

People with chronic kidney disease: Who to refer, when to refer, and the impact on outcomes

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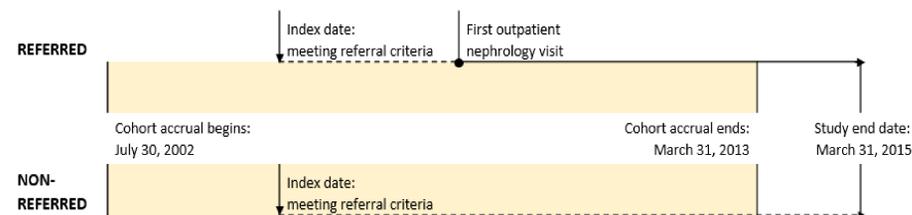
5. Centre for Health Evaluation and Outcome Sciences (CHEOS, jointly affiliated with PHCRI and UBC) 6. Canadian Network for Observational Drug Effect Studies (CNODES)

Background

- Chronic kidney disease (CKD) is common and associated with increased risks of morbidity and death
- Most people with CKD are cared for by primary care physicians, who must decide whether to refer them for specialist nephrology care and when to do it, if needed
- The Kidney Disease: Improving Global Outcomes (KDIGO) recommends early nephrology referral for people with CKD who have eGFR<30 ml/min/1.73m² or a consistent finding of significant albuminuria (A3),¹ based on many observational studies showing better outcomes after dialysis start in people who received longer predialysis nephrology care²
- We propose this project considering that prior studies:
 - focused on individuals who started dialysis, rather than the broader population of CKD patients
 - designed to examine the effects of duration of predialysis care, rather than the important variables available that may influence decision-making at the time when referral decisions are made

Methods

- Data Sources:** Population-based, provincial-wide administrative and lab databases
- Study population:** We will:
 - identify Albertans aged ≥18 years with CKD (G3-4 or A2-3) for >90 days between July 30, 2002 and March 31, 2013
 - include people who met either, or both, of referral criteria of eGFR<30 ml/min/1.73m² or a consistent finding of albuminuria A3
 - exclude those who *i)* already met either of the above referral criteria when their CKD was ascertained, *ii)* were on renal replacement treatment prior to the index date, or *iii)* saw a nephrologist prior to the index date



- Exposures:** We will use the initiation of outpatient nephrology visit as a proxy of nephrology referral as we do not have information on when referrals were submitted
 - Primary: initial nephrology visit as an outpatient vs never saw a nephrologist
 - Secondary: the time from the index date to the first outpatient nephrology visit, early (≤1 year) vs late (>1 year) visit

- Outcomes:**
 - Primary: all-cause mortality
 - Secondary: progression to end-stage kidney failure, occurrence of major cardiovascular events, and hospital/emergency department visits
- Covariates:** Demographics, comorbidities, prescription drug use, and laboratory measurements
- Analysis plan:** We will use the following methods for addressing immortal time bias and minimizing confounding:
 - time-dependent Cox and count models, to assess the associations between referral (vs. no referral) and outcomes
 - sequential Cox models and exposure density sampling with additional matching on important predictors of kidney failure, to examine the effect of early referral (vs. late or no referral) and to identify which patient group would benefit most from referral

Objectives

- To evaluate the impact of nephrology referral and its timing on outcomes of people who met the KDIGO's criteria for referral
- To identify which patient group would benefit from current nephrology referral criteria, if benefits exist

Expected results & Implications

- We expect to observe benefits from early nephrology referral; our study power will allow to detect smaller effects, if they exist
- This work will provide for the first time high-quality evidence to inform referral decisions in the CKD population, referral guidelines and future research

References

- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013;3:112-9.
- Smart NA, Dieberg G, Ladhani M, Titus T. Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. *Cochrane Database Syst Rev.* 2014;6:CD007333.

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