OPEN

Economic Analysis of Renal Replacement Therapy Modality in Acute Kidney Injury Patients With Fluid Overload

Olivier Ethgen, PhD[1,2]

Raghavan Murugan, MD, MS, FRCP[3]

Jorge Echeverri, MD[4]

Michael Blackowicz, PhD[1,4]

Kai Harenski, MD[5]

Marlies Ostermann, PhD[6]

OBJECTIVES: Acute kidney injury (AKI) and fluid overload (FO) are among the top reasons to initiate intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT). Prior research suggests CRRT provides more precise volume control, but whether CRRT is cost-effective remains unclear. We assessed the cost-effectiveness of CRRT for volume control compared with IHD from a U.S. healthcare payer perspective.

DESIGN: Decision analytical model comparing health outcomes and healthcare costs of CRRT versus IHD initiation for AKI patients with FO. The model had an inpatient phase (over 90-d) followed by post-discharge phase (over lifetime). The 90-day phase had three health states: FO, fluid control, and death. After 90 days, surviving patients entered the lifetime phase with four health states: dialysis independent (DI), dialysis dependent (DD), renal transplantation, and death. Model parameters were informed by current literature. Sensitivity analyses were performed to evaluate results robustness to parametric uncertainty.

SETTING: ICU.

PATIENTS OR SUBJECTS: AKI patients with FO.

INTERVENTIONS: IHD or CRRT.

MEASUREMENTS AND MAIN RESULTS: The 90-day horizon revealed better outcomes for patients initiated on CRRT (survival: CRRT 59.2% vs IHD 57.5% and DD rate among survivors: CRRT 5.5% vs IHD 6.9%). Healthcare cost was 2.7% (+$2,836) higher for CRRT. Over lifetime, initial CRRT was associated with +0.313 life years (LYs) and +0.187 quality-adjusted life years (QALYs) compared with initial IHD. Even though important savings were observed for initial CRRT with a lower rate of DD among survivors (–$13,437), it did not fully offset the incremental cost of CRRT (+$1,956) and DI survival (+$12,830). The incremental cost-per-QALY gained with CRRT over IRRT was +$10,429/QALY. Results were robust to sensitivity analyses.

CONCLUSIONS: Our analysis provides an economic rationale for CRRT as the initial modality of choice in AKI patients with FO who require renal replacement therapy. Our finding needs to be confirmed in future research.

KEY WORDS: acute kidney injury; cost-effectiveness; fluid overload; renal recovery; renal replacement therapy; ultrafiltration

Acute kidney injury (AKI) is a common complication in critically ill patients admitted to the ICU (1). AKI is associated with worse patient prognosis when it is accompanied by fluid accumulation, which is present in more than two-thirds of patients (2). The need to hemodynamically stabilize the patient typically requires fluid resuscitation and vasopressor support, which can result in fluid overload (FO) that may be compounded by decreased fluid excretion due to AKI. Several studies have reported that FO

DOI: 10.1097/CCE.0000000000000921

KEY POINTS

Question: Is initial continuous renal replacement therapy (CRRT) cost-effective versus initial intermittent hemodialysis (IHD) in acute kidney injury (AKI) patients with fluid overload?

Findings: Initial CRRT was associated with +0.313 life years (LYs) and +0.187 quality-adjusted life years (QALYs) compared with initial IHD. Even though important savings were observed for initial CRRT with a lower rate of dialysis dependent among survivors (–$13,437), it did not fully offset the incremental cost of CRRT (+$1,956) and dialysis independent survival (+$12,830). The incremental cost-per-LYs gained and incremental cost-per-QALY gained of initial CRRT over initial IHD were +$6,237 and +$10,429, respectively, both below the prevailing willingness-to-pay thresholds in the United States.

Meaning: There is an economic rationale for CRRT as the initial modality of choice in AKI patients with fluid overload and who require renal replacement therapy.

is independently associated with increased morbidity and mortality and reduced renal recovery (3–7).

AKI and FO are among the top reasons to initiate renal replacement therapy (RRT), commonly delivered either as intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT). An observational analysis demonstrated that negative mean daily fluid balance during CRRT was consistently associated with improved clinical outcomes (8). These relationships were confirmed in other studies showing that better volume control during CRRT was related to better patient outcomes (9, 10).

Compared with IHD, CRRT offers more effective 24-hour fluid removal for several reasons: 1) slower and better tolerability of fluid removal; 2) slower but sustained solute clearance avoiding rapid fluctuations in solutes, electrolytes, and fluid shifts; 3) greater prescription flexibility to respond to changes in patient needs and hemodynamics; and 4) ease of machine use. Achieving the target fluid balance is particularly challenging in hemodynamically unstable patients for whom CRRT is the modality of choice (11, 12). CRRT has been shown to reduce the likelihood of dialysis dependence among survivors when used as initial modality (13, 14), although other studies have found no difference in the likelihood of renal recovery (15).

Nonetheless, there are wide variations in RRT practice globally and CRRT might not always be available. In addition, the cost-effectiveness of using CRRT for fluid management compared with IHD is unclear. This is important because FO is associated with increased resource utilization and impacts patients' well-being (16). Use of CRRT for early fluid management might offset the costs related to CRRT and FO and therefore may be cost-effective in the long term.

This prompts the need for comparing CRRT and IHD in the management of fluid accumulation in AKI patients, considering both health outcomes and cost implications. We investigated from a U.S. healthcare payer perspective the cost-effectiveness of CRRT versus IHD.

METHODS

Analytic Model

Using Microsoft Excel (Microsoft Corporation, Redmond, WA), we designed a decision analytical model to compare outcomes and costs of initiating CRRT versus IHD for AKI patients with FO. The model had two analytic phases: an inpatient phase (daily cycles over 90-d time horizon) followed by a post-discharge phase (yearly cycles over lifetime horizon). This distinction was made to better simulate the impact of both short-term clinical decisions during the inpatient stay and long-term prognosis associated with the outcomes of the inpatient stay.

The 90-day phase was a partitioned survival model. Survival curves were extrapolated and the areas under those curves used to estimate the distribution over time of patients across three mutually exclusive health states: FO, controlled fluid status, or death. At hospital discharge, we differentiated between survivors who were dialysis dependent (DD) and those who were dialysis independent (DI), indicating renal recovery.

At 90 days, DD and DI survivors entered the lifetime horizon phase. This was a health-state transition model comprised of four states: DI, DD, renal transplantation, or death. DI patients could transition to DD or death. DD patients could transition to transplantation, death, or DI. **Figure 1** shows both the 90-day and the lifetime model phases. Model parameters were informed by literature.

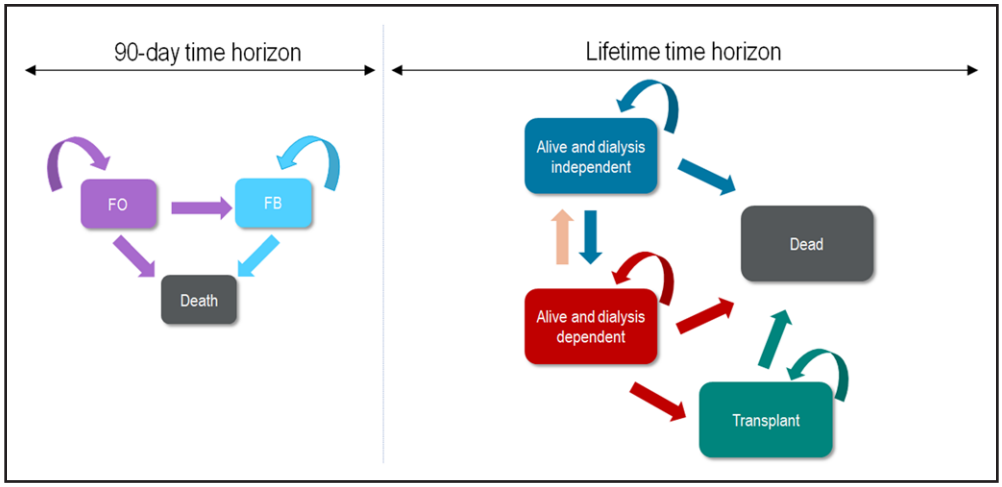

Figure 1. Model schematic. FB = fluid balance, FO = fluid overload.

Clinical Data

For the 90-day phase, survival was extrapolated using a Weibull function on two data points: the 100% survival at model inception and the expected 90-day survival rate of patients for whom fluid control was achieved set at 60% from a study published in 2012 for patients who do not switch RRT modalities (17). Patients not achieving fluid control entailed an increased risk of death. Assuming proportional hazards, this excess risk of death was applied by means of a hazard ratio (HR) greater than 1, set at 1.25 in the base case (2). Time to volume control as determined by clinicians was modeled in a similar manner, using a Weibull function on two data points: all patients with FO at model inception and the median time to achieve target fluid balance with initial use of CRRT, set at 4 days in the base case from a study published in 2020 (10). A delayed time to fluid control was modeled for patients initiated with IHD, extending the median time to achieve target fluid balance by 2 extra days.

DD at 90-day for patients who initiated CRRT was estimated at 5.5% as reported in a 2022 study (18). Rate of DD for patients with initial modality of IHD was assumed to be higher, with a HR of 1.25 as suggested in a large retrospective study in 2014 (19). As switches between RRT modalities are common in practice, we hypothesized that 45% of patients initiated with CRRT would be switched to IHD and that 13% of patients initiated with IHD would be switched to CRRT as found in a 2009 study (20). As switch from CRRT to IHD usually reflects improvement in hemodynamic status, we stipulated that these patients would have a mortality benefit over those who remained on CRRT, patterned with a HR of 1.05. Switch from IHD to CRRT was conservatively assumed to have no effect on mortality.

The model assumed daily treatment with CRRT or IHD. Overall RRT duration was assumed to be 5 days for both initial CRRT and initial IHD (21, 22). In case of switches, the second modality was assumed to represent 60% of the overall RRT duration. ICU and hospital length of stay (LoS) were modeled independently from fluid or DD status. LoS was instead a function of patient survival, survivors constantly exhibiting longer ICU and hospital LoS compared with patients dying in hospital (17, 22, 23). In the base case, ICU LoS was set at 7 and 10 days for nonsurvivors and survivors, respectively, as described in a 2020 publication (22). Hospital LoS was set at 9 and 29 days for hospital nonsurvivors and survivors, respectively, as reported in 2018 and 2020 studies (22, 23).

For the lifetime phase, survival of DI patients was estimated using age- and gender-dependent general population annual mortality risk in 2019 (24), while DD and transplant patient survival were estimated using their corresponding age- and gender-matched annual mortality risks from the U.S. Renal Data System (USRDS) registry in 2020 (25).

Health Utilities

Health utility refers to the level of desirability or preference for a certain health state. It usually ranges between 0 (death) to 1 (perfect health). All intermediate states between can then be ordered on this utility scale. In the analysis, the health utility of a stay in the ICU was set at 0.130 (26). Health utility of DI at discharge was assumed to be decremented by 4.0% from the age and gender-matched U.S. population norms (27). This decrement was applied over the remaining patients' lifetime as evidence suggests that impaired quality of life and functioning subsist over the long term (28, 29).

Regarding health utility evolution over lifetime as DI survivors age, we interpolated the published U.S. population norms based on the Euroqol questionnaire at 5

dimensions index (30). Interpolation was done continuously over the 18–100 years old span using a logistic equation. DD survivors were assigned a utility decrement of –0.110 from the age- and gender-matched population norms (31). This decrement was stipulated to last over the entire remaining lifetime of DD survivors. Renal transplant patients were assumed to return to age- and gender-matched population norms. Finally, the average between ICU health utility and hospital discharge health utility (in either DI or DD states) was used to assign health utility to the non-ICU hospital stay.

Healthcare Costs

The analysis was performed from a U.S. healthcare payer perspective. Only direct healthcare costs were considered. Resource utilization were first quantified by RRT duration, ICU LoS, and hospital LoS. All resources were then costed by applying a daily cost to RRT and LoS (26, 32–35).

Daily cost estimates were derived from published literature from the years 2003–2022 and expressed in 2021 $ (U.S. dollars) using the Consumer Price Index for Medical Care Services from the U.S. Bureau of Labor Statistics (36). The cost of the first ICU day was set at $14,471 and daily costs of each subsequent ICU day at $6,630. The daily cost of a hospital ward was taken from the hospital-adjusted expenses per inpatient day estimated by the Kaiser Family Foundation and set at $2,710 (37). Patients dying in hospital were assumed to incur a 25% greater cost compared with those who survived.

Daily costs of CRRT and IHD were estimated to be $872 and $273, respectively. These estimates were based on a comprehensive micro-costing study of CRRT and IHD in which actual resources and supplies used by 261 patients were measured and costed (supplies, replacement fluid, dialysate, RRT machinery amortization, nursing, laboratory tests, and physician billing) (32).

For the lifetime horizon phase, we assigned a yearly cost to DI and DD survivors. DI survivors were assigned the U.S. per-capita healthcare spending (38) and DD survivors the corresponding USRDS Network cost data, covering payment for all patients receiving dialysis under Medicare as their primary insurance (25). These post-hospital costs reflected all costs related to healthcare resources used for those patients who survived the hospitalization. Latest cost estimates available were inflated to 2021 $ and continuously interpolated from available age-group cost estimates to be inputted in the model as a function of survivors' ages.

Base-Case Analysis

Health outcomes and healthcare costs were accumulated cyclically by health states and averaged for a simulated cohort of 1,000 patients initially receiving either CRRT or IHD, with an average age of 67 years and 44% women (23). Health outcomes consisted of survival and DD rates for the 90-day phase, life years (LYs) and quality-adjusted life years (QALYs) gained for the lifetime phase. Incremental cost-effectiveness ratios (ICERs) expressed as incremental cost-per-DI survivor, incremental cost-per-LYs gained, and incremental cost-per-QALY gained were computed. For the lifetime horizon, both health outcomes and costs were discounted at 3% per annum (39).

Sensitivity Analyses

Deterministic sensitivity analyses were carried out, consisting of sequential variations of all base-case values within their 95% CI or interquartile range (IQR) bounds, whichever was available. When CI or IQR were missing, a ±30% range variation was used instead. Results were graphically presented as Tornado diagrams, displaying the 10 most impactful parameter variations. A probabilistic analysis was done with 1,000 iterations Monte-Carlo simulation of all parameters sampled simultaneously across appropriate distributions characterizing the uncertainty in their estimation. Utilities and proportions were simulated with beta distributions, costs with gamma distributions, and risk ratios with log-normal distributions. All other parameters were simulated with normal distributions. Results were presented as a scatter plot on the incremental cost-effectiveness plane, with corresponding average differences and nonparametric 95% CI.

All inputs are summarized in **Supplemental Table** (http://links.lww.com/CCX/B196). The study was based on literature and assumptions only and did not involve human subjects or access to private individual information. As such, it did not fall under board's guideline as human subjects' research and institutional review board or ethics committee approval was not sought.

RESULTS

The 90-day horizon revealed better outcomes for initial use of CRRT with greater 90-day survival (CRRT 59.2% vs IHD 57.5%) and lower DD rate among survivors (CRRT 5.5% vs IHD 6.9%) (**Table 1**). Cost was 2.7% (+$2,836) higher for initial CRRT, mainly due to higher costs attributed to RRT modality in the CRRT branch of the model (+$1,956).

Better 90-day outcomes for initial CRRT resulted in better long-term outcomes. Initial CRRT provided +0.313 LYs and +0.187 QALYs compared with initial IHD over patients' lifetime. Even if important savings were observed for initial CRRT with the lower rate of DD among survivors (–$13,437), they did not fully offset the incremental cost of CRRT (+$1,953) and DI survival (+$12,830). The incremental cost-per-LY gained and incremental cost-per-QALY gained were +$6,237 and +$10,429, respectively (Table 1). These were both below the prevailing willingness-to-pay thresholds in the United States, usually about $100,000/QALY (40, 41).

Results of the deterministic sensitivity analysis on the lifelong outcomes are detailed in **Supplemental Figure 1** (http://links.lww.com/CCX/B196). The greater chance of survival for CRRT patients switching

TABLE 1.
Base-Case Results

Outcomes	Initiate Continuous Renal Replacement Therapy	Initiate Intermittent Hemodialysis	Difference
90-d			
Health outcomes			
Survival at 90-d (%)	59.2	57.5	+1.7 pp
DD at 90-d among survivors (%)	5.5	6.9	−1.4 pp
Healthcare resources			
RRT duration (d)	5.0	5.0	0.000
Length of stay (d)	29.6	29.2	+0.391
ICU	8.8	8.7	+0.051
Hospital	20.8	20.5	+0.340
Costs			
Total	$106,058	$103,222	+$2,836
RRT	$3,550	$1,594	+$1,956
ICU stay	$66,028	$65,690	+$338
Hospital stay (non-ICU)	$26,665	$26,026	+$639
Lifelong			
Health outcomes			
LYs	10.720	10.407	+0.313
QALYs	6.061	5.874	+0.187
Costs			
Total	$494,138	$492,184	+$1,953
Dialysis independence	$299,949	$287,119	+$12,830
DD	$8, 460	$99,897	–$13,437
Transplant	$1,671	$1,946	–$275
Incremental cost-effectiveness ratio			
Incremental cost-per-LY gained			+$6,237
Incremental cost-per-QALY gained			+$10,429

DD = dialysis dependence, LYs = life years, pp = percentage point, QALYs = quality-adjusted life years, RRT = renal replacement therapy.

to IHD versus CRRT patients remaining on CRRT was the most influential parameter in the model. The increased risk of DD at 90 days for survivors who initiated IHD was also an influential parameter on the ICER. The highest ICER was +$80,315/QALY, obtained without the consideration of an increased risk of DD for survivors at 90 days for those initiated with IHD.

Supplemental Figure 2 (http://links.lww.com/CCX/B196) shows the scatter plot and the cost-effectiveness acceptability curve obtained from the probabilistic sensitivity analysis. The average QALY gained was +0.074 (95% nonparametric CI [−0.072 to +0.256]) and the average incremental cost was +$1,853 (95% CI [−$31,589 to +$34,474]). Initial CRRT had a greater than 50% and 75% chance of being the most cost-effective option from a decision-maker willingness-to-pay of $20,000 and $100,000/QALY gained, respectively.

DISCUSSION

Our model-based analysis demonstrated that for the management of FO in patients with AKI, the initial use of CRRT is cost-effective compared with IHD. Initiation of CRRT was associated with better long-term outcomes, providing +0.313 LYs and +0.187 QALYs compared with initial IHD. Even if savings were notable for initial CRRT because of the lower rate of DD among survivors (−$13,437), they did not fully offset the incremental cost of CRRT (+$1,956) and DI survival (+$12,830). The incremental cost-per-LY gained and the incremental cost-per-QALY gained were +$6,237 and +$10,429, respectively, which are below the prevailing willingness-to-pay threshold in the United States (40, 41). These results were robust to both deterministic and probabilistic sensitivity analyses.

There is wide variability in CRRT availability and practices worldwide (42). CRRT is perceived to be more costly and resource intensive compared with IHD. This may dissuade the use of CRRT as initial modality. However, in a multinational survey of fluid management practices, more than 70% of clinicians used CRRT as initial modality of choice for fluid management (43, 44). The apparent upfront costs of CRRT appeared to be justified by the clinical and humanistic benefit, with a lifelong ICER per QALY consistently under prevailing thresholds in the United States. However, our analysis needs to be properly adapted to resource-limited settings before drawing wide-reaching global recommendations.

To our knowledge, this is the first economic modeling work comparing CRRT and IHD as first RRT modality for fluid management in AKI patients. Previous studies have compared the economics of RRT modalities for patients with AKI overall (26) or in cardiac surgery-associated AKI (35). The current study focused on AKI patients with FO, a specific group with higher risk of mortality. Thus, our study adds to the body of evidence that RRT initiation with CRRT versus IHD is cost-effective in the management of critically ill patients with AKI and FO.

In our analysis, the benefit of CRRT over IHD appears to be driven by the mortality benefit conferred by optimized fluid management and the lower rate of dialysis dependence among survivors (17, 19). Even if survival benefit of one modality over another has not been clearly established, evidence suggests that initial CRRT enhances the chances of achieving target fluid balance (10). In turn, successful fluid management has been shown to be associated with better survival (17). In our analysis, it is the combination of these two main benefits that translated into a survival benefit for patients initiated on CRRT. This survival benefit was then enhanced further by the greater likelihood of renal recovery among survivors who received CRRT.

CRRT and IHD do not have the same fluid removal profile. The body of evidence lacks direct comparative data. We have thus assembled within a consistent modeling framework multiple components and features of RRT dispersedly informed by the literature. We balanced model simplicity and representativeness of reality to reasonably assess the cost-effectiveness of RRT modalities in AKI patients with FO. Our model may not embrace some specific clinical scenarios, but extensive sensitivity analyses were carried out on all parameters to account for variability and uncertainty.

Switches between modalities are generally indicative of patient evolution. This was accounted for in sensitivity analyses for switches in both directions. In the base case, patients switching from CRRT to IHD were assumed to have a mortality benefit over those remaining on CRRT, reflecting improvement of their hemodynamic status. On the other hand, patients switching from IHD to CRRT were assumed to have no mortality difference with those remaining on IHD. The

latter assumption is conservative as the mortality of patients unable to transition from CRRT is high. Both-way switches appeared to be among the top 10 most influential parameters in the model (**Supplemental Fig. 1**, http://links.lww.com/CCX/B196).

There are different ways of delivering CRRT and IHD. The multiple components contributing to daily costs vary among centers and countries. In some ICUs, CRRT can be directly delivered by the ICU staff operating readily available CRRT platforms while IHD has to be delivered by renal dialysis nurses, implying the borrowing of external resources. Other ICUs have both modalities readily available and operable by their own trained staff. In other instances, CRRT may not even be available at all. In our analysis, both modalities were assumed to be interchangeably available and operable in the ICU. This may impede the generalizability of our findings given the variation of practices across ICUs worldwide.

Our model intended to palliate a lack of evidence. FO is considered as a potential condition in which RRT modalities may have differential outcomes. However, comparative data are lacking between CRRT and IHD for management of FO in AKI patients. This is probably due to the difficulty in making direct clinical comparisons, notably through randomized clinical trials. There would be significant challenges in designing a reasonable protocol with clear clinical equipoise between volume control and noncontrol in hemodynamically unstable patients that would warrant safe and justified randomization. This provided the rationale for our modeling study.

Our modeling exercise has some limitations. First, we did not consider that patients in the "fluid balance" state may transit back to the "fluid overload" state. Our model focuses on scenarios that are more common in clinical practice. Such transition can happen in a small proportion of patients when they develop acute complications or have sudden worsening of their critical illness after a period of clinical stability and achieving fluid balance. However, most of these patients are likely to die, which is captured in our analysis. Second, complications of CRRT and IHD were not accounted for in the analysis. There are numerous complications related to CRRT and IHD and fitting models for each of those complications would have been beyond the scope of our study. Furthermore, randomized clinical trials comparing CRRT and IHD showed no significant differences in adverse events between the two modalities (45, 46). Third, our analysis only captured direct healthcare costs. Indirect costs are generally substantial and should be factored in to comprehensively inform societal and policy decisions (47, 48).

Finally, parameters were informed by the literature, based on scattered results from RRT studies designed for other purposes. This is precisely the objective of modeling, to bring together in a coherent analytical framework a set of data to address a specific research question, when evidence cannot be generated in a direct and timely manner. As such, we believe that our work has fulfilled its role and now fills an important gap previously left unchartered. Nevertheless, our work remains more suggestive than affirmative and needs to be complemented by further research.

In conclusion, our model-based analysis provides an economic rationale for CRRT initiation as the modality of choice in AKI patients with FO requiring RRT. This finding is to be confirmed by properly designed future research.

1 *Department of Public Health, Epidemiology & Health Economics, University of Liège, Liège, Belgium.*

2 *SERFAN Innovation, Namur, Belgium.*

3 *Program for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA.*

4 *Baxter Healthcare Corporation, Deerfield, IL.*

5 *Baxter Deutschland GmbH, Unterschleissheim, Germany*

6 *Department of Critical Care & Nephrology, King's College London, Guy's & St Thomas' Hospital, London, United Kingdom.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Dr. Ethgen was involved in conceptualization, methodology, formal analysis, and writing–original draft. Dr. Murugan was involved in conceptualization, methodology validation, and writing–review & editing. Dr. Echeverri was involved in project administration, resources, and writing–review & editing. Blackowicz was involved in project administration, resources, and writing–review & editing. Dr. Harenski was involved in project administration, resources, and writing–review & editing. Dr. Ostermann was involved in conceptualization, methodology, formal analysis, validation, and writing–review & editing. All authors critically reviewed and approved the final version for submission.

Drs. Ethgen and Murugan are authors of the publication and have received consulting fees from Baxter Healthcare Corporation for developing the present economic model. Dr. Ostermann is an author of the publication and received fees for developing the present model which were used to support research activities in the

institution. Dr. Echeverri, Dr. Blackowicz, and Dr. Harenski are full-time employees of Baxter International with ownership interest.

For information regarding this article, E-mail: o.ethgen@uliege.be

The results presented in this article have not been published previously in whole or in part. The present economic analysis was funded by Baxter Healthcare Corporation. This publication was subject to review by internal employees from Baxter Healthcare Corporation prior to submission for protection of Confidential Information. However, the authors retain full responsibility for the content of this publication.

The present economic model has not been registered on clinical.trials.gov.

REFERENCES

1. Hoste EAJ, Kellum JA, Selby NM, et al: Global epidemiology and outcomes of acute kidney injury. *Nat Rev Nephrol* 2018; 14:607–625
2. Balakumar V, Murugan R, Sileanu FE, et al: Both positive and negative fluid balance may be associated with reduced long-term survival in the critically ill. *Crit Care Med* 2017; 45:e749–e757
3. Raimundo M, Crichton S, Martin JR, et al: Increased fluid administration after early acute kidney injury is associated with less renal recovery. *Shock* 2015; 44:431–437
4. Zhang L, Chen Z, Diao Y, et al: Associations of fluid overload with mortality and kidney recovery in patients with acute kidney injury: A systematic review and meta-analysis. *J Crit Care* 2015; 30:860.e7–e13
5. Zhang J, Crichton S, Dixon A, et al: Cumulative fluid accumulation is associated with the development of acute kidney injury and non-recovery of renal function: A retrospective analysis. *Crit Care* 2019; 23:392
6. Messmer AS, Zingg C, Müller M, et al: Fluid overload and mortality in adult critical care patients - a systematic review and meta-analysis of observational studies. *Crit Care Med* 2020; 48:1862–1870
7. Fang J, Wang M, Gong S, et al: Increased 28-day mortality due to fluid overload prior to continuous renal replacement in sepsis associated acute kidney injury. *Ther Apher Dial* 2022; 26:288–296
8. Bellomo R, Cass A, Cole L, et al; RENAL Replacement Therapy Study Investigators: An observational study fluid balance and patient outcomes in the randomized evaluation of normal vs. augmented level of replacement therapy trial. *Crit Care Med* 2012; 40:1753–1760
9. Bouchard J, Soroko SB, Chertow GM, et al: Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int* 2009; 76:422–427
10. Hall A, Crichton S, Dixon A, et al: Fluid removal associates with better outcomes in critically ill patients receiving continuous renal replacement therapy: A cohort study. *Crit Care* 2020; 24:279
11. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group: KDIGO clinical practice guideline for acute kidney injury. *Kidney Int* 2012; 2(Suppl 1):1–138
12. Ostermann M, Joannidis M, Pani A, et al; 17th Acute Disease Quality Initiative (ADQI) Consensus Group: Patient selection and timing of continuous renal replacement therapy. *Blood Purif* 2016; 42:224–237
13. Bell M, Granath F, Schön S, et al; SWING: Continuous renal replacement therapy is associated with less chronic renal failure than intermittent haemodialysis after acute renal failure. *Intensive Care Med* 2007; 33:773–780
14. Schneider AG, Bellomo R, Bagshaw SM, et al: Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: A systematic review and meta-analysis. *Intensive Care Med* 2013; 39:987–997
15. Liang KV, Sileanu FE, Clermont G, et al: Modality of RRT and recovery of kidney function after AKI in patients surviving to hospital discharge. *Clin J Am Soc Nephrol* 2016; 11:30–38
16. Child DL, Cao Z, Seiberlich LE, et al: The costs of fluid overload in the adult intensive care unit: Is a small-volume infusion model a proactive solution? *Clinicoecon Outcomes Res* 2015; 7:1–8
17. Vaara ST, Korhonen A-M, Kaukonen K-M, et al; FINNAKI Study Group: Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: Data from the prospective FINNAKI study. *Crit Care* 2012; 16:R197
18. Murugan R, Kerti SJ, Chang C-CH, et al: Association between net ultrafiltration rate and renal recovery among critically ill adults with acute kidney injury receiving continuous renal replacement therapy: An observational cohort study. *Blood Purif* 2022; 51:397–409
19. Wald R, Shariff SZ, Adhikari NKJ, et al: The association between renal replacement therapy modality and long-term outcomes among critically ill adults with acute kidney injury: A retrospective cohort study. *Crit Care Med* 2014; 42:868–877
20. Palevsky PM, O'Connor TZ, Chertow GM, et al: Intensity of renal replacement therapy in acute kidney injury: Perspective from within the Acute Renal Failure Trial Network Study. *Crit Care* 2009; 13:310
21. Bellomo R, Cass A, Cole L, et al; RENAL Replacement Therapy Study Investigators: Intensity of continuous renal-replacement therapy in critically ill patients. *N Engl J Med* 2009; 361:1627–1638
22. Bagshaw SM, Wald R, Adhikari NKJ, et al; STARRT-AKI Investigators; Canadian Critical Care Trials Group; Australian and New Zealand Intensive Care Society Clinical Trials Group; United Kingdom Critical Care Research Group; Canadian Nephrology Trials Network; Irish Critical Care Trials Group: Timing of initiation of renal-replacement therapy in acute kidney injury. *N Engl J Med* 2020; 383:240–251
23. Bonnassieux M, Duclos A, Schneider AG, et al; AzuRéa Group: Renal replacement therapy modality in the ICU and renal recovery at hospital discharge. *Crit Care Med* 2018; 46:e102–e110
24. Social Security: Actuarial Life Table. 2019. Available at: https://www.ssa.gov/oact/STATS/table4c6.html. Accessed December 6, 2021
25. U.S. Renal Data System: 2020 Annual Data Report, 2020. Available at: https://adr.usrds.org/2020. Accessed December 6, 2021

26. Ethgen O, Schneider AG, Bagshaw SM, et al: Economics of dialysis dependence following renal replacement therapy for critically ill acute kidney injury patients. *Nephrol Dial Transplant* 2015; 30:54–61
27. Mayer KP, Ortiz-Soriano VM, Kalantar A, et al: Acute kidney injury contributes to worse physical and quality of life outcomes in survivors of critical illness. *BMC Nephrol* 2022; 23:137
28. Oeyen S, De Corte W, Benoit D, et al: Long-term quality of life in critically ill patients with acute kidney injury treated with renal replacement therapy: A matched cohort study. *Crit Care* 2015; 19:289
29. Soliman IW, Frencken JF, Peelen LM, et al: The predictive value of early acute kidney injury for long-term survival and quality of life of critically ill patients. *Crit Care* 2016; 20:242
30. Jiang R, Janssen MF, Pickard AS: US population norms for the EQ-5D-5L and comparison of norms from face-to-face and online samples. *Quality Life Res* 2021; 30:803–816
31. Wyld M, Morton RL, Hayen A, et al: A systematic review and meta-analysis of utility-based quality of life in chronic kidney disease treatments. *PLoS Med* 2012; 9:e1001307
32. Manns B, Doig CJ, Lee H, et al: Cost of acute renal failure requiring dialysis in the intensive care unit: Clinical and resource implications of renal recovery. *Crit Care Med* 2003; 31:449–455
33. Dasta JF, McLaughlin TP, Mody SH, et al: Daily cost of an intensive care unit day: The contribution of mechanical ventilation. *Crit Care Med* 2005; 33:1266–1271
34. Srisawat N, Lawsin L, Uchino S, et al; BEST Kidney Investigators: Cost of acute renal replacement therapy in the intensive care unit: Results from The Beginning and Ending Supportive Therapy for the Kidney (BEST kidney) study. *Aust Crit Care* 2010; 14:R46
35. Ethgen O, Zarbock A, Koyner JL, et al: Early vs. delayed initiation of renal replacement therapy in cardiac-surgery associated acute kidney injury: An economic perspective. *J Crit Care* 2022; 69:153977
36. U.S. Bureau of Labor Statistics: Consumer Price Index Medical Care Services. Available at: http://www.bls.gov/data/2021. Accessed December 5, 2021
37. State Health Fact of the Kaiser Family Foundation (KFF): Hospital Adjusted Expenses per Inpatient Day, 2021. Available at: https://www.kff.org/health-costs/state-indicator/ expenses-per-inpatient-day/2021. Accessed May 28, 2021
38. Papanicolas I, Marino A, Lorenzoni L, et al: Comparison of health care spending by age in 8 high-income countries. *JAMA Network Open* 2020; 3:e2014688
39. Institute for Clinical and Economic Review: ICER's Reference Case for Economic Evaluations: Principles and Rationale, Current As of January 31, 2020, 2020. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_Reference_Case_013120.pdf
40. Phelps CE: A new method to determine the optimal willingness to pay in cost-effectiveness analysis. *Value Heath* 2019; 22:785–791
41. Vanness DJ, Lomas J, Ahn H: A health opportunity cost threshold for cost-effectiveness analysis in the United States. *Ann Intern Med* 2021; 174:25–32
42. Uchino S, Bellomo R, Morimatsu H, et al: Continuous renal replacement therapy: A worldwide practice survey. The beginning and ending supportive therapy for the kidney (B.E.S.T. kidney) investigators. *Intensive Care Med* 2007; 33:1563–1570
43. Murugan R, Ostermann M, Peng Z, et al: Net ultrafiltration prescription and practice among critically ill patients receiving renal replacement therapy: A multinational survey of critical care practitioners. *Crit Care Med* 2020; 48:e87–e97
44. Chen H, Murugan R: Survey of U.S. critical care practitioners on net ultrafiltration prescription and practice among critically ill patients receiving kidney replacement therapy. *J Crit Care Med* 2021; 7:272–282
45. Vinsonneau C, Camus C, Combes A, et al; Hemodiafe Study Group: Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: A multicentre randomised trial. *Lancet* 2006; 368:379–385
46. Schefold JC, von Haehling S, Pschowski R, et al: The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): A prospective randomized controlled trial. *Crit Care* 2014; 18:R11
47. Laukkanen A, Emaus L, Pettilä V, et al: Five-year cost-utility analysis of acute renal replacement therapy: A societal perspective. *Intensive Care Med* 2013; 39:406–413
48. Griffiths J, Hatch RA, Bishop J, et al: An exploration of social and economic outcome and associated health-related quality of life after critical illness in general intensive care unit survivors: A 12-month follow-up study. *Crit Care* 2013; 17:R100