and guidance she provided other patients and those new to the world of PH. The initiatives that stemmed from her passion for helping other PH patients will have a lasting impact on the Canadian PHamily. We honour Lynn's contributions, knowing that her memory will shine a bright periwinkle light on all the PHighters following her example and putting up a strong and brave fight against PH.

I first met Lynn-Marie in February 2013, a few months after I joined PHA Canada's Board of Directors, when she attended the Western Canada PH Symposium in Vancouver. Lynn-Marie had been elected to the PHA Canada Board of Directors in September 2011, and I knew of a few remarkable aspects of her journey with PAH. Diagnosed in 1998, at a time when few treatment options were available and no national support network existed, Lynn-Marie became the first patient in Alberta to be treated with intravenous epoprostenol (Flolan®). As we worked together, I learned of our shared experiences and interests and of her extraordinary contributions to the community. Lynn-Marie was courageous and she exuded personal warmth that brought hope and strength to the many patients and families who reached out to her for support. I am privileged to have known Lynn-Marie, to have worked with her, and to have experienced her kindness, generosity, and the goodwill she extended to everyone she came into contact with.

Contributed by: Roberta Massender, Vice-Chair, PHA Canada Board of Directors, Richmond, BC



Ruth Dolan and Lynn-Marie Cox at our 2015 National Conference.

Tribute to Harry Kingston

PHA Canada Director, 2013–2017

Harry lived by the phrase "never surrender" and his dedication to fostering PHA Canada's vision of a better life for all Canadians affected by PH never faltered. Committed to seeing the PH community thrive, Harry took a leading role in supporting PHighters locally through the Ottawa PH Support Group and actively advocated on behalf of patients. His legacy will not be forgotten; in his memory, we will continue to PHight for all those who, like him, will "never surrender" to PH.

PAH is an unforgiving disease and time is of the essence in getting a diagnosis. Harry knew this well and, along with his wife Teri, committed himself to bringing awareness to this disease.

Harry was an accomplished man with a clear sense of direction and purpose. He was a Distinguished Toastmaster, a Christian man who devoted himself to his church, volunteered with the Ottawa Police Service as Neighbourhood Watch Coordinator, and a Board Member of PHA Canada. He fought to improve the lives of Canadians with this devastating disease at the same time dealing with his own illness. In June, Harry knew that he and Teri had suffered enough. He joined our Board call on the evening of Monday, June 26th urging Board members to continue the PHight. He passed away the next morning.

Harry treated everyone with respect and honoured relationships. He will be missed by many and be remembered for his compassion and commitment to helping others.

Contributed by: Carolyn Doyle-Cox, Advanced Practice Nurse, Ottawa Pulmonary Hypertension Clinic and PHA Canada Board Member, Ottawa, ON

It is with a heavy heart that I recollect my time of knowing a gentleman by the name of Harry Kingston. I met Harry after he joined PHA Canada's Board of Directors in 2013. As a Founding Board member, I volunteered to mentor Harry as he joined the Board and proceeded to spend endless hours of his time working tirelessly to further the mission and values of our organization. Harry was a man with an unwavering sense of duty, not only to this country, but also to the PH community. Harry, with the extraordinary support of his wife Teri, advocated selflessly on behalf of all persons affected by pulmonary hypertension. Harry helped bring awareness to this rare disease on local, provincial, and national scales. Knowing Harry over the last four years was a privilege for me. His dedication to our community, even on the toughest days, continues to inspire me.

Contributed by: Darren Bell, PHA Canada Founding Board Member, Vancouver, BC

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