Data Creation Plan for Secondary Analyses

Name and Number of Study	The association of elevated baseline serum creatinine and decreased eGFR and other markers of chronic kidney disease with key outcomes according to accelerated or standard timing of renal replacement therapy initiation in the STARRT-AKI trial
Principal Investigator(s)	Sean Bagshaw, Ron Wald, Ary Serpa Neto, Rinaldo Bellomo et al.
DCP Update History	Version 1 – January 21, 2022
Short Description of Research Question	It is possible that the presence of baseline chronic kidney disease (CKD), defined by baseline serum creatinine and/or estimated glomerular filtration rate (eGFR) and the additional presence of markers of kidney dysfunction/disease might have influenced the impact of RRT initiation strategies on key outcomes of the STARRT AKI trial. We therefore asked the question: Did high baseline serum creatinine and/or low eGFR and other markers of chronic kidney disease modify key outcomes according to accelerated or standard timing of RRT initiation in the STARRT-AKI trial?
List of Datasets Used	Data obtained during the STARRT-AKI trial
Time of Data Extraction	January 2022

Defining the Cohort	
Cohort	Patients with evidence of a chronically elevated baseline creatinine and/or a low eGFR prior to randomization (CKD), based on KDIGO consensus definitions for CKD.
Exclusion Criteria	Patients without a baseline eGFR or serum creatinine Patients with a normal serum creatinine or eGFR
Size of Cohort	Estimated to be approximately 30% of the total cohort depending on definitions.

	GFR categories in CKD		
	Category	**GFR ml/min/1.73 m^2**	**Terms**
	G1	≥90	Normal or high
	G2	60-89	Mildly decreased*
	G3a	45-59	Mildly to moderately decreased
	G3b	30-44	Moderately to severely decreased
	G4	15-29	Severely decreased
	G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level.
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Assign Albuminuria category as follows:

Albuminuria categories in CKD

Category	**ACR (mg/g)**	**Terms**
A1	<30	Normal to mildly increased
A2	30-300	Moderately increased*
A3	>300	Severely increased**

Abbreviations: ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion ACR >2220 mg/g

Time Frame Definitions	
Accrual Start/End Dates	From randomization to trial treatment
Max Follow-up Date	To 90-day follow up after randomization

Variable Definitions	
Main Exposure or Risk Factor	Presence of baseline CKD (see Form 6 risk factors)
Baseline Characteristics (Table 1 data)	Same as in STARRT-AKI main analysis; however, stratified by the presence or absence of CKD.

Covariates (To Inform Model Development)	Same as in STARRT-AKI main analysis.
Outcome(s) Definitions	Same as in STARRT-AKI main analysis, with a focus on 90-day all-cause mortality, RRT dependence at 90-day, and RRT-free days at 90-days.

Outline of Analysis Plan	
Primary Outcome Variables	Mortality at 90 days
Secondary Outcome Variables	Same as in STARRT-AKI main analysis.
Detailed Analysis Plan	Comparative analysis of process of care, outcome and adverse events as in the primary STARRT-AKI study but split by the presence of CKD or its absence and according to different levels of CKD and adjusting for other factors related to CKD (see Form 6) and the location of baseline data acquisition (outpatient vs. inpatient)
Proposed Tables and Figures	Same as in STARRT-AKI main analysis; however, stratified by CKD status and further stratified by baseline severity of CKD, if feasible.

Mock Tables and Figures (legends):

Table 1: Baseline Characteristics According to the Presence of CKD.

Table 2: Clinical Outcomes According to CKD According to the Presence of CKD.

Table 3: Clinical Outcomes According to Allocation Group.

Figure Legend:

Figure 1. Flow diagram.

Figure 2. Survival stratified by CKD status and allocated RRT initiation strategy.

Figure 3. Forest plot of outcomes by CKD status and allocated RRT initiation strategy.

Figure 4. Summary of RRT-free days by CKD status.