SUPPLEMENT

Supplementary content for Dixon SN, et al. Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD): Statistical Analysis Plan of a Registry-Based, Cluster-Randomized Clinical Trial. *Can J Kid Health Dis.* 2022: doi 10.1177/20543581221131201

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Appendix 1. Administrative information for the EnAKT LKD Statistical Analysis Plan (SAP)

Full study title: Quality Improvement Intervention to Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD) in Patients With Chronic Kidney Disease: A Pragmatic, Registry-based, Cluster-Randomized Clinical Trial

Acronym: EnAKT LKD

Registration: EnAKT LKD is registered with the U.S. National Institute of Health at clincaltrials.gov (NCT03329521 available at https://clinicaltrials.gov/ct2/show/NCT03329521)

Published Study Protocol Version: 1.0 (April 15, 2021)

SAP Version: 1.0 (August 26, 2022)

SAP Revision History

Version number	Description	Date	Timing
Version 1.0	Revised SAP to Canadian Journal of Kidney Health and Disease (CJKHD) as version 1.0 with changes based on response to reviewers.	August 26, 2022	Completed prior to any outcome analysis

Roles and responsibilities:

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Roles and contributions:
Senior statistician responsible: Stephanie N. Dixon
Principal investigator: Amit X. Garg
Primary writer of Statistical Analysis Plan: Stephanie N. Dixon
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Signatures: We the undersigned, certify that we have read this Statistical Analytic Plan and approve it as adequate in scope of the main analyses of the EnAKT LKD trial.

Primary SAP writers:

Name: Stephanie N. Dixon

Signature: 

Date: August 26, 2022

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Date: August 26, 2022

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Name: Amit X. Garg

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Date: August 26, 2022

Table S1. Statistical Analysis Plan (SAP) checklist v 1.0 2019

Section/Item	Index	Description	Reported in section
Section 1: Administrative information			
Trial and Trial registration	1a	Descriptive title that matches the protocol, with SAP either as a forerunner or subtitle, and trial acronym (if applicable)	Appendix 1
	1b	Trial registration number	Appendix 1
SAP Version	2	SAP version number with dates	Appendix 1
Protocol Version	3	Reference to version of protocol being used	Appendix 1
SAP revisions	4a	SAP revision history	Appendix 1
	4b	Justification for each SAP revision	Appendix 1
	4c	Timing of SAP revisions in relation to interim analyses, etc.	Appendix 1
Roles and responsibility	5	Names, affiliations, and roles of SAP contributors	Appendix 1
Signatures of:	6a	Person writing the SAP	Appendix 1
	6b	Senior statistician responsible	Appendix 1
	6c	Chief investigator/clinical lead	Appendix 1
Section 2: Introduction			
Background and rationale	7	Synopsis of trial background and rationale including a brief description of research question and brief justification for undertaking the trial	Introduction
Objectives	8	Description of specific objectives or hypotheses	Trial objectives and hypotheses
Section 3: Study Methods			
Trial design	9	Brief description of trial design including type of trial (e.g., parallel group, multi-arm, crossover, factorial) and allocation ratio and may include brief description of interventions	Trial Design
Randomization	10	Randomization details, e.g., whether any minimization or stratification occurred (including stratifying factors used or the location of that information if it is not held within the SAP)	Randomization
Sample size	11	Full sample size calculation or reference to sample size calculation in protocol (instead of replication in SAP)	Sample Size
Framework	12	Superiority, equivalence, or noninferiority hypothesis testing framework, including which comparisons will be presented on this basis	Hypothesis Testing Framework

Section/Item	Index	Description	Reported in section
Statistical interim analysis and stopping guidance	13a	Information on interim analyses specifying what interim analyses will be carried out and listing of time points	Interim Analysis
	13b	Any planned adjustment of the significance level due to interim analysis	Na
	13c	Details of guidelines for stopping the trial early	Na
Timing of final analysis	14	Timing of final analysis, e.g., all outcomes analysed collectively or timing stratified by planned length of follow-up	Timing of Outcome Assessment and Analysis
Timing of outcome assessments	15	Time points at which the outcomes are measured including visit “windows”	Trial Design
Section 4: Statistical Principals			
Confidence intervals and *P* values	16	Level of statistical significance	Confidence Intervals and P-Values: Level of Statistical Significance
	17	Description and rationale for any adjustment for multiplicity and, if so, detailing how the type 1 error is to be controlled	Confidence Intervals and P-Values: Level of Statistical Significance
	18	Confidence intervals to be reported	Confidence Intervals and P-Values: Level of Statistical Significance
Adherence and Protocol deviations	19a	Definition of adherence to the intervention and how this is assessed including extent of exposure	Adherence and Protocol Deviations

Section/Item	Index	Description	Reported in section
	19b	Description of how adherence to the intervention will be presented	Analysis Methods
	19c	Definition of protocol deviations for the trial	Adherence and Protocol Deviations
	19d	Description of which protocol deviations will be summarized	Adherence and Protocol Deviations
Analysis populations	20	Definition of analysis populations, e.g., intention to treat, per protocol, complete case, safety	Analysis Population
Section 5: Trial Population			
Screening data	21	Reporting of screening data (if collected) to describe representativeness of trial sample	Na
Eligibility	22	Summary of eligibility criteria	Eligibility Criteria
Recruitment	23	Information to be included in the CONSORT flow diagram	Recruitment-Flow Diagram (Figure S1 of supplement)
Withdrawal/ Follow-up	24a	Level of withdrawal, e.g., from intervention and/or from follow-up	Withdrawal and Loss to Follow-up
	24b	Timing of withdrawal/lost to follow-up data	Withdrawal and Loss to Follow-up
	24c	Reasons and details of how withdrawal/lost to follow-up data will be presented	Withdrawal and Loss to Follow-up
Baseline patient characteristics	25a	List of baseline characteristics to be summarized	Table S2 of the supplement
	25b	Details of how baseline characteristics will be descriptively summarized	Baseline Characteristics
Section 6: Analysis			

Section/Item	Index	Description	Reported in section
Outcome definitions		List and describe each primary and secondary outcome including details of:	Outcome Definitions & Table S3 of Appendix 5
	26a	Specification of outcomes and timings. If applicable include the order of importance of primary or key secondary end points (e.g., order in which they will be tested)	Confidence Intervals and P-Values: Level of Statistical Significance; Appendix 5
	26b	Specific measurement and units (e.g., glucose control, hbA1c [mmol/mol or %])	Outcome Definitions
	26c	Any calculation or transformation used to derive the outcome (e.g., change from baseline, QoL score, Time to event, logarithm, etc.)	Outcome Definitions
Analysis methods	27a	What analysis method will be used and how the treatment effects will be presented	Analysis of the Primary Outcome; Analysis of the Secondary Outcomes; Additional Analyses
	27b	Any adjustment for covariates	Analysis of the Primary Outcome
	27c	Methods used for assumptions to be checked for statistical methods	Analysis of the Primary Outcome
	27d	Details of alternative methods to be used if distributional assumptions do not hold, e.g., normality, proportional hazards, etc.	Analysis of the Primary Outcome

Section/Item	Index	Description	Reported in section
	27e	Any planned sensitivity analyses for each outcome where applicable	Additional Analyses
	27f	Any planned subgroup analyses for each outcome including how subgroups are defined	Additional Analyses
Missing data	28	Reporting and assumptions/statistical methods to handle missing data (e.g., multiple imputation)	Missing Data and Other Considerations
Additional analyses	29	Details of any additional statistical analyses required, e.g., complier-average causal effect analysis	Additional Analyses
Harms	30	Sufficient detail on summarizing safety data, e.g., information on severity, expectedness, and causality; details of how adverse events are coded or categorized; how adverse event data will be analysed, i.e., grade 3/4 only, incidence case analysis, intervention emergent analysis	Harms & Data Monitoring
Statistical software	31	Details of statistical packages to be used to carry out analyses	Statistical Software
References	32a	References to be provided for nonstandard statistical methods	References
	32b	Reference to Data Management Plan	Availability of Data and Materials
	32c	Reference to the Trial Master File and Statistical Master File	Availability of Data and Materials
	32d	Reference to other standard operating procedures or documents to be adhered to	Study methods & References

Taken from the paper: Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Doré C, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA. 2017;318(23):2337-43[1].

Abbreviations: CONSORT[2–4], Consolidated Standards of Reporting Trials; hbA1c, haemoglobin A1c; QoL, quality of life; SAP, statistical analysis plan.

For more information visit: https://www.equator-network.org/reporting-guidelines/guidelines-for-the-content-of-statistical-analysis-plans-in-clinical-trials/

The development of this checklist was funded by the MRC Hubs for Trials Methodology Research

Appendix 2: Secondary outcome details

All secondary outcomes outlined in the published protocol[5] will be analyzed in the multistate model framework as defined in our primary analysis. The simplest multistate model is a single transition between a non-event state to the event of interest. In this setting, the multistate frame framework can be used to obtain estimates analogous to a traditional Cox Proportional Hazard model.[6] The five secondary outcome definitions are outlined in **Table S2**, along with details on how outcomes will be measured and corresponding methods. Analyses of secondary outcomes will be performed in the order they appear in **Table S2**.

Outcomes in **Table S2** focus on the steps towards receiving a living donor kidney transplant. Therefore, all analyses of secondary outcomes will be censored at time of receipt of a deceased donor kidney transplant (precludes a patient from receiving a living donor kidney transplant).

Table S2*: Secondary outcome definitions, outcome details, and proposed methods for analysis*

Secondary Outcome definitions	**Outcome details**	**Methods**
1. A potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient and/or a patient receives a living donor transplant (composite of step 2 and/or 4 of primary outcome).	Bivariate outcome with time and status indicator for 3 potential states: 1. No activity 2. Donor candidate contacts a transplant centre and begins their evaluation 3. Intended recipient receives a living donor transplant	As with the primary analysis, a constrained clustered multistate model will be used to have a single intervention effect for the transition rate across all activities.

Secondary Outcome definitions	Outcome details	Methods
2. Time to first occurrence of a potential living kidney donor beginning their evaluation at a transplant centre to donate a kidney to the patient (step 2 of primary outcome).	Classic time-to-event analysis with bivariate outcome of a continuous event time and binary censoring indicator (1 if the step occurs and 0 if the individual is censored).	Use the multistate model framework to complete a Cox Proportional Hazards model with bootstrapping at the cluster-level to control for the correlation in CKD programs.
3. A transplant centre receives a patient's complete referral package from a chronic kidney disease program and at least one potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient (requires both step 1 and 2 of the primary outcome)	Classic time-to-event analysis with bivariate outcome of a continuous event time and binary censoring indicator (1 if both components occur and 0 if the individual is censored). NOTE: Both conditions are required to be met before the event is observed (i.e., time of at which both events are attained).	Use the multistate model framework to complete a Cox Proportional Hazards model with bootstrapping at the cluster-level to control for the correlation in CKD programs.
4. A patient receives a living donor kidney transplant (a portion of step 4 in the primary outcome).	Classic time-to-event analysis with bivariate outcome of a continuous event time and binary censoring indicator (1 if the living donor kidney transplant occurs and 0 if the individual is censored).	Use the multistate model framework to complete a Cox Proportional Hazards model with bootstrapping at the cluster-level to control for the correlation in CKD programs.
5. Pre-emptive living donor kidney transplant (restricted to patients who were not receiving dialysis when they entered the trial and not on dialysis at the time of transplant) (a portion of step 4 in the primary outcome).	Classic time-to-event analysis with bivariate outcome of a continuous event time and binary censoring indicator (1 if the pre-emptive living donor kidney transplant occurs and 0 if the individual is censored).	Use the multistate model framework to complete a Cox Proportional Hazards model with bootstrapping at the cluster-level to control for the correlation in CKD programs.

Secondary Outcome definitions	Outcome details	Methods
	NOTE: Only patients approaching the need for dialysis in a multi-care kidney clinic at index date are included in the analysis and they will be censored at initiation of maintenance dialysis.	

Primary outcome includes (1) patient referred to a transplant centre for evaluation, (2) a potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient, (3) patient added to the deceased donor transplant waitlist, and (4) patient receives a kidney transplant from a living or deceased donor.

Appendix 3: Additional considerations for the analysis

Many analyses rely on the asymptotic theory, i.e., *large numbers.* In cluster randomization trials, it is possible to have a small number of large clusters. It has been suggested that a minimum of 30 to 40 clusters is needed for patient-level random effects models, and 40 to 50 clusters is needed for generalized estimating equations.[7] We will add a small sample correction based on degrees of freedom; however, this approach has not been explored for our context, i.e., clustered multistate model framework. Specifically, we will use a Student's *t* distribution for our statistical tests (as opposed to relying on the normal distribution). Similarly, we will use the Student's *t* distribution to calculate the margin of error in the confidence intervals. Another consideration is the methodology and application of survival models to cluster randomization trials is quite limited.[8] Other work has used a random effect to control for the clustering.[9] We have decided to use bootstrapping at the cluster level so that our inferences remain valid.

Appendix 4: summary of clarifications

*** All updates below were made without reviewing any between-group trial outcome data (viewing and analysis will only occur after the trial period is over and the final version of the statistical analysis plan has been accepted for publication) and were done after the start of the EnAKT LKD Trial period (November 1, 2017).**

** Additional table of updates available on https://clinicaltrials.gov/ct2/show/record/NCT03329521

Table S3. Table of Clarification (August 26, 2022)

Revision	Details of Revision	Rationale
Eligibility Criteria for Trial Population included in the Statistical Analysis	**Added clarification:** In the footnote of Table 1, we added "Using the 2021 Chronic Kidney Disease–Epidemiology Collaboration Equation, without race.[10]"	We did not change the requirement for the estimated GFR (eGFR < 15 mL/min/1.73 m^2) but did provide clarification on the equation used to calculate eGFR.
Eligibility Criteria for Trial Population included in the Statistical Analysis	**Added clarification:** In Table 1, we added "To ensure stability of kidney function, at least two eGFR or two KFRE measures were required to enter the cohort and these measures had to be separated by at least >90 days but within 365 days."	Previously reported " persistent evidence " but did not detail how this would be determined.
Eligibility Criteria (Contraindication to transplantation)	**Changed from**: "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	We further refined the eligibility criteria based on an analysis we conducted in patients approaching the need for dialysis or receiving dialysis, where we compared 80+ baseline characteristics between patients who did and did not receive a kidney transplant during follow-up.[12] We also further refined our eligibility criteria to exclude individuals receiving conservative renal care as these individuals would not receive a kidney transplant as they have opted for conservative care to manage their kidney

Revision	Details of Revision	Rationale
	care home, and <u>any comorbidities</u> likely to preclude transplantation."[11] **<u>Changed to:</u>** "We also further refined the eligibility criteria based on an analysis we conducted in patients approaching the need for dialysis or receiving dialysis, where we compared 80+ baseline characteristics between patients who did and did not receive a kidney transplant during follow-up.[12] We found that >97% of patients with one or more of the following characteristics did not receive a transplant in follow-up, and so patients with these characteristics will not enter the trial for analysis: an ESKD adapted Charlson comorbidity index score[13] ≥7 (a higher score represents greater comorbidity), age >75 years, home oxygen use, dementia, living in a long-term care facility, receiving ≥1 physician house call in the past year, or any of the following cancers: bladder, cervical, colorectal, liver, lung, lymphoma, or active multiple myeloma.[12] Of note, not all these comorbidities are listed in provincial referral and listing criteria for kidney transplant[14]; however, as described above, few individuals with these characteristics receive a transplant in practice. We have also clarified that receiving conservative renal care will be considered a contraindication to transplant as these patients have decided not to purse dialysis or transplantation."	disease which means they will not be pursuing a kidney transplant.

Revision	Details of Revision	Rationale
Primary Outcome details	**<u>Added clarification to wording (no change in outcomes):</u>** The four steps include: Step I: patient referred to a transplant centre for evaluation, Step II: a potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient, Step III: patient added to the deceased donor transplant waitlist, and Step IV: patient receives a kidney transplant from a living or deceased donor.	The primary outcome was listed in the published protocol.[5] The outcome did not changed but we updated the language.
Secondary Outcome details	**<u>Added clarification to wording in Table S2 (no change in outcomes):</u>** 1. A potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient and/or a patient receives a living donor transplant (composite of step 2 and/or 4 of primary outcome). 2. Time to first occurrence of a potential living kidney donor beginning their evaluation at a transplant centre to donate a kidney to the patient (step 2 of primary outcome). 3. A transplant centre receives a patient's complete referral package from a chronic kidney disease program and at least one potential living kidney donor begins their evaluation at a transplant centre to donate a kidney to the patient (requires both step 1 and 2 of the primary outcome)	All secondary outcomes were listed in the published protocol.[5] No outcomes where changed but we found that the interpretation could be subjective. As such, we added additional detail.

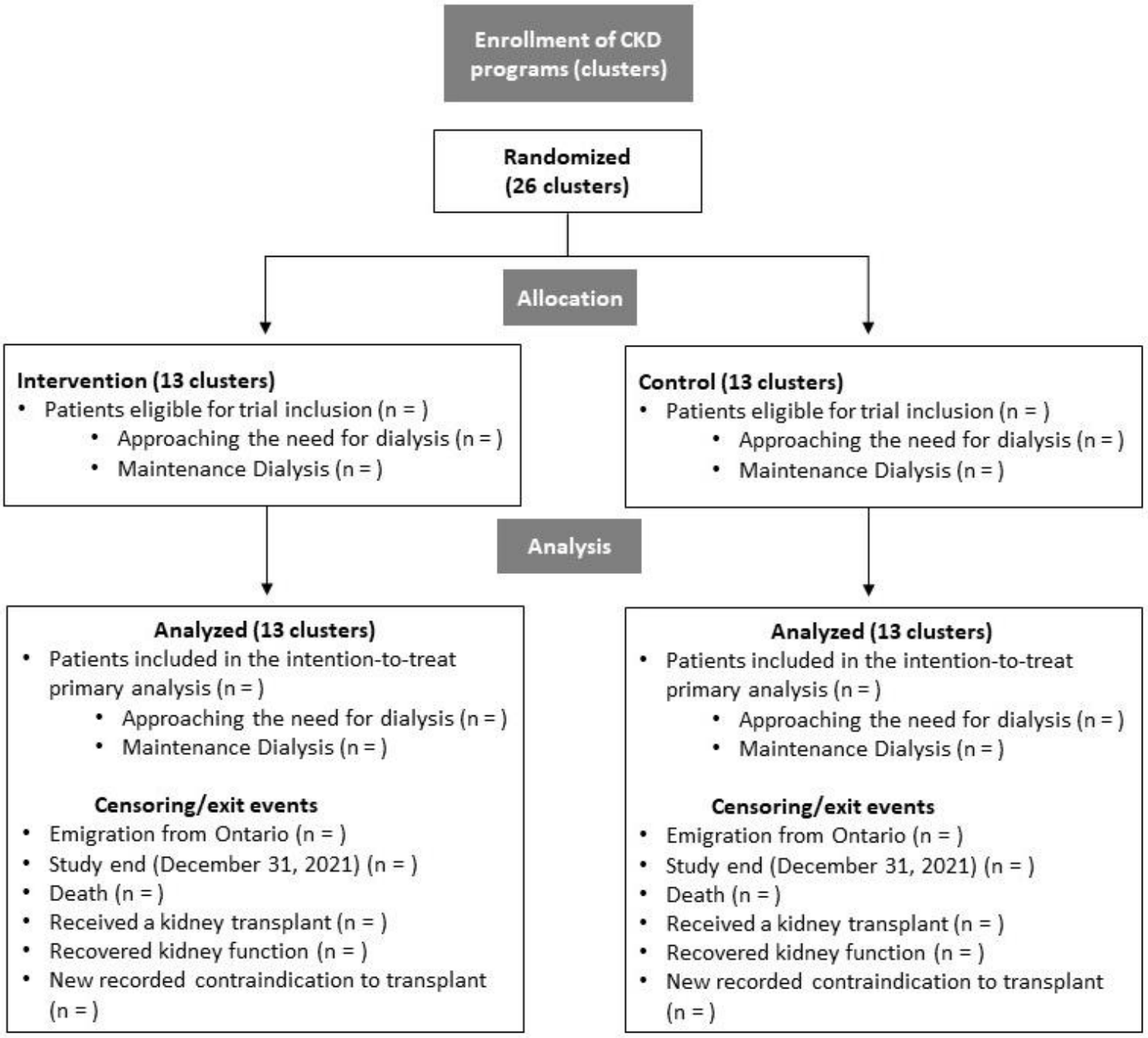
Revision	Details of Revision	Rationale
	4. A patient receives a living donor kidney transplant (a portion of step 4 in the primary outcome). 5. Pre-emptive living donor kidney transplants (restricted to patients who were not receiving dialysis when they entered the trial and not on dialysis at the time of transplant) (a portion of step 4 in the primary outcome).	
Withdrawal and Loss to Follow-up	**<u>Added clarification:</u>** In the published protocol, we state "…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."[11] We added additional clarification of the exits here, stating "We will use administrative databases to follow all patients, with emigration from the province being the only reason for loss to follow-up (<0.5% of Ontarians emigrate each year). Otherwise, a patient's observation time will only stop on the trial end date (December 31, 2021), death, receipt of a kidney transplant, evidence of recovered kidney function, or on the date a recorded contraindication to transplant occurs (as defined in criteria 2 of Table 1) with the exception of aged >75 years."	In the published protocol we stated that we would stop the observation period once a patient became ineligible. However, we wanted to explicitly state that this also includes evidence of a recovered kidney function as patients with recovered kidney function would not be taking steps towards transplantation.

Revision	Details of Revision	Rationale
Analysis of Trial Outcomes	**Changed from**: "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 patient-level variables ignoring intervention and clustering effects. Second stage: residuals from the first stage are aggregated at the cluster level as the outcome."[5] **Changed to:** "The primary outcome will be analysed using a patient-level constrained multistate model adjusting for the clustering within CKD programs. Bootstrapping at the cluster level will be used to maintain valid inference in the presence of correlated outcomes within CKD programs. We are interested in the global intervention effect for all completed steps towards transplantation. That is, we will be constraining the intervention effect to be the same for each state transition in our primary analysis. This approach will provide a single estimate of the relative rate (i.e., hazard ratio) of steps completed towards receiving a transplant among patients in CKD programs in the intervention group versus the usual-care group.[25,26]"	To preserve the statistical power this approach requires a weighting based on the estimated theoretical variance of cluster means.[7] This estimate requires an estimate of the between and within cluster variances, which can result in fragile estimates when sample sizes are small. Using such weights could also result in less statistical precision. Patient-level analyses are used more frequently due to their ease, and increase in statistical power.[7] An additional benefit of a patient level analysis is that it will naturally accommodate the variable cluster sizes found in Ontario CKD programs. The impact of the variation in cluster size on power will be negligible when the coefficient of variation (CV) is <0.239.[15] The primary outcome is a composite of 4 steps completed toward receiving a kidney transplant; however, these steps will not have a count distribution since a patient can only experience a maximum of 4 steps. Instead, these steps can be considered to create the different states on the path toward transplantation. As such, a multistate statistical model is better suited to handle this type of data
Additional Analysis	**Added Clarification:** "As specified in our protocol, the primary analysis for this trial will not account for pandemic-related changes in transplant activity.[8]	Given the challenges of delivering the intervention during the COVID-19 pandemic, we will perform a pre-specified analysis of our primary and secondary outcomes

Revision	Details of Revision	Rationale
	However, we will conduct an additional analysis in which patients' follow-up times will be truncated on the date transplant activity was first suspended in Ontario as described below. We are also conducting a concurrent process evaluation using surveys and interviews to understand how the intervention was delivered in each CKD program, and we will ask respondents how the pandemic affected these activities.[17]"	restricting the trial period and follow up from November 1st, 2017 to December 20th, 2019 with follow up to March 16th, 2020. March 16th, 2020 aligns with the suspension of transplant activity in Ontario. It is possible any beneficial effect of the intervention will be more pronounced in the pre-pandemic period.
Subgroup (removed race and immigration status)	**Changed from**: "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)."[5] **Changed to:** "In our protocol, we have 10 prespecified subgroup analyses listed as exploratory analyses for the EnAKT LKD trial. [5] After consultation with our project partners, we no longer plan to	We updated our subgroup analyses by removing race (white vs. other) and immigration status.

Revision	Details of Revision	Rationale
	perform 2 of these subgroup analyses of the intervention effect; specifically, we will not report results by race (white vs. other) (as we do not have access to self-reported race which is considered the gold standard for determining individuals' race and ethnicity, specifically ethnicity information in the Ontario Renal Reporting System was collected by data leads in each CKD program at the time of patient registration, based on charting by clinical staff who could ask patients to self-identify ethnicity but who were not mandated to do so)[16,17] or immigration status."	
Subgroup (addition)	**Added:** "In addition to the subgroup analyses described in our protocol, we will also conduct subgroup analyses based on how the patient entered the trial (ie, through patients approaching the need for dialysis or maintenance dialysis as well as if patients entered on November 1, 2017 or during the accrual period)."	We updated our subgroup analyses by including an analysis based on how the patient entered the trial. This was always an intended analysis but was not explicit in the published protocol.

Figure S1. Example flow of Chronic Kidney Disease (CKD) Programs (clusters) and patients in the EnAKT LKD Trial[a]



[a] No loss to follow-up is expected other than if a patient emigrates from Ontario (expected in less 0.5% of patients/year).

Table S4: Baseline variables*

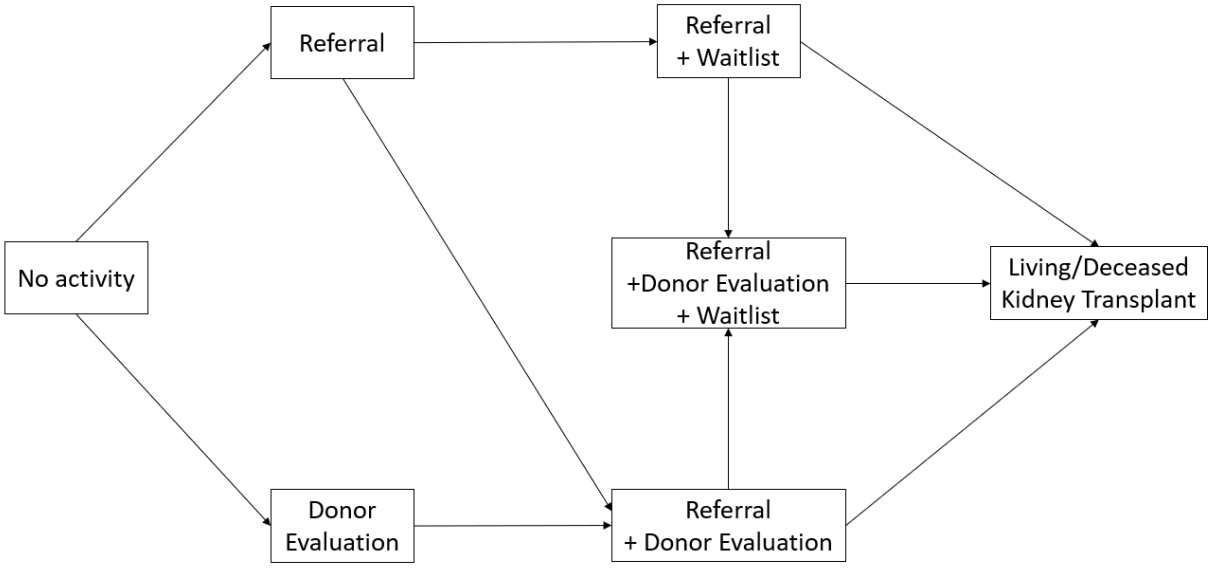
Baseline characteristic
Demographics
Age
Sex
Neighbourhood income quintile
Rural residence
Kidney-specific characteristics
Primary CKD treatment modality (i.e., in-centre hemodialysis, other form of dialysis, or approaching the need for dialysis)
Comorbidities
Stroke/Transient ischemic attack (TIA)
Chronic Obstructive Pulmonary Disease
Congestive heart failure
Chronic Liver disease
Venous thromboembolism
Depression
Coronary artery disease
Hypertension
Diabetes
Peripheral vascular disease
Fracture
Previous receipt of a kidney transplant
End-stage renal disease modified Charlson comorbidity index
Healthcare Utilization
Number of hospitalizations in prior year
Number of visits to emergency department in prior year
At least 1 intensive care unit visit in prior year
Program Factors
Historical rate of kidney transplant

*Baseline characteristic list details some of the baseline characteristics we will include in our final manuscript.

Appendix 5: Multistate models – transitions between states towards transplantation

The states towards transplantation for the primary outcome combines the relevant steps towards receiving a living donor kidney transplant (LKT) and deceased donor kidney transplant (DKT). Patients can simultaneously complete steps towards receiving a living or deceased donor kidney transplant, which have different steps. For example, a patient on the deceased donor waitlist may have a potential living kidney donor contact a transplant centre and begin their evaluation to donate a kidney to them. As such, we are using a flexible state progression in our model rather than an ordered state progression and accounted for the cumulative steps when creating our states (see **Figure S2**). In the primary analysis, we are constraining on the intervention effect to estimate a single relative rate across all transitions. In the additional analysis, an unconstrained multistate model will be used, which will produce an estimate of the intervention effect for each of the transitions (i.e., the arrows in **Figure S2**).

Figure S2*: Multistate model diagram for transitions towards both living and deceased donor kidney transplantation**



*Patients can start with no activity, or in one of the other states other than LKT/DKT. The patients may experience up to four steps. For example, if multiple potential living kidney donors begin their evaluation to donate to the same patient, only the date the first potential donor contacts the transplant centre will be counted as a step towards transplantation.

References:

1. Gamble C, Krishan A, Stocken D, et al. Guidelines for the content of statistical analysis plans in clinical trials. *JAMA - J Am Med Assoc*. 2017;318(23):2337-2343. doi:10.1001/jama.2017.18556

2. Kwakkenbos L, Juszczak E, Hemkens LG, et al. Protocol for the development of a CONSORT extension for RCTs using cohorts and routinely collected health data. *Res Integr Peer Rev*. 2018;3(1):1-9. doi:10.1186/s41073-018-0053-3

3. Campbell MK, Piaggio G, Elbourne DR, Altman DG. Consort 2010 statement: Extension to cluster randomised trials. *BMJ*. 2012;345(7881):1-21. doi:10.1136/bmj.e5661

4. Zwarenstein M, Treweek S, Gagnier JJ, et al. Improving the reporting of pragmatic trials: An extension of the CONSORT statement. *Bmj*. 2008;337(7680):1223-1226. doi:10.1136/bmj.a2390

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