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Subjective Ratings of Mental and Physical Health Correlate With EQ-5D-5L Index Values in Survivors of Critical Illness: A Construct Validity Study*

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OBJECTIVES: Survivors of critical illness commonly show impaired health-related quality of life (HrQoL). We investigated if HrQoL can be approximated by brief, easily applicable items to be used in primary care.

DESIGN: Secondary analysis of data from the multicenter, cluster-randomized controlled Enhanced Recovery after Intensive Care trial (ClinicalTrials.gov: NCT03671447) and construct validity study.

SETTING: Ten participating clusters of ICUs in the metropolitan area of Berlin, Germany.

PATIENTS: Eight hundred fifty ICU survivors enrolled in a mixed, medical or surgical ICU when they had an expected ICU length of stay of at least 24 hours, were at least 18 years old, and had statutory health insurance coverage.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Patients received follow-ups scheduled 3 and 6 months after ICU discharge. HrQoL was assessed with the EuroQol 5-Dimension 5-Level (EQ-5D-5L), and patients were asked to rate their current mental and physical health state from 0 (worst) to 10 (best). We fitted prediction models for the EQ-5D-5L index value using these two items and additional covariates, applying stepwise regression and adaptive lasso. Subjective mental health (Spearman: 0.59) and subjective physical health (Spearman: 0.68) correlated with EQ-5D-5L index values and were better predictors of EQ-5D-5L index values in the two-item regression (normalized root mean squared error [nRMSE] 0.164; normalized mean absolute error [nMAE] 0.118; R^2_{adj} 0.43) than the EQ-5D Visual Analog Scale (nRMSE 0.175; nMAE 0.124; R^2_{adj} 0.35). Stepwise regression with additional covariates further increased prediction performance (nRMSE 0.133; nMAE 0.1; R^2_{adj} 0.51).

CONCLUSIONS: Asking patients to rate their subjective mental and physical health can be an easily applicable tool for a first impression of the HrQoL in primary care settings.

KEY WORDS: critical care; postintensive care unit care; postintensive care syndrome; primary care; quality of life

The demand for intensive care medicine has been increasing (1, 2) and is forecasted to further grow in the future (3). At the same time, ICU mortality rates are steadily declining (4). Various studies have shown that the growing cohort of survivors of critical illness commonly faces long-term impairments of their health-related quality of life (HrQoL) (5–10). This might be attributable to long-term sequelae of their mental health, cognition,

***See also p. 418.**

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KEY POINTS

Question: Do two brief items asking patients to rate their mental and physical health reflect the health-related quality of life (HrQoL) in critical illness survivors?

Findings: In this secondary analysis of 850 post-ICU patients of the Enhanced Recovery after Intensive Care (ERIC) trial, we fitted prediction models of the EQ-5D-5L index value using two items asking patients to rate their current mental and physical health. These two items are better predictors of the EQ-5D-5L index value than the EQ-5D-5L Visual Analog Scale.

Meaning: Asking patients to rate their mental and physical health depict two easily applicable, free-to-use tools to approximate post-ICU patients' HrQoL in primary care.

or physical functions (11), summarized as postintensive care syndrome (PICS) (12). Although HrQoL of critically ill patients appears already worse than in a matched reference population prior to ICU admission, ICU treatment further diminishes HrQoL (8, 13).

The most commonly used instruments to assess post-ICU HrQoL are the Short Form 36 (SF-36) (14) and the EuroQol-5Dimension (EQ-5D) (10, 15). The EQ-5D includes an assessment of the five dimensions mobility, self-care, usual activities, pain/discomfort, and anxiety/depression that are either rated on a three-level (EQ-5D-3L) or five-Level (EQ-5D-5L) scale (16) and converted to an index value (17). In the second part of the EQ-5D, patients rate their current overall health on a vertical Visual Analog Scale (VAS) from 0 to 100. International (18–21) and national (22) consensus statements on care for ICU survivors uniformly recommended application of the EQ-5D to assess HrQoL.

Worse HrQoL may lead to worse patient satisfaction and increased utilization of healthcare resources (6). Despite the importance of HrQoL and recommendations to assess it (23), HrQoL appears to be measured primarily in study settings, if measured at all. Specialized ICU recovery centers or routine post-ICU follow-up exist (24) but are not common practice (25–29). In absence of follow-up structures, post-ICU patients often consult their general practitioners with little experience in the sequelae of critical illness and their impact on HrQoL (30, 31).

In their proposed measurement instrument set for PICS, Spies et al (22) introduced two short, easily applicable items to approximate HrQoL for primary care settings. Patients were asked to rate their current mental health state and current physical health state on a scale from 0 (worst) to 10 (best). In conjunction, patients specified current mental (e.g., difficulties reading) or physical (e.g., difficulties climbing stairs) health concerns. The separation of ratings of mental and physical health and the connection with specific health concerns might be an advantage over the EQ-5D, but feasibility of this assessment was piloted on 17 patients only (22).

It is unknown, first, if the two items on subjective mental and physical health ratings adequately reflect a patient's HrQoL and second, which current health concerns are frequently reported by patients that score low ratings on these items. Aim of this study was to assess how well the subjective mental and physical health ratings predict the EQ-5D-5L index value compared with the EQ-5D VAS and which current health concerns are frequently reported by post-ICU patients.

MATERIALS AND METHODS

Study Design, Study Population, and Setting

We conducted a secondary analysis of the multicenter, stepped-wedge cluster-randomized controlled Enhanced Recovery after Intensive Care (ERIC) trial (ClinicalTrials.gov: NCT03671447) (32, 33). ERIC was approved by the Institutional Review Board of Charité—Universitätsmedizin Berlin (EA1/006/18) on January 26, 2018. The presented analysis is original, has not been published before, adhered to the ethical standards of the Declaration of Helsinki from 1964 and its later amendments, and adhered to the Transparent Reporting of multivariable predication model for Individual Prognosis Or Diagnosis (TRIPOD) statement (**Supplement A**, http://links.lww.com/CCM/H251) (33).

Patients were enrolled in one of 10 participating clusters of ICUs in the metropolitan area of Berlin, Germany, if they had an expected ICU length of stay of greater than or equal to 24 hours in a mixed, medical, or surgical ICU, were at least 18 years old, and had

statutory health insurance coverage. Patients or legal representatives gave written informed consent. For this analysis, we analyzed ERIC trial participants who were discharged alive from the ICU and completed one or two follow-ups.

Follow-Ups

Patients received two follow-ups scheduled 3 and 6 months after ICU discharge. Follow-ups were conducted by trained study personnel either in the study center or as home visits. In the rare event that a personal visit was not possible, follow-ups were conducted via phone or mail. Follow-ups were conducted using a recently proposed instrument set for PICS assessment (22). For this analysis, we included data from each patient's first follow-up.

EQ-5D-5L, Subjective Mental and Physical Health, and Current Health Concerns

HrQoL was assessed using the EQ-5D-5L. Participants rate mobility, self-care, usual activities, pain/discomfort, and anxiety/depression from 1 (no problems) to 5 (unable/extreme problems). Results are converted to country-specific index values (1: best possible HrQoL; 0: death; below 0: health state worse than death) (15, 35). We applied two novel, brief items of self-reported, subjective mental and physical health (22). Patients were asked to rank their mental and physical health status in the last week on a VAS from 0 (worst) to 10 (best) (**Supplement B**, http://links.lww.com/CCM/H251). Before filling in the subjective health items, patients indicated (yes/no) if they experienced one or more of the following: nightmares, mood changes, anxiety attacks, outbursts, depressive symptoms, difficulties sleeping, difficulties remembering phone numbers, difficulties remembering familiar names, difficulties concentrating, difficulties reading, less contact to friends, and trying not to think of the ICU (mental health), as well as difficulties walking, difficulties climbing chairs, difficulties swallowing, digestive problems, incontinence, fatigue, lack of strength, and pain (physical health).

Covariates

Our models included covariates that were previously considered predictors of reduced HrQoL (7–10, 36–39). Demographic data, Simplified Acute Physiology Score (SAPS) II at ICU admission, ICU admission date, and reason of admission were collected at study enrollment. Results of routine delirium screening instruments were documented during ICU treatment, and duration of mechanical ventilation and discharge date were documented after ICU discharge. During follow-ups, patients were asked if they live in a partnership or marriage and about their highest education. Patients or their general practitioner were asked which of the following organ systems were impaired prior to ICU admission: 1) pulmonary system, 2) metabolic system, 3) kidneys and urogenital system, 4) cardiovascular system, 5) bones, joints, and muscles, and 6) CNS.

Statistical Analysis

Descriptive statistics are presented as median and interquartile range (IQR) or as mean and SD for continuous variables and as frequencies (*n*, %) for categorical variables. EQ-5D-5L conditions were converted to index values using the German value set (17). Correlations between EQ-5D-5L index values, EQ-5D VAS, and subjective mental and physical health state were quantified using Spearman rank correlation coefficients and violin plots.

We estimated different regression models to predict the EQ-5D-5L index value. First, using linear regression, we used the VAS (independent variable) to predict the EQ-5D-5L index value (dependent variable).

Second, we estimated regression models with the subjective mental and physical health states as independent variables (two-item models), after calculating the variance inflation factor to check for multicollinearity. A variance inflation factor of greater than or equal to 3 was considered relevant multicollinearity (40). We randomly split the sample in 10 equally sized parts; the models were fitted with nine of 10 parts and validated with the remaining part (41).

Third, we estimated additional regression models after adding the following predefined covariates: number of organ systems affected prior to ICU admission, age, sex, body mass index (BMI), length of mechanical ventilation, time between ICU discharge and follow-up, ICU length of stay, SAPS II at ICU admission, admission due to trauma (yes/no), delirium (yes/no), university degree (yes/no), and partnership/

marriage (yes/no). Regression models were fitted using stepwise regression with backward elimination. With this method, a model that includes all independent variables is compared with a model where the least significant variable is omitted (42, 43). Iteration with the next least significant variable yields a model where all nonsignificant variables have been removed. In another approach, we estimated regression models with the adaptive least absolute shrinkage and selection operator (LASSO), which performs estimation and selection of a subset of regression covariates from a set of many covariates (44, 45).

For all models, we fitted polynomials up to the third degree. To prevent overfitting, we used 10-fold cross-validation for stepwise regression and lasso. Cross-validation split the sample randomly into 10 equal subsamples (41). The model is fitted with nine of 10 subsamples (training sample), and the tenth subsample is used for validation. This process was repeated 10 times.

Goodness of fit was determined using the normalized root mean squared error (nRMSE) between the observed and predicted values, the normalized mean absolute error (nMAE), the adjusted R^2, and the width of empirical and theoretical 95% limits of agreement (LoA). Normalization was performed with the range of EQ-5D-5L index values in our dataset. Theoretical LoA were computed with ± 1.96 SD (residuals) (46). Bland-Altman plots were prepared for the best-fitting two-item model and the best-fitting stepwise regression or adaptive LASSO model. We excluded cases for which at least one covariate was missing. Significance was defined at less than 0.05. Statistical analysis was performed using Stata17 SE (StataCorp LLC, College Station, TX).

RESULTS

Characteristics of the Study Population and Follow-Ups

Of 1,463 patients enrolled in the study, 1,304 patients were discharged alive from the ICU. Eight hundred fifty patients received at least one follow-up (**Fig. S1**, http://links.lww.com/CCM/H251), with a median of 3.2 months (IQR, 2.8–4.5) after discharge. Patients showed a variety of admission diagnoses, two of three patients received mechanical ventilation, and about one in five patients had delirium during ICU treatment (**Table 1**).

TABLE 1.
Patient Characteristics of the Study Population Upon ICU Admission

Characteristics[a]	Study Population ($N = 850$)
Age, yr, median (IQR)	67 (56–77)
Female, *n* (%)	383 (45.1)
Length of ICU stay, d ($N = 849$), median (IQR)	5 (2–10)
Mechanical ventilation ($N = 846$), *n* (%)	569 (66.9)
Mechanical ventilation, hr ($N = 846$), median (IQR)	10.5 (0–111)
Delirium,[b], *n* (%)	190 (22.4)
Simplified Acute Physiology Score II at admission, median (25–75th percentile)	29 (17–41)
Organ systems affected prior to ICU admission,[c] median (IQR)	3 (2–5)
Body mass index, kg/m^2, median (IQR)	26.1 (23.4–29.7)
Admission type ($N = 840$), *n* (%)	
Medical	358 (42.6)
Emergency surgery	238 (28.3)
Elective surgery	244 (29.1)
Admission diagnosis, *n* (%)	
Respiratory	88 (10.4)
Sepsis/infection	124 (14.6)
Gastrointestinal	91 (10.7)
Cardiovascular	238 (28)
Trauma	74 (8.7)
Neurologic	62 (7.3)
Metabolic/endocrine	37 (4.4)
Oncologic	124 (14.6)
Other[d]	12 (1.4)
University degree ($N = 835$), *n* (%)	125 (15)
In partnership/marriage ($N = 843$), *n* (%)	463 (54.9)

IQR = interquartile range.
[a]*n* other than 850 in brackets.
[b]At least one positive delirium screening during ICU stay.
[c]As assessed by the general practitioner or study personnel. Organ systems were defined as follows: 1) pulmonary system, 2) metabolic system, 3) kidneys and urogenital system, 4) cardiovascular system, 5) bones, joints, and muscles, and 6) CNS.
[d]Other includes multiple organ failure, trimalleolar fracture, urolithiasis, acute kidney injury (3 patients), placement of catheter for hemodialysis, reduced vigilance of unknown cause, bilateral ureter stenosis with recurrent urinary tract infections, spinal deformity, medication-induced osteonecrosis of the jawbone, and inguinal seroma.

EQ-5D-5L Domain Items, EQ-5D-5L Index Scores, and Subjective Health State

EQ-5D-5L assessments indicate a high level of morbidity in our cohort (**Table 2**). The median EQ-5D-5L index value was 0.78 (IQR 0.45–0.91), and the mean EQ-5D-5L index value was 0.66 (SD 0.33). On average, patients reported an EQ-5D VAS of 60 (median, IQR 45–80). Median subjective mental and physical health were 7 (IQR 5–9; n = 840) and 6 (IQR 4–8, n = 848), respectively. Violin plots, which visualize summary statistics and the data's density functions, display the relationship between subjective mental and physical health states and EQ-5D-5L index values (**Fig. 1**). Spearman rank correlation coefficients between the subjective mental and physical health states and the EQ-5D-5L index value were 0.59 and 0.68, respectively (**Table S1**, http://links.lww.com/CCM/H251). This correlation shows that higher subjective mental and physical health state scores are associated with higher EQ-5D-5L index values. With 0.65, the Spearman rank correlation coefficient for the EQ-5D VAS and the EQ-5D index value was in a similar range.

Best-Fitting Models: Two-Item Linear Regression and Linear Stepwise Regression

With a variance inflation factor between the subjective mental and physical health states of 1.66, we did not detect relevant multicollinearity. Among the two-item models, which use the subjective mental and physical health status to predict EQ-5D-5L index values, linear regression showed the best fit (**Table 3**) (**Table S2**, http://links.lww.com/CCM/H251). Subjective mental and physical health status explains 43% of the variance in the EQ-5D-5L index value. The low nMAE (0.118) and nRMSE (0.164) indicate good prediction performance.

Including previously defined covariates and fitting regression models with stepwise regression or adaptive Lasso increased the goodness of fit (Table S2, http://links.lww.com/CCM/H251). Models estimated with stepwise regression showed higher goodness of fit than models estimated with adaptive LASSO. The subjective mental health state, subjective physical health state, the number of affected organ systems prior to ICU admission, and the BMI were significant in all tested models, but delirium, SAPS II, time since ICU discharge, and ICU length of stay were excluded in all models (**Table S3**, http://links.lww.com/CCM/H251). The best-fitting model was estimated using stepwise regression with

TABLE 2.
Results of the EuroQol-5D-Five-Level Domain Items and Index Score

EuroQol-5D-Five-Level Items	Study Population (N = 850)
Mobility, *n* (%)	
No problems	269 (31.7)
Slight problems	138 (16.2)
Moderate problems	181 (21.3)
Severe problems	179 (21.1)
Extreme problems/unable to do	83 (9.8)
Self-care, *n* (%)	
No problems	462 (54.4)
Slight problems	117 (13.8)
Moderate problems	122 (14.4)
Severe problems	83 (9.8)
Extreme problems/unable to do	66 (7.8)
Usual activities, *n* (%)	
No problems	244 (28.7)
Slight problems	179 (21.1)
Moderate problems	166 (19.5)
Severe problems	153 (18)
Extreme problems/unable to do	108 (12.7)
Pain/discomfort, *n* (%)	
No problems	227 (26.7)
Slight problems	254 (29.9)
Moderate problems	238 (28)
Severe problems	120 (14.1)
Extreme problems/unable to do	11 (1.3)
Anxiety/depression, *n* (%)	
No problems	418 (49.2)
Slight problems	188 (22.1)
Moderate problems	160 (18.8)
Severe problems	70 (8.2)
Extreme problems/unable to do	14 (1.7)
Index score[a]	
Median (IQR)	0.78 (0.45–0.91)
Mean (SD)	0.66 (0.33)
Minimum; maximum	−0.549; 1
Visual Analog Scale (N = 728)	
Median (IQR)	60 (45–80)
Mean (SD)	59.3 (23.3)
Minimum; maximum	0; 100

IQR = interquartile range.

[a]Calculated from the single items as follows: (1—[mobility + self-care + usual activities + pain/discomfort + anxiety/depression]).

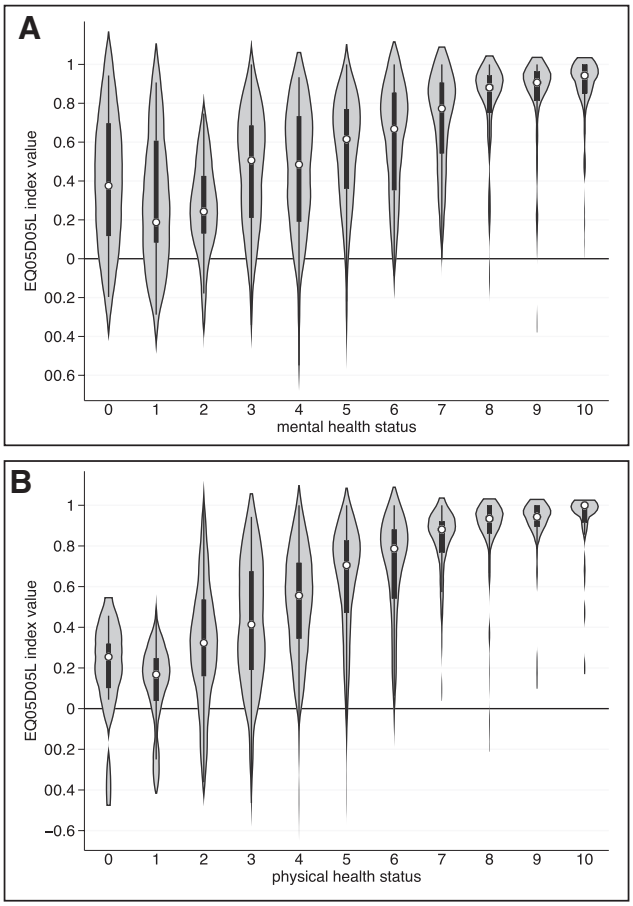

Figure 1. *Violin plots* showing ratings of subjective mental (**A**) and physical (**B**) health state and corresponding EuroQol 5-Dimension 5-Level (EQ-5D-5L) index scores.

linear coefficients (nRMSE 0.133; nMAE 0.1), explaining 51% of the variation in the EQ-5D-5L index values. Interestingly, explaining the EQ-5D-5L index value with the VAS only showed the worst fit of all tested models (nRMSE 0.175, nMAE 0.124, and R^2_{adj} 0.35).

The Bland-Altman plots for the best-fitting two-item model and the best-fitting stepwise regression model indicate that prediction performance becomes better with higher EQ-5D-5L index values. For EQ-5D-5L index values below 0.7, predicted EQ-5D-5L index values are, on average, above observed values, and for EQ-5D-5L index values above 0.7, predicted EQ-5D-5L index values tend to be below observed values (**Fig. 2**).

Current Health Concerns and Subjective Health Status

Patients with high ratings of subjective mental health state reported the absence of any current mental health concerns more frequently than patients with low ratings of their subjective mental health state. For example, 60% (73/121) with a subjective mental health state of 10 indicated the absence of any current mental health concerns. Patients with low ratings of their subjective mental health state frequently described current mental health concerns, particularly mood changes, depressive symptoms, and difficulties sleeping (**Fig. 3*A*)**.

Patients with high ratings of their subjective physical health state frequently reported the absence of any current physical health concern: On the one hand, 59% (19/32) with a subjective physical health state of 10 reported that they did not have any current physical health concern. On the other hand, patients with low subjective physical health state frequently reported various physical health concerns, in particular difficulties walking, difficulties climbing stairs, lack of strength, fatigue, and pain (**Fig. 3*B***).

DISCUSSION

This secondary analysis of a large multicenter trial shows that asking ICU survivors to rate their current mental and physical health state on a scale from 0 (worst) to 10 (best) serves as an excellent predictor of the magnitude of their EQ-5D-5L index value. These two items are brief and can easily be applied in primary care settings to approximate patients' HrQoL.

Several previous studies have reported reductions in HrQoL in survivors of critical illness for up to 5 years after ICU discharge (5–10). With a median of 0.78 (IQR 0.45–0.91), the EQ-5D-5L index value in our analysis was comparable with previous studies (10). For example, a large multicenter study on ICU survivors found median EQ-5D-5L index values of 0.73 1–3 years after ICU discharge (47). In only 10.7% of our follow-ups, patients reported the absence of problems in all EQ-5D-5L dimensions, which was much lower compared with 36.4% in the general population (17).

Two items rating subjective mental and physical health to approximate HrQoL of critical illness survivors have recently been introduced by Spies et al (22). The authors proposed that patients should be assessed for PICS in primary care settings 3 months after ICU discharge, and in case of PICS-related impairments, patients should be transferred to specialized ICU rehabilitation centers. Although the two items of mental and physical health were piloted on 17 patients and considered feasible, the

TABLE 3.

Coefficients and Goodness of Fit of the Best-Fitting Two-Item Regression Model, the Overall Best-Fitting Model, and the EuroQol 5-Dimension Visual Analog Scale Model

	Two-Item Regression (Linear)			Stepwise Regression (Linear)			EQ-5D VAS Regression (Linear)		
Covariate	**Coefficient**	**SE**	***p***	**Coefficient**	**SE**	***p***	**Coefficient**	**SE**	***p***
Physical health state[a]	0.067	0.005	< 0.001	0.057	0.005	< 0.001			
Mental health state[a]	0.029	0.005	< 0.001	0.035	0.005	< 0.001			
Organ systems affected prior to ICU admission, *n*[b]				−0.018	0.005	<0.001			
Mechanical ventilation, hr				< −0.001	< 0.001	0.005			
Body mass index, kg/m^2				−0.004	0.001	0.009			
EQ-5D VAS[c]							0.008	< 0.001	< 0.001
Constant	0.083	0.027	0.002	0.270	0.049	< 0.001	0.189	0.028	< 0.001
Goodness of fit									
Normalized root mean squared error	0.164			0.133[d] (0.155[e])			0.175		
Normalized mean absolute error	0.118			0.1[d] (0.112[e])			0.124		
R^2_{adj}	0.43			0.51			0.35		
95% limits of agreement									
Empiricial	−0.508; 0.499			−0.47; 0.486			-0.588; 0.529		
Theoretical	± 0.483			± 0.461			± 0.513		

EQ-5D = EuroQol 5-Dimension, VAS = Visual Analog Scale.

[a]From 0 (worst) to 10 (best).

[b]As assessed by the general practitioner or study personnel. Organ systems were defined as follows: 1) pulmonary system, 2) metabolic system, 3) kidneys and urogenital system, 4) cardiovascular system, 5) bones, joints, and muscles, and 6) CNS.

[c]From 0 (worst) to 100 (best).

[d]Best-fitting model after tenfold cross-validation.

[e]Mean of the tenfold cross-validations.

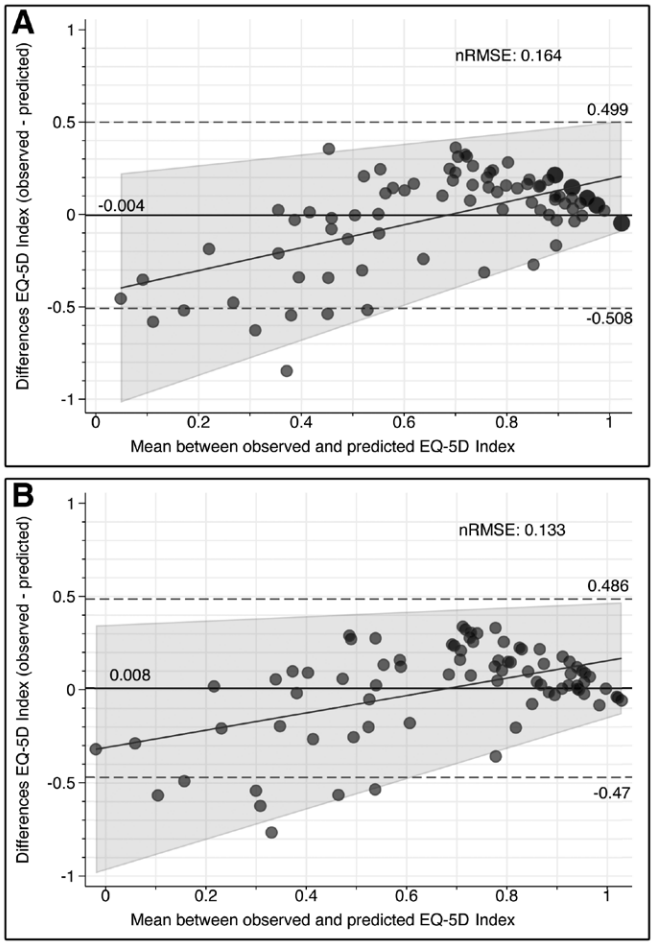

Figure 2. Bland-Altman plot for the best-fitting two-item model (linear) (**A**) and the best-fitting stepwise regression model (linear) (**B**). EQ-5D = EuroQol 5-Dimension, nRMSE = normalized root mean square error.

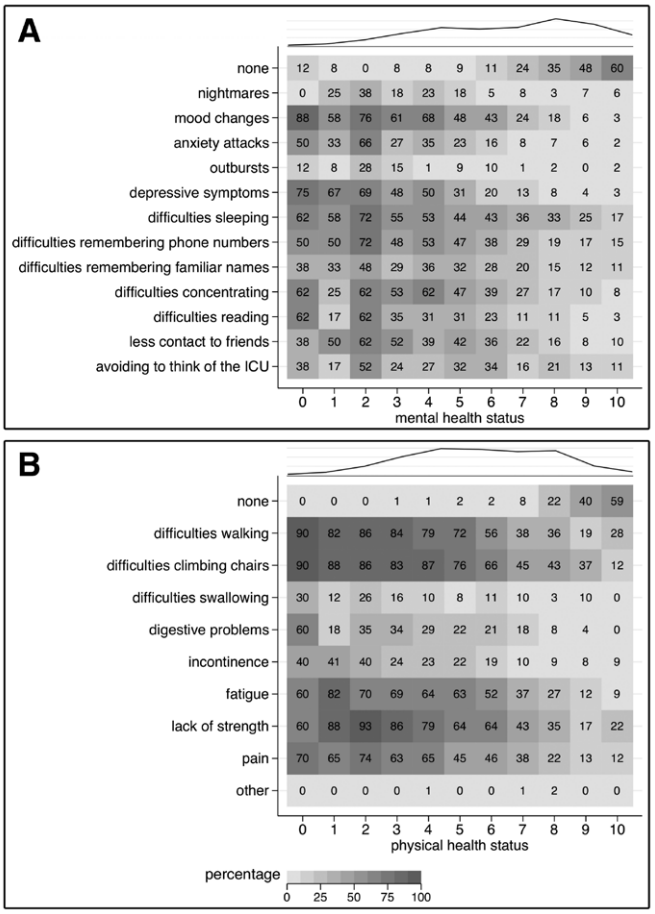

Figure 3. A, Subjective mental health state and current mental health concerns ($n = 840$; density function displayed above heatmap). **B**, Subjective physical health state and current physical health concerns ($n = 848$; density function displayed above heatmap). Other includes shortness of breath, leg edema, loss of vision, and vertigo.

authors acknowledged that measurement properties of the assessments are indispensable (22).

The two items of current mental and physical health showed high correlation coefficients with the EQ-5D-5L index value. Linear regression analysis revealed that a combination of these two items explained 43% of the variation in the EQ-5D-5L index values. Still, goodness of fit parameters of our prediction model (nRMSE, nMAE, LoA, and Bland-Altman plot) indicated differences between predicted and observed EQ-5D-5L index values. We are not aware of studies that explored the minimum clinically important difference in EQ-5D-5L index values for survivors of critical illness, but the minimum clinically important difference for other interventions has been found to vary substantially from 0.03 to 0.52 (48). Although the clinical importance of the differences in predicted and observed EQ-5D-5L index values in our analysis is unknown, we can conclude that the two items on subjective mental and physical health provide good estimates of the EQ-5D-5L index value.

The prediction performance of the subjective mental and physical health status can be increased when the number of affected organ systems prior to ICU admission, length of mechanical ventilation, and BMI are taken into consideration. These variables are usually easily available, and taking this information into consideration can refine a general practitioner's impression of the HrQoL. Interestingly, the time after ICU discharge was not significantly associated with the EQ-5D-5L index value in our analysis, even though previous studies found fluctuations of HrQoL within 1 year after ICU discharge (10).

When patients stated a low subjective mental health status, they frequently reported mood changes, depressive symptoms, and difficulties sleeping; when patients

stated a low subjective physical health status, they frequently reported difficulties walking, difficulties climbing stairs, lack of strength, fatigue, and pain. For patients with low subjective mental or physical health, general practitioners could therefore target their diagnostics toward these health concerns. This is particularly true for depression, which has several treatment options and was shown to be a strong predictor of HrQoL (36).

There are great variations in the organization of post-ICU care between hospitals and healthcare systems (26, 27). For many patients, post-ICU care is organized by primary care physicians (31) and outpatient specialists (49), who might lack experience in sequelae of critical illness (30). The two items on subjective mental and physical health, which do not have a copyright and are free to use, can be applied as a brief tool that adequately reflects HrQoL in these outpatient settings. If a patient scores low on these items, the primary care physician can either conduct a more elaborate assessment of HrQoL (e.g., the SF-36), conduct further diagnostics in relevant PICS domains, or refer the patient to post-ICU specialists.

This analysis is subject to strengths and limitations. We analyzed a large cohort of ICU survivors who were treated in 10 clusters and showed a wide range of admission diagnoses. We were able to include many variables in our prediction models that were shown to have an association with HrQoL, including pre-ICU morbidity. Furthermore, follow-ups were conducted on more than three quarters of study participants who were discharged alive and survived up to 8 months after ICU care. As a limitation, our data might have been subject to survivor bias (50), as we only analyzed patients who did not pass away before their follow-up. Also, patients with particularly impaired HrQoL might have been more likely to be lost to follow-up or to withdraw from the study. Finally, by its nature, this secondary analysis is hypothesis-generating only.

CONCLUSIONS

We showed that asking survivors of critical illness to rank their current subjective mental and physical health from 0 (worst) to 10 (best) is a good reflection of their HrQoL as determined using the EQ-5D-5L index value. The two items on subjective mental and physical health can easily be applied in primary care settings to rapidly assess the HrQoL of survivors of critical illness.

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Drs. Paul and Cittadino have contributed equally to this work.

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Data will be made available from the corresponding author upon a reasonable request.

REFERENCES

1. Halpern NA, Pastores SM: Critical care medicine in the United States 2000–2005: An analysis of bed numbers, occupancy rates, payer mix, and costs. *Crit Care Med* 2010; 38:65–71
2. Statistisches Bundesamt [German Federal Statistical Office], Grunddaten der Krankenhäuser 2015 and 2019 [basic data of hospitals 2015 and 2019]. Statistisches Bundesamt: Wiesbaden, Germany, 2016 and 2021. Available from: https://www.statistischebibliothek.de/mir/receive/DESerie_mods_00000124. Accessed November 28, 2022
3. Needham DM, Bronskill SE, Calinawan JR, et al: Projected incidence of mechanical ventilation in Ontario to 2026: Preparing for the aging baby boomers*. *Crit Care Med* 2005; 33:574–579
4. Kaukonen K-M, Bailey M, Suzuki S, et al: Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA* 2014; 311:1308–1316
5. Alam N, Nannan Panday RS, Heijnen JR, et al: Long-term health related quality of life in patients with sepsis after intensive care stay: A systematic review. *Acute Med* 2017; 16:164–169
6. Cuthbertson BH, Scott J, Strachan M, et al: Quality of life before and after intensive care. *Anaesthesia* 2005; 60:332–339
7. Desai SV, Law TJ, Needham DM: Long-term complications of critical care. *Crit Care Med* 2011; 39:371–379
8. Dowdy DW, Eid MP, Sedrakyan A, et al: Quality of life in adult survivors of critical illness: A systematic review of the literature. *Intensive Care Med* 2005; 31:611–620
9. Oeyen SG, Vandijck DM, Benoit DD, et al: Quality of life after intensive care: A systematic review of the literature. *Crit Care Med* 2010; 38:2386–2400
10. Gerth AMJ, Hatch RA, Young JD, et al: Changes in health-related quality of life after discharge from an intensive care unit: A systematic review. *Anaesthesia* 2019; 74:100–108
11. Marra A, Pandharipande PP, Girard TD, et al: Co-occurrence of post-intensive care syndrome problems among 406 survivors of critical illness. *Crit Care Med* 2018; 46:1393–1401
12. Needham DM, Davidson J, Cohen H, et al: Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. *Crit Care Med* 2012; 40:502–509
13. Geense WW, Zegers M, Peters MAA, et al: New physical, mental, and cognitive problems 1 year after ICU admission: A prospective multicenter study. *Am J Respir Crit Care Med* 2021; 203:1512–1521
14. Chrispin PS, Scotton H, Rogers J, et al: Short form 36 in the intensive care unit: Assessment of acceptability, reliability and validity of the questionnaire. *Anaesthesia* 1997; 52:15–23
15. The EuroQol Group: EuroQol - A new facility for the measurement of health-related quality of life. *Health Policy* 1990; 16:199–208
16. Thompson AJ, Turner AJ: A comparison of the EQ-5D-3L and EQ-5D-5L. *Pharmacoeconomics* 2020; 38:575–591
17. Ludwig K, Graf von der Schulenburg JM, Greiner W: German value set for the EQ-5D-5L. *Pharmacoeconomics* 2018; 36:663–674
18. Angus DC, Carlet J; 2002 Brussels Roundtable Participants: Surviving intensive care: A report from the 2002 Brussels Roundtable. *Intensive Care Med* 2003; 29:368–377
19. Major ME, Kwakman R, Kho ME, et al: Surviving critical illness: What is next? An expert consensus statement on physical rehabilitation after hospital discharge. *Crit Care* 2016; 20:354
20. Mikkelsen ME, Still M, Anderson BJ, et al: Society of critical care medicine's international consensus conference on prediction and identification of long-term impairments after critical illness. *Crit Care Med* 2020; 48:1670–1679
21. Needham DM, Sepulveda KA, Dinglas VD, et al: Core outcome measures for clinical research in acute respiratory failure survivors. An international modified Delphi consensus study. *Am J Respir Crit Care Med* 2017; 196:1122–1130
22. Spies CD, Krampe H, Paul N, et al: Instruments to measure outcomes of post-intensive care syndrome in outpatient care settings – Results of an expert consensus and feasibility field test. *J Intensive Care Soc* 2021; 22:159–174
23. Pallanch O, Ortalda A, Pelosi P, et al: Effects on health-related quality of life of interventions affecting survival in critically ill patients: A systematic review. *Crit Care* 2022; 26:126
24. Sevin CM, Bloom SL, Jackson JC, et al: Comprehensive care of ICU survivors: Development and implementation of an ICU recovery center. *J Crit Care* 2018; 46:141–148
25. Griffiths JA, Barber VS, Cuthbertson BH, et al: A national survey of intensive care follow-up clinics. *Anaesthesia* 2006; 61:950–955
26. Egerod I, Risom SS, Thomsen T, et al: ICU-recovery in Scandinavia: A comparative study of intensive care follow-up in Denmark, Norway and Sweden. *Intensive Crit Care Nurs* 2013; 29:103–111
27. Van Der Schaaf M, Bakhshi-Raiez F, Van Der Steen M, et al: Recommendations for intensive care follow-up clinics; Report from a survey and conference of Dutch intensive cares. *Minerva Anestesiol* 2015; 81:135–144

28. Jeitziner M-M, Nydahl P: Surviving an intensive care unit stay – Do we know if intensive care unit survivors go back to life? *Intensive Crit Care Nurs* 2022; 72:103262
29. Unroe M, Kahn JM, Carson SS, et al: One-year trajectories of care and resource utilization for recipients of prolonged mechanical ventilation: A cohort study. *Ann Intern Med* 2010; 153:167–175
30. Sevin CM, Jackson JC: Post-ICU clinics should be staffed by ICU clinicians. *Crit Care Med* 2019; 47:268–272
31. Ågård AS, Lomborg K, Tønnesen E, et al: Rehabilitation activities, out-patient visits and employment in patients and partners the first year after ICU: A descriptive study. *Intensive Crit Care Nurs* 2014; 30:101–110
32. Adrion C, Weiss B, Paul N, et al; ERIC Study Group: Enhanced Recovery after Intensive Care (ERIC): Study protocol for a German stepped wedge cluster randomised controlled trial to evaluate the effectiveness of a critical care telehealth program on process quality and functional outcomes. *BMJ Open* 2020; 10:e036096
33. Spies CD, Paul N, Adrion C, et al: Effectiveness of an intensive care telehealth programme to improve process quality (ERIC): A multicentre stepped wedge cluster randomised controlled trial. *Intensive Care Med* 2023 Jan 16. [online ahead of print]
34. Collins GS, Reitsma JB, Altman DG, et al: Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. *BMC Med* 2015; 13:1
35. Herdman M, Gudex C, Lloyd A, et al: Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011; 20:1727–1736
36. Zaninotto P, Falaschetti E, Sacker A: Age trajectories of quality of life among older adults: Results from the English longitudinal study of ageing. *Qual Life Res* 2009; 18:1301–1309
37. Bastian K, Hollinger A, Mebazaa A, et al; FROG-ICU Study Investigators: Association of social deprivation with 1-year outcome of ICU survivors: Results from the FROG-ICU study. *Intensive Care Med* 2018; 44:2025–2037
38. Wang S, Mosher C, Perkins AJ, et al: Post-intensive care unit psychiatric comorbidity and quality of life. *J Hosp Med* 2017; 12:831–835
39. Whynes DK, Group T: Correspondence between EQ-5D health state classifications and EQ VAS scores. *Health Qual Life Outcomes* 2008; 6:94
40. Thompson CG, Kim RS, Aloe AM, et al: Extracting the variance inflation factor and other multicollinearity diagnostics from typical regression results. *Basic Appl Soc Psych* 2017; 39:81–90
41. Blum A, Kalai A, Langford J: Beating the hold-out: Bounds for K-fold and progressive cross-validation. In: Proceedings of the Twelfth Annual Conference on Computational Learning Theory. Santa Cruz, CA, Association for Computing Machinery, 1999
42. Mantel N: Why stepdown procedures in variable selection. *Technometrics* 1970; 12:621–625
43. Heinze G, Wallisch C, Dunkler D: Variable selection – A review and recommendations for the practicing statistician. *Biom J* 2018; 60:431–449
44. Zou H: The adaptive lasso and its oracle properties. *J Am Stat Assoc* 2006; 101:1418–1429
45. Tibshirani R: Regression shrinkage and selection via the lasso. *J R Stat Soc Ser B Stat Methodol* 1996; 58:267–288
46. Klapproth CP, van Bebber J, Sidey-Gibbons CJ, et al: Predicting EQ-5D-5L crosswalk from the PROMIS-29 profile for the United Kingdom, France, and Germany. *Health Qual Life Outcomes* 2020; 18:389
47. Orwelius L, Nordlund A, Nordlund P, et al: Pre-existing disease: The most important factor for health related quality of life long-term after critical illness: A prospective, longitudinal, multicentre trial. *Crit Care* 2010; 14:R67
48. Coretti S, Ruggeri M, McNamee P: The minimum clinically important difference for EQ-5D index: A critical review. *Expert Rev Pharmacoecon Outcomes Res* 2014; 14:221–233
49. Kosilek RP, Baumeister SE, Ittermann T, et al: The association of intensive care with utilization and costs of outpatient healthcare services and quality of life. *PLoS One* 2019; 14:e0222671
50. Hofhuis JGM, Spronk PE, van Stel HF, et al: The impact of critical illness on perceived health-related quality of life during ICU treatment, hospital stay, and after hospital discharge: A long-term follow-up study. *Chest* 2008; 133:377–385