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# Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Disease (WE-ROCK)

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**Introduction**: Continuous renal replacement therapy (CRRT) is used for the symptomatic management of acute kidney injury (AKI) and fluid overload (FO). Contemporary reports on pediatric CRRT are small and single center in design. Large international studies evaluating CRRT practice and outcomes are lacking. Herein, we describe the design of a multinational collaborative.

**Methods**: The Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Disease (WE-ROCK) is an international collaborative of pediatric specialists whose mission is to improve short- and long-term outcomes of children treated with CRRT. The aims of this multicenter retrospective study are to describe the epidemiology, liberation patterns, association of fluid balance and timing of CRRT initiation, and CRRT prescription with outcomes.

**Results:** We included children (n = 996, 0–25 years) admitted to an intensive care unit (ICU) and treated with CRRT for AKI or FO at 32 centers (in 7 countries) from 2018 to 2021. Demographics and clinical characteristics before CRRT initiation, during the first 7 days of both CRRT, and liberation were collected. Outcomes include the following: (i) major adverse kidney events at 90 days (mortality, dialysis dependence, and persistent kidney dysfunction), and (ii) functional outcomes (functional stats scale).

**Conclusion**: The retrospective WE-ROCK study represents the largest international registry of children receiving CRRT for AKI or FO. It will serve as a broad and invaluable resource for the field of pediatric critical care nephrology that will improve our understanding of practice heterogeneity and the association of CRRT with clinical and patient-centered outcomes. This will generate preliminary data for future interventional trials in this area.

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n recent years, our understanding of AKI and the pathologic state of FO in critically ill children and young adults has increased exponentially. Fluid balance (FB) is the difference between total input and output and is often expressed as "daily or cumulative" over a defined duration of time. The 26th Pediatric Acute Disease Quality Initiative defined FO as a pathologic state of FB associated with clinically observable events.<sup>1</sup>

AKI and pathologic FO have been shown to occur commonly among critically ill children and young

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<sup>&</sup>lt;sup>11</sup>The members of the WE-ROCK Investigators are listed in the Appendix.

adults.<sup>2,3</sup> Across 3 international multicenter studies, AKI and the development of FO have been shown to be associated with increased morbidity and mortality.<sup>4-6</sup> As the deleterious impact of AKI and FO has become clear, the field has transitioned toward the prevention, mitigation, and the optimization of interventions to improve outcomes.

Approximately 1% to 5% of critically ill children and young adults with the most severe form of AKI are treated with CRRT. Much of our understanding for prescribing CRRT and the impact on outcomes of critically ill children receiving CRRT are derived from small single center studies and the seminal work of the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) registry. The ppCRRT registry represents the largest registry of pediatric patients treated with CRRT and included 13 centers in the United States.<sup>7–17</sup> This study collected data from 2001 to 2005 and served to set the framework for research and clinical care in pediatric CRRT.<sup>7,8,11,13,15–18</sup> In the nearly 20 years since ppCRRT, there have been significant advances in pediatric and neonatal critical care nephrology technology, practices, education, devices, access, and quality improvement.<sup>18,19</sup> A summary of the published CRRT studies that assessed associations with mortality are included in Table 1. To continue to move the field forward, improve practices, and drive research priorities, a contemporary international multicenter cohort evaluating pediatric and neonatal CRRT is greatly needed.

The WE-ROCK investigator group was established in 2020 comprising pediatric intensivists, pediatric cardiac intensivists, advanced practice nurses, and pediatric nephrologists to develop the mission, vision, strategy, and necessary infrastructure for sustained collaboration to drive the field forward. These primary centers, along with several experts in the field, formed the steering committee for what would become a multinational group that expanded to 32 institutions in 7 countries (USA, Canada, United Kingdom, Italy, Spain, Austria, and Australia) (Figure 1). The WE-ROCK study group was developed with the global aims to better understand the epidemiology, practice differences, as well as the short- and long-term clinical and patient-centered outcomes of children receiving CRRT for AKI and FO.

As the first step to accomplish the global aims, the WE-ROCK investigators collected data from what will be the largest study of children receiving CRRT (n = 996) for AKI or FO. The aims of the initial study from the WE-ROCK investigator group include the following: (i) describe the demographics and predictors of successful CRRT liberation, (ii) understand the current CRRT techniques and practices, (iii) evaluate the

association of the timing of CRRT and pathologic FO at initiation with outcomes, and (iv) assess the patientcentered outcomes using the functional status scale (FSS).<sup>28</sup> The results of these primary studies will enhance our understanding of CRRT practice to facilitate future large multicenter prospective studies and standardize the delivery of care in this population at high risk for morbidity and mortality. Here, we describe the methods, infrastructure, and the formation of the initial studies from the WE-ROCK investigators, the WE-ROCK registry.

### METHODS

#### Design

The WE-ROCK registry is a retrospective multicenter study of pediatric patients receiving CRRT for AKI and FO who were admitted to the pediatric, neonatal, or cardiac ICU from January 1, 2018, to December 31, 2021. Data were entered into the registry from January to August 2022.

#### Setting

Thirty-two institutions in 7 countries (United States of America, Canada, United Kingdom, Italy, Spain, Australa, and Australia) across 4 continents contributed data to the registry (Figure 1). Site principal investigators are listed in Supplementary Table S1 and represent pediatric nephrologists, intensivists, and advanced practice providers. A summary of the total hospital and ICU bed capacity, excluding the neonatal ICU are also summarized in Supplementary Table S1. Centers were classified into small ( $\leq$ 30 ICU beds), medium (>30–60 ICU beds) and large (>60 ICU beds) (Supplementary Figure S1).

#### Population

Eligible participants who fulfill all inclusion criteria and meet no exclusion criteria.

#### **Inclusion Criteria**

The following inclusion criteria were established to capture as many potential study patients as possible who received CRRT:

- Birth to <25 years of age
- Primary CRRT indication of AKI or FO

#### **Exclusion Criteria**

The exclusion criteria are the following:

- Patients with history of end stage kidney disease defined as dialysis dependence before admission.
- Infants with a known diagnosis of severe congenital anomalies of the kidney and urinary tract resulting in end stage kidney disease.

#### Table 1. Characteristics and outcomes of single and multicenter CRRT studies in children

Study	Population	RRT type	Time	Sample size	Incidence of RRT	Survival
Kaddourah <i>et al.</i> 4	Multicenter, prospective N = 73	HD, PD CRRT	3-month period in 2014	73	1.5% of enrolled ICU patients. 5.8% of patients with AKI	67% by 28 days after admission
Jetton <i>et al.</i> <sup>5</sup>	Multicenter, retrospective N = 25	HD, PD CRRT	3-month period in 2014	25	1.2% of enrolled neonates. 4.1% of neonates with AKI	76% to hospital discharge
Chanchlani <i>et al.</i> ª20	Healthcare administrative database, Ontario N = 375	HD, PD CRRT	2010–2015	375	0.65 per 1000 person years in 2015	81% at 30 days
Riley et al.21	Single center, Texas $N = 311$	CRRT	2004–2013	311	Not specified	45% at discharge
Al-Ayed et al.22	Single center, Saudi Arabia N = 96	CRRT	2009–2015	96		50% at discharge
Holt et al.23	Single center, Saskatchewan	CRRT	2007–2020	82		79% at discharge
Erkol Tuncer et al.24	Single center, Turkey	CRRT	2010-2015	50		42% at discharge
Lee <i>et al.</i> <sup>25</sup>	Single center, Korea	CRRT	2003-2016	263		30% at discharge
Tain <i>et al</i> . <sup>26</sup>	Taiwan's health care delivery system	HD, PD, CRRT	2010–2017	412	6.59% of 23,759 encounters in 412 pediatric patients	66.4% at discharge
Yetimakman <i>et al.</i> <sup>27</sup>	Single center, Turkey	CRRT	2009-2016	104		51% at discharge

CRRT, continuous renal replacement therapy; HD, hemodialysis; PD, peritoneal dialysis; RRT, renal replacement therapy.

<sup>a</sup>Chanchlani *et al.*<sup>20</sup> describe dialysis over multiple years. Only the recent cohort from 2010-2015 is reported here.

- Patients receiving CRRT for a non-AKI/FO indication even if it developed during the course of treatment (i.e., ingestion, inborn errors of metabolism, and hyperammonemia).
- Patients on extracorporeal membrane oxygenation concurrently with CRRT or within the 7 days before CRRT initiation
- Patients without end stage kidney disease who received peritoneal dialysis (PD) in the same ICU admission before CRRT initiation (i.e., patients in the cardiac ICU who received PD postsurgically)
- Children receiving CRRT with the CARPEDIEM device (Medtronic Inc) because of an existing registry focusing solely on this device.

# Variable Collection

A detailed summary of collected variables is included in Supplementary Table S2. A manual of procedures was created and disseminated to all participating sites. Education on data collection was provided during monthly collaboration calls and members of the steering committee and data analysts at Cincinnati Children's Hospital Medical Center (CCHMC) were available *ad hoc* for additional queries. Demographic data, including sex, self-reported ethnicity, race, date of birth, date of ICU admission, and date of CRRT initiation were collected for all patients. Race is being included as a variable because of the potential for differences in outcomes.

# **Baseline Characteristics**

Data at ICU admission included the admitting diagnosis, comorbidities, sepsis, Pediatric Risk of Mortality III (PRISM-III) score,<sup>29</sup> height, preillness or dry weight (if available), admission weight, baseline and admission serum creatinine (SCr). Baseline SCr was defined as the lowest SCr (mg/dl) within 90 days before admission. If the baseline was not known or not available, it was back-calculated using the bedside CKiD equation<sup>30</sup> using an estimated glomerular filtration rate of 100 ml/min per 1.73 m<sup>2</sup> as has been previously described and validated.<sup>31</sup>

# **CRRT** Initiation

Data at CRRT initiation included SCr and urinary neutrophil gelatinase associated lipocalin immediately before initiation, presence of sepsis, vasoactiveinotrope score,<sup>32</sup> Pediatric Logistic Organ Dysfunction 2 (PELOD-2) score<sup>33</sup> in the 24 hours prior, FB, and loop diuretic challenge. Hourly urine output was recorded for the 6 hours before, and 6 hours following administration of a loop diuretic. Data on FB were used to calculate percent FO from ICU admission to CRRT initiation, and from dry weight to CRRT initiation using the following equations as previously described.<sup>10</sup>



Figure 1. Map of participating WE-ROCK centers. Symbols denote center. WE-ROCK, Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Disease.

%FO = 
$$\frac{\text{Fluid in} - \text{Fluid out (l)}}{\text{ICU Admission Weight (kg)}} \times 100$$

Or

%FO

$$= \frac{\text{Daily Weight } (\text{kg}) - \text{ICU Admission Weight } (\text{kg})}{\text{ICU Admission Weight } (\text{kg})}$$

 $\times 100$ 

#### Daily CRRT Data

Data were collected from day 0 (defined as the time from CRRT initiation until the start of the next morning shift) until the first CRRT liberation attempt (if before day 7), day 7, or death, whichever came first. A shift was defined as the time at which nursing staff change over. Daily data included weight, FB, urine output, urine neutrophil gelatinase associated lipocalin, SCr, highest serum glucose, phosphorus, and platelet count. Details of CRRT prescription, including device, modality, filter, dose, CRRT fluid type, and anticoagulation were also collected.

#### **CRRT** Liberation Data

If CRRT liberation was attempted at any time during CRRT days 0 to 28, additional information was collected on the first liberation attempt only. Successful CRRT liberation was defined as  $\geq$ 72 hours off renal support therapy, without need for reinitiation of CRRT, hemodialysis, or PD.<sup>34</sup> In the event of a successful liberation, daily weight, net FB, urine output, urine neutrophil gelatinase associated lipocalin, SCr, and serum cystatin C were recorded for up to 7 days post CRRT liberation. No liberation data was collected for those who were not successfully liberated at the first attempt. Only data about the first liberation attempt was captured to identify critical metrics that would be used to identify risk factors for failure of the first attempt.

#### **Outcomes Data**

Specific variables included total ventilation time, length of stay (ICU and hospital), mortality, dialysis dependence, and SCr for those not dependent on

#### Interventions

No intervention was performed.

### **Ethics and Dissemination**

WE-ROCK was proposed as human subject research. Therefore, each participating site sought ethics or institutional review board approval with a waiver of informed consent or parental permission. Data use agreements were signed between each site and the host site (CCHMC). WE-ROCK investigators will disseminate data through peer reviewed publications and presentations at educational conferences.

# Research Electronic Data Capture

Data entry of the variables of interest was performed by participating sites using a web-based database, Research Electronic Data Capture (REDCap)<sup>35</sup> hosted by CCHMC. REDCap is a mature, secure web application for building and managing online surveys and databases. Through this system, each participating site was assigned a unique code by the project managers. For sites that were allowed to enter limited protected health information (date of birth and date of admission) by their institutional review board and data use agreement, age and durations were automatically calculated. Sites which were not allowed to enter dates by their data use agreement, entered the ages and durations manually using a separate calculator that was provided to them. All participating sites used the same case report forms. The electronic case report forms were designed by the steering committee. Research personnel from each site are able to access the data from their site for the purposes of using it to generate quality metrics and create dashboards for improvement. Project managers from the Heart Institute Research Core and Center for Acute Care Nephrology at CCHMC could access data from other sites and were responsible for data management, including corresponding with site principal investigators for data queries and communication of missing data elements. The data integrity and cleaning process occurred from September 1 to January 31, 2023. This was performed in an iterative process by creating rules within REDCap which were sent to site investigators for review and completion. All statistical analyses will be conducted at CCHMC.

# Primary and Secondary Outcomes

Our primary outcome was major adverse kidney events at 90 days (MAKE-90) from CRRT initiation defined as a composite of death, dialysis dependence, or persistent kidney dysfunction (a >25% decline in estimated glomerular filtration rate).<sup>36</sup> The rationale for MAKE-90 is on the basis of the reported estimated median length of stay (42 days, interquartile range 28–71) for children who receive CRRT.<sup>21</sup> Secondary outcomes included successful liberation, ICU mortality, hospital mortality, MAKE at 30 days, length of stay, duration of mechanical ventilation, and functional outcomes using the FSS<sup>28</sup> at hospital discharge, 6 months and 1 year after discharge (survivors only). MAKE at 30 days has not been rigorously evaluated in children. This large, multicenter collaborative will allow us to evaluate whether MAKE at 30 days is a valid outcome metric in children receiving CRRT.

# Analysis

Analysis of data will be conducted independently based on each specific aim using SAS software v9.4 (SAS Institute, Cary, NC, USA). Patients missing data for primary and secondary outcomes will not be included. Multiple imputation will be considered for predictor variables and will be handled separately for each aim as follows:

1. The first aim is to describe liberation patterns among children receiving CRRT and the association with MAKE-90 outcomes. Patients will be divided into the following groups: liberation never attempted, reinstituted (liberation not successful), and liberation successful. We will describe the predictors of liberation success, as well as the risk factors associated with MAKE-90. Liberation success was defined as not needing any dialytic therapy (CRRT, PD, or hemodialysis) within 72 hours of a liberation attempt. We hypothesized as follows: (i) that there would be specific factors associated with liberation success, including only patients who had a trial of liberation; and (ii) that patients with successful liberation would have improved MAKE-90 outcomes compared to those who never had liberation attempted or who failed a liberation attempt. Multivariable logistic regression will be used to assess the factors associated with successful liberation. The model will account for clustering within hospitals and include confounders based on clinical knowledge. Some of the confounders to be included are illness severity, time to CRRT initiation from ICU admission, duration of CRRT to first liberation attempt. A second multivariable logistic regression will be used to assess the association between liberation patterns and MAKE-90. The primary predictors are the liberation patterns (liberated, reinstituted, and never attempted), with the outcome of MAKE-90.

- 2. The second aim is to describe the patient population and technical aspects of CRRT with regard to modality, filter type, prescription, catheter size and location, and anticoagulation to gain insight into which methods may lead to better outcomes and generate hypotheses for clinical trials in pediatric CRRT. These data will be presented descriptively with consideration of stratification by center-level characteristics.
- 3. The third aim is to evaluate association of the timing to initiation of CRRT and FO with MAKE-90 outcomes. Time to CRRT start will be assessed as a continuous and categorical variable with early CRRT initiation defined as within  $\leq$ 48 hours from ICU admission, and late CRRT initiation defined as >48 hours from ICU admission. This time frame was selected on the basis of the work by Buccione and colleagues, where the median time to CRRT start was 40 hours.<sup>37</sup> We hypothesized that longer time to CRRT initiation from ICU admission would be associated with worse MAKE-90 outcomes. Multivariable regression will be used to assess the association between time to CRRT initiation measured in days and MAKE-90. Confounding variables will be selected based on known clinical knowledge. The model will also account for clustering between centers. Secondary outcomes will include ventilation duration and ICU length of stay. Regression models will also be used to determine the association between time to CRRT start and duration of ventilation. We will also perform a propensity score analysis and integrate it into the multivariable model.
- 4. The fourth aim is to evaluate a patient-centered outcome using the FSS.<sup>28</sup> The FSS evaluates patient-centered outcomes across 6 domains, namely mental status, sensory, communication, motor function, feeding, and respiratory function. This tool describes functional outcomes in a reliable, reproducible well-defined way for a wide range of pediatric patients and varied inpatient environments.<sup>28</sup> We will evaluate the change in FSS from premorbid baseline at ICU discharge and at 6 months and 1 year after ICU discharge using outpatient notes as described above among survivors only. We hypothesize that survivors will have worse functional status than their premorbid baseline at all follow-up time points and there will be specific factors associated with development of a new morbidity. A new morbidity will be defined as an increase in FSS score of  $\geq$ 3. Multivariable regression will be used to assess these associations.

We will also separately evaluate a subgroup of patients who weigh < 10 kg in which we will describe the associations between CRRT dosing and outcomes, and evaluate the relationship between body surface areabased CRRT dosing and weight-based dosing. Other subanalyses will be performed based on the submission, review, and approval of ancillary proposals by the ancillary subcommittee (discussed below). Analytical plans for each ancillary proposal will be developed as it pertains to the research question.

#### Oversight

A 12-member steering committee comprising physicians (intensivists, cardiac intensivists, and nephrologists), an advance practice provider, and a nurse was established for study oversight and to develop subcommittees. Each of the subcommittees is chaired by a member of the steering committee and the cochair is a member at large. The subcommittees are each made up of 8 to 10 additional members on a volunteer basis who will serve a term of up to 2 years. The subcommittees include protocol development, protocol implementation, ancillary proposal, and manuscript. Ancillary proposal submission opportunities will be available twice yearly and submitted using a protocol and analysis plan template through REDCap and will be reviewed and scored using a rigorous committee driven peer review process based on science and feasibility. All abstracts and manuscripts will undergo deidentified rigorous review by the manuscript committee before submission. The protocol development and implementation committees will review new proposals that would involve new data collection, and this is discussed in more detail in the discussion section.

## DISCUSSION

The WE-ROCK investigator group has created the largest international multicenter registry of children treated with CRRT. The WE-ROCK study and resulting registry includes 996 children from 32 centers in 7 countries across 4 continents. The registry includes a diverse mix of centers from across the globe with a broad range of patient populations, representing the largest, most inclusive international pediatric CRRT study to date. This WE-ROCK investigator group and the initial registry will provide invaluable data to improve our understanding of pediatric CRRT practices and outcomes around the world.

Contemporary studies evaluating current CRRT practices and outcomes are greatly needed because current CRRT practice in critically ill children are derived from the seminal work by the ppCRRT registry, which was performed over almost 2 decades ago. Since that time there have been small single center studies that have added important data to the literature, which have also highlighted an increasing heterogeneity in CRRT practice. A recent survey disseminated to WE-ROCK participants using a modified Delphi approach highlighted this significant practice heterogeneity among WE-ROCK study centers,38 which is consistent with findings from a recent survey of European<sup>39</sup> and Japanese centers.<sup>40</sup> Understanding how these variations in practice associate with outcomes in critically ill children is essential for advancing our knowledge, determining best practice, and improving outcomes of children as was highlighted in a recent commentary on standardizing care in pediatric CRRT.<sup>41</sup> The 26th Acute Disease Quality Initiative recently published recommendations and highlighted the need for the development and execution of updated studies in pediatric cohorts investigating AKI outcomes, CRRT practices, and outcomes in children treated with CRRT.<sup>1</sup> The WE-ROCK study group is poised through the foundational work described in the design of this international multicenter retrospective study to fill this important void in the literature.

There are several strengths of this registry. This robust international research database captures 325 unique variables beginning with patient demographics, granular data for the first 7 days of both CRRT and the first liberation attempt as well as outcomes. We have captured CRRT practices from 7 countries with plans to expand to several more interested groups that are onboarding, including countries that are not yet represented. With the potential for improved survival, we are evaluating novel patient-centered outcomes using the FSS in children. One of the most important goals and strengths of the WE-ROCK study group is to create a collaborative that would be capable of growing and evolving to include new centers and answer new questions brought forth. As an example, institutional review board and data use agreements are pending from additional regional and international centers. We are actively identifying ways to expand to centers in Asia, Central and South America, Africa, and the Middle East. The repository of data collected will inform critical care nephrologists for many years, and allow for analysis of many epidemiologic associations through subsequent secondary studies. Finally, we have built a robust infrastructure founded on the principles of inclusivity, diversity, and collaboration. Our founding principles will easily extend to collaboration with other existing multicenter and multinational groups, including those which have focused on other acute kidney injury support therapies such as PD, prolonged intermittent renal replacement therapy, and hemodialysis. Indeed, this will allow us to enhance global knowledge together, inclusive of resource limited environments. WE-ROCK has been designed to foster collaboration through participant engagement on

subcommittees for the purposes of improvement of care, multidisciplinary research, career development, and academic advancement. We are actively working on expanding the repository to encompass children supported by CRRT for other indications, such as acute liver failure, or with other circulatory therapies such as extracorporeal membrane oxygenation. The results from the aims described will serve as foundational preliminary data for future prospective studies including participating centers that encompass novel patient-centered outcomes. Furthermore, we have already begun to identify ways to develop near real time quality improvement dashboards for which centers will be able to benchmark their own data using the collaborative data. Important demographic predictors of outcomes, such as sex and social determinants of health will also be the subject of future prospective work to delineate why these differences exist.

The WE-ROCK registry has several limitations. All sites are tertiary or quaternary care centers in high resource countries. Translation of the findings of the proposed analyses will be limited to centers with similar practice models and resources. Centers from low-income and middle-income countries often utilize other methods for acute management of AKI and FO. We did not collect data for other modalities of renal support therapy to limit heterogeneity and capture a robust population of a single dialysis modality. As described above, this limitation can be overcome by our founding principles of collaboration with other groups. The retrospective study design results in missing data points, particularly around details of hourly urine output quantification and response to diuretic challenges, as well as results of specific laboratory tests that may not be considered standard of care, or available at all included centers. It is also possible that we will encounter missing data around MAKE-90 outcomes and FSS reporting at 6 and 12 months post hospitalization. After the database was closed, there were 996 patients in the registry. During the data cleaning process, 16 were identified as being dialysis-dependent or having received CRRT before the start of the study period, thereby leaving 980 patients. MAKE-90 outcome data were not available for 11 patients, thereby leaving 969 (98.8% of the entire cohort) for evaluation of MAKE-90. In subsequent analyses, if MAKE-90 is missing in a large proportion of patients, we will perform a sensitivity analysis to evaluate for differences between groups to limit bias. We will only be able to establish associations, not causality. Because we are only including patients who receive CRRT, we will not be able to identify risk factors for needing CRRT. We are only capturing the first liberation attempt and if it was successful, potentially missing out on other factors that may contribute to recovery and/or survival.

#### Conclusion

The WE-ROCK investigator group has created a diverse, multidisciplinary research collaborative that will provide an invaluable resource to study CRRT practices and outcomes in a broad cohort of critically ill children. In this initial study performed by the WE-ROCK study group, we will aim to better understand the predictors of successful CRRT liberation, current CRRT techniques and practices, the association of CRRT timing and FB with outcomes; and assess patientcentered outcomes in children treated with CRRT. Most importantly, the WE-ROCK study group has created a robust enduring infrastructure, capable of answering the current questions and performing future prospective interventional and observational studies that will serve to be a driving force to improve outcomes in children treated with CRRT.

# **APPENDIX**

# Members of the WE-ROCK CollaborativeInvestigators

The following individuals served as collaborators and investigators for the WE-ROCK studies. They collaborated in protocol development and review, data analysis, and participated in drafting or review of the manuscript, and their names should be citable by PubMed.

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# SUPPLEMENTARY MATERIAL

#### Supplementary File (PDF)

**Figure S1.** Histogram summarizing the number of centers by size according to intensive care unit bed capacity. Hospitals were classified by the total intensive care unit bed capacity inclusive of the cardiac intensive care unit and excluding the neonatal intensive care unit. Small is  $\leq$ 30 beds, medium is >30 to 60 beds and large is >60 beds.

**Table S1.** Site, city, country, principal investigator of WE-ROCK registry, total hospital bed capacity and intensive care unit bed capacity.

**Table S2.** Summary of variables collected. This table summarizes each of the variables collected by category, including baseline and demographics, pre-CRRT initiation, Daily CRRT data for 7 days, additional CRRT information (liberation), daily liberation form for 7 days and outcomes.

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