

Proceedings From a Canadian Nephrology Forum: Nephrology Is Back

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Abstract

Purpose of conference: On January 18, 2020, the Nephrology is Back learning day forum was held in Toronto, ON, Canada. The objectives of the meeting were to describe recent advances in nephrology for community and academic nephrologists and patients, and to define challenges and opportunities for integration of new data into clinical practice. The intent was to test a unique forum for continuing medical education integrating physician and patient experiences with the goal of encouraging change in practice.

Sources of information: Program content was based on current literature and clinical experience. Additional information was provided by patient partners who attended the meeting to provide their perspective on current issues in nephrology.

Methods: A steering committee (A.L., A.S., and D.S.) developed goals and an outline for the content to be covered over the course of the meeting and led the recruitment of speakers. Speakers were asked to develop their presentations independently following direction by the committee, based on primary sources, including their own experiences. Presentations were followed by discussion including both physicians and patients, and participants had an opportunity to evaluate the conference and its outcomes.

Key findings: We present a unique approach to providing continuing medical education by including both physicians and patients in the learning process. Patient perspectives accompanying presentations around data and other clinical topics provided a much different environment from other knowledge translation exercises. We believe this represents an innovative approach for knowledge translation that allows physicians to address clinical topics in a novel manner, including the integration of new findings into practice and the need to cascade this education to their peers.

Limitations: Because the conference was a one-time event, it has been difficult to assess the actual clinical impact of the knowledge translation exercise and whether physician behaviors have changed as a result of the activity. The conference could also have included broader representation from across Canada.

Implications: The success of this test forum among both physicians and patient partners suggests that the inclusion of patient partners in learning could have an important role in future educational initiatives.

Abrégé

Objectif de la conférence: La journée d'apprentissage *Nephrology is Back* s'est tenue à Toronto (Ontario) au Canada le 18 janvier 2020. Cette réunion visait à décrire les plus récentes avancées de la néphrologie pour les néphrologues des centres communautaires et universitaires, de même que pour les patients, et à cerner les occasions d'intégrer ces nouvelles données dans la pratique clinique et les défis rencontrés. L'intention était de tester un forum de formation médicale continue intégrant les expériences des médecins et des patients afin d'entraîner des changements dans la pratique.

Sources: Le contenu du programme s'inspirait de la documentation actuelle et de l'expérience clinique. L'invitation de patients partenaires à donner leur point de vue sur les enjeux actuels en néphrologie a fourni des informations supplémentaires.

Méthodologie: Le comité directeur (AL, AS et DS) a élaboré les objectifs de la réunion et un plan du contenu à couvrir, en plus de diriger le recrutement des intervenants. Ces derniers ont été invités à préparer leur présentation de façon indépendante en suivant les directives du comité, en se basant sur des sources primaires et en intégrant leurs expériences personnelles. Ces présentations ont été suivies de discussions impliquant tant des médecins que des patients, et les participants ont évalué la conférence et ses issues.

Principaux résultats: Nous présentons une approche de formation médicale continue unique qui intègre à la fois l'avis des médecins et de patients partenaires au processus d'apprentissage. Le point de vue des patients sur les données et les autres sujets abordés pendant les présentations a fourni un environnement très différent des exercices d'application des



connaissances habituels. Nous sommes d'avis qu'il s'agit d'une approche innovante pour l'application des connaissances et qu'elle offre aux médecins une nouvelle façon d'aborder certains sujets, notamment l'intégration des plus récentes découvertes à la pratique et la nécessité de transmettre ces apprentissages aux pairs.

Limites: Il s'agissait d'un événement ponctuel. Il est donc difficile d'évaluer l'impact clinique réel de cette conférence sur la transmission des connaissances et de déterminer si les comportements des médecins ont changé à la suite de l'activité. La conférence aurait également bénéficié d'une meilleure représentation au niveau national.

Conclusion: Le succès de cette conférence rassemblant à la fois des médecins et des patients partenaires suggère que l'inclusion de ces derniers au processus d'apprentissage pourrait jouer un rôle de premier plan dans les futures activités d'apprentissage.

Keywords

ADPKD (autosomal dominant polycystic kidney disease), diabetes, diabetic nephropathy, SGLT2, Canadian

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Purpose of Conference

Although kidney disease is an important and costly health issue, there is limited information to help guide patient care in many instances, and clinical trials have suffered from important design issues.¹ In addition to the challenges associated with designing high-quality clinical trials, there are a low number of nephrology-specific trials in comparison with other specialties.² However, the recent history of nephrology also contains some major successes, including trials in autosomal dominant polycystic kidney disease (ADPKD) and in chronic kidney disease (CKD) among patients with type 2 diabetes (T2D).³⁻⁵ Despite these successes, focus groups and personal observations from several leading Canadian nephrologists suggest that integration of new findings and knowledge, including therapeutic options and new approaches in the practice of Canadian nephrology, has been slower than similar options among other specialty fields.

To help increase uptake of newer therapeutic options and encourage changes in physician behavior, a meeting of nephrologists and patient partners in learning from across the Canadian province of Ontario was held to describe some of the recent advances in nephrology for community and academic nephrologists and patients, and to define challenges and opportunities for integration of new data into clinical practice.

Sources of Information

The Steering Committee (A.L., D.S., and A.S.) drew on current literature, education needs assessments, personal experience, and conversations with other nephrologists in the creation of the meeting goals and agenda. Speakers, who were selected for their expertise in a given topic, used published data and their own experience in constructing the day's presentations. Uniquely, 10 patients with kidney disease were also included as partners in learning to provide their own insights and contribute patient perspectives to the day's proceedings.

Methods

Planning

A Steering Committee (A.L., D.S., and A.S.) came up with the concept for the meeting and approached pharmaceutical companies with a presence in nephrology to provide funding. Meeting goals and an agenda were set in discussions via teleconference. The primary goals were to encourage change in practice and uptake of medications with relatively recent strong evidence of benefit in nephrology but insufficient adoption by nephrologists in the opinion of the Committee, to positively impact patient lives, and to test a new format for

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continuing medical education (CME) that includes patients to provide a different perspective on issues in nephrology. Speakers for each portion of the agenda were selected by the Committee based on their expertise within the proposed content for the presentation.

Meeting Objectives

The objectives of the meeting as described to participants were as follows:

- Describe recent advances in nephrology demonstrated in ADPKD and CKD in T2D;
- Define new opportunities for implementation of recent clinical trial data into nephrology practice;
- Define barriers to integration of new data into routine clinical practice in nephrology;
- Improve the understanding of ongoing trials to identify future opportunities to improve patient care.

Role of the Funding Source

Funding was provided to liV Medical Education Agency by Janssen Inc and Otsuka Canada Pharmaceutical, Inc as an unrestricted educational grant. There was no input into content of the meeting or choice of speakers by the funders. Representatives of both funding organizations were present at the event but did not contribute to presentations or discussions.

Invitees

A wide variety of nephrologists from across Ontario were invited to attend. Participants could use a website to register for their attendance, which was free of charge. Leveraging a pan-Canadian SPOR (strategy for patient-oriented research) network, CanSOLVE CKD (www.cansolveckd.ca), and other sources, patients with diverse backgrounds were included among the participants as partners in learning.

Meeting Execution

The meeting took place on January 18, 2020, and 7 presentations were scheduled from 8:00 AM to 1:00 PM. The introductory session described a brief history of advances in nephrology; noting the recent development of “a culture of complacency” among some current practitioners, where the adoption of new therapies seems to be relatively slow despite strong evidence. It was speculated that this may be the result of the relatively high number of negative clinical trials in nephrology and low number of trials in comparison with other specialties.² It was emphasized that there was reason to be excited to be in the practice of nephrology at this time and reason to hope for improved patient outcomes, for new discoveries, and for a higher level of knowledge about and participation in research by both patients and physicians.

Key Findings

This meeting represented a novel approach to providing CME by including both physicians and patients in the learning process. Discussions following presentations around data and other clinical topics included both physicians and patient partners and provided an innovative mechanism for knowledge translation that allowed physicians to address clinical topics in a novel manner.

Genetics of Chronic Kidney Disease and Polycystic Kidney Disease

Issues in differential diagnosis of cystic kidney diseases were described, including the challenge of cyst burden often being substantial before diagnosis when there is no apparent family history.⁶ Considerations around genetic factors in ADPKD severity were detailed, including the adverse influence of *PKD1* or *PKD2* mutations on survival, discordance in presentation within families, and unrecognized mutations across 60 different modifier genes being present within about one-third of patients.⁷⁻⁹

Indications for genetic testing in suspected ADPKD were also reviewed. Genetic testing was said to not be necessary for all patients, such as those with a classic presentation and family history of ADPKD. It should be considered clinically indicated for patients with no apparent family history, those requiring disease exclusion at a young age, and for prenatal or preimplantation diagnosis. Other features, such as early severe presentation, syndromic features, and discordance between imaging and actual renal function may help contribute to a differential diagnosis.¹⁰

Current research in ADPKD includes the examination of renal parenchymal imaging as a viable analysis of disease progression and the use of artificial intelligence in imaging to discover patterns of kidney involvement that would not be evident to conventional assessment.

From the patient perspective, questions arose around the relevance of new scientific data to clinical outcomes and whether genetic factors in ADPKD irrevocably determine outcomes. Presenters conferred with the patient partners, noting that new trial data are encouraging for patients and should provide hope for better outcomes and described genetics are one potential determinant of illness, and other factors (socioeconomic, cultural, etc.) contribute to disease manifestation and progression.

Sodium-Glucose Cotransporter-2 (SGLT2) Inhibition and Cardiorenal Protection for Patients With Diabetes

Several potential mechanisms of action for the cardiorenal protection provided by SGLT2 inhibitor (SGLT2i) class of medications were described, including the potential involvement of SGLT2 inhibition in tubuloglomerular

feedback resulting in the constriction of afferent arterioles into the nephron.^{11,12} It was also noted that SGLT2i treatment is associated with a reduction in proinflammatory signaling and may affect hypoxia-related pathways, which may contribute to both renal and cardiac protection by SGLT2i medications and account for the independence of these effects from glucose lowering.^{13,14} The need for further research to better define the mechanisms of action of SGLT2 inhibitors for renal and cardiac protection was acknowledged.

Discussion included speculation that the renal protective effects of SGLT2i seen in patients with T2D⁵ would extend to patients without diabetes.

Advances in Polycystic Kidney Disease

Height-adjusted total kidney volume (HiTKV) changes precede changes in estimated glomerular filtration rate (eGFR) and may thus be a better marker for disease progression in ADPKD as it would enable earlier intervention.¹⁵ In a review of trial results and clinical pearls in ADPKD treatment, it was emphasized that there seems to be a greater benefit of tolvaptan among patients who experience a greater reduction in urine osmolality.¹⁶ Nephrologists were encouraged to titrate the tolvaptan dose and water intake to ensure a urine osmolality <280 mOsm/kg is maintained.

CREDESCENCE: A Landmark Study in DKD

The current standard of care for diabetic nephropathy is associated with an important residual risk for patients.¹⁷⁻¹⁹ A recent trial of SGLT2 inhibitors in patients with T2D and renal impairment⁵ was hailed as a landmark in the treatment of diabetic nephropathy, and ongoing trials of SGLT2 inhibitors in patients with CKD, both with and without T2D, were also described. A pressing need for nephrologists to adopt SGLT2 inhibitors based on these positive trial results was emphasized, with it being noted that only 40% of nephrologists across 4 Canadian provinces had prescribed an SGLT2 inhibitor at the time of the presentation.²⁰ A call to action was put forth for Canadian nephrologists to increase their use of SGLT2 inhibitors in patients with CKD and T2D.

Physicians discussed a need to optimize continuity of care between endocrinologists and nephrologists in patients with CKD and T2D with respect to SGLT2 inhibitors. The independence of the cardiorenal and metabolic effects from its effects on glucose was emphasized, and it was said that both specialties should feel an obligation to ensure that patients are able to benefit from the medication. Accountability and even peer pressure among nephrologists were considered important in ensuring the adoption of best practices and incorporation of new data into practice. An analogy was drawn to angiotensin-converting enzyme (ACE) inhibitors and angiotensin II

receptor blocker (ARB) medications, and nephrologists were called upon to help take the lead with adopting SGLT2 inhibitors into their practices and educating primary care practitioners to implement these changes in their own practices.

What Is “Clinical Inertia” and What Might We Do About It?

A presentation on topics in implementation science is followed, noting that the successful incorporation of evidence into actual practice is a multifactorial process involving multiple actors all changing their behaviors within relatively complex environments.²¹ The 4 key considerations in implementing change were described as the parties whose behavior needs to change, the factors influencing their behavior, strategies to effect changes, and outcome measures.²² Defining the behaviors that need to be changed can be framed in terms of the desired actions and actors, the context in which the action should be performed, the target for the action, and the time when the action should occur.²³ A variety of tools can encourage behavior change in one or more of the above key domains, including education, audit and feedback, reminders, incentives, and addition of resources.²⁴ It was emphasized that behavior change requires that actors be capable of effecting the change, be motivated to make the change, and have the opportunity to do so.

Nephrology Trials in Canada: Toward a New Era

A final presentation described several interconnected ways to potentially address challenges in Canadian kidney research such as increasing public awareness and funding and creating research networks. Engaging patients and front-line care providers in the design of research projects may help prevent premature stoppage or discontinuation of trials due to low recruitment, address high dropout rates, and ensure health care personnel are invested in research projects.²⁵ Even fundamental priorities of research are different between clinicians, who tend to focus on mortality outcomes, and patients, who are more concerned with topics such as communication and information delivery, symptoms, and quality of life.^{26,27} It was also emphasized that research results need to be disseminated to the public and especially to those patients who participate in a trial. Failing to convey results of effectiveness to trial participants may be detrimental to perceptions of value of research and hence also to trial recruitment and retention. Showing a meaningful impact of research on practice is critical in addressing barriers to funding, logistics, and stakeholder buy-in.

Discussion after the presentation emphasized the importance of including patients in setting research priorities and the potential advantages of having patients who have participated in clinical trials work as “research

ambassadors” to help encourage other patients to enroll in studies and trials.

Patient Perspectives

A group of 10 patients with diverse kidney journeys was in attendance and led a group discussion from their perspective. Commenting on the day’s presentations, they recognized that adoption of new or improved practices is an issue that affects all industries and professions, but wanted a better understanding of why not all doctors are using the very latest and best-proven therapies to delay progression of kidney disease.

From a patient education perspective, they cautioned that patients are often underestimated in terms of their intelligence and that many of them would appreciate efforts to help them understand research findings so that they can be more active partners in their own treatment. Patients agreed that they have a responsibility to educate themselves about their condition and the available treatments, and some patients said they attempt to primarily use peer-reviewed literature as their research material. However, paywalls on research and learning resources were an absolute barrier for many. Another barrier to their education is the fatigue experienced by many patients with kidney disease before initiation of treatment. Reading material could be provided for patients to review as they are able.

With respect to medications, patients expressed particular concern about side effects and drug-drug interactions. Enhancing understanding of relative and absolute risks of side effects was seen as extremely important for both patients and physicians, and that learning around this key topic might be best undertaken as a collaboration between both groups to ensure that data are interpreted correctly and can be clearly communicated. Patients and physicians agreed on a need for the development of better methods to communicate concepts of relative and absolute risk, and how to improve understanding so individual doctors may use these concepts in decision making.

In terms of research, it was noted that the need for demonstration of patient engagement within research (ie, in the context of grant applications) could be addressed by the inclusion of patients in the planning process rather than a qualitative research component. Patient perspectives can be highly useful in research design, from practical considerations such as input on frequency of follow-ups and visits to prioritizing research questions. One patient remarked, “Our job is to sit on your side of the table and ask the questions that you would ask if you knew what we know about this side of kidney disease,” highlighting the experiential knowledge possessed by patients that is critical to setting research priorities. Patients also remarked that research advisory and ethics boards seem to be focused on protecting institutions from liability rather than protecting patients and that patients themselves might be willing to accept more risk than institutions would allow.

Meeting Evaluation

In a postmeeting survey, all participants indicated that the meeting had met its stated objectives, and all agreed or strongly agreed that the meeting had been relevant to their practice, increased their understanding and awareness of key topics, and that they would use the information they had learned in their practice. Participants were asked to select 1 or 2 adjectives to describe the meeting from a provided list, and the most common responses included “innovative,” “interesting,” and “impactful.” Several participants briefly described changes they would make to their practices based on the information presented, including pushing for better education for patients and colleagues, exploring strategies to improve patient engagement, reviewing barriers to change in the context of implementation science, and providing better explanations to patients around the rationale for treatments. Key barriers identified to making changes included early patient identification and referral, clinic and practitioner resources, and medication costs and access.

Conclusions

Using an interactive approach including patients, practicing physicians, and researchers, this meeting constituted the first endeavor in Canadian nephrology to “share learning” in real time between these groups of stakeholders. Based on the positive participant evaluations, this approach proved successful with participants, and all stakeholders appreciated the value of engaging patients to help modify or inform individual physician behavior.

From the physician perspective, data and clinical pearls were shared around indications for genetic testing in ADPKD, potential mechanisms of organ protection by SGLT2i, and the uses of tolvaptan and SGLT2 inhibitors in specific patient populations. These presentations provided the evidence behind newer therapies to help fulfill the goal of encouraging their adoption by physicians. Principles of implementation science as discussed in this meeting could help effect behavior change among nephrologists and contribute to overcoming therapeutic inertia, such as that seen with adoption of SGLT2i medications among nephrologists.

Patients brought a new perspective to CME. Physicians were able to directly ask questions to help inform their understanding of issues in kidney disease as experienced by patients. Patients expressed concerns about lack of uptake of new therapies, barriers to their ability to educate themselves on their disease such as paywalls to credible sources, safety and drug-drug interactions, and communication of absolute and relative risk in medicine. Interactions between physicians and patients in this context differentiated this meeting from others in nephrology and provided valuable information to physicians about the opinions and real-life experiences of patients in nephrology practices. Patients also expressed a desire to be more engaged with research and to

bring their experiential knowledge of living with kidney disease into the planning of research initiatives.

The limitations of this approach to medical education include the one-time nature of the event, making it difficult to assess the actual clinical impact of the knowledge translation exercise and whether physician behaviors have changed as a result of the activity. The conference could also have included broader representation from across Canada.

We hope to undertake further events with a similar structure and in additional regions to help promote the successful evolution of nephrology.

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Ethics Approval and Consent to Participate

No patient consent or ethics approval was required for this narrative review.

Consent for Publication

All authors consent to the publication of this research.

Availability of Data and Materials

No data or materials are available for this review.

Author Contributions

D.S., A.S., and A.L. planned the meeting, set the agenda, and facilitated the discussion. A.L. and I.C.H. drafted the first version of the manuscript. D.S., A.S., D.C., M.B.L., L.M., and R.S.S. reviewed and revised the manuscript and approved the final draft. A.L. and I.C.H. drafted the responses to reviewers and took responsibility as corresponding author. All authors edited and approved the final manuscript.

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References

- Baigent C, Herrington WG, Coresh J, et al. Challenges in conducting clinical trials in nephrology: conclusions from a Kidney Disease-Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int.* 2017;92(2):297-305. doi:10.1016/j.kint.2017.04.019.
- Chatzimanouil MKT, Wilkens L, Anders HJ. Quantity and reporting quality of kidney research. *J Am Soc Nephrol.* 2019;30(1):13-22. doi:10.1681/ASN.2018050515.
- Torres VE, Chapman AB, Devuyst O, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. *N Engl J Med.* 2012;367(25):2407-2418. doi:10.1056/NEJMoa1205511.
- Torres VE, Chapman AB, Devuyst O, et al. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. *N Engl J Med.* 2017;377(20): 1930-1942. doi:10.1056/NEJMoa1710030.
- Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med.* 2019;380(24):2295-2306. doi:10.1056/NEJMoa1811744.
- Grantham JJ, Torres VE, Chapman AB, et al. Volume progression in polycystic kidney disease. *N Engl J Med.* 2006;354(20):2122-2130.
- Hwang YH, Conklin J, Chan W, et al. Refining genotype-phenotype correlation in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol.* 2016;27(6):1861-1868. doi:10.1681/ASN.2015060648.
- Lanktree MB, Guiard E, Li W, et al. Intrafamilial variability of ADPKD. *Kidney Int Rep.* 2019;4(7):995-1003. doi:10.1016/j.ekir.2019.04.018.
- Groopman EE, Marasa M, Cameron-Christie S, et al. Diagnostic utility of exome sequencing for kidney disease. *N Engl J Med.* 2019;380(2):142-151. doi:10.1056/NEJMoa1806891.
- Lanktree MB, Iliuta IA, Haghghi A, Song X, Pei Y. Evolving role of genetic testing for the clinical management of autosomal dominant polycystic kidney disease. *Nephrol Dial Transplant.* 2019;34(9):1453-1460. doi:10.1093/ndt/gfy261.
- Heerspink HJ, Perkins BA, Fitchett DH, Husain M, Cherney DZI. Sodium glucose cotransporter 2 inhibitors in the treatment of diabetes mellitus: cardiovascular and kidney effects, potential mechanisms, and clinical applications. *Circulation.* 2016;134(10):752-772. doi:10.1161/CIRCULATIONAHA.116.021887.
- Kidokoro K, Cherney DZI, Bozovic A, et al. Evaluation of glomerular hemodynamic function by empagliflozin in diabetic

- mice using in vivo imaging. *Circulation*. 2019;140(4):303–315. doi:10.1161/CIRCULATIONAHA.118.037418.
13. Dekkers CCJ, Petrykiv S, Laverman GD, Cherney DZ, Gansevoort RT, Heerspink HJL. Effects of the SGLT-2 inhibitor dapagliflozin on glomerular and tubular injury markers. *Diabetes Obes Metab*. 2018;20(8):1988-1993. doi:10.1111/dom.13301.
 14. van Raalte DH, Cherney DZI. Sodium glucose cotransporter 2 inhibition and renal ischemia: implications for future clinical trials. *Kidney Int*. 2018;94(3):459-462. doi:10.1016/j.kint.201805026.
 15. Chapman AB, Bost JE, Torres VE, et al. Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol*. 2012;7(3):479-486. doi:10.2215/CJN.09500911.
 16. Devuyst O, Chapman AB, Gansevoort RT, et al. Urine osmolality, response to tolvaptan, and outcome in autosomal dominant polycystic kidney disease: results from the TEMPO 3:4 trial. *J Am Soc Nephrol*. 2017;28(5):1592-1602. doi:10.1681/ASN.2016040448.
 17. Bakris GL. Maximizing cardiorenal benefit in the management of hypertension: achieve blood pressure goals. *J Clin Hypertens (Greenwich)*. 1999;1(2):141-147.
 18. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med*. 2001;345(12):861-869.
 19. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med*. 2001;345(12):851-860.
 20. IQVIA. IMS Health Canada. Report, IQVIA Canada Inc., Montreal Canada; 2019.
 21. Eccles MP, Mittman BS. Welcome to implementation science. *Implement Sci*. 2006;1:1. doi:10.1186/1748-5908-1-1.
 22. French SD, Green SE, O'Connor DA, et al. Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework. *Implement Sci*. 2012;7:38. doi:10.1186/1748-5908-7-38.
 23. Presseau J, McCleary N, Lorencatto F, Patey AM, Grimshaw JM, Francis JJ. Action, actor, context, target, time (AACTT): a framework for specifying behaviour. *Implement Sci*. 2019;14(1):102. doi:10.1186/s13012-019-0951-x.
 24. Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Ann Behav Med*. 2013;46(1):81-95.
 25. Flythe JE, Hilliard T, Castillo G, et al. Symptom prioritization among adults receiving in-center hemodialysis: a mixed methods study. *Clin J Am Soc Nephrol*. 2018;13(5):735-745. doi:10.2215/CJN.10850917.
 26. Tong A, Craig JC, Nagler EV, et al. Composing a new song for trials: the Standardized Outcomes in Nephrology (SONG) initiative. *Nephrol Dial Transplant*. 2017;32(12):1963–1966. doi:10.1093/ndt/gfx288.
 27. Manns B, Hemmelgarn B, Lillie E, et al. Setting research priorities for patients on or nearing dialysis. *Clin J Am Soc Nephrol*. 2014;9(10):1813-1821. doi:10.2215/CJN.01610214.