

Development of PREPARE (PREdicting PATients' Long-Term Outcome for REcovery): A Practically Usable Prediction Model for Quality of Life of ICU Survivors

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Abstract

BACKGROUND Though numbers of Intensive Care Unit (ICU) survivors have been increasing, using data on patient-reported long-term physical and mental functioning post-ICU during ICU admission is rare. Individualised information about long-term quality of life (QoL) supports ICU physicians' decision making and empowers patients to better manage their disease during ICU admission and recovery and rehabilitation. We aimed to develop a prediction model for ICU survivors' change in QoL one year after ICU admission.

METHODS This is a sub-study of an ongoing multicenter prospective cohort study (MONITOR-IC study), in which long-term outcomes of ICU patients are measured up to five years after ICU admission. Adult patients admitted ≥ 12 hrs to the ICU between July 2016 and January 2019 were included. Moribund patients were excluded. Multivariable linear regression and best subsets regression analysis (SRA) were used for building the prediction model. Change in QoL after one year was quantified using the EuroQol five-dimensional (EQ-5D-5L) questionnaire (Dutch range: -0.446–1), and Short-Form 36 (SF-36, range: 0–100). Models were internally validated

RESULTS Data on 1308 ICU survivors was used to build the **PREdicting PAtients' long-term outcome for Recovery**, PREPARE, prediction model. The best model contained 33 predictors, using the EQ-5D. Explained variance (R^2) was 58.0%. Using SRA, we reduced the number of predictors to 5 ($R^2=55.3\%$): QoL before admission; sex; Clinical Frailty Scale; a cerebral embolism, occlusion, bleeding or infarction prevalent at or within one hour of admission; and having been admitted to the ICU from the operating room, from the same hospital's nursing ward. The prediction model using the EQ-5D to quantify QoL had better predictive performance than the best SF-36 model ($R^2=40.6\%$).

CONCLUSIONS We developed PREPARE, a prediction model for ICU survivors' QoL one year after ICU admission that is practically usable due to the small number of predictors, measurable within the first 24 hours of admission. The next step is to test and evaluate the use of this prediction model in conversations between ICU physicians and patients and their families to ultimately improve patient outcomes.

TRIAL REGISTRATION ClinicalTrials.gov: NCT03246334 on August 11, 2017.

Background

Every year, millions of patients are admitted to an intensive care unit (ICU) worldwide. Due to advances in critical care medicine the number of patients that survive their critical illness has been steadily increasing (1). However, over the last two decades, it has become more clear how devastating and long-lasting the consequences of critical illness can be for ICU survivors and their families. Physical, mental and cognitive health symptoms can persist for months or even years post-discharge, severely affecting quality of life (QoL). Many patients and families are unaware of this fact, and are often too optimistic about long-term

health expectations, underestimating the possible time and effort needed to return to their previous health state and associated life activities (2, 3).

As highlighted by the COVID-19 pandemic (4), incorporating QoL aspects in treatment decision making is incredibly important (5). Expected ICU survivors need conversations about good quality of survivorship: what it entails for a particular person, whether it can be achieved, and what is necessary to achieve it.

Due to a general lack of epidemiological data on long-term health outcomes for ICU survivors, long-term prognosis is often based on caregivers' expert opinion and experience. Even though this is of invaluable importance in clinical practice, ICU physicians and nursing staff cannot always reliably predict future QoL (6-8). As it is not only the patient's survival that matters, but also their QoL, taking a more holistic point of view and broadening focus from being primarily on vital parameters is essential. Therefore, to improve communication between the patient and their family and ICU clinicians regarding long-term outcomes of critical illness and ICU treatment, more patient reported outcome measures (PROMs) are needed. Prediction models can aid the incorporation of PROMs in clinical decision making, and provide a more tailored prognosis regarding long-term health outcome.

Prediction modelling within the ICU has been predominantly focused on modelling short-term mortality (9, 10). Few models consider long-term health outcomes (11-13), let alone long-term QoL (14). Even rarer is a clear path towards its use in clinical practice. Therefore, the aim of the current study was to develop a model to predict the QoL of ICU survivors one year after ICU admission, with the clear goal of its use in clinical practice.

Methods

Study design and population

Data were obtained through an ongoing multicenter prospective cohort study (MONITOR-IC study), in which long-term outcomes of ICU patients are measured up to five years after ICU admission ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03246334): NCT03246334). ICU patients aged 16 years or older were excluded when they had been admitted to the ICU for less than 12 hours, had a life expectancy of less than 48 hours, or could not read or speak the Dutch language. The MONITOR-IC study protocol has been previously published and can be referred to for further detail (15).

For this ancillary study, data of patients who were admitted to a university hospital between July 2016 and January 2019 were used. The population included medical, planned and emergency surgery admission types. The follow-up period was one year.

The study has been approved by the research ethics committee of the Radboud University Medical Centre, CMO region Arnhem-Nijmegen (number 2016–2724). All patients, or their legal representative, provided written informed consent.

Data collection

Patients were asked to complete self-administered questionnaires regarding their health status before and one year after ICU admission. In the case of unplanned ICU admissions, patients were asked to recall their health situation before admission and complete the questionnaire retrospectively as soon as possible after admission. Patients with a planned ICU admission filled in the baseline questionnaire at the outpatient clinic before ICU admission, while patients with unplanned ICU admissions were asked to fill in the questionnaire retrospectively as soon as possible after ICU admission. E-mail and telephone reminders were used in the case of non-response for 4 or 6 weeks, respectively. After 90 days of non-response, patients were excluded. If patients were unable to fill in either questionnaire, this task was performed by their proxies.

Outcome measure

The outcome measure, change in QoL one year after ICU admission, was quantified using the EQ-5D-5L questionnaire (16), as specifically calibrated for the Dutch population (17), and the Short-Form 36 (SF-36) questionnaire (18). The SF-36 is a staple of ICU QoL research (19). Its 36 questions are used to describe both the physical and the mental health aspects of QoL, compiled into the physical component summary (PCS) and the mental component summary (MCS). Both the PCS and MCS range from 0 – 100, a higher score means a better QoL. The EQ-5D is generally used in health technology assessment studies. It consists of five questions each highlighting different aspects of QoL. The Dutch EQ-5D-5L range is -0.446 – 1 (17), a higher score means a better QoL. Both QoL questionnaires were included in order to compare the resulting models on performance (explained variance, adjusted R^2).

Predictors

Candidate predictors consisted of PROMs and other variables that were part of the questionnaire filled in by the patients or proxies as part of the MONITOR-IC study, and of medical patient characteristics collected in the electronic health record (EHR). Two of the PROMs used as a candidate predictor in this study were frailty, measured using the Dutch Clinical Frailty Scale (CFS) (20), and the Visual Analog Scale (VAS). Examples of other questionnaire variables are marital status and education level. All PROMs and other variables collected in the MONITOR-IC database can be found in the study protocol (15). EHR data included information about the first 24 hours of a patient's admission to the ICU, as well as hospital and ICU length of stay. This was supplemented with the Acute Physiology and Chronic Health Evaluation IV (APACHE IV) score and physiological factors like blood pressure. All of these variables were collected by the Dutch National Intensive Care Evaluation registry (NICE: <https://stichting-nice.nl/>), with standardized definitions as specified in their data dictionary.

A preselection of possible predictors from the MONITOR-IC database was executed based on expert opinion (21). The full list of candidate predictors can be found in the Additional Files (Additional File 1).

Statistical analysis

In order to satisfy the regression assumption of normal dependent variable distribution, the outcome measure was defined as change in QoL after one year, i.e. QoL one year after ICU admission minus QoL before ICU admission (at baseline). To produce both a statistically sound and practically useable prediction model for ICU survivors' change in QoL after one year, multivariable linear regression analysis was applied to find the model that best fit the data, followed by best subsets regression analysis (SRA). To assess the bias in predictions, we visualised the predicted changes in EQ-5D scores versus the actual changes in EQ-5D scores in a calibration plot, which can be found in the Additional File (Additional File 2).

Linear regression modelling: choosing the best fit model

To obtain the model that best fit the data with respect to Akaike's Information Criterion (AIC) (22), a stepwise selection procedure was performed. This model is subsequently referred to as the best fit model. The adjusted R^2 ($a-R^2$) and mean square error (MSE) were calculated to indicate the predictive performance of the model.

Best subsets regression modelling: choosing the best practical model

SRA was used to identify the best practical model for use in daily clinical practice, and to compare its performance to the best fit model. We considered a 'practical' model to be easy to use and thus small in terms of the number of predictors needed, while still providing an adequate prediction performance. SRA is a means for model selection that consists of testing all possible combinations of predictor variables while restricting the number of variables allowed in the prediction model. The R function `regsubsets` from the R package `leaps` was used to identify different best models of different sizes, ranging from the best one-variable model up to the best ten-variable model (23). The best practical model was chosen based on $a-R^2$ differences of $<0.5\%$ in pairwise comparisons based on an increasing number of variables to balance the number of variables in the model and the increase in the amount of variation explained in the model.

Internal validation

For all models, we performed interval validation through bootstrap sampling (24). For each of the 2000 bootstrap samples, we fit the model on the bootstrap dataset and predicted the outcomes on the full dataset and calculated the R^2 and MSE from these predictions. We then calculated the mean R^2 and MSE across bootstrap samples as well as standard errors (SEs). Good internal validation would result in mean bootstrap R^2 's that are similar to the model $a-R^2$, and low SEs.

Complete case analysis was applied, meaning that the prediction model has explicitly been developed using survivor data.

Some additional analyses were explored and can be viewed in Additional Files 3 and 4. These include a preliminary analyses using the SF-36 questionnaire to quantify QoL and a prediction model including confirmed deaths.

The variance inflation factor (VIF) was used to identify multicollinearity in the models. Variables with $VIF > 5$ were removed from the model.

All analyses were performed in R, version 3.6.2, using the readxl, MASS, haven, tidyr, ggplot2, plyr, gamlss, lmerTest, foreign, varhandle, leaps and xlsx packages (23, 25-34). We used the Transparent Reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) to check that our reporting adhered to their recommendations for the reporting of studies developing a prediction model (35).

Results

A total of 2291 patients were admitted to the university hospital between July 2016 and January 2019. Of these, 780 (34.0%) were excluded because their one-year outcome measurements were missing, either due to death ($n = 184$, 8.0%) or other, unknown reasons ($n = 596$, 26.0%), resulting in a dataset of 1511 patients, of whom 1308 (57.1%) records had no other missing non-outcome data (Figure 1).

Baseline patients characteristics

The median age of the study population was 65.0 years (interquartile range [IQR] = 57-71) and the majority was male (67.9%). Their median QoL, as quantified using the EQ-5D describing the period before ICU admission, was 0.8 (IQR = 0.7-0.9). Over two thirds of the sample were admitted for planned surgery (72.7%). The median APACHE-IV score was 48.0 (IQR = 38-60). All baseline study population characteristics can be found in Table 1.

Quality of life questionnaire

Two practical prediction models were developed using the SF-36, to describe the change in PCS and MCS score. The best change in PCS model had an $a-R^2 = 40.6\%$, and the best change in MCS model had an $R^2 = 38.5\%$, more details can be found in the Additional File (Additional File 3). The EQ-5D yielded better results in terms of predictive performance ($a-R^2 = 55.3\%$) and was further preferred to the SF-36 due to the smaller size of the questionnaire. This means an advantage when used in clinical practice. It was therefore selected for further analysis.

While our main goal was to develop a prediction model for ICU survivors, we explored the option the EQ-5D questionnaire provides to give confirmed deaths a value of '0'. Due to the increased heterogeneity in the outcome measure variation, this yielded a lower predictive performance ($a-R^2 = 35.0$). See Additional File 4 for full results.

Best fit model (EQ-5D)

A total of 69 candidate predictors (excluding variable categories) were included in the linear regression analysis (Additional File 1). Stepwise selection resulted in a model with 34 predictors as the best fitting model (lowest AIC). Minimum thrombocyte level in first 24 hours was removed due to evidence of multicollinearity, and the model was refit with 33 predictors. The strongest predictor in this best fit model

was the baseline EQ-5D QoL score ($\beta = -0.79$, 95% CI: $-0.83 - -0.75$), a higher score was associated with a lower change in QoL after one year. Other negatively associated predictors were being admitted with a cerebrovascular accident (CVA) (which includes a cerebral embolism, occlusion, bleeding or infarction prevalent before or within one hour of admission) ($\beta = -0.11$, 95% CI: $-0.18 - -0.04$), chronic respiratory insufficiency ($\beta = -0.15$, 95% CI: $-0.24 - -0.06$) and a higher frailty score ($\beta = -0.01$, 95% CI: $-0.02 - -0.01$). Male sex was associated with a higher change in EQ-5D score after one year ($\beta = 0.05$, 95% CI: $0.03 - 0.07$). The full summary of the best fit regression model is depicted in Table 2.

Best subsets regression analysis

If, through SRA, the number of predictors in the model was restricted to one, the model was most likely to include the baseline EQ-5D QoL score. The $a-R^2$ ranged from 51.1% for the smallest model, to an $a-R^2$ value of 56.2% for the largest model. The $a-R^2$ from all models were similar to their bootstrap mean R^2 , showing good internal validation. The predictive performance of the model in terms of $a-R^2$ improved by less than 0.5% when we moved from the best five-variable model to the best six. The balance struck by the model that was restricted to five predictors between a high mean $a-R^2$, a low mean square prediction error, and a small number of relatively easily accessible variables was therefore deemed the most efficient, and was selected as the final model. There was no evidence of multicollinearity, with variance inflation factors <2 for all variables across the 10 models. The full summary of the best subsets regression analysis can be found in Table 3.

Best practical model analysis

The five predictors most likely to be included in the best subsets model restricted to five predictors were studied with linear regression analysis. Baseline EQ-5D QoL score was negatively associated with the outcome ($\beta = -0.76$, 95% CI: $-0.81 - -0.72$), as were frailty score ($\beta = -0.02$, 95% CI: $-0.03 - -0.01$) and having been admitted with a cerebral vascular accident (CVA) ($\beta = -0.14$, 95% CI: $-0.20 - -0.07$). Male sex and being admitted from the operating room from the nursing ward within the same hospital were positively associated with the outcome ($\beta = 0.05$, 95% CI: $0.03 - 0.07$) and $\beta = 0.07$, 95% CI: $0.05 - 0.10$), respectively.

This best practical model, named PREPARE (PREdicting PATient's long-term outcome for REcovery) had an $a-R^2$ of 55.3%. A visual demonstration of the best practical model can be viewed in Figure 2. The red dot demarcates the predicted change in QoL after one year for a fictional patient.

The calibration plot shows that the relationship between the predicted changes in EQ-5D and the actual changes in EQ-5D is linear with slope = 1 (95% CI: $0.95 - 1.05$) and intercept = 0 (95% CI: $-0.01 - 0.01$), indicating that the model is well calibrated. The calibration plot can be viewed in the Additional Files (Additional File 2).

Discussion

We have developed a prediction model for change in ICU survivors' QoL one year after ICU admission that has both considerable predictive value and is well calibrated, as supported by internal validation. The small number of predictors, all available within the first 24 hours of admission, increases the feasibility of using the PREPARE model in clinical practice. Moreover, the prediction model based on the less-burdensome five-question EQ-5D questionnaire had better predictive value than the longer SF-36 QoL questionnaire, which is more commonly used in the ICU (19).

Prediction models focusing purely on quality of life, and not on mortality, are rare in critical care. A timely and continuous conversation about long-term outcomes is an indispensable part of future intensive care medicine for expected ICU survivors. Using a prediction model as an enrichment to ICU professionals' knowledge enables them to provide patients with a more objective prediction of their long-term outcomes. This in turn empowers ICU patients and their families to be more involved in clinical decision-making and helps to manage their expectations for their long-term recovery, facilitating an individualized, preparatory approach instead of a reactionary one.

As far as we are aware, only Oeyen et al. have developed a series of increasingly practically usable prediction models for the general ICU population's long-term QoL (14). Although our overall conclusions are similar, the major difference between our studies is the inclusion of patients who died in the year after admission, an approach we rejected due to our focus on good survivorship. We also had more planned surgical patients and we incorporated more physiological patient characteristics within the first 24 hours of admission. We consider this study an elaboration on their foundational work, with a focus on good survivorship and a proposed method of prediction model visualisation for incorporation of the results in clinical practice.

Past implementation of prediction modelling in ICU practice has been impeded by doubts about model accuracy (14, 36). Even though any prediction for long-term health can only ever be used as a supplement to ICU professionals' knowledge and experience, these fears are understandable. Though we consider the predictive performance of our PREPARE model to be more than acceptable, medical professionals familiar with prediction modelling might think our model performance inferior to the predictive performance measurements of other oft used prediction models in ICU practice (SAPS III aROC: 0.86 (10), APACHE IV aROC: 0.88 (9) predict patients' chance to die in hospital). Considering the difficulty of predicting a long-term PROM such as QoL, we deem the current achieved model performance based only on variables available within the first 24 hours of admission to be a substantive step in the right direction. All the same, the CIs of our model predictions are still wide, and the model performance can be improved upon. For instance by using a larger pool of patient data by extracting more detailed patient data from the EHR, instead of only data from the first 24 hours. Whether inputting new data pertaining to the whole ICU admission will make the model less practical remains to be seen. Perhaps the gains in model performance will be sufficiently large to offset this potential setback.

Like other studies detailing the prediction of physical long-term health post ICU admission, we have shown that among our predictors the pre-ICU QoL is by far the most important predictor for long-term QoL

(used as the sole predictor $a-R^2 = 51.1\%$) (37-39). Conversations about pre-ICU health status are already an important part of many ICU physician's manner of providing care. Doing so with the added help of a more standardized set of questions and data on hundreds of former patients will only make these conversations more valuable and objective.

Talking about both the opportunities and the disadvantages of an ICU admission in a frank manner is important to prepare patients and families for the road ahead (5). Stressing the importance of pre-ICU health can be an important source of comfort and preparedness. Our study is new evidence supporting the importance of all aspects of pre-ICU health in ICU treatment decision making. The significance of pre-ICU health status extends to another one of our findings: the relative unimportance of age. Age is generally one of the most crucial factors considered when performing triage (40, 41). While it was associated with our outcome in the full model, our results show that baseline QoL and frailty score are more important predictors of long-term QoL than age, which is supported by literature (42).

This is a large prospective cohort study based on ICU patients' past and long-term health. Though second of its kind, it demonstrates the possibility of achieving a good predictive performance combined with a reduction of the number of predictors needed, compared to its predecessor in purpose (14).

This study has some limitations. There is a possible bias in the relatively healthier ICU patient group that agreed to participate in the MONITOR-IC study, and by extension, are included in the prediction model. More than two thirds of the study population were admitted due to planned surgery. Generally, these patients are more prepared for an ICU stay and have better outcomes. Even though our prediction model is for ICU survivors only, this sample may be slightly better off than the general ICU survivor population. This could have caused our predictions to be slightly overoptimistic. Moreover, though proxies filling in the questionnaire when patients were unable to might have introduced a small underestimation of their QoL scores (43), we believe that excluding these patients would have led to bias as well (44). We consider our choice to use complete case analysis on ICU survivors to be best due to the improved model performance, though we realize that it is not always clear who will survive long-term. However, we still believe that the new information the model provides will be a valuable contribution to the improved ICU care of today, with its shifting focus towards good survivorship.

Lifting a model from the pages of theory and putting it into clinical practice is not an easy feat. In order to further model implementation, the next step is external validation. While the overrepresentation of planned ICU admissions in our sample might pose a challenge, the small number of predictors needed for the model has caused us to consider this an achievable goal. A pilot study using the prediction model in existing conversations between ICU physicians and patients and their families is conducted at the moment. In this pilot study, ICU physicians are asked to judge patients' likeliness of long-term survival. If physicians are confident in this matter, the change in QoL prediction is introduced into a conversation with family, in order to start looking ahead to the future while still on the ICU. If both the external validation, using data from secondary centers to further improve model generalisability, and the pilot

study provide conclusive evidence to the model's value in practice, a large trial will be conducted to evaluate the effect of using QoL data in ICU treatment on patient outcomes and experiences.

Conclusions

In conclusion, we have developed the PREPARE model, a prediction model for ICU survivors' change in QoL one year after ICU admission that is usable in clinical practice due to the small number of predictors, all available on the first day of admission. The explained variance of 55.3%, as supported by internal validation, marks the model as a potential helpful complement to ICU professionals' knowledge and expertise in conversations with patients and their families. In future, long-term QoL information should be integrated in ICU care to better inform ICU decision making and to aid ICU survivors in managing their long-term health expectations.

List Of Abbreviations

in order of appearance

PREPARE: PREdicting PATients' long-term outcome for Recovery

ICU: Intensive Care Unit

QoL: Quality of Life

SRA: Subsets Regression Analysis

EQ-5D-5L: EuroQol five-dimensional questionnaire

SF-36: Short-Form 36 questionnaire

PROM: Patient Reported Outcome Measure

CMO: Committee on Research Involving Human Subjects

PCS: Physical Component Summary (of the SF-36 questionnaire)

MCS: Mental Component Summary (of the SF-36 questionnaire)

EHR: Electronic Health Record

CFS: Clinical Frailty Scale VAS: Visual Analogue Scale

APACHE: Acute Physiology and Chronic Health Evaluation

NICE: (Dutch) National Intensive Care Evaluation registry

AIC: Akaike's Information Criterion

a-R²: adjusted R²

MSE: Mean Square Error

SE: Standard Error

VIF: Variance Inflation Factor

CVA: Cerebro Vascular Accident

Declarations

Ethics approval and consent to participate

The study has been approved by the research ethics committee of the Radboud University Medical Centre, CMO region Arnhem-Nijmegen (number 2016–2724). All patients, or their legal representative, provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NW, MvDB, HvdH and MZ contributed substantially to the conception of the work. Each author contributed substantially to the design of the work. NW, MvDB and MZ contributed substantially to the acquisition of the data. NW and JR contributed substantially to the analysis of the data. Each author

contributed substantially to the interpretation of the data. NW drafted the manuscript. Each author contributed substantially to the revision of the work.

Each author approved the submitted version. Each author agrees to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Tables

Table 1.
Patient characteristics at baseline (ICU admission)

Variable	Median (25 th -75 th percentile) or N (%)
Sex: male	888 (67.9)
Age	65.0 (57.0-71.0)
Frailty	3 (2.0-3.0)
EQ-5D-5L score	0.8 (0.7-0.9)
SF-36 PCS score	41.9 (32.3-51.1)
SF-36 MCS score	52.0 (41.4-57.6)
APACHE IV score	48.0 (38.0-60.0)
Education level:	
· High	376 (28.7)
· Medium	574 (43.9)
· Low	358 (27.4)
Admission type:	
· Planned Surgery	951 (72.7)
· Emergency surgery	140 (10.7)
· Medical	217 (16.6)
Mechanically ventilated 24 hours after admission	1020 (78.0)
Comorbidity (chronic conditions):	
· Immunological insufficiency	66 (5.0)
· Malignant hematological disease	18 (1.4)
· Metastasized neoplasm	58 (4.4)
· Cirrhosis	0 (0)
· Chronic cardiovascular insufficiency	37 (2.8)
· Chronic respiratory insufficiency	16 (1.2)
· Chronic renal insufficiency	21 (1.6)

Table 2.
Best fit model summary, including 33 predictors

Predictor	Coefficient	95% CI	p-value
Baseline EQ-5D score	-0.79	-0.83 – -0.75	<0.001
Age at baseline	-0.00	-0.00 – -0.00	0.13
Sex: male	0.05	0.03 – 0.07	<0.001
Weight	-0.00	-0.00 – 0.00	0.09
Frailty	-0.01	-0.02 – -0.01	<0.001
Education level			
· High education	0.03	0.00 – 0.06	0.02
· Medium education	0.03	0.01 – 0.05	0.01
Admission type			
· Planned surgery	0.03	-0.01 – 0.07	0.10
Admission source (from same hospital):			
· CCU, ICU or Special Care Unit	0.10	0.01 – 0.18	0.02
· Operating room from nursing ward	0.03	-0.00 – 0.01	0.07
Dysrhythmia	0.03	-0.01 – 0.07	0.12
CVA (present at admission)	-0.11	-0.18 – -0.04	0.00
Intracranial mass effect	-0.07	-0.14 – 0.00	0.06
Chronic respiratory insufficiency	-0.15	-0.24 – -0.06	0.00
Acute renal failure	-0.05	-0.11 – 0.01	0.11
Chronic COPD	-0.03	-0.06 – -0.01	0.12
Minimum heartrate in first 24 hours	-0.00	-0.00 – -0.00	0.04
Maximum heartrate in first 24 hours	0.00	-0.00 – 0.00	0.18
Minimum systolic blood pressure in first 24 hours	0.00	-0.00 – 0.00	0.09
Maximum systolic blood pressure in first 24 hours	-0.00	-0.00 – 0.00	0.10
Mean minimum blood pressure in first 24 hours	-0.00	-0.00 – 0.00	0.15
Minimum temperature in first 24 hours	-0.01	-0.02 – -0.00	0.13
Maximum potassium level in first 24 hours	-0.02	-0.04 – 0.00	0.02
Maximum sodium level in first 24 hours	-0.00	-0.01 – -0.00	0.02

Maximum bicarbonate level in first 24 hours	-0.00	-0.01 – -0.00	0.03
Bilirubin level in first 24 hours	0.00	0.00 – 0.00	0.03
Minimum albumin level in first 24 hours	-0.00	-0.00 – 0.00	0.10
Maximum albumin level in first 24 hours	0.00	-0.00 – 0.00	0.36
Maximum thrombocyte level in first 24 hours	0.00	-0.00 – 0.00	0.20
Maximum glucose level in first 24 hours	-0.00	-0.01 – 0.00	0.05
APACHE probability score at baseline	0.21	0.08 – 0.34	0.00
APACHE IV probability score at baseline	-0.21	-0.32 – -0.10	<0.001
One previous admission to the ICU	-0.05	-0.09 – -0.01	0.02

Table 3. Best subsets regression analysis summary

Variable name ↓	Number of variables in model →	1	2	3	4	5	6	7	8	9	10	Best fit: 34
Baseline EQ-5D-5L score												
Admission source: Operating room*												
Sex: male												
Frailty												
CVA (present at admission)												
Chronic respiratory insufficiency												
Maximum sodium levels in first 24 hours												
One previous ICU admission												
Minimum heartrate in first 24 hours												
Bilirubin levels in first 24 hours												
Model Adjusted R² %		51.1	53.1	54.0	54.8	55.3	55.6	55.7	55.9	56.0	56.2	58.0
Mean Square Error of prediction (model)		0.033	0.032	0.031	0.030	0.030	0.030	0.030	0.030	0.030	0.029	0.029
Mean bootstrap R² % (SE)		51.0 (0.13)	53.0 (0.14)	54.0 (0.15)	54.7 (0.16)	55.1 (0.25)	55.3 (0.26)	55.5 (0.27)	55.7 (0.27)	55.8 (0.28)	55.9 (0.34)	57.6 (0.45)

Figures

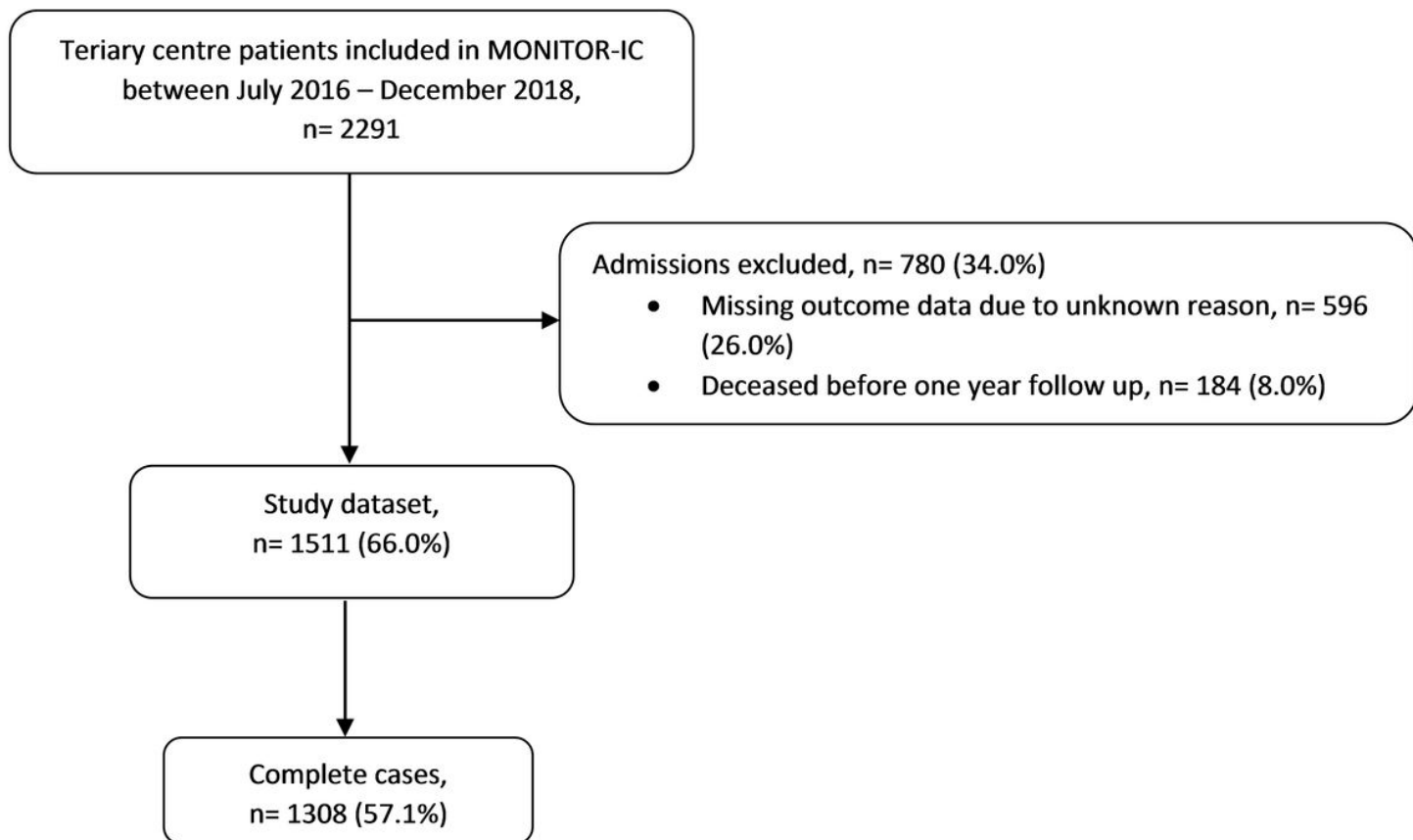


Figure 1

Study population flowchart

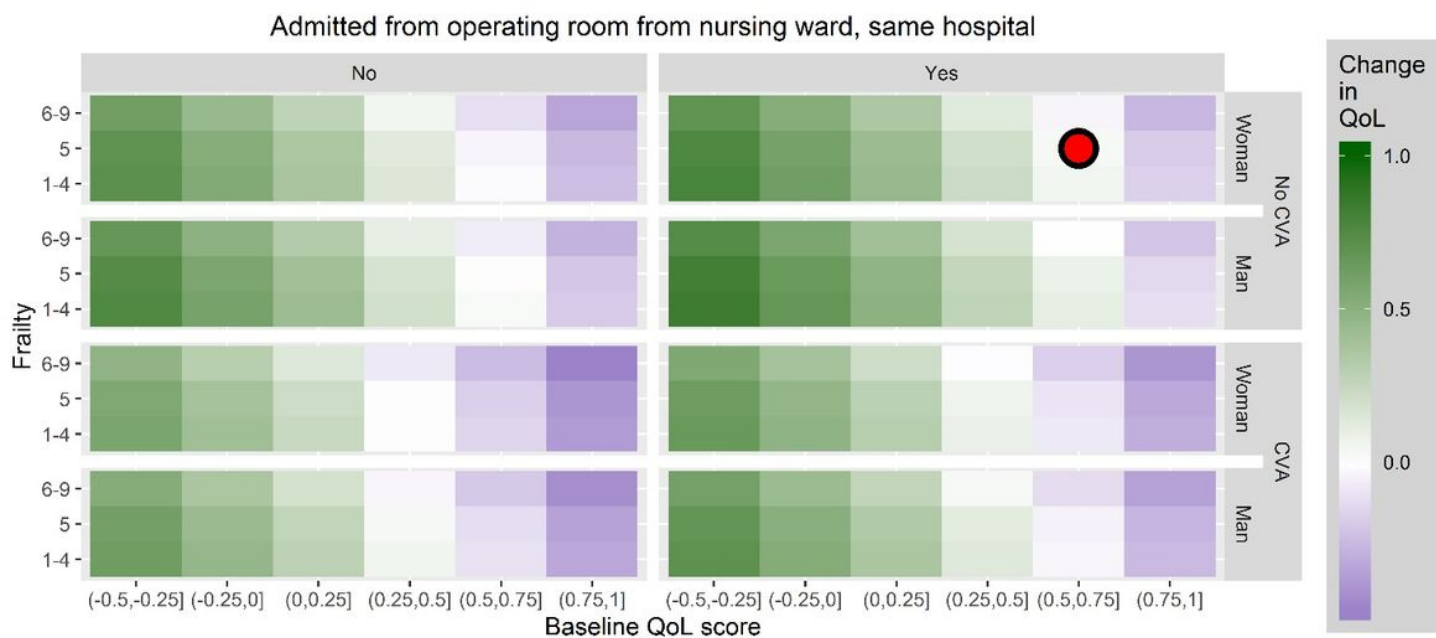


Figure 2

Risk table visualising the PREPARE model. The PREPARE model has five predictors and is described by the following formula: $\text{Change in QoL} = 0.63 + \text{Baseline QoL score} \times -0.77 + \text{Admission source: operating room from nursing ward, same hospital} \times 0.07 + \text{Male sex} \times 0.05 + \text{Frailty score} \times -0.02 + \text{CVA (present at admission)} \times -0.14$ The red dot demarcates the predicted change in QoL ($\Delta = 0.04$, 95% CI: $-0.31 - 0.38$) after one year for a fictional female patient who is pre-frail (Frailty score = 5), had a baseline QoL score of 0.70 and who was admitted after a planned surgery with no CVA present.

Supplementary Files

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