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Cultivating Innovative, Pragmatic, Randomized Controlled Registry Trials Embedded in Hemodialysis Care: Conference Proceeding From Gardener's Grove 2023

Bryn Tannar[1], Patricia Olar[1], Shane Kilburn[1,2], Kathleen Brown-Blake[1,2], Ahmed A. Al-Jaishi[2,3], Peter G.Blake[1,4,5], Kristin K. Clemens[2,6,7,8], Charles Cook[9], Laura M. Dember[10,11], Stephanie N. Dixon[1,2,6], Cory E. Goldstein[12,13], Areef Ishani[14,15], Catherine Joyes[16], Conor Judge[17,18], James C. Kaufman[19,20], Susan Q. Mackenzie[9,21], Taylor McLinden[1,2,6], Amber O. Molnar[2,18], Alicia Murdoch[22], Gihad Nesrallah[23,24], Sanjay Pandeya[25,26], Claudio Rigatto[25,27,28], Pavel S. Roshanov[1,4,6,29], Melissa Schorr[1,18], Samuel A. Silver[2,30], Rona M. Smith[31,32], Leanne Stalker[33], Navdeep Tangri[27,28], Monica Taljaard[12,13], Karthik K. Tennankore[34], Hans Vorster[5], Charles Weijer[6,35,36], Myles Wolf[37], Merrick Zwarenstein[2,6], and Amit X. Garg[1,2,4,6,38]

Abstract

Purpose of the Conference: Hemodialysis is a life-sustaining treatment for patients with end-stage kidney disease. However, patients on dialysis continue to face poor quality of life and short life expectancies. Despite this, the nephrology community conducts the fewest randomized controlled trials of any medical discipline, relying instead on expert opinion to guide many aspects of hemodialysis care. There is a need to conduct high-quality pragmatic randomized controlled trials in hemodialysis to drive evidence-based practice. To this end, the Innovative Clinical Trials in Hemodialysis Centers initiative, with the support of the Canadian Institutes of Health Research and its Strategy for Patient-Oriented Research, funded the development of 6 pragmatic trial protocols. Gardener's Grove 2023 created a space to support the development of these trials and increase awareness and knowledge of past, ongoing, and future innovative, pragmatic, randomized controlled registry trials embedded in routine hemodialysis care. This report summarizes the proceedings of this conference.

Sources of information: The conference included 6 panel presentations, each featuring an overview of a new pragmatic trial followed by expert panel feedback from patient partners, nephrologists, researchers, and health care providers. The conference also included 10 educational sessions led by clinicians and researchers with experience in the fields of kidney medicine and clinical trials.

Methods: Gardener's Grove 2023 was a 4-day virtual conference held in March of 2023. Recordings of all the conference presentations were later published on the Gardener's Grove website and are summarized in the Supplemental Appendix of this report.

Key Findings: The conference brought together 118 Canadian and international researchers, patients, and health care providers to collaborate on 6 pragmatic trials intended to test interventions to improve hemodialysis care. The proposed trials included (1) PREventing FracturEs in REnal Disease (PREFERRED), (2) DIALysis with EXpanded solute removal (DIALEX), (3) Sodium fOr diaLysis oUTcome rEduction (SOLUTE), (4) Finding the right blood pressure target for patients on dialysis, (5) DIuretic Use in patients with Residual renal function on hemodialysis (DIURESED), and (6) Lower vs higher dialysate bicarbonate concentration in patients receiving hemodialysis (Dial-Bicarb). All of these interventions were widely supported

and received valuable feedback from panelists and conference attendees. The education sessions focused on various design and execution elements of pragmatic, randomized controlled registry trials embedded in routine care.
Limitations: The conference could have been improved by streamlining session topics and pacing, allowing additional time for discussions, strengthening online network opportunities, and improving survey response rates. A follow-up conference is planned to take place in a few years, and the coordinators will aim to implement these changes.
Implications: Gardener's Grove 2023 successfully created a space for patients, researchers, and health care providers to support the development of 6 new pragmatic trials in hemodialysis care. Since Gardener's Grove 2023, several of these trials have secured CIHR funding, obtained ethics approval, and are actively preparing to launch their interventions.

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Objectifs de la conférence: L'hémodialyse est un traitement vital pour les personnes souffrant d'insuffisance rénale terminale. Les patients sous hémodialyse voient cependant leur qualité et leur espérance de vie réduites. Malgré cela, la communauté de la néphrologie est celle parmi toutes les disciplines médicales qui mène le moins d'essais contrôlés randomisés, s'appuyant plutôt sur l'opinion d'experts pour guider de nombreux aspects des soins d'hémodialyse. Des essais contrôlés, randomisés, pragmatiques de haute qualité sont nécessaires en hémodialyse pour encourager une pratique fondée sur des données probantes. C'est pourquoi l'Initiative sur les essais cliniques novateurs dans les centres d'hémodialyse, avec l'appui des Instituts de recherche en santé du Canada et de la Stratégie de recherche axée sur le patient, finance l'élaboration de six protocoles d'essais pragmatiques en hémodialyse. La conférence Gardener's Grove de 2023 a créé un espace pour soutenir le développement de ces essais et accroître la sensibilisation et la connaissance sur les essais innovants, pragmatiques, randomisés et contrôlés—passés, en cours et futurs—intégrés dans les soins courants d'hémodialyse. Le présent rapport résume les travaux de cette conférence.
Sources de l'information: La conférence prévoyait six présentations de panel, chacune donnant un aperçu d'un nouvel essai pragmatique suivi des commentaires d'experts, de partenaires patients, de néphrologues, de chercheurs et de prestataires de soins. Dix séances de formation animées par des cliniciens et des chercheurs ayant une expérience en médecine rénale et en essais cliniques figuraient également au programme.
Méthodologie: Gardener's Grove 2023 est une conférence virtuelle de quatre jours qui s'est tenue en mars 2023. Les enregistrements de toutes les présentations ont ensuite été publiés sur le site Web de Gardener's Grove; ils sont résumés dans l'annexe supplémentaire du présent rapport.
Principaux résultats: La conférence a réuni 118 chercheurs, patients et prestataires de soins canadiens et internationaux pour collaborer à six essais pragmatiques pour tester des interventions visant à améliorer les soins d'hémodialyse. Les essais proposés sont les suivants : 1) l'essai PREFERRED (*PREventing FracturEs in REnal Disease*); 2) l'essai DIALEX (*DIALysis with EXpanded solute removal*); 3) l'essai SODIUM (*Sodium fOr diaLysis oUTcome rEduction*); 4) un essai portant sur les cibles de pression artérielle pour les patients sous dialyse (*Finding the right blood pressure target for patients on dialysis);* 5) l'essai DIURESED (*DIuretic Use in patients with Residual renal function on hemodialysis*); et 6) l'essai Dial-Bicarb comparant les effets d'une concentration faible ou élevée de bicarbonate dans le dialysat. Toutes les interventions ont reçu de précieux commentaires des panélistes et des participants à la conférence, qui les ont largement appuyées. Les séances de formation ont mis l'accent sur les divers éléments de conception et d'exécution des essais contrôlés, randomisés, pragmatiques intégrés aux soins courants.
Limites: La conférence pourrait être améliorée en allégeant les sujets, en accélérant le rythme des séances, en laissant plus de temps aux discussions, en augmentant les possibilités de réseautage en ligne et en améliorant les taux de réponse aux sondages. Une conférence de suivi est prévue dans quelques années; les coordinateurs viseront à mettre en œuvre ces changements.
Conclusion: La conférence Gardener's Grove 2023 a réussi à créer un espace où patients, chercheurs et prestataires de soins se sont réunis pour soutenir l'élaboration de six nouveaux essais pragmatiques dans le contexte des soins d'hémodialyse. Depuis la conférence, plusieurs de ces essais ont obtenu du financement des IRSC, obtenu l'approbation du comité d'éthique et se préparent activement à lancer leurs interventions.

Keywords
chronic kidney disease, hemodialysis, pragmatic trial, randomized controlled trial, registry-based randomized trial, clinical trial, patient-oriented research, conference

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Background

Chronic kidney disease is a growing global public health problem that is now one of the leading causes of death in the industrialized world.[1] Hemodialysis is a life-sustaining treatment that approximately 3 million people worldwide, including 23 000 Canadians, rely on for managing end-stage kidney disease (ESKD).[2] However, the quality of life for patients on dialysis is poor, life expectancy is short, and maintenance dialysis costs the health care system approximately $100,000 per patient per year.[3] Between 15% and 30% of patients die within 1 year of starting dialysis, and the average life expectancy of a person on dialysis is less than 3 years.[4,5] This life expectancy has remained unchanged for 20 years, due, in part, to a paucity of high-quality randomized controlled trials (RCTs) that have been conducted to inform evidence-based hemodialysis care.[5,6] Previously completed trials frequently failed to inform best practices due to issues such as small sample size, low power, low adherence to trial protocols, and reduced generalizability.[7-9] Consequently, much of dialysis care delivery is based on expert opinion.

Several logistical challenges limit the implementation of RCTs in hemodialysis. For one, the compromised health of patients, coupled with the substantial treatment demands they already face, can discourage participation in trials that have complex protocols. Second, because many patients (especially those in rural settings) receive hemodialysis at community hospitals without onsite research coordinators, they are overlooked from participating in clinical trials that require research staff to facilitate patient enrollment, intervention delivery, and data collection. Third, even in centers that have research coordinators, high costs associated with coordinator involvement can render the execution of these trials prohibitively expensive.[10]

[1]London Health Sciences Centre, ON, Canada
[2]Institute for Clinical Evaluative Sciences, Kidney, Dialysis and Transplantation Research Program, London, ON, Canada
[3]Public Health Agency of Canada, Ottawa, ON, Canada
[4]Division of Nephrology, Department of Medicine, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada
[5]Ontario Renal Network, Cancer Care Ontario, Toronto, Canada
[6]Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada
[7]Division of Endocrinology and Metabolism, Department of Medicine, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada
[8]St. Joseph's Health Care London, ON, Canada
[9]Grand River Hospital, Transplant Ambassador Program, Kitchener, ON, Canada
[10]Division of Renal, Electrolyte, and Hypertension, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA
[11]Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA
[12]Clinical Epidemiology Program, Ottawa Hospital Research Institute, ON, Canada
[13]School of Epidemiology and Public Health, University of Ottawa, ON, Canada
[14]Minneapolis VA Health Care System, MN, USA
[15]Department of Medicine, University of Minneapolis, MN, USA
[16]Department of Clinical Research, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada
[17]Galway University Hospital, Ireland
[18]Division of Nephrology, Department of Medicine, McMaster University, Hamilton, ON, Canada
[19]Division of Nephrology, Department of Medicine, Grossman School of Medicine, New York University, NY, USA
[20]VA New York Harbor Healthcare System, NY, USA
[21]The Kidney Patient and Donor Alliance Canada, Calgary, AB, Canada
[22]Can-SOLVE CKD Network, Vancouver, BC, Canada
[23]Temerty Faculty of Medicine, University of Toronto, ON, Canada
[24]Department of Medicine, Humber River Health, Toronto, ON, Canada
[25]Canadian Society of Nephrology, Winnipeg, MB, Canada
[26]Halton Healthcare, Oakville, ON, Canada
[27]Division of Nephrology, Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, MB, Canada
[28]Chronic Disease Innovation Centre, Seven Oaks Hospital, Winnipeg, MB, Canada
[29]Population Health Research Institute, Hamilton, ON, Canada
[30]Division of Nephrology, Kingston Health Sciences Center, Queen's University, ON, Canada
[31]University of Cambridge, UK
[32]Cambridge University Hospitals NHS Foundation Trust, UK
[33]The Kidney Foundation of Canada, National Office, Montreal, QC, Canada
[34]Division of Nephrology, Department of Medicine, Dalhousie University, Halifax, NS, Canada
[35]Department of Philosophy, Western University, London, ON, Canada
[36]Division of Critical Care Medicine, Department of Medicine, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada
[37]Division of Nephrology, Department of Medicine, Duke Clinical Research Institute, School of Medicine, Duke University, Durham, NC, USA
[38]Victoria Hospital, London Health Sciences Centre, ON, Canada

Corresponding Author:
Amit X. Garg, Victoria Hospital, London Health Sciences Centre, 800 Commissioners Road, Room ELL-215, London, ON N6A 5W9, Canada.
Email: amit.garg@lhsc.on.ca

A possible solution to this problem is to design and conduct more pragmatic RCTs. Pragmatic RCTs are conducted in real-world settings and may overcome these logistical challenges by integrating interventions into routine hemodialysis care.[2] These trials rely heavily on local sites to effectively support the intervention and ensure strict protocol adherence.[11]

Early collaboration with these sites is crucial, as is providing comprehensive education on the trial's objectives and procedures to empower staff in implementing the intervention accurately. Fostering continuous dialogue with local site personnel is also critical, as it enables the collection of valuable feedback and facilitates the timely resolution of any concerns.[11] In some clinical settings, the high degree of collaboration and communication with local sites required may pose a barrier to trial implementation, but the value of a pragmatic design in improving real-world applicability can produce evidence-based clinical guidelines that can more feasibly inform best practice over traditional RCTs.

The outpatient hemodialysis setting is particularly well suited for pragmatic trials because hemodialysis patients are intensively monitored on a weekly basis, and interventions can be administered by health care staff as they are in routine care, effectively reducing costs and lowering barriers to participation. Pragmatic trials also feature broad inclusion criteria, improving equity by including representative patient populations not typically included in traditional trials, such as patients with multiple comorbidities.[12] The information needed for the trial can come from existing administrative databases and data-rich registries. Finally, when it is appropriate to do so, some of these trials may use an altered approach to patient consent, which can be efficiently done in routine care avoiding the need for research coordinators at participating sites.[13] Altogether, these features of pragmatic RCTs can substantially improve efficiency and reduce implementation costs compared to traditional RCTs.[14] Importantly, pragmatic RCTs promote interventions that are scalable and sustainable, and intervention delivery in the trial mimics how the intervention would be applied in busy routine practice.

These trials are also important tools in achieving the goals of a learning health system. By leveraging advancements in health information technology, pragmatic RCTs promote innovation by generating new knowledge as a natural by-product of health care delivery.[15]

The frequently contradictory information arising from observational research has created an urgent need for hemodialysis care to be the subject of high-quality, patient-oriented research conducted through large-scale pragmatic RCTs. These trials are essential to establish robust, evidence-based standards of care and to guide the decision-making processes of patients, health care providers, and policymakers.

We received a peer-reviewed grant to help develop and implement large-scale pragmatic RCTs to address critical issues in hemodialysis care. This was a 4-year grant from the Canadian Institutes of Health Research (CIHR) Strategy for Patient-Oriented Research (SPOR) innovative Clinical Trials (iCT) initiative (nominated principal investigator Dr Amit Garg). This initiative focuses on large-scale pragmatic trials which:

- Embed intervention delivery within routine hemodialysis care administered by health care providers and not research coordinators;
- Consider different approaches to randomization, where 1 option is cluster randomization at the level of hemodialysis units;
- May use altered procedures to obtain patient consent to trial participation; and
- Leverage existing linked health care registries and administrative databases to provide all baseline, follow-up, and outcome information for the trial.

Trial protocols are co-developed with patients receiving hemodialysis, family members, caregivers, health care providers, health administrators, and researchers as full partners.[16]

Patient and caregiver involvement has been crucial to advocating for the needs and interests of patients in clinical research, whereas consultation with health care providers and health administrators has lent insight into the challenges and feasibility associated with delivering trial interventions in busy health care environments.

In 2018, we hosted our first conference on this theme: a 2-day event that engaged stakeholders and nurtured intervention proposals through structured presentations, rapid-fire proposals, facilitated group discussions, and expert panel feedback.[17] The success of the 2018 conference prompted the organization of this second event: a 4-day virtual conference held in March of 2023. The conference expanded upon the original workshop to include 6 panel presentations and 10 educational sessions.

To prepare for the conference, representatives from several organizations formed a committee to develop the agenda, create conference materials, coordinate with speakers and panelists, and select trial proposals. To source these proposals, we put out an open call for innovative trial proposals across multiple networks. A total of 9 proposals were submitted and were evaluated by the selection committee based on criteria such as feasibility, efficiency, trial readiness, scalability, sustainability, impact, and patient engagement. With a budget of $300,000, 6 proposals were selected, each receiving $50,000 for robust protocol development. The teams of each of these proposals presented their trial protocol as a panel presentation at the conference.

Conference Introduction

Between March 27 and 30, 2023, the conference brought together Canadian and international participants to collaborate

on pragmatic trials intended to test interventions to improve hemodialysis care. Participants included patients receiving hemodialysis, health care providers, health care administrators, and researchers (clinical trialists, biostatisticians, methodologists).

The conference was called Gardener's Grove to set the tone for a nurturing and synergistic space that, similar to gardening, would allow trial ideas to be planted, grow, and ultimately flourish. Each day of the conference featured a variety of panel presentations and educational sessions led by clinicians and researchers with experience in the fields of kidney medicine and clinical trials (see Supplemental Appendix Figure A1 for the complete conference agenda). Time was also provided for networking. The conference was hosted on PheedLoop, a virtual event platform that hosts live presentations and facilitates active feedback from attendees. PheedLoop also allowed attendees to easily access additional information about the conference, speakers, educational sessions, and panel presentations.

The conference was moderated by Dr Amit Garg, Dr Claudio Rigatto, who is a professor at the University of Manitoba, Mr Hans Vorster, who has lived experience with hemodialysis and is an investigator on the iCT in Hemodialysis Centers CIHR SPOR grant, and Ms Alicia Murdoch, who is Project Manager of the Canadian Nephrology Trials Network. Prior to commencing the conference, Elder Eli Baxter, an Anishinaabe Marten Falls First Nations member and accomplished author, delivered a traditional Anishinaabe Land Acknowledgement.

Conference Goals

1. Increase awareness and knowledge of past, ongoing, and future innovative, pragmatic, randomized controlled registry trials embedded in routine hemodialysis care.
2. Foster opportunities to partner and collaborate on the development of current and future trials across stakeholder groups.
3. Identify new trial concepts that would be appropriate to develop further and launch as large-scale innovative trials by 2026.

The trial ideas discussed at the conference focused on interventions with the potential to reduce complications associated with dialysis and improve the overall health and well-being of individuals with kidney disease who require hemodialysis.

Collaboration

Representatives from different stakeholder groups evaluated and discussed the proposed pragmatic trials to strengthen their planning and support their implementation. Knowledge sharing and collaboration were central to the activities of the conference and were fostered in several ways:

- All panel presentations received constructive feedback from a multidisciplinary panel that included patients, researchers, health care providers, and health administrators (Supplemental Appendix Table C2).
- Both educational sessions and panel presentations were subject to audience questions and feedback through PheedLoop's anonymous online chat feature.
- Conference attendees were encouraged to connect during designated networking sessions through the interactive video meeting forum SpatialChat. Specific chat rooms were created for each day's speakers for those who wished to further discuss the topic of an educational session or intervention proposal (Supplemental Appendix Figure A2).

Surveys collecting feedback and suggestions for improvement were provided at 3 time points: (1) following each intervention proposal, (2) at the end of each day of the conference, and (3) at the conclusion of the conference. Intervention proposal feedback was provided to pertinent presenters at the end of the conference.

Conference Attendees

The conference was attended by 118 individuals, of which 12 were patients, family members, and caregivers (Supplemental Appendix Table B1). Other attendees included multiple physicians, nurses, nurse practitioners, researchers, research personnel, trainees, health and research administrators, patient participation facilitators, industry partners' representatives, ethicists, and one of each of the following: medical scientific liaison, community programs coordinator, social worker, patient advocacy groups, and an implementation support practitioner and knowledge translation broker. A total of 103 participants (87.2%) were Canadian and 15 were international. Canadians attended from 8 provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, and Newfoundland and Labrador). International attendees were from Ireland, New Zealand, Uganda, the United Kingdom, and the United States (Colorado, Georgia, Maryland, Massachusetts, Minnesota, New York, North Carolina, and Pennsylvania).

Participants included representatives from several organizations, including the CIHR, the Canadian Nephrology Trials Network (CNTN), The Canadian Society of Nephrology, Health Data Research Network (HDRN) Canada, the CanSOLVE CKD Network, the Kidney Foundation of Canada (KFOC), the Public Health Agency of Canada, the Ontario ICES Kidney, Dialysis and Transplantation (KDT) provincial program, Ontario Health, the Ontario Renal Network

(ORN), the Ontario SPOR SUPPORT Unit (OSSU), U.S. Renal Care, Renal Research Institute, and the patient-led Transplant Ambassador Program.

Calls for conference involvement were sent to attendees of the previous 2018 conference and to team members who participated in trials in hemodialysis care. Further marketing of the conference was coordinated with the Ontario Renal Network ORN, Trillium Gift of Life Network (TGLN), Can-SOLVE, CNTN, Kidney Foundation of Canada (KFOC), HDRN Canada, Canadian Donation and Transplant Research Program, CSN, Baxter, DCI, Chief Medical, Fresenius, ASN, the PKD Foundation, Western Research, the Schulich School of Medicine & Dentistry at Western University, ICES, OSSU, and the Transplant Ambassador Program (TAP), which invited participating patients. In addition, key patient partners who contributed to the development of this conference were instrumental in identifying other potential patient participants, ensuring diverse representation across patient populations.

During conference registration, individuals were invited to indicate their interest in serving as a panelist for one of the panel presentations. Those who expressed interest were subsequently assigned to one of the trial proposals, with the goal of having 1 patient partner, nephrologist, researcher, and health care provider on each panel. Prior to the conference, these registrants were contacted with details of their assigned panel presentation and provided with an information package.

Panel Presentations

Gardener's Grove 2023 hosted 6 panel presentations. Each panel presentation was structured as a 30-minute trial proposal followed by 20 minutes of expert panel feedback and another 10 minutes for audience feedback. Panelists and audience members were encouraged to consider the following 4 criteria when providing feedback to best support the design and development of the proposed pragmatic RCT:

1. What is this intervention's potential to improve the health of patients receiving in-center hemodialysis or improve the system caring for them?
2. Do the intervention's benefits likely outweigh any risks?
3. If proven beneficial, can the intervention be incorporated broadly into routine hemodialysis care?
4. What will help nurture this idea?

The proceedings from 1 intervention proposal are reported below, whereas the remaining 5 are summarized in Supplemental Appendix Table C2.

Intervention Proposal: Lower vs Higher Dialysate Bicarbonate Concentration in Patients Receiving Hemodialysis (Dial-Bicarb)

Nephrologists Dr Amber Molnar of McMaster University and Dr Samuel Silver of Queen's University shared their proposal for an innovative, pragmatic trial to determine whether providing a lower vs higher concentration of dialysate bicarbonate alters the risk of outcomes important to patients and their care providers.

This trial aims to address the metabolic acidosis that is commonly experienced as a complication of kidney failure. When untreated, metabolic acidosis can lead to bone demineralization, muscular atrophy, fractures, and increased mortality.[18-20] Hemodialysis can counter metabolic acidosis by supplying the body with bicarbonate ions from dialysis fluid that help regulate acid-base homeostasis and increase serum pH to within normal range.[21]

However, due to the intermittent schedule of hemodialysis, correction of metabolic acidosis can occur too rapidly during the hemodialysis session, leading to metabolic alkalosis by the end of each hemodialysis treatment.[22] This rapid shift in patient acid-base balance can also be harmful, affecting heart function, blood pressure, bone metabolism, and muscles, and contributing to painful muscle cramps. Unfortunately, the optimal amount of dialysate bicarbonate remains unknown, and previous studies present conflicting data (see Supplemental Appendix Table C2 for more information).

Consequently, the dialysate bicarbonate concentration provided in routine care varies depending on the hemodialysis unit where a patient receives treatment.[23] Some dialysis units in Canada add bicarbonate to a concentration of 32 mmol/L, whereas others add it to a concentration of 38 mmol/L. Robust information from large-scale RCTs comparing health outcomes in patients receiving lower vs higher dialysate bicarbonate concentration would alter the current status quo, where bicarbonate concentrations are largely determined by clinician discretion.

Drs Molnar and Silver defined their research question as the following: in outpatients receiving maintenance hemodialysis, does using a higher (38 mmol/L) vs lower (32 mmol/L) dialysate bicarbonate concentration as a center policy for 4 years alter the risk of (1) all-cause (non-elective) hospitalization or all-cause mortality and (2) patient-reported muscle cramps? Both the higher and lower dialysate bicarbonate concentrations fall within the range of standard care in Canada.

To test the research question, participating hemodialysis units will be randomized through covariate-constrained randomization into either the high-dialysate or low-dialysate bicarbonate groups. The study will have broad inclusion criteria but will exclude those who receive nocturnal dialysis or

dialysis on a frequent schedule. The trial will use an opt-out consent model and obtain follow-up data through linked registries.

If the trial reveals that a lower rather than higher dialysate bicarbonate concentration leads to improved health outcomes, then this represents an easily scalable intervention that may be readily translated into clinical practice in hemodialysis units globally at no added cost. This change in practice could help reduce hospitalizations and premature deaths among the more than 2 million people on hemodialysis worldwide.

During the conference, the following themes were discussed in a conversation between Drs Molnar and Silver and their expert panel, which included patient Mr Frank Ansell, nephrologist Dr Bonnie Richardson of Saskatchewan Health Authority, researcher Dr Danielle Nash of London Health Sciences Centre, and nephrologist and senior medical director Dr Eduardo Lacson Jr of Dialysis Clinic, Inc:

- Many nephrologists may recommend dialysate bicarbonate concentrations in the higher range of standard care (ie, ~38 mmol/L) if their patients are particularly acidotic (with pre-dialysis serum bicarbonate concentrations around 15-17 mmol/L). In cases like this, the study should consider how to convince nephrologists randomized to the low-dialysate bicarbonate group to adhere to their intervention arm.
- Substudies could be introduced to monitor serum oxygen saturation, assess patients' acid-base status, or even adjust dialysate potassium and magnesium levels. These substudies may allow the trial to lend some insight into the potential relationship between dialysate bath composition and metabolic alkalosis, hyperkalemia, and hypercapnia.
- In light of the study's planned waived consent model, the researchers are encouraged to adequately inform patients about the trial and make them aware of their right to opt out at any point. Drs Molnar and Silver agreed, stating that informative pamphlets and posters will be distributed to participating dialysis centers. They also emphasized that the trial has been designed with patient partners who feel comfortable with the opt-out model, given that both concentrations are currently used as standard care in Canada.
- There may exist a U-shaped relationship between dialysate bicarbonate concentration and health. If this is the case, it may be interesting to consider a 3-armed trial that randomizes hemodialysis units to low-dose, medium-dose, and high-dose dialysate bicarbonate. However, it is acknowledged that it may prove infeasible to acquire enough clusters or achieve sufficient separation between the 3 groups.
- The study is encouraged to consider if any additional patient-reported outcomes may reflect a direct path between bicarbonate concentration and health more strongly than muscle cramps.
- The study is encouraged to consider potential confounding variables (eg, co-morbidities) that may provide further justification for why nephrologists prescribe the dialysate bicarbonate concentrations that they do.

Audience members additionally encouraged collaborating with multidisciplinary teams such as dieticians and suggested oral bicarbonate supplementation as an alternative option, considering patients' bicarbonate levels may fluctuate drastically between dialysis sessions.

Overall, the responses collected from live polling questions, a post-presentation survey, and contributions from the panel demonstrated support for Drs Molnar and Silver's design and research question, indicate that pursuing this trial would be of interest to the nephrology community. There was strong agreement that the intervention has the potential to improve patient health and be readily translated into routine hemodialysis care.

Following the conference, significant advancements have been made in the Dial-Bicarb trial. In July 2023, Drs Molnar and Silver secured $1 682 998 in funding from the Canadian Institutes of Health Research (CIHR), and in August, they secured $205 521.25 in funding from Accelerating Clinical Trials (ACT). In addition, to increase the trial's power, the design has shifted from cluster randomization to individual randomization. Patients at each participating dialysis unit will be randomly allocated into one of 2 study arms in a 1:1 ratio to receive a dialysate bicarbonate concentration of either 32 or 38 mmol/L. Furthermore, in April 2024, the study obtained its initial provincial ethics approval, paving the way for trial recruitment to commence in hemodialysis centers across Ontario in 2025.

Educational Sessions

Gardener's Grove 2023 hosted 10 educational sessions. The sessions varied in length from 15 to 60 minutes and were followed by question-and-answer periods facilitated through PheedLoop's anonymous online chat feature. This allowed researchers and clinicians to discuss the crucial role of pragmatic trials in clinical research and share insights gained through their unique experiences in trial conduct. The knowledge-sharing promoted through these sessions can help support future trial teams to recognize potential challenges and pitfalls early in the trial planning process and to develop solutions to overcome them.

Two educational sessions are summarized below. Supplemental Appendix Table D1 identifies some important takeaways from the remaining 8 educational sessions.

Implementing Without Coordinators for Pragmatic Trials/MyTEMP

Dr Amit Garg advocated for responsibly implemented strategies in some pragmatic trials that can be conducted without the need for research coordinators to be present in dialysis centers. Dr Garg referred to the recent MyTEMP trial, in which methods of obtaining consent, delivering the intervention, and collecting data were achieved in the absence of research coordinators and were done in a way that made the trial feasible and possible without compromising patient welfare.[24] In lieu of a research coordinator, multilingual informational posters, letters, and presentations can be used to inform patients, substitute decision-makers, and family advisory councils about ongoing trials and patients' right to opt out. An alteration to the consent process may be ethically employed in cases where trial participation poses little additional risk to patients beyond what they would experience in usual care. Guidance for when an alteration of the standard consent process may be considered is provided in article 3.7A in the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.[25] In addition, standard treatments may be delivered by usual care providers (although training may be needed) with baseline and follow-up data obtained through linked administrative databases and registries, eliminating the need for on-site research coordinators to support these activities. Eliminating the use of research coordinators could allow trials to become better integrated within routine care and critically reduce the staggering costs required to run trials by as much as 75-90%. In turn, this would permit a greater number of meaningful trials to be done.

Practical Experience in Pragmatic Trials

Dr Sandra Eldridge, Honorary Professor of Queen Mary University of London, spoke about her experiences with past pragmatic trials and shared her advice for managing common challenges. Throughout her presentation, Dr Eldridge prompted future trialists to consider the following. First, she advised investigators to expect and prepare for unanticipated barriers to recruitment. Second, Dr Eldridge recommended that large trial teams use streamlined communication channels to ensure a global understanding of expectations and time scales. Third, background research and a pilot study are needed to guide the trial protocol and execution. Fourth, she emphasized that adherence in pragmatic trials may not be forced, but strategies to increase authentic engagement by clinical personnel and patients should be considered. Finally, Dr Eldridge championed the use of blinding within the trial team to prevent bias from influencing data collection and analysis.

Patient Engagement

The conference provided a space for patient partners to be actively involved in shaping trial proposals that could directly impact the care they receive. One patient panelist was included in each panel presentation, 2 patients were involved in the conference's ethics presentation, and patient partner Mr Hans Vorster was engaged as a conference moderator. In panel discussions, patient partners provided personal insight from their unique experiences on maintenance hemodialysis and shared their ideas on the potential benefits and limitations of panel presentations' proposals. Importantly, they were offered a platform to highlight their priorities when receiving care. Notably, the presenters supported the tenets of CIHR's Strategy for Patient-Oriented Research and consistently encouraged patient engagement throughout the design and development of their trials. As an example, Dr Karthik Tennankore's panel presentation (summarized in Supplemental Appendix Table C2) featured a video delivered by a patient partner as she explained the challenges she has faced managing her blood pressure while on dialysis.

Next Steps

Conference participants described the overall conference experience as educational, informative, and collaborative (see Figure 1 for full word cloud).

Addressing suggestions for improvement received from the 2018 conference, this conference increased the allocated time for structured panel feedback to further nurture trial proposals, included a patient or caregiver in each expert panel to encourage their contribution to discussions with trial investigators, expanded networking opportunities, and introduced a greater number of surveys to obtain participant feedback. These surveys were administered at 3 time points throughout the conference: at the end of each panel presentation, at the end of each day, and at the conclusion of the conference. Feedback collected following each panel presentation has been compiled and returned to the trial presenters. They will use this information to either strengthen their current concept or to pivot to a better trial concept that uses an alternative approach or intervention to have a positive impact. Comments and suggestions collected from the end-of-day and post-conference surveys are reported in Supplemental Appendices E1 and E2.

This conference had several successes:

- Participants indicated the conference was well organized, and the presenters indicated they felt well supported. The expert panel reviews were viewed as particularly valuable in providing information from diverse perspectives to strengthen trial protocols.
- Patients, families, and caregivers were provided a positive and inclusive space to express their opinions,

Figure 1. One-word summary from attendees of the overall conference experience presented in a word cloud.

concerns, and priorities directly with trial teams and researchers. Their involvement in the conference enriched the feedback trialists received, giving them a unique view of the impact of trials on patients, and presented patients with numerous opportunities where they could contribute to future projects in patient-oriented research.
- The conference's anonymous commenting platform was able to capture audience.
- Members' immediate impressions and questions, as they arose without interfering with ongoing presentations, encouraging participation from those who were less likely to engage with presentations in person.
- The virtual nature of the conference enabled attendance and contribution from clinicians, patients, researchers, and health administrators across Canada and internationally, connecting members of the nephrology community who share the common goal of wanting to improve hemodialysis care. The conference was accessible from the comfort of people's homes or offices, eliminating the expenses and requirement for days off work associated with in-person attendance.

Areas for improvement include the following:

- Including more patient-friendly language integrated into presentations to promote patient understanding and input.
- Involving patients in moderating the conference, including possibly providing opening remarks, commenting on their understanding of the importance of hemodialysis research, sharing their personal experiences with hemodialysis, or lending insight on some concerns about participating in pragmatic trials.
- Having fewer speakers present on fewer topics during some of the education sessions to improve the pacing of the presentations. This would improve audience members' ability to follow along and process the valuable information being presented.
- Expanding the time allotted for panel and audience discussion, so that a greater number of audience comments and feedback can be addressed. Audience members could also be given the option to unmute themselves, which may facilitate discussions.
- Encouraging greater networking participation if a future conference is hosted online. Moderators could initiate conversations with a specific question, comment, or topic of discussion to draw audiences. A shift back to a hybrid or in-person conference may also promote networking more organically.
- Better supporting trial-makers, stakeholders, and trial development by implementing strategies to increase survey response rates. Allocating dedicated time during the conference for participants to complete these surveys could significantly improve response rates in the future.
- Possibly using an alternative virtual platform in future conferences. The PheedLoop platform to host the conference posed a few complications, including an inability to extend the screen to full size for audience members and an inability to pin or search notifications, making it difficult for users to locate the conference link and password.

Trial Advancements

An ultimate goal of the conference was to advance innovative trials toward implementation, with a specific focus on evaluating the merits of the presented trials through panel discussion and enhancing their design before actual implementation. Following the conference, the Dial-Bicarb trial, led by Drs Amber Molnar and Samuel Silver (summarized in Supplemental Appendix Table C2), secured $1 682 998 in funding from CIHR and $205 521.25 from ACT. Furthermore, in April 2024, the study obtained ethics approval, with the trial recruitment set to begin in 2025. Additional advancements in the remaining 5 trial proposals are summarized in Supplemental Appendix Table C3.

Conclusion

The conference successfully provided a platform for nephrology patients, providers, and health care policymakers to cultivate and nurture support for 6 new trial ideas. The partnerships and promising trial ideas forged during the conference will continue to be developed to facilitate future large-scale trials to enhance the health and well being of patients receiving maintenance dialysis. Furthermore, promising trial proposals will be supported in future conferences to continue advancing innovative large-scale pragmatic RCTs. A follow-up conference will be planned to take place in a few years.

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ORCID iDs

Bryn Tannar https://orcid.org/0009-0005-4524-6850
Kristin K. Clemens https://orcid.org/0000-0001-9636-5597
Stephanie N. Dixon https://orcid.org/0000-0002-7566-6574
Cory E. Goldstein https://orcid.org/0000-0002-0229-5039
Amber O. Molnar https://orcid.org/0000-0003-4549-0202
Claudio Rigatto https://orcid.org/0000-0002-8306-8072
Pavel S. Roshanov https://orcid.org/0000-0003-3908-1955
Samuel A. Silver https://orcid.org/0000-0002-1843-6131
Navdeep Tangri https://orcid.org/0000-0002-5075-6370
Amit X. Garg https://orcid.org/0000-0003-3398-3114

Supplemental Material

Supplemental material for this article is available online.

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