



## Data Creation Plan for Secondary Analyses

Name and Number of Study	The association of regional practice variation and patient outcomes in the STARRT AKI trial.
Principal Investigator(s)	Ary Serpa Neto, Rinaldo Bellomo, Sean Bagshaw, Ron Wald, et al.
DCP Update History	Version 1 – July 16, 2022 Version 2 – July 18, 2022
Short Description of Research Question	<p>It is possible that significant practice variation existed within the STARRT-AKI trial. Such practice variation could have affected processes of care in terms of fluid management (i.e., fluid balance) and choice of RRT modality and, thereby, translated into differences in patient outcomes.</p> <p>We therefore asked these questions. In the STARRT-AKI trial:</p> <ol style="list-style-type: none"> <li>1. Did regional practice (regional defined as North America, Europe, Australia and New Zealand, China and Brazil) vary significantly in terms of baseline patient characteristics, fluid balance and modality of RRT?</li> <li>2. If present, did such practice variation show an association with key primary and secondary patient outcomes?</li> <li>3. If present, did such practice variation show interaction with RRT initiation strategy (i.e., accelerated vs. standard) and primary and secondary patient outcomes?</li> </ol>
List of Datasets Used	Data obtained during the STARRT-AKI trial
Time of Data Extraction	July to August 2022

Defining the Cohort	
Cohort	Full mITT cohort; with patients stratified by region
Exclusion Criteria	No exclusion

Size of Cohort	Full cohort with 994 patients in North America, 1143 patients in Europe, 556 patients in ANZ and 263 patients in China (n=255) and Brazil (n=8) combined.
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Time Frame Definitions	
Accrual Start/End Dates	From randomization to trial treatment and final outcome
Max Follow-up Date	To 90-day follow up after randomization

Variable Definitions	
Main Exposure or Risk Factor	Randomization within a specified region
Baseline Characteristics (Table 1 data)	Same as in STARRT-AKI main analysis; however, stratified by region
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	<p>Comparative analysis of process of care, outcome and adverse events as in the primary STARRT-AKI study but stratified by region. Unadjusted and adjusted comparison for process of care features (e.g., fluid balance and choice of RRT) and patient outcomes. Interaction tests for effect of region on process of care variables, randomized allocation and outcomes.</p> <p>Due to the smaller numbers of patients contributed from China (n=255) and Brazil (n=8), these countries may be excluded from the main analysis.</p>

	In addition, selected countries with large contributions, such as Canada (n=866) and France (760) may be looked at individually in further sensitivity analysis. These will not be reported in the main descriptive analysis.
Proposed Tables and Figures	Same as in STARRT-AKI main analysis; however, stratified by region and adjusted for baseline differences in patient characteristics.

**Mock Tables and Figures (legends):**

**Table 1:** Baseline characteristics according to region.

**Table 2:** Comparison of process of care variables according to region

**Table 3:** Clinical outcomes according to CKD according to region.

**Table 4:** Adjusted clinical outcomes according to region.

**Figure Legend:**

**Figure 1.** Flow diagram.

**Figure 2.** Fluid balance stratified by region.

**Figure 3.** Forest plot of outcomes by region.

**Figure 4.** Summary of RRT-free days stratified by region.