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Improving the quality of the performance and delivery of continuous renal replacement therapy (CRRT) to critically ill patients across a healthcare system – QUALITY CRRT

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Manuscripts

Improving the quality of the performance and delivery of continuous renal replacement therapy (CRRT) to critically ill patients across a healthcare system – QUALITY CRRT

Dawn Opgenorth¹, Ellen Reil², Vincent Lau¹, Nancy Fraser³, Danny J Zuege^{3,4}, Xiaoming Wang², Sean M. Bagshaw^{1,3}, Oleksa G. Rewa^{1,3}

¹ Department of Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta and Alberta Health Services

² Alberta Health Services

³ Critical Care Strategic Clinical Network, Alberta Health Services

⁴ Department of Critical Care Medicine, Cumming School of Medicine, University of Calgary and Alberta Health Services

Corresponding Author

Oleksa G. Rewa

Assistant Professor

Department of Critical Care Medicine

University of Alberta

CSB 2-124 8440 112th St NW

Edmonton, Alberta

T6G 2B7

t. 780 263 3280

f. 780 492 1500

e. rewa@ualberta.ca

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Abstract (235 words)

Introduction: Continuous Renal Replacement Therapy (CRRT) is a continuous form of dialysis used to support critically ill patients with acute kidney injury. The ideal delivery of CRRT requires ongoing monitoring and reporting to adjust practice and deliver optimal therapy.

However, this practice occurs variably.

Methods: QUALITY CRRT is a multi-center, prospective, stepped-wedged, interrupted time-series evaluation of the effectiveness, safety and cost of implementing a multi-faceted CRRT quality assurance and improvement program across an entire healthcare system. This study will focus on the standardization of CRRT programs with similar structure, process and outcome metrics by the reporting of CRRT Key Performance Indicators (KPIs). The primary outcome will be the quarterly performance of CRRT KPIs. Secondary outcomes will include patient-centered outcomes and economic outcomes. Analysis will compare pre- and post-implementation groups as well as for the performance of KPIs using an interrupted time-series methodology. The health economic evaluation will include a within-study analysis and a longer-term model-based analysis.

Discussion: The effective delivery of CRRT to critically ill patients ideally requires a standardized approach of best practice assessment and ongoing audit and feedback of standardized performance measures. QUALITY CRRT will test the application of this strategy stakeholder engagement and stepped-wedged implementation across an entire healthcare system.

Ethics and Dissemination: This study has received ethics approval. We will plan to publish the results in a peer-reviewed journal.

Trial Registration: clinicaltrials.gov, NCT04221932, first posted 9 January 2020.

Strengths and Limitations

- **Quality CRRT involves the implementation of CRRT KPIs across an entire healthcare system**
- **Study includes pilot program followed by broader stepped-wedged roll out of CRRT KPIs across all ICUs performing CRRT**
- **Included CRRT KPIs informed from current evidence-base as well as stakeholder surveys**
- **Study limited to CRRT and does not include IRRT**

Introduction

Continuous renal replacement therapy (CRRT) is a continuous method of blood purification that provides slow uninterrupted clearance of uremic toxins and enables acid-base, electrolyte and volume homeostasis while preserving hemodynamic stability.[1, 2]

CRRT is the most common initial form of dialysis in ICU settings

The recent epidemiological study, AKI-EPI, revealed that CRRT was the most common form of initial acute RRT for patients with severe AKI.[3] These patients have greater illness severity, are more likely to die and have significantly increased healthcare utilization when compared to their non-CRRT critically ill counterparts.[2] As our population ages, becomes more medically complex, and presents with greater severity of illness, the utilization of CRRT is likely to increase and become an increasingly vital component of life-sustaining therapy.[3]

CRRT is expensive but there are substantial opportunities to improve costs

CRRT is a costly and labour intensive resource.[4] In the setting of increasingly constrained healthcare resources, intervention is needed which may identify and eliminate inefficiencies, improve performance, and decrease waste while improving provider satisfaction and achieving better patient outcomes.[5, 6] Currently, performance indicators for CRRT are not routinely measured, and as such, we are not in a position to understand or identify the inefficiencies or gaps in the quality of care of CRRT delivered to our sickest patients.[6]

Current CRRT practices are not standardized

In our healthcare system, CRRT is delivered as per individual unit protocols and practice patterns and is not consistently monitored (i.e., initiation strategies, anticoagulation techniques, dose delivered, ultrafiltration, etc). Discrepancies from best practices and lack of standardization

of CRRT delivery can result in unplanned CRRT interruptions, decreased treatment time, inadequate dose delivery, and impaired clearance of toxic metabolites which can lead to worsened patient outcomes.[7, 8]

Such suboptimal practice variation may relate to the lack of well-developed key performance indicators (KPIs) for CRRT delivery and performance, and the associated audit and feedback function such KPIs can facilitate. KPIs are measures that can be used to monitor the performance of healthcare delivery.[9] They are necessary and can improve reliability of care, standardize complex interventions, and provide a platform to measure and monitor performance and the impact of practice changes.[10, 11]

Recently, previous phases of work have identified and prioritized KPIs for CRRT care.[12, 13] Implementing these CRRT KPIs may change practice to provide effective, validated and standardized CRRT.[12, 13] Though several previous programs of work have looked to implement these CRRT KPIs into clinical practice, but no program has rigorously tested the implementation of this structure and monitoring across an entire healthcare system.[14-16]

Objectives and Research Questions:

Primary Objective

The primary objective is to improve the quality of care delivered to critically ill patients receiving CRRT in Alberta, as measured by CRRT KPI performance.

Secondary Objectives

These will include patient centered outcomes (i.e., ICU mortality and length of stay, duration of

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3 CRRT therapy, 90-day renal recovery) and cost of health services, including unit specific CRRT
4 costs.
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8 9 **Research Hypotheses:**

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12 1. Can we improve the performance of CRRT programs through the implementation of
13 evidence-based clinical practice guidelines and provision of targeted multi-faceted CRRT
14 audit, feedback and education sessions?
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16
17 2. Will the implementation of standardized CRRT programs our healthcare system's ICUs
18 result in decreased healthcare systems costs?
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21 3. What is the impact of a multi-faceted quality assurance and improvement program on the
22 efficacy and safety of care in critically ill patients requiring CRRT across our healthcare
23 system?
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35 **Methods**

36 **Trial Design**

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38 The QUALITY CRRT trial is a pragmatic, multi-center, population-level, stepped-wedged,
39 interrupted time series evaluation of the implementation of an evidence-based CRRT quality
40 assurance and improvement program to standardize the delivery of CRRT in the 15 adult
41 general and cardiac ICUs and 3 pediatric ICUs in our healthcare system that provide CRRT
42 (Table 1). It conforms with the SPIRIT Checklist for study protocols (see Appendix 1).
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51 **Trial Oversight**

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3 QUALITY CRRT will be led by a small but specialized Steering Committee whose members
4 bring extensive experience with CRRT programs and clinical leadership, implementation science
5 and healthcare systems research. This pan-provincial team will be based at the University of
6
7
8 Alberta Hospital and will include representation from the Critical Care Strategic Network of
9
10
11 Alberta Health Services (the provincial body which provides provincial liaison, networking and
12
13
14 coordination of adult and pediatric critical care in Alberta).[17] The Steering Committee will be
15
16
17 responsible for program management, development and implementation of minimum standards
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19
20 for CRRT programs, KPI reporting, targeted education and overall trial management.
21
22
23

24 **Patient and Public Involvement**

25
26 While this study currently does not directly include patients in its design, the Critical Care
27
28 Strategic Clinical Network includes patient representatives on its core committee and is
29
30 represented on the study team. The study objectives and research hypotheses have been
31
32 developed along with these members. Finally, the results of this study will be disseminated to
33
34 patients and families leveraging the strengths of the Critical Care Strategic Clinical Network
35
36 through online resources, publications and public engagement events (i.e., Café Scientifiques).
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43 **Population and Eligibility**

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45 This study will be conducted at all ICUs in Alberta capable of providing CRRT. All subjects in
46
47 this study will be critically ill patients (i.e., pediatric and adult) receiving CRRT as part of their
48
49 care. There will be no exclusion criteria. The inclusion criteria are purposely broad in scope to
50
51 capture a systems level sample of critically ill patients where new monitoring and policy may
52
53 be implemented, and outcomes measured on a population-based level.
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3 All new ICU admissions receiving CRRT in the 15 adult and 3 pediatric ICUs in Alberta who
4 provide this therapy will be included in this project. In 2019, there were 12,132 adult and 1,592
5
6 pediatric admissions per year with 5.6% and 1.4% of these patients (i.e., 680 adult and 22
7
8 pediatric patients) receiving CRRT. As this study will be conducted over a 4-year period, thus
9
10 data on approximately 3,000 adult and pediatric (i.e., 2900 adult and 100 pediatric) patients will
11
12 be included in this project.
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16 17 18 **Interventions, duration and frequency of follow-up**

19
20 The project consists of a 24-month baseline phase to measure current CRRT practice and a 24-
21
22 month intervention phase to implement a standardized CRRT program targeting ICUs-based
23
24 CRRT KPIs and monitor performance and compliance of participating sites. Data from the 24-
25
26 month intervention phase will be used to model long-term health economic outcomes.
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30 31 **Baseline Phase**

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33 Baseline data collection: baseline clinical and resource utilization data will be collected on all
34
35 patients having received receiving CRRT between November 1, 2017 and October 31, 2019.
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38 Stakeholder survey: A healthcare system-wide survey of care providers and stakeholders at
39
40 participating ICUs will be conducted to identify and establish agreement on the most appropriate
41
42 KPIs to measure at their ICU during the intervention phase. The survey will be administered
43
44 through Survey Monkey (www.surveymonkey.com).
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47 48 **Intervention Phase**

49
50 KPI benchmark reporting: The primary study intervention will be the implementation of audit
51
52 and feedback on CRRT KPI benchmarks identified by the individual ICU teams in the baseline
53
54 survey. We will implement a minimal bundle of potential CRRT KPIs with evidence to measure
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3 will include CRRT program structure, filter life, downtime, delivered dose, ultrafiltration
4 achieved, alarms, adverse events, ICU mortality and renal recovery (Table 2).[6, 12, 13]
5
6 Reports will be implemented and reviewed with ICU stakeholders ad hoc and at quarterly
7
8 intervals.
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11
12 Prior to implementation of the reports, each ICU will receive multi-faceted education strategies
13 tailored to their site and informed by local CRRT leaders, champions and stakeholders (Table
14 3). Education strategies will include, 1) inter-professional grand rounds, seminars and webinars
15 supported by a web-based information repository, 2) identification of site champions to provide
16 onsite advocacy and education. The intervention will be multidisciplinary, targeting CRRT
17 prescribers, nurses, unit operational leaders and educators. After the intervention is
18 implemented quarterly audit and feedback reports and quarterly tele/videoconference and/or in-
19 person visits will be conducted to support the ICUs. The content of this feedback and methods
20 will be individualized to individual ICU needs and preferences.
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34 While the initial education strategy will contain similar themes across all sites, each site will be
35 encouraged to facilitate and participate with our working group in their own audit and
36 educational activities to address unit specific shortcomings in their CRRT KPI performance. A
37 central website repository of troubleshooting tools that will be hosted by the Critical Care
38 Strategic Network of Alberta Health Services will be available for sites who are not achieving
39 KPI benchmarks.
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48 The CRRT KPI reporting program will be implemented in a stepped fashion with a pilot
49 occurring at the GSICU at the UAH over a 3-month period to ensure feasibility, proper
50 reporting and compliance. This will lead to optimization of the tools prior to more generalized
51 use. The pilot will be followed by a stepped-wedge roll out at centers across Alberta over the
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subsequent 12 months.

Intervention data collection: At the end of the intervention phase, clinical and resource utilization data will be collected on all patients receiving CRRT during the 24-month intervention period (Table 4).

Outcomes

Primary Outcome

The primary endpoint measures are quarterly changes in the performance of the CRRT process

KPIs:

- Average filter lifespan, measured in hours
- Downtime, as percentage of prescribed time
- Delivered dose, as a percentage of prescribed dose
- Ultrafiltration achieved, as a percentage of prescribed ultrafiltration
- Alarms as recorded per machine, per day

Secondary Outcomes

Patient centered

- Mortality - ICU, hospital, 90-day post discharge
- Length of stay - ICU and hospital
- Duration of CRRT treatment in hours
- Renal recovery 90-days post ICU discharge

Health economic

- Supply costs - dialysis filters, fluids, dialysis catheters

- Medication costs – anticoagulation, renal specific replacement medications (e.g. erythropoietin analogues, calcium binders, etc.)
- Health care worker costs – physician billing, nursing (hrs)
- ICU and hospital stay costs (length of stay)
- Progression to end stage renal disease - projected chronic dialysis costs
- Quality of life adjusted years (QALYs)
- Health-related Quality of Life (HRQoL)
- Total health care costs

Data Management

Data elements will include patient centered variables: (i.e., demographics, type of admission [medical, surgical, trauma]), clinical characteristics (i.e., comorbid diseases, primary diagnosis), illness severity (i.e., APACHE II, Sequential Organ Failure Assessment [SOFA], Clinical Frailty Score [CFS]), treatment intensity (i.e., duration of renal replacement therapy, mechanical ventilation, vasoactive therapy), ICU and hospital lengths of stay, and outcomes (i.e., renal recovery, mortality, HRQoL); and CRRT associated cost data: (i.e., filter use, prescription/dose, machine alarms/down time, coagulation, adverse events, re-hospitalizations, progression of renal disease). A schedule of data variables to be captured is summarized in Appendix 2.

Data sources will include TRACER and Enterprise data repository, AHS Data Integration, Management and Reporting (DIMR) administrative databases, the Nephrology Information System (NIS), the Patient based Renal Information System (PARIS) and Baxter Healthcare Inc.[18]

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3 All study documents will be kept in a locked filing cabinet in a locked office, and computer files
4 will be encrypted and stored on a secure network for 5 years following completion of the study.
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8 9 **Co-Enrollment**

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11 QUALITY CRRT is a pragmatic, real world, quality improvement and assurance program. Due
12 to the healthcare systems scope of the program, there are no patient-level interventions.
13

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15 Accordingly, there will be no limitations to co-enrollment or specific patient or clinician
16 practices.
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20 21 22 **Statistical Analyses**

23
24 Analysis will be conducted between the pre- and post-implementation groups. Analyses of the
25 primary and secondary outcomes will involve summary measures obtained by aggregating the
26 endpoints. Analyses will be performed using SAS Enterprise Guide 7.1 (Cary, North
27 Carolina, USA). Baseline comparisons will be performed using chi-squared test for equal
28 proportions with results to be reported as frequencies with percentages. Continuous normally
29 distributed variables will be compared using t-tests and reported as means with standard
30 deviation, while non-parametrically distributed will be compared using Wilcoxon rank sum
31 tests and reported as medians and interquartile ranges (IQRs). In case of small sample size,
32 Fisher's exact test will be used.
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47 Interrupted time series (ITS) analyses using autoregressive integrated moving average
48 (ARIMA) models will be employed for important risk factors to account for temporal trends
49 and to determine whether there were changes in the clinic outcomes at the intervention period
50 (compared with the baseline period) and associated with implementation of the evidence-based
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3 acute RRT pathway.
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6 Cost-effectiveness or net-benefit (investment-return) analysis using a decision tree will be
7
8 adopted to compare return (or benefit, B) and investment (or cost, C) of the evidence-based
9
10 RRT pathway. Reduction of healthcare systems costs including inpatient services (length of
11
12 stay of primary admission, number of readmissions, and readmission LOS), outpatient services
13
14 (emergency room visits, and clinic visits), physician services (specialist visits, and general
15
16 practitioner visits), and ongoing new end-stage renal disease will be estimated based on
17
18 generalized linear models. Cost-effectiveness will be analyzed by estimating incremental cost
19
20 and effectiveness based on quality-adjusted life years (QALYs) gained. QALYs will be
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22 calculated based on health-related quality of life as measured by the 5Q-5D-5L and SF-36 in
23
24 adults and the PedsQL in children.
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29 **Performance of CRRT KPIs**

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32 Our primary outcome will be the iterative performance of selected CRRT KPIs. Based on prior
33
34 work, KPIs might include filter life (measured in hours), delivered dose (measured in
35
36 mL/kg/hr), downtime (measured in percentage of time), ultrafiltration realized (measured in
37
38 percentage of prescribed) and access alarms (measured in total number per day). We will aim
39
40 to both compare the performance of these KPIs to historical controls, as well as prospectively
41
42 through an interrupted time-series analysis. The interrupted time-series analysis will allow us
43
44 to follow variable changes over time, allow for assessment of gradual change, and is consistent
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46 with traditional quality improvement initiatives.
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51 **Patient-Centered Outcomes Analysis**

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53 The patient-centered outcome analysis will include ICU, hospital and 90-day mortalities, ICU
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55 and hospital lengths of stay, duration of CRRT treatment, and renal recovery measured at 90-
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3 days months. While this study is not designed to evaluate the effect that the implementation of
4
5 the reporting of CRRT KPIs will have on mortality, lengths of treatment and stay or renal
6
7 recovery, these are important patient-centered outcomes that will need to be considered as
8
9 balancing measures for CRRT KPI reporting and implementation of our multi-faceted
10
11 knowledge translation intervention.
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14 15 **Health Economic Evaluation**

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17 The economic evaluation will comprise two parts: 1) a within-study analysis, and 2) a longer-
18
19 term, model-based analysis.
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23 The within-study analysis will focus on costs and outcomes collected during the study period. It
24
25 will include total quarterly unit-specific CRRT-associated costs following the implementation
26
27 of the CRRT KPI reporting program. This endpoint will be determined from our provincial CIS
28
29 and Alberta Blue Cross databases. Specifically, we will evaluate and compare the 1) costs of
30
31 supplying CRRT filters, 2) costs of CRRT fluids, 3) cost of CRRT anticoagulation and, 4) costs
32
33 and utilization of dialysis catheters. Costs will be calculated in part using CRRT process
34
35 measures captured by our CRRT KPIs (i.e., filter life and number of filters used,
36
37 anticoagulation modality, dose delivered, and effluent used, etc.). CRRT-associated costs were
38
39 selected as an important secondary outcome as these will be most immediately affected with the
40
41 implementation of the CRRT KPI quality assurance program across unit.
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47 We will also determine healthcare systems costs to include total ICU and hospital stay
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49 associated costs, ongoing new end-stage renal disease (i.e., chronic RRT) costs, total healthcare
50
51 costs, and outcomes [mortality, quality-adjusted life years (QALY)]. Modelling analysis will
52
53 provide cost estimates from both a healthcare system and societal perspective (capturing costs
54
55 to the health service, social care providers and patients). Results will be reported as the
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3 incremental net benefit and incremental cost-effectiveness ratios. Uncertainty will be captured
4
5 in the analyses through probabilistic sensitivity analysis and reported using cost-effectiveness
6
7 acceptability curves, showing the likelihood the intervention will be cost-effective over a range
8
9 of values of willingness-to-pay for specific outcomes.
10
11

12 13 **Planned Subgroup Analyses**

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15 Pre-specified subgroup analysis will include ICU patients to 1) adult vs. pediatric, 2) female vs.
16
17 male, 3) academic vs. community ICUs, 4) cardiovascular ICUs vs. medical/surgical ICUs, 5)
18
19 high volume vs. low volume centers (i.e., as per quartiles) 6) patients requiring acute RRT vs.
20
21 those on chronic dialysis. Adult, pediatric, female and male patients are fundamentally different
22
23 patient populations and deserve specific study.
24
25

26
27 Cardiovascular ICU patients differ from general medical/surgical patients as often these
28
29 patients are immediately post-operative, have a specific timing of insult (i.e., cardiac surgery)
30
31 and hence have different pathophysiology related to their critical illness. It is important to
32
33 delineate academic vs. community ICUs as, for mechanically ventilated patients (i.e., another
34
35 form of critical life-sustaining therapy) with acute respiratory distress syndrome (ARDS),
36
37 mortality rates differ significantly.[19] Finally, higher ARDS hospital case volume has also
38
39 been associated with lowers ARDS hospital mortality and it will be important to determine if
40
41 this association is present in CRRT.[20] We will perform the above analyses for health
42
43 economic evaluations, patient and process of care measures to include our pre-specified
44
45 primary and secondary outcomes for each subgroup. Each analysis will be accompanied by a
46
47 test for interaction between treatment and subgroup to ascertain whether effects differ
48
49 significantly between subgroups.
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56 **Ethics Approval and Consent to Participate**

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3 This project is an evaluation of impact of a multi-faceted CRRT quality assurance and
4 improvement program on patient outcomes and health care resource utilization in Alberta ICUs
5 delivering CRRT. All diagnostic and management strategies are within standard of care and all
6 data with relevance to the project are already routinely captured as part of standard patient care
7 by means of machine specific data cards or clinical charting. No added trial-specific
8 investigations or clinical documentation is required.
9

10
11 This evaluation was reviewed by the University of Alberta Health Research Ethics Board
12 (HREB) (Pro00075274 January 22, 2020) and a waiver of consent was granted based on the
13 premise this project represents health services implementation and evaluation compatible with a
14 quality assurance and improvement initiative (see Appendix 3).
15

16
17 Any protocol modifications will be submitted to the appropriate relevant parties.
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19

20 21 22 23 24 25 26 27 28 29 30 31 **Dissemination**

32
33 The findings of QUALITY CRRT will directly inform and guide policy on establishing
34 evidence-based best-practices guidelines for delivering CRRT in Alberta ICUs. In addition,
35 establishing evidence-based benchmarks across the entire health care system will enable
36 systematic evaluation of CRRT performance. These outcomes will help create a framework for
37 the standardization of CRRT programs across Alberta and other jurisdictions providing CRRT.
38 (Table 2).
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47
48 Alberta's comprehensive ICU clinical information and analytics infrastructure (Connect Care,
49 eClinical TRACER) will be leveraged to implement a CRRT Quality Dashboard, accessible to
50 all Alberta ICU practitioners. The dashboard will contain statistics on KPI benchmarks to
51 provide real-time feedback on individual ICUs performance in delivering CRRT.
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3 A central website containing a summary of CRRT guidelines and best practices and a repository
4 of troubleshooting tools on attaining KPI benchmarks will be developed and made available to
5
6 all Alberta CRRT practitioners.
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10 We are proposing to publish the study results. Further, this work will be presented at local,
11 provincial and national critical care and nephrology meetings. Finally, QUALITY CRRT will
12 serve as the basis for a broader program of work, DIALYZING WISELY, which will aim to
13 transform the fashion in which acute dialysis is conducted in Alberta.
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23 Discussion

24
25 The importance of the quality and management for critically ill patients with acute kidney injury
26 requiring CRRT has been previously recognized.[5, 6] Previous studies have focused on single
27 unit or individual hospital-level quality improvement and assurance interventions (Table 5).[14-
28 16] Griffin et al., first conducted such a quality improvement study at the University of Colorado
29 Hospital where they assessed the magnitude in variability in CRRT dosing. They followed
30 specific implementation that included optimizing their electronic medical record to calculate
31 CRRT dosing in real-time to then comment on dosing and provide guidance and education in
32 order to better adhere to national guidelines. This led to the doubling of the rate of appropriate
33 CRRT dosing, and reduction in variability.[14] Mottes et al., at the University of Cincinnati
34 Children's Hospital, created a 'CRRT Dashboard' which tracked important KPIs such as 'filter
35 life,' 'mean prescription dose,' and 'fluid balance,' and found that this platform provided a
36 significant means for measuring adherence to robust standards on the delivery of CRRT,
37 specifically in the process of care.[15] Finally, most recently a group from the University of
38 Kentucky Medical Centre reported the development, implementation, and subsequent outcomes
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3 associated with a quality assurance system to support the provision of CRRT in the ICU.[16]
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5 This was the largest program to date, numbering 1185 adult patients on CRRT over a 34-month
6
7 period. Using the monitoring of evidence-based KPIs and targeted education, they doubled the
8
9 appropriate use of citrate-based anticoagulation, improved the appropriateness of CRRT-dosing,
10
11 increased filter life while decreasing machine alarms and maintaining similar CRRT duration and
12
13 patient mortality while reducing CRRT-costs. While these programs demonstrate that the
14
15 implementation of evidence-derived KPI-based CRRT quality assurance programs are effective
16
17 in improving the efficiency and quality of CRRT, none of these programs have sought to do this
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19 on an entire healthcare systems level. QUALITY CRRT will build on the experience of these
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21 programs in order to scale such a quality improvement and assurance initiative across a
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23 provincial health system of ICUs which provide CRRT.
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31 **Strengths & Limitations**

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33 While QUALITY CRRT focuses on standardizing CRRT programs across an entire provincial
34
35 healthcare system by ensuring a robust framework is in place and the monitoring of CRRT
36
37 performance and delivery occurs, this is limited to only continuous RRT. Intermittent RRT can
38
39 also occur in the acute setting for critically ill patients in the ICU. Accordingly, the experience
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41 and infrastructure realized in QUALITY CRRT will pave the work for additional critical care
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43 nephrology programs aimed at improving all forms acute RRT (i.e., continuous and intermittent)
44
45 in the ICU.
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52 **Contributorship Statement**

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3 SMB and OGR were responsible for the conception, design and planning of this study. XW and
4
5 VL were responsible for data analysis and interpretation of the data. All authors were part of
6
7 reporting and drafting of this manuscript.
8
9

10 11 12 **Competing Interests** 13

14 Drs. SBM and OGR have received honoraria from Baxter Healthcare Inc.

15
16
17 The study sponsors had no role in protocol development, trial management or data analysis and
18
19 reporting.
20
21

22 23 24 **Funding** 25

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27
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Table 1. Alberta ICUs Delivered CRRT

Site	City	ICU Type	Hospital Type	Beds
University of Alberta Hospital General Systems ICU	Edmonton	Mixed	Academic	32
Mazankowski Alberta Heart Institute Cardiovascular ICU	Edmonton	Cardiac surgery	Academic	24
Mazankowski Alberta Heart Institute Cardiac ICU	Edmonton	Cardiac	Academic	8
Royal Alexandra Hospital ICU	Edmonton	Mixed	Academic	25
Grey Nuns Hospital ICU	Edmonton	Mixed	Community	8
Misericordia Hospital	Edmonton	Mixed	Community	10
Sturgeon Hospital ICU	Edmonton	Mixed	Community	5
Stollery Children's Hospital Pediatric ICU	Edmonton	Mixed	Academic	16
Stollery Children's Hospital Pediatric Cardiac ICU	Edmonton	Cardiac	Academic	16
Foothills Medical Centre ICU	Calgary	Mixed	Academic	28
Foothills Medical Centre Cardiovascular ICU	Calgary	Cardiac surgery	Academic	16
Foothills Medical Centre Cardiac ICU	Calgary	Cardiac	Academic	18
Peter Lougheed Centre ICU	Calgary	Mixed	Academic	18
Rockyview General Hospital ICU	Calgary	Mixed	Community	10
South Health Campus ICU	Calgary	Mixed	Community	10
Chinook Regional Hospital ICU	Lethbridge	Mixed	Regional	7
Red Deer Regional Hospital ICU	Red Deer	Mixed	Regional	12
Alberta Children's Hospital Pediatric ICU	Calgary	Mixed	Academic	15

Table 2. Standardized Elements of CRRT Programs

Program Element	Operational Definition	Benchmark
CRRT Leadership	Presence of both CRRT physician and clinical nurse educator	100%
CRRT Education	Number of CRRT providers with training/ total number of CRRT providers	100%
Filter Life	Number of filters lasting 72 hours/ Total number of filters used	> 50% of filters
Delivered Dose	Actual delivered dose in ml/Kg/h / Prescribed dose in ml/Kg/h	> 85% of dose and between 25-30 ml/Kg/h
Downtime	Time CRRT not running per day/ Each day of CRRT prescription	< 15%
Ultrafiltration	Actual ultrafiltration achieve in ml/Kg/h/ Prescribed ultrafiltration in ml/Kg/h	>85% of prescription
Access Alarms	Number of alarms recorded per machine per day of therapy	< 5 alarms
Adverse Events	Number of adverse events as per RLS per quarter	0 events
ICU Mortality	Patient survival to ICU discharge	> 50%
Renal Recovery	Number of patients still requiring RRT at 90-days	< 10%

*CRRT Program Elements are shaded from white to light grey to dark grey as per the Donabedian framework of *structure*, *process* and *outcome*. Specific CRRT KPIs are in bold. Benchmarks have been taken from our internal and external validation of the KPIs. Our primary outcome will measure the performance of specific CRRT process KPIs.

Table 3. Components of the multi-faceted intervention and knowledge implementation strategy

Strategy	Description
Education	<ul style="list-style-type: none"> • Site grand rounds and inter-professional seminars • Monthly video/teleconferencing sessions • Site specific educational sessions by inter-professional content experts and local champions • Provide a summary of current guidelines and best practice • Development of website for repository of evidence supporting implementation including banked webinar of project • In-person or virtual visits with ICU leadership, champions and investigator teams
Coaching	<ul style="list-style-type: none"> • Provide ongoing resources for interpretation of KPI reports • Common troubleshooting advice cards • Provide clinical decision support resources
Audit and Feedback	<ul style="list-style-type: none"> • Baseline and monthly reports of process of care indicators of implementation of the intervention • Comparative performance relative to peer ICUs across province • Quarterly video/teleconferencing sessions to discuss provincial KPI reports
Reminders	<ul style="list-style-type: none"> • Promotional items (posters; bulletins) • Weekly electronic communication to local site champions to ensure ongoing review of KPI reports and access to additional resources

Table 4. Project Timeline

Activity by Quarter	2020				2021				2022				2023		
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3
	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep
Approvals															
Ethics approval/renewal - HREB	■				■				■				■		
Ethics approval/renewal - CHREB		■				■				■				■	
CTA/Administrative approvals	■														
DDA – Edmonton/Calgary/Regional		■													
Baseline phase															
Recruit Executive/Steering committee			■	■											
Conduct survey			■												
Extract baseline data - UAH			■												
Extract baseline data – all sites			■	■											
Develop education strategies			■	■	■	■									
Intervention phase															
Initiate pilot GSICU						■									
Initiate other sites						■	■	■	■						
Implement education strategies						■	■	■	■	■	■	■	■	■	■
CRRT KPI reporting						■	■	■	■	■	■	■	■	■	■
Protocol Manuscript						■	■	■	■						
Extract intervention phase data														■	
Study Manuscript															■

Table 5. Previous CRRT QI Initiatives

Study	Setting	Sample Size	KPI(s) studied	Intervention	Outcomes
Griffin et al. 2019	<ul style="list-style-type: none"> Single center Adult Medical/Surgical Nephrology prescription 	<ul style="list-style-type: none"> 837 CRRT treatment sessions 	<ul style="list-style-type: none"> Delivered dose 	<ul style="list-style-type: none"> Stakeholder engagement Modification to EMR Training of ICU nurses Standardization of protocol Improved documentation Modification of order sets Result dissemination 	<ul style="list-style-type: none"> Increased in treatments achieving dose (66.3% vs. 33.3%, p<0.001) Decline in under-dose treatments (11.7% vs. 20.7%, p<0.001) Decline in over-dosed treatments (22% vs. 46%, p<0.001)
Mottes et al. 2019	<ul style="list-style-type: none"> Single center Pediatric Newborn, cardiac, pediatric Nephrology prescription 	<ul style="list-style-type: none"> 184 patients 2090 patient days 	<ul style="list-style-type: none"> Filter life Unplanned filter changes Prescribed effluent dose Delivered vs. prescribed effluent dose Fluid balance 	<ul style="list-style-type: none"> Development of CRRT quality dashboard Provided targeted provider based CRRT education 	<ul style="list-style-type: none"> Mean filter life increase from 50 to 56 hours Unplanned filter change 33% to 15% Mean delivered dose increased from 2400ml/hr/1.73m² to 2845ml/hr/1.73m² Delivered time increased from 81.1% to 92.7% Increase in achievement of daily desired fluid balance from 69.2% to 83.3%
Ruiz et al. 2020	<ul style="list-style-type: none"> Single center Adult Medical/Surgical Nephrology prescription 	<ul style="list-style-type: none"> 1185 patients 7420 patient-days 	<ul style="list-style-type: none"> CRRT modality Anticoagulation Delivered dose Delivered/Prescribed dose Filter life CRRT access alarms 	<ul style="list-style-type: none"> Assembly of multidisciplinary team Standardization of CRRT protocol Improvement of CRRT charting Report of CRRT QI metrics Education to clinicians and ICU nurses 	<ul style="list-style-type: none"> Increase in CVVHDF use (92.4% to 100%, p<0.001) Increase in RCA use (23.1% to 39.5%, p<0.001) Improved filter life (26 to 31.2h, p=0.02) Decrease in access alarms (2.95 to 1.68/d, p=0.02)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	1
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 19

1	Roles and	#5b	Name and contact information for the trial sponsor	1
2	responsibilities:			
3	sponsor contact			
4	information			
5				
6				
7	Roles and	#5c	Role of study sponsor and funders, if any, in study	18
8	responsibilities:		design; collection, management, analysis, and	
9	sponsor and funder		interpretation of data; writing of the report; and the	
10			decision to submit the report for publication, including	
11			whether they will have ultimate authority over any of	
12			these activities	
13				
14	Roles and	#5d	Composition, roles, and responsibilities of the	7
15	responsibilities:		coordinating centre, steering committee, endpoint	
16	committees		adjudication committee, data management team, and	
17			other individuals or groups overseeing the trial, if	
18			applicable (see Item 21a for data monitoring committee)	
19				
20				
21				
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24				
25				
26	Introduction			
27				
28	Background and	#6a	Description of research question and justification for	4
29	rationale		undertaking the trial, including summary of relevant	
30			studies (published and unpublished) examining benefits	
31			and harms for each intervention	
32				
33				
34				
35	Background and	#6b	Explanation for choice of comparators	4
36	rationale: choice of			
37	comparators			
38				
39				
40	Objectives	#7	Specific objectives or hypotheses	5,6
41				
42				
43	Trial design	#8	Description of trial design including type of trial (eg,	6
44			parallel group, crossover, factorial, single group),	
45			allocation ratio, and framework (eg, superiority,	
46			equivalence, non-inferiority, exploratory)	
47				
48				
49	Methods:			
50	Participants,			
51	interventions, and			
52	outcomes			
53				
54				
55				
56	Study setting	#9	Description of study settings (eg, community clinic,	6
57			academic hospital) and list of countries where data will	
58				
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be collected. Reference to where list of study sites can be obtained

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4	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)
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11	Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered
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16	Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)
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23	Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)
24			
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27			
28	Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial
29			
30			
31			
32	Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
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43	Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)
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50	Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations
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57	Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size
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60			

1 **Methods:**

2 **Assignment of**
3 **interventions (for**
4 **controlled trials)**
5
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7			
8	Allocation: sequence	#16a	Method of generating the allocation sequence (eg,
9	generation		computer-generated random numbers), and list of any
10			factors for stratification. To reduce predictability of a
11			random sequence, details of any planned restriction (eg,
12			blocking) should be provided in a separate document
13			that is unavailable to those who enrol participants or
14			assign interventions
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18			
19	Allocation	#16b	Mechanism of implementing the allocation sequence
20	concealment		(eg, central telephone; sequentially numbered, opaque,
21	mechanism		sealed envelopes), describing any steps to conceal the
22			sequence until interventions are assigned
23			
24			
25			
26	Allocation:	#16c	Who will generate the allocation sequence, who will
27	implementation		enrol participants, and who will assign participants to
28			interventions
29			
30			
31	Blinding (masking)	#17a	Who will be blinded after assignment to interventions
32			(eg, trial participants, care providers, outcome
33			assessors, data analysts), and how
34			
35			
36	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is
37	emergency unblinding		permissible, and procedure for revealing a participant's
38			allocated intervention during the trial
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41 **Methods: Data**
42 **collection,**
43 **management, and**
44 **analysis**
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49	Data collection plan	#18a	Plans for assessment and collection of outcome,
50			baseline, and other trial data, including any related
51			processes to promote data quality (eg, duplicate
52			measurements, training of assessors) and a description
53			of study instruments (eg, questionnaires, laboratory
54			tests) along with their reliability and validity, if known.
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Reference to where data collection forms can be found, if not in the protocol

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4	Data collection plan:	#18b	Plans to promote participant retention and complete
5	retention		follow-up, including list of any outcome data to be
6			collected for participants who discontinue or deviate
7			from intervention protocols
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10			
11	Data management	#19	Plans for data entry, coding, security, and storage,
12			including any related processes to promote data quality
13			(eg, double data entry; range checks for data values).
14			Reference to where details of data management
15			procedures can be found, if not in the protocol
16			
17			
18			
19	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary
20			outcomes. Reference to where other details of the
21			statistical analysis plan can be found, if not in the
22			protocol
23			
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25			
26	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and
27	analyses		adjusted analyses)
28			
29			
30	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-
31	population and		adherence (eg, as randomised analysis), and any
32	missing data		statistical methods to handle missing data (eg, multiple
33			imputation)
34			
35			
36	Methods: Monitoring		
37			
38			
39	Data monitoring:	#21a	Composition of data monitoring committee (DMC);
40	formal committee		summary of its role and reporting structure; statement of
41			whether it is independent from the sponsor and
42			competing interests; and reference to where further
43			details about its charter can be found, if not in the
44			protocol. Alternatively, an explanation of why a DMC is
45			not needed
46			
47			
48			
49			
50	Data monitoring:	#21b	Description of any interim analyses and stopping
51	interim analysis		guidelines, including who will have access to these
52			interim results and make the final decision to terminate
53			the trial
54			
55			
56			
57	Harms	#22	Plans for collecting, assessing, reporting, and managing
58			solicited and spontaneously reported adverse events
59			
60			

and other unintended effects of trial interventions or trial conduct

Auditing [#23](#) Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor n/a

Ethics and dissemination

Research ethics approval [#24](#) Plans for seeking research ethics committee / institutional review board (REC / IRB) approval 15

Protocol amendments [#25](#) Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) 16

Consent or assent [#26a](#) Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) n/a

Consent or assent: ancillary studies [#26b](#) Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable n/a

Confidentiality [#27](#) How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial 11

Declaration of interests [#28](#) Financial and other competing interests for principal investigators for the overall trial and each study site 18

Data access [#29](#) Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators n/a

Ancillary and post trial care [#30](#) Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation n/a

Dissemination policy: trial results [#31a](#) Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the

public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

5	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of	16
6	authorship		professional writers	
9	Dissemination policy:	#31c	Plans, if any, for granting public access to the full	n/a
10	reproducible research		protocol, participant-level dataset, and statistical code	

13 Appendices

15	Informed consent	#32	Model consent form and other related documentation	n/a
16	materials		given to participants and authorised surrogates	
19	Biological specimens	#33	Plans for collection, laboratory evaluation, and storage	n/a
20			of biological specimens for genetic or molecular analysis	
21			in the current trial and for future use in ancillary studies,	
22			if applicable	

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 27 Commons Attribution License CC-BY-NC. This checklist was completed on 16. June 2021 using
 28 <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with
 29 [Penelope.ai](#)
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Appendix 2. List of data variables

Data Variable	Data source	Description
ICU location	TRACER/Enterprise	admission ICU
Age	TRACER/Enterprise	years
Sex	TRACER/Enterprise	M/F
BMI	TRACER/Enterprise	n/a
Date of Hospital Admission	TRACER/Enterprise	dd/mm/yyyy
Date of ICU Admission	TRACER/Enterprise	dd/mm/yyyy
Admission class	TRACER/Enterprise	med/surg/neuro/trauma
ICU discharge location	TRACER/Enterprise	unit/hospital
ICU Admission Diagnosis CV Respiratory Gastrointestinal Genitourinary/Renal Endocrinological/Metabolic Neurological Trauma Burn Sepsis Surgery	TRACER/Enterprise	yes/no
Co-morbidities AIDS Chronic Dialysis Chronic Heart Failure Respiratory Insufficiency Cirrhosis Diabetes Mellitus Hepatic Failure Immune Suppression Leukemia Lymphoma Metastatic Cancer Coronary Artery Disease	TRACER/Enterprise	yes/no
Clinical Frailty Scale	TRACER/Enterprise	number
APACHE II Score	TRACER/Enterprise	number
SOFA score	TRACER/Enterprise	number
Invasive/non-invasive ventilation	TRACER/Enterprise	hrs/min
Vasopressors (include type)	TRACER/Enterprise	hrs/min
CRRT Duration	TRACER/Enterprise	hrs/min
Cumulative daily fluid balance prior to RRT	TRACER/Enterprise	mls
Creatinine, urea, pH, bicarbonate, potassium on day of RRT initiation	TRACER/Enterprise	result

Renal Recovery at ICU Discharge	TRACER/Enterprise	y/n - IHD
Renal Recovery at Hospital Discharge	NIS/PARIS/DIMR	y/n - IHD/PD
Renal Recovery at 90 days	NIS/PARIS/DIMR	y/n - IHD/PD
ICU Mortality	TRACER/Enterprise	A/D
Hospital Mortality	TRACER/Enterprise	A/D
90-day Mortality	DIMR	A/D
ICU length of Stay	TRACER/Enterprise	days
Hospital Length of Stay	TRACER/Enterprise	days
Number of admissions to site	TRACER/Enterprise	aggregate
Patient days	TRACER/Enterprise	aggregate
Ventilator days	TRACER/Enterprise	aggregate
Dialysis days	TRACER/Enterprise	Days CRRT/IHD/SLED
CRRT data	Baxter	aggregate
Filter life		aggregate
Reasons for retiring filters		aggregate
Treatment time lost		aggregate
Prescription/dose		aggregate
Machine alarms		aggregate
Machine down times		aggregate
Type of coagulation		aggregate
Blood flow rates		aggregate
Filtration fraction		aggregate
Adverse events		aggregate
Economic data	DIMR	aggregate
Cost of filters, fluids, anticoagulation medications, dialysis catheters		aggregate
Patient life-years gained		aggregate
Quality of life adjusted years (QUALY)		aggregate
Re-hospitalizations		aggregate
Recurrence/chronic RRT		aggregate
Health care provider related costs		aggregate

308 Campus Tower
University of Alberta, Edmonton, AB T6G 1K8
p. 780.492.9724 (Biomedical Panel)
p. 780.492.0302 (Health Panel)
p. 780.492.0459

Approval Form

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14 Date: January 22, 2020
15
16 Study ID: Pro00075274
17
18 Principal Investigator: Oleksa Rewa
19
20 Study Title: Improving the quality of the performance and delivery of CRRT to critically ill patients in Alberta
21
22 Approval Expiry Date: Thursday, January 21, 2021
23
24
25 Sponsor/Funding Agency: Baxter Healthcare Inc
26
27
28
29 Sponsor/Funding Agency: University Hospital Foundation UHF

Project ID	Project Title	Speed Code	Other Information
View RES0044818	Development of a CRRT Quality Dashboard (QUALITY CRRT)		Baxter Healthcare
View RES0040497	QUALITY ICU	ZAAIH	UHF - Kaye Fund

41 Thank you for submitting the above study to the Health Research Ethics Board - Health Panel. Your application, including the following, has been reviewed and approved on behalf of the committee;

- 44 • Quality CRRT Survey (1/22/2020)
- 45 • Items to Be Included in Medical Record Review (1/22/2020)
- 46 • Quality CRRT Protocol (11/26/2020)

48 The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. It has been determined that a portion of the research described in the ethics application is retrospective review for which consent for
49 access to personally identifiable health information would not be reasonable, feasible or practical. Consent therefore is not required for access to personally identifiable health information described in the ethics application. In order to comply with
50 the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

51 Any proposed changes to the study must be submitted to the REB for approval prior to implementation. A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew
52 on or before the renewal expiry date (Thursday, January 21, 2021), you will have to re-submit an ethics application.

53 Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries
54 regarding Alberta Health approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Anthony S. Joyce, PhD.
Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).



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BMJ Open

Improving the quality of the performance and delivery of continuous renal replacement therapy (CRRT) to critically ill patients across a healthcare system – QUALITY CRRT: A Study Protocol

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Manuscripts

Improving the quality of the performance and delivery of continuous renal replacement therapy (CRRT) to critically ill patients across a healthcare system – QUALITY CRRT: A Study Protocol

Dawn Opgenorth¹, Ellen Reil², Vincent Lau¹, Nancy Fraser³, Danny J Zuege^{3,4}, Xiaoming Wang², Sean M. Bagshaw^{1,3}, Oleksa G. Rewa^{1,3}

¹ Department of Critical Care Medicine, Faculty of Medicine and Dentistry, University of Alberta and Alberta Health Services

² Alberta Health Services

³ Critical Care Strategic Clinical Network, Alberta Health Services

⁴ Department of Critical Care Medicine, Cumming School of Medicine, University of Calgary and Alberta Health Services

Corresponding Author

Oleksa G. Rewa

Assistant Professor

Department of Critical Care Medicine

University of Alberta

CSB 2-124 8440 112th St NW

Edmonton, Alberta

T6G 2B7

t. 780 263 3280

f. 780 492 1500

e. rewa@ualberta.ca

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Tables 5

Appendices 3

Keywords: Critical Care Medicine; Intensive Care; Continuous Renal Replacement Therapy; Dialysis; Quality; Key Performance Indicators

Trial Registration: clinicaltrials.gov, NCT04221932, first posted 9 January 2020

Protocol Version: 1.0, June 15 2020

Abstract (232 words)

Introduction: Continuous Renal Replacement Therapy (CRRT) is a continuous form of dialysis used to support critically ill patients with acute kidney injury. The ideal delivery of CRRT requires ongoing monitoring and reporting to adjust practice and deliver optimal therapy. However, this practice occurs variably.

Methods: QUALITY CRRT is a multi-center, prospective, stepped-wedged, interrupted time-series evaluation of the effectiveness, safety and cost of implementing a multi-faceted CRRT quality assurance and improvement program across an entire healthcare system. This study will focus on the standardization of CRRT programs with similar structure, process and outcome metrics by the reporting of CRRT Key Performance Indicators (KPIs). The primary outcome will be the quarterly performance of CRRT KPIs. Secondary outcomes will include patient-centered outcomes and economic outcomes. Analysis will compare pre- and post-implementation groups as well as for the performance of KPIs using an interrupted time-series methodology. The health economic evaluation will include a within-study analysis and a longer-term model-based analysis.

Discussion: The effective delivery of CRRT to critically ill patients ideally requires a standardized approach of best practice assessment and ongoing audit and feedback of standardized performance measures. QUALITY CRRT will test the application of this strategy stakeholder engagement and stepped-wedged implementation across an entire healthcare system.

Ethics and Dissemination: This study has received ethics approval. We will plan to publish the results in a peer-reviewed journal.

Trial Registration: clinicaltrials.gov, NCT04221932, first posted 9 January 2020.

Strengths and Limitations

- **Quality CRRT involves the implementation of CRRT KPIs across an entire healthcare system**
- **Study includes pilot program followed by broader stepped-wedged roll out of CRRT KPIs across all ICUs performing CRRT**
- **Included CRRT KPIs informed from current evidence-base as well as stakeholder surveys**
- **Study limited to CRRT and does not include IRR**

Introduction

Continuous renal replacement therapy (CRRT) is a continuous method of blood purification that provides slow uninterrupted clearance of uremic toxins and enables acid-base, electrolyte and volume homeostasis while preserving hemodynamic stability.[1, 2]

CRRT is the most common initial form of dialysis in ICU settings

The recent epidemiological study, AKI-EPI, revealed that CRRT was the most common form of initial acute RRT for patients with severe AKI.[3] These patients have greater illness severity, are more likely to die and have significantly increased healthcare utilization when compared to their non-CRRT critically ill counterparts.[2] As our population ages, becomes more medically complex, and presents with greater severity of illness, the utilization of CRRT is likely to increase and become an increasingly vital component of life-sustaining therapy.[3]

CRRT is expensive but there are substantial opportunities to improve costs

CRRT is a costly and labour intensive resource.[4] In the setting of increasingly constrained healthcare resources, intervention is needed which may identify and eliminate inefficiencies, improve performance, and decrease waste while improving provider satisfaction and achieving better patient outcomes.[5, 6] Currently, performance indicators for CRRT are not routinely measured, and as such, we are not in a position to understand or identify the inefficiencies or gaps in the quality of care of CRRT delivered to our sickest patients.[6]

Current CRRT practices are not standardized

In our healthcare system, CRRT is delivered as per individual unit protocols and practice patterns and is not consistently monitored (i.e., initiation strategies, anticoagulation techniques, dose delivered, ultrafiltration, etc). Discrepancies from best practices and lack of standardization

1
2
3 of CRRT delivery can result in unplanned CRRT interruptions, decreased treatment time,
4 inadequate dose delivery, and impaired clearance of toxic metabolites which can lead to
5 worsened patient outcomes.[7, 8]
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9
10 Such suboptimal practice variation may relate to the lack of well-developed key performance
11 indicators (KPIs) for CRRT delivery and performance, and the associated audit and feedback
12 function such KPIs can facilitate. KPIs are measures that can be used to monitor the performance
13 of healthcare delivery.[9] They are necessary and can improve reliability of care, standardize
14 complex interventions, and provide a platform to measure and monitor performance and the
15 impact of practice changes.[10, 11]
16
17

18
19
20 Recently, previous phases of work have identified and prioritized KPIs for CRRT care.[12, 13]
21
22 Implementing these CRRT KPIs may change practice to provide effective, validated and
23 standardized CRRT.[12, 13] Though several previous programs of work have looked to
24 implement these CRRT KPIs into clinical practice, but no program has rigorously tested the
25 implementation of this structure and monitoring across an entire healthcare system.[14-16]
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41 **Objectives and Research Questions:**

42 **Primary Objective**

43
44 The primary objective is to improve the quality of care delivered to critically ill patients
45 receiving CRRT in Alberta, as measured by CRRT KPI development, monitoring and
46 performance.
47
48
49
50
51

52 **Secondary Objectives**

1
2
3 These will include patient centered outcomes (i.e., ICU mortality and length of stay, duration of
4 CRRT therapy, 90-day renal recovery) and cost of health services, including unit specific CRRT
5
6 costs.
7
8
9

10 **Research Hypotheses:**

- 14 1. Can we improve the performance of CRRT programs through the implementation of
15 evidence-based clinical practice guidelines and provision of targeted multi-faceted CRRT
16 audit, feedback and education sessions?
17
18
- 22 2. Will the implementation of standardized CRRT programs our healthcare system's ICUs
23 result in decreased healthcare systems costs?
24
25
- 28 3. What is the impact of a multi-faceted quality assurance and improvement program on the
29 efficacy and safety of care in critically ill patients requiring CRRT across our healthcare
30 system?
31
32
33

34 **Methods**

35 **Trial Design**

36
37 The QUALITY CRRT trial is a pragmatic, multi-center, population-level, stepped-wedged,
38 interrupted time series evaluation of the implementation of an evidence-based CRRT quality
39 assurance and improvement program to standardize the delivery of CRRT in the 15 adult
40 general and cardiac ICUs and 3 pediatric ICUs in our healthcare system that provide CRRT
41
42 (Table 1). It conforms with the SPIRIT Checklist for study protocols (see Appendix 1).
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53 **Trial Oversight**

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3 QUALITY CRRT will be led by a small but specialized Steering Committee whose members
4 bring extensive experience with CRRT programs and clinical leadership, implementation science
5 and healthcare systems research. This pan-provincial team will be based at the University of
6
7
8 Alberta Hospital and will include representation from the Critical Care Strategic Network of
9
10
11 Alberta Health Services (the provincial body which provides provincial liaison, networking and
12
13
14 coordination of adult and pediatric critical care in Alberta).[17] The Steering Committee will be
15
16
17 responsible for program management, development and implementation of minimum standards
18
19
20 for CRRT programs, KPI reporting, targeted education and overall trial management.
21
22
23

24 **Patient and Public Involvement**

25
26 While this study currently does not directly include patients in its design, the Critical Care
27
28 Strategic Clinical Network includes patient representatives on its core committee and is
29
30 represented on the study team. The study objectives and research hypotheses have been
31
32 developed along with these members. Finally, the results of this study will be disseminated to
33
34 patients and families leveraging the strengths of the Critical Care Strategic Clinical Network.
35
36 This will be conducted through online resources, publications, and public engagement events
37
38 (i.e., Café Scientifiques).
39
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45 **Population and Eligibility**

46
47 This study will be conducted at all ICUs in Alberta capable of providing CRRT. All subjects in
48
49 this study will be critically ill patients (i.e., pediatric and adult) receiving CRRT as part of their
50
51 care. There will be no exclusion criteria. The inclusion criteria are purposely broad in scope to
52
53 capture a systems level sample of critically ill patients. This will be done so that these new KPI
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3 monitoring processes may be developed and implemented as policy, and outcomes measured on
4
5 a population level.
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7

8 All new ICU admissions receiving CRRT in the 15 adult and 3 pediatric ICUs in Alberta who
9
10 provide this therapy will be included in this project. In 2019, there were 12,132 adult and 1,592
11
12 pediatric admissions per year with 5.6% and 1.4% of these patients (i.e., 680 adult and 22
13
14 pediatric patients) receiving CRRT. As this study will be conducted over a 4-year period, thus
15
16 data on approximately 3,000 adult and pediatric (i.e., 2900 adult and 100 pediatric) patients will
17
18 be included in this project.
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21
22

23 **Interventions, duration and frequency of follow-up**

24
25 The project consists of a 24-month baseline phase to measure current CRRT practice and a 24-
26
27 month intervention phase to implement a standardized CRRT program targeting ICUs-based
28
29 CRRT KPIs and monitor performance and compliance of participating sites. Data from the 24-
30
31 month intervention phase will be used to model long-term health economic outcomes.
32
33
34

35 **Baseline Phase**

36
37
38 Baseline data collection: baseline clinical and resource utilization data will be collected on all
39
40 patients having received receiving CRRT between November 1, 2017 and October 31, 2019.

41
42
43 Stakeholder survey: A healthcare system-wide survey of care providers and stakeholders at
44
45 participating ICUs will be conducted to identify and establish agreement on the most appropriate
46
47 KPIs to measure at their ICU during the intervention phase. The survey will be administered
48
49 through Survey Monkey (www.surveymonkey.com).
50
51

52 **Intervention Phase**

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54
55 KPI benchmark reporting: The primary study intervention will be the implementation of audit
56
57
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1
2
3 and feedback on CRRT KPI benchmarks identified by the individual ICU teams in the baseline
4 survey. We will implement a minimal bundle of potential CRRT KPIs with evidence to measure
5
6 will include CRRT program structure, filter life, downtime, delivered dose, ultrafiltration
7
8 achieved, alarms, adverse events, ICU mortality and renal recovery (Table 2).[6, 12, 13]
9
10 Reports will be implemented and reviewed with ICU stakeholders ad hoc and at quarterly
11
12 intervals.
13
14
15

16
17 Prior to implementation of the reports, each ICU will receive multi-faceted education strategies
18
19 tailored to their site and informed by local CRRT leaders, champions and stakeholders (Table
20
21 3). Education strategies will include, 1) inter-professional grand rounds, seminars and webinars
22
23 supported by a web-based information repository, 2) identification of site champions to provide
24
25 onsite advocacy and education. The intervention will be multidisciplinary, targeting CRRT
26
27 prescribers, nurses, unit operational leaders and educators. After the intervention is
28
29 implemented quarterly audit and feedback reports and quarterly tele/videoconference and/or in-
30
31 person visits will be conducted to support the ICUs. The content of this feedback and methods
32
33 will be individualized to individual ICU needs and preferences.
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38
39 While the initial education strategy will contain similar themes across all sites, each site will be
40
41 encouraged to facilitate and participate with our working group in their own audit and
42
43 educational activities to address unit specific shortcomings in their CRRT KPI performance. A
44
45 central website repository of troubleshooting tools that will be hosted by the Critical Care
46
47 Strategic Network of Alberta Health Services will be available for sites who are not achieving
48
49 KPI benchmarks.
50
51

52
53 The CRRT KPI reporting program will be implemented in a stepped fashion with a pilot
54
55 occurring at the GSICU at the UAH over a 3-month period to ensure feasibility, proper
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3 reporting and compliance. This will lead to optimization of the tools prior to more generalized
4 use. The pilot will be followed by a stepped-wedge roll out at centers across Alberta over the
5
6 subsequent 12 months.
7
8

9
10 Intervention data collection: At the end of the intervention phase, clinical and resource
11 utilization data will be collected on all patients receiving CRRT during the 24-month
12
13 intervention period (Table 4).
14
15

16 17 18 **Outcomes**

19 20 **Primary Outcome**

21 The primary endpoint measures are quarterly changes in the performance of the CRRT process

22
23
24
25 KPIs:

- 26 • Average filter lifespan, measured in hours
- 27 • Downtime, as percentage of prescribed time
- 28 • Delivered dose, as a percentage of prescribed dose
- 29 • Ultrafiltration achieved, as a percentage of prescribed ultrafiltration
- 30 • Alarms as recorded per machine, per day

31 32 33 34 35 36 37 38 39 **Secondary Outcomes**

40 Patient centered

- 41 • Mortality - ICU, hospital, 90-day post discharge
- 42 • Length of stay - ICU and hospital
- 43 • Duration of CRRT treatment in hours
- 44 • Renal recovery 90-days post ICU discharge

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54 Health economic

- Supply costs - dialysis filters, fluids, dialysis catheters
- Medication costs – anticoagulation, renal specific replacement medications (e.g. erythropoietin analogues, calcium binders, etc.)
- Health care worker costs – physician billing, nursing (hrs)
- ICU and hospital stay costs (length of stay)
- Progression to end stage renal disease - projected chronic dialysis costs
- Quality of life adjusted years (QALYs)
- Health-related Quality of Life (HRQoL)
- Total health care costs

Data Management

Data elements will include patient centered variables: (i.e., demographics, type of admission [medical, surgical, trauma]), clinical characteristics (i.e., comorbid diseases, primary diagnosis), illness severity (i.e., APACHE II, Sequential Organ Failure Assessment [SOFA], Clinical Frailty Score [CFS]), treatment intensity (i.e., duration of renal replacement therapy, mechanical ventilation, vasoactive therapy), ICU and hospital lengths of stay, and outcomes (i.e., renal recovery, mortality, HRQoL); and CRRT associated cost data: (i.e., filter use, prescription/dose, machine alarms/down time, coagulation, adverse events, re-hospitalizations, progression of renal disease). A schedule of data variables to be captured is summarized in Appendix 2.

Data sources will include TRACER and Enterprise data repository, AHS Data Integration, Management and Reporting (DIMR) administrative databases, the Nephrology Information System (NIS), the Patient based Renal Information System (PARIS) and Baxter Healthcare Inc.[18]

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2
3 All study documents will be kept in a locked filing cabinet in a locked office, and computer files
4 will be encrypted and stored on a secure network for 5 years following completion of the study.
5
6
7

8 9 **Co-Enrollment**

10
11 QUALITY CRRT is a pragmatic, real world, quality improvement and assurance program. Due
12 to the healthcare systems scope of the program, there are no patient-level interventions.
13

14
15 Accordingly, there will be no limitations to co-enrollment or specific patient or clinician
16 practices.
17
18
19

20 21 22 **Statistical Analyses**

23
24 Analysis will be conducted between the pre- and post-implementation groups. Analyses of the
25 primary and secondary outcomes will involve summary measures obtained by aggregating the
26 endpoints. Analyses will be performed using SAS Enterprise Guide 7.1 (Cary, North
27 Carolina, USA). Baseline comparisons will be performed using chi-squared test for equal
28 proportions with results to be reported as frequencies with percentages. Continuous normally
29 distributed variables will be compared using t-tests and reported as means with standard
30 deviation, while non-parametrically distributed will be compared using Wilcoxon rank sum
31 tests and reported as medians and interquartile ranges (IQRs). In case of small sample size,
32 Fisher's exact test will be used.
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47 Interrupted time series (ITS) analyses using autoregressive integrated moving average
48 (ARIMA) models will be employed for important risk factors to account for temporal trends
49 and to determine whether there were changes in the clinic outcomes at the intervention period
50 (compared with the baseline period) and associated with implementation of the evidence-based
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3 acute RRT pathway.
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6 Cost-effectiveness or net-benefit (investment-return) analysis using a decision tree will be
7
8 adopted to compare return (or benefit, B) and investment (or cost, C) of the evidence-based
9
10 RRT pathway. Reduction of healthcare systems costs including inpatient services (length of
11
12 stay of primary admission, number of readmissions, and readmission LOS), outpatient services
13
14 (emergency room visits, and clinic visits), physician services (specialist visits, and general
15
16 practitioner visits), and ongoing new end-stage renal disease will be estimated based on
17
18 generalized linear models. Cost-effectiveness will be analyzed by estimating incremental cost
19
20 and effectiveness based on quality-adjusted life years (QALYs) gained. QALYs will be
21
22 calculated based on health-related quality of life as measured by the EQ-5D-5L in adults and
23
24 the PedsQL in children. Patients will be sent letters with study team contact information in
25
26 order for them to contact our team in order to complete these questionnaires.
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30

31 **Performance of CRRT KPIs**

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34 Our primary outcome will be the iterative performance of selected CRRT KPIs. Based on prior
35
36 work, KPIs might include filter life (measured in hours), delivered dose (measured in
37
38 mL/kg/hr), downtime (measured in percentage of time), ultrafiltration realized (measured in
39
40 percentage of prescribed) and access alarms (measured in total number per day). We will aim
41
42 to both compare the performance of these KPIs to historical controls, as well as prospectively
43
44 through an interrupted time-series analysis. The interrupted time-series analysis will allow us
45
46 to follow variable changes over time, allow for assessment of gradual change, and is consistent
47
48 with traditional quality improvement initiatives.
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51

52 **Patient-Centered Outcomes Analysis**

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54 The patient-centered outcome analysis will include ICU, hospital and 90-day mortalities, ICU
55
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2
3 and hospital lengths of stay, duration of CRRT treatment, and renal recovery measured at 90-
4 days months. While this study is not designed to evaluate the effect that the implementation of
5 the reporting of CRRT KPIs will have on mortality, lengths of treatment and stay or renal
6 recovery, these are important patient-centered outcomes that will need to be considered as
7 balancing measures for CRRT KPI reporting and implementation of our multi-faceted
8 knowledge translation intervention.
9
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15

16 **Health Economic Evaluation**

17
18 The economic evaluation will comprise two parts: 1) a within-study analysis, and 2) a longer-
19 term, model-based analysis.
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21
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23

24
25 The within-study analysis will focus on costs and outcomes collected during the study period. It
26 will include total quarterly unit-specific CRRT-associated costs following the implementation
27 of the CRRT KPI reporting program. This endpoint will be determined from our provincial CIS
28 and Alberta Blue Cross databases. Specifically, we will evaluate and compare the 1) costs of
29 supplying CRRT filters, 2) costs of CRRT fluids, 3) cost of CRRT anticoagulation and, 4) costs
30 and utilization of dialysis catheters. Costs will be calculated in part using CRRT process
31 measures captured by our CRRT KPIs (i.e., filter life and number of filters used,
32 anticoagulation modality, dose delivered, and effluent used, etc.). CRRT-associated costs were
33 selected as an important secondary outcome as these will be most immediately affected with the
34 implementation of the CRRT KPI quality assurance program across unit.
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48 We will also determine healthcare systems costs to include total ICU and hospital stay
49 associated costs, ongoing new end-stage renal disease (i.e., chronic RRT) costs, total healthcare
50 costs, and outcomes [mortality, quality-adjusted life years (QALY)]. Modelling analysis will
51 provide cost estimates from both a healthcare system and societal perspective (capturing costs
52
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1
2
3 to the health service, social care providers and patients). Results will be reported as the
4
5 incremental net benefit and incremental cost-effectiveness ratios. Uncertainty will be captured
6
7 in the analyses through probabilistic sensitivity analysis and reported using cost-effectiveness
8
9 acceptability curves, showing the likelihood the intervention will be cost-effective over a range
10
11 of values of willingness-to-pay for specific outcomes.
12
13

14 15 **Planned Subgroup Analyses**

16
17 Pre-specified subgroup analysis will include ICU patients to 1) adult vs. pediatric, 2) female vs.
18
19 male, 3) academic vs. community ICUs, 4) cardiovascular ICUs vs. medical/surgical ICUs, 5)
20
21 high volume vs. low volume centers (i.e., as per quartiles) 6) patients requiring acute RRT vs.
22
23 those on chronic dialysis. Adult, pediatric, female and male patients are fundamentally different
24
25 patient populations and deserve specific study.
26
27

28
29 Cardiovascular ICU patients differ from general medical/surgical patients as often these
30
31 patients are immediately post-operative, have a specific timing of insult (i.e., cardiac surgery)
32
33 and hence have different pathophysiology related to their critical illness. It is important to
34
35 delineate academic vs. community ICUs as, for mechanically ventilated patients (i.e., another
36
37 form of critical life-sustaining therapy) with acute respiratory distress syndrome (ARDS),
38
39 mortality rates differ significantly.[19] Finally, higher ARDS hospital case volume has also
40
41 been associated with lowers ARDS hospital mortality and it will be important to determine if
42
43 this association is present in CRRT.[20] We will perform the above analyses for health
44
45 economic evaluations, patient and process of care measures to include our pre-specified
46
47 primary and secondary outcomes for each subgroup. Each analysis will be accompanied by a
48
49 test for interaction between treatment and subgroup to ascertain whether effects differ
50
51 significantly between subgroups.
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Ethics Approval and Consent to Participate

This project is an evaluation of impact of a multi-faceted CRRT quality assurance and improvement program on patient outcomes and health care resource utilization in Alberta ICUs delivering CRRT. All diagnostic and management strategies are within standard of care and all data with relevance to the project are already routinely captured as part of standard patient care by means of machine specific data cards or clinical charting. No added trial-specific investigations or clinical documentation is required.

This evaluation was reviewed by the University of Alberta Health Research Ethics Board (HREB) (Pro00075274 January 22, 2020) and a waiver of consent was granted based on the premise this project represents health services implementation and evaluation compatible with a quality assurance and improvement initiative (see Appendix 3).

Any protocol modifications will be submitted to the appropriate relevant parties.

Dissemination

The findings of QUALITY CRRT will directly inform and guide policy on establishing evidence-based best-practices guidelines for delivering CRRT in Alberta ICUs. In addition, establishing evidence-based benchmarks across the entire health care system will enable systematic evaluation of CRRT performance. These outcomes will help create a framework for the standardization of CRRT programs across Alberta and other jurisdictions providing CRRT. (Table 2).

Alberta's comprehensive ICU clinical information and analytics infrastructure (Connect Care, eClinical TRACER) will be leveraged to implement a CRRT Quality Dashboard, accessible to

1
2
3 all Alberta ICU practitioners. The dashboard will contain statistics on KPI benchmarks to
4
5 provide real-time feedback on individual ICUs performance in delivering CRRT.
6
7

8 A central website containing a summary of CRRT guidelines and best practices and a repository
9
10 of troubleshooting tools on attaining KPI benchmarks will be developed and made available to
11
12 all Alberta CRRT practitioners.
13
14

15 We are proposing to publish the study results. Further, this work will be presented at local,
16
17 provincial and national critical care and nephrology meetings. Finally, QUALITY CRRT will
18
19 serve as the basis for a broader program of work, DIALYZING WISELY, which will aim to
20
21 transform the fashion in which acute dialysis is conducted in Alberta.
22
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28 **Discussion**

29
30 The importance of the quality and management for critically ill patients with acute kidney injury
31
32 requiring CRRT has been previously recognized.[5, 6] Previous studies have focused on single
33
34 unit or individual hospital-level quality improvement and assurance interventions (Table 5).[14-
35
36 16] Griffin et al., first conducted such a quality improvement study at the University of Colorado
37
38 Hospital where they assessed the magnitude in variability in CRRT dosing. They followed
39
40 specific implementation that included optimizing their electronic medical record to calculate
41
42 CRRT dosing in real-time to then comment on dosing and provide guidance and education in
43
44 order to better adhere to national guidelines. This led to the doubling of the rate of appropriate
45
46 CRRT dosing, and reduction in variability.[14] Mottes et al., at the University of Cincinnati
47
48 Children's Hospital, created a 'CRRT Dashboard' which tracked important KPIs such as 'filter
49
50 life,' 'mean prescription dose,' and 'fluid balance,' and found that this platform provided a
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2
3 significant means for measuring adherence to robust standards on the delivery of CRRT,
4 specifically in the process of care.[15] Finally, most recently a group from the University of
5
6 Kentucky Medical Centre reported the development, implementation, and subsequent outcomes
7
8 associated with a quality assurance system to support the provision of CRRT in the ICU.[16]
9
10 This was the largest program to date, numbering 1185 adult patients on CRRT over a 34-month
11
12 period. Using the monitoring of evidence-based KPIs and targeted education, they doubled the
13
14 appropriate use of citrate-based anticoagulation, improved the appropriateness of CRRT-dosing,
15
16 increased filter life while decreasing machine alarms and maintaining similar CRRT duration and
17
18 patient mortality while reducing CRRT-costs. While these programs demonstrate that the
19
20 implementation of evidence-derived KPI-based CRRT quality assurance programs are effective
21
22 in improving the efficiency and quality of CRRT, none of these programs have sought to do this
23
24 on an entire healthcare systems level. QUALITY CRRT will build on the experience of these
25
26 programs in order to scale such a quality improvement and assurance initiative across a
27
28 provincial health system of ICUs which provide CRRT.
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38 **Strengths & Limitations**

39
40 While QUALITY CRRT focuses on standardizing CRRT programs across an entire provincial
41
42 healthcare system by ensuring a robust framework is in place and the monitoring of CRRT
43
44 performance and delivery occurs, this is limited to only continuous RRT. Intermittent RRT can
45
46 also occur in the acute setting for critically ill patients in the ICU. Accordingly, the experience
47
48 and infrastructure realized in QUALITY CRRT will pave the work for additional critical care
49
50 nephrology programs aimed at improving all forms acute RRT (i.e., continuous and intermittent)
51
52 in the ICU.
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Contributorship Statement

SMB and OGR were responsible for the conception, design and planning of this study. ER assisted in the development of CRRT KPIs. VL and XW have assisted in creating the analysis plan and will work with interpretation the data. DO, NF and DZ assisted with manuscript preparation. All authors approved the final drafting of this manuscript.

Competing Interests

Drs. SBM and OGR have received honoraria from Baxter Healthcare Inc.

The study sponsors had no role in protocol development, trial management or data analysis and reporting.

Funding

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Table 1. Alberta ICUs Delivered CRRT

Site	City	ICU Type	Hospital Type	Beds
University of Alberta Hospital General Systems ICU	Edmonton	Mixed	Academic	32
Mazankowski Alberta Heart Institute Cardiovascular ICU	Edmonton	Cardiac surgery	Academic	24
Mazankowski Alberta Heart Institute Cardiac ICU	Edmonton	Cardiac	Academic	8
Royal Alexandra Hospital ICU	Edmonton	Mixed	Academic	25
Grey Nuns Hospital ICU	Edmonton	Mixed	Community	8
Misericordia Hospital	Edmonton	Mixed	Community	10
Sturgeon Hospital ICU	Edmonton	Mixed	Community	5
Stollery Children's Hospital Pediatric ICU	Edmonton	Mixed	Academic	16
Stollery Children's Hospital Pediatric Cardiac ICU	Edmonton	Cardiac	Academic	16
Foothills Medical Centre ICU	Calgary	Mixed	Academic	28
Foothills Medical Centre Cardiovascular ICU	Calgary	Cardiac surgery	Academic	16
Foothills Medical Centre Cardiac ICU	Calgary	Cardiac	Academic	18
Peter Lougheed Centre ICU	Calgary	Mixed	Academic	18
Rockyview General Hospital ICU	Calgary	Mixed	Community	10
South Health Campus ICU	Calgary	Mixed	Community	10
Chinook Regional Hospital ICU	Lethbridge	Mixed	Regional	7
Red Deer Regional Hospital ICU	Red Deer	Mixed	Regional	12
Alberta Children's Hospital Pediatric ICU	Calgary	Mixed	Academic	15

Table 2. Standardized Elements of CRRT Programs

Program Element	Operational Definition	Benchmark
CRRT Leadership	Presence of both CRRT physician and clinical nurse educator	100%
CRRT Education	Number of CRRT providers with training/ total number of CRRT providers	100%
Filter Life	Number of filters lasting 72 hours/ Total number of filters used	> 50% of filters
Delivered Dose	Actual delivered dose in ml/Kg/h / Prescribed dose in ml/Kg/h	> 85% of dose and between 25-30 ml/Kg/h
Downtime	Time CRRT not running per day/ Each day of CRRT prescription	< 15%
Ultrafiltration	Actual ultrafiltration achieve in ml/Kg/h/ Prescribed ultrafiltration in ml/Kg/h	>85% of prescription
Access Alarms	Number of alarms recorded per machine per day of therapy	< 5 alarms
Adverse Events	Number of adverse events as per RLS per quarter	0 events
ICU Mortality	Patient survival to ICU discharge	> 50%
Renal Recovery	Number of patients still requiring RRT at 90-days	< 10%

*CRRT Program Elements are shaded from white to light grey to dark grey as per the Donabedian framework of *structure*, *process* and *outcome*. Specific CRRT KPIs are in bold. Benchmarks have been taken from our internal and external validation of the KPIs. Our primary outcome will measure the performance of specific CRRT process KPIs.

Table 3. Components of the multi-faceted intervention and knowledge implementation strategy

Strategy	Description
Education	<ul style="list-style-type: none"> • Site grand rounds and inter-professional seminars • Monthly video/teleconferencing sessions • Site specific educational sessions by inter-professional content experts and local champions • Provide a summary of current guidelines and best practice • Development of website for repository of evidence supporting implementation including banked webinar of project • In-person or virtual visits with ICU leadership, champions and investigator teams
Coaching	<ul style="list-style-type: none"> • Provide ongoing resources for interpretation of KPI reports • Common troubleshooting advice cards • Provide clinical decision support resources
Audit and Feedback	<ul style="list-style-type: none"> • Baseline and monthly reports of process of care indicators of implementation of the intervention • Comparative performance relative to peer ICUs across province • Quarterly video/teleconferencing sessions to discuss provincial KPI reports
Reminders	<ul style="list-style-type: none"> • Promotional items (posters; bulletins) • Weekly electronic communication to local site champions to ensure ongoing review of KPI reports and access to additional resources

Table 4. Project Timeline

Activity by Quarter	2020				2021				2022				2023		
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3
	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep
Approvals															
Ethics approval/renewal - HREB	■				■				■				■		
Ethics approval/renewal - CHREB		■				■				■				■	
CTA/Administrative approvals	■														
DDA – Edmonton/Calgary/Regional		■													
Baseline phase															
Recruit Executive/Steering committee			■	■											
Conduct survey			■												
Extract baseline data - UAH			■												
Extract baseline data – all sites			■	■											
Develop education strategies			■	■	■	■									
Intervention phase															
Initiate pilot GSICU						■									
Initiate other sites						■	■	■	■						
Implement education strategies						■	■	■	■	■	■	■	■	■	■
CRRT KPI reporting						■	■	■	■	■	■	■	■	■	■
Protocol Manuscript						■	■	■	■						
Extract intervention phase data														■	
Study Manuscript															■

Table 5. Previous CRRT QI Initiatives

Study	Setting	Sample Size	KPI(s) studied	Intervention	Outcomes
Griffin et al. 2019	<ul style="list-style-type: none"> Single center Adult Medical/Surgical Nephrology prescription 	<ul style="list-style-type: none"> 837 CRRT treatment sessions 	<ul style="list-style-type: none"> Delivered dose 	<ul style="list-style-type: none"> Stakeholder engagement Modification to EMR Training of ICU nurses Standardization of protocol Improved documentation Modification of order sets Result dissemination 	<ul style="list-style-type: none"> Increased in treatments achieving dose (66.3% vs. 33.3%, p<0.001) Decline in under-dose treatments (11.7% vs. 20.7%, p<0.001) Decline in over-dosed treatments (22% vs. 46%, p<0.001)
Mottes et al. 2019	<ul style="list-style-type: none"> Single center Pediatric Newborn, cardiac, pediatric Nephrology prescription 	<ul style="list-style-type: none"> 184 patients 2090 patient days 	<ul style="list-style-type: none"> Filter life Unplanned filter changes Prescribed effluent dose Delivered vs. prescribed effluent dose Fluid balance 	<ul style="list-style-type: none"> Development of CRRT quality dashboard Provided targeted provider based CRRT education 	<ul style="list-style-type: none"> Mean filter life increase from 50 to 56 hours Unplanned filter change 33% to 15% Mean delivered dose increased from 2400ml/hr/1.73m² to 2845ml/hr/1.73m² Delivered time increased from 81.1% to 92.7% Increase in achievement of daily desired fluid balance from 69.2% to 83.3%
Ruiz et al. 2020	<ul style="list-style-type: none"> Single center Adult Medical/Surgical Nephrology prescription 	<ul style="list-style-type: none"> 1185 patients 7420 patient-days 	<ul style="list-style-type: none"> CRRT modality Anticoagulation Delivered dose Delivered/Prescribed dose Filter life CRRT access alarms 	<ul style="list-style-type: none"> Assembly of multidisciplinary team Standardization of CRRT protocol Improvement of CRRT charting Report of CRRT QI metrics Education to clinicians and ICU nurses 	<ul style="list-style-type: none"> Increase in CVVHDF use (92.4% to 100%, p<0.001) Increase in RCA use (23.1% to 39.5%, p<0.001) Improved filter life (26 to 31.2h, p=0.02) Decrease in access alarms (2.95 to 1.68/d, p=0.02)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	1
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 19

1	Roles and responsibilities:	#5b	Name and contact information for the trial sponsor	1
2	3			
4	4			
5	5			
6	6			
7	7			
8	8	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	18
9	9			
10	10			
11	11			
12	12			
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15	15			
16	16			
17	17			
18	18	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7
19	19			
20	20			
21	21			
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25	25			
26	26			
27	27			
28	28			
29	29	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
30	30			
31	31			
32	32			
33	33			
34	34			
35	35	#6b	Explanation for choice of comparators	4
36	36			
37	37			
38	38			
39	39			
40	40	#7	Specific objectives or hypotheses	5,6
41	41			
42	42			
43	43	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	6
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52	52			
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54	54			
55	55			
56	56	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will	6
57	57			
58	58			
59	59			
60	60			

be collected. Reference to where list of study sites can be obtained

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4	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)
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11	Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered
12			
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16	Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)
17			
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23	Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)
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27			
28	Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial
29			
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31			
32	Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
33			
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43	Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)
44			
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50	Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations
51			
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57	Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size
58			
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Methods:**Assignment of interventions (for controlled trials)**

Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	n/a
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	n/a
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7,8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a

Methods: Data collection, management, and analysis

Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known.	10,11
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Reference to where data collection forms can be found, if not in the protocol

1			
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4	Data collection plan:	#18b	Plans to promote participant retention and complete
5	retention		follow-up, including list of any outcome data to be
6			collected for participants who discontinue or deviate
7			from intervention protocols
8			
9			
10	Data management	#19	Plans for data entry, coding, security, and storage,
11			including any related processes to promote data quality
12			(eg, double data entry; range checks for data values).
13			Reference to where details of data management
14			procedures can be found, if not in the protocol
15			
16			
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18			
19	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary
20			outcomes. Reference to where other details of the
21			statistical analysis plan can be found, if not in the
22			protocol
23			
24			
25			
26	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and
27	analyses		adjusted analyses)
28			
29			
30	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-
31	population and		adherence (eg, as randomised analysis), and any
32	missing data		statistical methods to handle missing data (eg, multiple
33			imputation)
34			
35			
36	Methods: Monitoring		
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39	Data monitoring:	#21a	Composition of data monitoring committee (DMC);
40	formal committee		summary of its role and reporting structure; statement of
41			whether it is independent from the sponsor and
42			competing interests; and reference to where further
43			details about its charter can be found, if not in the
44			protocol. Alternatively, an explanation of why a DMC is
45			not needed
46			
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50	Data monitoring:	#21b	Description of any interim analyses and stopping
51	interim analysis		guidelines, including who will have access to these
52			interim results and make the final decision to terminate
53			the trial
54			
55			
56			
57	Harms	#22	Plans for collecting, assessing, reporting, and managing
58			solicited and spontaneously reported adverse events
59			
60			

1			and other unintended effects of trial interventions or trial	
2			conduct	
3				
4	Auditing	#23	Frequency and procedures for auditing trial conduct, if	n/a
5			any, and whether the process will be independent from	
6			investigators and the sponsor	
7				
8				
9	Ethics and			
10	dissemination			
11				
12				
13	Research ethics	#24	Plans for seeking research ethics committee /	15
14	approval		institutional review board (REC / IRB) approval	
15				
16				
17	Protocol amendments	#25	Plans for communicating important protocol	16
18			modifications (eg, changes to eligibility criteria,	
19			outcomes, analyses) to relevant parties (eg,	
20			investigators, REC / IRBs, trial participants, trial	
21			registries, journals, regulators)	
22				
23				
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25	Consent or assent	#26a	Who will obtain informed consent or assent from	n/a
26			potential trial participants or authorised surrogates, and	
27			how (see Item 32)	
28				
29				
30	Consent or assent:	#26b	Additional consent provisions for collection and use of	n/a
31	ancillary studies		participant data and biological specimens in ancillary	
32			studies, if applicable	
33				
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35				
36	Confidentiality	#27	How personal information about potential and enrolled	11
37			participants will be collected, shared, and maintained in	
38			order to protect confidentiality before, during, and after	
39			the trial	
40				
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42				
43	Declaration of	#28	Financial and other competing interests for principal	18
44	interests		investigators for the overall trial and each study site	
45				
46				
47	Data access	#29	Statement of who will have access to the final trial	n/a
48			dataset, and disclosure of contractual agreements that	
49			limit such access for investigators	
50				
51				
52	Ancillary and post trial	#30	Provisions, if any, for ancillary and post-trial care, and	n/a
53	care		for compensation to those who suffer harm from trial	
54			participation	
55				
56				
57	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial	7,16
58	trial results		results to participants, healthcare professionals, the	
59				
60				

public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

1 2 3 4 5 6 7 8	Dissemination policy: authorship	#31b Authorship eligibility guidelines and any intended use of professional writers	16
9 10 11 12	Dissemination policy: reproducible research	#31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a

13 Appendices

15 16 17 18	Informed consent materials	#32 Model consent form and other related documentation given to participants and authorised surrogates	n/a
19 20 21 22 23 24 25	Biological specimens	#33 Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

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 27 Commons Attribution License CC-BY-NC. This checklist was completed on 16. June 2021 using
 28 <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with
 29 [Penelope.ai](#)
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Appendix 2. List of data variables

Data Variable	Data source	Description
ICU location	TRACER/Enterprise	admission ICU
Age	TRACER/Enterprise	years
Sex	TRACER/Enterprise	M/F
BMI	TRACER/Enterprise	n/a
Date of Hospital Admission	TRACER/Enterprise	dd/mm/yyyy
Date of ICU Admission	TRACER/Enterprise	dd/mm/yyyy
Admission class	TRACER/Enterprise	med/surg/neuro/trauma
ICU discharge location	TRACER/Enterprise	unit/hospital
ICU Admission Diagnosis CV Respiratory Gastrointestinal Genitourinary/Renal Endocrinological/Metabolic Neurological Trauma Burn Sepsis Surgery	TRACER/Enterprise	yes/no
Co-morbidities AIDS Chronic Dialysis Chronic Heart Failure Respiratory Insufficiency Cirrhosis Diabetes Mellitus Hepatic Failure Immune Suppression Leukemia Lymphoma Metastatic Cancer Coronary Artery Disease	TRACER/Enterprise	yes/no
Clinical Frailty Scale	TRACER/Enterprise	number
APACHE II Score	TRACER/Enterprise	number
SOFA score	TRACER/Enterprise	number
Invasive/non-invasive ventilation	TRACER/Enterprise	hrs/min
Vasopressors (include type)	TRACER/Enterprise	hrs/min
CRRT Duration	TRACER/Enterprise	hrs/min
Cumulative daily fluid balance prior to RRT	TRACER/Enterprise	mls
Creatinine, urea, pH, bicarbonate, potassium on day of RRT initiation	TRACER/Enterprise	result

Renal Recovery at ICU Discharge	TRACER/Enterprise	y/n - IHD
Renal Recovery at Hospital Discharge	NIS/PARIS/DIMR	y/n - IHD/PD
Renal Recovery at 90 days	NIS/PARIS/DIMR	y/n - IHD/PD
ICU Mortality	TRACER/Enterprise	A/D
Hospital Mortality	TRACER/Enterprise	A/D
90-day Mortality	DIMR	A/D
ICU length of Stay	TRACER/Enterprise	days
Hospital Length of Stay	TRACER/Enterprise	days
Number of admissions to site	TRACER/Enterprise	aggregate
Patient days	TRACER/Enterprise	aggregate
Ventilator days	TRACER/Enterprise	aggregate
Dialysis days	TRACER/Enterprise	Days CRRT/IHD/SLED
CRRT data	Baxter	aggregate
Filter life		aggregate
Reasons for retiring filters		aggregate
Treatment time lost		aggregate
Prescription/dose		aggregate
Machine alarms		aggregate
Machine down times		aggregate
Type of coagulation		aggregate
Blood flow rates		aggregate
Filtration fraction		aggregate
Adverse events		aggregate
Economic data	DIMR	aggregate
Cost of filters, fluids, anticoagulation medications, dialysis catheters		aggregate
Patient life-years gained		aggregate
Quality of life adjusted years (QUALY)		aggregate
Re-hospitalizations		aggregate
Recurrence/chronic RRT		aggregate
Health care provider related costs		aggregate

308 Campus Tower
 University of Alberta, Edmonton, AB T6G 1K8
 p. 780.492.9724 (Biomedical Panel)
 p. 780.492.0302 (Health Panel)
 p. 780.492.0459

Approval Form

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14 Date: January 22, 2020
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16 Study ID: Pro00075274
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18 Principal Investigator: Oleksa Rewa
19
20 Study Title: Improving the quality of the performance and delivery of CRRT to critically ill patients in Alberta
21
22 Approval Expiry Date: Thursday, January 21, 2021
23
24
25 Sponsor/Funding Agency: Baxter Healthcare Inc
26
27
28
29 Sponsor/Funding Agency: University Hospital Foundation UHF

Project ID	Project Title	Speed Code	Other Information
View RES0044818	Development of a CRRT Quality Dashboard (QUALITY CRRT)		Baxter Healthcare
View RES0040497	QUALITY ICU	ZAAIH	UHF - Kaye Fund

41 Thank you for submitting the above study to the Health Research Ethics Board - Health Panel. Your application, including the following, has been reviewed and approved on behalf of the committee;

- 44 • Quality CRRT Survey (1/22/2020)
- 45 • Items to Be Included in Medical Record Review (1/22/2020)
- 46 • Quality CRRT Protocol (11/26/2020)

48 The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. It has been determined that a portion of the research described in the ethics application is retrospective review for which consent for
 49 access to personally identifiable health information would not be reasonable, feasible or practical. Consent therefore is not required for access to personally identifiable health information described in the ethics application. In order to comply with
 50 the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

51 Any proposed changes to the study must be submitted to the REB for approval prior to implementation. A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew
 52 on or before the renewal expiry date (Thursday, January 21, 2021), you will have to re-submit an ethics application.

53 Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries
 54 regarding Alberta Health approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,
 Anthony S. Joyce, PhD.
 Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

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