Appendix Table A1. Workshop Agenda

	Pre-Workshop Opportunities - Saturday, June 2, 2018	
07:30 - 08:30	Breakfast	
08:30 - 10:00	CIHR Module 1 Curriculum in Patient-Oriented Research	
10:00 - 10:15	Break	
10:15 - 12:30	CIHR Module 1 Curriculum in Patient-Oriented Research	
12:30 - 13:30	Lunch	
13:30 - 14:55	Ethics Group Meeting*	
15:00 - 15:55	iCT in HD Steering Committee Meeting*	
After 15:00	Hotel Check-in – Hilton Mississauga Meadowvale	
16:00 - 16:55	ICES KDT Research Program Investigators Meeting*	
17:00 - 17:55	Patient & Care-giver Circle	
18:00 - 19:30	Social Cocktail Dinner	
19:30 - 21:30	Teambuilding and Networking Event	
	Workshop - Sunday, June 3, 2018	
7:00 - 7:45	Breakfast	
	Introduction, Orientation, & Goals for the Day	
	MyTEMP Update	Amit X. Garg

	Patient Voice	Hans Vorster
	Panel presentation: Intra-Dialytic Exercise Trial	Clara Bohm
	What are the ethical considerations in doing these trials?	Charles Weijer
	Panel Presentation: Dialysate Magnesium Trial	Eduardo Lacson Jr.
10:15 - 10:30	Break	
	Welcomes	
	Ongoing Trial Updates	
	Panel Presentation: Dialyzable Beta-Blockers Trial	Matthew Weir
12:00 - 12:50	Lunch	
	Housekeeping	
	Panel Presentations	
	▪ Hemodialysis Catheters Trial	Amber Molnar
	▪ Frequency of Bloodwork Trial	Samuel Silver
14:20 - 14:30	Break	
	Panel Presentation: Diabetic Care Trial	Kristin Clemens
	Rapid Fire Proposal Presentations	
	Closing Remarks & Next Steps	

Note. * = denotes meetings by invitation only

Appendix Table A2. List of Workshop Participants

Participant Name	Organization	Participant Type	Location
Aakil Patel	Western University	Research Personnel	London, ON
Abhijat Kitchlu	University of Toronto	Nephrologist	Etobicoke, ON
Ajaya Sharma	London Health Sciences Centre	Researcher	London, ON
Alison Thomas	St. Michael's Hospital	Nurse / Nurse Practitioner	Toronto, ON
Amber Molnar	McMaster University	Nephrologist	Hamilton, ON
Amit Garg	ICES Western & KDT, London Health Sciences Centre, Western University	Nephrologist	London, ON
Ann Young	University of Toronto	Trainee	Toronto, ON
Ayodele Odutayo	University of Toronto	Trainee	Toronto, ON
Betty Hogeterp	Lakeridge Health	Nurse / Nurse Practitioner	Oshawa, ON
Brenden Cote	Waterloo-Wellington Regional Patient and Family Advisory Council	Patient / Care-giver	Waterloo, ON
Catherine Clase	McMaster University	Nephrologist	Hamilton, ON

Channing Liberty	The Ottawa Hospital	Nurse / Nurse Practitioner	Finch, ON
Chantal Lainesse	Sterile Care Inc.	Researcher	Markham, ON
Charles Cook	Transplant Ambassador Program Volunteer	Patient / Care-giver	Kitchener, ON
Charles Weijer	Western University	Researcher	London, ON
Claire Harris	British Columbia Provincial Renal Agency	Nephrologist	Vancouver, BC
Clara Bohm	University of Manitoba	Nephrologist/Researcher	Winnipeg, MB
Cory Goldstein	Western University	Trainee	London, ON
Craig Lindsay	Scarborough Health Network	Patient / Care-giver	Toronto, ON
Daniel Tascona	Ontario Renal Network	Nephrologist	Orillia, ON
Danielle Nash	ICES KDT	Research Personnel	London, ON
David Berry	Sault Area Hospital	Nephrologist	Sault Ste. Marie, ON
Deborah Zimmerman	The Ottawa Hospital	Nephrologist	Ottawa, ON
Derek Benjamin	Royal Victoria Regional Health Centre	Nephrologist	Barrie, ON
Douglas Smith	London Health Sciences Centre	Patient / Care-giver	London, ON
Eduardo Lacson	Dialysis Clinic Inc., Tufts Medical	Nephrologist	Boston, MA

Jr.	Center Nephrology		
Eli Rabin	Niagara Health System	Nephrologist	St. Catharine's, ON
Elisabeth Fowler	Kidney Foundation of Canada	Primary Appointment at Kidney Foundation of Canada	Ottawa, ON
Emma Hahn	ICES KDT	Research Personnel	London, ON
Eric McArthur	ICES KDT	Research Personnel	London, ON
Erika Basile	Western University	Other; Director, Office of Human Research Ethics	London, ON
Flory Tsobo-Muanda	Western University, ICES KDT	Trainee	London, ON
Francyelle Fernandez	London Health Sciences Centre	Nurse / Nurse Practitioner	Whitby, ON
Gihad Nesrallah	Humber River Hospital	Nephrologist	North York, ON
Gisell Castillo	Ottawa Hospital Research Institute	Researcher	Ottawa, ON
Gord Field	London Health Sciences Centre	Patient / Care-giver	London, ON
Gregory Hundemer	Brigham & Women's Hospital	Nephrologist	Arlington, MA
Hans Vorster	Ontario Renal Network	Patient / Care-giver	Kingston, ON

Ian Barrett	St. Michael's Hospital	Non-Nephrologist, Non-Nurse Allied Health Professional	Toronto, ON
Jack Tu	ICES	Researcher	Toronto, ON
Jade Dirk	ICES KDT	Research Personnel	London, ON
James Scholey	University of Toronto	Nephrologist	Toronto, ON
Janice McCallum	London Health Sciences Centre	Renal Program Administrator	
Jeff Perl	St. Michael's Hospital	Nephrologist	Toronto, ON
Jennifer MacRae	University of Calgary	Nephrologist	Calgary, AB
Jessica Sontrop	London Health Sciences Centre	Research Personnel	London, ON
John Antonsen	British Columbia Provincial Renal Agency	Nephrologist	Victoria, BC
John Riley	Ontario SPOR SUPPORT Unit	Other; Funder	Toronto, ON
Jordan Ward	ICES KDT	Research Personnel	London, ON
Jovina Bachynski	Halton Healthcare	Nurse / Nurse Practitioner	Oakville, ON
Justin Slater	ICES KDT	Researcher	London, ON
Karen Kelln	Sterile Care Inc	Other; Vendor	Markham, ON
Kathleen Quinn	London Health Sciences Centre	Trainee	London, ON
Kristin Clemens	ICES Western	Researcher	London, ON
Kyla Naylor	ICES KDT	Trainee	London, ON
Laura Dember	University of Pennsylvania	Researcher	Philadelphia,

			PA
Leah Getchell	ICES KDT	Research Personnel	London, ON
Len Usvyat	Fresenius Medical Care	Researcher	Boston, MA
Lianne Barnieh	Western University	Researcher	Calgary, AB
Malvinder S. Parmar	Timmins and District Hospital	Nephrologist	Timmins, ON
Manish Sood	University of Ottawa	Nephrologist	Ottawa, ON
Marisa Battistella	University Health Network	Researcher	Toronto, ON
Matthew Oliver	Sunnybrook Health Sciences Centre	Nephrologist	Toronto, ON
Matthew Weir	London Health Sciences Centre	Nephrologist	London, ON
Meg Jardine	The George Institute for Global Health	Researcher	Sydney, AUS
Michael Pandes	Mackenzie Health	Nephrologist	Richmond Hill, ON
Michael Walsh	McMaster University	Researcher	Hamilton, ON
Michael Zappitelli	The Hospital for Sick Children	Researcher	Toronto, ON
Michelle Hughes	Orillia Soldiers Memorial Hospital	Nurse / Nurse Practitioner	Orillia, ON

Misty Dudley	N/A	Patient / Care-giver	Chatham-Kent, ON
Navdeep Tangri	University of Manitoba	Nephrologist	Winnipeg, MB
Nazanine Gholami	St-Joseph Health Centre	Non-Nephrologist, Non-Nurse Allied Health Professional	Etobicoke, ON
Patricia Chan	Michael Garron Hospital	Nephrologist	Toronto, ON
Pavel Roshanov	McMaster University	Trainee	Hamilton, ON
Peter Blake	Ontario Renal Network	Nephrologist	London, ON
Phil McFarlane	St. Michael's Hospital	Nephrologist	Toronto, ON
Reem Mustafa	University of Kansas Medical Center	Nephrologist	Overland Park, KS
Rey Acedillo	Thunder Bay Regional Health Sciences Centre	Nephrologist	Thunder Bay, ON
Rita Suri	McGill University Health Center	Nephrologist	Montreal, QC
Ron Wald	St. Michael's Hospital	Nephrologist	Toronto, ON
Samiksha Singh	St. Michael's Hospital	Nurse / Nurse Practitioner	Toronto, ON
Samuel Silver	Queen's University	Nephrologist	Kingston, ON
Sarah Bota	ICES KDT	Research Personnel	London, ON
Sean Leonard	ICES KDT	Research Personnel	London, ON
Shane Kilburn	ICES KDT	Research Personnel	London, ON

Shannon Fogarasi	Kidney Foundation of Canada-Ontario Branch	Primary Appointment at Kidney Foundation of Canada	Mississauga, ON
Shasikara Kalatharan	N/A	Patient / Care-giver	Markham, ON
Stephanie Dixon	ICES KDT	Research Personnel	London, ON
Stephanie Winn	Health Sciences North	Renal Program Administrator	Sudbury, ON
Susan Huang	London Health Sciences Centre	Nephrologist	London, ON
Vinusha Kalatharan	Western University	Patient / Care-giver	Markham, ON

Appendix B. Ongoing innovative, pragmatic, cluster-randomized registry trial: Major Outcomes With Personalized Dialysate TEMPerature: Cluster Randomized Controlled Trial (MyTEMP)

While hemodialysis can be a life-sustaining treatment, half of all persons on hemodialysis experience large drops in blood pressure during treatment.[48,49] This can cause dizziness, fatigue, and muscle cramping.[48,50,51] Repeated exposure can lead to cumulative ischemic injury of the heart and brain, which may manifest as heart attacks, strokes, and even death.[49,52,53]

Hemodialysis uses a standard dialysis fluid (called dialysate) temperature of 36.5 °C, a practice based on tradition. Small-scale RCTs have shown that lowering the dialysate temperature (0.5 to 1 °C below each person's body temperature) can reduce the frequency of large drops in blood pressure.[54] This results in beneficial outcomes, including decreased likelihood of cardiovascular and cerebrovascular diseases, reduced symptoms (fatigue, pain, and dizziness), and increased likelihood of survival.[48,49,52–56]

In addition, personalized dialysate temperatures are well-tolerated by persons undergoing hemodialysis, will not incur additional financial costs, may lead to reduced health care costs, and are easy to implement world-wide.[57] To investigate this at a large scale and be able to influence practice, the following research question was proposed for MyTEMP:

Do patients in hemodialysis centres, which are randomized to provide temperature-reduced personalized hemodialysis protocol for a period of four years, have a different composite event rate for the time to first cardiovascular-related mortality or hospitalization for major cardiovascular events compared with patients in hemodialysis centres that provide standard-temperature hemodialysis protocol of 36.5 °C?

Hospitalization for major cardiovascular events is defined as a non-fatal hospitalization of myocardial infarction, ischemic stroke, or congestive heart failure.

MyTEMP underwent three years of trial development, which involved:

- Developing the trial protocol in consultation with stakeholders (e.g., Patient and Family Advisory Councils).
- Performing analyses for:
    - Trial implementation (i.e., understanding potential study barriers and facilitators)[57]

    - Mechanistic studies (i.e., physiological effect of personalized dialysate temperatures on the heart and brain)[55,56]
    - Economics (e.g., health care costs, staff education costs)
    - Updated systematic review[54]
- Analyzing historical records (e.g., determining baseline characteristics, study outcomes of interest) from health care administrative data holdings at ICES and ORN's Ontario Renal Reporting System (ORRS).
- Applying for ethics approval through Research Ethics Board (REB) presentations, discussions, and a review of the trial protocol.
- Receiving participation agreements from 84 hemodialysis units in Ontario.
- Securing funding and partnerships with the CIHR, Heart and Stroke Foundation of Canada, KFOC, ORN, OSSU.
- Performing data analyses (e.g., modelling, randomization)

Through Clinical Trials Ontario (CTO) and its centralized research ethics board approval process (Streamlined Research Ethics Review System), MyTEMP received ethics approval for an altered method of patient consent involving no consent documentation.[27,58] This cluster-randomized trial started in April 2017 (ID: NCT02628366) and will run in hemodialysis centres for four years. Follow-up is expected to be near-complete with the only losses occurring due to emigration (<0.2% of patients participants[59]). The cost for the trial was determined to be 1/20th of a traditional RCT.[60] The main challenge will be

ensuring high adherence in hemodialysis units to their assigned group. As of April 2018, the intervention group had an adherence rate of 86%, whereas the control group had an adherence rate of 94% rate. Ensuring that both groups are at least at 90% adherent will improve the ability to detect a difference between the groups (if a difference truly exists).

The implementation and conduct of this large-scale, innovative, pragmatic, cluster-randomized registry trial was made possible through an Ontario-wide partnership of patients, health care providers, researchers, and renal program administrators. Furthermore, this collaboration of different stakeholders will help ensure that the research findings will help inform health care policy and patient care. Finally, the experience, infrastructure, and relationships built from this trial will be leveraged to prepare new, similar trials to improve the lives of persons on hemodialysis.

Appendix Table C1. Panel Presentations for Intervention Proposals

Proposal	Presenter	Summary of Proposal	Expert Panel and Audience Feedback
1. *The case for intradialytic exercise programming*	Clara J. Bohm *MD, MPH,* *Assistant Professor,* *University of Manitoba*	Persons on HD have low physical activity levels, decline in physical function over time, and struggle with daily physical tasks.[61–64] They are at increased risk of falls, hospitalization, CVD, and mortality.[61,65,66] In addition, persons on HD have identified treatment of symptoms, promotion of heart health, treatment of depression, and effect of lifestyle interventions as important research priorities.[67] Small RCTs have shown that exercise during HD (intradialytic exercise) improves physical function, mood, CV health, HD symptoms, and overall quality of life.[68] Furthermore, intradialytic	• Patient or care-giver perspective: Persons on hemodialysis may be more interested in outcomes impacting quality of life. For those with intensive dialysis schedules, addressing mental and physical fatigue during recovery periods is a priority. Exercising allows persons on hemodialysis to take an active role in their own recovery, which can empower them and support their mental health. However, there are specific patient concerns that may pose an obstacle and need to be addressed, including: physical weakness during dialysis, ability

exercise has been shown to be safe, accessible, and beneficial to almost all persons on HD.[69,70] However, the long-term effects of intradialytic exercise on adverse outcomes such as hospitalization and mortality are not clear and few HD units currently offer exercise programs for their parents. A two-year innovative, pragmatic, cluster-randomized registry trial will be held to investigate the following question: *Do HD units that implement an intradialytic cycling program for their adult chronic HD patients have a different rate of all-cause hospitalization than HD units that do not implement such a program?* Consenting HD units will be randomized into an intervention or control group. The

to access the exercise equipment (e.g., patients with leg grafts), and securing funding exercise experts and equipment for all HD units.

• Existing exercise programs can be resource-demanding. Many dialysis units, especially small rural ones, do not have the funding for equipment and support staff (e.g., physiotherapist). This may affect the program's sustainability and scalability, making large-scale implementation challenging. The role of a physiotherapist could be minimized to monitoring exercise programs and their patients on a monthly basis. Regular staff may be able to volunteer their time to run the program. Finally,

	intervention group's units will implement an intradialytic cycling program, whereas the control group will operate at usual standard of care. In the intervention group, an exercise expert will provide a graded level of supervision for the program, which will be promoted by unit staff and individualized for each person's ability and safety. In addition to outcomes of hospitalization, falls, and mental health consultations, the study will also look for outcomes in symptoms, quality of life, and health care costs. The exercise program is expected to decrease the rate of hospitalization in persons on HD through improvements to physical function, cardiovascular function and	less costly exercise tools could be used. • Persons on hemodialysis may be excluded from exercise programs in different ways. Current exercise programs may have to be halted for the purposes of the study. Those with debilitating conditions, such as amputations or vascular diseases, may have difficulty participating. An exercise protocol that is adaptable to individual needs, such as providing passive stretching for weaker patients, is one way of addressing this challenge. • A pilot study could determine the proportion of patients likely to participate in an exercise

		symptom burden.	regimen, and whether this would be improved through informing them of the potential health benefits. They may not wish to exercise and may want to consent individually.
2. *Dialysate magnesium outcomes*	Eduardo Lacson Jr. *Senior Medical Director for Clinical Science and Quality Initiatives for DCI, Associate Professor, Tufts University*	Persons on HD frequently have low levels of serum magnesium, which is associated with decreased function of the heart, kidneys, and other organs.[71–80] Although a poor diet and medication interference are common culprits, HD itself can also remove small amounts of magnesium from the blood during treatment.[81,82] Increasing the concentration of dialysate magnesium is one way to ensure that persons on HD	• Patient or care-giver perspective: Symptom benefit is an important and feasible outcome for persons on hemodialysis, as they can suffer from severe cramps and pain. If these symptoms can be improved through modifying the dialysate magnesium concentration, the trial has the potential to improve quality of life for persons on hemodialysis. This would also provide an

have sufficient levels of magnesium. A four-year, innovative, pragmatic, cluster-randomized registry trial is proposed to investigate the following question: *Compared to HD units practicing standard care, do HD units that use a higher concentration of dialysate magnesium have increased patient serum magnesium levels and an associated risk reduction in mortality?* The primary outcome of interest will be all-cause mortality. Secondary outcomes include: CV mortality and hospitalization, all-cause hospitalization, patient satisfaction, and quality of life (e.g., pain, cramps). The intervention is expected to reduce mortality risk and improve patient experience (e.g., less cramps), while opportunity to educate clinicians on the impact of magnesium levels on symptoms.

• A cluster-randomized trial with modified consent is a suitable study design for the proposal. The intervention is simple, part of routine health care, low risk, and takes effect at the HD unit/program level.

• The relationship between magnesium levels and mortality may have confounding variables. Low magnesium levels may be a marker for another issue, and changing the dialysate magnesium concentration may not improve mortality rate.

		causing minimal changes to patient care, health care costs, and routine health care services. Additionally, the program can be easily scalable, generalizable, and applicable for clinical practice. If increasing dialysate magnesium is shown to improve health, it could then become standard care for persons receiving hemodialysis.	
3. *Beta blocker optimization in hemodialysis*	Matthew A. Weir *MD, FRCPC, MSc, Assistant Professor, Schulich School of Medicine,*	β-adrenergic receptor antagonists (β-blockers) reduce CV mortality, which afflicts nearly half of all persons receiving HD[49,83,84]. Some β-blockers, such as atenolol and metoprolol, show 'high dialyzability'; they are more efficiently removed from circulation by HD than others	• Patient or care-giver perspective: Persons on hemodialysis may be protective of their current medication regimen or unwilling to add to their pill burden. Clinicians, including nephrologists and cardiologists, may need to carefully explain the

Western University	with 'low dialyzability' (e.g., bisoprolol and carvedilol)[85–87]. For persons on HD, this may reduce the effectiveness of their prescribed β-blocker and increase the risk of negative CV outcomes, including mortality[88]. As an innovative, pragmatic, cluster-randomized registry trial, the proposed program investigates the following question: *Do patients in HD units in which a β-blocker has been optimized for dialytic clearance have a lower risk of death in major CV events compared to patients in HD units where β-blockers are prescribed as usual?* HD units will be cluster-randomized, through covariate-based constrained randomization, into an intervention or control group. Informed consent will be requested	rationale behind drug prescription changes and scheduling and establish trust with each patient. This may be difficult when clinicians may be resistant to changes in medication without the support of official guidelines. Educational materials and personalized feedback may need to be provided for each unit. Individual participant consent may be needed so that they understand and agree to changes in their medication. • In addition to dialytic clearance, the effect of β-blockers on outcomes may be influenced by: the pharmacodynamics of specific β-blockers, the extent to which dialytic clearance eliminates a

from the medical directors of each HD unit. In the intervention group, clinicians will be educated on the optimal β-blocker prescription for individual persons receiving HD. For example, persons using β-blockers with high dialyzability (metaprolol or atenolol) will have their clinician advised to switch their prescription to a β-blocker with low dialyzability (e.g., bisoprolol). Clinicians in the control group will practice at the usual standard of care. Using health administrative data, outcomes of interest include mortality, major CV events (e.g., sudden cardiac death), and the rates at which specific β-blockers are prescribed. The intervention is expected to be non-intrusive and may reduce mortality

specific β-blocker, the person's adherence to their medication, the timing of drug administration (e.g., pre- or post-dialysis), and the effect of residual renal function on drug clearance.

• The study may not be sufficiently powered due to a limited number of persons on hemodialysis who are available to switch their current β-blocker prescription to an optimal one. Additionally, there may not be adequate prescription drug coverage for specific β-blockers, which could exclude some from participating. The study may need to include those who have indicators for β-blocker use and have not yet been prescribed a specific β-blocker.

		and major CV events for persons receiving HD.	
4. Testing a new locking solution for better hemodialysis catheter care	Amber O. Molnar *MD, MSc,* *Assistant Professor,* *Division of Nephrology,* *McMaster University*	Catheter locks, which are chemical solutions instilled into tunneled catheters between HD sessions, are used to prevent catheter-related bacteremia and catheter dysfunction (blockages and blood clotting).[89,90] Otherwise, these complications lead to increased rates of hospitalization, mortality, morbidity (e.g., endocarditis), and catheter exchange.[91–95] Although trisodium citrate 4% is a widely used catheter lock solution in Canada, tetrasodium EDTA 4% has recently been approved for use by Health Canada. Although both possess desirable anti-microbial and anti-thrombotic	• Patient or care-giver perspective: This trial has value in changing practice, as catheters represent a lifeline to patients on hemodialysis; they may be resistant to changing catheter locks without evidence. As patients using catheters have to accept some associated risk of negative health outcomes, increasing their safety is worthwhile to patients. Patients would also benefit from education on catheter use, such as differences between catheter types (e.g., temporary versus long-term) and maintaining/cleaning their

properties, they have not been rigorously compared. As an innovative, pragmatic, cluster-randomized registry trial, the proposed study will investigate the following question: *Do HD units that adopt citrate-based catheter locks versus EDTA-based catheter locks have different rates of catheter-related bacteremia and catheter exchanges?* The intervention will be a simple, routine component of HD care, delivered at the HD unit/program level, and individual consent will be waived. Using health administrative data, outcomes of interest include catheter-related bacteremia and catheter exchanges. Additionally, linked dialysis medical records (e.g., tissue plasminogen activator [tPA], dialysis catheters.

• The proposal may be well-suited as a classical RCT in collaboration with pharmaceutical industry partners. This may provide more funding opportunities and expedite knowledge translation of the trial's findings.

• If the two catheter lock solutions are comparable in outcomes, the financial cost of each type may be an important criterion in determining the ideal catheter lock.

• There may be multiple reasons for catheter removal or tissue plasminogen activator (tPA) use, which may not be captured without linking

adequacy) will be used to measure catheter dysfunction and related costs. Feasibility concerns will be addressed during trial preparation, including: achieving sufficient statistical power (based on the number of persons on HD with catheters in Ontario), establishing a baseline rate of catheter-related bacteremia, and meeting the financial cost of catheter locks (through fostering industry partnerships). As catheters are commonly used and catheter-related complications remain a concern, the study is expected to determine the ideal catheter lock and inform best practice for catheter-related care.

additional data sources.

- For non-sterile catheters, biofilm buildup eventually affects function and occludes over time. This is an issue that may be addressed by a sub-study.
- Bacteremia rates may be too low, resulting in insufficient statistical power for answering the study question.
- Persons on hemodialysis may be interested in outcomes related to patient symptoms and satisfaction, including: vascular access satisfaction, duration of dialysis treatment, and number of repeat visits.

5. *Frequency of routine bloodwork for patients on hemodialysis*	Samuel A. Silver *MD, MSc, Assistant Professor, Division of Nephrology, Queen's University*	Routine blood work is an important component of dialysis care, allowing health care providers to monitor the health of their patients, the effectiveness of their hemodialysis sessions, and treatment-related complications (e.g., anemia). Although dialysis care guidelines recommend blood work to be performed every one to three months, the effect of blood work frequency on patient outcomes has yet to be determined.[96–99] A lower frequency of blood work may potentially reduce test-related patient anxiety and health care costs, while allowing health care providers	• Patient or care-giver perspective: Routine blood tests allow persons on hemodialysis to monitor their health and serve to address their worries (e.g., anemia, medication changes). While some patients may prefer less frequent bloodwork, reducing the frequency of blood work may negatively impact other patients' satisfaction with their care and the quality of interaction with their health care providers. Patients may not necessarily be concerned about cost and undergoing bloodwork. They will need to be informed and

more time to focus on other aspects of dialysis care. As an innovative, pragmatic, cluster-randomized registry trial, the proposed program investigates the following question*: Do HD units that perform less frequent routine blood work have no worse clinical outcomes for patients than hemodialysis units that do more frequent routine blood work?* HD units will be randomized into groups for more (4-week interval) or less (6-week interval) frequent routine blood work. The program is expected to be non-intrusive, a regular component of HD care, low cost, and scalable. Individual informed consent will be waived. Linked health care administrative and laboratory data (e.g., electrolyte imbalances) will be

educated prior to the study.

• The frequency at which blood work is performed is based on tradition, with little supporting evidence. The proposal has the potential to address a vital question in dialysis care.

• Variation in blood work practice may alter patient outcomes. Due to large patient volumes, some units stagger their patients for bloodwork throughout the month. A fixed interval may increase workload and decrease quality of care. Additionally, units may differ on when blood tests are administered relative to the two-day long interdialytic interval, which may impact the risk of

used to determine outcomes of interest, including: all-cause mortality, all-cause hospitalization, and health care costs. The program is expected to determine whether less frequent blood work is non-inferior for patient outcomes and has the potential to improve patient experience, increase health care provider availability, and reduce costs related to blood tests.

adverse patient outcomes. Adjustments to the study plan may be needed to standardize for variations.

- All-cause mortality may be too broad to capture whether patient outcomes are affected by blood work frequency. Mortality rates for specific causes (e.g., sudden cardiac death) may differ from one another, due to being affected by changes in frequency for specific routine blood tests (e.g., potassium). Outcomes that are more sensitive to the potential harms and benefits of reducing blood work frequency may be needed.
- Specific blood tests may need to be administered

			more frequently. For example, vascular calcification is a concern for persons with chronic kidney disease, and is affected by phosphate levels. This requires well-regulated care by the nephrologist, with frequent blood tests for phosphate levels.
6. *Bringing diabetes care expertise to the hemodialysis unit*	Kristin K. Clemens *MD, MSc, Assistant Professor, Departments of Medicine & Epidemiology and*	Persons with diabetes, chronic kidney disease, and on HD face many challenges, including: poor glycemic control, reduced quality of life, and juggling a dialysis schedule with diabetes-related tasks (e.g., insulin injections). [31] They are also more likely to face diabetes-related complications (e.g., CVD). [32] Consequently, they	• Patient or care-giver perspective: The intervention aligns closely with patient-oriented research by addressing the difficulty persons have coordinating diabetes and kidney care. However, they will need care at all times, which may conflict with the scheduling of CDEs, health care providers,

Biostatistics, Western University, Adjunct ICES Scientist	have a high care burden, difficulty meeting all their health care needs, and decreased overall quality of care.[30] To improve coordination of care for these patients, CDEs will provide a patient-grown diabetes case management program (chronic care model) at HD units as part of the health care team.[33] A two-year, innovative, pragmatic, cluster-randomized registry trial will be implemented to investigate the following question: *Do Ontario HD units which adopt the intervention of a CDE-delivered diabetes case management program have a lower rate of diabetes-related complications for patients compared to HD units operating under standard care?* Participating Ontario	and the diabetes case management program. In addition, they may be resistant to changes in their care which they perceive as troublesome or not helpful. Their needs and expectations will need to be taken into account during program development. • Through reducing wait-times, the intervention has the potential to relieve the care burden on persons on hemodialysis and prevent a multi-morbidity cascade effect leading to hospitalization and other complications. • A significant portion of First Nations, Inuit, and Métis persons on hemodialysis have diabetes, are

HD units will be randomized into an intervention or control group. CDEs will be assigned to units in the intervention group, providing individualized patient treatment plans for use by health care staff. Units in the control group will practice standard care. A composite outcome will be generated using diabetes-related complications, including: foot ulcers, cardiovascular and cerebrovascular events, hospitalization for hyper- and hypoglycemia. Secondary outcomes will include hemoglobin A1c (HbA1c), quality of life, and annual vision screening. The program is expected to improve outcomes and coordination of care for these patients while minimizing their care burden.

on hemodialysis, and have difficulty managing blood sugar levels; they will particularly benefit from the program. However, a key challenge will be implementing the program in smaller and more remote hemodialysis units, which will be difficult to access for CDEs.

• Patient outcomes of interest need to ensure that they are a result of diabetes-related complications.

• To address potential financial costs for implementing the study, a factorial approach could be used to determine which specific intervention is the most cost-effective (e.g., foot care versus glycemic control).

Note. CDE = certified diabetes educator; CV = cardiovascular; CVD = cardiovascular disease; HD = hemodialysis; RCT = randomized controlled trial.

Appendix Table C2. Rapid Fire Ideas for Intervention Proposals

Presenter	Rapid Fire Idea	Audience Feedback
Amit X. Garg *MD, PhD, Professor,* *Western University*	• Full use of oral diuretics for persons receiving hemodialysis	• Patient or care-giver perspective: This intervention may prove beneficial for persons on hemodialysis, such as through lowering fluid removal targets during hemodialysis. • As participants may already be taking diuretics (e.g., patients who are non-anuric), cluster randomization of units may be difficult compared to individual-level randomization.
	• Use of ultrapure dialysis fluid for hemodialysis	• No feedback was given.
	• Incorporating mindfulness and meditation interventions in hemodialysis programs	• While a promising trial idea, such interventions may be complex and may raise issues for trial design, including:

		standardization of treatment, appropriateness for a cluster-randomized trial, and suitability for modified (waived) consent. • Validated questions have been used for other chronic illnesses in screening for mood disorders (e.g., depression). Such screening tools may be useful for this study.
Navdeep Tangri *MD, PhD, Associate Professor, University of Manitoba*	• Determining ideal pre-hemodialysis blood pressure targets (150/90 versus 130/80 mmHg) for better outcomes in persons receiving hemodialysis	• As a cluster-randomized trial, randomization of hemodialysis units will have to address age and blood pressure management strategies, in addition to randomizing for blood pressure targets. Each unit can employ a blood pressure management strategy, which is in turn modified slightly for each patient. Units in the control group can

operate at usual care. However, waived informed consent may be difficult, as detailed patient safety information may need to be collected.

• In the patient population, blood pressure targets are individualized and dependent on many variables. An explanatory individual-level RCT may be more appropriate to start with, as it may be difficult to get ethics approval for a modified/simplified method of consent.

• In determining ideal pre-hemodialysis blood pressure targets, additional considerations and variables need to be addressed, including: time of blood pressure measurement, averaging multiple measurements, ultrafiltration goals and rates, volume status, and hypotension episodes.

Deborah Zimmerman *MD, FRCPC, Associate Professor,* *Division of Nephrology,* *The Ottawa Hospital and* *the University of Ottawa*	• Determining ideal dialysate calcium levels (1.25 versus 1.50 mmol/L) for better outcomes in cardiovascular disease and transplant candidacy	• The trial idea addresses an important issue in hemodialysis units. Vascular calcification and calcific uremic arteriolopathy (CUA) may be some of the concerns related to dialysate calcium levels. The study would help to provide evidence on the benefits and risks of dialysate calcium levels that is not just based on surrogate outcomes.
Amber O. Molnar *MD, MSc, Assistant Professor,* *Division of Nephrology,* *McMaster University*	• Determining ideal ultrafiltration rates for better outcomes in persons receiving hemodialysis	• Ultrafiltration rates may be auto-adjusted using hemodialysis machines. • For certain units, a large portion of the persons receiving hemodialysis have consistently high fluid gains. The study may need to take this into consideration during trial design. • Ultrafiltration rates may be used as a quality measure for

	hemodialysis care. • The study may cause longer hemodialysis times, which could negatively impact the study's adherence to treatment.
• Testing a permissive shower technique for improved vascular access satisfaction in persons on hemodialysis with a catheter	• Patient or care-giver perspective: Enabling showers with some measure of training and support is important for persons on hemodialysis as a quality of life issue. • The intervention as a study may pose questions during trial development, including: what the primary endpoint is (e.g., entry site monitoring), how to accurately capture bacteremia, and how to monitor patient satisfaction. • If the intervention involves complex, one-on-one training for individual patients, informed consent may be achieved

		with each individual during training and an individual-level RCT may be more appropriate.
Samuel A. Silver *MD, MSc, Assistant Professor,* *Division of Nephrology,* *Queen's University*	• Effect of low versus high dialysate bi-carbonate levels on outcomes for persons on hemodialysis	• No feedback was given.
	• Determining the effect of vitamin D and K supplementation on cardiac and bone outcomes for persons receiving hemodialysis	• No feedback was given.
Marisa Battistella *BSc Phm, Pharm D, ACPR,*	• Implementing a de-prescribing algorithm in hemodialysis units across Ontario	• For persons on hemodialysis, reducing their pill burden is an important issue.

Associate Professor, *Leslie Dan Faculty of Pharmacy,* *University of Toronto*		• Pharmacogenetics may be helpful when included in decision-making tools for de-prescribing medications. • Cluster-randomized clinical trials may not be the best approach for this intervention. The decision-making tools could benefit from being implemented in clinical practice as an observational trial so that patient-reported outcomes could be followed.
Malvinder S. Parmar *MB, MS, FRCPC, FACP, FASN,* *Professor, Internal Medicine &* *Nephrology, Timmins and District* *Hospital and the*	• Determining the effect of a vegetarian diet on outcomes for persons receiving hemodialysis	• No feedback was given.

Note. RCT = randomized controlled trial.