Data Creation Plan for Secondary Analyses

Name and Number of Study	A Comparison of Teaching vs. Community ICU sites – A Secondary Analysis of the STARRT-AKI Study
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DCP Update History	July 18, 2023 (Version 1) August 8, 2023 (Version 2) October 19, 2023 (Version 3)
Short Description of Research Question	Significant variations may exist between teaching and community hospitals with respect to patient demographics, processes of care and patient outcomes. The STARRT-AKI trial enrolled patients in both teaching and non-teaching hospitals. It provides a unique opportunity to compare patient characteristics and outcomes between hospital types as well as to evaluate whether there are differences in outcomes by trial intervention. It also provides an opportunity to compare recruitment rates and protocol adherence in teaching and community hospitals. We therefore asked these questions, in the STARRT-AKI trial: 1. Were there differences in recruitment, baseline characteristics, trial performance (i.e., consent rate, exclusion of eligible patients; co-enrolment rate; protocol violations) and processes of care (i.e., time to KRT; KRT modality) stratified by hospital type (teaching and community) in the STARRT-AKI trial? 2. Are there differences in the primary and secondary outcomes and adverse events stratified by hospital type (teaching and community) in the STARRT-AKI trial? 3. Is there evidence of interaction with hospital type and KRT initiation strategy (i.e., accelerated vs. standard) in the primary and key

	secondary outcomes (i.e., composite of KRT dependence and death at 90-days; KRT dependence at 90-days; KRT-free days at 90-days)?
List of Datasets Used	Data obtained during the STARRT-AKI trial. Additional data regarding hospital information (i.e., number of hospital beds, number of beds in ICU, number of yearly ICU admissions, services offered, urban vs. rural setting and any previous research participation) to be collected by study team.
Time of Data Extraction	TBD

Defining the Cohort	
Cohort	STARRT-AKI cohort (3019 patients)
Exclusion Criteria	None
Size of Cohort	2927

Time Frame Definitions	
Accrual Start/End Dates	October 2015 to September 2019
Max Follow-up Date	90 days from randomization

Variable Definitions	
Main Exposure or Risk Factor	Hospital Type – Teaching vs. Community (as per CIHI definitions)
Baseline Characteristics (Table 1 data)	Same as STARRT-AKI main analysis stratified by Hospital Type
Covariates **(To Inform Model Development)**	Patient Characteristics: Age (Years), body weight (kg), female sex (%), baseline serum creatinine (sCr), baseline eGFR (ml/min/1.73 m2), known chronic kidney disease, hypertension, diabetes mellitus, heart failure, liver disease, admission type, diagnosis, SOFA score at randomization, SAPS II score at randomization, sCr at randomization, mg/dl, hemoglobin at randomization, serum urea at randomization, cardiopulmonary bypass, aortic aneurysm repair, other vascular surgery, trauma, sepsis, receipt of

	mechanical ventilation, receipt of vasoactive medication, cumulative fluid balance at randomization. Site Characteristics: Type of hospital (teaching vs. community), type of ICU admission (medical, surgical, cardiac), geographical location. Community sites will be further classified as small, medium, and large (as per CIHI definitions - https://www.cihi.ca/sites/default/files/document/peer-group-methodology_en.pdf). Hospital characteristics will be ascertained (hospital beds, ICU beds, regional vs. urban/metropolitan, etc.) At KRT initiation: time from ICU admission, days from hospital admission, SOFA score components, TOTAL SOFA score, urine output in preceding 24 hours, cumulative fluid balance at KRT initiation, sCr, serum urea, serum potassium, bicarbonate, pH, hemoglobin.
Outcome(s) Definitions	Primary: death at 90 days. Secondary: KRT dependence at 90-days; composite of KRT dependence or death at 90-days; KRT-free days at 90-days. Tertiary: trial performance measures; frequency of adverse events.

Outline of Analysis Plan	
Primary Outcome Variables	Death at 90 days
Secondary Outcome Variables	Secondary: KRT dependence at 90-days; composite of KRT dependence or death at 90-days; KRT-free days at 90-days; ICU length of stay. Tertiary: Trial performance measures (recruitment rate; exclusion of eligible patients; protocol violations); frequency of adverse events.
Detailed Analysis Plan	Comparative analysis of recruitment, patient characteristics, processes of care, outcomes, and adverse events as in the primary STARRT-AKI study but stratified by type of center (i.e., teaching vs. community). Unadjusted and adjusted comparison from process of care features and patient outcomes. Interaction tests for effect of type of center on process of care variables, randomized allocation, and outcomes. Specifically, the following analyses will be undertaken: 1. Evaluation of patients enrolled in teaching vs. community hospitals. We hypothesize that patients in teaching hospitals will be older, having greater comorbidity burden and higher illness acuity compared to community hospitals. We will further evaluate the performance of patients recruited in teaching vs. community hospitals. We hypothesize that patients in teaching hospitals will have higher consent rates, less exclusion of eligible patients, higher

	co-enrolment rates and fewer protocol violations. We will also assess whether adherence and site features mediate any differences in outcomes between teaching vs. community hospitals. This analysis will only be performed if there is an interaction between hospital type and intervention arm. Sites will be divided according to quartiles of adherence and the effect of the different strategies will be tested in linear or logistic models with the interaction for adherence quartiles. Finally, we will evaluate processes of care in teaching vs. community hospitals. We hypothesize that in teaching hospitals there will be increased time to KRT initiation and greater relative use of CKRT compared with IHD. 2. Evaluation of primary outcomes and secondary outcomes in patients enrolled in teaching vs. community hospitals. We hypothesize that that there are no differences in these outcomes between teaching vs. community. We will also evaluate adverse events in patients enrolled in teaching vs. community hospitals. We hypothesize that there will no differences in adverse events between teaching and non-teaching hospitals. We will also 3. Evaluation of the interaction between the type of center (i.e., teaching vs. community hospital) and strategy for initiation of KRT and outcomes. This will be performed by regression models (i.e., logistic or linear, as appropriate) for the outcomes adjusted for hospital type, intervention arm and their interaction. We will present marginal odds ratios for the effects of KRT initiation and strategy according to hospital type. We hypothesize that there will be no differences in timing of initiation and outcomes between teaching vs. community hospitals. 4. To determine if the variation in KRT is explained by patient vs. site-specific (i.e., teaching vs. community hospital) features using a hierarchical model. This analysis will be performed only for the standard group of patients in the STARRT-AKI trial. A model that predicts KRT modality will be created using relevant patient baselines features as covariates and site as a random intersect. The contribution of fixed effects and site will be estimated by the repeatability index which decomposes the model explained variance according to fixed and random effects. We hypothesize that patient features will explain more of the variability vs. enrolling site.
Proposed Tables and Figures	Same as in STARRT-AKI main analysis; however, stratified by type of center and adjusted for baseline differences in patient characteristics. We will also present the proposed models in items 3 and 4 above.