

Effect of a multicomponent intervention to improve patient access to kidney transplant and living kidney donation

a pragmatic, cluster-randomized trial



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we continue to learn so much from the NIH collaboratory ...

Réseau de recherche sur les données de santé du Canada
Health Data Research Network Canada
Pragmatic Trials Training Program

funded by



CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

hosted by



2-year training program

- 29 future trial leaders
- 11 post docs
- 35 highly qualified personnel

total 75 trainees

starts in July 2024

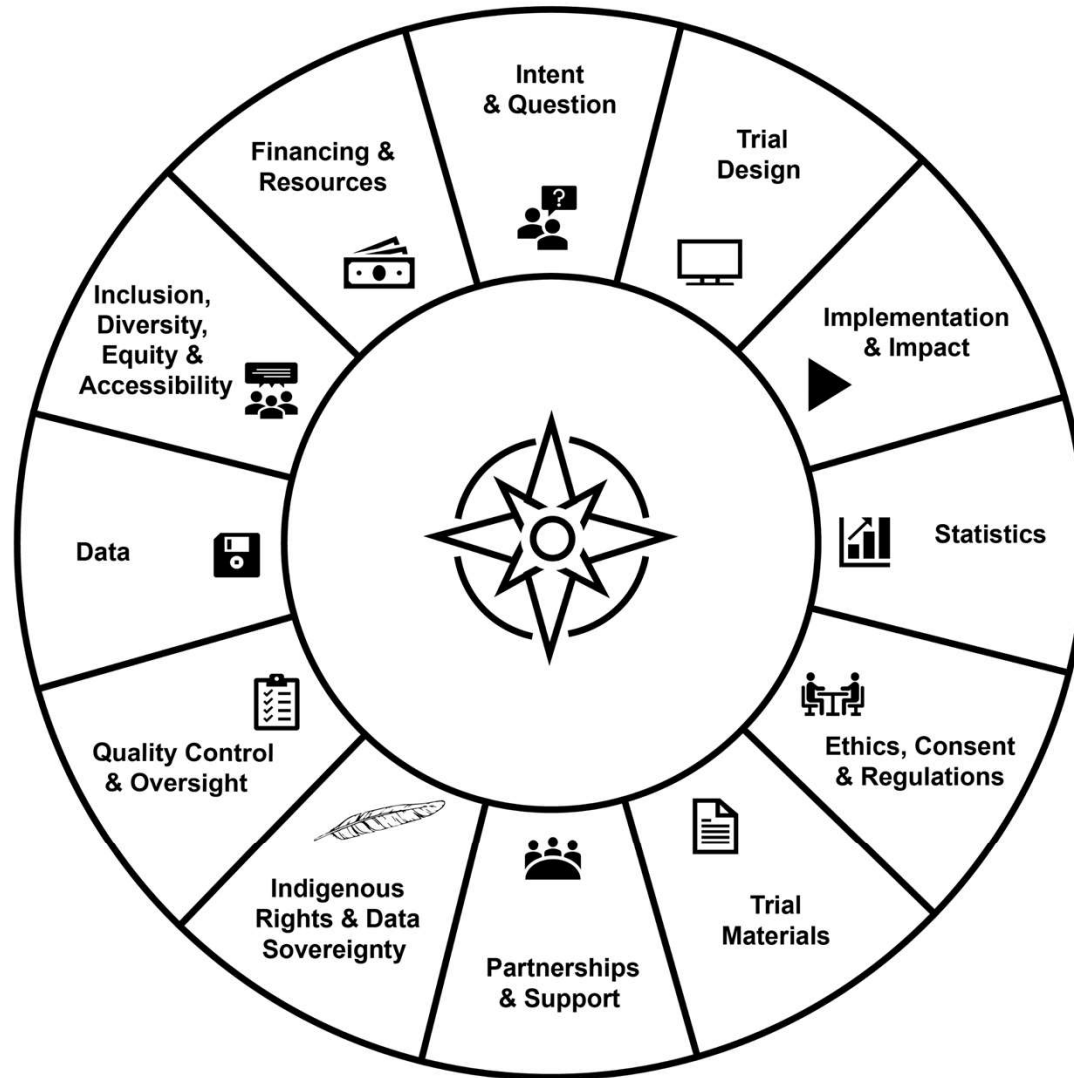
pragmatictrialstraining.ca

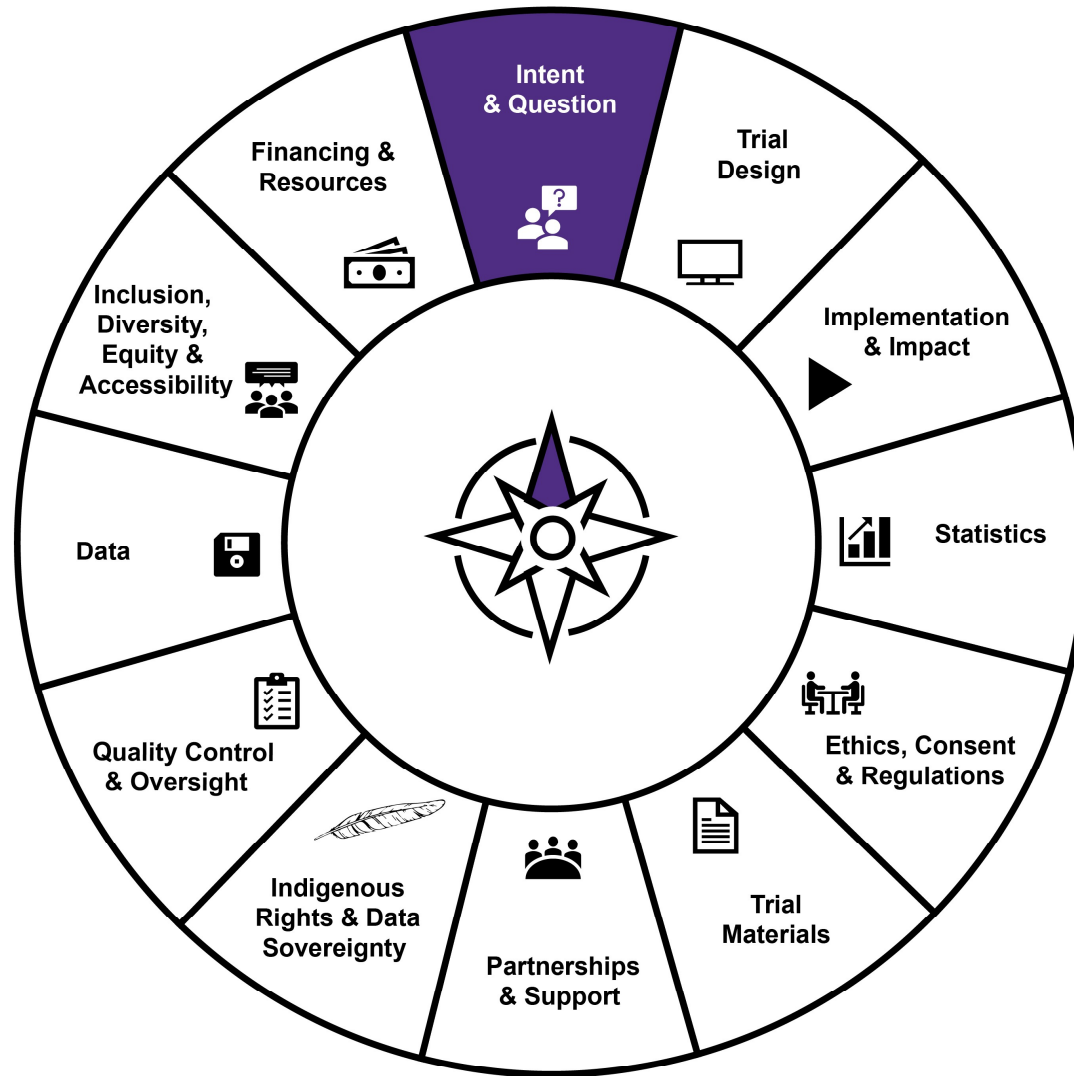
hdrn.ca



thank you to Dr. Kevin Weinfurt
for all the support & collaboration
member of program advisory committee

newly created educational materials will be free
and hopefully of use to this community





renal program-wide use of

**multicomponent
intervention**

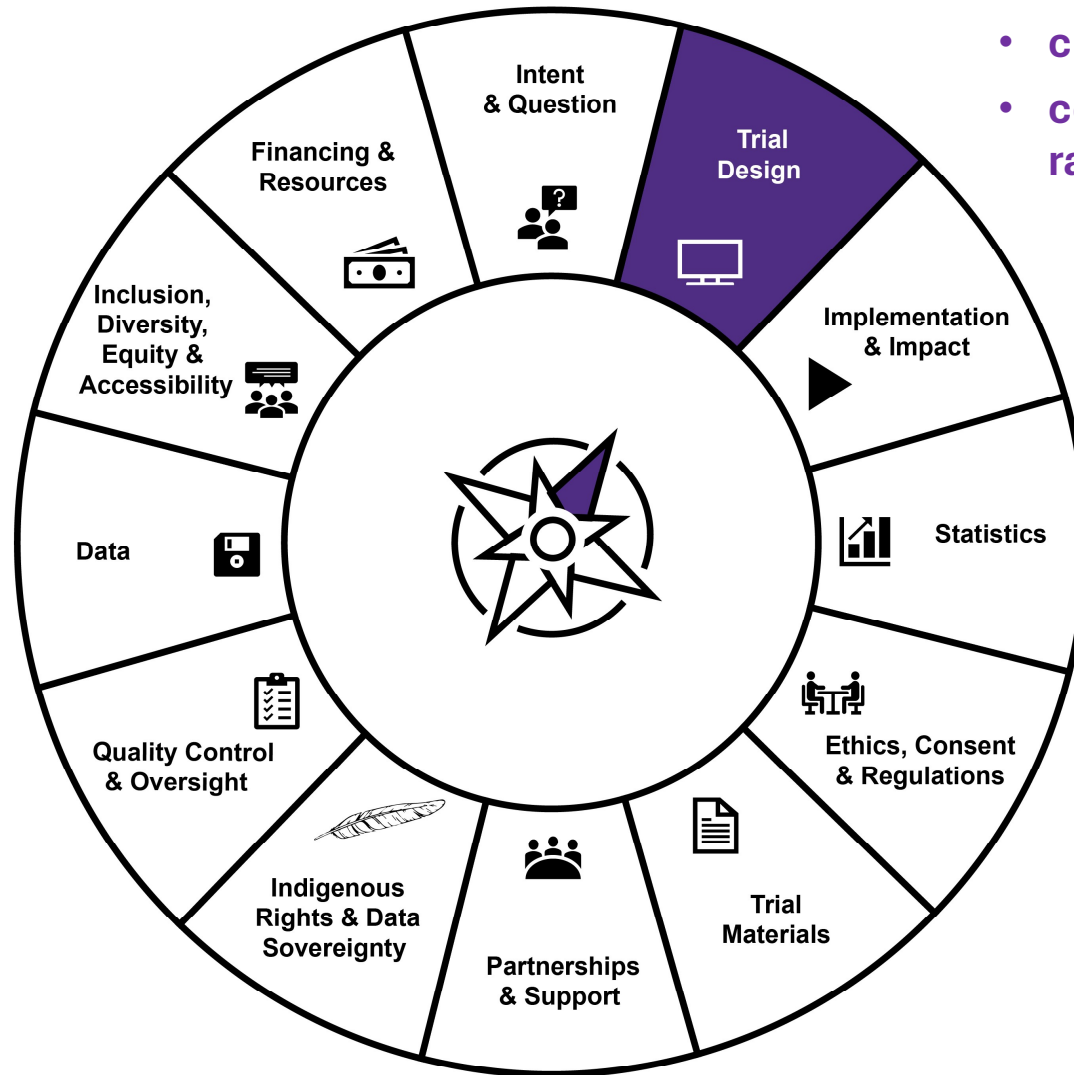
superior

usual care

in
completing steps
towards receiving
a transplant

Primary Intent

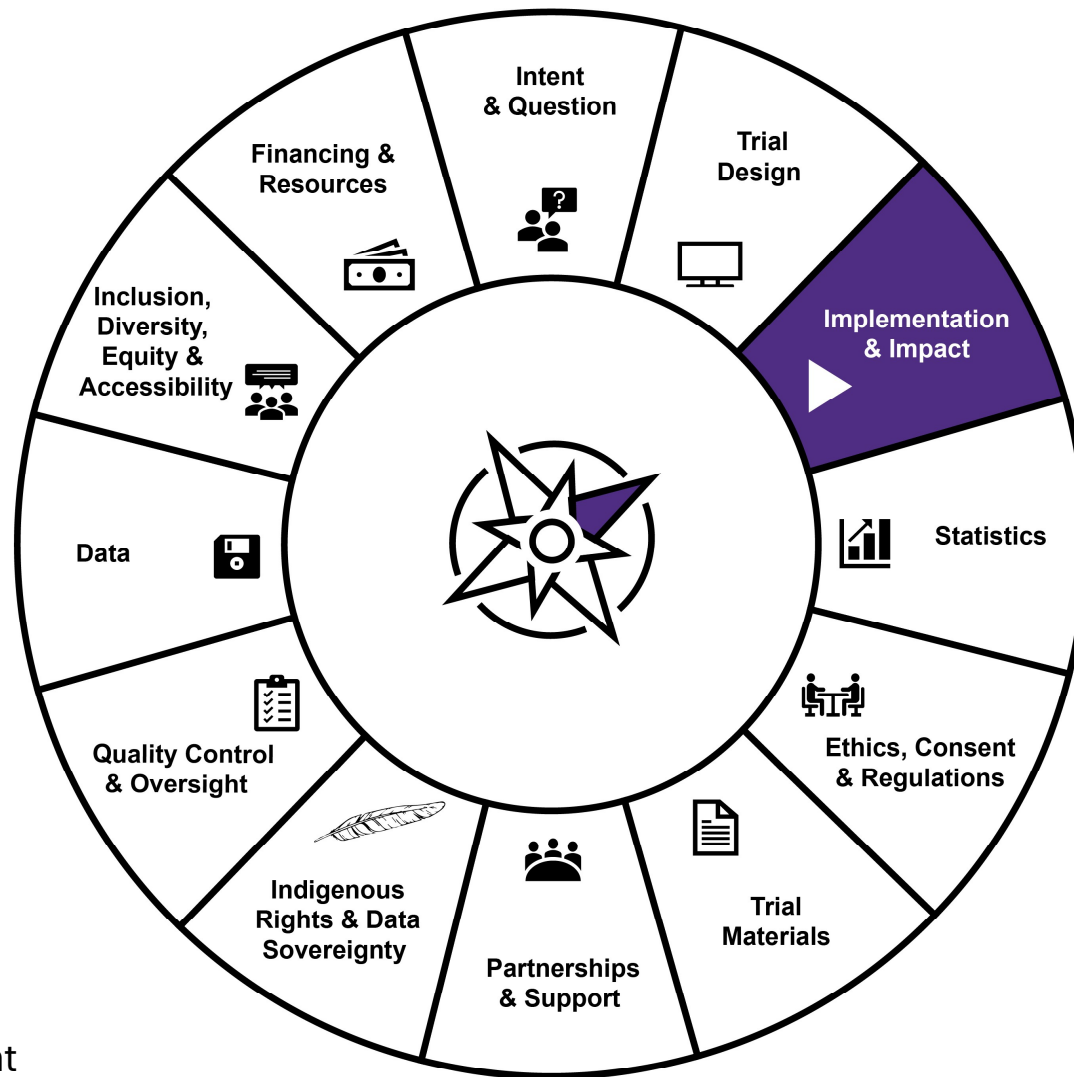
Inform whether the provincial renal agency in Ontario, Canada should continue to use the intervention or modify their approach



- cluster randomized
- covariate constrained randomization

Trial protocol

Yohanna S et al.
 Can J Kidney Health Dis
 2021 Apr 15



Trial embedded in routine care across

- 26 specialized clinics for patients approaching the need for dialysis
- 26 home dialysis programs
- 97 hemodialysis units

More than 3400 nurses and 230 nephrologists provided this care

Separate process evaluation

Surveyed and interviewed health professionals to understand

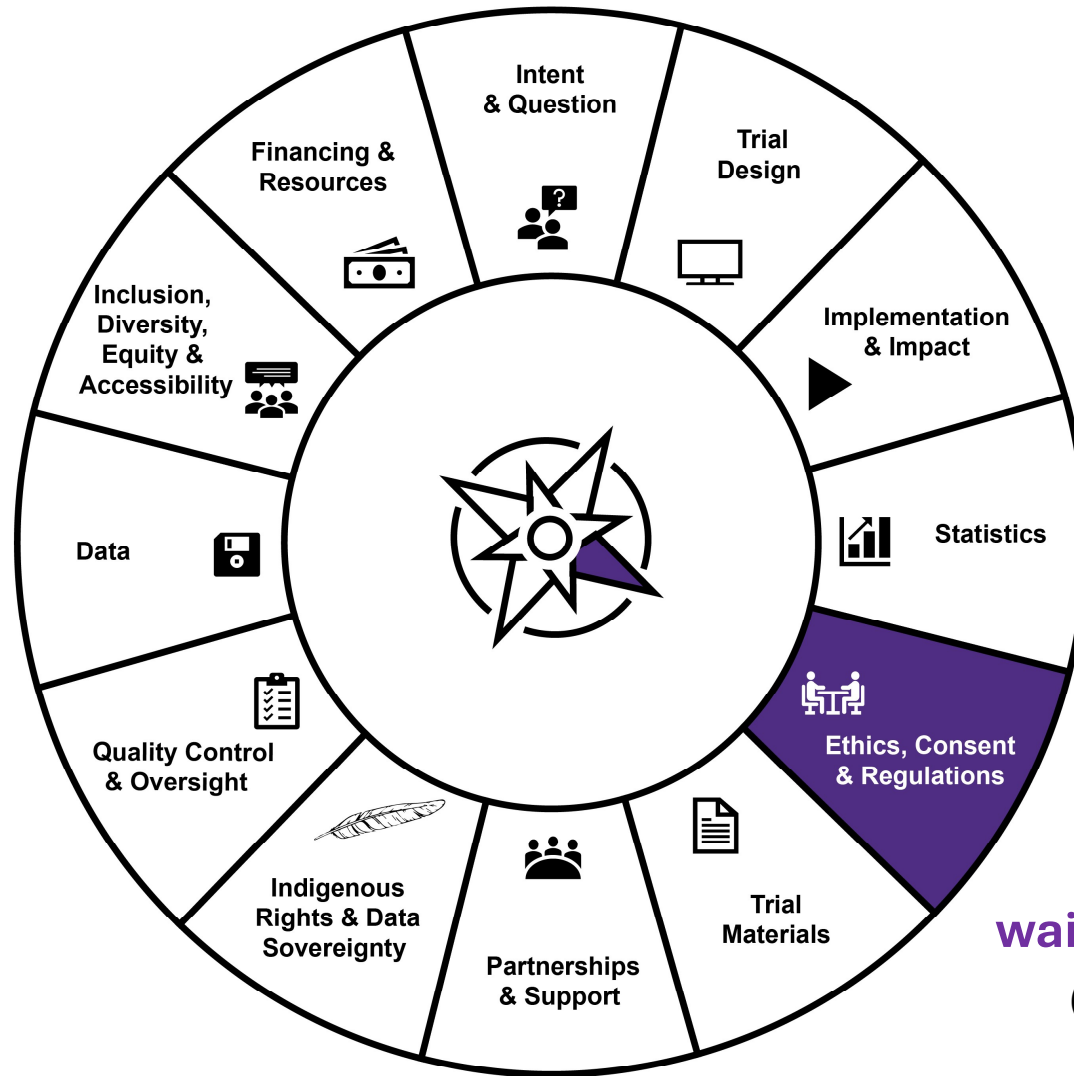
- Did intervention address intended barriers?
- Did implementation occur as planned?

Process evaluation protocol

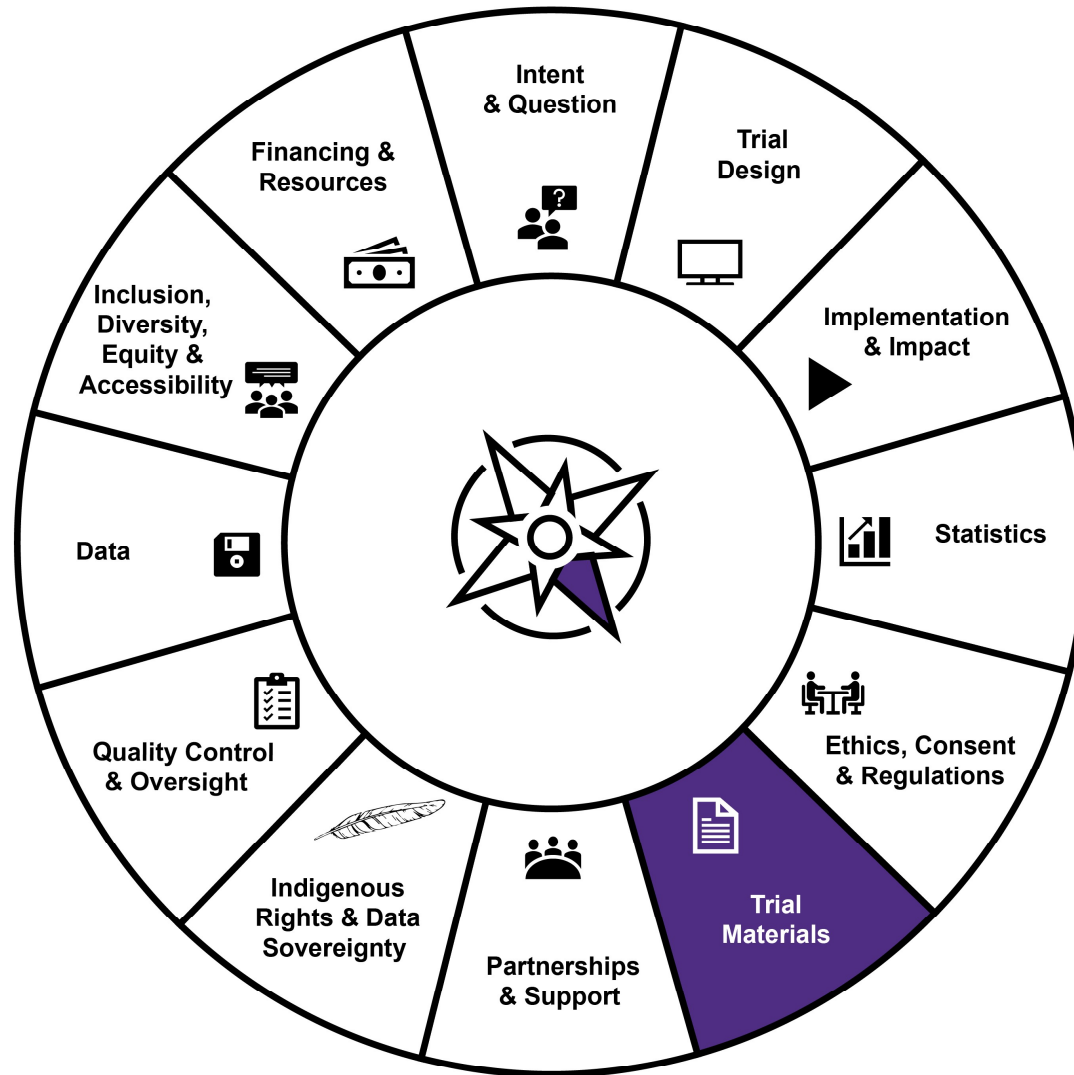
Yohanna S et al.

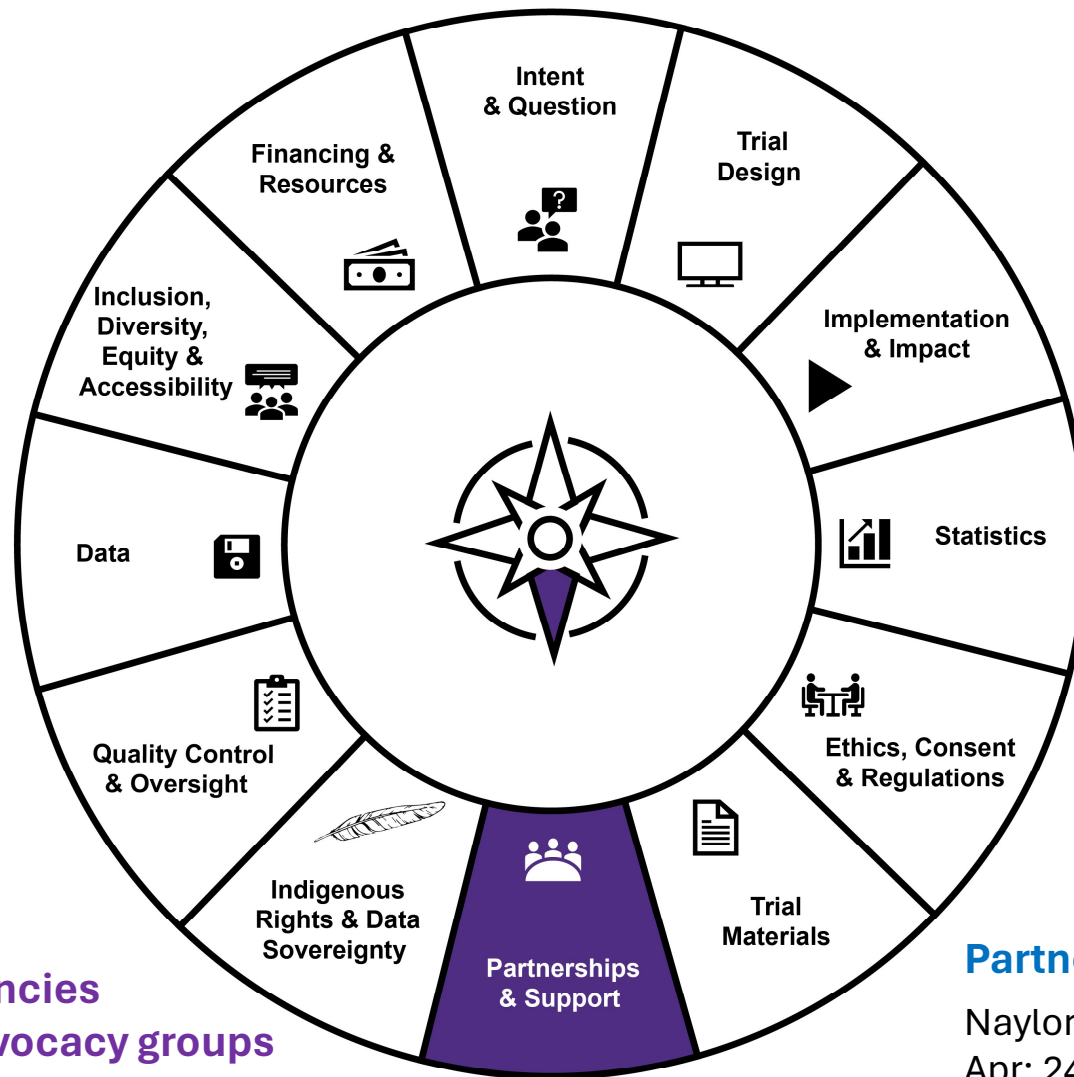
Can J Kidney Health Dis
2022 Mar 19

- paper under development



REB (IRB) approved
waived patient consent
(no patient notification during the trial)

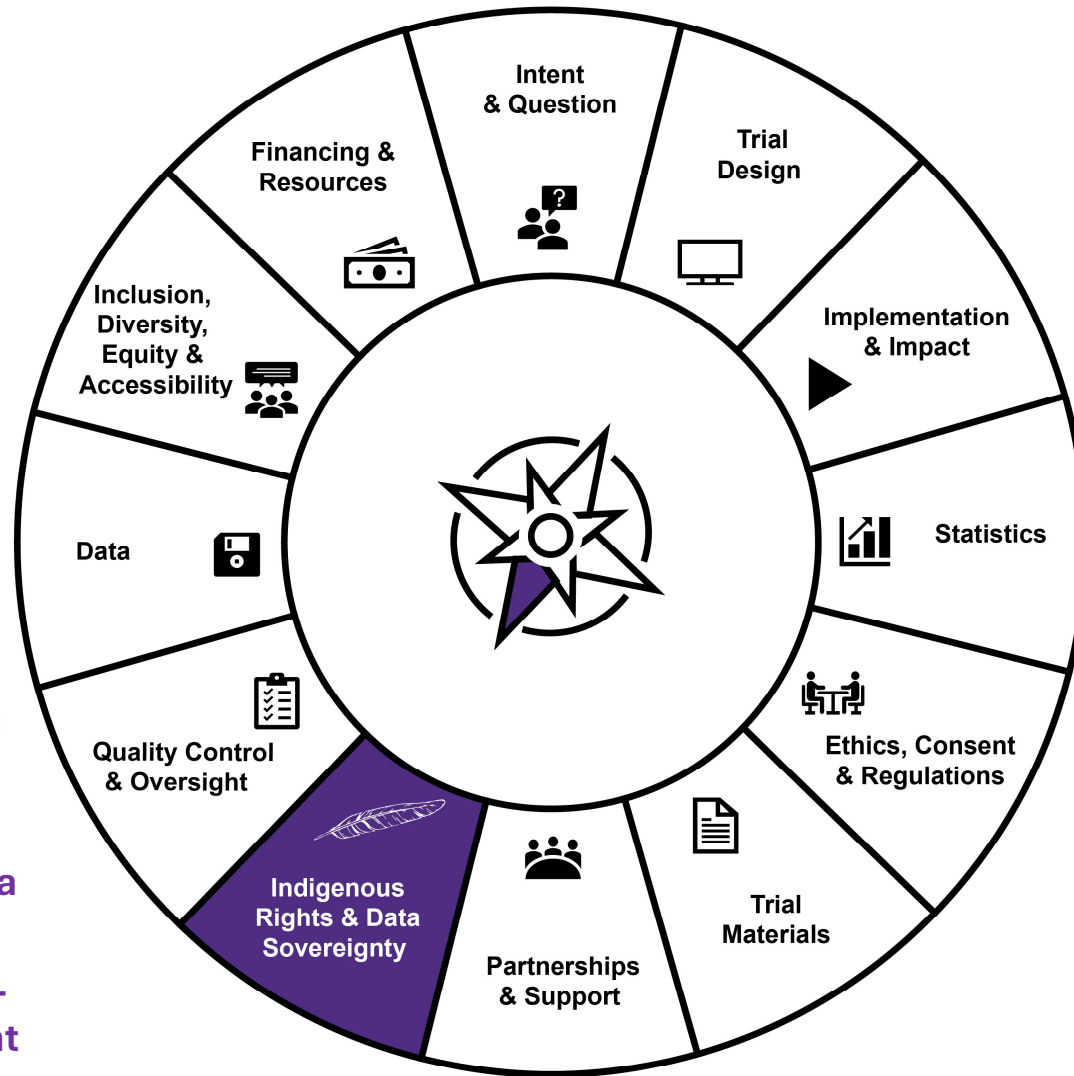




- 2 provincial renal agencies
- patient and family advocacy groups
- patients' part of the intervention

Partnering with patients

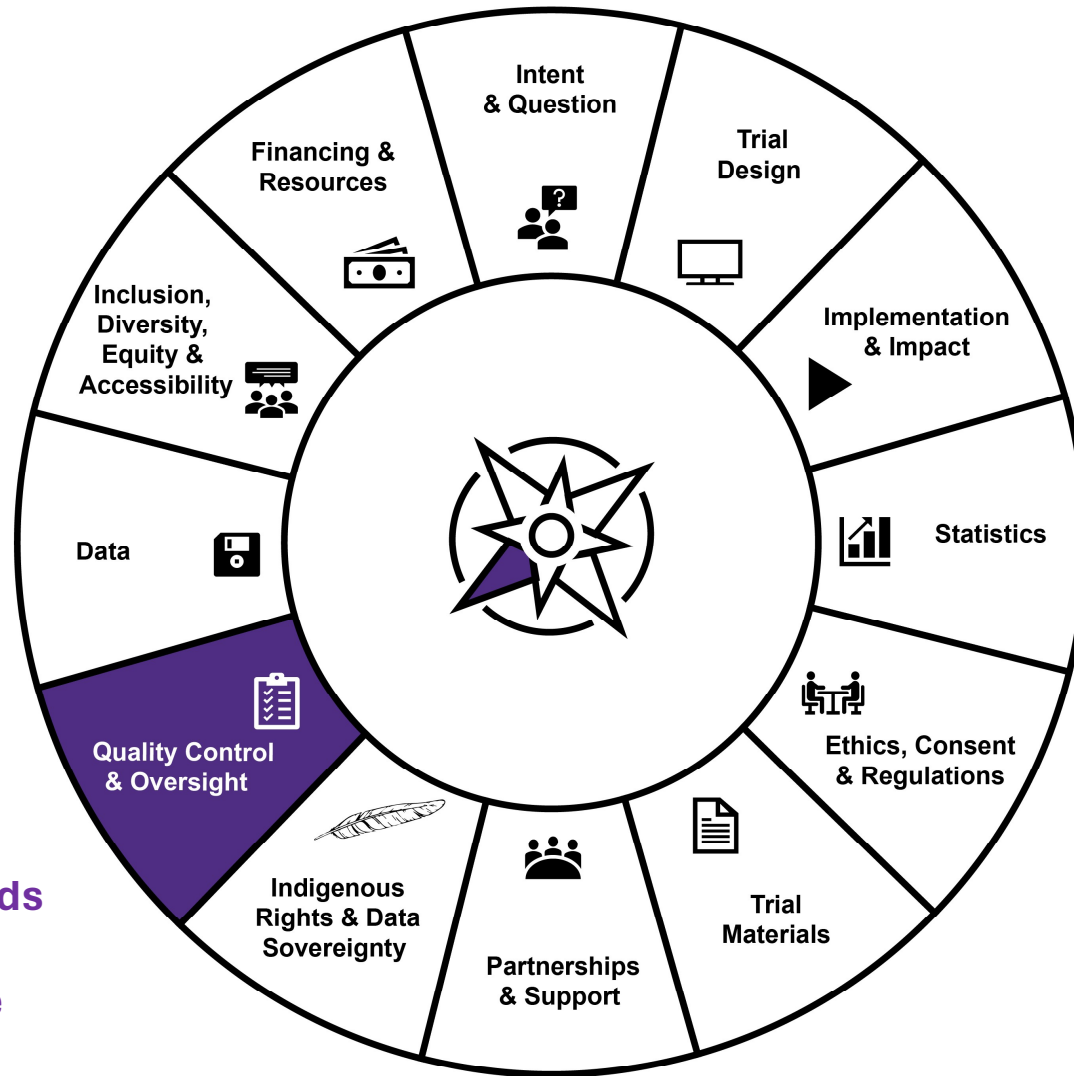
Naylor K. Healthc Q 2022
Apr; 24(SP):69-73



Recognize Indigenous peoples in Canada are disproportionately affected by kidney disease

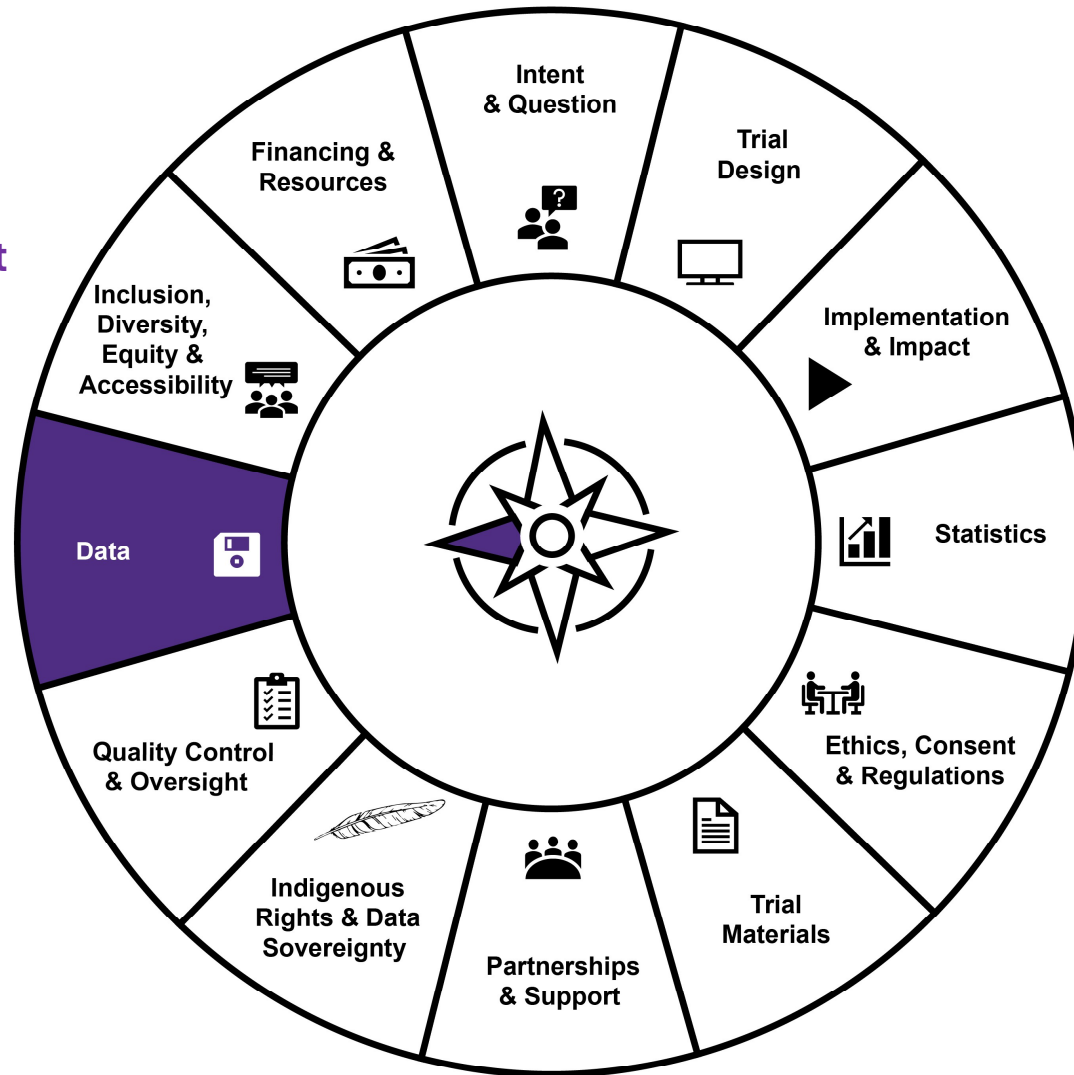
Contribute to a history of randomized trials done in a respectful way

Co-authored with prior co-Chair of Indigenous patient council

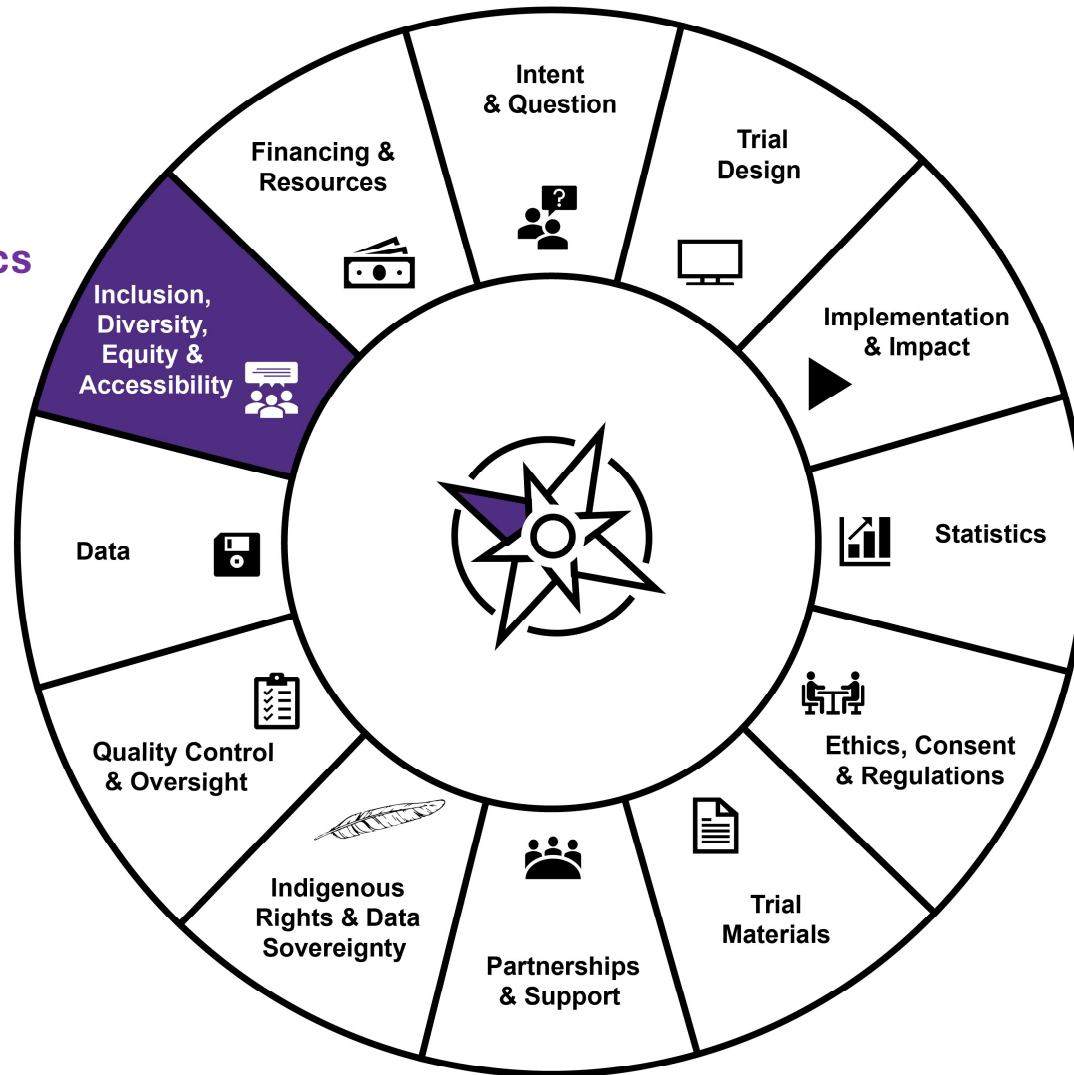


the occasional step a patient received towards transplant was not recorded in healthcare databases

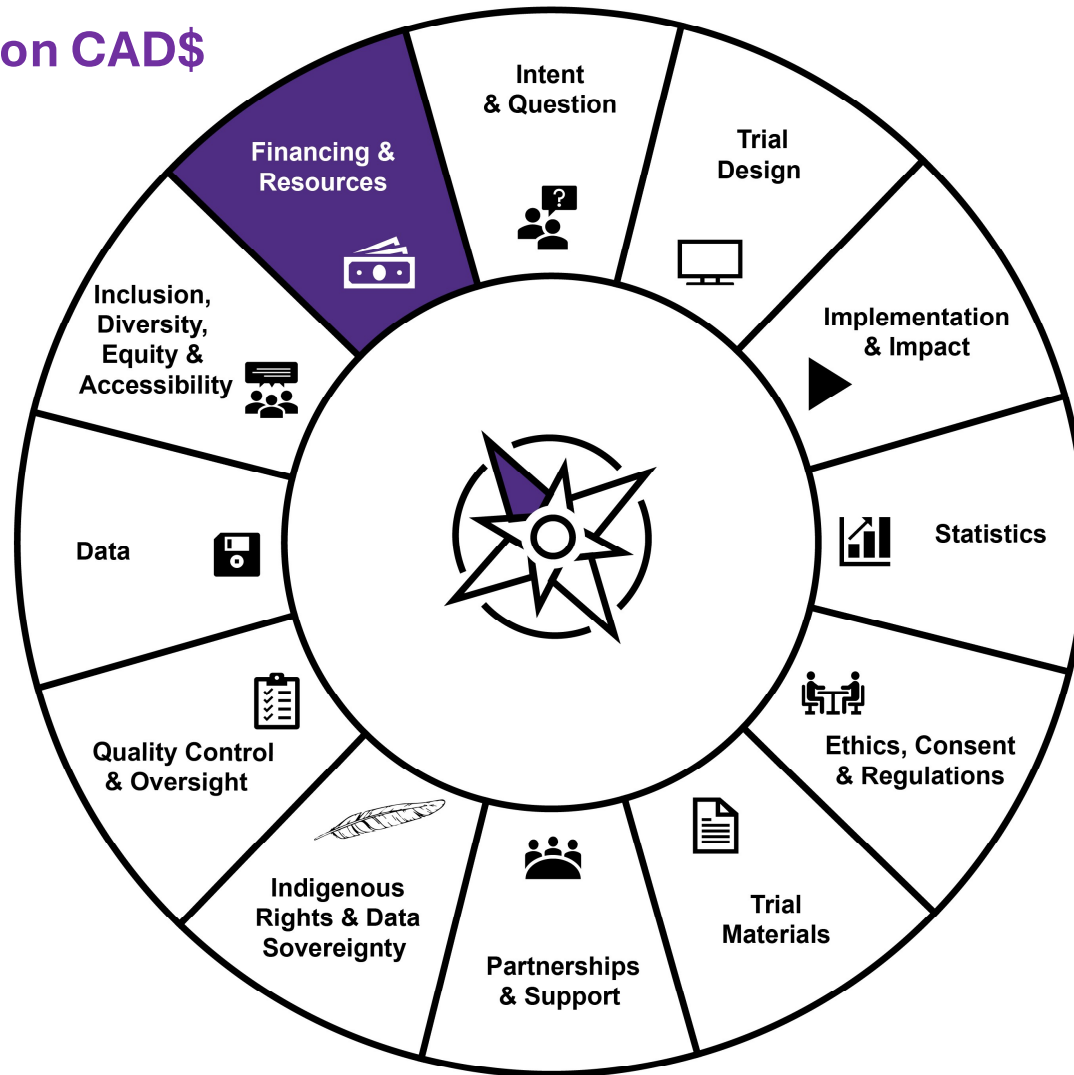
**data sharing agreement
between two provincial
agencies**

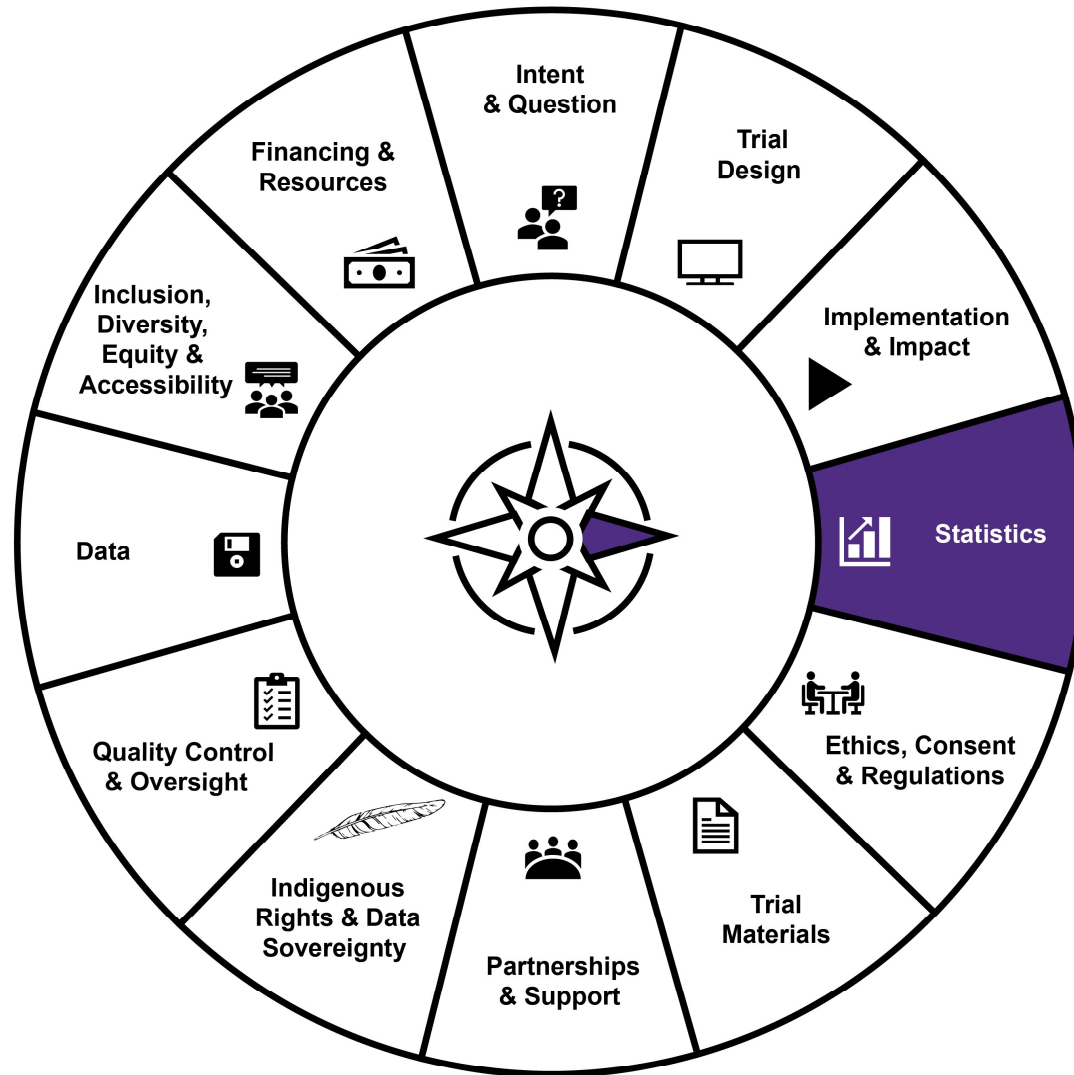


**elected not to report
race-ethnicity in paper
baseline characteristics**



~ 1.5 million CAD\$





Statistical analytic plan

Dixon SN. Can J Kidney Dis
2022 Nov 22:9

Methods

› [Can J Kidney Health Dis.](#) 2022 Nov 22;9:20543581221131201. doi: 10.1177/20543581221131201. eCollection 2022.

Enhance Access to Kidney Transplantation and Living Kidney Donation (EnAKT LKD): Statistical Analysis Plan of a Registry-Based, Cluster-Randomized Clinical Trial

Stephanie N Dixon ^{1 2 3 4}, Kyla L Naylor ^{1 2 3 4}, Seychelle Yohanna ⁵, Susan McKenzie ⁶, Dmitri Belenko ⁷, Peter G Blake ^{8 9}, Candice Coghlan ¹⁰, Rebecca Cooper ^{8 11}, Lori Elliott ⁸, Leah Getchell ^{1 2 12}, Vincent Ki ^{8 13}, Istvan Mucsi ^{7 14}, Gihad Nesrallah ^{7 15}, Rachel E Patzer ¹⁶, Justin Presseau ^{17 18}, Marian Reich ¹⁹, Jessica M Sontrop ^{1 2 4}, Darin Treleaven ^{5 11}, Amy D Waterman ²⁰, Jeffrey Zaltzman ^{11 21}, Amit X Garg ^{1 3 4 5 8 9}

On behalf of the EnAKT investigators



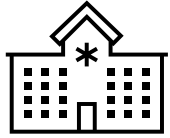
Considerations

- **Objective:** To evaluate the effect of a multicomponent intervention designed to target several barriers that prevent eligible patients from completing key steps toward receiving a kidney transplant
- **Design:**
 - 2-arm parallel-group Cluster-Randomized Trial
 - Stratified covariate-constraint randomization
- **Type of outcome & data collection**
- **Interpretation or estimand of interest**



EnAKT LKD

Primary outcome



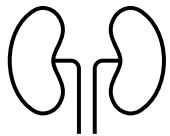
Referral: Patient referred to a transplant center for evaluation,



Donor evaluation: A potential living kidney donor contacts a transplant centre to begin their evaluation to donate a kidney to the patient

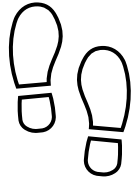


Wait list: Patient added to the deceased donor transplant wait list, and



Kidney Transplant: Patient receives a kidney transplant from a living or deceased donor.

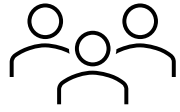
Primary outcome



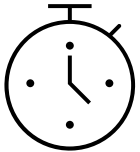
Only “new” steps during trial period are counted



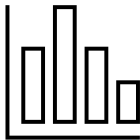
Completion of any individual step is only counted once



Correlation of outcomes within clusters by design



Variable follow up time



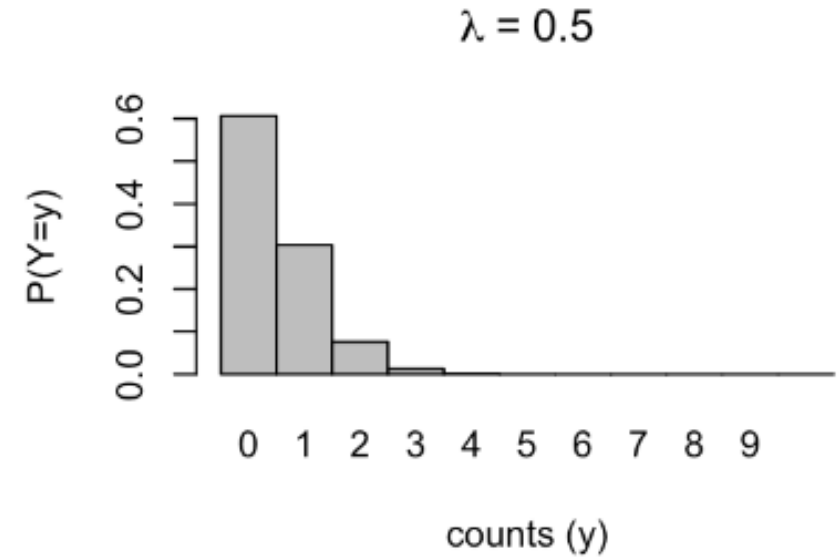
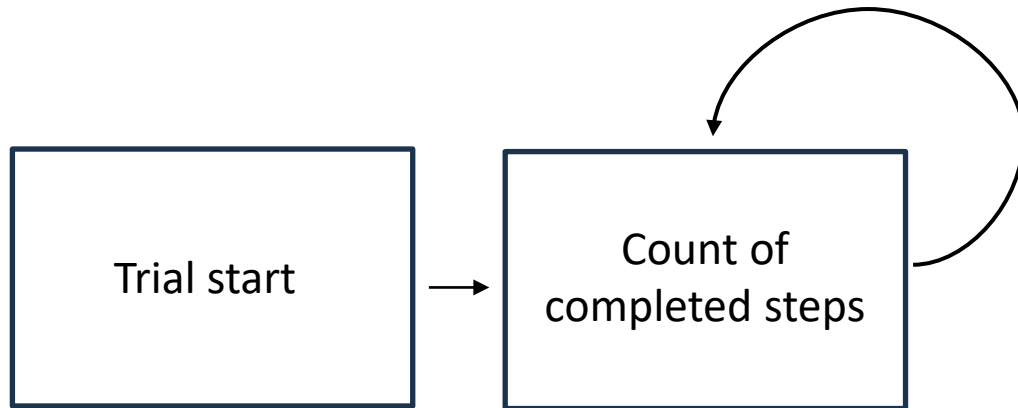
Find an appropriate distribution



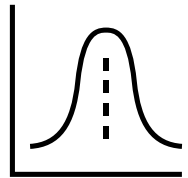
Adjustments for stratified covariate constrained randomization

Outcome framework

Treat as a count or recurrent event?



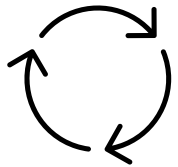
https://bookdown.org/ks6017/GLM_bookdown3/chapter-4-poisson-regression-and-extensions.html



Not a count distribution
Treats all steps as equal

Outcome framework

Progressive recurrent event?

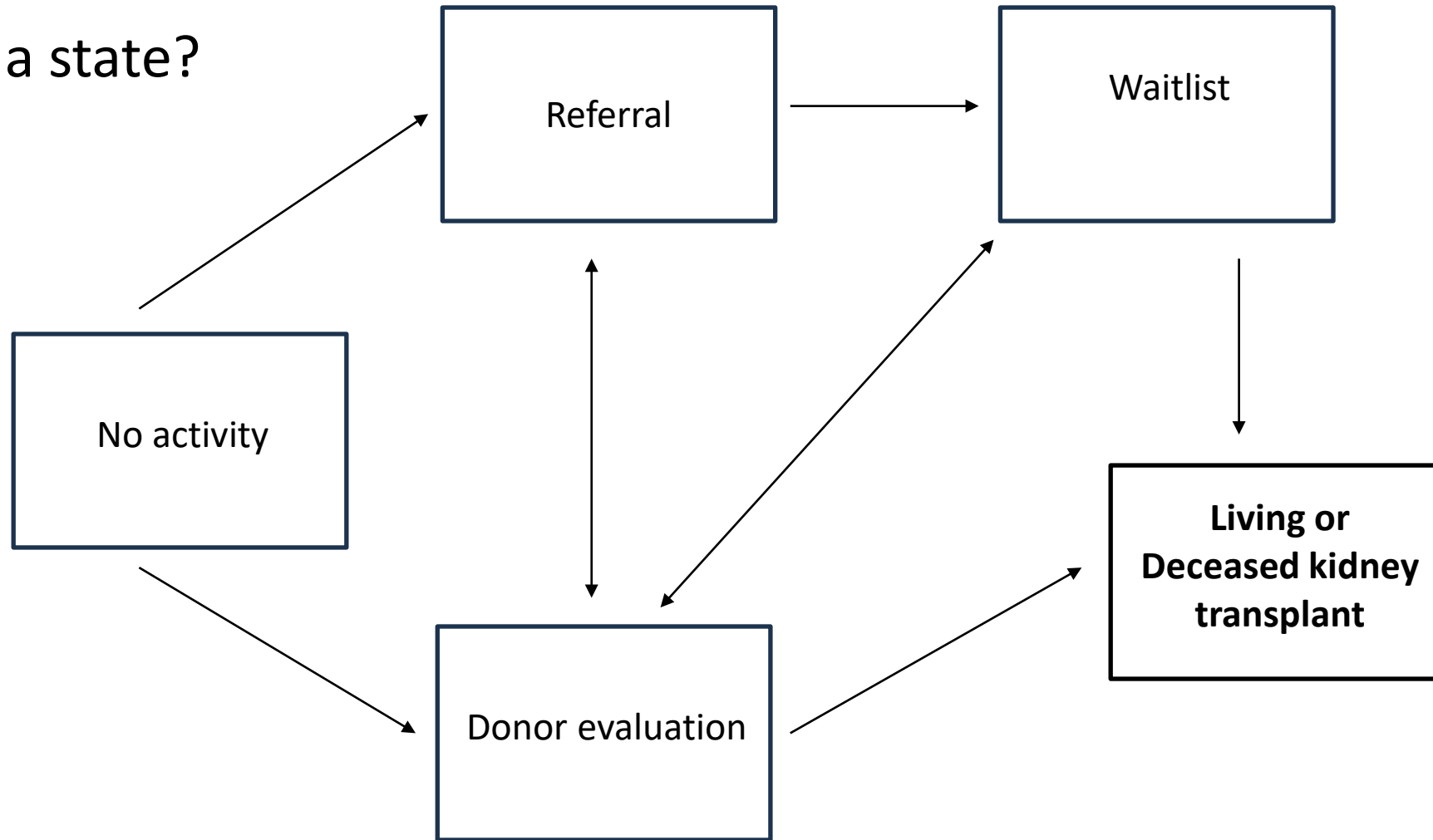


Does not distinguish the type of steps

Order is important for some steps but not others

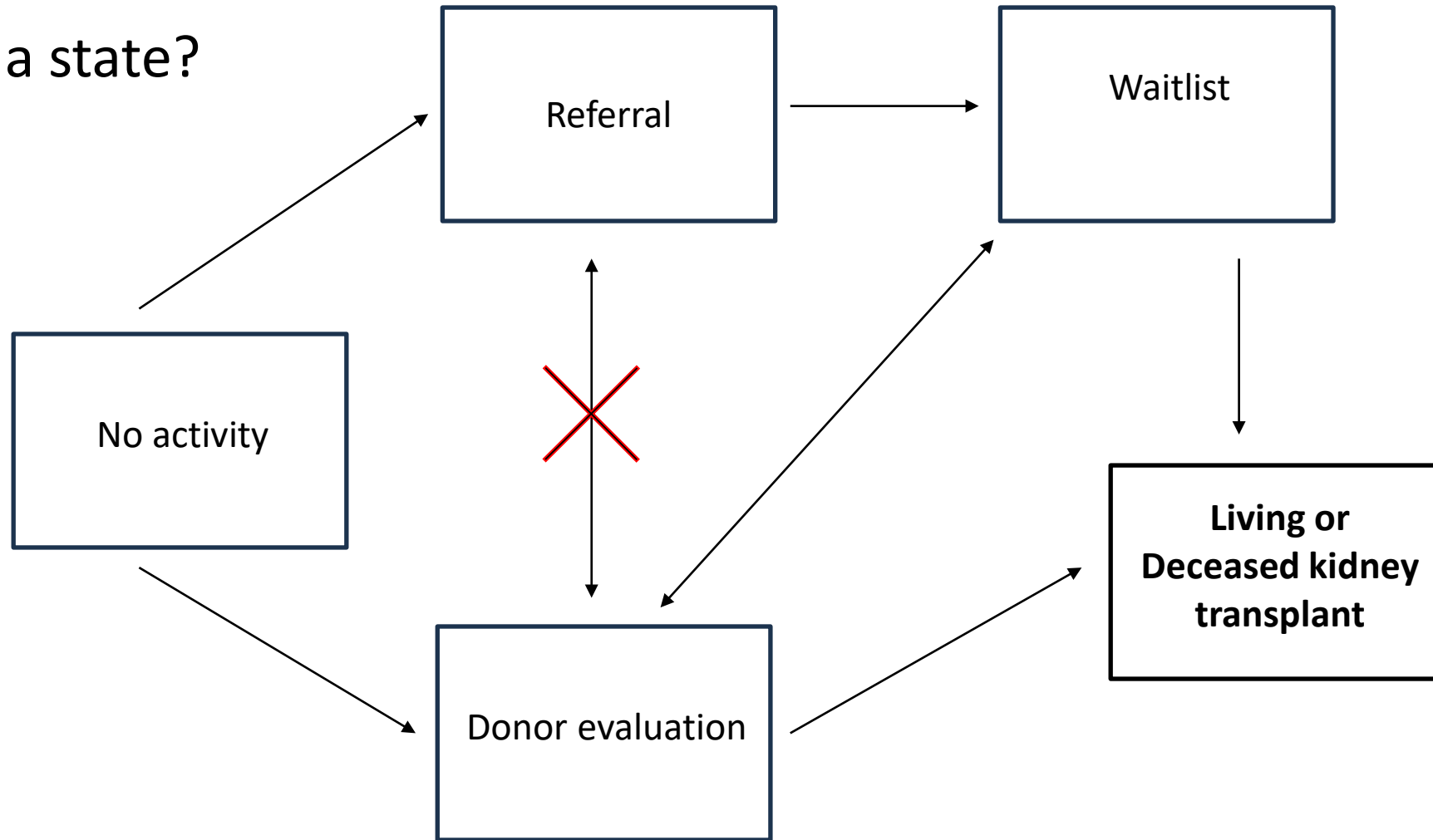
Outcome framework

Treat as a state?

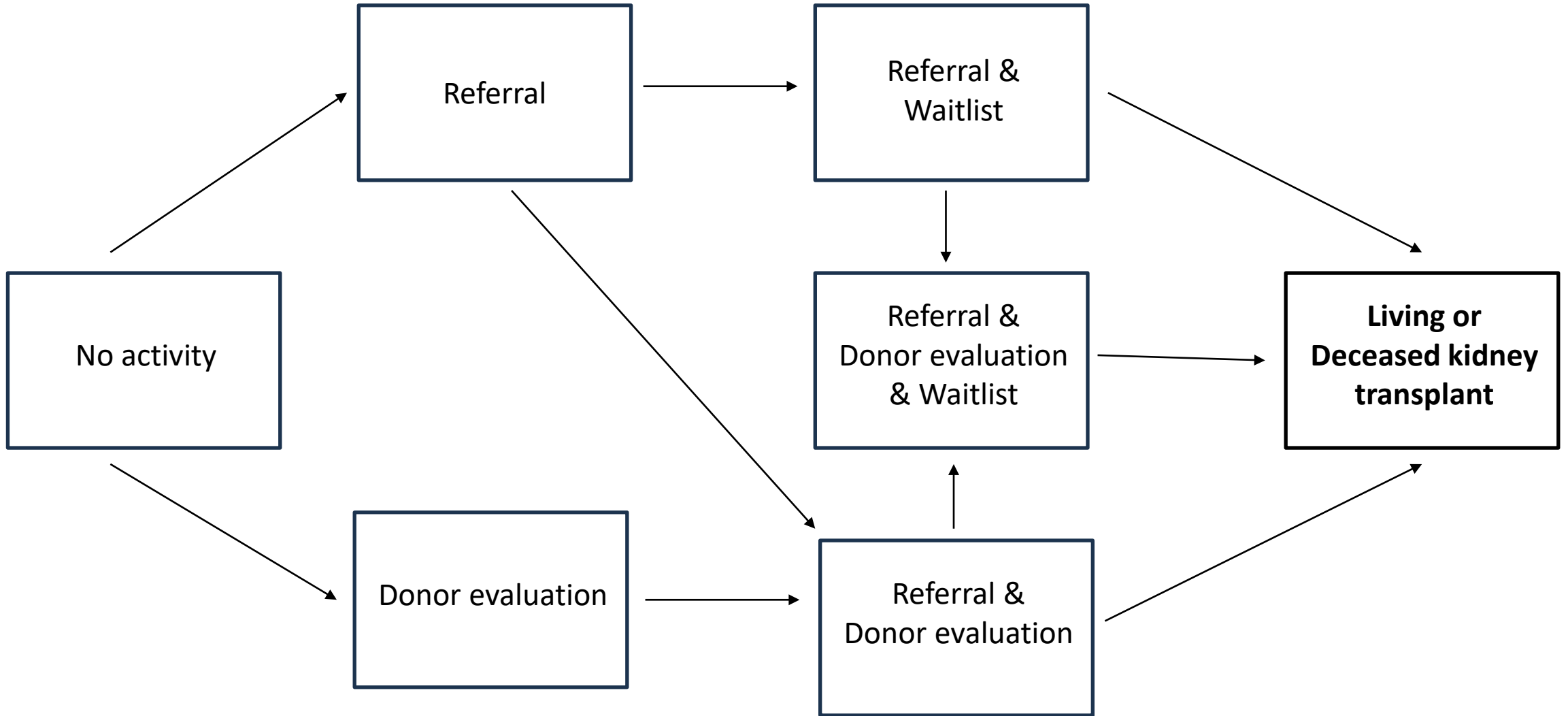


Outcome framework

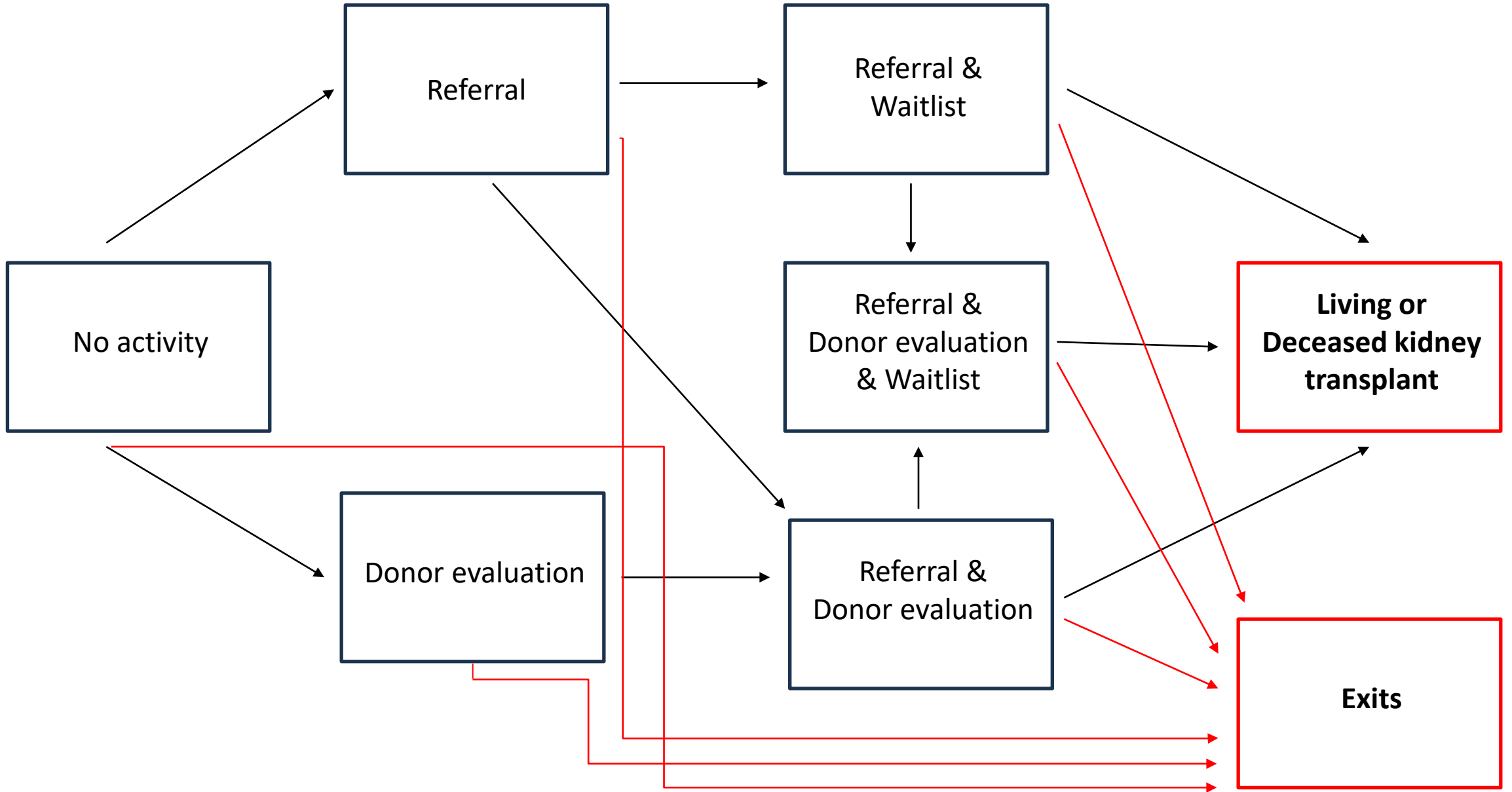
Treat as a state?



Outcome framework



Outcome framework





Primary Analysis

- By Design, we need to account for:
 - Correlation of outcomes in kidney programs (the “clusters”)
 - Variables used in the stratified constrained randomization
- Single marginal participant averaged treatment effect
- Analyzed according to index program’s intervention allocation
- Cohort, characteristics, outcomes and terminating events at ICES
- Terminating events: All patients were follow-up until transplant, loss to follow up, and intercurrent events (i.e., death and contraindication to transplant)

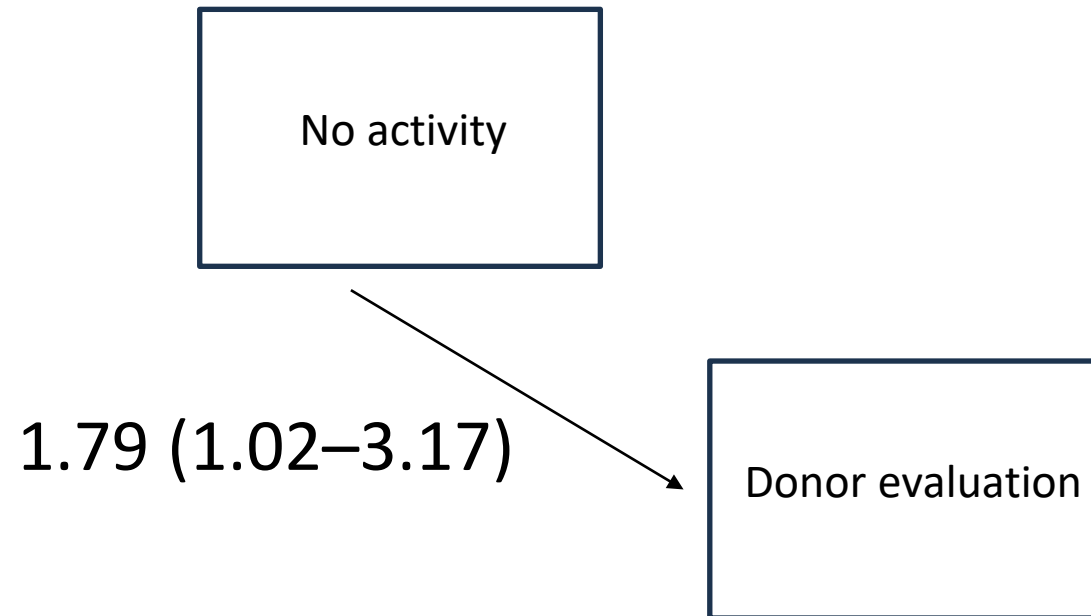
Primary Analysis

- Multistate model (MSM)
- Allowed for different baseline hazards for the different transitions
- Constrained on the transitions to obtain a single intervention effect
 - In additional analyses, we explored all transitions separately
- Consider terminating events

Primary Analysis

- Adjusted hazard rate: 1.00 (0.87-1.15)
- Unconstrained rates: no intervention effect for most transitions

Hypothesis generating:



Primary Analysis

- 26 Kidney programs (13 per arm)
 - Adjustment needed depending on model when < 40 cluster in trial

› [Int J Epidemiol. 2018 Jun 1;47\(3\):1012. doi: 10.1093/ije/dyy057.](#)

Cluster randomized trials with a small number of clusters: which analyses should be used?

[Clémence Leyrat, Katy E Morgan, Baptiste Leurent, Brennan C Kahan](#)

**On behalf of the EnAKT LKD
investigators**

Thank you for listening



EnAKT LKD