The Kidney Foundation of Canada Research Awards

2021 Awardees and Lay Summaries

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ALLIED HEALTH KIDNEY SCHOLARSHIP

Victoria Riehl-Tonn

University of Calgary

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2022	$5,000	Nursing



Sex, Gender, and Quality of Life in Patients Initiating Hemodialysis

Kidney failure is an irreversible, progressive decline in kidney function. As kidney function declines, the ability of the kidneys to function and excrete fluid and wastes is decreased. In Canada, more than 40,000 people are living with kidney failure that require life-sustaining kidney replacement therapy in the form of dialysis. Hemodialysis uses a dialysis machine that removes blood to filter and clean it, before returning it back to the body.

Currently, all patients initiating hemodialysis are given the same treatment prescription of 4 hours thrice weekly. This is known as conventional hemodialysis. However, it has been shown that quality of life in the dialysis population is worse than the general population. Furthermore, females on dialysis have a worse quality of life than males. Quality of life is a predictor of hospitalizations and mortality in dialysis patients. This is important, and quality of life has been identified by patients as a research priority. Incremental hemodialysis is a new initiative in Alberta that aims to improve quality of life for dialysis patients. With incremental hemodialysis, patients start on a lower dose (less than thrice weekly) and gradually increase their dialysis prescription as their residual kidney function declines.

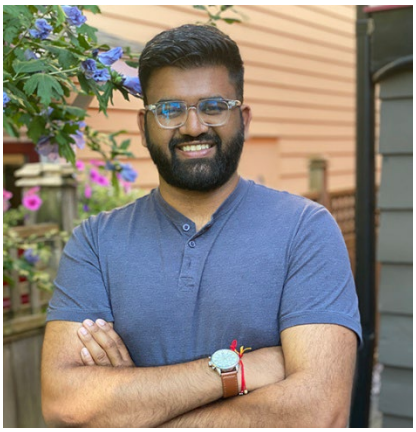
The aim of incremental hemodialysis is to ease the transition onto hemodialysis and gradually adjust dialysis prescription to eventually be at thrice weekly dialysis. Easing patients onto hemodialysis reduces treatment burden and is associated with better tolerance of treatment and better quality of life. My project is a prospective cohort study with a 3-month follow-up time to find the association between quality of life and incremental and conventional hemodialysis, stratified by sex and gender. My population is incident kidney failure patient's initiation hemodialysis in Alberta. My exposure is incremental hemodialysis which will be compared to conventional hemodialysis. My outcome is quality of life, which will be measured using the standardized and valid Kidney Disease Quality of life-36 item (KDQOL-36) questionnaire. The setting is all Alberta Kidney Care clinics.

ALLIED HEALTH DOCTORAL FELLOWSHIP

Rohit Singla

The University of British Columbia

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$50,000	Chronic Kidney Disease



Quantifying Kidney Fibrosis Non-invasively with Smart Ultrasound

Chronic kidney disease (CKD) prevents the body from performing vital functions such as blood filtering, blood pressure maintenance, and waste elimination. With diabetes, obesity, hypertension, and an aging population all increasing, CKD impacts over 1 in 10 adults globally.

CKD follows a common histopathological pathway which results in the accumulation of fibrosis within the kidney. Due to deficiencies in how it is identified, fibrosis goes unnoticed until CKD has reached the latter, more severe, stages. Similarly, kidney transplantation has not seen significant improvements in long-term donor organ survival outcomes, driven by a similar sub-clinical accruement of fibrosis. The sole method for evaluating for fibrosis is invasive biopsy, which has limitations including needle phobia, patient pain, risk of hemorrhage, hematuria, and infection, and sampling error. Repeated protocol biopsies, while performed in certain centers, are not routinely performed in adults. This limits the ability to temporally monitor the response to treatment.

This work proposes the use of ultrasound (US) and machine learning (ML) to non-invasively assess fibrotic load in a volumetric and real-time manner. US is commonly used to image the kidney but is challenging to use and interpret. ML can assist with this by allowing computer algorithms to automatically learn patterns and

perform tasks without being explicitly programmed. It has shown record breaking capabilities in medical imaging. However, ML parameters and how they link to the disease state is difficult to interpret. An US imaging method called S-WAVE may be the missing link. Shear wave absolute vibroelastography (S-WAVE) is a new highly accurate variant of ultrasound elastography that provides volumetric tissue stiffness measurements and at larger imaging depths. S-WAVE has shown that for certain diseases, stiffness correlates with severity.

Additionally, changes in glomeruli diameter in the early stages of damage cause fundamental changes to the raw ultrasound signal itself. ML can enable the easy measurement of glomeruli diameter. Using both SWAVE and glomeruli diameter together may yield a long-sought biomarker for renal fibrosis. This work proposes creating the new algorithms using US, ML, and S-WAVE to quantitatively measure fibrosis. In a single-center prospective cohort study on patients receiving all-cause kidney biopsy, patients will undergo a smart kidney ultrasound. Their SWAVE and glomeruli diameter results compared against biochemical and biopsy results. In turn, this may optimize resource usage, improve monitoring capabilities, and improve long-term outcomes.

ALLIED HEALTH KIDNEY RESEARCH GRANTS

Dr. Marisa Battistella

University Health Network

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2021	$98,353	Dialysis



Deprescribing in Patients on Hemodialysis

Patients on hemodialysis (HD) take more pills per day on average than any other chronically ill patient population. On average, a patient on HD takes 15 medications per day, of which 70% may not be appropriate. The medications may not be appropriate because patients on HD are rarely included in clinical trials for new medications, and therefore the efficacy and safety data that exists for the general population may not actually apply to them.

Tools to guide the re-assessment and discontinuation (deprescribing) of these specific medications that lack evidence for efficacy and safety in patients on HD are needed. These tools will help reduce the number of medications being taken and may also reduce the potential negative consequences of taking so many medications (e.g. adverse drug reactions, drug-drug interactions, non-adherence, increased risk of cognitive impairment, impaired balance and falls, and increased risk of hospitalization, and mortality).

Our study group identified nine medications that are often inappropriately prescribed to patients on HD. These medications are: Alpha-1 Blockers, Benzodiazepines & Z-Drugs, Gabapentinoids, Loop Diuretics, Prokinetic Agents, Proton Pump Inhibitors, Quinine, Statins, Urate Lowering Agents.

We developed and validated tools to help medical teams and patients in outpatient HD units with identifying and stopping these medications. The next step for our working group will be to perform a study where we test these tools in practice at an HD centre in Toronto. We believe that this study will help decrease the number of medications per patient and decrease inappropriate medication use in the HD unit. The results of this study will help us make improvements to our deprescribing tools that will make them easy-to-use and adaptable to all patients. The goal of this study is to improve patient experiences by optimizing medication use and prescribing patterns in HD units across Canada.

Kara Schick-Makaroff

University of Alberta

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Dialysis



Tailoring a Pathway for Mental Health Care for Albertans on Dialysis

"*I have met many, many medical staff that are scared of depression and anxiety. Any mental health issues - they don't even wanna talk about them, period. So, if they're asking the depression question and think, 'Oh my goodness. He is a seven out of ten, wow! I wonder what's going on there?' But once they ask that question, they really need to be prepared to do something about it.*" (An Albertan home dialysis participant from our study on quality of life.)

Mental health concerns are very common for people on dialysis. Up to four out of 10 experience depression and anxiety. This has likely increased due to COVID-19, similar for many Canadians. But dialysis patients are also isolated and now have different health care services. Albertans on dialysis have said that their mental health is a top priority. Unfortunately, mental health symptoms are rarely addressed or treated in dialysis. The patient quoted above expressed this so well. Dialysis clinicians do not feel prepared to address mental health.

Here is what one nephrologist said in our previous study on quality of life: "*You know, things such as anxiety, depression – those aren't things that we're particularly well adept at managing. So, the truth is, most nephrologists, my guess is, would just as soon not hear about things that don't really fall into their scope of practice.*" We want to address this gap in dialysis care. We plan to work together with people on dialysis, community members, clinicians, leaders, and researchers to create a document, called a "pathway", to guide mental health care.

- First, we will find out what is currently done for mental health care in dialysis across Alberta. We will interview patients, clinicians, and administrators. We will also send a survey to clinicians.
- Second, we will speak with clinicians in primary care and mental health to find out how dialysis patients can access their help.
- Third, we will look at the tools currently used by dialysis patients to report on their mental health symptoms, and the quality of their overall care. And we will see how their responses can be used to provide them with the best care.
- Fourth, we will use all of this information to draft a pathway. We will invite patients, clinicians, leaders, and researchers to give their feedback.

We will revise the pathway based on their recommendations. In so doing, we bring together those in the kidney community to create the best mental health care for those on dialysis. Our research will address a major gap in our understanding about how to address and provide support to people on dialysis who are experiencing mental health symptoms. Our findings may ultimately improve the quality of life for Canadians on dialysis living with mental health symptoms. Results may also be applied to kidney programs across Canada and internationally.

KIDNEY HEALTH RESEARCH GRANTS

Dr. Rami Al Batran

University of Montreal

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$150,000	Screening & Prevention



Could a ketogenic diet slow the progression of diabetic kidney disease?

The incidence of diabetic kidney disease (DKD; also known as diabetic nephropathy) has more than doubled in the past decades, largely due to the increasing prevalence of diabetes. Approximately 30 to 40% of all diabetic patients will develop DKD, and many of them will eventually require dialysis and/or kidney transplantation. Thus, DKD imposes an enormous burden on our health care system and patients' quality of life.

The current clinical management of DKD stabilizes but does not improve kidney function, indicating a substantial treatment gap. Therefore, there remains an unmet need for innovative treatment strategies to prevent, improve, treat and reverse DKD. Indeed, lifestyle modifications, a combination of dietary interventions and increased physical activity, are frequently recommended to diabetic patients to reduce the incidence of DKD and slow its progression.

The ketogenic diet (KD), a high-fat, low-carbohydrate diet with adequate protein, has attracted greater attention recently as a potential weight-loss strategy, likely due to the obesity epidemic. Also, KD has been shown

to increase levels of ketone bodies in animals and humans. Ketone bodies are important fuels for the kidneys; however, little is known about their role in the diabetic kidneys.

We speculate that increasing circulating ketone bodies via feeding diabetic mice a KD will reduce the incidence of DKD and slow its progression. We will test our hypothesis by inducing diabetes in mice and measuring ketone body metabolism rates in the diabetic kidneys. Then, we will feed these mice a KD and assess its effects on kidney function. These experimental approaches will help us to investigate whether changes in ketone body metabolism contribute to the development of DKD, and to determine whether KD can be used as an approach to reduce the incidence of DKD and slow its progression. It is our hope that the ideas put forth in this study will bring new ways of thinking into the field of ketone body metabolism and will lead to exciting new research directions.

Dr. Khaled Barakat

University of Alberta

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Quality of Life



Development of SHP2 inhibitors as a treatment for Acute kidney injury

Acute kidney injury is a sudden incident of kidney damage, which can also affect other organs such as the brain, heart, and lungs. The mortality rates associated with AKI are still high, therefore, the goal of identifying novel therapeutic targets and modalities to prevent and treat AKI is critically needed. Our proposal will focus on contributing to this goal by blocking the activity of one of the recently identified hallmarks in Acute kidney injury. Our team recently identified tools that have been shown to interact very strongly with this target and the objective of our proposal is to validate this approach as a possible treatment for Acute kidney injury. Findings

from our proposal will advance the development of a new generation of promising and new treatments to prevent Acute kidney injury.

Dr. Darren Bridgewater

McMaster University, Faculty of Health Sciences

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Kidney Development



Nephron development: A role for Shroom3 in nephron progenitor morphogenesis

Patients with kidney disease have changes in a gene called SHROOM3. Through basic science studies, our work was the first to validate that SHROOM3 as playing important functions in the kidney and when these functions are disrupted this leads to kidney disease. We now wish to build on these exciting studies. To that end we have exciting new data that shows the kidney disease could be due to alterations during early development of the kidney. Therefore, in this proposal we will investigate Shroom3 functions in the earliest stages of kidney development to determine how the changes during kidney development could lead to disease.

It is our hypothesis that disruptions in the Shroom3 gene lead to disruptions in Shroom3 function causing structural and functional abnormalities that contribute to kidney disease. Specifically, we will determine how Shroom3 effects the development of the kidney and examine how Shroom3 helps in the cells ability to communicate. We will also utilize human biobanks to further understand the changes in the Shroom3 gene as a contributor to kidney disease. To generate new treatments for kidney disease we must first understand the molecules and mechanisms of how and where they work. These studies will be the first to examine how changes in Shroom3 expression or function regulate the earliest stages of kidney formation and will yield vital new insights into how kidney cells form, work, and heal.

Dr. Jean-François Cailhier

Centre Hospitalier de l'Université de Montréal

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Renal Failure



Deciphering the inflammatory proprieties of crystalloids: Why Saline is bad?

Inflammation is present in all intensive care patients. Leukocytes, white blood cells are important in the inflammatory response. However, when the inflammation is too great, the compensatory mechanisms of the patients are overwhelmed, and the patients can then have complications such as acute kidney injury (AKI) or other dysfunctions. The immune system of these patients goes from a period of hyperactivation to a period of immune fatigue associated with immunosuppression leading to infections. Any stimuli can then contribute to overstimulate leukocytes, exacerbating renal and tissue damage, leading to immunological fatigue. Critical care patients, in addition to receiving antibiotics, also receive fluids in the form of crystalloids.

Three solutions are available clinically: Normal Saline, Ringer's Lactate and PlasmaLyte. Recently, normal saline, with a higher concentration of chlorine, has been associated with more AKI and other bad kidney events, with no real explanation. However, the impact of fluids on the modulation of inflammation and their role in renal insults and immunosuppression in intensive care patients are unknown.

Our hypothesis is that Normal Saline is the solution with the worst inflammatory impact, thus causing more AKI. In order to test our hypothesis, we will study the inflammatory modulation induced by the infusion of each of the solutions in cardiac surgery patients. Furthermore, we will perform experiments on their leukocytes to understand the mechanism by which sodium actives them.

We will also evaluate the inflammatory impact and the consequences on renal function of the various crystalloids in a murine model of renal insult: ischemia-reperfusion. The absence of excessive inflammation prior

to the surgery at the time of administration in cardiac surgery patient will make it possible to assess any modulation induced by these solutions on the activation of leukocytes and the production of associated inflammatory cytokines. The murine model of renal ischemia by arterial clamping and contralateral nephrectomy will reproduce a clinical condition often found in intensive care patients. Immunological analyzes and with immune stimulation in vitro will be carried out to evaluate the inflammatory potential of the fluids in vivo and in vitro. We will assess leukocyte activation by flow cytometry and the measurement of plasma levels of inflammatory proteins various techniques. This study will provide further insight into the immunomodulatory impact of clinically used fluids and its role in the increased incidence of AKI as seen with Normal Saline. It will identify the type of crystalloids with the least inflammatory and nephrotoxic potential. These results will lead to a greater understanding of immunological effects to allow personalized use of solutions in the clinic.

Dr. John Chan

University of Montreal

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Diabetes



Oxidative Stress and Regulation of SGLT2 Expression in Diabetic Kidney

90% of glucose filtered by the kidney is reabsorbed in renal proximal tubules (RPTs) by a protein called sodium-glucose cotransporter 2 (SGLT2). Since SGLT2 expression is upregulated and SGLT2-mediated glucose reabsorption is increased in the diabetic kidney, selective inhibition of SGLT2 expression and activity is a therapeutic target of the treatment of diabetes. The mechanism(s) of upregulation of renal SGLT2 gene expression in diabetes is, however, not fully understood. In this proposal, Dr. John Chan is examined a protein, called nuclear factor erythroid 2-related factor 2 (NRF2) how this protein is involved to upregulate the expression

of renal SGLT2 in excerbating kidney damage in diabetes. Dr. Chan's studies will identify whether NRF2 could be a therapeutic target in preventing nephropathy progression in diabetes.

Dr. Edward Clark

Ottawa Hospital Research Institute

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Dialysis



Albumin to Enhance Recovery from Severe Acute Kidney Injury

Background: Sudden damage to the kidneys, causing a decrease in their function, is called acute kidney injury (AKI). AKI often happens to critically ill patients in an intensive care unit (ICU). Dialysis is a blood-cleaning procedure that replaces some of the kidneys' usual functions. For patients with severe AKI, dialysis can be life-saving. Patients that need dialysis for severe AKI have a very high risk of death (50% or more), require long stays in ICU and incur high costs to the health care system. Many patients who survive don't recover enough kidney function to stop dialysis treatments when they are discharged from ICU. Sometimes they require dialysis permanently afterwards. Dialysis does not repair kidney damage but does prevent death from kidney failure. This allows damaged kidneys and other organs to heal over time. In fact, dialysis itself may cause additional damage.

Additional damage occurs because critically ill patients often have a drop in their blood pressure (hypotension) caused by dialysis treatments. The hypotension caused by dialysis is harmful to the kidneys, heart, and other organs. As a result, hypotension during dialysis may increase the risk of death and limit kidney recovery. Albumin is a protein normally found in the blood. Patients with higher levels of albumin in their blood have less hypotension during dialysis. Intravenous albumin is a blood product that is widely used to treat

hypotension. Some doctors prescribe intravenous albumin to be given to critically ill patients during dialysis to prevent hypotension. However, the use of intravenous albumin for this purpose depends more on doctors' preferences than science, data, or evidence. Intravenous albumin is also very expensive. Our research team recently completed a study showing intravenous albumin prevents hypotension during dialysis in critically ill ICU patients with AKI.

This study had too few patients to determine if intravenous albumin has an impact on outcomes that are most important to patients such as the risk of death or the need for permanent dialysis.

Method: We will undertake a study of patients with AKI that need dialysis for AKI in an ICU at 5 Canadian hospitals. Patients that consent to the study will be randomly assigned to be given either intravenous albumin or an equal amount of a placebo (saline intravenous fluid) during dialysis treatments. We will then measure the difference in the numbers of patients that die or need permanent dialysis in the two groups to determine if intravenous albumin is effective.

Conclusion: If this study finds intravenous albumin reduces death or the need for permanent dialysis, it is a widely available treatment that can be used for more patients with severe AKI. If not, an expensive but ineffective treatment that is already being used by some doctors can be stopped with the money currently spent on intravenous albumin being better used elsewhere.

Dr. Kristin Kyomi Clemens

London Health Sciences Centre Research Inc. (Lawson Health Research Institute)

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$99,999	Dialysis



Prevent Fractures for Renal Disease-1 (PREFERRED-1)

Preventing bone fractures in hemodialysis with denosumab: a pilot study for a large clinical trial (PREFERRED-1)

Background: One in 10 women and one in 20 men who receive hemodialysis (a treatment for kidney failure which filters waste and water from blood) will suffer a fracture due to brittle bones. “Fragility” fractures not only lead to pain and loss of quality of life, but admissions to hospitals, nursing homes, and even death. Fragility fractures are also extremely costly to our healthcare system.

Purpose: Despite the risk of fragility fracture in hemodialysis, there are no research studies on how to best prevent them in this population. Most "fracture-preventing" medications available for use in those with normal kidneys either can’t be used in hemodialysis or have severe side effects (e.g heart attack). Although a medication called denosumab (Prolia) is approved for use in dialysis, there have been no large research studies to determine if it can safely and effectively prevent fracture.

Procedure: Our team of doctors, researchers and patients will conduct a clinical trial to learn whether denosumab prevents fractures and can be safely used in adults on hemodialysis. Our trial will be conducted in “real-world” dialysis units, using existing data to capture patient characteristics and outcomes, and will be conducted at a fraction of the cost of a traditional clinical trial. Before conducting our large trial of denosumab, we propose a small "pilot" study (PREFERRED-1) to ensure that a large trial is possible, and that enough patients will participate.

Outcomes: With completion of PREFERRED-1 we will understand how well we can conduct a larger trial examining fracture outcomes with denosumab, an outcome that matters most to patients and providers. We will also explore how safe this medication is in people using hemodialysis.

Relevance to patients: People using hemodialysis are routinely excluded from research studies. They are denied treatments that could improve their care, outcomes and quality of life. PREFERRED-1 will purposively include and study these individuals and spark the creation of needed knowledge to better care for those with kidney disease. Where people with kidney disease have expressed the desire for healthcare providers to work together and coordinate their healthcare, PREFERRED-1 will also bring together doctors, researchers and patients to study a treatment that can be delivered in a patient-centered manner (i.e. dialysis unit). With patients included as full research partners in PREFERRED-1, they will feel valued, supported and listened to in their healthcare.

Dr. Casimiro Gerarduzzi

Hôpital Maisonneuve-Rosemont

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$150,000	Kidney Biology



Investigating the Provisional-Immune Matrix in Kidney Injury via SMOC2

Background: The smallest parts of our body that work to keep us alive are called cells. Cells need the area where they live to be healthy, similar to people living in a home. This home, which we call the extracellular matrix (ECM), is made from many different building blocks and pieces needed for cells (people) to grow inside. Patients with various kidney diseases show signs of damage to the ECM home of kidney cells. This damage to the ECM home makes cells less healthy and unable to work well. As a result, cells turn into construction workers by repairing the damage using new ECM building blocks, which rebuild their ECM home to return to their usual job.

Purpose: Understanding how kidney cells fix damage from diseases could be used to help them heal faster and better. We will study how kidney cells prepare themselves and work together to repair. We also want to discover which specific building blocks cells need and how cells use them to repair their ECM home.

Procedure: Cells make a checklist of materials it needs to replace those damaged in an injured kidney. This list is like the “blueprint” of building materials needed to renovate a house. In this case, the blueprints are those used to fix a damaged kidney. Through our laboratory experiments, we will read the blueprint list that kidney cells use to repair their damaged ECM home. Once we find key building blocks from this kidney list, we will use them to study how they work with kidney cells.

Outcome: We found in a cell’s blueprints a building block that it uses for repair. Our identified building block helped start cells to repair their damaged ECM home because it was part of the foundation onto which cells need to rebuild. It also helped organize cells from other areas of the body to help kidney cells to heal. Relevance to patients: The discovery of a blueprint of building blocks would allow us to design drugs or supplements to treat kidney diseases. Such designs could help introduce each “building block” faster or fill in those missing from the list for a complete and quicker repair of a damaged ECM home. As a result, this will help cells rescue kidney function. Also, we would be able to find differences in building blocks when comparing a list taken from a healthy kidney with that of a damaged kidney. These differences could alert doctors when a patient has an injured kidney. Overall, this information could help kidney patients heal faster, which would improve the standard cost and quality of life for kidney patients.

Dr. Rémi Goupil

CIUSSS du Nord-de-l'Ile-Montréal

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Hypertension



CENTRAL-CKD

Purpose: In patients with the most severe form of chronic kidney disease, blood pressure (BP) control can be difficult as the margin of error between a too low BP and a too high BP is quite thin. Keeping the BP in the appropriate range helps minimise the risk of progression towards dialysis and the risk of cardiovascular complications. Also, it helps reduce side effects of medication and symptoms related to inappropriate BP. However, the way we currently measure BP, with a cuff installed on the upper arm (or brachial BP), can be highly inaccurate to determine the BP that is in the large vessels in the body (or aortic BP). It is important to have the best estimation of this last BP as it is the one that directly impact the heart, the brain and the kidneys. These past years, central BP devices have been developed and we can now have a better estimation of the aortic BP. We think that better estimating aortic BP with central BP devices instead of using brachial BP values will allow us to improve the life of people with severe kidney disease.

Procedure: This study will assign at random 116 patients with severe kidney disease to a central BP target or to a brachial BP target. These two BP will be measured at the same time by one machine. The patients, doctors and investigators will not know what target was allocated (blinded trial). During the study, the patients will be taken care of as usual by their kidney doctors who will not know if the BP that is provided is a central or a brachial BP.

Outcome: This study aims to determine the feasibility of doing a larger trial aimed at verifying which strategy is best for outcomes that are more important to patients, but also to determine which strategy results in the lower arterial stiffness after 12 months, as a marker of cardiovascular disease.

Relevance to patients: The CENTRAL-CKD study has the potential to change how we treat high blood pressure in patients with severe kidney disease, to reduce the burden associated with this condition.

Dr. Gregory Hundemer

Ottawa Hospital Research Institute

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$122,340	Screening & Prevention



The Impact of Subclinical Primary Aldosteronism on Kidney Disease

Background: Hypertension (high blood pressure) management generally involves a 'one size fits all' approach. Employing a more personalized approach targeting the specific cause of an individual patient's hypertension provides the opportunity to improve long-term health.

Primary aldosteronism (PA) is a very common, yet often unrecognized, cause of hypertension caused by excess production of a hormone called aldosterone. Excess aldosterone causes the body to retain salt, raises blood pressure, and damages the kidneys. Indeed, PA leads to disproportionately high rates of kidney disease compared with other forms of hypertension. Importantly, the adverse health consequences of PA are preventable with early treatment using medications (called mineralocorticoid receptor antagonists) that directly block the effects of aldosterone. These medications used to treat PA are distinct from the blood pressure medications that are routinely used to treat other forms of hypertension.

Recently, a growing body of evidence has demonstrated that milder forms of PA ('Subclinical PA') are exceedingly common in the general population yet go undetected in modern-day medical practice. Whether Subclinical PA leads to increased rates of kidney disease remains unknown.

Purpose: To study the impact of Subclinical PA on kidney disease.

Procedure: We will investigate Subclinical PA using CARTaGENE – a study which enrolled over 20,000 Québec residents in 2009-2010 and captured a vast amount of health information on these individuals. A subset of these individuals had blood and urine samples collected and stored both at the beginning of the study and 7 years later. We will use the stored blood and urine samples to measure aldosterone levels among these individuals to identify those with Subclinical PA and compare their rates of kidney disease to those participants without Subclinical PA. We will also employ a state-of-the-art technique called proteomics which will allow us to study the effects of aldosterone at the molecular level to gain an understanding of the precise mechanisms by which Subclinical PA may damage the kidney.

Outcome: We anticipate that individuals with Subclinical PA will develop higher rates of kidney disease compared to individuals without Subclinical PA.

Relevance to Patients: If indeed individuals with Subclinical PA experience higher rates of kidney disease, the logical next step will be to study whether using medications that specifically target Subclinical PA (and are not used routinely in the treatment of hypertension) will prevent kidney disease in this large, but currently unrecognized, population. This study will provide a much-needed step toward a more personalized approach to hypertension management that will serve to prevent future kidney disease.

Dr. Tony Kiang

University of Alberta

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$98,778	Transplantation



p-Cresol and mycophenolate interaction in adult kidney transplant patients

Mycophenolate (or mycophenolic acid) is a commonly used medication for life-long maintenance to prevent the body from rejecting the transplanted kidney. Mycophenolate is usually prescribed in a fixed regimen, and almost all patients would receive the same starting dose. Unfortunately, many patients show

large variations and high blood concentrations of mycophenolate, which can result in severe side effects such as reduced white blood cell counts and infection. In many transplant centres in Canada, more than one quarter of the kidney transplant patients develop severe side effects to mycophenolate. The exact reasons why so many patients have high and variable mycophenolate blood concentrations remain unknown.

Recently, our lab has found a potential cause: that a blood toxin called "p-cresol" which is accumulated in this patient population may be the culprit of the high blood concentrations and the toxic responses observed of mycophenolate. Using innovative human test tube models, we found that p-cresol reduced the body's ability to eliminate mycophenolate, therefore effectively pushing up its blood levels. As the blood concentrations of p-cresol are also highly variable, p-cresol could be one of the major reasons for the large variation observed of mycophenolate blood levels in patients.

Our clinical experiment will confirm our thinking in adult kidney transplant patients where we will compare the blood concentrations of both p-cresol and mycophenolate, using cutting edge approaches in our field. If we are correct, health care professionals can actively manage (i.e. reduce) the blood levels of p-cresol (e.g. through diet regimens or synbiotics) which should significantly reduce the chance of developing mycophenolate-associated side effects. Due to reduced variations (or uncertainties) in mycophenolate dosing, the patient's overall experience to mycophenolate will also be improved. This study directly addresses the vision and mission of the Kidney Foundation of Canada by improving the health of the transplanted kidney and the quality-of-lives of our patients through innovative research.

Dr. Ngan Lam

University of Calgary

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$97,138	Screening & Prevention



Follow-up and Outcomes of Critically Ill Patients with Acute Kidney Injury

More than half of patients in the intensive care unit (ICU) get kidney injury. These patients do worse than those who do not get kidney injury. Sometimes, patients with kidney injury in the ICU are sick enough to need dialysis. In Alberta, this type of dialysis is usually managed by the ICU doctors, not the kidney doctors. That means, when patients get better and go home, they may never see a kidney doctor, even if there is still kidney damage leftover. Follow-up care for these patients may help in the prevention, early detection, and management of kidney diseases.

Currently, it is unclear how often patients with kidney disease in the ICU are getting follow-up care and if it is effective in preventing diseases. There is a need for high-quality research to better understand what follow-up care these patients are getting and what should be monitored to keep them healthy. We want to study how often patients with kidney disease in the ICU get follow-up care after they go home from hospital. We also want to understand if this follow-up care leads to better health for them.

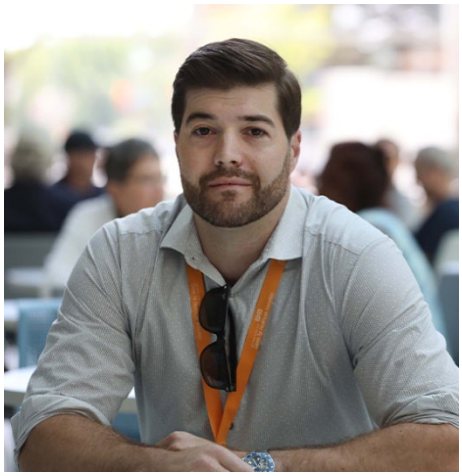
We have a large database called the Alberta Kidney Disease Network that we will use to answer these questions. One of the unique features of this database is that it has all the blood and urine tests done anywhere in the province. We will be able to find all the patients who were admitted to the ICU in Alberta since 2002 and had kidney injury. Based on the test results, we will know how severe their kidney injury was and whether they needed dialysis. We will also find out how well their kidneys were working when they left the hospital and if they had any follow-up for kidney health afterwards.

Our research will help us understand how often patients with kidney injury in the ICU get follow-up, and what some of the barriers are. Understanding these factors will help us find ways to prevent patients from getting kidney failure and heart disease. Overall, we will find important gaps in care for patients who go home from the hospital after being in the ICU. This will help us improve the experiences and kidney health for these patients.

Dr. Dylan Mackay

University of Manitoba

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$148,437	Quality of Life



Dietary potassium liberalization in pre-dialysis patients

Chronic kidney disease (CKD) is a major public health concern. More than 1 in 10 Canadians have CKD and the rates continue to rise. CKD is a leading cause of disability and death around the world and is very expensive to treat.

Potassium is a mineral we get from our food, especially fruits and vegetables, that plays a key role in maintaining numerous bodily functions and the kidney is where potassium levels in the blood are controlled. High blood potassium happens in approximately 10% of patients with CKD and is associated with increased death. High blood potassium is most often seen when people have diabetes or are taking medications that increase potassium levels, but patients with CKD are still told to eat less potassium, which means avoiding many nutritious fruits and vegetables. This recommendation is unfortunately based on little evidence, and it is unclear if lowering potassium from fruit and vegetables even lowers blood potassium. Furthermore, eating a lower potassium diet is not easy; it reduces what people with CKD can eat and can hurt their quality of life.

In this 16-week study, we will test if changing the amount of potassium people with CKD are eating with fruits and vegetables changes the amount of potassium in their blood. We will do this by providing people with fruits and vegetables that are high or low in potassium for a period 6 weeks. We will then provide these same participants with fruits and vegetables that they didn't receive in the first 6 weeks, for 6 weeks in what is called a randomized crossover design. In a randomized crossover design everyone gets both treatments, but the order they get them in is chosen at random, like a coin toss. Twenty participants will be recruited to this study. We will measure blood potassium during the study and see if it changes due to the change in potassium in the fruits and vegetables provided. We think that changing the amount of potassium that participants eat through fruit and vegetables will not really lead to a different level of potassium in the participants blood, and we think having higher potassium fruits and vegetables in their diet will lead to an increase in the participants quality of life. This study's results could change the dietary recommendation given to people living CKD and potentially allow them to eat a greater variety of food.

Dr. Amber Molnar

McMaster University

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$143,302	Screening & Prevention



Impact of a Change in Eligibility Criteria for Multi-care Kidney Clinics

Background: Kidney disease affects many people and is costly. Kidney care in Ontario costs an estimated 650 million dollars per year. In Ontario, patients with low kidney function are cared for in specialty clinics called Multi-care Kidney Clinics. These kidney clinics have a team of health professionals that includes kidney doctors, nurses, dietitians, pharmacists, and social workers. The goal of Multi-care Kidney Clinics is to improve patient health, protect kidney function, and better prepare patients for dialysis and kidney transplant. Prior to 2016, any patient with kidney function estimated at 30% or lower could receive care in a Multi-care Kidney Clinic. In April 2016,

the Ontario Government changed what types of patients could be followed in Multi-care Kidney Clinics. Patients now need to have lower kidney function or a higher risk of kidney failure to receive care in these specialty clinics. Our study will look at how this change affected the health of patients with low kidney function.

Methods: We have access to information collected from all healthcare visits across Ontario. We expect to study approximately 70,000 patients with low kidney function (30% or lower) followed by a kidney doctor. We will look at patient health outcomes such as preparation for dialysis, proper medication use, kidney function and hospital admissions. We will measure these outcomes both before and after April 2016 (when the change in patient access to Multi-care Kidney Clinics occurred). If a change in patient outcomes is seen after April 2016, this suggests that restricting access to Multi-care Kidney Clinics affected patient health.

Importance to patient care: Patients, doctors and healthcare administrators have asked that this research be done. Our results will guide future changes to Multi-care Kidney Clinic access in Ontario. However, our study results are also relevant to other provinces with similar types of kidney clinics. The information gained from this study will be shared across Canada and internationally. The results of this research will help ensure that patients with low kidney function have access to the right care.

Dr. Istvan Mucsi

University Health Network

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$99,450	Transplantation



Emotion/Symptom-focused Engagement for Kidney/Kidney-Pancreas Recipients

Nearly half of kidney and pancreas recipients have traumatic stress, depression or anxiety as well as fatigue, pain, nausea and sleep problems after their transplant. These symptoms interfere with the enjoyment of life they expect with a new organ. The symptoms might come from ongoing illnesses, worries about organ

rejection, or worries about the donor's health in case of transplant from a living donor. Currently, many of these symptoms go unnoticed and untreated. Addressing them improves patient-doctor communication, helps patients stick to their treatment plan, and improves their health generally.

We have developed a supportive treatment for patients with cancer that combines treatments to manage pain, sleep problems, nausea, shortness of breath with counselling based on cognitive behavioral therapy to help to deal with these and emotional (anxiety, depression) symptoms. Cognitive behavioural therapy is based on the idea that our thoughts, feelings, physical sensations and actions are related, and that negative thoughts and feelings can trap us in bad circles. Cognitive behavioural therapy helps us break overwhelming problems into smaller parts. Getting this kind of therapy is known to help patients with patients deal with their symptoms.

In this project, we will adapt this treatment for kidney and pancreas transplant recipients. We will then test to see if it works and if patients and doctors like it. The results and the information gained on how well and easily the treatment can be used routinely in clinics will lead to a bigger study to confirm its usefulness. Eventually, we expect the new treatment to deliver better care by bringing the patient voice to the front of kidney and pancreas transplant care; more satisfaction with care among patients and doctors; better general health after transplant; better enjoyment of life for transplant recipients and caregivers; and cost savings for healthcare systems.

Dr. Annie-Claire Nadeau-Fredette

Hôpital Maisonneuve-Rosemont

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2024	$148,691	Chronic Kidney Disease/Dialysis



QUALIFY CKD-to-HOME

Prospective Changes in Quality of Life and Frailty in Chronic Kidney Disease Patients Transitioning to Home versus in-Center Dialysis (QUALIFY CKD-to-HOME)

Background: For people with advanced kidney disease who choose to have dialysis, deciding which type of dialysis is best can be challenging. Many kidney programs will recommend home dialysis (peritoneal dialysis and home hemodialysis) because we think these techniques have advantages compared to hemodialysis performed in hospitals. These advantages include more autonomy, facility to travel, flexible schedule and, in some cases, lower risk of being hospitalized or dying. Studies have shown that quality of life, having the ability of participate in life and not having too much fatigue are very important to patients. It is thought that the quality of life of people receiving their dialysis at home is often better than the one of people receiving dialysis in a hospital. However, we do not know how the start of dialysis changes the quality of life of people who choose home dialysis in comparison to people choosing hemodialysis in a hospital. We also believe that people who receive dialysis at home often have a better health, mobility, and function level than people with dialysis in hospital who are often frailer. Currently, it is uncertain if people receiving home dialysis can maintain their functioning level after start of dialysis. We also do not know if frail people starting dialysis at home will have a better functioning level after 1 year than those starting dialysis in hospital.

Method: We will perform a prospective study following adult with advanced kidney disease who progress to dialysis and receive home or hospital-based dialysis. In this study, we aim to examine the change in patients' quality of life and their frailty status (health, mobility and function) before start of dialysis up to 12 months after

dialysis start. We are especially interested in comparing the differences between people doing home dialysis and hospital-based dialysis. We will use questionnaires to measure quality of life and several tools to evaluate frailty.

Conclusion: We hope that the results of this study will improve the care of people starting dialysis, both at home and in hospital. This study will inform kidney teams on periods where patients may need more support after start of dialysis, especially when treated at home, and help to design interventions to improve patient's experience on dialysis.

Dr. Shaifali Sandal

The Research Institute of the McGill University Health Centre

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$100,000	Transplantation



Health System-Level Barriers to Living Donor Kidney Transplantation

Background: Living donor kidney transplantation (LDKT) is the best treatment option for patients with kidney failure. But even though we know this, the number of patients getting LDKT in Canada has not risen in the last ten years. There are also very different rates of LDKT in different provinces. We don't know why this is. When researchers have tried to help increase rates of LDKT, they have usually tried to do this by focusing on individual people, such as patients. They have suggested teaching patients more about LDKT, for example. But focusing on individual people ignores how complicated healthcare is and how many different people and places are involved in LDKT. In Canada, there are no national guidelines for LDKT and each province has a different way of organizing things when it comes to LDKT.

Methods: We think that differences in how provinces organize LDKT may help to explain why rates are so different across Canada. So, we want to know more about what provinces are doing differently to help understand why some have higher amounts of LDKT than others, and how they do it. To do this we will conduct

something called a ‘comparative case study’. This means that we will learn and compare how three different provinces, which have high, medium, and low rates of LDKT, do things when it comes to LDKT. We will learn about all the people and places involved in LDKT in these three provinces, by talking to people, watching what they do, and reading documents, like policies, that they follow. Then we will compare how these provinces do things to understand what helps to provide LDKT and what makes it harder.

Relevance: By doing this study, we hope that we can make suggestions for how Canadian provinces can help boost their rates of LDKT. Other studies of LDKT have tended to look at individual parts of a healthcare system – our study is the first one that will look at all of the different people and places involved, and how they are connected. By doing this, we hope that we can make suggestions for improvements that are grounded in how healthcare operates in real life. Overall, we want to help promote LDKT in Canada, because it is the treatment option for kidney failure that benefits patients the most.

CDTRP KFOC RESEARCH INNOVATION GRANT

Dr. Tom Blydt-Hansen

University of British Columbia

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$30,000	Transplantation



Predictors and Patient Experiences that Enable Access to Care of Post-Traumatic Stress in Pediatric Solid Organ Transplant Recipients

Living with end-stage organ disease is associated with an accumulation of traumatic medical and surgical events. Despite successful restoration of organ function by transplantation, many children and adolescents go on to develop post-traumatic stress (PTS) symptoms. Although this mental health condition is associated with long-term impairments in wellbeing, it continues to be overlooked by many transplant clinics.

To address this prevalent issue, the objectives of this study are to identify risk factors and patient experiences that may be used to improve early identification and access to treatment of PTS symptoms in pediatric heart, kidney, and liver transplant recipients.

First, clinical and demographic variables will be reviewed in the transplant database to develop a screening tool that predicts PTS. Trauma severity will be measured by the Child Trauma Score Questionnaire.

Then, interviews with transplant patients and their families will be conducted to understand common experiences that impede or facilitate awareness of PTS, access to resources, and readiness to engage with mental health services.

This exploration of patient and caregiver experiences with PTS will enable us to design and implement patient-centered mental health resources. By combining these approaches, we hope to establish a clear pathway for the early identification of transplanted children and their families living with PTS and facilitate their access to mental health services.

Amanda Vinson

Nova Scotia Health Authority

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2021-2023	$30,000	Transplantation



Identifying Sex-Based Disparities in Referral for Transplant, Activation on the Waitlist and Kidney Transplantation

Kidney transplantation is the best treatment for patients with kidney failure (KF). However, there is some evidence that women may be less likely to receive a kidney transplant than men. Whether this applies to Canada is unknown, and whether there are barriers to Canadian women being referred for transplant consideration, accepted and placed on the transplant waitlist once referred, or receiving a transplant once on the waitlist (or all of the above) requires study.

In this study we will examine differences in access to kidney transplant for men and women in two ways. First, we will create a series of identical cases of male and female patients with KF. We will present a combination of these cases to kidney specialists from across Canada and ask whether they would consider the patient possibly

eligible for transplant and refer them for formal consideration and placement on the transplant waitlist, or not. We will then determine if there is a difference in referral rates for men versus women, and if the gender of the responding doctor impacts this result (ex. are female doctors more or less likely to refer female patients)?

Second, we will explore rates of kidney transplant in patients with KF from Nova Scotia between 2010-2020 to determine if there was a difference between male and female patients in the likelihood of being referred for transplant consideration, accepted and placed on the transplant waitlist once referred, or receiving a transplant once on the waitlist.

This study will be important to identify if there is a difference in transplant rates in Canada between men and women, and if so, why? Identifying these differences is the first step towards fixing them.