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Economic evaluation of different treatment modalities in acute kidney injury

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Abstract

Background. Major controversy exists regarding the preferred treatment option for acute kidney injury (AKI). The purpose of this study was to assess the incremental cost-effectiveness of continuous renal replacement therapy (CRRT) versus intermittent renal replacement therapy (IRRT) and conservative (CONS) AKI treatment in Belgium.

Methods. An area-under-the-curve model based on survival analysis was used to estimate costs and health outcomes using a 2-year time horizon. Input data were derived from the multi-centre Stuivenberg Hospital Acute Renal Failure 4 study.

Results. Analyses indicated that in-hospital mortality, hospitalization costs and hospital length of stay differed significantly between treatment modes. Follow-up mortality rates and follow-up cost per day showed no significant difference between the treatment modes. Utility values, which improved gradually after admission to the hospital, revealed no significant differences between the three treatment strategies. CONS treatment was associated with a 2-year cost of 33 802€ and 0.54 quality-adjusted life years (QALYs). The CRRT was the most expensive therapy with a cost of 51 365€ leading to 0.57 QALYs. The cost and QALYs associated with IRRT were 43 445€ and 0.50, respectively. One-way sensitivity analyses indicated the 'in-hospital mortality' as the variable with the greatest influence on the results. Probabilistic sensitivity analysis resulted in a significant difference in treatment costs but no significant difference in QALY gain.

Conclusions. This study has indicated that the most expensive treatment (CRRT) associated with an incremental cost of approximately €7920 generates only a minor non-significant increase in QALYs of 0.07 compared with IRRT. Additionally, the results revealed that the RRTs did not result in a significant increase in QALYs despite their higher cost compared with the CONS treatment. From a health economic perspective, the latter seems to be the preferred treatment strategy.

Keywords: acute kidney injury; cost-effectiveness; renal replacement therapy; SHARF

Introduction

Approximately 1 out of 4 critically ill patients admitted to the intensive care unit (ICU) develops acute kidney injury (AKI) leading to high mortality rates (over 50% in ICU) and a substantial economic burden [1–3]. Although there seems to be an overall consensus on treating severely ill AKI patients with renal replacement therapy (RRT) instead of the conservative therapy (CONS), the best treatment modality for AKI remains a matter of debate, since evidence is lacking to generalize this opinion [4, 5]. Moreover, evidence for the type of dialysis and the starting time [6–11] remains conflicting. Recent RCTs and meta-analyses showed similar benefit with either continuous RRT (CRRT) or intermittent RRT (IRRT) [12–18]. This was confirmed in the multi-centre Stuivenberg Hospital Acute Renal Failure 4 (SHARF4) study, in which the modality of RRT had no impact on ICU outcome. In addition, the study revealed a higher hospital mortality in AKI patients receiving RRT versus conservative treatment, which could not only be explained by higher disease severity in the RRT group. The long-term mortality outcome of AKI was not related to treatment modality during hospitalization [4, 18, 19].

Health care resources are limited, and in order to gain the highest value for money, policy makers should obtain better insights into the costs and benefits of medical treatments. Owing to the high morbidity, mortality and costs associated with AKI and its treatment, it is recommended that the cost-effectiveness of the different treatment methods be assessed, taking into account the latest available evidence, hence allowing health care payers to make more profound decisions in their resource allocation. Few cost-effectiveness studies have been performed in this area, and within our knowledge the conservative treatment option was never included in any health economic evaluation. Hence, the purpose of our study was to examine the clinical and economic effect of the different AKI treatment modalities (conservative, IRRT and CRRT) based on the multi-centre prospective partially randomized SHARF4 study including 1303 AKI patients with a 2-year follow-up period. The outline and detailed results of this study are reported extensively elsewhere [19].

Materials and methods

We aimed to determine the preferred treatment methods for AKI, taking into account both the associated costs and health benefits. Our cost-effectiveness evaluation was based on an area-under-the-curve model. Survival analysis, using individual patient data, was applied to estimate time to event data. Events considered in this study were hospital mortality and short-term follow-up mortality [20]. The survival model was able to deal with the problem of censoring, which frequently occurs in databases containing follow-up data. Mortality estimates and a cost per day for each treatment modality were calculated. The study was performed from a payer perspective taking into account only direct medical costs, based on true Belgian cost data.

Study population

Data were derived from the multi-centre SHARF4 study, which started in April 2001 and ended in March 2004 [19]. Nine Belgian ICUs participated in the study. Only adult ICU patients with a serum creatinine of >2 mg/dL were included. For all these patients, disease severity was defined by calculating the SHARF score. This score was developed and validated in previous SHARF projects as a specific severity scoring system for AKI [21, 22]. The SHARF4 study was a partially randomized observational study. The decision regarding the treatment mode (conservative, CRRT, IRRT) was at the discretion of the responsible physician, taking into account the rules of good clinical practice. Patients in need of RRT were assigned to daily IRRT (during 4–6 h daily) or CRRT after randomization or according to local practice. About half of the RRT patients were included in a randomized way; however, basic characteristics as well as severity scores (SHARF, APACHE II and SOFA) were comparable between both the randomized patient group and the non-randomized group. For the economic analysis, a database of 1303 AKI patients admitted to one of the nine participating Belgian ICUs was used. One hospital was not able to deliver the hospital billing data, and therefore, these records were deleted from the health economic analyses leaving us with 1208 AKI patient records from eight different hospitals. RRT, either IRRT (intermittent haemodialysis) or CRRT (continuous veno-venous hemofiltration), was initiated in 364 and 249 patients, respectively. Follow-up data after hospital discharge were collected for all the 601 AKI patients surviving hospitalization. A total of 203 survivors were interviewed at home by trained medical students and study nurses with a mean of 20.1 months after hospital discharge. Follow-up health care costs were documented for 172 patients. The median IRRT treatment consisted of four sessions (one session per day) with a median duration of 4 h, and the median CRRT treatment lasted 4 days with a mean substitution of 1.8 L/h or 23.0 mL/kg. Conservative treatment consisted of volume, electrolyte and acid–base homeostasis management and specific drug management. For more information on the treatment modalities, we refer the reader to the effectiveness papers [4, 18, 19].

Data collection

The SHARF database contains individual patient information on hospital length of stay, index hospitalization costs, 1-year follow-up costs, Short-Form 36 (SF-36) scores, mortality during index hospitalization and follow-up mortality.

(i) Using a payer perspective, the current analyses take into account only direct medical costs and no additional societal costs. Hence, the economic impact of absenteeism from work due to the illness, or the time investment of family members taking care of the patient was not considered. Costs included both public insurance payments and patient out-of-pocket payments, comprising ambulatory costs, medication costs and hospitalization costs. The costs were retrospectively collected for each patient separately. Two different sources were used in order to calculate the total direct medical costs. Individual cost data associated with the index hospitalization were collected from the hospital billing data gathered from the different participating hospitals. The billing data include all the costs and expenses made during the index hospitalization for each individual separately. They are a sum of physician costs, investigation costs, dialysis costs, medication costs and overhead costs such as hospital maintenance and hospital administration. Follow-up costs (after index hospitalization discharge until Year 1) were provided by the public health insurance companies. The total health care costs, AKI related as well as non-AKI related, were gathered during this 1-year follow-up period. No follow-up costs were available for the second year.

(ii) Hospital mortality was registered during the SHARF4 study. Long-term mortality was checked in the national register at 1 and 2 years after discharge.

(iii) Within the SHARF4 trial, long-term quality of life was assessed by using the Medical Outcome Survey SF-36 during home visits (20.1 months after discharge). To convert the SF-36 scores into a utility level, an algorithm supplied by Brazier (University of Sheffield) was used [23]. Since no short-term quality of life data were included in the SHARF database, these were gathered from the literature. From a recently published study a short-term utility score of 0.4 (60 days after hospital admission) was extracted [24]. It is assumed that the quality of life progresses equally with the burden of disease. To estimate a daily utility

Table 1. Summary of input data for the health economic model

	CONS (SE)	IRRT (SE)	CRRT (SE)
Hospital length of stay	29 days (1.5)	38 days (2.2)	38 days (2.2)
Mean cost index hospitalization	13 569€ (850€)	25 169€ (1427€)	30 447€ (2491€)
Follow-up cost/day	63€ (6€)	63€ (6€)	63€ (6€)
Utility hospital	0.13 × ln(*t*)–0.101	0.13 × ln(*t*)–0.11	0.13 × ln(*t*)–0.11
Utility follow-up first period	0.13 × ln(*t*)–0.101	0.13 × ln(*t*)–0.11	0.13 × ln(*t*)–0.11
Utility follow-up after 20.1 months	0.69 (0.15)	0.69 (0.15)	0.69 (0.15)
Unadjusted hospital survival	57.60% (17.28%)	46.40% (13.92%)	35.70% (10.71%)

Summary of input parameters in the cost-effectiveness model. SE, standard error; CONS, conservative treatment; IRRT, intermittent renal replacement therapy; CRRT, continuous renal replacement therapy. These data were used in the PSA to account for the range of uncertainty associated with each mean value.

value between hospital admission and 2-year follow-up, the logarithmic equation 0.13 × ln(*t*)–0.101 was applied, on the basis of the assumption that the quality of life improvement follows a logarithmic distribution (see Table 1).

Statistical methods

Statistical analyses were performed using PASW 18. One-way analysis of variance was used for statistical comparison of cost estimates, utility estimates and hospital length of stay. Chi-square test was used to assess in-hospital mortality. Logistic regression was applied to adjust these mortality rates for severity of illness by including the SHARF-, APACHE II- and SOFA-scores into the logistic model. The mean severity score within each treatment group was calculated. For each additional point on the SHARF scale between the conservative method and the RRT treatments, 2.8% mortality was extracted from the hospital mortality percentage. With regard to follow-up mortality, a survival curve was simulated utilizing Kaplan–Meier.

Cost-effectiveness analysis

Based on the aforementioned input data a health-economic model was built for each treatment modality to calculate the costs and health benefits. Because it concerns an acute illness in a population with poor prognosis and since the follow-up outcomes after the acute episode were the same among treatment groups, a 2-year time horizon was used with no lifetime projection, in order to limit uncertainty inherent to long-term projections.

An incremental cost-effectiveness ratio (ICER), defined as the difference in the total costs (numerator) divided by the difference in total health gains (denominator), was calculated for the different treatment options [25]. The ICER is represented by the formula: $(\text{costs}_{\text{treatment A}} - \text{costs}_{\text{treatment B}})/(\text{effectiveness}_{\text{treatment A}} - \text{effectiveness}_{\text{treatment B}})$.

The health gains are expressed in quality-adjusted life years (QALYs). A QALY is a common outcome measure, often used in health economic evaluations. This measure allows easy comparison between different study results. A QALY combines both the quantity (duration) and the quality of life. The latter is represented by a value ranging between 0 and 1, where 0 represents death and 1 represents perfect health. To calculate the total QALYs associated with a certain treatment, the quality of life value (=utility value) is multiplied by the time period one spends in a given disease state [25].

QALYs and cost for each of the AKI treatments were calculated as follows. The survival curve was analysed for the three different patient groups. Daily survival percentages were calculated and these were used to estimate the area under the survival curve from hospital discharge until year 2. Daily cost and quality of life values are then multiplied by the daily percentage of survivors. Summing up these costs and QALYs per day results in the total cost and the total QALYs for the patient cohort over the 2-year timeframe [26]. Applying this method for all the three treatment modalities allowed us to calculate the incremental effects and incremental costs.

A willingness to pay threshold of 30 000€ per QALY gained, a commonly used threshold in Belgium, was applied. This threshold refers to the amount one would want to pay for an additional life year in perfect health. Sensitivity analyses were performed to account for the effect of the uncertainty associated with the different input parameters, on the model's outcome. One-way sensitivity analyses were completed to asses the variation in the cost-effectiveness outcomes by varying individual input parameters over plausible ranges. Hence, this allowed evaluation of the individual influence associated with the uncertainty range around each variable. The results of the uncertainty ranges around the input parameters are represented in Tornado diagrams. Additionally, a probabilistic sensitivity analysis (PSA) was performed. One-way sensitivity analyses evaluate the effect of the uncertainty range of one parameter at a time, whereas a PSA allows assessment of the effect of the uncertainty of all the parameters simultaneously. The uncertainty of each input parameter is represented by a probability distribution, defined by the mean and the standard error of each parameter (see Table 1). As proposed by Briggs *et al.* [20] in order to perform a PSA, beta distributions were used to represent the uncertainty around the utility values and the in-hospital mortality, and gamma distribution were used for cost data and hospital length of stay. The PSA was based on 1000 iterations, whereby for each simulation a random draw was taken from each of the input parameter distributions.

For a more detailed description of the principles and methodologies of a cost-effectiveness analysis, the reader is referred to the article of Palmer [27].

Results

Analysis of the database

Hospital length of stay. The mean hospital length of stay differed significantly between the conservative treatment and RRTs, with a mean of 29 days [95% confidence interval (CI) = 26 days–32 days] for the first and 38 days (95% CI = 33 days–42 days) for the latter, with no significant difference between IRRT and CRRT (see Table 1).

Outcome. In-hospital mortality differed significantly between the different treatment groups, even after correction for disease severity (SHARF). Unadjusted mortality equals 42.4% for the conservative treatment modality, 53.60% for IRRT and 64.30% for CRRT (see Table 1). With regard to long-term mortality rates, survival analysis showed no significant difference between the different treatment group; therefore, one overall follow-up survival table was used. At 730 days after ICU admission, total mortality amounted to 66% (95% CI = 63–68%).

Quality of life data. No significant difference in utility data between the treatment groups at interview was found; hence, at a 20.1-month follow-up, a utility score of 0.69 (95% CI = 0.67–0.71) was used for all treatment modalities. Similar values were found in the literature, validating our score. The daily utilities from admission to interview followed a logarithmic distribution.

Cost estimates. Based on billing data, significant differences were found between the mean hospitalization costs in the three treatment groups. The CONS therapy was the least expensive one with a mean hospital cost of 13 569€ (95% CI = 11 895€–15 242€). The RRTs were more expensive with a mean hospital cost of 30 447 € (95% CI = 25 522€–35 372€) and 25 169€ (95% CI = 22 357€–27 982€) for CRRT and IRRT, respectively (see Table 1).

With regard to follow-up costs during the first year after the event, no significant difference was found between groups, and hence, an equal follow-up cost of 63 € (95% CI = 51€–75€) per day for each treatment modality was incorporated in our cost-effectiveness analysis based on the overall mean cost (see Table 1). These follow-up costs, based on public health insurance data, were collected for each patient separately. They included physician visits, hospitalization, dialysis and medication. No second-year follow-up costs were available; therefore, we assumed them to be equal to the first-year follow-up cost. Costs were discounted at 3% yearly. With regard to the costs, it is important to report on the relation between renal outcome and total cost with end stage renal disease patients generating the highest follow-up cost. At discharge, 13% of the patients were on dialysis (8% of conservative group, 22% of IRRT group, 15% of CRRT group), and after a 1-year follow-up 10.4% of the patients were on dialysis (6% of conservative group, 16% of IRRT group, 14% of CRRT group).

Model outputs

Below are the results of the base case analyses and the sensitivity analyses. The figures, adjusted for severity, were used in the calculation of these cost-effectiveness results.

Basecase. The conservative AKI treatment was the least expensive treatment with a mean total cost, including initial hospitalization costs and follow-up costs over a 2-year period, of 33 802€. The RRT modalities are more expensive with a mean total cost of 43 445€ for IRRT and 51 365€ for CRRT, the latter being the most expensive treatment of all. The conservative treatment was associated with a health gain of 0.54 QALYs, IRRT was associated with a health gain of 0.50 QALYs and CRRT was associated with a health gain of 0.57 QALYs. The ICER of CRRT versus IRRT amounts to 114 012€/ QALY. The ICER of CRRT versus CONS equals 590 410€/QALY. In addition, the conservative treatment dominated the IRRT modality, since IRRT has a higher cost and a lower QALY gain (see Table 2).

One-way sensitivity analysis. The results of the sensitivity analysis are shown in the tornado diagrams in Figure 1. The variables of interest are those for which a significant difference was found between the treatment groups. The results were sensitive to changes in in-hospital mortality, hospital length of stay and hospitalization costs (represented by the grey bars in Figure 1). For both comparisons (IRRT versus CONS and CRRT versus CONS), the in-hospital mortality seems to be the parameter with the most significant influence on the ICER, whereas the mean hospital length of stay has only a limited effect on the ICER.

Probabilistic sensitivity analysis. Figure 2 shows a scatterplot of the cost-effectiveness simulation for the three different treatment modalities based on 1000 iterations. The difference in cost between conservative treatment and RRTs appears clearly from this graph as well as the lack of significant difference in QALYs.

The cost-effectiveness planes representing the ICERs for the different treatment comparisons (CRRT versus IRRT, CRRT versus conservative approach, IRRT versus

Table 2. Results of cost-effectiveness analysis

Therapies compared	Incremental cost	Incremental QALY	ICER
CRRT versus CONS	17 563€	0.0297	590 410€/QALY
IRRT versus CONS	9643€	−0.0397	Dominant
CRRT versus IRRT	7919€	0.0694	114 012€/QALY

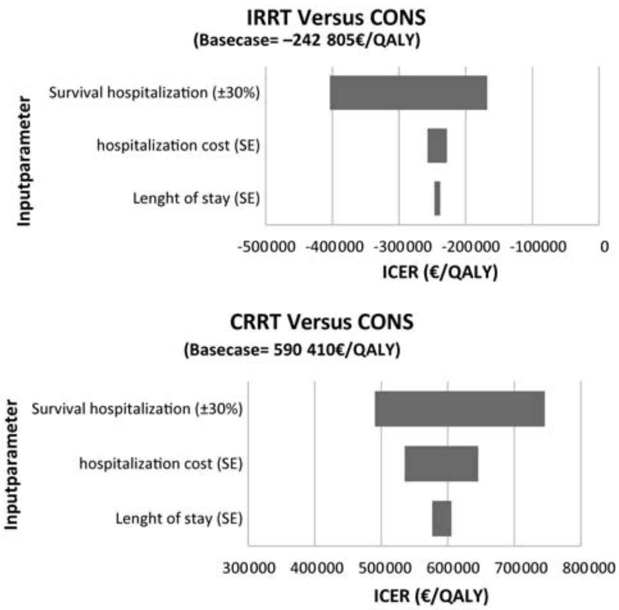

Fig. 1. Tornado diagrams. The input parameters 'in-hospital mortality', 'hospitalization cost' and 'hospital length of stay' are varied within their range of uncertainty in these one-way sensitivity analyses. The effects of these variables on the ICER are represented by grey bars. The input parameter hospital survival has the greatest influence. The hospitalization cost and the hospital length of stay have a smaller influence on the results. CONS, conservative treatment; IRRT, intermittent renal replacement therapy; CRRT, continuous renal replacement therapy; ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life year.

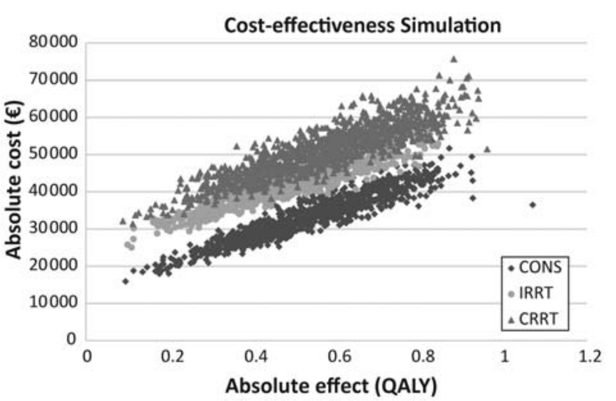

Fig. 2. Cost-effectiveness simulation for each treatment based on 1000 trials. The scatterplots represent the claud of uncertainty associated with the results of each treatment. The absolute results are shown. No significant difference in QALY gain can be found between the treatments. The results show a difference in costs, with the conservative treatment as the least expensive one. CONS, conservative treatment; IRRT, intermittent renal replacement therapy; CRRT, continuous renal replacement therapy.

conservative approach) in relation to a willingness to pay treshhold of 30 000€ per QALY are shown in Figure 3. For all the three comparisons, the scatter is situated mainly above the willingness to pay treshhold, which is represented by the diagonal line, hence visualizing the favourable outcome for the conservative treatment.

Discussion

The results of our analysis reveal that CRRT is not cost-effective compared with IRRT. CRRT does in fact increase the total quality of life, albeit not significantly; however, the supplementary cost per additional QALY associated with this therapy far exceeds the willingness to pay threshold of 30 000€/QALY. In addition, compared with a conservative treatment method, both renal replacement methods were not cost-effective, despite the fact that the severity of illness was taken into account.

Our findings confirm the results of the few economic evaluations already performed in this area. Klarenbach *et al.* [28] assessed the cost-effectiveness of continuous RRT versus intermittent haemodialysis within a Canadian context. This study assumed a lifetime time horizon and included renal recovery explicitly in their analytic model. Their analysis indicated that CRRT was associated with similar health outcomes but with a higher cost ranging from CAN$1100 to CAN$3700 per patient. A study by Hamel *et al*. during the 1990s evaluated the cost-effectiveness of dialysis and continuing aggressive therapy versus 'doing nothing'. The overall result amounted to CAN$128 200 per QALY, far exceeding the willingness to pay threshold [29].

Our study has some limitations that need to be addressed to correctly interpret the results. The area-under-the-curve model has the limitation that survival curves are based on extrapolation of the data. To avoid making strong assumptions by extrapolating the SHARF4 findings into long-term outcomes, a 2-year time horizon starting from the index event was taken into account. However, it can be assumed that the different treatment methods will be associated with different co-morbidities and associated costs in the long run. For example, recent studies have indicated a better renal recovery in patients treated with CRRT [30, 31]. Follow-up costs, gathered during the first year after the hospital discharge, were also utilized as the second-year follow-up cost; therefore, an overestimation of treatment cost may have occurred. With regard to the utility scores, a logarithmic equation was hypothesized on the basis of both literature and SHARF4 data since only one estimate per patient was available in our database. Hence, a slightly negative utility value was calculated for the first 2 days on ICU. Since these patients are most likely to be anxious and to suffer from pain, not able to walk and not able to dress themselves or execute daily activities, our utility scores were assumed to approach the reality, where such a disease state can be perceived as an inferior state versus the death state. Utility values starting from the home visits (20.1 months) until 2 years after discharge were considered to be constant in time. Literature findings confirmed this assumption, since long-term follow-up utility levels approached our 2-year follow-up values [32]. In addition, there is a lot of ongoing debate on use of QALYs. According to some, QALYs do not take into account all dimensions of health care.

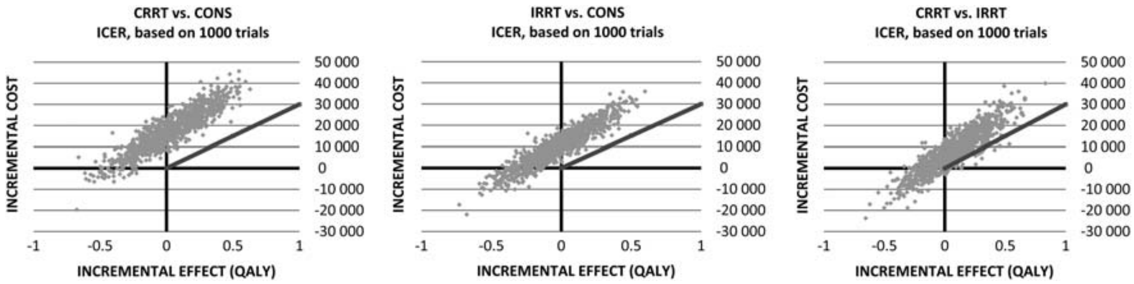

Fig. 3. Cost-effectiveness planes. Scatter plot representing the results of the PSA varying all input parameters simultaneously. The diagonal line represents the willingness to pay threshold of 30 000€ per QALY. ICER, incremental cost-effectiveness ratio; CRRT, continuous renal replacement therapy; IRRT, intermittent renal replacement therapy; CONS, conservative treatment. The figures show cost-effectiveness clouds located above the willingness to pay threshold, demonstrating the favourable outcome for the conservative treatment.

Furthermore, they do not account for the effect of the illness on the patients' environment like carers and family members. Some feel that the generic measurement instruments are not sensitive enough to capture disease-specific characteristics [33]. However, within the current study, quality of life was assessed using the SF-36 questionnaire, which is already far more detailed than the frequently used EQ-5D questionnaire.

This analysis was performed on the basis of a health care perspective considering only direct cost. Cost associated with absenteeism and care from family members were not taken into account, leading to an underestimation of the true cost. However, the strength of our study lies in the sensitivity analysis. We performed both one-way sensitivity analysis and PSA. This enabled us to assess the impact of the uncertainty around the input parameters and to test the robustness of the results.

This study has indicated that the most expensive treatment (CRRT) associated with an incremental cost of ~7920€ generates only a minor non-significant increase in QALYs of 0.07 compared with IRRT, resulting in an ICER of 114 012€/QALY, hence far exceeding the willingness to pay threshold of 30 000€/QALY. Additionally, the results revealed that both RRTs associated with an additional cost between €9643 and €17 563 compared with the CONS therapy did not result in a significant increase in quality of life. Hence, from a health economic perspective CONS therapy seems to be the preferred treatment strategy.

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References

1. de Mendonca A, Vincent JL, Suter PM *et al*. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. *Intensive Care Med* 2000; 26: 915–921
2. Ympa YP, Sakr Y, Reinhart K *et al*. Has mortality from acute renal failure decreased? A systematic review of the literature. *Am J Med* 2005; 118: 827–832
3. Chertow GM, Burdick E, Honour M *et al*. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 2005; 16: 3365–3370
4. Van Berendoncks AM, Elseviers MM, Lins RL. Outcome of acute kidney injury with different treatment options: long-term follow-up. *Clin J Am Soc Nephrol* 2010; 5: 1755–1762
5. Ghahramani N, Shadrou S, Hollenbeak C. A systematic review of continuous renal replacement therapy and intermittent haemodialysis in management of patients with acute renal failure. *Nephrology (Carlton)* 2008; 13: 570–578
6. Prowle JR, Bellomo R. Continuous renal replacement therapy: recent advances and future research. *Nat Rev Nephrol* 2010; 6: 521–529
7. Rabindranath K, Adams J, Macleod AM *et al*. Intermittent versus continuous renal replacement therapy for acute renal failure in adults. *Cochrane Database Syst Rev* 2007; CD003773
8. Van Biesen W, Vanholder R, Lameire N. Dialysis strategies in critically ill acute renal failure patients. *Curr Opin Crit Care* 2003; 9: 491–495
9. Jakob SM, Frey FJ, Uehlinger DE. Does continuous renal replacement therapy favourably influence the outcome of the patients? *Nephrol Dial Transplant* 1996; 11: 1250–1255
10. Kanagasundaram NS, Paganini EP. Critical care dialysis—a Gordian knot (but is untying the right approach?). *Nephrol Dial Transplant* 1999; 14: 2590–2594
11. Ronco C, Bellomo R, Ricci Z. Continuous renal replacement therapy in critically ill patients. *Nephrol Dial Transplant* 2001; 16 (Suppl 5): 67–72
12. Mehta RL, McDonald B, Gabbai FB *et al*. A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. *Kidney Int* 2001; 60: 1154–1163
13. Augustine JJ, Sandy D, Seifert TH *et al*. A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. *Am J Kidney Dis* 2004; 44: 1000–1007
14. Uehlinger DE, Jakob SM, Ferrari P *et al*. Comparison of continuous and intermittent renal replacement therapy for acute renal failure. *Nephrol Dial Transplant* 2005; 20: 1630–1637
15. Vinsonneau C, Camus C, Combes A *et al*. 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
16. Tonelli M, Manns B, Feller-Kopman D. Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. *Am J Kidney Dis* 2002; 40: 875–885
17. Kellum JA, Angus DC, Johnson JP *et al*. Continuous versus intermittent renal replacement therapy: a meta-analysis. *Intensive Care Med* 2002; 28: 29–37
18. Lins RL, Elseviers MM, Van der Niepen P *et al*. Intermittent versus continuous renal replacement therapy for acute kidney injury patients admitted to the intensive care unit: results of a randomized clinical trial. *Nephrol Dial Transplant* 2009; 24: 512–518
19. Elseviers MM, Lins RL, Van der Niepen P *et al*. Renal replacement therapy is an independent risk factor for mortality in critically ill patients with acute kidney injury. *Crit Care* 2010; 14: R221

20. Briggs AH, Claxton K, Sculpher MJ. *Decision Modelling for Health Economic Evaluation*. Oxford: Oxford University Press, 2006.
21. Lins RL, Elseviers M, Daelemans R *et al*. Prognostic value of a new scoring system for hospital mortality in acute renal failure. *Clin Nephrol* 2000; 53: 10–17
22. Lins RL, Elseviers MM, Daelemans R *et al*. Re-evaluation and modification of the Stuivenberg Hospital Acute Renal Failure (SHARF) scoring system for the prognosis of acute renal failure: an independent multicentre, prospective study. *Nephrol Dial Transplant* 2004; 19: 2282–2288
23. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 2002; 21: 271–292
24. Johansen KL, Smith MW, Unruh ML *et al*. Predictors of health utility among 60-day survivors of acute kidney injury in the Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network Study. *Clin J Am Soc Nephrol* 2010; 5: 1366–1372
25. Morton RL, Howard K, Webster AC *et al*. The cost-effectiveness of induction immunosuppression in kidney transplantation. *Nephrol Dial Transplant* 2009; 24: 2258–2269
26. Messori A. Survival curve fitting using the Gompertz function: a methodology for conducting cost-effectiveness analyses on mortality data. *Comput Methods Programs Biomed* 1997; 52: 157–164
27. Palmer AJ. Health economics—what the nephrologist should know. *Nephrol Dial Transplant* 2005; 20: 1038–1041
28. Klarenbach S, Manns B, Pannu N *et al*. Economic evaluation of continuous renal replacement therapy in acute renal failure. *Int J Technol Assess Health Care* 2009; 25: 331–338
29. Hamel MB, Phillips RS, Davis RB *et al*. Outcomes and cost-effectiveness of initiating dialysis and continuing aggressive care in seriously ill hospitalized adults. SUPPORT investigators. Study to understand prognoses and preferences for outcomes and risks of treatments. *Ann Intern Med* 1997; 127: 195–202
30. Bell M, Granath F, Schon S *et al*. 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
31. Uchino S, Bellomo R, Kellum JA *et al*. Patient and kidney survival by dialysis modality in critically ill patients with acute kidney injury. *Int J Artif Organs* 2007; 30: 281–292
32. Ahlstrom A, Tallgren M, Peltonen S *et al*. Survival and quality of life of patients requiring acute renal replacement therapy. *Intensive Care Med* 2005; 31: 1222–1228
33. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull* 2010; 96: 5–21

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