Risk factors for long-term invasive mechanical ventilation:a retrospective longitudinal study using German health claims data

Franziska C Trudzinski (franziska.trudzinski@med.uni-heidelberg.de)
Thoraxklinik-Heidelberg gGmbH https://orcid.org/0000-0002-0980-7586

Julia Dorothea Michels
Thoraxklinik-Heidelberg gGmbH

Benjamin Neetz
Thoraxklinik-Heidelberg gGmbH

Jan Meis
Heidelberg University: Universitat Heidelberg

Michael Müller
Thoraxklinik-Heidelberg gGmbH

Axel Kempa
SLK-Kliniken Heilbronn GmbH

Claus Neurohr
Robert Bosch Hospital: Robert-Bosch-Krankenhaus GmbH

Armin Schneider
Wangen Hospital: Fachkliniken Wangen

Herth Felix
Thoraxklinik-Heidelberg gGmbH

Joachim Szecsenyi
Heidelberg University: Universitat Heidelberg

Elena Biehler
Heidelberg University: Universitat Heidelberg

Thomas Fleischhauer
Heidelberg University: Universitat Heidelberg

Michael Wensing
Heidelberg University: Universitat Heidelberg

Simone Britsch
UMM: Universitatsklinikum Mannheim

Janina Schubert-Haack
aQua göttingen

Thomas Grobe

aQua Göttingen

Timm Frerk

aQua Göttingen

Research Article

Keywords:

Posted Date: March 1st, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2599890/v1

Abstract

Purpose

Long-term invasive mechanical ventilation (IMV) is a major burden for those affected and causes high costs for the health care system. Early risk assessment is a prerequisite for the best possible support of high-risk patients during the weaning process. We aimed to identify risk factors for long-term IMV within 96 hours after the onset of IMV.

Methods

The analysis was based on data from the AOK Baden-Württemberg; patients who received IMV ≥ 96h and were discharged between 2015 and 2017 were analysed. Health claims data were considered for the previous year and 30 days after hospitalisation. Long-term IMV was defined as evidence of invasive home mechanical ventilation (HMV), IMV≥ 500h, or readmission with (re)prolonged ventilation. The performance of the model was evaluated on a 2018 data-set.

Results

7.584 hospitalisations were analysed. Criteria for long-term IMV were met in 38.3% of cases, of which 13.9% had evidence of HMV, 73.1% were ventilated >500 hours and/or 40.3% were rehospitalised with IMV. Several risk factors could be identified, including pre-existing conditions, admission diagnosis, prescribed aids and procedures. By combining all these factors into a final model, the risk for long-term IMV could be estimated with a sensitivity and specificity of respectively 49 and 80% on the test data set (when classifiying patients based on their predicted probability with a cut-off of 41.15%).

Conclusion

Based on health claims data alone, the risk for long-term IMV could be estimated with an acceptable predictive quality as early as 96 hours after the start of IMV.

Take Home Message

Using health insurance data of 7.584 invasively ventilated patients from Germany, the risk for long-term ventilation could be determined based on the diagnoses and aid prescriptions of the previous 365 days in combination with the admission diagnosis and the operations and procedures of the first 96h after Initiation of Invasive mechanical ventilation.

Introduction

The increasing number of patients who cannot be successfully weaned from invasive mechanical ventilation (IMV) after an acute stay in the intensive care unit (ICU) is a drawback of modern intensive care medicine (ICM) [1]. Even patients that carry a high risk of weaning failure can often be successfully

weaned from IMV in specialised weaning centres [2]. However, transfer to long-term IMV facitilites after weaning failure often occurs directly from the ICU, without prior assessment in one of these centres. Even when a patient is transferred to a weaning centre, this often occurs after a long inpatient history of receiving IMV. It has been shown that the duration of previous IMV is an independent risk factor for weaning failure with subsequent discharge to invasive home mechanical ventilation [3–5]. The outpatient care of patients receiving out-of-hospital IMV is time-consuming, expensive and also ties up trained nursing staff who are urgently needed in inpatient care. The cause of the rare and often late transfer of patients at risk for long-term IMV to specialised care has several reasons. In addition to a long wait list and limited capacity of specialised centres, these individuals are critically ill patients with difficult to predict disease trajectories, making anticipatory care planning challenging. The volume of acute or postoperatively invasively ventilated patients who undergo prolonged weaning incurs large costs and ties up valuable critical care resources. The recent international, multicentre, observational study WEAN SAFE with 5869 critically ill adult patients, shows that only 65% of patients who received invasive ventilation for more than 2 days were successfully weaned on day 90 [6]. It is estimated, that weaning takes about 40% of the total ventilation time, which is particularly due to the patients, who require prolonged weaning [7]. Ideally, these patients should receive special support throughout the course of IMV. To achieve this, reliable tools are needed to assess the risks of long-term IMV as early as possible during the ICU stay. So, there is an urgent need for comprehensive data on this important topic [8]. We aimed to conduct an analysis of risk factors for long-term IMV early in the course of treatment after intubation. For this purpose, we used data from the largest statutory health insurance fund in Germany. In addition to the intensive care stay that led to the need for mechanical ventilation, data from the previous year and the subsequent 30 days of the corresponding hospitalisation were also considered. This work is part of the multicentre PRiVENT study project, which aims to investigate innovative forms of care for invasively ventilated patients.

Methods

The basis for the analysis is the claims data of *Allgemeine Ortskrankenkasse Baden-Württemberg* (AOK-BW), the largest nationwide health insurance company with around 4.38 million insured people, which corresponds to around 5.96% of the population covered by statutory health insurance in Germany. The validity follows to the requirements of German health claims data. The limitations are in the lack of diagnoses and procedures that are not relevant for profit. The data were provided in pseudonymised form and analysed by the Institute for Applied Quality Improvement and Research in Health Care, aQua, in close exchange with a team of experienced clinicians. The consulting team consisted of 3 specialists in pneumology and internal medicine with additional qualifications in intensive care medicine, and a respiratory therapist. The exploratory data analyses were based on a systematic literature review [8] and the clinical knowledge of the interprofessional team.

Patients

The patients studied were AOK-BW insured patients, who underwent invasive mechanical ventilation during a hospital stay with discharge between January 2015 and December 2017. To specifically identify high-risk patients, only patients who were invasively ventilated for ≥ 96 hours, were over 30 years of age, and had a medical comorbidity were included. Patients with evidence of previous invasive HMV, or neuromuscular disease without potential for ventilator weaning, although this would further improve the predictive quality of the model, were excluded from the analysis as it is clear, that these patients are already at high risk for long-term IMV without the presence of other risk factors. Patients, who died within the first 11 days after initiation of invasive ventilation, were also excluded from the analysis. In order to capture pre-diagnoses and chronic conditions and to document the sustainability of weaning from ventilation, the patient had to be insured with AOK-BW within the previous 365 days and 30 days after discharge from the hospital. The inclusion and exclusion criteria as well as their definitions are shown in Table 1.

Table 1

Selection criteria The table shows the inclusion and exclusion criteria of the study, and the respective definitions of the given parameters. Abbreviations: HMV invasive mechanical home ventilation, ICD international statistical classification of diseases and related health problems, OPS official classification of operational procedures in Germany.

Inclusion criteria	Definition
At least 96 hours of ventilation	Ventilation hours ≥ 96 (counting method according to the German Coding Guidelines)
At least 30 years old	Start of inpatient treatment [year] - Year of birth ≥ 30
At least one comorbidity	One of the following ICDs coded in the 365 days prior to the ventilation case: J44, M41, J60-J70, J84, I50, I25, E10-E14, E66.01, E66.02, C00-C97, F05, F10.4-16.4 (in each case those ending in .4), F18.4, F19.4, F20-29, G62.80, G72.80, N17, N18
Insurance periods	In calendar years in which the pre-review period (365 days before the start of the inpatient stay), the ventilation case and the post-review period (30 days after discharge) fall, the insured person must have been insured with AOK-BW for at least 365 days.
Exclusion criteria	
Neuromuscular diseases	Exclusion of insureds with a coded condition with ICD G12.2 and/or G71 within 365 days prior to the ventilator case.
No prior invasive HMV	OPS 8716.01, 8716.11, 8716.21, „Tracheostomy ventilator aids “12.50.99.0002, ICD (Z99.1, Z43.0, ICD Z99.1) within 365 days prior to the ventilator case.
No death within 11 days following the initiation of ventilation	No death (discharge reason ≠ death) within 11 days of the first date on which access for invasive ventilation was coded (OPS 5311, 5312, 8701, 8704).

Outcomes

Long-term IMV was defined as follows; evidence of invasive home mechanical ventilation after discharge, or total duration of ventilation ≥ 500 hours, or re-hospitalisation with (re)prolonged ventilation (IMV ≥ 96h). The criteria and operationalisations of outcomes are listed in Table 2.

Table 2

Outcomes The table shows the different definitions of the three outcomes studied; long-term IMV defined as evidence of invasive mechanical home ventilation, IMV ≥ 500h and/or readmission with (re)prolonged ventilation. Abbreviations: HMV invasive mechanical home ventilation, IMV invasive mechanical ventilation, ICD international statistical classification of diseases and related health problems, OPS official classification of operational procedures in Germany. * the specified no. 12.50.99.0002 is an AOK-BW specific code.

Criteria	Definition
Evidence of home invasive ventilation after discharge	
Initiation of home mechanical ventilation - Invasive HMV after weaning failure and within 30 days.	OPS 8716.01
Control or optimisation of a previously initiated HMV within 30 days	OPS 8716.11
Termination of previously initiated home ventilation within 30 days	OPS 8716.21
Tracheostomy ventilator aids prescribed after start of ventilation and within 30 days of discharge	Nr. 12.50.99.0002*
Inpatient: dependence (long term) on respirator after start of ventilation AND	ICD Z99.1
Care of a tracheostoma after the start of ventilation and within 30 days after discharge	ICD Z43.0
Outpatient: Dependence (long-term) on respirator AND. Care of a tracheostoma in the quarter following the end of the respirator claim.	ICD Z99.1 ICD Z43.0
Total duration of ventilation ≥ 500 hours	
Total duration of ventilation is 500 or more hours	Ventilation hours ≥ 500
Re-hospitalisation with (re)prolonged ventilation	
Re-hospitalisation with (re)prolonged ventilation within 30 days after discharge	Re-hospitalisation with initiation of prolonged ventilation within 30 days of discharge (with ventilation hours ≥ 96).

Predictors

Data from International Statistical Classification of Diseases and Related Health Problems (ICD), official classification of operational procedures in Germany (OPS), and prescriptions for medical aids were considered. In addition to the data on the hospitalisation at which the invasive ventilation was initiated, information on the previous year the subsequent 30 days of the corresponding hospitalisation were also considered. Predictors were selected stepwise based on exploratory data analysis in close communication with the consulting team. All relevant independent predictors were combined in a final regression model. An overview of the time periods of the predictors and results is shown in Fig. 1.

Statistical methods

Binary logistic regression models were estimated to predict the risk for long-term IMV. To investigate the predictive value of the final model, the probabilities determined in regression models were evaluated by Receiver Operating Characteristic (ROC) analyses. The performance of the model was evaluated on a 2018 AOK data-set (which was not used in the training the model). Statistical analyses were performed using SAS Enterprise Guide 7.1.

Results

Regression analyses

By the end of the 30-day follow-up, the criteria for long-term IMV were met in 2905 of 7584 cases (38,3%). Of these cases, 13,9% showed evidence of invasive HMV, 73,1% were ventilated for at least 500 hours and/or 40,3% were re-hospitalised receiving IMV within the follow-up period of 30 days after discharge. Among the baseline predictors, only nursing home placement immediately prior to hospitalisation was relevant, and this was associated with a favourable prognosis; age or gender did not play a role. In terms of preexisting conditions documented in the year preceding the corresponding hospitalisation, or chronic diseases, registered in the course of the inpatient stay, thyroiditis, eating disorders, rheumatic mitral valve disease (insufficiency or stenosis), pneumothorax, obesity and chronic obstructive pulmonary disease (COPD) as well as dependence (at least 3 completed months) on aspirator and/or non-invasive respirator carried an increased risk of long-term IMV. Whereas a prior diagnosis of dementia or peritonitis showed a favourable prognosis with respect to the risk of long-term IMV. Of the admission diagnoses, cardiac arrhythmias were associated with a favourable prognosis while cerebral infarction and acute pancreatitis entailed an increased risk for long-term IMV. In the analysis of the operations and procedures documented in the preceding year of the corresponding hospitalisation, the previous tracheostomy was particularly unfavourable, whereas the application of a dialysis shunt was associated with a lower risk of long-term IMV. Surgeries and procedures associated with increased risk of long-term IMV during the first four days of IMV included bronchoscopies, native computed tomography of the chest, cranial magnetic resonance imaging with contrast, cerebrospinal fluid system procedures (drainage, shunt, catheterisation), positioning in a rotating or sandwich bed, the transfusion of plasma components, the use of extracorporeal pulmonary support and the complex treatment of colonisation or infection with

multidrug-resistant pathogens. Radical cervical lymphadenectomy and autologous blood collection and transfusion showed favourable prognosis in terms regarding outcome. All investigated predictors with the corresponding odds ratios and confidence intervals (CI) are shown in Table 3.

Table 3
predictor

The table shows all predictors of the model with the respective odds ratios and the corresponding confidence intervals. In addition to the master data, diagnoses as well as operations and procedures of the previous 365 days, before the intensive care stay and operations and procedures during the hospital stay up to 95 h after intubation were considered. Abbreviations: COPD chronic obstructive pulmonary disease, PECLA pumpless extracorporeal lung assist, ECCO2R Extracorporeal CO2 removal, vv veno-venous, va veno-arterial, ECMO extracorporeal membrane oxygenation, CI confidence interval.

Predictor	**Definition**	**Odds Rato**	**Lower CI**	**Upper CI**	**P value**
Baseline predictors		**1.56**	**1.05**	**2.32**	
Intercept		0.32	0.22	0.46	< 0.001
Age (years)		1.00	1.00	1.01	0.276
Gender (female)		0.93	0.84	1.03	0.149
Nursing home accommodation	Nursing home accommodation immediately before hospitalisation	0.67	0.50	0.90	0.009
Diagnoses					
Pre-existing medical conditions (in 365 days prior to the ventilator case).					
Thyroiditis	ICD E06	1.50	1.01	2.22	0.045
Dementia	ICD F00-F03	0.66	0.55	0.80	< 0.001
Eating disorders	ICD F50	1.99	1.09	3.65	0.026
Rheumatic mitral valve disease (insufficiency or stenosis)	ICD I05	1.89	1.35	2.65	< 0.001
Peritonitis	ICD K65	0.45	0.26	0.78	0.004
Pneumothorax	ICD J93	2.10	1.12	3.93	0.020
Admission diagnosis					
Cardiac arrhythmia	ICD I49	0.51	0.31	0.86	0.011
Cerebral infarction	ICD I63	1.54	1.17	2.03	0.002
Acute pancreatitis	ICD K85	2.64	1.50	4.63	0.001
Diseases (previous disease, admission diagnosis, ventilation case).					

Predictor	Definition	Odds Rato	Lower CI	Upper CI	P value
Dependence (at least 3 completed months) on aspirator and/or respirator.	ICD Z99.0, Z99.1	5.13	4.03	6.52	< 0.001
COPD	ICD J44	1.30	1.17	1.44	< 0.001
Pulmonary or abdominal metastasis	ICD C78	0.49	0.35	0.68	< 0.001
Operations and procedures					
Operations and procedures in the 365 days prior to the ventilator case.					
Tracheostomy, permanent or temporary	OPS 5311, 5312	2.17	1.67	2.82	< 0.001
Creation of a dialysis fistula, shunt or bypass	OPS 5393	0.36	0.18	0.72	0.003
Operations and procedures during the ventilation case up to 95h after intubation.					
Bronchoscopy	OPS 1620	1.18	1.07	1.31	0.001
Native computed tomography of the chest	OPS 3202	1.19	1.03	1.37	0.019
Computed tomography and/or magnetic resonance imaging of the the cranium with imaging contrast medium	OPS 3220, 3820	1.36	1.16	1.59	< 0.001
Operations on the spinal cerebrospinal fluid system (drainage, shunt, catheter; also, removal)	OPS 5038	2.61	1.31	5.22	0.007
Tracheostomy, permanent or temporary	OPS 5311, 5312	3.97	3.43	4.60	< 0.001
Radical cervical lymphadenectomy	OPS 5403	0.20	0.10	0.40	< 0.001
Chest tube	OPS 8144	1.38	1.18	1.62	< 0.001
Positioning treatment in a special bed (e.g. positioning in a rotating or sandwich bed)	OPS 8390.0	2.31	1.70	3.13	< 0.001
Autologous blood collection and transfusion	OPS 8803	0.65	0.47	0.90	0.010
Transfusion of plasma components and genetically engineered plasma proteins	OPS 8810	1.36	1.17	1.58	< 0.001
PECLA, ECCO2R, vv- und va ECMO und Prä-ECMO-Therapie	OPS 8852	1.80	1.35	2.39	< 0.001
Complex treatment for colonization or infection with multidrug-resistant pathogens	OPS 8987	1.49	1.21	1.84	< 0.001

Perfomance of the model on 2018 AOK BW data set

The diagnostic value of the combination of all these factors was investigated using ROC analyses; the c-value on the training data set is 0.700 and can be classified as an acceptable predictive value according to Hosmer and Lemeshow [9].

In order to test our generated model, we used it on health claims data from 2018. The AUC value was c = 0.679, slightly lower than the result based on the test data, but also still showed acceptable predictive quality [9]. Thus, we could validate the predictivce model on an independent data set comfirming its value. The ROC curves for the training and the test data are shown in Fig. 2.

Discussion

In the face of increasingly complex intensive care interventions and an aging population, the prevention of long-term IMV is one of the great challenges in modern intensive care medicine. Our aim was to identify risk factors for long-term ventilation early after initiation of invasive mechanical ventilation. Using data from more than 7.500 inpatient hospitalisations, we identified a set of risk factors that can be assessed in the first four days after intubation. Drawing on the knowledge of a consulting multiprofessional team and a systematic literature review [8], we examined a wide range of different factors in exploratory analyses. This approach allowed us to identify multiple previously unknown risk factors, but also favourable conditions with respect to subsequent invasive long-term IMV. In contrast with the literature [2, 10, 11], age did not play a role in our anaysis. As outlined in previous studies, COPD [2, 11, 12], evidence of previous dependence on a ventilator invasive or noninvasive [2, 13], colonisation with multidrug-resistant pathogens [14] and cerebral infarction [15] were confirmed as risk factors in our study population. Other risk factors not previously described include medical history, preexisting conditions, admission diagnoses, resource prescriptions, and procedures performed within the first 96h after initiation of IMV.

Unexpectedly, nursing home accommodation immediately before hospitalisation was a prognostically favourable factor, which can best be explained by the fact that the treating intensivists performed a thorough pre-selection of these patients with regard to the general prognosis before initiating IMV. Among admission diagnoses, thyroiditis, eating disorders, rheumatic mitral valve disease and acute pancreatitis were identified as risk factors for subsequent long term IMV. In the case of thyroiditis, hypothyroidism, which often develops during the course of the disease, probably plays a role. However, both hyperthyroidism [16] and hypothyroidism [17][15] can affect respiratory function through muscle weakness. In the context of eating disorders, in addition to general cachexia-related muscle weakness, hypophosphatemia [18] may also be play a role, as indicated by a small study on the effect of serum phosphorus concentration on ventilatory weaning [19]. Rheumatic mitral valve disease is the most

common valvular heart disease [20] and can lead to heart failure via tricuspid regurgitation, which in turn is a known risk factor for long-term ventilation [20].

Pre-existing dementia and previous placement of a dialysis fistula, as well as peritonitis, cardiac arrhythmias, and pulmonary or abdominal metastases as admission diagnoses turned out to be favourable factors with respect to subsequent long-term ventilation. The association of known dementia with delirium [21] in the context of acute hospitalisation may have led to the administration of more sedative medications and, via this, to an increase in the duration of ventilation, but without requiring subsequent long-term ventilation. In the case of the above-mentioned admission diagnoses, both cardiac arrhythmias and peritonitis are causally treatable diseases, which allows termination of ventilation after successful completion of treatment. The same is true for patients with a dialysis fistula; here, the likely pathogenesis of respiratory failure is volume overload, which can be rapidly corrected. With regard to metastases and dementia, we assume a selection bias; usually, only patients with a very favourable prognosis are admitted to an intensive care unit in this situation [22].

Of the operations and procedures studied within the first 96h initiation of IMV were particularly procedures that indicate a pulmonary cause of the need for ventilation found to be risk factors, such as bronchoscopy or computed tomography of the chest. Also, the early tracheostomy, which was associated with a very high risk, is certainly an indicator that the treating physicians already suspected prolonged weaning. Patients with particularly complex prolonged ICU courses were also at increased risk for long-term ventilation, indicative of the use of Extracorporeal lung assist (ECLA) or extracorporeal membrane oxygenation (ECMO), positioning therapy, transfusion of plasma components or coagulation factors. The use of a chest tube as a further risk factor indicates either a pre-existing pulmonary condition or complications related to barotrauma or iatrogenesis [23]. In addition, procedures suggestive of leading neurological problems such as cerebral spinal surgeries, cerebrospinal fluid system surgeries, or cranial imaging were also predictors for unfavourable outcomes. In contrast, radical cervical lymphadenectomy, or autologous blood collection and transfusion, usually as part of elective surgery, showed a favourable prognosis with respect to subsequent long-term ventilation. The combination of all identified risk factors makes it possible to assess the prognosis with regard to subsequent long-term ventilation in the first days of intensive medical care with an acceptable predictive accuracy. The predictive value of this model, could be confirmed based on a subsequent validation cohort. Strengths of this model are the large number of patients, the validation in a later cohort and the 30-day follow-up.

Despite the steadily increasing number of long-term ventilated patients, the associated individual suffering and the high costs for the health care systems, there are only a few studies that have dealt with the determination of risk factors of invasive ventilation [8].

One of the largest studies on ventilatory weaning by Béduneau et al, the WIND study, provides a multicentre population of 2,729 ventilated patients and identified age, Sequential Organ Failure Assessment (SOFA) Score at admission, duration of MV before the first separation attempt and medical admissions as risk factors for weaning failure. However, the study did not aim to identify risk factors but

to describe the weaning process, according to a new operational classification [10]. Two smaller studies from China with 302 and 343 patients investigated risk factors for prolonged mechanical ventilation and weaning failure and found age > 74 years and COPD as well as Glasgow Score and $PaCO_2$ (at the beginning of the first spontaneous breathing trial) as risk factors [12, 24]. The most comprehensive study dealing with weaning failure is the study by Windisch et al. It is a retrospective analysis of a German weaning registry, here the data of 11.424 patients transferred to a specialised weaning centre were examined, the need to continue with invasive ventilation was most strongly associated with the duration mechanical ventilation prior to transfer from the ICU, a low body mass index, pre-existing neuromuscular disorders and advanced age [2].

The current WEAN SAFE study also examined factors associated with weaning failure. Demographic factors independently associated with weaning failure included older age, weakened immune system and frailty. Critical illness-related factors associated with weaning failure were severity of critical illness as measured by the SOFA score, cardiac arrest or a non-traumatic neurological event as the reason for admission to the ICU, pre-existing limitations of care, and the degree of respiratory dysfunction (respiratory rate and lower partial pressure of arterial oxygen relative to FiO_2) and ventilatory support (dynamic driving pressure and PEEP) used at the time of the first disconnection attempt. Among the potentially modifiable factors, the presence of deep sedation levels at the time of the first weaning attempt was associated with weaning failure; and the time interval between the development of weaning criteria and the first weaning attempt was independently associated with weaning failure [6]. In addition to consistent and timely implementation of weaning attempts when weaning criteria are met, we need models that allow us to identify high-risk patients as early as possible.

Limitations

The main drawback of our study includes the use of data on health care services designed for reimbursement with all the associated problems [25] as well as the fact that only data from a statutory health insurance fund was used. Data that was not available but might also be predictive is for example social support in the home setting or if outpatient specialised health support is available.

Conclusion

Despite the limitations mentioned above, based on health claims data data alone, the risk for long-term ventilation could be determined early in the ventilatory course with an acceptable prediction quality. We expect that the prediction quality can be further improved by combining the existing model with additional clinical information, such as neurological status, respirator settings, breathing mechanics, blood gas parameters and other biomarkers. Whether the application of this model is useful in clinical practice and whether it can contribute to better care for invasive patients is currently being investigated in the multicentre PRiVENT project.

Declarations

Contributors:

The PRiVENT study group:

Thoraxklinik Heidelberg:Felix Herth, Franziska Christina Trudzinski, Julia Dorothea Michels, Michael Müller, Benjamin Neetz, Gabriele Iberl, Beatrice Müller; Universitätsklinikum Heidelberg Abteilung Allgemeinmedizin & Versorgungsforschung: Martina Bentner, Elena Biehler, Thomas Fleischhhauer, Johanna Forstner, Gerhard Fuchs, Nicola Litke, Markus Qreini, Selina von Schumann, Noemi Sturm, Joachim Szecsenyi, Aline Weis, Michel Wensing; aQua: Janina Schubert-Haack, Timm Frerk, Anja Klingenberg; SLK Klinik Löwenstein: Alex Kempa, Biljana Joves, Andreas Rheinhold; RBK Schillerhöhe: Claus Neurohr, Alessandro Ghiani, Nina Lutz, Swenja Walcher, Konstantinos Tsitouras, Joanna Paderewska; Selina Briese. Waldburg-Zeil Kliniken Fachkliniken Wangen: Armin Schneider, Christoph Andritschky, Patrick Gehrig, Joachim Sugg, Susanne Hirschmann; Universitätsklinikum Heidelberg Medizinische Klinik 4 für Gastroenterologie, Infektionskrankheiten, Vergiftungen: Uta Merle; Universitätsklinikum Heidelberg Klinik für Anästhesiologie: Mascha Fiedler; SRH Kurpfalzkrankenhaus: Jens Regula; Siloah St. Trudpert Klinikum: Miriane Bomeken; Städtisches Klinikum Karlsruhe: Sebastian Stier; GRN-Klinik Schwetzingen: Jens Müller; Universitätsklinikum Mannheim Medizinische Klinik 1 Kardiologie, Angiologie, Hämostaseologie und Internistische Intensivmedizin: Simone Britsch; Universitätsklinikum Mannheim Klinik für Anästhesiologie und Operative Intensivmedizin: Jörg Krebs; Helios Klinikum Pforzheim: Ute Oltmanns; St. Josefskrankenhaus: Tom Terboven; SLK Klinikum am Gesundbrunnen: Marcus Hennersdorf; SLK Klinikum am Plattenwald: Neslihan Satir; Caritas-Krankenhaus Bad Mergentheim: Mathias Borst; Klinikum Heidenheim: Brigitte Mayer; Klinikum Crailsheim: Wolfgang Reikow; Ostalb Klinikum Aalen: Markus Kredel; St. Anna-Virngrund-Klinik Ellwangen: Konstantin Frey; Hohenloher Krankenhaus: Holger Wolff; Die Filderklinik: Florian Seidlitz; SRH Klinikum Karlsbad-Langensteinbach: Stefanie Bientzle; Zollernalb Klinikum: Boris Nohé; Robert-Bosch-Krankenhaus: Sebastian Allgäuer; Diakonie-Klinikum Stuttgart: Dr. med. Alexej Schöpp; RKU Ulm: Christoph Schlegel; Dr. Imke Hübner; Krankenhaus Landkreis Freudenstadt: Andrezj Kuzniar; Universitätsklinikum Tübingen Klinik für Anästhesie und Intensivmedizin: Helene Häberle; Universitätsklinikum Tübingen Medizinische Klinik: Reimer Riessen; Klinikum am Steinenberg: Benjamin Schempf; Klinikum Landkreis Tuttlingen: Ingo Rebenschütz; St. Elisabethen Klinikum Ravensburg: Professor Andreas Straub; Hegau-Bodensee-Klinikum Singen 1 Medizinische Klinik Singen, Kardiologie und internistische Intensivmedizin: Marc Kollum; Alb-Donau-Kreis Krankenhaus Blaubeuren: Markus Winter; Dr. Paul Hartveg; Alb-Donau-Kreis Krankenhaus Ehingen: Andreas Junginger; Oberschwabenklinik Westallgäu – Klinikum in Wangen: Dr. Helmut Beck; Universitätsklinikum Ulm: Peter Hartveg; Klinikum Friedrichshafen, Klinik für Anästhesiologie und Intensivmedizin: Mathias Vogel.

Funding: This PRiVENT study is fully funded by the Innovation Fund of the Federal Joint Committee (G-BA), grant number: 01NVF19023.

Competing interests: Joachim Szecsenyi holds stock of the aQua Institut. Other authors declare none.

Ethics approval and consent to participate: The study protocol version 1.0 was first approved by the ethics committee of the Medical Faculty Heidelberg prior to the start of the study (S-352/2018) on 18th September 2020, version 1.4. was approved on 27th April 2021. Patient consent for publication: Not required.

Trial registration number: The PRiVENT study is registered at ClinicalTrials.gov (NCT05260853).

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

This manuscript follows STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

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Figures

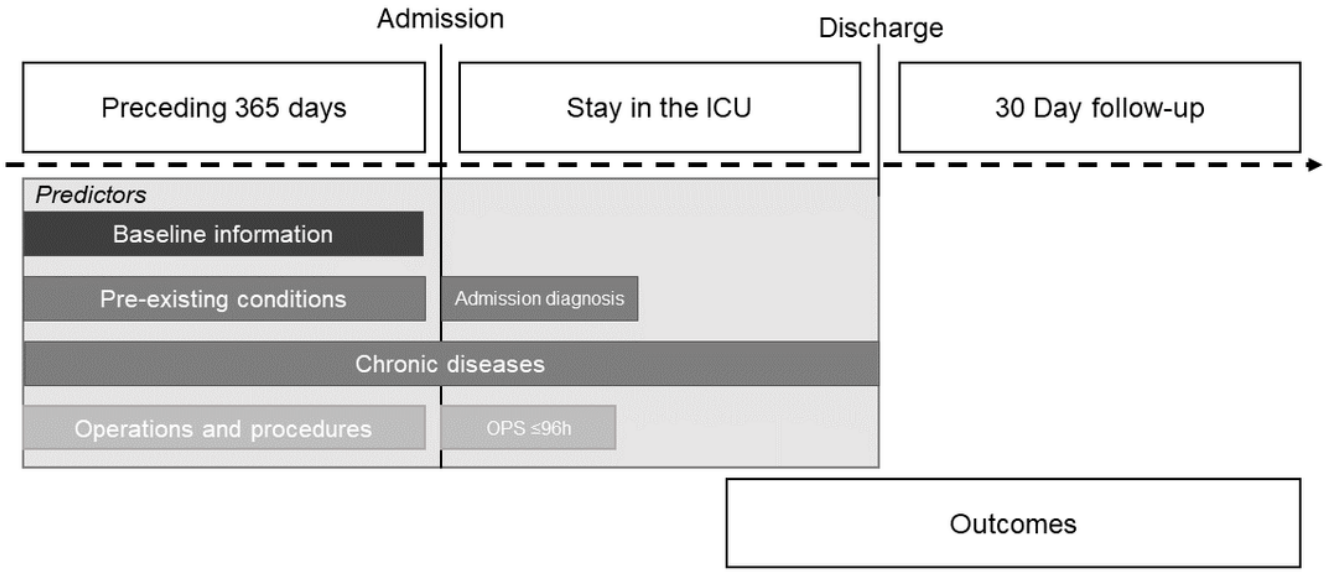

Figure 1

Overview of the time periods of predictors and outcomes

The analysis was based on data from the AOK Baden-Württemberg; patients who received IMV ≥ 96h and were discharged between 2015 and 2017 were analysed. Health claims data were considered, in each case for the previous year and 30 days after hospitalisation. Abbreviations: OPS official classification of operational procedures in Germany.

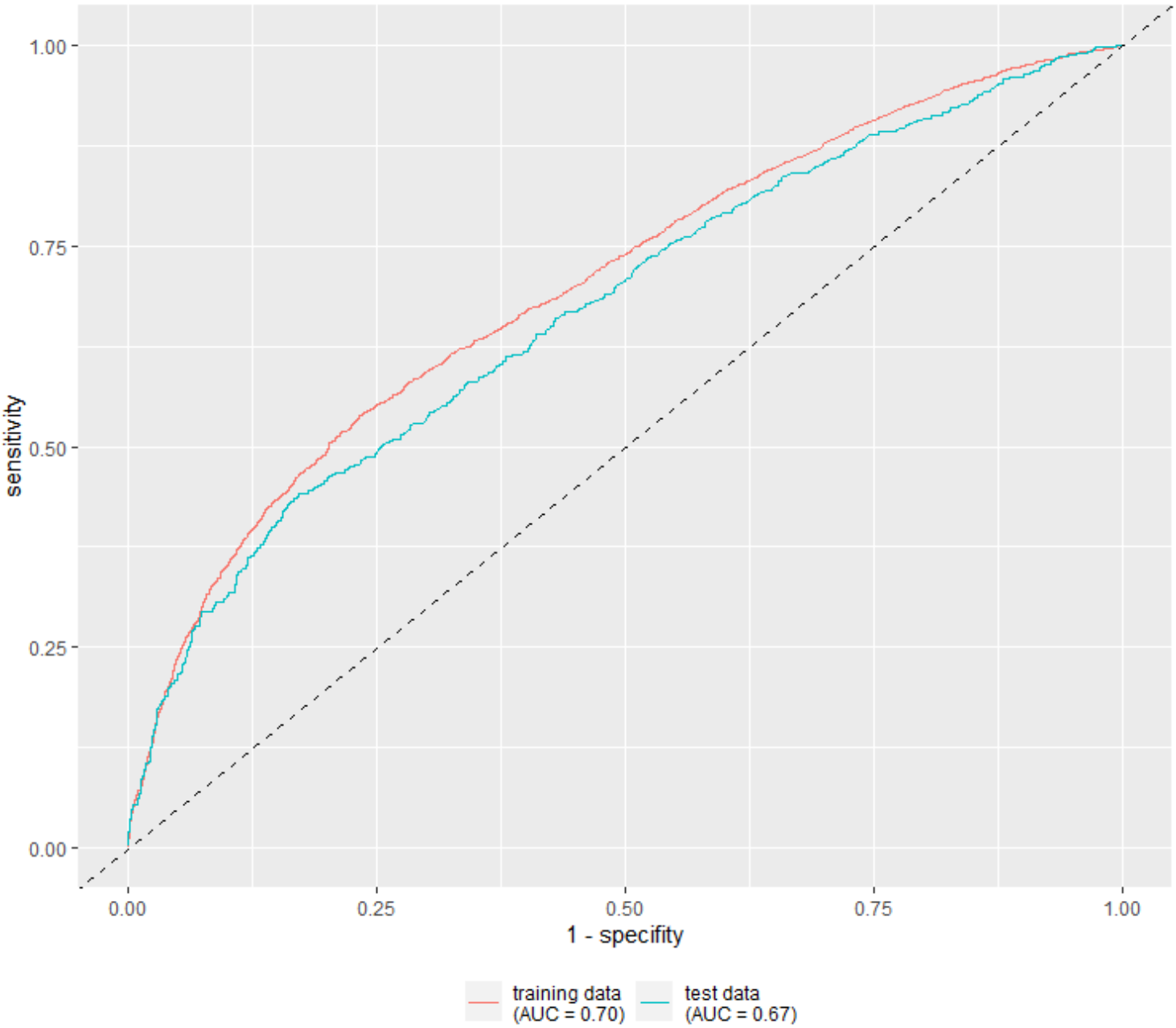

Figure 2

ROC for training and test data

The figure shows the ROC curves of the model for the training data set (red) and the test data set (blue). Abbreviations: ROC receiver operating characteristic, AUC Area Under the Curve

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STROBEchecklistRiskfactorsforlongtermIMV.doc