Canadian Society of Nephrology/ Société canadienne de néphrologie CSN/SCN

CANADIAN JOURNAL OF KIDNEY HEALTH AND DISEASE
Journal canadien de la santé et de la maladie rénale

Clinical Research Protocol

Canadian Journal of Kidney Health and Disease
Volume 8: 1–18

DOI: 10.1177/2054358121997266
journals.sagepub.com/home/cjk
SAGE

A Quality Improvement Intervention to Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD) in Patients With Chronic Kidney Disease: Clinical Research Protocol of a Cluster-Randomized Clinical Trial

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Abstract

Background: Many patients with kidney failure will live longer and healthier lives if they receive a kidney transplant rather than dialysis. However, multiple barriers prevent patients from accessing this treatment option.

Objective: To determine if a quality improvement intervention provided in chronic kidney disease (CKD) programs (vs. usual care) enables more patients with no recorded contraindications to kidney transplant to complete more steps toward receiving a kidney transplant.

Design: This protocol describes a pragmatic 2-arm, parallel-group, open-label, registry-based, cluster-randomized clinical trial—the Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD) trial.

Setting: All 26 CKD programs in Ontario, Canada, with a trial start date of November 1, 2017. The original end date of March 31, 2021 (3.4 years) has been extended to December 31, 2021 (4.1 years) due to the COVID-19 pandemic.

Participants: During the trial, the 26 CKD programs are expected to care for more than 10 000 adult patients with CKD (including patients approaching the need for dialysis and patients receiving dialysis) with no recorded contraindications to a kidney transplant.

Intervention: Programs were randomly allocated to provide a quality improvement intervention or usual care. The intervention has 4 main components: (1) local quality improvement teams and administrative support; (2) tailored education and resources for staff, patients, and living kidney donor candidates; (3) support from kidney transplant recipients and living kidney donors; and (4) program-level performance reports and oversight by program leaders.

Primary Outcome: The primary outcome is the number of key steps completed toward receiving a kidney transplant analyzed at the cluster level (CKD program). The following 4 unique steps per patient will be counted: (1) patient referred to a transplant center for evaluation, (2) at least one living kidney donor candidate contacts a transplant center for an intended recipient and completes a health history questionnaire to begin their evaluation, (3) patient added to the deceased donor transplant wait list, and (4) patient receives a kidney transplant from a living or deceased donor.

Planned Primary Analysis: Study data will be obtained from Ontario's linked administrative healthcare databases. An intent-to-treat analysis will be conducted comparing the primary outcome between randomized groups using a 2-stage approach. First stage: residuals are obtained from fitting a regression model to individual-level variables ignoring intervention and clustering effects. Second stage: residuals from the first stage are aggregated at the cluster level as the outcome.

Limitations: It may not be possible to isolate independent effects of each intervention component, the usual care group could adopt intervention components leading to contamination bias, and the relatively small number of clusters could mean the 2 arms are not balanced on all baseline prognostic factors.
Conclusions: The EnAKT LKD trial will provide high-quality evidence on whether a multi-component quality improvement intervention helps patients complete more steps toward receiving a kidney transplant.
Trial registration: Clinicaltrials.gov; identifier: NCT03329521.

Abrégé
Contexte: Plusieurs patients atteints d'insuffisance rénale vivront plus longtemps et en meilleure santé s'ils reçoivent une greffe de rein plutôt que des traitements de dialyze. De nombreux obstacles empêchent cependant les patients d'accéder à la transplantation.
Objectif: Déterminer si une intervention visant l'amélioration de la qualité menée dans les programs d'insuffisance rénale chronique (IRC) permettrait à davantage de patients sans contre-indications à une greffe d'aller plus loin (comparativement aux soins habituels) dans le processus menant à la transplantation.
Type d'étude: Ce protocole décrit un essai clinique pragmatique ouvert, à deux bras, en groupes parallèles, à répartition aléatoire en grappes et fondé sur un registre — l'essai *Enhance Access to Kidney Transplantation and Living Kidney Donation* (EnAKT LKD).
Cadre: Les 26 programs d'IRC de l'Ontario (Canada). L'essai a débuté le 1er novembre 2017 et devait initialement se terminer le 31 mars 2021 (3,4 ans); cette date a été reportée au 31 décembre 2021 (4,1 ans) en raison de la pandémie de COVID-19.
Sujets: Au cours de l'essai, on estime que les 26 programs d'IRC prendront en charge plus de 10 000 adultes atteints d'IRC (y compris des patients approchant le besoin de dialyze et des patients dialysés) sans contre-indications à une greffe.
Interventions: Les programs ont été répartis aléatoirement pour intégrer une intervention d'amélioration de la qualité ou pour prodiguer les soins habituels. L'intervention consiste en quatre composantes principales: (1) des équipes locales d'amélioration de la qualité et de soutien administratif; (2) de l'information et des ressources sur mesure pour le personnel, les patients et les donneurs vivants; (3) du soutien pour les receveurs et les donneurs vivants; et (4) des rapports sur le rendement au niveau du program et une surveillance assurée par les chefs de program.
Principaux résultats: Le principal critère d'évaluation est le nombre d'étapes clés complétées en vue de la réception d'une greffe de rein tel qu'analysé au niveau de la grappe (program d'IRC). Pour chaque patient, quatre étapes spécifiques seront comptabilisées: (I) le patient est aiguillé vers un center de transplantation pour évaluation; (II) au moins un donneur vivant de rein contacte un center de transplantation pour un receveur en particulier et amorce son évaluation en remplissant un questionnaire sur ses antécédents médicaux; (III) le patient est ajouté à la liste d'attente pour une transplantation d'un donneur décédé, et (IV) le patient reçoit une greffe de rein d'un donneur vivant ou décédé.
Principale analyze envisagée: Les données sont tirées des bases de données administratives du système de santé ontarien. Une analyze en intention de traiter sera effectuée en comparant le principal critère d'évaluation entre les groupes

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répartis aléatoirement à l'aide d'une approche en deux étapes. Première étape: obtention de valeurs résiduelles en adaptant un modèle de régression aux variables de niveau individuel et en ignorant les effets de l'intervention et du regroupement. Deuxième étape: les valeurs résiduelles de la première étape agrégées au niveau du groupe constitueront le résultat.
Limites: Il pourrait ne pas être possible d'isoler les effets indépendants de chaque composante de l'intervention. L'équipe prodiguant les soins habituels pourrait adopter des composantes de l'intervention menant à un biais de contamination. Le nombre relativement faible de groupes pourrait signifier que les deux bras ne sont pas équilibrés sur tous les facteurs pronostiques de base.
Conclusion: L'essai EnAKT LKD fournira des données de haute qualité sur la question de savoir si une intervention à composantes multiples visant l'amélioration de la qualité aide effectivement les patients à franchir davantage d'étapes vers une transplantation rénale.

Keywords
cluster-randomized clinical trial, quality improvement intervention, kidney transplant, living kidney donation, protocol

Received December 20, 2020. Accepted for publication January 2, 2021.

Background

Patients with kidney failure need regular dialysis treatments or a kidney transplant to survive. Compared with dialysis, a kidney transplant offers patients a better quality of life and many gain 10 or more years of life expectancy.[1,2] A transplant also costs the healthcare system less—over a 5-year period, every 100 kidney transplants saves the healthcare system about $20 million in averted hospital-based dialysis costs (Canadian data).[3,4] Living donor transplants offer further advantages, including superior graft and patient survival compared with deceased donor transplants.[5,6] Unfortunately, many patients with kidney failure who would benefit from a transplant will never receive one. There is a chronic shortage of organs from deceased donors, and in Canada, the rate of living donor kidney transplantation has stagnated since 2006.[7-9] Currently, more than 40,000 patients are living with kidney failure in Canada and 3000 are on a waiting list for a deceased donor kidney transplant.[10]

In addition to the shortage of transplantable kidneys, several other barriers impede patient access to transplantation (Table 1).[11-15] Patients and frontline healthcare providers often lack knowledge or have misconceptions about transplantation and living kidney donation. Many patients have difficulty discussing the option of living donor transplantation with family and friends. Furthermore, the evaluation process for transplantation and living kidney donation is complex involving multiple steps (Figures 1 and 2) including appointments, tests, and consultations, making it difficult to navigate the healthcare system to complete the evaluation. As a result, many patients who are potentially eligible for a transplant are not appropriately evaluated, and many never receive a transplant.[12] Significant variation in access to kidney transplants is evident across Ontario (Canada's most populous province), even after accounting for differences in patient characteristics.[16]

In an effort to improve access to kidney transplantation in Ontario, 2 government-funded organizations formed a partnership in 2015: The Ontario Renal Network (ORN, part of Ontario Health), which manages the delivery of renal services across the province, and the Trillium Gift of Life Network (TGLN), which coordinates organ donation and transplant care. This partnership resulted in the development of a multi-component quality improvement intervention designed to improve access to kidney transplantation and living kidney donation in Ontario (in Canada, health services are publicly funded and provincially administered). Here we describe the development of this intervention and the protocol of a pragmatic 2-arm, parallel-group, open-label, registry-based, cluster-randomized clinical trial that will evaluate its province-wide implementation and impact.

Development of the Quality Improvement Intervention and Its Components

An 18-member panel was convened to understand how access to kidney transplantation and living kidney donation might be improved in Ontario. The panel was led by a physician Provincial Medical Lead in Access to Kidney Transplantation for the ORN (A Garg) and included provincial experts in quality improvement and transplantation (S Yohanna), administrative healthcare data (K Naylor), education (I Musci), and patient support (S McKenzie), as well as patients, frontline healthcare professionals, administrators, clinicians, and representatives from the ORN and TGLN. The panel sought input from multiple stakeholders between 2015 and 2017, including a patient-led workshop,[11] chronic kidney disease (CKD) program staff, transplant personnel, and other experts in the field. Three task groups were also created to help plan the intervention: the first focused on education, the second on patient support from kidney transplant recipients and living kidney donors, and the third on data and performance monitoring. These activities led to the

Table 1. Barriers to Receiving a Kidney Transplant.

Category	Barriers
Patient	• Poor transplant knowledge. • Misconceptions about eligibility, kidney transplant, and living kidney donation. • Fear or uncertainty about transplant. • Comfortable with dialysis. • Low health literacy. • Not ready to pursue a transplant. • Difficulty sharing their story of kidney failure and asking loved ones for a kidney. • Feels undeserving of a living donor kidney transplant. • Feels guilt and anxiety about putting the health of a loved one at risk. • Cultural beliefs prevent considering a transplant. • Difficulty completing the necessary testing and appointments. • Lives far from the transplant center making it difficult to complete the transplant evaluation.
Living donor candidate	• Lack of knowledge about living kidney donation. • Financial costs of evaluation. • Complexity of the living donor evaluation process. • Cultural beliefs prevent considering living kidney donation. • Shared risk factors with the recipient (e.g. obesity or familial diseases).
Healthcare professional	• Not trained to provide transplant education and therefore uncomfortable discussing kidney transplantation with patients and families.
Chronic kidney disease (CKD) program	• Other initiatives in kidney care (e.g. the promotion of home dialysis or fistula use) may compete with transplant-related initiatives. • No standardized process to identify eligible patients for education and transplant referral. • Educational material on transplantation may require high health literacy or be culturally insensitive. • Transplant education may not include patients' family or friends. • Transplant education is not sufficiently repetitive. • Lack of time and resources to adequately educate and promote kidney transplant.
Transplant center	• Kidney transplant referral eligibility criteria are not clear or standardized across transplant centers. • Evaluation process for potential kidney transplant recipients and living donor candidates is long and burdensome. • Lack of communication with CKD programs to help move patients through the evaluation process.
Health system	• Lack of accountability for ensuring equal access to kidney transplants. • Misaligned financial incentives (e.g. remuneration to CKD programs for home dialysis starts is lost if patients receive a kidney transplant). • No policies to ensure financial neutrality for living kidney donors.

Note. Barriers identified from our patient-led workshop and from conversations with patients and healthcare providers. We also identified barriers from the literature, including *Kidney Int*[12]; *CJASN*[13]; *Nephrol Dial Transplant*[14]; *Transplantation*.[15]

development of several strategies for improving access to kidney transplantation.

The panel recognized that barriers to receiving a transplant are complex and exist at multiple levels including the patient, living donor, health professional, CKD program, and healthcare system (Table 1). The panel recommended that the strategies which address these barriers be combined and included as components of a province-wide quality improvement intervention but acknowledged the difficulty then to clearly attribute any observed intervention effects to specific components which may interact synergistically. In designing this intervention, the panel reviewed best practices in the literature including other quality improvement interventions in dialysis and transplantation,[17-21] and considered the costs, feasibility, and likelihood of uptake of different components in the Ontario setting. The development of each component is described briefly below, and the implementation details are provided in the methods section.

1. Quality improvement teams and administrative support: To support intervention implementation and improve program performance, the panel recommended that local quality improvement teams be established at each CKD program. The panel also recommended that CKD programs receive administrative support to support their teams.
2. Improved transplant education for patients and healthcare providers: The need for more effective transplant-related education was identified by the 2016 patient-led workshop[11] and confirmed in a needs

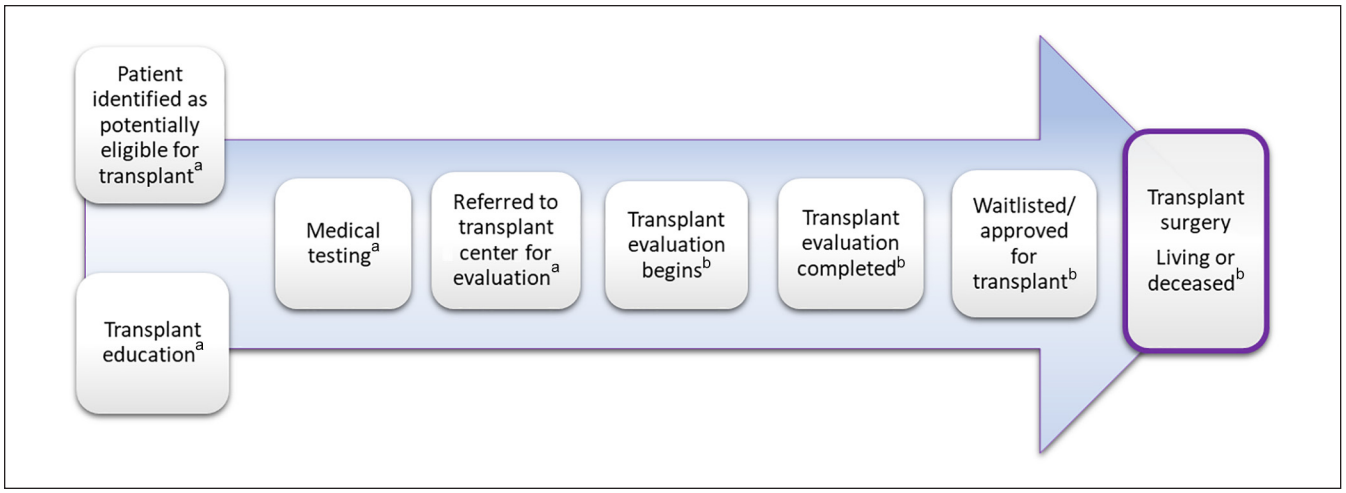

Figure 1. Steps to receiving a living or deceased donor kidney transplant for patients in Ontario, Canada.
[a]Occurs within the chronic kidney disease program.
[b]Occurs within the transplant center.

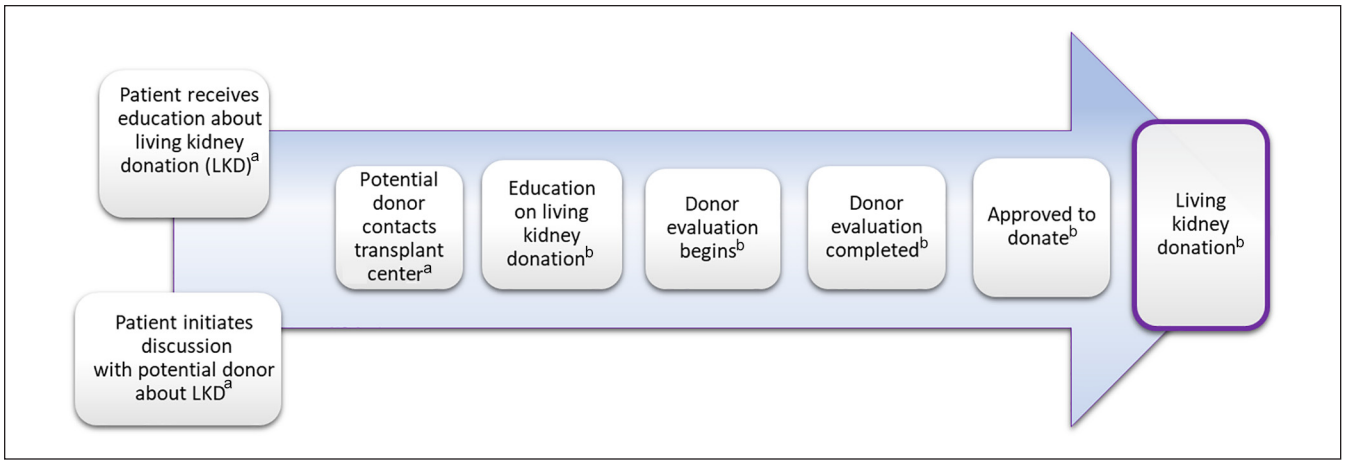

Figure 2. Steps to living kidney donation (LKD) for patients in Ontario, Canada.
[a]Occurs within the chronic kidney disease program; family members and friends who attend clinic visits can also receive education. The chronic kidney disease program can also facilitate discussions with potential donors about LKD.
[b]Occurs within the transplant center.

assessment conducted by the education task group. The task group surveyed nurses and other healthcare providers in Ontario's 26 CKD programs and 6 adult kidney transplant centers and conducted semistructured interviews with patients and living kidney donors in Ontario. This work revealed that only about one quarter of frontline kidney healthcare providers in Ontario felt comfortable discussing kidney transplantation with their patients, and over one third of patients in advanced CKD clinics (referred to as multi-care kidney clinics) were not adequately informed about kidney transplantation as a treatment option. This was a concern, as early transplant education has been shown to increase referral rates and decrease disparities in access to transplantation.[22-31] Furthermore, a systematic review and meta-analysis found educational interventions improve measures of living donor transplant activity (e.g. donor contacts and living kidney donor transplant rate).[32] The education task group also conducted an environmental scan and literature review, consulted with experts to understand best-practice recommendations for transplant education, and curated many high-quality educational resources that could be used in Ontario.

The task group also recommended CKD programs be supported in their use of a new Ontario version of Explore Transplant (etontario.org/), a personalized educational program that incorporates guided discussions tailored to a CKD patient's stage of readiness for considering transplant.[33-35] A randomized controlled

trial found that patients on maintenance dialysis who received the Explore Transplant program compared to standard education had greater transplant knowledge, were more likely to start the transplant evaluation, and had more living donor candidates evaluated.[33,34] The United States version of Explore Transplant was adapted to meet the needs of Ontario patients (an effort led by I Mucsi and A Waterman), and the program's videos include Ontario patients and healthcare professionals.[35]

3. Access to support: Better access to support from kidney transplant recipients and living kidney donors was strongly recommended by the 2016 patient-led workshop.[11] On the recommendation of the workshop, a task group focused on patient support developed a new patient-led, volunteer-driven, grassroots, support program—the Transplant Ambassador Program (TAP: transplantambassadors.ca; see Supplemental Appendix 1 for a screenshot of the TAP website). The program was built upon prior work in this area.[26,36] The effort was led by S McKenzie, a recipient of a kidney from a living donor and L Getchell whose mother received a living kidney from her father.
4. Program-level performance monitoring: Traditionally, Ontario's CKD programs have not received feedback on how well their patients are completing key steps toward receiving a kidney transplant (e.g. number of referrals to transplant centers). The data and performance monitoring task group collated feedback from relevant stakeholders and recommended existing data be leveraged and shared between transplant centers and CKD programs with the goal of improving care. This prompted the creation of a data-sharing agreement between TGLN and ORN to allow relevant transplant data to be combined with data from CKD programs and featured in program-level reports according to best practices in audit-and-feedback.[37] The task group recommended that these reports be reviewed in accountability meetings between the CKD programs and the ORN.

The Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD) Trial

The 4 components described above: quality improvement teams, education, transplant ambassador support, and performance monitoring are included in the quality improvement intervention currently being tested in a province-wide, cluster-randomized clinical trial: The Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD) trial (see Supplemental Appendix 2 for EnAKT LKD logo). The rigorous evaluation of this intervention will inform future decisions as to whether this intervention should be sustained and expanded. The trial objectives, methods, and analytic plan are outlined in the protocol below.

Objective

To determine if a quality improvement intervention provided in CKD programs (vs. usual care) enables more patients (with no recorded contraindications to kidney transplant) to complete more steps toward receiving a kidney transplant.

Methods

Study Design and Setting

EnAKT LKD is a pragmatic, 2-arm, parallel-group, open-label, registry-based cluster-randomized clinical trial. Registry-based trials use existing information in administrative databases to perform randomization and to obtain data on baseline variables and outcomes.[38] The intervention was designed to impact entire CKD programs, so program-level (cluster) randomization was adopted for logistical reasons and to minimize cross-group contamination. The CKD programs were randomly allocated (1:1) to receive the quality improvement intervention or to continue care as usual. Recommended guidelines were followed to prepare this protocol (Standard Protocol Items: Recommendations for Interventional Trials [SPIRIT]; Supplemental Appendix 3)[39] and to describe the intervention (Template for Intervention Description and Replication [TIDieR]; Supplemental Appendix 4).[40]

As of November 1, 2017, the province of Ontario (Canada) had 26 regional CKD programs (also referred to as Regional Renal Programs). On April 1, 2018, one of the programs separated into 2; however, these will continue to be treated as a single unit of randomization during the trial. The programs are listed online (https://www.ontariorenalnetwork.ca/en/about/regional-renal-programs [last accessed Jan 30, 2020]). The CKD programs oversee 26 multi-care kidney clinics (which provide care for patients approaching the need for dialysis), 22 home dialysis programs, and 97 hemodialysis units. Staff in the dialysis units and multi-care kidney clinics are responsible for identifying patients who are potentially eligible to receive a kidney transplant. In Ontario, the CKD programs are responsible for completing and submitting a comprehensive referral package to one of the 6 provincial transplant centers (Kingston General Hospital, London Health Sciences Center, St. Joseph's Healthcare Hamilton, St. Michael's Hospital, the Ottawa Hospital, or the University Health Network). This differs from the practice in the United States, where all that is needed for a CKD program to make a transplant referral is to provide a patient's name and contact information. The referral package in Ontario consists of tests needed by the transplant center to assess transplant eligibility, including up-to-date cancer screening tests, blood work, and cardiac assessment (the full list of required tests is available on the TGLN website).[41] Staff in the multi-care

kidney clinics help patients plan for future kidney replacement therapy, including the possibility of a pre-emptive living kidney donor transplant (receipt of a transplant without any need for dialysis treatments). CKD program staff can raise awareness with family members and friends who come with patients to their appointments about opportunities to be evaluated as a living kidney donor. Interested donor candidates for an intended recipient then contact the transplant center to receive more information and begin their evaluation by completing a health history questionnaire.

Inclusion Criteria

All 26 regional CKD programs in Ontario, Canada, were included in this trial. During the trial period, the 26 programs will provide healthcare to more than 13 000 adult patients receiving maintenance dialysis (including in-center hemodialysis, home hemodialysis, and peritoneal dialysis). Each CKD program also provides a multi-care kidney clinic for patients with CKD who are approaching the need for dialysis (during the trial period more than 15 000 patients will visit these clinics). While many of these patients will have contraindications to kidney transplant, based on a preliminary analysis of our data sources, we estimate there will be at least 10 000 patients from the 26 programs during the trial period with no recorded contraindication to receiving a kidney transplant (see Statistical analysis section below). At the time of the final analysis, prespecified selection criteria will be applied to select patients for inclusion in the analysis of trial outcomes. Patients younger than 18 years (estimated $<1\%$ of the total CKD population in Ontario) will be excluded as they are managed by different healthcare teams.

Intervention

CKD programs were randomly allocated 1:1 to provide usual care or the quality improvement intervention beginning November 1, 2017. The original trial end date was planned for March 31, 2021 (3.4-year trial period); however, on March 16, 2020, nearly all kidney transplants and evaluations for deceased and living donor transplants were suspended in Ontario due to the COVID-19 pandemic. Thus, the trial period has been extended to December 31, 2021 (4.1-year trial period) and may be extended further depending on the progression of the pandemic.

Usual care. CKD programs randomly allocated to the usual-care group will continue to support access to kidney transplantation and living kidney donation as usual. In Ontario, CKD program health professionals have not traditionally placed a heavy emphasis on this activity in their day-to-day work. For example, they are not given provincially organized tools or support to form local quality improvement teams to understand and improve local performance, examine current transplant referral and education pathways, or set goals for improvement. Nor do they receive provincially derived detailed reports on transplant performance, have provincial meetings to discuss their performance, or have transplant recipients and living kidney donors present in clinical environments to support patients.

The EnAKT LKD quality improvement intervention. The 4 components of the EnAKT LKD quality improvement intervention (quality improvement teams, education, support from kidney transplant recipients and living kidney donors, and performance monitoring) are described in detail below. CKD programs were encouraged to implement all intervention components, but this was not mandated, and programs were given flexibility in how they implemented each component.

1. Local quality improvement teams and administrative support. The aim of this component is to establish a local quality improvement team to examine, understand, and improve local program performance, implement the intervention components, and champion local initiatives to enhance access to kidney transplantation and living kidney donation. The teams include a champion (the team lead), an executive sponsor (usually a member of hospital administration), local personnel with quality improvement experience, a clinical leader, and at least 2 patients, at least one of whom is also involved in TAP (more details provided in component 3).[42]

A 2-day, in-person quality improvement workshop was held for all team members. The workshop provided training on solving quality-of-care problems within healthcare organizations with a specific focus on enhancing access to kidney transplantation and living kidney donation.[43] Training modules were posted online after the workshop. Each CKD program in the intervention group received an instructional document titled "Quality Improvement Program Implementation Guide", which describes the principles behind using quality improvement strategies to improve healthcare delivery and processes of care and advice on how to build a quality improvement team. Teams were given instructions on creating aim statements (i.e. actionable goals); for example:

> At our CKD program, during the period from November 1, 2017 to October 31, 2018, we aim to increase the number of our patients who have a potential living donor contact the transplant center for evaluation from 20 per year to at least 25 per year.

Teams were also trained in using the Plan-Do-Study-Act (PDSA) model to carry out local improvement projects.[44] PDSA cycles are short, rapid-cycle changes that test potential "change" ideas on a small scale (i.e. tested within each QI team) (an example of a PDSA cycle worksheet can be found at http://www.ihi.org/resources/Pages/Tools/PlanDoStudyActWorksheet.aspx and instructions for the PDSA cycle in Supplemental Appendix 5). With guidance from the ORN-TGLN administration, each team developed

a charter with program-specific aims and measures for tracking progress (an instructional document for creating the project charter is shown in Supplemental Appendix 6 and an instructional document for creating program-specific aims is shown in Supplemental Appendix 7). Teams presented their charters to the ORN-TGLN administration and to the other teams at the beginning of the trial for input and were encouraged to meet regularly during the trial to discuss, review, and develop a plan to improve performance.[45] Teams were encouraged to create process maps of their program's current educational practices and transplant referral pathways and they reviewed their CKD program's first performance report (see component 4). At the start of the trial period, quality improvement teams, TAP leads and co-leads (see component 3), transplant center nephrologists and coordinators, living donor program nephrologists and coordinators, and ORN-TGLN leadership and staff attended an in-person 2-day launch event for the trial. The launch event included lectures from experts on improving access to transplant and provided a detailed overview of the trial.

During the trial, quality improvement team leaders and other team members meet monthly via teleconference or in-person to share progress and to discuss strategies for overcoming barriers. In-person visits from the Provincial Medical Lead in Access to Kidney Transplantation occurred as needed. Additional provincial support and resources were given to 13 CKD programs, including $10 000 per year to support intervention implementation and other local initiatives. Administrative support was also provided by staff at the ORN and TGLN (approximately 3 full-time equivalent positions); these personnel included a business strategist, a senior analyst, an analyst, and a project manager.

2. Education. This component aims to increase the knowledge that healthcare providers, patients, and their families have about kidney transplantation and living kidney donation. The education component is being implemented by an EnAKT LKD education team (led by 3 transplant education experts: I Mucsi, A Waterman, and D Belenko) in collaboration with each CKD program's quality improvement team. Each program was given materials and methods to develop a strategy to improve kidney transplant education to best suit their local practice. Programs were encouraged to develop additional educational resources, optimize patient education infrastructure, and disseminate the EnAKT LKD education initiative to staff and patients. The education team provided additional support when needed. A more detailed description of some of the key elements is provided below.

Education for healthcare providers. To ensure providers have the knowledge and resources to provide high-quality transplant education to patients and potential living donors, several educational resources were developed and made available to healthcare providers in CKD programs as follows:

Educational toolkits. A set of up-to-date educational resources on transplant-related topics was collated, reviewed, and posted online at renalnetwork.on.ca/TransplantProviderHub (see Table 2 for key resources and see Supplemental Appendix 8 for an example document created for the EnAKT LKD trial on when to refer patients to a transplant center). This set of resources also included an app and an online calculator we adapted for healthcare professionals to estimate and communicate a patient's predicted survival with a transplant versus dialysis in Ontario (http://dialysisvstransplant.ca).

The Ontario core transplant curriculum. Slide decks and webinars were made on several topics, including the risks and benefits of transplantation (living and deceased), transplant referral and eligibility criteria, the deceased donor kidney allocation system, and the evaluation process for potential kidney transplant recipients and living kidney donors. Live webinars were recorded so that they could also be watched by staff at a later time.

Explore Transplant training. Explore Transplant is a personalized education and coaching program designed to help kidney patients and their families fully consider transplantation and living kidney donation as treatment options.[46] In-person training on administering the Ontario version of this program (etontario.org) was provided at the trial launch event, with the option for CKD programs to request additional training during the trial as needed from the program creator (A Waterman). The training is tailored to frontline healthcare providers including nurses, nurse practitioners, social workers, and patients who are involved in educating patients about transplantation. The training includes an interactive group activity to help participants experience and understand 4 key concepts: considering transplant, transplant evaluation, living donor transplant, and making the decision.[46] Participants use role play to learn how to address questions or concerns that patients or family members may raise.

Education for patients, families, and potential donors. To ensure patients and potential donors have the knowledge to make informed decisions about transplantation and living kidney donation, a set of up-to-date educational resources was assembled, including the Explore Transplant Ontario educational package. Programs were also encouraged to host educational and social networking events.

Educational toolkits and resources. An online resource hub for patients and individuals considering living kidney donation was created and posted online at https://renalnetwork.on.ca/TransplantPatientHub. The hub contains transplant-related educational materials including resources created by the ORN and patients on finding a living kidney donor (Supplemental Appendix 9). All materials, including brochures, videos, guides, and handbooks, were reviewed by multiple stakeholders, including patients, prior to their use.

Table 2. Select Educational Resources on Kidney Transplantation and Living Kidney Donation Created for the Enhance Access to Kidney Transplantation and Living Kidney Donation Trial.

Topic	Description
Provider materials	renalnetwork.on.ca/TransplantProviderHub
When to refer a patient to a transplant center for kidney transplant evaluation	Provides an overview of the referral criteria and timing of referral for kidney transplant.
Online risk calculator: dialysis vs. transplantation in Ontario	An online risk calculator designed for doctors, social workers, nurses, and other healthcare professionals to estimate a patient's 3-year survival with dialysis vs a kidney transplant. http://dialysisvstransplant.ca
Patient and donor materials	https://renalnetwork.on.ca/TransplantPatientHub
Explore transplant Ontario	An educational program to help patients with kidney failure make informed decisions about kidney transplant and living kidney donation. The program is designed for patients with kidney failure, their families and friends, potential living donors, and healthcare providers. The program website also provides contact information for all the adult transplant centers in Ontario. https://etontario.org/
Finding a living kidney donor	A handout to help patients feel comfortable with sharing their stories and finding a living kidney donor.
Living kidney donation posters	Posters to raise awareness about living kidney donation.
Becoming a living kidney donor in Ontario	A handout describing the living kidney donation process for those considering donating a kidney.
Living kidney donors from outside of Canada	A handout outlining the process of living kidney donation and key considerations for international donors.

Explore Transplant. The Explore Transplant Ontario program (including a mass production of educational DVDs for patients and informational packages) was offered at no charge to all CKD programs in the intervention arm.[35] The full content of Explore Transplant Ontario was made available for staff and patients at the CKD programs of the intervention arm on a password-protected website (etontario.org). Using a model of behavioral change, the Explore Transplant program guides patients through 5 stages of readiness that precede the adoption of a new health behavior (i.e. precontemplation, contemplation, preparation, action, and maintenance). Patients are coached to take meaningful actions toward considering and pursuing transplantation based on their stage of readiness. Staff at participating CKD programs deliver this program to interested patients at multi-care kidney clinic visits or during dialysis sessions.

Social networking. CKD programs were encouraged to host workshops and social networking events such as educational movie nights. Such events give patients and their families the opportunity to share their stories and learn how social media platforms can be used to communicate their need for a kidney transplant.

3. The Transplant Ambassador Program (TAP). The TAP (transplantambassadors.ca) is a new provincial patient-led support program with the aim of supporting patients and their families in learning more about kidney transplantation and living kidney donation. Transplant ambassadors, those with lived experience of living kidney donation or transplantation, can play an invaluable role in helping patients and their families consider and pursue transplantation as a treatment option. These ambassadors volunteer to spend time in multi-care kidney clinics and dialysis centers to connect and talk with interested patients and families about their experience with transplantation and/or living kidney donation. They can share their stories, provide both practical advice and emotional support, inspire family and friends to consider living kidney donation, help with navigation through the transplant process, connect patients with the educational resource hub described above, and motivate patients to complete essential steps on the pathway to receiving a transplant. As volunteers, they can often spend more time than healthcare providers discussing transplantation with patients and families. These transplant ambassadors wear bright green vests with the TAP logo and a large-print invitation to "Ask me about Kidney Transplantation." These vests make it easy to identify ambassadors as kidney donors or recipients. Transplant ambassadors receive training in effective mentorship and communication, on maintaining patient confidentiality, and on delivering transplant education (while not providing medical advice).

A provincial coordinator assists with the implementation of the program, including inviting and onboarding living donors and recipients to serve as ambassadors. It was recommended that each CKD program have 2 local patient leads who also help train ambassadors and manage the TAP program locally. These patient volunteers are recruited from local patient and family advisory councils or by posters or mailed letters, or referral from healthcare professionals. Provincial oversight of TAP is provided by cofounder S McKenzie.

4. Program-Level Performance Monitoring. The aim of this component is to leverage existing administrative health data and facilitate data-sharing between CKD programs and

transplant centers. Performance reports on key transplant metrics and patient transplant eligibility lists are regularly shared with CKD programs to foster a quality improvement culture. The ORN monitors these reports and provides support to help programs improve areas of weakness.

Quarterly performance reports on key transplant metrics. Quarterly program-level performance reports summarize several transplant-related metrics for a given program, including the number of kidney transplant referrals, the number of living donor candidates who contacted a transplant center for an intended recipient to begin their evaluation, the number of patients added to the transplant waitlist, the number of pre-emptive transplants performed (i.e. recipients who did not receive dialysis before their transplant), the number of living donor kidney transplants performed, the number of deceased donor kidney transplants performed, and the overall number of transplants performed. The reports also include process measures that relate to the implementation and delivery of the intervention, such as the number of patients who completed the Explore Transplant Ontario program. The local quality improvement teams can also request additional metrics for inclusion in their performance report. Sample reports were user-tested and reviewed by experts in audit and feedback before the trial started to refine the design. Input was sought from the CKD programs on the perceived relevance of the metrics, the ease of interpretation, and the perceived actionability of the reports. The reports are given to each CKD program's local quality improvement team and reviewed in accountability meetings with the ORN. A sample report is provided in Supplemental Appendix 10 and a list of available metrics is provided in Supplemental Appendix 11.

Transplant eligibility lists for CKD programs. Each program's quality improvement team receives updated lists of patients who are potentially eligible for transplant referral (see Supplemental Appendix 12 for additional detail on types of patients who may be flagged in these lists); this report also includes a list of patients who have been in the transplant evaluation phase for more than 1 year. The teams are encouraged to share relevant lists with staff in their peritoneal dialysis programs, hemodialysis programs, and multi-care kidney clinics. The goal of these notifications is to encourage staff to help patients move through the evaluation process and to ensure patients do not get "lost in the system." Programs can deem a patient currently ineligible or never eligible to receive a kidney transplant (patients in the latter category do not appear in future reports).

Ethical Considerations

The EnAKT LKD trial was designed in accordance with the Tri-Council Policy Statement—Second Edition (TCPS-2)[47] and the Ottawa Statement on the Ethical Design and Conduct of Cluster-Randomized Trials.[48] The protocol received ethics approval from the Western University Health Sciences Research Ethics Board (REB approval #108408), which serves as the REB of record for this multi-site study (Western University is the institutional site where provincial data will be accessed for this study). The REB agreed that the trial met the criteria for waived patient consent for trial enrolment (details in Supplemental Appendix 13). The intervention is being delivered as part of the ORN's provincial quality improvement strategy (and individual patient consent is not required to implement these strategies). Given the resources required, it was impractical to provide the quality improvement intervention to all 26 CKD programs at once; the 13 programs randomly assigned to usual care will be the focus for quality improvement after the trial period is over.

De-identified baseline and outcome data for this trial will be obtained from provincial administrative healthcare databases housed at ICES (www.ices.on.ca/). ICES is a prescribed entity under section 45 of Ontario's Personal Health Information Protection Act. Section 45 authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects conducted under section 45, by definition, do not require review by a Research Ethics Board. The data used in this project was/will be conducted under section 45 and be approved by ICES' Privacy and Compliance Office. Secure access to these data is governed by policies and procedures that are approved by the Information and Privacy Commissioner of Ontario. Approval for the use of data from TGLN is obtained from the REB at Western University. Any additional surveys to CKD program staff to understand what was done during the trial, both in the intervention and usual-care group, will also receive REB approval.

Randomization

Sequence generation, allocation concealment, and implementation. The 26 CKD programs were randomly allocated to the intervention or usual-care arm (1:1) using a covariate-constrained randomization approach (detailed below), with stratification by historic transplant center referral patterns (CKD programs typically refer patients to 1-2 of 6 transplant centers in Ontario). The allocation scheme was computer-generated in London, ON, in February 2017 using SAS version 9.4 (SAS Institute Inc., NC Cary) and concealed from the primary study investigator and CKD programs. The study team notified CKD programs of their assigned allocation in February 2017. This 9-month lead time was chosen to give programs allocated to the intervention group enough time to establish their quality improvement teams and to manage schedules so team members could attend the in-person quality improvement launch event at the start of the trial period.

Covariate-constrained randomization. We performed the covariate-constrained randomization (a method that has been shown to produce intervention groups that are well-balanced on measured baseline characteristics) in the following steps.[49-51]

We first identified there were 270 possible ways to randomly allocate the 26 CKD programs accounting for the transplant center stratification. We randomly selected a scheme from those with the best balance on a set of patient-level and program-level baseline characteristics (i.e. schemes with minimal standardized differences between groups on the constrained variables). Given that ICES data sources are lagged by approximately 6 to 12 months and that the randomization had to be performed in advance of the trial start date, the baseline data used in the covariate-constrained randomization were based on data available in healthcare databases at the time of randomization. Therefore, at the final analytic stage, we will present baseline characteristics at trial entrance.

Blinding

The nature of the intervention makes it infeasible to blind patients, healthcare professionals, CKD programs, or transplant centers to the treatment assignment; however, the primary outcome (the number of key steps completed toward receiving a kidney transplant) will be assessed from administrative healthcare data, which are collected and recorded using standardized auditable procedures that are not influenced by treatment assignment.

Loss to Follow-Up

In this province-wide trial, patient outcomes will be assessed from provincial administrative healthcare databases, and thus the only reason for loss to follow-up will be emigration from the province. While it will not be possible for this trial to accurately censor the observation time for loss to follow-up in our data sources, the emigration rate from Ontario is less than 0.5% per year[52] and this rate is likely lower in patients with kidney failure.

Data Collection and Data Sources

Baseline and outcome data will be primarily ascertained from provincial administrative healthcare databases housed at ICES. These data sets are linked using unique encoded identifiers and analyzed at ICES for both the trial planning (e.g. power calculations) and for trial results. More information about some of the key databases that will be used in this study is provided in Supplemental Appendix 14. Ongoing efforts are in place to improve and/or verify the accuracy of transplant data (before and during the trial) at all transplant centers regardless of whether CKD programs are in the intervention or control group.

Process measures and process evaluation. Process measures on the implementation and uptake of the intervention will be obtained from the ORN (some of these measures appear in the performance-level reports, such as the number of interactions with a transplant ambassador). Other measures that will be collected include health professional attendance to webinars, the number of Explore Transplant Ontario packages distributed and used by patients including their potential donors, and the number of data reports given to the CKD programs. Utilization of the content available at the Explore Transplant Ontario website is monitored automatically by participating renal programs and by user type (patient or provider). Descriptive data on intervention uptake will be reported in the final manuscript.

Our quality improvement intervention is complex, requiring multiple people to modify a variety of behaviors and activities. Specifically, the intervention has several interacting and flexible components that target patients, healthcare professionals, and administrative processes. While the main trial results will provide information on the effectiveness of the intervention, information on *why* and *how* the intervention was effective or ineffective can be made clear using a process evaluation. Following guidelines from the UK Medical Research Council, we plan to conduct a separate process evaluation of this intervention.[53] We will use an implementation science-informed mixed-methods approach to evaluate fidelity to the intervention and the potential mechanisms of change. An online survey will be distributed to staff in all 26 CKD programs (including programs in the usual-care group) to record activities used during the trial period to help patients access kidney transplantation. These data will be reported in the final manuscript and will also be used to determine if the usual-care group used strategies employed by the intervention group during the trial. We will publish a protocol and the results for the EnAKT LKD process evaluation in a peer-reviewed manuscript. Separate in-depth evaluations for both the education and Transplant Ambassador Program components are also being planned.

Primary Outcome

In Ontario there are key steps that need to be completed to receive a kidney transplant. The primary outcome of the EnAKT LKD trial is the average number of these steps completed per 100 person-years during the trial period, analyzed at the cluster-level. Each step will only be counted once per patient (the first time it occurs), and each patient can contribute a maximum of 4 steps to their group total. The 4 steps are shown in Box 1.

Box 1. Primary Outcome: Steps Completed Toward Receiving a Kidney Transplant.

Step I	A transplant center receives a patient's complete transplant referral package from a chronic kidney disease program.
Step II	A living kidney donor candidate contacts a transplant center for an intended recipient and completes a health history questionnaire to begin their evaluation.
Step III	A patient is activated on the deceased donor transplant wait list.
Step IV	A patient receives a kidney transplant from a living or deceased donor.

Patients who complete steps before the trial starts can contribute new steps during the trial period; for example, a patient referred to a transplant center before the start of the trial may have a living kidney donor candidate contact a transplant center during the trial (which could be a result of the quality improvement intervention); the latter would be counted as a completed step in the trial.

Secondary Outcomes

Given that the average wait time for a deceased donor kidney transplant is 5 years in Ontario, our intervention is likely to have only a small impact on the rate of deceased donor kidney transplants.[54] For this reason, we have prespecified 5 secondary outcomes to examine the impact of our intervention on living kidney donor activity (the definitions of each outcome are shown in Box 2):

Box 2. Secondary Outcomes: Living Kidney Donor Transplant Activity.

Secondary outcomes	Description
1 Step II or a component of step IV	A living donor candidate contacts a transplant center for a patient and completes a health history questionnaire to begin their evaluation or a patient receives a living donor transplant.
2 Step II	A living kidney donor candidate contacts a transplant center for a patient and completes a health history questionnaire to begin their evaluation.
3 Step I and II	A transplant center receives a patient's complete referral package from a chronic kidney disease program and a living kidney donor candidate contacts a transplant center for a patient and completes a health history questionnaire to begin their evaluation.
4 Component of step IV	A patient receives a living donor kidney transplant.
5 Component of step IV restricted to pre-emptive transplants	Pre-emptive living donor kidney transplants (restricted to patients who were not receiving dialysis when they entered the trial and not on dialysis at the time of transplant).

Other Outcomes

We will consider several other outcomes in an exploratory analysis, such as the remaining steps of the primary outcome analyzed separately. Additional outcomes are described in Supplemental Appendix 15.

Balancing Measures

Balancing measures are metrics that track whether changes designed to improve one area of the health system do not introduce problems in other aspects of care.[55] For example, promoting kidney transplantation may lead to more ineligible patients referred and cause system-level inefficiencies. Similarly, the average wait time for the donor and recipient evaluation might be lengthened if more demand is placed on healthcare resources. For these reasons, we will examine several balancing measures (Supplemental Appendix 16). Some of these measures will be compared between the 2 groups during the trial period, while others will be assessed as a change from before the trial to during the trial.

Statistical Power

Statistical power calculations for the primary outcome (the number of steps completed toward receiving a kidney transplant) were informed by an analysis of historical administrative healthcare data in Ontario (from November 1, 2016, to October 31, 2017). We acknowledge at the time of performing the analysis that not all steps toward receiving a kidney transplant were accurately recorded in our data sources, leading to an underestimate of the number of steps. That said, we analyzed 13 532 patients from the 26 CKD programs (6477 CKD patients not receiving dialysis and 7055 patients receiving dialysis with no recorded contraindications to kidney transplantation [e.g. not residing in long-term care, no dementia, and no home oxygen]). In this analysis, we observed 2455 steps completed during this 1-year period, corresponding to an incidence rate of 23 steps per 100 person-time years. This suggests a 3.5-year trial should have at least 80% power to detect a rate ratio of 1.5 (this corresponds to patients in the intervention group completing an average of 12 more steps per 100 person-years than patients in the control group [35 steps vs. 23 steps, respectively]; 2-sided $\alpha = 0.05$). These calculations were done using the sample size equation for comparing incidence rates (accounting for the coefficient of variation in CKD programs) in Hayes and Moulton.[56]

Statistical Analysis

Trial population: Patient selection and observation time. In Ontario, eligibility criteria for adult referral to a kidney transplant center and for transplant wait-listing are set by the TGLN.[57] We will follow these criteria to select patients for inclusion in the analysis of trial outcomes. However, as we are using administrative data sources to assess patient eligibility, we will not be able to accurately ascertain information for several criteria such as uncontrolled psychiatric symptoms; active irreversible ischemic progressive heart disease; substance abuse, including substantial smoking and functional capacity; and an informed decision to never pursue a kidney transplant. This means, some transplant-ineligible

patients will be included in the analysis (which would underestimate the overall rate of completing steps toward receiving a kidney transplant); however, the proportion of transplant-ineligible patients is expected to be similar in the 2 comparison groups and should not influence the rate ratio estimated in the primary analysis. To ensure our sample is representative of patients who have historically received kidney transplants in Ontario, we will apply additional exclusion criteria (described below) and censor the observation time when a patient is no longer eligible for transplant in follow-up (described below).

Eligibility criteria. We will include adults (aged 18 to 80 years) who are registered in one of Ontario's 26 CKD programs as outpatients, including patients attending multi-care kidney clinics (i.e. approaching the need for dialysis) and those receiving outpatient maintenance dialysis (including in-center hemodialysis and at-home hemodialysis or peritoneal dialysis). For patients attending multi-care kidney clinics, the following additional inclusion criteria will be applied: persistent evidence of an estimated glomerular filtration rate (eGFR) less than 15 mL/min per 1.73 m^2 or at least a 25% estimated chance of requiring kidney replacement therapy within 2 years as assessed by the kidney failure risk equation (kidneyfailurerisk.com).[58] Although older age is not an absolute contraindication to transplant, few people over age 80 are healthy enough to receive a transplant, and transplants in this age group are rare in Ontario; we will therefore exclude those ≥80 years of age. Additional exclusion criteria include evidence of any recorded contraindications to transplant including dementia, use of home oxygen (a sign of serious pulmonary disease), living in a long-term care home, and any comorbidities likely to preclude transplantation. We will also exclude patients with invalid or missing data on date of birth or sex, and patients who are not permanent residents of Ontario (<1% will be excluded for a reason of invalid or missing data).

Observation time. A patient's follow-up time will begin on November 1, 2017, or on the earliest date when all eligibility criteria were met up until 3 months before the trial end date (3 months is the expected minimum time to complete early steps toward receiving a kidney transplant). Patients can only enter the analytic cohort once and will be followed until the trial end date; a patient's observation time will be stopped at the end of study or if they die, receive a kidney transplant, or become ineligible (using the same criteria above), whichever comes first. Given the maximum follow-up time is less than 5 years (for those who enter the trial at the beginning of the trial period), patients who become ineligible will not re-enter the analytic cohort even if they meet the eligibility criteria again within the trial period. While a small proportion of patients may transfer between CKD programs during follow-up, based on previous work we expect over 90% of patients' observation time will be spent receiving care at the same program their follow-up time began in or at another program in the same intervention arm.

Analysis of trial outcomes. As per the intention-to-treat principle, all patients will be analyzed according to their CKD program's random allocation on their date of cohort entry as defined above. We will account for the study design and covariate-constrained randomization in our analysis. The primary outcome is at the cluster level (the rate of completing steps toward receiving a kidney transplant [per 100 person-years]) and will be compared between groups using a 2-stage approach because we have 26 clusters randomized (13 per arm).[59-62] In the first stage of the model, residuals are obtained from fitting a regression model to the individual-level count data adjusting for prespecified individual-level confounders while ignoring the intervention and clustering effects.[62] In the second stage, the residuals from the first stage are aggregated at the cluster level and used as the outcome. This model fits cluster-level variables and the treatment effect. No interim analyses are planned. Only the biostatistician performing the analysis will have access to the outcome data.

Additional exploratory analyses. In additional exploratory analyses we will consider subgroup analyses to determine if the intervention improved access to kidney transplant in the following subgroups, recognizing that some of these categorizations are imperfect: receiving maintenance dialysis at the time of trial entry (in-center or home dialysis), sex (male vs. female), race (white vs. other), immigration status, geography (average distance from the patient's place of residence to the transplant center), income quintile (measured by neighborhood-level median income), and measures of marginalization (i.e. residential instability, material deprivation, ethnic concentration, and dependency).

Statistical significance. To avoid type I errors due to multiple comparisons,[63-65] we will use the fixed-sequence procedure, a stepwise multiple-testing procedure where 2-sided hypothesis tests for superiority will be performed at the 0.05 significance level in a prespecified order. We will test the primary outcome first. This will be followed by the 5 secondary outcomes (in the same order as shown in Box 2). Once a hypothesis test is not significant, no further testing will be done. Rather, the analyses of any subsequent secondary outcomes, as well as additional outcomes and other analyses will be reported as point estimates with 95% confidence intervals (without *p* values); we will indicate that interval widths are not adjusted for multiple testing and therefore inferences drawn may not be reproducible. We will conduct all analyses using Statistical Analysis Software version 9.4 (SAS Institute, Cary, NC).

Timeline

The quality improvement intervention began on November 1, 2017. Once the trial period is complete (the end date has

been extended to December 31, 2021 due to the COVID-19 pandemic), the trial data will be updated and linked, and the final analysis will be completed within approximately a year of the end date. The primary and secondary outcomes will be analyzed and summarized in the final report.

Data Monitoring, Harms, and Auditing

Given that the trial intervention poses minimal risk and the data are stored in provincial administrative healthcare databases, no interim analyses are planned, and there is no Data Safety and Monitoring Board. However, the ORN will host monthly calls with the CKD programs, and TGLN will be in regular contact with the transplant centers; this will provide opportunities for any concerns about the intervention to be expressed. As previously described in the section on balancing measures, we will also collect information on unintended effects of the trial (e.g. an increase in incomplete referrals).

Characterizing the Trial Within the Pragmatic-Explanatory Continuum

We aimed to design a pragmatic randomized clinical trial, whereby the intervention is delivered under real-world conditions and trial results are generalizable to the usual community of users. In contrast, an explanatory approach delivers an intervention under ideal conditions to maximize the likelihood that the intervention produces its anticipated benefit. A trial is neither purely pragmatic nor purely explanatory; rather it falls on a continuum between pragmatic to explanatory.[66] We used the PRagmatic Explanatory Continuum Indicator Summary (PRECIS-2), to confirm that this trial is highly pragmatic (Supplemental Appendix 17).[67] Small reductions in pragmatism resulted from (1) providing speciality training to healthcare providers in the intervention arm but not the usual-care group, (2) the delivery of educational materials such as Explore Transplant Ontario to the intervention group, and (3) asking CKD programs in the intervention group to collect information on process measures, which may encourage better adherence to the intervention.

Dissemination Policy

We will publish trial results in an open-access journal regardless of the direction of the effect. All listed authors in the protocol will be given the opportunity to participate in subsequent publications related to the trial. We will not use professional writers. The data set for this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the data set publicly available, access can be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification. We will communicate any important protocol modifications on clinicaltrials.gov/.

Discussion

Despite the well-known benefits of kidney transplantation, most Canadian patients with kidney failure do not receive a transplant.[9] Strategies that address barriers to transplantation may help more patients gain access to a transplant. Randomized controlled trials provide some of the best estimates of intervention effects; however, few clinical trials have tested strategies for improving access to transplantation. This protocol describes a quality improvement intervention designed to increase access to kidney transplantation and living kidney donation in Ontario, Canada.

A previously published randomized controlled trial in the state of Georgia, United States used a multi-component intervention (comprised of transplant education, engagement activities, and quality improvement initiatives) targeting patients with kidney failure within hemodialysis clinics and found the intervention resulted in a ~7.3% absolute increase in 1-year transplant referrals compared with standard care.[68] There are important differences in the Canadian and United States' healthcare systems (e.g. universal versus nonuniversal healthcare), and contextual factors in the delivery of a quality improvement intervention that justify the need for our current evaluation.

Our pragmatic, cluster-randomized clinical trial includes all CKD programs in Ontario that care for more than 15 000 patients with CKD and 13 000 patients receiving dialysis—over one-third of these patients are potentially eligible for a transplant. Our trial results should therefore produce results that are highly translatable into clinical practice. Kidney care is delivered in a similar way in other Canadian provinces, so we expect the results to generalize well across Canada, and the results to be of international interest as many countries share a goal of improving access to kidney transplantation and living kidney donation.[69] The intervention was developed, refined, and implemented by a wide range of stakeholders across Ontario, with input from CKD and transplant centers, medical experts, patients, administrators, physicians, frontline staff, and allied health professionals. Patients were involved in all stages of the design to increase the quality and relevance of the intervention. The intervention is grounded in quality improvement, focuses on patient engagement, and uses data as the basis for monitoring performance.[70] This approach has improved healthcare outcomes in other settings.[71,72] We engaged medical directors and lead nephrologists at each of the 26 CKD programs before program randomization to support successful implementation of the intervention. The ORN hosts a Leadership Forum several times a year which brings together leadership and administrative positions, and the intervention was discussed and vetted several times at these meetings. The unique design of this

trial allows us to continuously monitor the progress at each of the CKD programs, troubleshoot barriers, and improve the delivery and uptake of the intervention components. The use of administrative databases will allow us to have near complete follow-up of our key outcomes (<0.5% lost to follow-up).[52]

The following challenges and limitations may impact the evaluation of this multi-component quality improvement intervention.

First, multiple identified barriers to kidney transplantation and living kidney donation may be addressed by the components of our quality improvement intervention but it may not be possible to isolate the independent effects of each component. Our intervention has several flexible components that target patients, healthcare professionals, and administrative processes, and these components may interact together synergistically. We will conduct a separate process evaluation using a mixed-methods approach to better understand the uptake and effects of the individual components.[53]

Second, given the limited supply of deceased donor kidneys, our intervention is likely to have less of an effect on the rate of deceased donor kidney transplants. The average wait time for a deceased donor kidney in Ontario is 5 years,[54] and this wait time is likely to increase substantially as a result of the COVID-19 pandemic with kidney transplant activity (both kidney transplant work-ups and kidney transplants) decreasing substantially for several months during the trial. For this reason, change in living donor transplant activity is prioritized as a key secondary outcome.

Third, there is a risk of contamination bias if changes in transplant center practices in the intervention group influence practices in the usual-care group; for example, if educational toolkit materials are unintentionally disseminated to CKD programs in the usual-care group. To assess the potential for contamination bias, as part of our process evaluation, we will administer an online survey near the end of the trial to select staff in all 26 CKD programs (including those in the usual-care group) to assess which activities were used to help patients access kidney transplantation during the trial period.

Fourth, while our intervention is designed to increase the number of patients being referred for transplant, if many referred patients are later deemed ineligible for transplant, this could overwhelm existing transplant center capacity and result in an inefficient use of healthcare resources. To address this limitation, we will seek to understand the overall impact of our intervention, including any unintended consequences through tracking several balancing measures. We recognize that our outlined balancing measures do not address patient experience (e.g. were the patients satisfied with the amount of transplant education provided) and do not address provider satisfaction (e.g. did the intervention increase staff workload). However, we will use our process evaluations to better understand some of these components.

Fifth, the relatively small number of clusters in this trial means that the intervention and usual-care groups may not be balanced on all baseline prognostic factors and this could influence between-group differences in trial outcomes. We will conduct a sensitivity analysis to determine if any between-group differences in outcomes persist after statistically adjusting for baseline factors.

Sixth, the use of administrative data in this study means that we cannot exclude all patients who are ineligible for a transplant. However, the criteria used to select patients for inclusion in the analysis is not expected to differ by study group.

Conclusion

Our quality improvement intervention was designed to help patients complete more steps toward receiving a kidney transplant. If our intervention is successful, more transplants may ultimately be performed and result in improved survival and a better quality of life for patients with CKD. Significant healthcare savings may also be realized. Over a 5-year period, every 100 kidney transplants saves the Canadian healthcare system about $20 million in averted dialysis costs.[3,4] Kidney transplantation thus achieves the *triple aim in healthcare*: better outcomes, better experience of care, and lower costs.[73] Healthcare systems are being redesigned to achieve this goal, and our intervention is in-line with this priority.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Western University Health Sciences Research Ethics Board (REB approval #108408), which serves as the REB of record for this multi-site study. The REB agreed that the trial met the criteria for waived patient consent for trial enrolment.

Consent for Publication

Consent for publication was obtained from all authors.

Availability of Data and Materials

The data set from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the data set publicly available, access can be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full data set creation plan and underlying analytic code are available from the authors upon request, understanding that the programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Acknowledgments

The authors thank Drs. Adeera Levin and Braden Manns for leading Canadians Seeking Solutions and Innovations to Overcome Chronic Kidney Disease (Can-SOLVE CKD), a patient-orientated research network to transform the care of people affected by kidney disease. They thank the Access to Kidney Transplantation and Living Donation Priority Panel and the ORN-TGLN Partnership Core

Project Team. They thank the following individuals for their assistance with the development of the trial protocol and/or their support for this activity: Ahmed Al-Jaishi, Jeanette Chua, Rebecca Cooper, Sonia Eusebio, Charlotte Grieve, Jeremy Grimshaw, Andrew Hinson, Karen Hornby, Andrew House, Noah Ivers, Lisa Joya, Joseph Kim, Iris Lui, Eric McArthur, Megan McCallum, Beth Montesi, Jocelyn Pang, James Rodrigue, Dior Sarr, Colleen Shelton, Kaveh Shojania, Vanessa Simoes, Amanda Stypulkowski, and Irina Voronin. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The study was completed at the ICES Western site, where core funding is provided by the Academic Medical Organization of Southwestern Ontario, the Schulich School of Medicine and Dentistry, Western University, and the Lawson Health Research Institute. Parts of this material are based on data and/or information compiled and provided by Canadian Institute for Health Information (CIHI) and MOHLTC. The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred. Parts of this material are based on data and information provided by Ontario Health (OH). The opinions, results, view, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of OH. No endorsement by OH is intended or should be inferred. The author(s) acknowledge that the data used in this study were provided by the Trillium Gift of Life Network (Toronto, Ontario), which is funded by the Government of Ontario. The opinions, results, view, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of TGLN. The authors thank IMS Brogan Inc. for use of their Drug Information Database. The research was conducted by members of the ICES Kidney, Dialysis and Transplantation team, at the ICES Western facility.

Author Contributions

A.X.G. conceived the original concept for the trial and was involved in organizing the team and obtaining funding. S.Y., K.L.N., P.B., S.D., and A.X.G. participated in designing the trial. S.M. and L.G. led the Transplant Ambassador Program. I.M., D.B., and A.D.W. led the educational component. K.N. guided the development of the data reports. S.D. contributed to the methodology. The O.R.N. was responsible for coordinating the project and interacting with the quality improvement teams. S.Y., K.L.N., J.M.S., and A.X.G. drafted the manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This trial is funded/sponsored by the ORN (part of Ontario Health) and the Canadian Institutes of Health Research (CIHR) SPOR Networks in Chronic Disease (Canadians Seeking Solutions and Innovations to Overcome Chronic Kidney Disease [Can-SOLVE CKD]). The Lawson Health Research Institute was a sponsor for this work. Partial funding to deliver the Explore Transplant Ontario educational program was provided by Astellas Pharma Canada Inc. A.X.G. is supported by the Dr. Adam Linton Chair in Kidney Health Analytics and is the joint ORN-TGLN Provincial Medical Lead for Access to Kidney Transplantation. He is also supported by a Clinician Investigator Award from the Canadian Institutes of Health Research.

Role of the Funders/Sponsors

The Ontario Renal Network (ORN, part of Ontario Health) was involved in the study design, data collection (but not the data collection of the primary or secondary outcomes), and the intervention delivery. The ORN will have no role in the analysis and interpretation of data. Representatives from the ORN will review the final manuscript describing the trial results but will have no ultimate authority over the decision to publish the manuscript (i.e. the study will be published regardless of the results). The other funders/sponsors had no role in the study design or data collection, and they will have no role in the analysis or interpretation of data, the writing of the final report, or the decision to publish the final manuscript.

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Supplemental Material

Supplemental material for this article is available online.

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