Trial Description Document

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Trial Title: UPRISING-CKD: Using personalized risk to improve nephrology guideline use for chronic kidney disease – A pragmatic randomized controlled trial in Connect Care

Content Area:

My current research program focuses on three major themes. I am exploring the perioperative experience of people with kidney disease, specifically focused on understanding what outcomes are most important to people with kidney failure and developing risk prediction models to target these patient-prioritized outcomes. Along with this interest in risk prediction, I also have an interest in use of risk tools to guide evidence-based interventions delivered in electronic health records.

Trainee Goal:

I am in the early stages of developing a pragmatic trial where we will use clinical decision support to inform outpatient chronic kidney disease management across Alberta (see plan below). With the support and knowledge gained in the HDRN pragmatic trials training program, I will develop the full protocol for this trial and enhance my skills as a future pragmatic trials leader in Canada.

Background:

One in ten Canadians are living with chronic kidney disease (CKD). In the last decade, there have been important scientific discoveries in the care of people with CKD care including novel medical therapies such as sodium-glucose like transporter 2 (SGLT2) inhibitors, non-steroidal mineralocorticoid receptor antagonists, glucagon-like peptide-1 receptor agonists (GLP-1RAs), in addition to important disease modifying medications such as renin-angiotensin system (RAS) inhibitors and statins. Despite being recommended by international kidney disease guidelines for use in CKD, substantial

implementation gaps remain in Canada where people with indications for these potentially life-extending therapies are not receiving recommended treatments. Alberta Health Services (AHS) has recently implemented a new province-wide Epic-based Clinical Information System called Connect Care, which provides a unique opportunity to use digital health technology to implement and evaluate clinical decision support interventions.

Trial Focus:

With the system-wide implementation of the clinical information system Connect Care, we will utilize evidence-based interventions as part of a multi-component digital solution. We will answer: **Does a digitally implemented multi-component intervention of therapies for people with CKD in routine clinical settings reduce the risk of long-term major adverse kidney or cardiovascular (CV) events?**

Method:

UPRISING-CKD is a pragmatic, parallel-arm RCT with patient-level randomization that will compare a risk-guided and patient-specific approach to implement guideline recommendations for people with CKD in outpatient clinic settings with usual care. Participants will be followed up to two years after randomization for major clinical outcomes. Follow-up will end at death or after two years, whichever comes first.

For this trial, we will adapt, co-design and implement the OPA and order set that identifies guideline-recommended therapeutic gaps, including RAS inhibitors, SGLT2 inhibitors, nsMRAs, (e.g., Finerenone), statins, and GLP-1RAs (e.g., Semaglutide). These gaps will depend on comorbidities, measures of outpatient kidney function (eGFR and proteinuria/albuminuria), and current medication and allergy lists. When a patient is randomized to the intervention arm, the OPA will alert their clinician to any medication gaps and provide options for each category to be ordered in real-time. In addition to medication recommendations, the order set will enable clinicians to easily order follow up labs either after medication reconciliation or as part of routine recommended CKD care. Further, if the patient is not already receiving nephrologist-guided care as an outpatient, and they have an indication based on predicted risk of kidney failure from the validated tools, the automated order set will include an ambulatory referral to kidney care programs in Alberta.

Our primary focus will be on effectiveness of the OPA, as defined by major adverse kidney or CV events at two years, defined as the composite outcome of death, kidney failure (i.e., receipt of maintenance dialysis or eGFR <15 mL/min/1.73m^2 for four weeks or more), or hospitalization with a most responsible diagnosis for heart failure, myocardial infarction, or stroke. We will also assess the implementation metrics of feasibility, fidelity, and scalability of the intervention within the clinical setting, examining how effectively the study procedures are carried out. We will identify any barriers or facilitators required for successful implementation of the OPA.