Comparing the cost-utility of renal replacement therapies delivered to critically ill patients with acute kidney injury in the United States

Martins R [1,2], Echeverri J [3], Koyner J [4], Harenski K [5], Wald R [6,7]

1. Global Market Access Solutions, Health Economics Unit, St-Prex, Switzerland
2. University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
3. Vantive Health LLC, Global Medical Affairs, Deerfield, Illinois, United States
4. Section of Nephrology, University of Chicago, Chicago, Illinois, United States
5. Vantive Health LLC, Unterschleissheim, Germany
6. Division of Nephrology, St. Michael's Hospital, University of Toronto,
7. Li Ka Shing Knowledge Institute, Toronto, ON, Canada.

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BACKGROUND

- Acute kidney injury (AKI) is common in intensive care unit (ICU) patients, with 5-15% requiring acute renal replacement therapy (RRT) [1]. Incomplete recovery is common, leading to important morbidity and mortality [2].
- Continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD) are widely recognized treatments for severe AKI [3].
- The choice of initial RRT modality depends on the patient's clinical status, including hemodynamic stability and volume status, as well as the resources and expertise available at the institution [4].
- There is no conclusive evidence of mortality differences among RRT modalities due to study limitations [5].
- CRRT appears to lower the risk of 90-day dialysis dependence (DD) when used as the initial treatment [6,7].

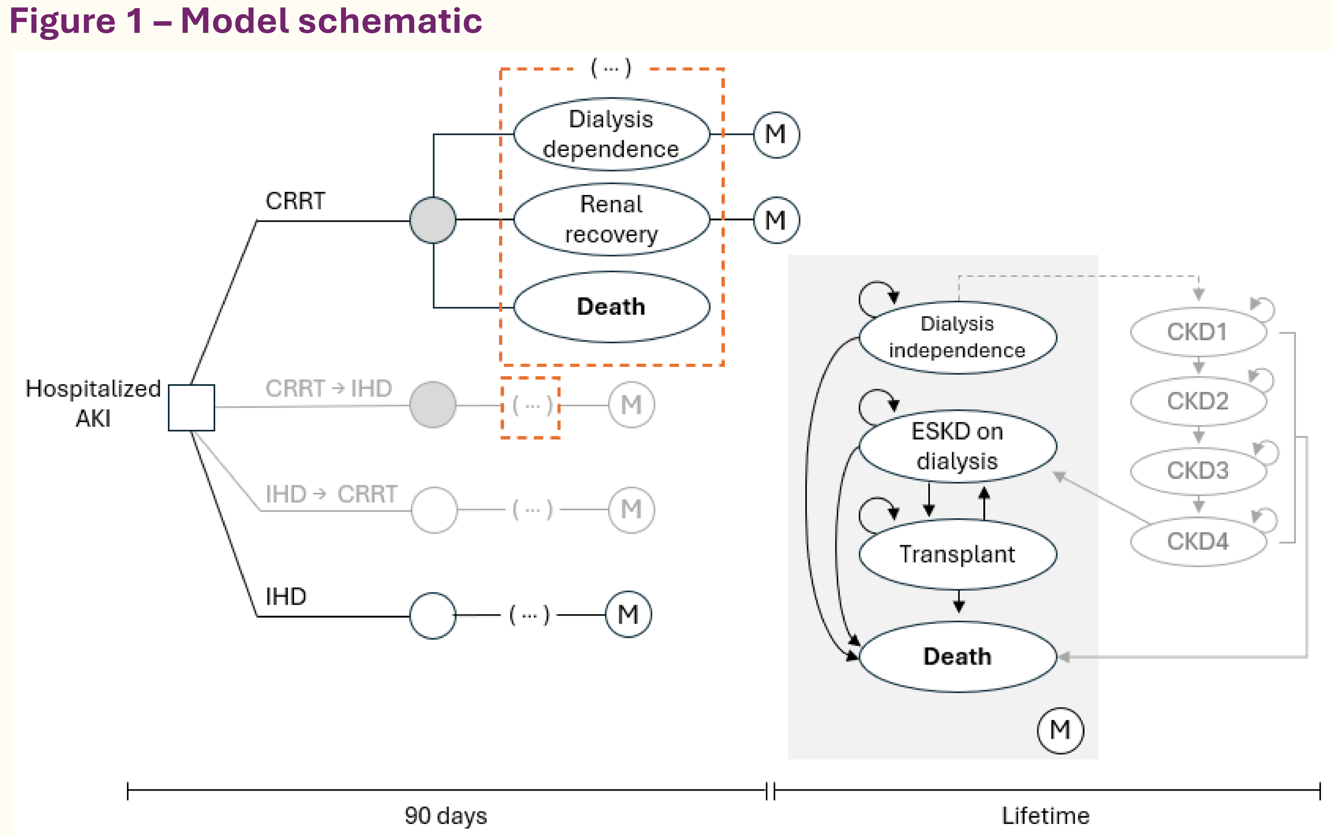
OBJECTIVES

- This analysis aims to consolidate the evidence on the cost-utility of CRRT compared with IHD for treating AKI in the ICU using a United States (US) third-party payer perspective. The analysis incorporates recent clinical evidence [6,7] and expands on previous modelling simplifications.

METHODS

- The analysis combined a decision tree modeling outcomes over 90 days since RRT initiation, and a semi-Markov model with annual cycles capturing lifetime consequences and costs of end-stage kidney disease (ESKD), dialysis, and kidney transplantation (**Figure 1**). Base case settings assumed RRT modality would not differentially impact mortality, hospital/ICU length-of-stay, or severity of dialysis independent chronic kidney disease (CKD).
- The effect of RRT on 90-day DD, used as a proxy for lifetime DD, was sourced from a propensity score-adjusted study, representative of the US population with AKI in ICU [6]. An ad hoc literature review and meta-analysis of non-randomized comparative studies was used to inform an alternative input for scenario analysis (**Table 1**).

Figure 1 – Model schematic



Acronyms: AKI, acute kidney injury; CKD, chronic kidney disease; ESKD, end-stage kidney disease; IHD, intermittent hemodialysis; M, Markov process. Light grey elements of the diagram represent structural variations explored in scenario analyses.

- Post-AKI CKD distribution [8] and transitions between CKD severity states [9] used in scenario analyses were informed by peer reviewed publications.
- The probabilities of ESRD-related death, renal transplantation, graft failure and the long-term impact of CKD on costs were mostly sourced from the US Renal Data System annual report [10].
- Preference-elicited utility values were obtained from peer-reviewed publications to calculate quality adjusted life-years (QALYs) and equal-value life years (evLYs) [11-15].
- The results were subject to half-cycle correction, 3% annual discounting, and were summarized as incremental cost-effectiveness ratios (ICER). ICERs were calculated as the ratio of the difference in costs over the difference in QALYs or evLYS between comparators and assessed at a $50K to $100K willingness-to-pay threshold. Uncertainty was explored in deterministic and probabilistic sensitivity analyses.

RESULTS

- Base case results suggest CRRT is associated with additional life years (0.269) and quality of life (0.223 QALYs or 0.236 evLYs), but higher costs ($4,864), compared with IHD. Further, CRRT was predicted to avoid 2.2 cases of DD and 2.1 ESKD-related deaths per 100 individuals requiring RRT for AKI in ICU. Consequently, CRRT was deemed cost-effective at $21,755/QALY or $20,590/evLY gained (**Table 1**).
- One-way sensitivity analysis showed that varying CRRT's effect on 90-day DD had the greatest impact on base case results (**Figure 2**). Nonetheless, additional scenarios utilizing alternative sources for this input suggest that base case conclusions persist.
- Scenarios varying the effect of CRRT on hospital and ICU length-of-stay yielded the intervention dominant compared with IHD.
- The mean of 20,000 Monte Carlo simulations suggested that according to base case settings, CRRT was associated with an 89.6% probability of being cost-effective compared with IHD, probabilistic ICER $23,860/QALY or $22,593/evLY gained (**Figure 3**).
- Modeling CKD progression further increased the base case ICER to $54,688/QALY or $49,586/evLY, with 50% of incremental costs related to CKD management. Additional scenarios showed that a modest effect of CRRT in reducing CKD progression (i.e. ≥5% decrease) substantially improved CRRT cost-effectiveness (**Figure 4**).

Table 1 – Base case and scenario analysis results

Scenario	Base case input	New input	Incremental				ICER		Probability cost-effective $50K/QALY
			Costs	LYs	QALYs	evLY	($/QALY)	($/evLY)	
Base case	-	-	$4,864	0.269	0.224	0.236	$21,755	$20,590	89.6%
Effect of CRRT on dialysis dependence - Wald 2023[7]	OR 0.680	OR 0.610	$5,118	0.329	0.274	0.289	$18,680	$17,682	94.0%
Effect of CRRT on dialysis dependence - MA NRCS	OR 0.680	OR 0.757	$4,628	0.212	0.177	0.187	$26,198	$24,793	91.8%
CRRT reduces mortality - Wald 2023[7]	CRRT=IHD	OR 0.900	$14,547	0.650	0.528	0.561	$27,525	$25,915	90.4%
CRRT reduces LOS hospital - Wald 2023[7]	CRRT=IHD	6 hospital free days	-$5,512	0.269	0.225	0.238	-$24,474	-$23,172	99.6%
CRRT reduces ICU stay - Wald 2023[7]	CRRT=IHD	2 ICU free days	-$4,187	0.269	0.225	0.238	-$18,609	-$17,618	99.6%
Switching RRT allowed	Not allowed	33.8% CRRT to IHD, 1.8% IHD to CRRT	$4,514	0.269	0.224	0.236	$20,188	$19,106	91.3%
Time horizon is 10 years	45 years	10 years	$1,626	0.113	0.098	0.103	$16,676	$15,730	80.2%
Discount rate 2%	3%	2%	$5,498	0.302	0.251	0.265	$21,940	$20,770	90.1%
Discount rate 1.5%	3%	1.5%	$5,863	0.321	0.266	0.281	$22,042	$20,870	90.9%
No CKD in DI	40% CKD 3-4	No CKD, GP costs and utilities	$2,631	0.277	0.235	0.244	$11,184	$10,773	92.2%
CKD progression is modeled	Not modeled	CKD distribution	$6,777	0.154	0.124	0.137	$54,688	$49,586	32.7%
CRRT avoids 5% of CKD progression (all severities)	Not modelled	CKD distribution	$4,935	0.286	0.242	0.264	$20,407	$18,660	99.7%

Figure 2 - Tornado diagram

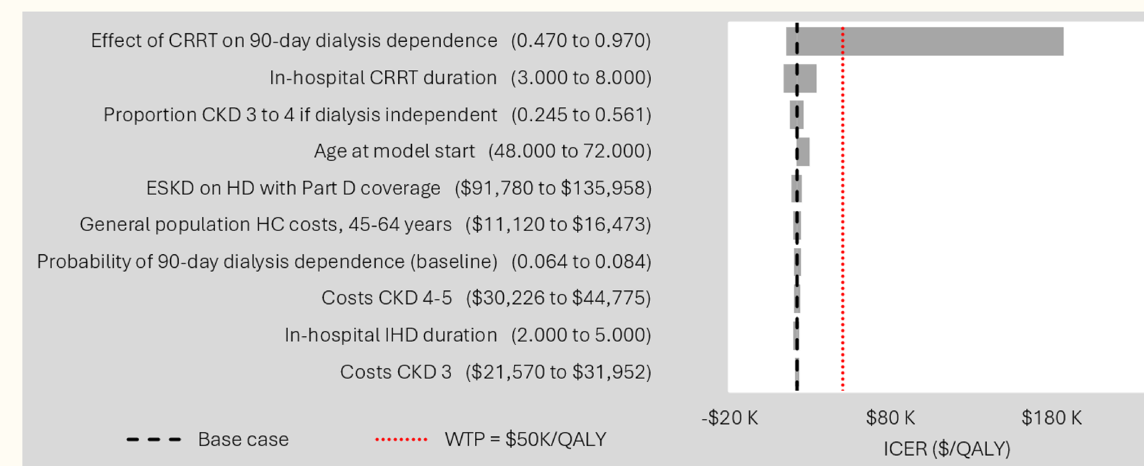


Figure 3 – Cost-effectiveness acceptability curve of CRRT vs IHD

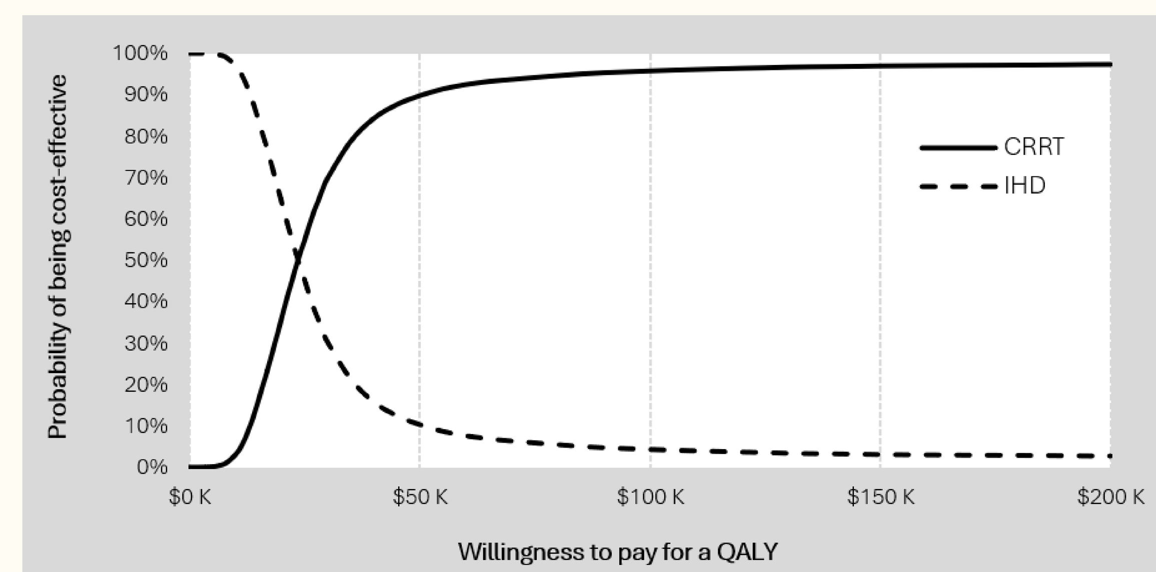
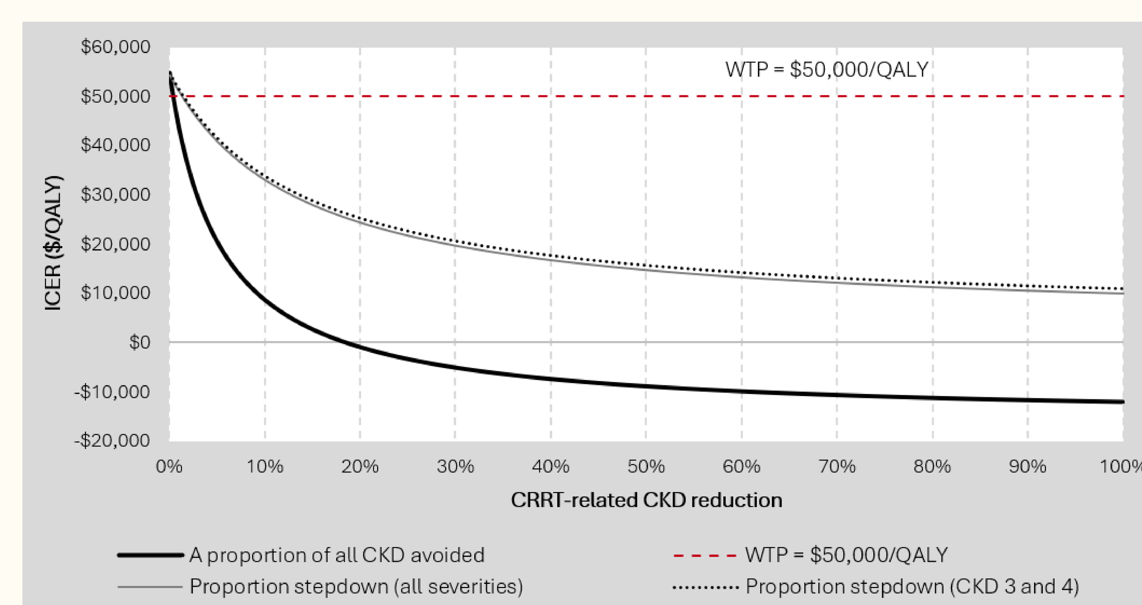


Figure 4 - Scenario analysis exploring CKD progression



Acronyms: CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; DI, dialysis independence; evLYs, equal value life years; ESKD, end stage kidney disease; GP, general population; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; IHD, intermittent hemodialysis; LOS, length of stay; LYs, life years; MA, meta-analysis; NRCS, non-randomized comparative studies; OR, odds ratios; QALY, quality-adjusted life year; RRT, renal replacement therapy; WTP, willingness to pay.

DISCUSSION

- Recent non-randomized comparative studies consensually point to CRRT being associated with a 25-39% reduction in DD. The economic consequences of reducing DD were shown sufficient to offset the higher upfront costs of CRRT, deeming the technology cost effective.
- There is limited evidence supporting a difference in short-term mortality related to RRT modality, nonetheless our model suggests that IHD is associated with excess ESRD-related mortality due to increased DD.
- **Strengths**: (1) Robust, reproducible methods aligned with national and international standards. (2) Inputs and clinical rationale validated by clinical experts. (3) Strengthens findings from previous cost-utility analyses. (4) Addresses data quality concerns by incorporating propensity score matched analysis from large, US representative sample. (5) Extensive sensitivity analyses which support base case results.
- **Weaknesses**: (1) Did not account for regional variations in clinical practice, and may not be generalizable to all US geographies. (2) Dialysis dependence at 90 days used as proxy for ESKD-D. (3) Dated source informing RRT costs, not US-specific. (4) Direct non-medical costs and indirect costs not accounted for in the analysis.

Conclusions

- CRRT is likely more cost-effective than IHD for managing severe AKI in ICUs in the US, potentially avoiding 2.2 deaths and 2.1 cases of permanent dialysis for every 100 patients treated.
- Long-term CKD costs, often overlooked, account for over 50% of the excess costs linked to CRRT in AKI patients. Further research is needed to assess how RRT modality affects CKD progression after severe AKI.

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