Original Article

Intensive care unit resources and patient-centred outcomes in severe COVID-19: a prospective single-centre economic evaluation

N. Schallner,[1] **J. Lieberum,**[2] **J. Kalbhenn,**[1] **H. Bürkle**[3] and **F. Daumann**[4]

1 Consultant, 2 Doctoral Student, 3 Chair, Department of Anesthesiology and Critical Care Medicine, Medical Center University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
4 Chair, Institute of Health Economics and Sports Economics, Institute of Sports Science, University of Jena, Germany

Summary
During the COVID-19 pandemic, ICU bed shortages sparked a discussion about resource allocation. We aimed to analyse the value of ICU treatment of COVID-19 from a patient-centred health economic perspective. We prospectively included 49 patients with severe COVID-19 and calculated direct medical treatment costs. Quality of life was converted into aggregated quality-adjusted life years using the statistical remaining life expectancy. Costs for non-treatment as the comparator were estimated using the value of statistical life year approach. We used multivariable linear or logistic regression to identify predictors of treatment costs, quality of life and survival. Mean (SD) direct medical treatment costs were higher in patients in ICU with COVID-19 compared with those without (£60,866 (£42,533) vs. £8282 (£14,870), respectively; $p < 0.001$). This was not solely attributable to prolonged ICU length of stay, as costs per day were also higher (£3115 (£1374) vs. £1490 (£713), respectively; $p < 0.001$), independent of overall disease severity. We observed a beneficial cost-utility value of £7511 per quality-adjusted life-year gained, even with a more pessimistic assumption towards the remaining life expectancy. Extracorporeal membrane oxygenation therapy provided no additional quality-adjusted life-year benefit. Compared with non-treatment (costs per lost life year, £106,085), ICU treatment (costs per quality-adjusted life-year, £7511) was economically preferable, even with a pessimistic interpretation of patient preferences for survival (sensitivity analysis of the value of statistical life year, £48,848). Length of ICU stay was a positive and extracorporeal membrane oxygenation a negative predictor for quality of life, whereas costs per day were a positive predictor for mortality. These data suggest that despite high costs, ICU treatment for severe COVID-19 may be cost-effective for quality-adjusted life-years gained.

Correspondence to: N. Schallner
Email: nils.schallner@uniklinik-freiburg.de
Accepted: 26 July 2022
Keywords: cost-utility analysis; COVID-19; health-related quality of life; outcome assessment; quality-adjusted life years

Introduction
Severe COVID-19 may necessitate ICU admission. Early studies report ICU admission rates as high as 10% of all cases [1], although more recent data suggest significantly lower rates of hospital and ICU admission [2, 3]. In the healthcare systems of Western European countries and North America, ICU beds make up < 10% of the total number of hospital beds, but accounts for > 20% of the total costs of inpatient care [4, 5]. During the early phase of the pandemic, the high demand for ICU beds to treat COVID-19

patients, in addition to numerous other critically ill patients, presented unprecedented challenges. To date, effective therapies are mainly limited to the early hyperinflammatory phases of infection. Treatment in ICU may require multiple episodes of prone positioning and organ replacement therapies such as extracorporeal membrane oxygenation (ECMO) and haemodialysis. Due to this complexity, therapy is demanding in terms of length of ICU stay, personnel and costs [6].

Health-related quality of life (HQoL) after severe COVID-19 is a societal concern, with increased survival rates after ICU admission and patients being eventually discharged with persistent symptoms more frequently compared with patients with severe COVID-19 who had not been admitted to ICU [7, 8]. Persistent physical and psychological consequences can be significant [8–11], but their influence on HQoL is underinvestigated although potentially heterogeneous, most likely due to variability in disease severity [9, 12–15]. With this discrepancy, a discussion regarding appropriate use of scarce and costly ICU resources must focus on patient-centred outcomes. Therefore, there is a need for an economic evaluation of the disease entity and its treatment by relating treatment costs to HQoL and survival. However, this cost-utility study is missing for severe COVID-19 following ICU admission.

Gained quality-adjusted life years (QALYs), defined as the product of HQoL and remaining life years, is the preferred measure of health outcome for cost-utility analyses, as it accounts for both quantity and quality of life. We aimed to assess the direct ICU-related costs in patients treated for severe COVID-19, including ECMO therapy, in relation to the gained QALYs to estimate the cost-utility of ICU treatment in this patient population.

Methods

Data collection for this prospective single-centre observational study took place in the tertiary care-level ICU and acute respiratory distress syndrome/ECMO centre of the Department of Anesthesiology and Critical Care at the medical centre of the University of Freiburg, Germany. This study is a secondary analysis of another on inflammatory markers in severe COVID-19 that was prospectively approved by the Institutional Ethics Review Board of the University of Freiburg and registered with the German Clinical Trials Register, but the secondary analysis was not explicitly defined in the German Clinical Trials Register. Informed consent was obtained either from patients, legal guardians or legal proxies. Reporting of the data adheres to the STROBE guidelines. Inclusion/exclusion criteria and indications for ECMO therapy are detailed in online Supporting Information Appendix S1. All patients admitted to ICU due to severe COVID-19 were screened for potential participation in the study between April 2020 and April 2021. Overall disease severity is described using the total simplified acute physiology score-2 (SAPS-2) and therapeutic intervention scoring system (TISS) scoring (see online Supporting Information Appendix S1). For comparisons, SAPS-2/TISS categories relevant for medical coding and billing were used. Patients with ICU length of stay < 24 h do not receive SAPS-2 scores and are therefore denoted as non-valued but were still included in the analysis.

A diagnosis-related group-based reimbursement represents an inaccurate estimate of true individual treatment costs, so the direct treatment costs related to the patients' entire ICU stay were calculated based on a detailed 'bottom-up' cost analysis by the Department for Medical Controlling, as described in online Supporting Information Appendix S1. The control population for the cost analysis consisted of patients treated in the same ICU during 2020 without a diagnosis of COVID-19.

For QALY calculation, HQoL was recorded using the EQ-5D-5L questionnaire 6 months after ICU discharge. Calculating the individual value of the HQoL was carried out as described by Ludwig et al. and validated for a German cohort as detailed in online Supporting Information Appendix S1 [16]. The calculated EQ-5D index as a proportion of 1 and the EQ-5D visual analogue scale (VAS), which is directly valued by the patient as a proportion of 100%, are reported. It was assumed that the number of years of life gained can be equated to the statistically remaining life expectancy (calculated using data from the German Federal Statistical Office's most recent period life table 2017/2019 [17]). Thus, QALYs for each patient were a factor in remaining life expectancy and the EQ-5D index. As we assumed 100% mortality in patients who did not receive ICU treatment, the observed QALYs are considered as incremental QALYs attributable to ICU treatment. In addition, the years of life lost were calculated as detailed in online Supporting Information Appendix S1.

For a comparative analysis of the incurred costs per QALY, we assumed that 100% of the patients admitted to the ICU with severe COVID-19 would not survive in a hypothetical alternative scenario of non-treatment. The 'value of a statistical life year' was used as a reference value for the costs of non-treatment. For the value of a statistical life year, the 'willingness to pay' approach and values from the meta-analysis by Schlander et al. [18] were used to calculate the average value of a statistical life year in the study population with a discount factor of 3% per annum for future costs using the following formula:

$$\text{Average costs per lost life year} = \frac{\text{discounted costs of lost life years}}{\text{Number of lost life years}}$$

The incremental cost-effectiveness ratio (ICER) for ECMO therapy was calculated as follows:

$$ICER_{ECMO} = \frac{\text{therapy costs with ECMO} - \text{therapy costs without ECMO}}{\text{QALYs with ECMO} - \text{QALYs without ECMO}}$$

To analyse the robustness of the data, sensitivity analyses were performed for the remaining life expectancy and for comparison with hypothetical non-treatment. No data are yet available regarding the individual reduction of life expectancy after severe COVID-19. We, therefore, used available data projecting a population-level reduction in life expectancy for several countries including the USA, UK and Germany ranging from several months to 2 y [19, 20]. On the basis of these data, we assumed an individual reduction in life expectancy after COVID-19 of 1, 2 and 5 y compared with the statistically remaining life years according to the period life table for the sensitivity analysis of QALY calculation and subsequent costs per QALY estimate. The sensitivity analysis regarding the hypothetical non-treatment was performed in three stages, varying the value of statistical life-years (willingness to pay approach vs. World Health Organization (WHO) definition) [18, 21, 22], time preferences (annual discount rates for future costs of 3% vs. 5%, respectively) and likelihood of mortality (assumed mortality in the case of non-treatment of 100% vs. 80%, respectively) (see online Supporting Information, Appendix S1).

Various independent variables that may have influenced costs, quality of life and mortality were analysed using multiple linear regression (therapy costs) or multivariable logistic regression analysis (HQoL and mortality).

Statistical analyses were performed with GraphPad Prism (version 9.2, GraphPad Software, Inc., San Diego, CA, USA). An a priori power calculation using G*Power software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) was done for the multiple regression model predicting therapy costs with an effect size f^2, 0.35; α, 0.05; power, 0.8; number of predictors, 6. This yielded a total sample size of 46. Costs per QALY were a secondary endpoint in a related study analysing inflammatory biomarkers. Statistical comparison of two groups with metric data was carried out after analysing normal distribution using the Shapiro–Wilk test, either using an unpaired t-test or non-parametrically using the Mann–Whitney U-test. Repeated measurements and before-and-after comparison were performed with the Wilcoxon rank-sum test. More than two groups were compared using one-way ANOVA with post-hoc Tukey test or Kruskal–Wallis test with post-hoc Dunn's comparison. Groups with categorical nominally scaled variables were compared using Fisher's exact test. Non-parametric linear correlation according to Spearman's ρ was used to assess the correlation between metric datasets. Three models for predicting the dependent variables of mortality, quality of life and therapy costs were developed using multiple linear or logistic regression to determine the relationship between the variables and various potentially independent variables (age; ICU length of stay; therapy costs; ECMO; sex; EQ-5D index; mortality). Receiver operating characteristic plots and actual vs. predicted plots were used to examine the predictive power of the models. In all analyses, a value of $p < 0.05$ was considered statistically significant.

Results

A total of 49 patients with COVID-19 were included between April 2020 and April 2021, and 796 patients treated in the ICU without COVID-19 during 2020 (Fig. 1). Patient characteristics are detailed in Table 1.

Mean (SD) direct ICU treatment costs amounted to £60,866 ($74,584; €72,701) (£42,533; $52,100; €50,800) per patient in the study population compared with £8282 ($10,146; €9888) (£14,870; $18,215; €17,758) in the control population ($p < 0.001$; Fig. 2). Increased treatment costs were not solely attributable to prolonged length of stay, as mean (SD) treatment costs per day were £3115 ($3816; €3720) (£1374; $1682; €1640) compared with £1490 ($1824; €1779) (£713; $873; €851) in the control population ($p < 0.001$; Fig. 2).

Higher disease severity was seen in patients with COVID-19 compared with those without, which, together with longer length of stay, partially explains higher total treatment costs (see online Supporting Information, Fig. S1). However, after adjusting the total SAPS-2/TISS scores for ICU length of stay, there was comparable disease severity per day in both COVID-19 and non-COVID-19 cohorts (Fig. 2; $p = 0.281$). Analysis of the costs per day and total treatment costs in relation to SAPS-2/TISS demonstrated significantly higher costs in patients with COVID-19 compared with those without who were in the same SAPS-2/TISS category (see online Supporting Information, Fig. S1; $p = 0.001$). A detailed analysis of the

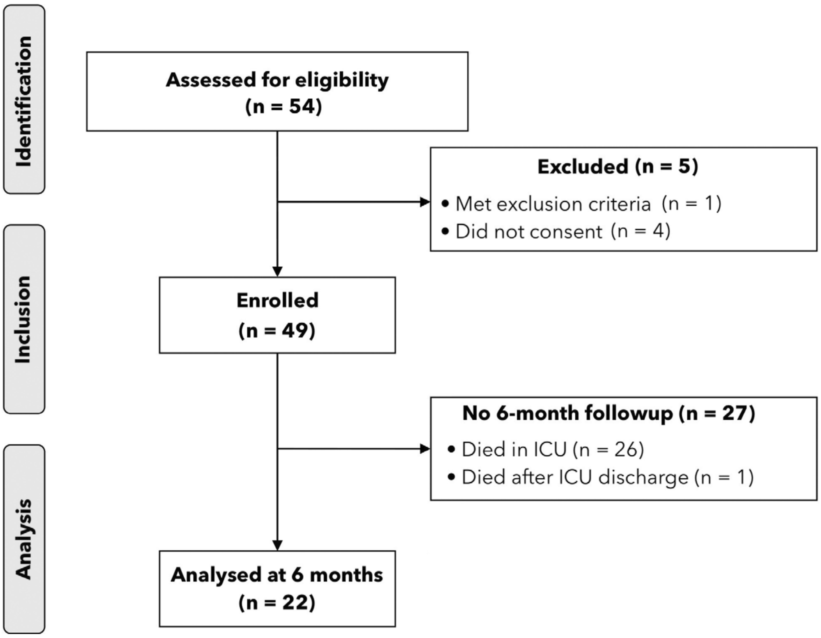

Figure 1 Flowchart of patient recruitment. Patients enrolled in the study (n = 49) were included in the cost-effectiveness analysis. Patients who were included at 6 months were included in the health-related quality of life and cost-utility analysis (n = 22).

relationship between treatment costs, sex and mortality is provided in Supporting Information (Figs. S2 and S3).

The overall mean (SD) EQ-5D index 6 months after discharge was 0.32 (0.40), while in the subpopulation of survivors, the mean (SD) EQ-5D was 0.72 (0.26) (Fig. 3; $p < 0.001$). Similarly, the EQ-5D VAS was 30.0 (35.3) overall and 66.8 (16.6) in the subpopulation of survivors (Fig. 3; $p < 0.001$).

Mean (SD) residual life expectancy in patients with COVID-19 was 24.8 (9.2) y, which was higher than the QALYs gained of 8.1 (10.4) y ($p < 0.001$). This may be explained by the high proportion of deceased patients and the reduction in HQoL following admission compared with before admission (Fig. 3; $p < 0.001$). The mean (SD) years of life lost due to mortality and impaired quality of life following admission compared with before admission was 16.7 (12.9) y (Fig. 3; $p < 0.001$). Comparing these with the COVID-19 cohort, the overall QALYs were significantly lower than the amount of QALYs in survivors (8.1 vs. 18.1 (7.6) y, $p = 0.005$) and compared with the years of life lost (8.1 vs. 16.7 y, $p = 0.002$).

Relating the total treatment costs for patients with COVID-19 to the total QALYs gained resulted in a cost per QALY ratio of £7511 ($9179; €8969). A sensitivity analysis with varying degrees of remaining life expectancy reduction due to COVID-19 resulted in cost per QALY ratios of £7821 ($9578; €9342) (1 y lost); £8157 ($9989; €9744) (2 y lost); and £9367 ($11,468; €11,190) (5 y lost), respectively (online Supporting Information, Table S1). The average costs per lost life year under the assumption of 100% mortality in the event of non-treatment resulted in a value of a statistical life year of £106,085 ($129,899; €126,688), which was greater than the calculated costs per QALY. The costs per lost life year were also higher than the mean total treatment costs per patient (£60,866; $74,528; €72,704; see online Supporting Information, Table S1).

We attempted to calculate an incremental cost-effectiveness ratio for ECMO therapy in patients with COVID-19. However, as there was selection bias in that ECMO was only used in severe cases, no QALY gain through ECMO therapy was detectable. Relevant additional costs due to ECMO therapy (£315,202; $385,812; €376,376) were accompanied by a total QALY deficit of 89.7 y within this subgroup compared with patients who did not receive ECMO. Therefore, no beneficial incremental cost-effectiveness for ECMO therapy was shown.

Sensitivity analysis regarding the value of a statistical life year assumption revealed that, even with the variation in variables representing a more pessimistic interpretation of the patients' preferences for survival, the costs per lost life year for non-therapy still exceeded the costs per QALY for ICU treatment, with the most pessimistic assumption resulting in a value of a statistical life year of £48,848 ($59,802; €58,356) (online Supporting Information, Table S2). The results of the individual assumptions differed significantly from one another (online Supporting Information, Fig. S4), indicating robustness of the sensitivity analysis.

Correlations between clinical, epidemiological and health-economic parameters are shown in online Supporting Information (Fig. S5). A multiple linear regression model was

Table 1 Characteristics of included patients with COVID-19. Values are mean (SD), number (proportion) or median (IQR [range]).

	Total n = 49	No ECMO n = 27	ECMO n = 22
Age	58.1 (10.5)	59.8 (10.1)	56.1 (10.9)
Sex; male	38 (78%)	22 (81%)	16 (73%)
ICU length of stay; days	16 (12–34 [1–85])	15 (7–22 [1–85])	18 (14–39 [1–55])
ECMO/ECLS			
Total	22 (45%)	-	22 (45%)
Male	16 (42%)	-	16 (42%)
Female	6 (55%)	-	6 (55%)
Mortality			
Total	26 (53%)	14 (52%)	12 (55%)
Male	18 (47%)	10 (46%)	8 (50%)
Female	8 (73%)	4 (80%)	4 (67%)
Duration of mechanical ventilation; h	367 (209–690 [0–1577])	344 (120–537 [0–1577])	419 (240–814 [11–1071])
Minimal PaO_2/FiO_2 ratio	75 (50–81 [40–182])	80 (67–90 [43–182])	59 (46–79 [40–95])
Modified Rankin Scale at 6 months	6 (2–6 [0–6])	5.5 (2–6 [0–6])	6 (2–6 [1–6])
Maximum NuDesc score	1 (0–3 [0–6])	1 (0–4 [0–6])	0.5 (0–1.5 [0–3])
Acute kidney injury			
Total	47 (96%)	26 (96%)	21 (95%)
Male	38 (100%)	22 (100%)	16 (100%)
Female	9 (82%)	4 (80%)	5 (83%)
Dialysed			
Total	21 (45%)	8 (31%)	13 (62%)
Male	17 (45%)	6 (27%)	11 (69%)
Female	4 (44%)	2 (50%)	2 (40%)
Thromboembolic events			
Total	27 (55%)	12 (44%)	15 (68%)
Male	23 (61%)	12 (55%)	11 (69%)
Female	6 (55%)	2 (40%)	4 (67%)

ECMO, extracorporeal membrane oxygenation; ECLS, external cardiac life support; NuDesc, Nursing Delirium Screening Scale.

adopted to predict the total treatment costs with the variables age, ICU length of stay, sex, costs per day and ECMO and multivariate logistic regression models were developed to predict HQoL (EQ-5D Index > 0.5 and EQ-5D Index > 0.8) and mortality (online Supporting Information, Table S3 and Fig. S5). ICU length of stay and costs per day were positive predictors of total treatment costs, while ICU length of stay (EQ-5D > 0.5 and EQ-5D > 0.8) was a positive and ECMO therapy (EQ-5D > 0.8) a negative predictor for favourable HQoL. Costs per day were a positive and ICU length of stay a negative predictor for mortality.

Discussion

In this single-centre observational study, we found that direct medical costs for the treatment of COVID-19 patients were higher than for other critically ill patients, which was not exclusively due to longer length of stay. Higher costs per day were not dependent on overall disease severity but rather specific to the study population. The cost-utility analysis indicated moderate costs of approximately £7511 ($9179; €8969) per QALY despite complexity and length of ICU treatment. Cost-utility remained favourable using several sensitivity analyses. In comparison with the fictitious costs of non-treatment or with the current implicit limits in some health care systems, treatment of COVID-19 patients was characterised by a high utility value.

Intensive care treatment costs are disproportionally high, considering ICU beds make up less than 10% of all in-patient beds [5, 23]. Data regarding daily treatment costs are rare and subject to significant fluctuations, ranging between £1020 ($1248; €1218) and £2720 ($3328; €3247) [4, 23–25]. The average daily treatment costs in the non-COVID-19 control cohort of our study lie within the range of these previous reports. Although this suggests that cost

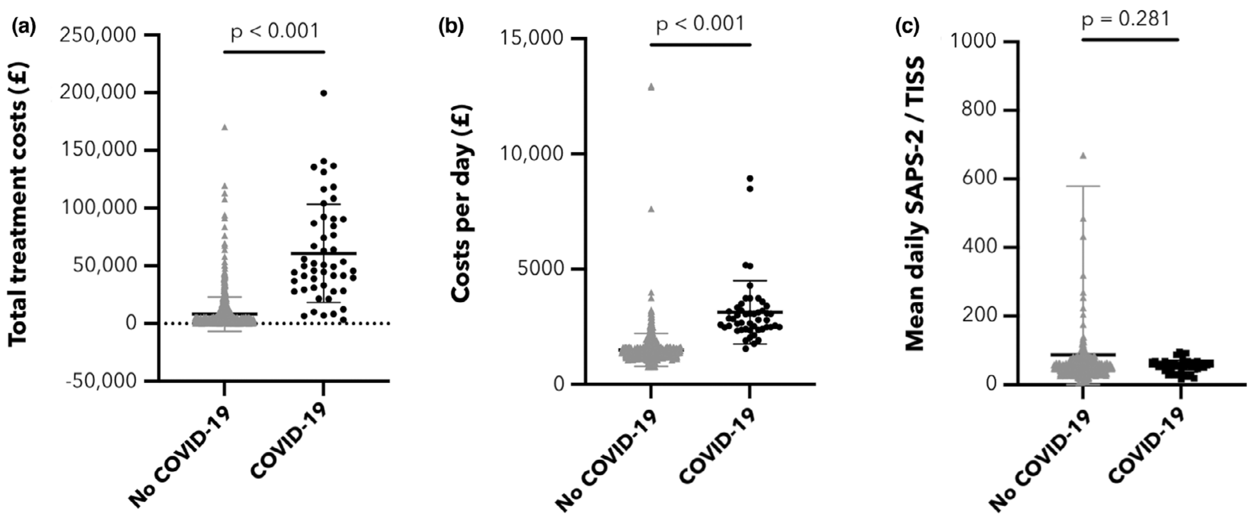

Figure 2 Comparison of ICU treatment costs and simplified acute physiology score-2 (SAPS-2)/therapeutic intervention scoring system (TISS) scores in patients with (black circles) and without (grey triangles) COVID-19. (a) Total treatment costs (£); (b) Treatment costs per day (£); (c) Mean daily SAPS-2/TISS scores. Circles and triangles are individual patients, thick lines are means and thin lines are SD.

comparisons are potentially suitable, generalising our results might not be appropriate due to differences in cost structures in different healthcare systems. Our findings might only be valid in countries with similar healthcare systems and standards of care as in Germany. However, daily therapy costs for treatment of patients with COVID-19 were more than twice as high as non-COVID-19 patients, regardless of overall severity scores, and total costs per patient were also many times higher. Although analysed according to overall disease severity, the control population was unmatched regarding organ support requirements and other aspects influencing costs. Therefore, the validity of directly comparing both populations is limited, yet the comparison supports the primary goal of depicting the overall cost burden due to the pandemic and the treatment of these complex patients, justifying a more in-depth health-economic cost-utility analysis.

Observed ICU mortality of 53% in the study population was high compared with acute lung failure in general and other viral pneumonia [26, 27], but also compared with previously published data on patients with severe COVID-19 [28]. Variation in mortality rates is reported for the latter, which might be due to country-specific and regional differences in healthcare systems, ICU capacities or temporal differences in the severity of COVID-19. While data from the early phase of the pandemic are in keeping with our mortality data [29, 30], recent meta-analyses suggest lower death rates [31, 32], particularly when including data involving SARS-CoV-2 variants [3]. It is possible that selection bias with patient factors such as comorbidities, external pre-treatment, higher disease severity and the need for ECMO therapy might explain the high mortality rates in our cohort. The patient population analysed represents a specific subgroup of patients with a small health economic impact from an overall societal point of view. However, we emphasise that the complex and costly treatment of these patients has the highest economic impact on an individual level and also sparked the strongest ethical controversy regarding the extent of treatment and the allocation of overall ICU treatment capacities, demanding an analysis of costs in relation to outcome.

Data now highlight long-term sequelae after severe COVID-19 [8–11]. Even though this suggests a concomitant reduction in quality of life, few studies have systematically analysed this. One UK study suggests deteriorating HQoL after ICU treatment compared with a milder disease course with overall good EQ-5D index scores of 70% [33], while this difference was not detectable in a French study [12]. Other international studies come to similar conclusions regarding deteriorating HQoL after ICU admission [9, 13, 15] with an overall heterogeneous HQoL distribution pattern. One meta-analysis suggests consistent HQoL values above 75% in patients with COVID-19 who were not admitted to ICU [14]. Lower HQoL values in our study population might be attributed to a patient selection toward more severe cases.

There are limited data on cost-utility of ICU treatment in general and even more so for COVID-19. In a recent Finnish study [23], the costs per QALY for ICU treatment averaged

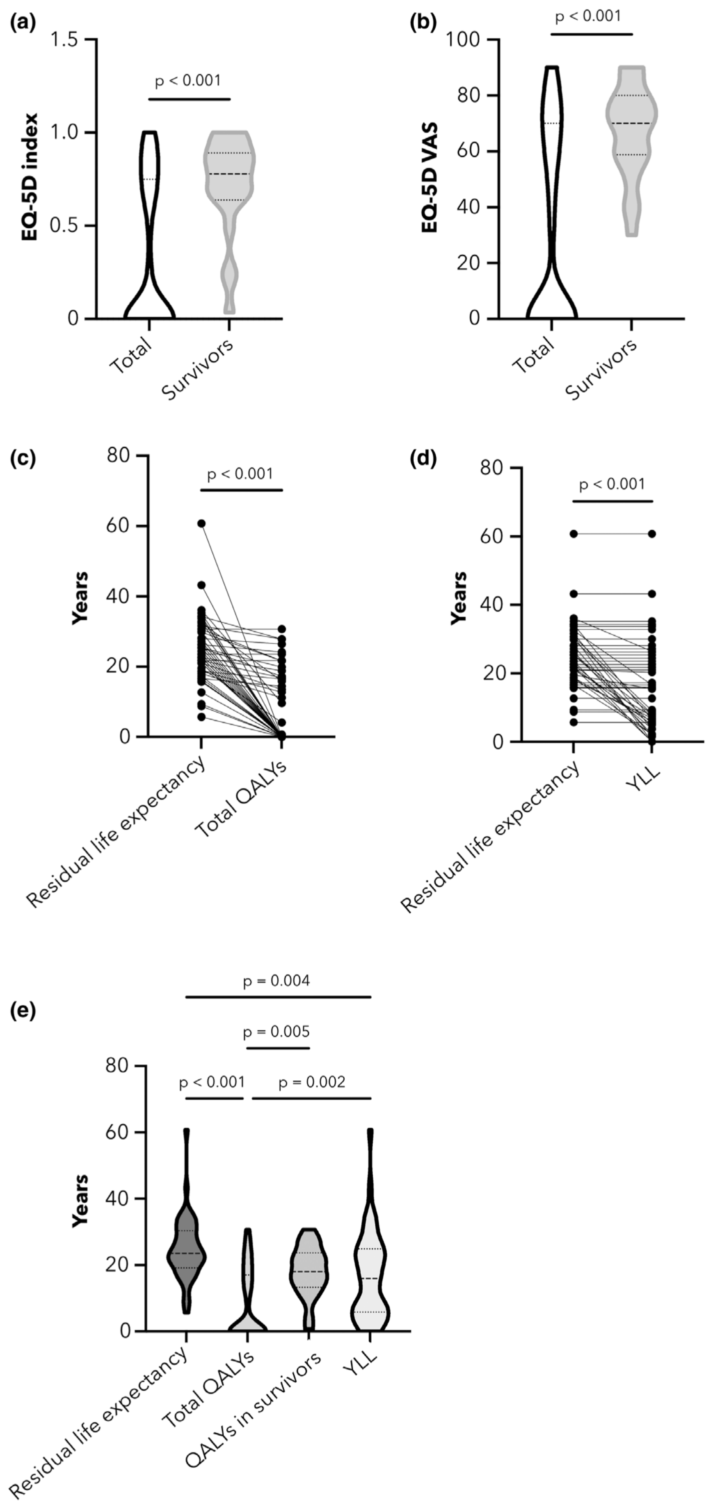

Figure 3 Health-related quality of life (HQoL) measured with the EQ-5D, gained quality-adjusted life years (QALYs) and years of life lost (YLL) after severe COVID-19. (a) Violin plot of the average EQ-5D index in the total study population and in survivors. (b) Violin plot of the average EQ-5D visual analogue scale (VAS) score in the total study population and in survivors. (c) Residual life expectancy versus total QALYs gained in an individual before-after comparison per patient. (d) Residual life expectancy versus YLL in an individual before-after comparison per patient. (e) Violin plots comparing average residual life expectancy in all patients, QALYs gained in all patients, QALYs in survivors only and YLL in all patients.

£6367 ($7789; €7600), which was comparable to the costs per QALY of our study (£7511; $9179; €8969). Different countries use limit ranges for cost-effectiveness of medical measures. Implicit threshold costs per QALY are assumed to be between £20,000 and £30,000 in the UK ($24,451; €23,866 and $36,677; €35,799) [34]. In the USA, the threshold of £41,208 ($50,381; €49,195) per QALY gained has been established in the literature [35]. To summarise, ICU treatment of patients with severe COVID-19 would be considered as cost-effective considering the above-mentioned thresholds.

The comparison with non-treatment as a hypothetical alternative showed a health-economic advantage for ICU treatment. The value of a statistical life year largely depends on a population's preferences and financial capabilities. Current estimates that use the concept of willingness to pay are based on these different preferences and therefore can be seen as accurate estimates [18]. In addition, a lower value of a statistical life year value of the WHO definition was used to account for more pessimistic population preferences regarding survival after COVID-19 [21]. Overall, the cumulative value for the value of statistical life-years in our calculation approximately corresponds to the generally accepted value of statistical life of £8.2 million ($9.8 m; €9.6 m) [36].

It was not possible to analyse which costs in the form of lost life years or medical follow-up costs were incurred through prioritisation decisions in healthcare systems in favour of the care of patients with COVID-19 but to the detriment of other patients. Total ICU capacity, which has been available to a lesser extent for other patients since the beginning of the pandemic, with the combination of delayed necessary operations, might have significantly influenced population health.

Several limitations of the study must be discussed. We attempted a detailed individual treatment cost analysis. Even though this can be classified as more accurate than the plain diagnosis-related group-based reimbursement values, inaccuracies remain related to the weighted tariffs and how treatments are assigned within the charge-based reimbursement system. Additionally, the indirect costs resulting from the illness and therapy, such as loss of productivity or reduced earning capacity, were not included in the calculation. Intangible costs such as pain and the loss of quality of life can be found in the results of the EQ-5D questionnaire and the QALY data, but no direct monetary value was assigned to them. Furthermore, direct medical follow-up costs, such as costs for rehabilitation, are not included in the analysis due to the lack of availability. As a result, the likelihood is that the actual treatment costs were underestimated. Second, a normal life expectancy according to the life table of the German population was assumed. Most patients did not present with relevant comorbidities, however, with this optimistic assumption, the remaining life expectancy and thus also the QALYs obtained could have been overestimated. Third, the small sample size might limit the generalisability of the data. In addition, the patient population was likely subject to a selection bias since patients with particularly severe disease courses were assigned to our ICU. Finally, a general critical appraisal applies to the QALY approach. It is based on the welfare consideration that the sum of the individual benefits results in the benefit for society and that society regards health as a matter of high prioritisation. If the goal is to maximise the collective benefit in health and thus create the conditions for individual benefit, it cannot represent the basis for individual medical decisions. By aggregating the benefits that arise in the entire population, the cost-utility analysis with the QALY approach can only serve as a basis for decision-making in allocation scenarios.

In summary, the data suggest that despite high costs, ICU treatment for severe COVID-19 is to be viewed as cost-effective and beneficial with regard to the patient-centred outcome quality of life and QALYs gained in relation to other medical measures and regarding the allocation of ICU resources. However, given long ICU length of stay, high treatment costs and excess mortality, better models for predicting mortality must be developed to guide future decisions on ICU resource allocation.

Acknowledgements

This study was prospectively registered with the German Clinical Trials Registry (ID DRKS00021522).

We thank the Department for Medical Controlling, University of Freiburg – Medical Center for helpful assistance with the cost analysis for this study. NS received research support from the German Research Foundation. No other competing interests declared. Open Access funding enabled and organized by Projekt DEAL.

References

1. Zhang JJY, Lee KS, Ang LW, Leo YS, Young BE. Risk factors for severe disease and efficacy of treatment in patients infected with COVID-19: a systematic review, meta-analysis, and meta-regression analysis. *Clinical Infectious Diseases* 2020; **71**: 2199–206.
2. Twohig KA, Nyberg T, Zaidi A, et al. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. *Lancet Infectious Diseases* 2022; **22**: 35–42.
3. Nyberg T, Ferguson NM, Nash SG, et al. Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2)

variants in England: a cohort study. *Lancet* 2022; **399**: 1303–12.
4. Martin J, Neurohr C, Bauer M, Weiss M, Schleppers A. Cost of intensive care in a German hospital: cost-unit accounting based on the InEK matrix. *Der Anaesthesist* 2008; **57**: 505–12.
5. Pastores SM, Dakwar J, Halpern NA. Costs of critical care medicine. *Critical Care Clinics* 2012; **28**: 1–10.
6. Rieg S, von Cube M, Kalbhenn J, et al. COVID-19 in-hospital mortality and mode of death in a dynamic and non-restricted tertiary care model in Germany. *PLoS One* 2020; **15**: e0242127.
7. Heesakkers H, van der Hoeven JG, Corsten S, et al. Clinical outcomes among patients with 1-year survival following intensive care unit treatment for COVID-19. *Journal of the American Medical Association* 2022; **327**: 559–65.
8. Huang L, Yao Q, Gu X, et al. 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. *Lancet* 2021; **398**: 747–58.
9. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; **397**: 220–32.
10. Romero-Duarte A, Rivera-Izquierdo M, Guerrero-Fernandez de Alba I, et al. Sequelae, persistent symptomatology and outcomes after COVID-19 hospitalization: the ANCOHVID multicentre 6-month follow-up study. *BMC Medicine* 2021; **19**: 129.
11. Jacobs LG, Gourna Paleoudis E, Lesky-Di Bari D, et al. Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection. *PLoS One* 2020; **15**: e0243882.
12. Garrigues E, Janvier P, Kherabi Y, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *Journal of Infection* 2020; **81**: e4–e6.
13. Todt BC, Szlejf C, Duim E, et al. Clinical outcomes and quality of life of COVID-19 survivors: a follow-up of 3 months post hospital discharge. *Respiratory Medicine* 2021; **184**: 106453.
14. Malik P, Patel K, Pinto C, Jaiswal R, Tirupathi R, Pillai S, Patel U. Post-acute COVID-19 syndrome (PCS) and health-related quality of life (HRQoL)-a systematic review and meta-analysis. *Journal of Medical Virology* 2022; **94**: 253–62.
15. Tabacof L, Tosto-Mancuso J, Wood J, et al. Post-acute COVID-19 syndrome negatively impacts physical function, cognitive function, health-related quality of life, and participation. *American Journal of Physical Medicine and Rehabilitation* 2022; **101**: 48–52.
16. Ludwig K, Graf von der Schulenburg JM, Greiner W. German value set for the EQ-5D-5L. *PharmacoEconomics* 2018; **36**: 663–74.
17. German Federal Statistical Office. Population by nationality and sex. https://www.destatis.de/EN/Themes/Society-Environment/Population/Current-Population/Tables/liste-current-population.html (accessed 06/07/2022).
18. Schlander M, Schwarz O, Hernandez D, Schaefer R. New estimates of the willingness-to-pay for a statistical life year: a systematic review of the empirical economic literature. *Value in Health* 2018; **21**: S111.
19. Aburto JM, Scholey J, Kashnitsky I, et al. Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries. *International Journal of Epidemiology* 2022; **51**: 63–74.
20. Islam N, Jdanov DA, Shkolnikov VM, et al. Effects of Covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries. *British Medical Journal* 2021; **375**: e066768.
21. Tan-Torres Edejer T, Baltussen R, Adam T, et al. *Making Choices in Health: WHO Guide to Cost-effectiveness Analysis*. Geneva: World Health Organization, 2003. https://apps.who.int/iris/bitstream/handle/10665/42699/9241546018.pdf;jsessionid=A8F13ABD00FED1F59F116460D1D44581?sequence=1 (accessed 05/08/2022).
22. German Federal Statistical Office. Gross domestic product. 2021. https://www.destatis.de/DE/Themen/Wirtschaft/Volkswirtschaftliche-Gesamtrechnungen-Inlandsprodukt/Tabellen/bip-bubbles.html (accessed 06/07/2022).
23. Jukarainen S, Mildh H, Pettila V, et al. Costs and cost-utility of critical care and subsequent health care: a multicenter prospective study. *Critical Care Medicine* 2020; **48**: e345–e355.
24. Moerer O, Plock E, Mgbor U, Schmid A, Schneider H, Wischnewsky M, Burchardi H. A German national prevalence study on the cost of intensive care: an evaluation from 51 intensive care units. *Critical Care* 2007; **11**: R69.
25. Tan SS, Bakker J, Hoogendoorn ME, et al. Direct cost analysis of intensive care unit stay in four European countries: applying a standardized costing methodology. *Value in Health* 2012; **15**: 81–6.
26. Luo L, Shaver CM, Zhao Z, Koyama T, Calfee CS, Bastarache JA, Ware LB. Clinical predictors of hospital mortality differ between direct and indirect ARDS. *Chest* 2017; **151**: 755–63.
27. Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ARDS have decreased over time. *Chest* 2008; **133**: 1120–7.
28. Piroth L, Cottenet J, Mariet AS, Bonniaud P, Blot M, Tubert-Bitter P, Quantin C. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. *Lancet Respiratory Medicine* 2021; **9**: 251–9.
29. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. *Journal of the American Medical Association Internal Medicine* 2020; **180**: 1345–55.
30. Kim L, Garg S, O'Halloran A, et al. Risk factors for intensive care unit admission and in-hospital mortality among hospitalized adults identified through the us coronavirus disease 2019 (COVID-19)-associated hospitalization surveillance network (COVID-NET). *Clinical Infectious Diseases* 2021; **72**: e206–14.
31. Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. *Anaesthesia* 2020; **75**: 1340–9.
32. Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. *Anaesthesia* 2021; **76**: 537–48.
33. Halpin SJ, McIvor C, Whyatt G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *Journal of Medical Virology* 2021; **93**: 1013–22.
34. Rumbold B, Weale A, Rid A, Wilson J, Littlejohns P. Public reasoning and health-care priority setting: the case of NICE. *Kennedy Institute of Ethics Journal* 2017; **27**: 107–34.
35. Padula WV, Sculpher MJ. Ideas about resourcing health care in the United States: can economic evaluation achieve meaningful use? *Annals of Internal Medicine* 2021; **174**: 80–5.
36. Robinson LA, Sullivan R, Shogren JF. Do the benefits of COVID-19 policies exceed the costs? Exploring uncertainties in the age-VSL relationship. *Risk Analysis* 2021; **41**: 761–70.

Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. Supplemental methods.

Figure S1. Cost comparison.

Figure S2. Treatment costs, age and mortality.

Figure S3. Sex-specific differences in costs and outcome.

Figure S4. Sensitivity analysis.

Figure S5. Correlations and regression models.

Table S1. Cost-utility analysis.

Table S2. Sensitivity analysis value of a statistical life year.

Table S3. Regression models for dependent outcome variables costs, HQoL and mortality.

