Instructions for Use

Pacmed Critical
Instructions for Use

English version

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1. Introduction

1.1. About Pacmed Critical

Pacmed Critical supports qualified intensive care unit medical professionals (e.g, intensivists, medical specialists) who are responsible for the care of patients and discharge processes with decision-making related to patient discharge.

The decision-support software specifically predicts the seven-day combined risk of patient readmission and mortality, at the moment of discharge to the regular ward, using historical patient data and a machine learning model. It has been developed and manufactured by Pacmed.

1.2. About these Instructions for Use

The Instructions for Use (IFU) is intended to assist users in the safe and effective use of the Pacmed Critical software product. Before attempting to use the software, users must read the IFU thoroughly, paying particular attention to all safety information, including all WARNINGS, it contains.

All users must also have received the Pacmed validated training provided by a representative allowed to give the training before using the software.

The IFU can be viewed and downloaded via a link on the user interface of the software. Versions in English and Dutch are available upon request and via the product webpage[1]. To request a hard copy of the IFU, please contact Pacmed (see 1.8 for details.). Be aware that a downloaded or hardcopy version of the IFU can become outdated: see section 1.2.1. below.

> [1] https://www.pacmed.ai/ifu

1.2.1. Updates to these Instructions for Use

The information in this IFU is subject to change without notice. If a new software version is released, the corresponding version of the IFU will be indicated. All versions of the IFU are available via Pacmed, with the corresponding software version number and publication date.

1.2.2. Paper format

Upon written request, a printed version of this IFU can be delivered at no additional cost and within 7 calendar days by sending a written request via email at support@pacmed.nl

1.2.3. About this Publication

Neither Pacmed nor anyone else involved in the development, production or delivery of the documentation can be held liable for any special, incidental or consequential damages, whether on the basis of breach of warranty, breach of contract, negligence, strict liability based on unlawful deed, or any other legal basis.

1.3. Use of the software

The software is intended to be installed and used only in accordance with the safety procedures and instructions given in this IFU and for the purpose for which it was designed, stated below in 1.3.1. However, users will at all times remain responsible for sound clinical judgement and best clinical procedure, regardless of what is stated in this IFU.

Use of this software is subject to the law in the jurisdiction of The Netherlands, the country in which it is being used. Users must only use the software product in such ways as do not conflict with applicable laws, or regulations which have the force of law.

In addition, use of the software product for purposes other than those intended and expressly stated by Pacmed, as well as incorrect use, may relieve Pacmed from all or some responsibility for resultant non-compliance, damage or injury.

1.3.1. Intended Use

Pacmed Critical is intended to support clinical decision making related to patients whose treatment includes intensive monitoring or organ support[2]. The tool predicts the probability of the patient's readmission to the department where they are receiving intensive monitoring or organ support and/or unexpected death. The predictions are intended as supplementary information that can support a user's clinical decision making and estimations about the optimal duration of intensive monitoring or organ support for a given patient.

> [2] These are patients who are typically found on the Intensive Care Unit (ICU) or Medium Care Unit (MCU). A need for intensive monitoring is defined as a need for recording of vital signs > 6 times /day. Patients on organ supportive therapy can be defined as those on: mechanical ventilation, high flow oxygen therapy, regular tracheobronchial toilet, inotropics, vasopression, extracorporeal membrane oxygenation, renal replacement therapy or sedation / anaesthetics.

1.3.2. Indications for Use

The user needs to take the predicted probability into account in clinical decision making by using the prediction into medical context. This means for example to:

- compare the probability with the average probability of readmission or mortality within the ICU where the tool is used;

- place the probability into context of other risks the user deems acceptable for the type of patient, and;

- do an assessment of the likelihood that future developments substantially change the probability.

Pacmed Critical should only be used as a complementary tool for clinical decision. The software is not intended to not replace medical expertise, hospital protocols, and any other relevant process.

1.3.3. Intended User

The intended users are qualified medical professionals (e.g. intensivists, nurses or other medical specialists) who are responsible for the care of patients who need intensive monitoring or organ support.

1.3.4. Intended Patient

Patients aged 18 years or older whose treatment has included intensive monitoring or organ support.

1.3.5. Intended Environment

Pacmed Critical shall be used in the hospital clinical settings where patients need intensive monitoring or organ support, this is typically the ICU.

1.3.6. Contraindications

Pacmed Critical is not intended for patients under 18 years. The device is not intended for patients admitted within less than 12 hours in the ICU and for patients who are not deemed eligible for discharge.

1.4. Clinical benefit

Pacmed Critical aims to improve patient outcomes by supporting clinicians to decide on the optimal timing of discharge for patients whose treatment includes intensive monitoring or organ support. Specifically it provides decision support to help clinicians either reduce the length of stay, or reduce patient readmission or mortality after discharge.

Pacmed Critical also improves clinicians' workflows by providing them with an effective overview of patients on the ICU.

1.5. Compatibility

Changes and/or additions to the software product should only be carried out by Pacmed. Such changes and/or additions must comply with all applicable laws and regulations which have the force of law within the jurisdictions concerned, and with best engineering practice.

1.6 Compliance

This software complies with relevant international and national standards, regulations and laws. Information on compliance will be supplied on request by your Pacmed representative (see 5.4).

1.7. Symbols Glossary

The following symbols may appear in the IFU and/or in the user interface:

Symbol	Symbol name	Symbol description
	Manufacturer	Indicates the name and address of the manufacturer of the software.
	Date of manufacture	Indicates the date that the version of the software was released.
LOT	Batch code	Indicates the version number of the software.
	Consult Instructions for Use	Indicates when the user must consult the Instructions for Use.
	Warning	Warnings are directions which when not followed could cause injury to the user, patient or other user, or could lead to clinical misdiagnosis.

		The presence of the symbol in the user interface indicates that the user must consult the IFU for an important warning related to the use of the software which cannot be displayed in the user interface itself.
CE	CE-mark	Pacmed Critical is CE certified under the European Medical Device Regulation (MDR)
MD	Medical Device (MD)	Indicates that it is a Medical Device
UDI	Unique Device Identifier (UDI)	The UDI is a globally harmonized, unique (alpha) numeric code used to identify the medical device. The UDI consists of a UDI-DI (Device Identifier) and a UDI-PI (Product identifier). The UDI-PI corresponds to the software version number.

1.8. Contact Information

	Pacmed Critical has been developed and produced by Pacmed B.V., Stadhouderskade 55 1072 AB, Amsterdam, Netherlands. For further information, please contact Pacmed: Website: https://pacmed.ai/ Email: support@pacmed.nl

Users can also contact the support desk by using the 'Feedback' button.

2. Safety

Before using this software, you must have read and understood all instructions and have followed the training to ensure safe and correct use. Be aware of the below warnings and specifications regarding the intended use, as stated in 1.3.

Negligence with regards to the safeguards found under 2 and 2.1 implies the risk of misuse of Pacmed Critical, with the risk of incorrect use and wrong interpretation of the results, possibly leading to safety risks for patients.

2.1. Important Safety Warnings

⚠	**WARNING:** The software product is not intended for use on mobile devices (tablets or mobile phones).

⚠	**WARNING:** The software product is not intended for the discharge of patients from the Intensive Care Unit to the Medium Care Unit.
⚠	**WARNING:** Pacmed Critical should only be used as a complementary tool for clinical decision making. The software is not intended to replace medical expertise, hospital protocols, and any other relevant process.
⚠	**WARNING:** The software tool is an extra source of information in the decision-making process for discharge of a patient to a step-down unit (e.g. general ward). It is not intended to be used for discharges of a patient from the ICU to the medium care unit. The software must never be used without consideration of all clinical, operational and any other patient information.
⚠	**WARNING:** The software shall not be used for treating and improving only one single feature that has a big impact on the prediction, with the sole purpose of decreasing the prediction probability.
⚠	**WARNING:** The software tool presents a seven-day readmission/mortality risk, displayed as a percentage. This represents a combined probability and must also be interpreted as such.
⚠	**WARNING:** The software must only be used for patients who are eligible for discharge. The predictions are unreliable for patients who, because of dependency on certain ICU-specific support or treatment cannot be discharged. The software therefore does not provide a prediction for these specific patients.
⚠	**WARNING:** The machine-learning model is trained on historical data and thus it depends on the patient population and hospital practices at the time of model training. Be aware that significant changes in the patient population and/or hospital practice may affect the performance of Pacmed Critical. It is advised not to rely only on the information regarding the risk of readmission/mortality displayed by Pacmed Critical.
⚠	**WARNING:** The readmission/mortality risk is a prediction made by a statistical model based on patient-, lab- and monitoring device data. Since this is a prediction, it is not 100% accurate and therefore a decision must never be made solely based on the readmission/mortality risk displayed.
⚠	**WARNING:** The software uses patient, lab and equipment data (see chapter 3 for further information). It does not currently use any information on medication, radiology diagnostic test results, surgery details and patient data from prior to admission (e.g. APACHE IV score).

⚠	**WARNING:** For each prediction the software shows the features that had the biggest impact on the prediction for an individual patient. These factors are calculated for the most recent prediction of this patient. During the admission of the patient the list with the most predictive features for an individual patient will change constantly. The predictive features which increase or decrease the readmission/mortality risk are displayed for individual patients in the software.
⚠	**WARNING:** The organ support specifications are more comprehensive than displayed in the software. The software only shows whether there is a form of support for any of the three organ systems and does not specify the type of support. Users must take this into account during interpretation and use in collaboration with local used Electronic Patient Database (EPD).
⚠	**WARNING:** The software shows the following information from the EPD per patient: bed number, name, patient number, date of birth, admission specialty and is therefore dependent on this information from the EPD.
⚠	**WARNING:** The software is developed for an adult patient population (aged 18 years old or older) only.
⚠	**WARNING:** The software is developed on patients that were discharged from ICU to the general ward (not to medium care unit), excluding: palliative care patients, patients with a 'Do Not Resuscitate/Intubate' order, patients that died during the ICU admission or transfers to the ICU of another hospital.
⚠	**WARNING:** The software may be used remotely by a qualified physician but only in consultation with another physician who is present in the ICU.

3. Product description

3.1. Model Introduction

Pacmed Critical is a software system that supports the decision to discharge patients from the Intensive Care Unit (ICU) to the general ward at the right time.

The method has been developed by a team of intensivists from Amsterdam UMC, location VUMC in collaboration with statisticians and machine-learning experts from Pacmed.[4]

The model is defined by learning from historical hospital data. After its definition, when it is meant to be used on a single patient, the model does not require further analysis on historical hospital data, only the data gathered about the patient under consideration is needed.

Patients with a 'Do Not Resuscitate/Intubate' order have been excluded from the data. As well as patients that died during the ICU admission or that were transferred to the ICU of another hospital.

The model employed in a version of Pacmed Critical used in a specific hospital is developed only with data of that specific hospital. No model is trained on a combination of data from multiple hospitals.

Periodic retraining of the model is done on the available dataset of that hospital, see paragraph 3.3.1 on the input data.

The software predicts the probability of readmission to the ICU or death of an ICU patient within seven days after discharge to the general ward, would this patient have been discharged at this moment. The software also presents the historical evolution of this probability during the patient's admission at the ICU (up to a maximum of 30 days) and shows the patient attributes ('predictors' or 'features') which are most important for the prediction according to the model.

The software predictions are continuously updated, and at least every 60 minutes. The model can provide the first prediction for an individual patient as soon as the patient has been admitted for at least 12 hours at the ICU. In certain conditions the model cannot provide a reliable prediction. When this happens, the software does not show a prediction. See **Appendix A** for further specification of these conditions.

> [4] An academic paper on the prediction model has been published in a peer-reviewed journal: Thoral, P.J. et al., Explainable Machine Learning on the AmsterdamUMCdb for ICU discharge decision support: uniting intensivists and data scientists . *Crit Care Exp 2021 Sep 10;3(9):e0529. doi: 10.1097/CCE.0000000000000529. PMID: 34589713; PMCID: PMC8437217*. Text available from: https://pubmed.ncbi.nlm.nih.gov/34589713/

3.2. Composition of the Outcome: Readmission/Mortality Risk

Since in literature readmission and mortality are both clearly defined as undesirable outcomes of a discharge[5], a negative outcome of the discharge is defined as either:

- ICU readmission within seven days after ICU discharge, which is defined as a transfer from the ICU to the general ward and back to the ICU or MCU during the same hospital stay

or

- Death within seven days after ICU discharge.

Important to note here is that patients with a 'Do not resuscitate/intubate' order have been excluded from the data. Also, patients that have died during the ICU stay, or patients transferred to another hospital are excluded from the data, as well as admissions that end with a discharge to the MCU.

Similarly, a positive outcome of the discharge is defined as no readmission or death within seven days after discharge to the general ward.

The model predicts the probability of a negative outcome if a patient would have been discharged right now. In consultation with medical experts, the choice has been made to not separately show the risk of readmission and the risk of mortality, but only the probability of the combination of both negative events happening. This is done to prevent an overload of information for the intensivist. Presenting a single risk of the combined negative outcome is hypothesised to improve comprehension, interpretability and thus added value for decision-making. Last, separately modelling the readmission risk from the mortality risk did not increase predictive performance of the model.

> [5] Hosein et al. 2013. A systematic review of tools for predicting severe adverse events following patient discharge from intensive care units. Critical Care. 17

3.3. Creating Predictive Features

The definition of a 'predictor' or 'feature' in this Instructions for Use is: a quantified aggregate (or summary statistic) of a value belonging to a patient, in a specific way over a specific time interval (e.g. the mean of heart rate over the first 24 hours of the ICU admission). Predictive features are used by the model to compute the prediction of readmission or mortality after discharge.

3.3.1. Input Data

In order to generate a prediction, the model uses data stored in the EPD. The software uses the following types of information:

- Patient information
- Admission information
- Laboratory test results
- Vital signs and device data
- Clinical Observations
- Lines, Drains and Airways (LDA); tube / tracheostoma and CVVH registration

Inter-hospital variability may cause slight changes when certain inputs are not available or when additional relevant input is available within these categories. See **Appendix A** for all inputs used for the model.

3.3.2. Validated Data

In order to create the features and do the prediction, the software only uses measurements that have been validated. Measurements that are not yet validated will not be used in the prediction. An example.

- A pH value is measured at 10:45h and not yet validated.
- At 11:00 the model makes a prediction for timestamp 11:00h using all validated data measured before 11:00h. The pH value of 10:45h will not be used at that point because it is not validated. However, any pH measurement measured and validated earlier that morning will be used.

- At 11:30h, the pH value measured at 10:45h is validated.

- Now the model will update the prediction of timestamp 11:00h, since now that prediction is allowed to use the pH value measured at 10:45h.

Because of this reason, predictions of Pacmed Critical can be updated retrospectively, when new validated data becomes available. For the user this means that the shown prediction might be different compared to an earlier moment. Therefore, when recently measured lab values or vital signs are about to be validated with values being substantially different from previously validated values, the user should consider re-evaluating the decision by reinspecting Pacmed Critical's prediction at a later point.

3.3.3. Composition of the Predictive Features

Patient values like lab values, vital signals and clinical observations are usually measured and/or registered multiple times during the stay. These values therefore have to be transformed into predictive features by creating so-called summary statistics. Per feature, together with medical experts a small set of summary statistics was selected which were deemed most clinically intuitive and predictive. In the current version of Pacmed Critical, most summary statistics are the average (or minimum or maximum) value over the last 24 hours, or the last measured value.

The model will impute the missing values with a parameter-specific, clinically sensible, value, e.g. the mean from the whole population or the last measured value.

Per type of feature, the statistics that are calculated and imputation techniques are shown in **Appendix C**.

This process yields a list of predictive features, validated by medical experts, that are included in the model. These selected features are used by the model to predict the risk of readmission or mortality after discharge to the general ward. In **Appendix C**, we list the full list of features that are selected by the prediction for model VUMC.

3.4. Creating the Prediction Model

The best predictive model for this application is a frequently used method in Machine Learning applications; an (Extreme) Gradient Boosted Trees model. This is a technique based on the creation of decision trees, which classifies patients according to their characteristics into high- or low-risk groups. In Figure 1 a simplified example of such a decision tree is shown. Note that the numbers shown in the example are fictitious.

The difference with traditional decision trees is that with Gradient Boosting, after every decision tree the patients that are predicted incorrectly by the model are modelled again in separate decision trees. As a consequence, more subtle (non-linear) effects can be modelled than with traditional methods like Logistic Regression or Proportional Hazard models. Gradient Boosting models therefore tend to outperform traditional techniques in terms of accuracy.
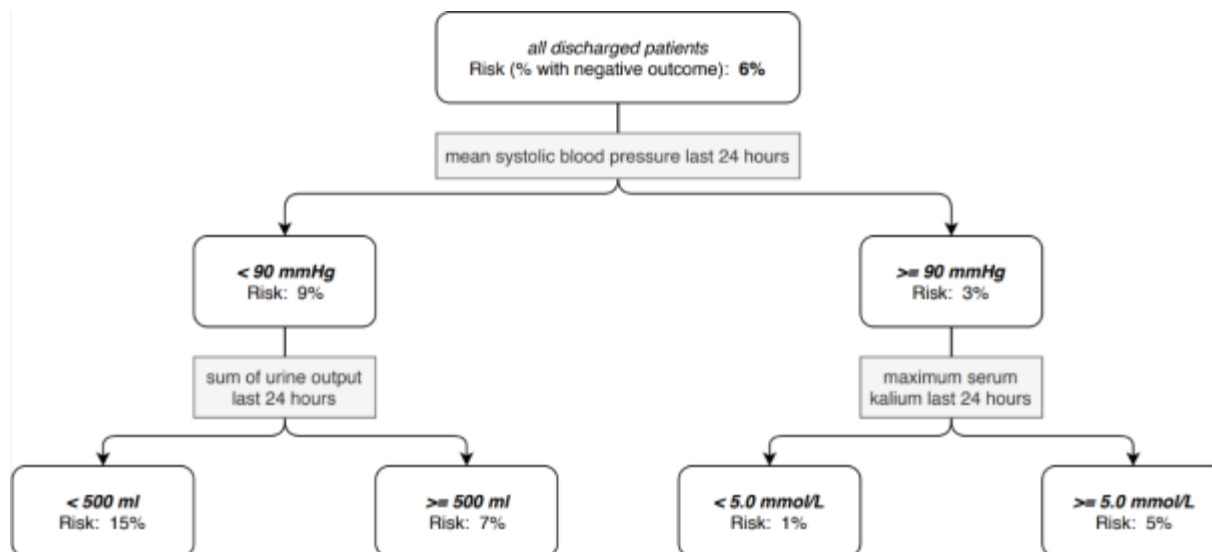
Figure 1: Simplified example of a decision-tree model

3.5. Model Performance

The performance of the model (i.e. a way to quantify how good the model is in discriminating successful ICU discharges by those followed by adverse events) is determined by cross-validation. This means that the model is trained iteratively on a subset of patients and then tested on the data from the remaining patients that the model has not yet 'seen'. This is done multiple times so that each patient is part of the test set once.

3.5.1. Area under the ROC-curve (AUC)

See **Appendix A** for the model accuracy. The model typically predicts a probability of readmission and/or mortality between 0% and 50%. A readmission/mortality probability of 8% signifies that the model expects that out of 100 patients with a similar profile who are discharged from the ICU, eight of them will be re-admitted or will die within seven days. It almost never happens that the model indicates a probability of adverse outcome higher than 50%. The user should remember that the average readmission/mortality probabilities are between 5% and 10%,% so that values do not need to be close to 100% to indicate high risk. Compared to the average readmission/mortality probability of 6%, a prediction of 12% already indicates an increased risk of negative outcome.

3.6. Creating Feature 'Importances'

Besides the risk of a negative outcome, the software presents the ten patient features that are most important for the risk prediction. This is done by calculating SHAP (Shapley Additive Explanations) values[6]. After the model is created, the SHAP calculates for each feature separately, what would have been the predicted risk if we would remove this feature from the model.

After the model is created, the SHAP algorithm associates to each feature of each patient a number (called the SHAP value). Such a number indicates how much the measured value of that specific feature contributes to the predicted readmission/mortality probability of that patient. The higher the SHAP value, the more that value for that feature increases the readmission/mortality probability and vice versa. In this way, it is possible to identify the features that are most predictive because they correspond to the ones with the higher or lower SHAP values.

Important to note is that if a feature is considered important according to this method, this does definitely not mean that a feature is causally related with readmission or mortality. It only tells us that in the historic database, this feature correlates with the risk of readmission or mortality after discharge. Therefore, this information should not be used for treatment decisions.

> [6] Lundberg S.M. and Lee, S. 2017. A Unified Approach to Interpreting Model Predictions [Online]. Available from: http://papers.nips.cc/paper/7062-a-unified-approach-to-interpreting-model-predictions

4. User instructions

4.1. Getting Started

In order to start using the software, the user needs to login to the hospital-specific network/domain. Most hospitals will require the use of a Microsoft account to do so. Once logged in, the user can visit a URL (provided by the hospital's ICT department) to start using the software. This URL is domain-specific and cannot be used by other people outside of the hospital's virtual environment.

Some hospitals may support remote access to the hospital's network, for example by means of a VPN connection. In this case the software can be used remotely, but still only by people with access to the network and authorised to use the software, and only in consultation with another physician who is present in the ICU.

Hospitals may choose to implement access to Pacmed Critical in the embedded browser view in the EHR system. Authentication in this case is done using Single Sign-On, so this requires the user to be logged in in the EHR to get access.

When logged in to the hospitals' network, the user should lock their device(s) at all times when leaving it unattended. Unauthorized users may get access to sensitive data if they fail to do so.

Log-in screen: in case the login information is forgotten, depending on the hospital configuration, a new login can be requested.

4.2. Department Monitor

An overview of all patients currently in the Intensive Care (IC) is displayed in the Department Monitor. In **Appendix B** an example of the Department Monitor user interface is shown, including an explanation of all elements shown.

Note on cursor: when navigating around the interface, the user's cursor will change from a standard pointer ➚ to a gloved hand ☝. This indicates that that element is clickable. Additional information may also be displayed when the user hovers their cursor over other elements.

4.3. Patient Detail screen

The Patient Detail screen displays additional information for an individual patient. This concerns the evolution of the predicted risk during admission and the 10 predictors that have the most impact on the most recent prediction for the readmission/mortality risk. In **Appendix B** an example of the Patient Detail screen is shown, including an explanation of all elements shown.

4.4. Error Messages

The user interface displays an error message when something goes wrong.

When this error message is displayed, a technical problem has occurred. The user is advised to wait a few minutes before refreshing the user interface to see if the problem has been solved in the meantime. When this is not the case, the user should contact Pacmed for support (see 1.8 for Contact Information).

5. Technical Specifications, Maintenance and Support

5.1. Software Installation and Removal

The software will be installed by Pacmed. If your department would no longer like to use the software, contact the Pacmed support team who will arrange uninstallation, taking care to remove any residual patient data, in line with agreements made and applicable laws and regulations.

5.2. Software Updates

Updates for this Pacmed software product can become available. Such updates are essential to keep the software product operating safely, effectively, and reliably. These can include security patches, updates of the model or general improvements. Pacmed will send release notes to a hospital contact person at least one day prior to releasing an update. The process surrounding delivery and installation of software updates is described in more detail in the Service Level Agreement. Please contact your functional administrator, key-user or the hospital project leader for more information, or contact support@pacmed.nl.

5.3. Technical Specifications

- Pacmed Critical has been developed to be used on screens with resolutions greater than 1440 x 900 (WXGA+)
- Pacmed Critical can not be used on mobile devices (tablets and mobile phones)
- Pacmed Critical and its IFU (in pdf format) can be used in the following browsers:
    - Microsoft Edge, all versions
    - Google Chrome, all versions
    - Mozilla Firefox, all versions

5.4. Support

Contact the Pacmed support desk to report any problems encountered with the software. You can contact Pacmed directly from the Interface (see 4.2) or use contact information provided in section 1.8.

In the unlikely case of any serious incident related to the use of the software tool, Pacmed will take all necessary follow-up actions as required by law.

Any serious incident that has occurred in relation to Pacmed Critical should be reported to Pacmed and the Ministry of Health, wellbeing and sports[7].

[7] medicaldevices@minvws.nl

5.5. Network Safety, Security and Privacy

Patient data used for Pacmed Critical is stored in the Cloud. Agreements on the type of data, security and more are covered by the Data Processing Agreement.

The software is only exposed within the hospital's network. The software is not exposed on the public internet. If a user is allowed to login from a remote location using VPN, then that user can use the software from outside the hospital but only in collaboration with another qualified physician actually present in the ICU at the moment of use.

It is advised that the workstations that the device is used on adhere to the following:

- Proper antivirus software (The device does not provide protection against viruses, malware, or any other threat)

- To optimize performance, it is recommended that the workstations are not used for multimedia purposes like gaming, music, video, and so forth.

- The device runs in a web browser. See section 5.3 for supported browsers and the minimal screen resolution for proper display of the device. Ensure that the software is not made available on systems that don't adhere to these requirements.

- The requirements for the virtual hardware of the application are validated by Pacmed during the installation. The hospital shall ensure that the workstations have sufficient resources to run a modern web browser.

This application is solely to be used within the internal (virtual) networks of the hospital. Do not enable outside traffic to access the application. If a user is allowed to login from a remote location using VPN, then that user can use the software from outside the hospital but only in collaboration with another qualified physician actually present in the ICU at the moment of use.

Risks of using the device outside the hospital environment include, but are not limited to:

- Information security risks: making Pacmed Critical available to the public internet exposes it to additional cybersecurity threats.

- Misuse of the device: lowering the barrier for access to the device increases the risk that untrained personnel access the device

- Data privacy: lowering the barrier for access to the device increases the risk that unauthorized people access the device (for instance when it is left unguarded in a public space).

The device is hosted by Pacmed and runs in the cloud

- A copy of the clinical data is stored in Pacmed's cloud environment. Pacmed does not keep another backup of this copy of the data. In case of failure, the data will be extracted again from the hospital's data source.

- Pacmed is responsible for patch management on the cloud systems and the device itself. Maintenance windows are specified in the Service Level Agreement.

- Containerized deployment of the device adds an additional layer of security.

- The security of the device has been assessed by means of a penetration test.

- The hospital network and Pacmed's cloud environment are connected by means of a secure site-to-site VPN. The hospital IT department will set up this VPN connection together with Pacmed.

The device implements state of the art token-based access control. User management is performed by Pacmed. Only trained personnel will be able to access the device. Only authorised Pacmed users are granted admin access to the device.

The device has been integrated with the hospital IT systems to:

- Enable easy access to the device. Optionally hospitals integrated the device in their EHR/PDMS systems. If such an integration has been set up, it has been validated during the installation by means of an acceptance test.

- Ensure the availability of recent clinical data. Pacmed has implemented monitoring systems to monitor the validity of the source data. The correctness of the source data in the hospital's data systems remains the responsibility of the hospital.

Appendix A – Model information VUmc

Input data

EHRS used for model development:	MetaVision, Epic
Period covered by the data:	01/01/2004 - - 01/10/2022
Number of admissions included in the dataset:	16027

Model performance

The model has an accuracy (measured in Area under the Receiver Operating Characteristic Curve (AUC)) of 0.77 when tested over the whole history using cross validation. This is comparable with with existing reference studies[8] and significantly higher than existing 'predictors' such as the SWIFT and SOFA scores. The model is also specifically tested for the last 12 months of admissions in the training data. In this period, the AUC is 0.72.

> [8] Gajic et al. 2008: AUC 0.75; Desautels et al. 2017: AUC 0.71; Jamei et al. 2017: AUC 0.78; Jo et al. 2015: AUC 0.76; Ouanes et al. 2012: AUC 0.74; Reini et al. 2012: AUC 0.80; Badawi et al. 2012: AUC 0.72; Frost et al. 2010: AUC 0.66; Campbell et al. 2008: AUC 0.74. See **Appendix D** for complete reference list.

Categories excluded from predictions

- Length of stay less than 12 hours
- Age < 18 years
- Renal support (CVVH(D), Continuous Veno-Venous Hemodialysis)
- Cardiovascular support
- Respiratory support in the past 2 hours, specifically:
    - Intubation
    - More than 8 l/min of oxygen
    - Oxygen administered via a non-rebreather mask
- When the patient's data differs greatly from patients in the training data. An 'out-of-domain-detection' model is used for this.

Organ support indicators

Respiratory support

The lung icon will be displayed in bold if the patient is dependent on any of the following support or treatment:

Presence in the last 2 hours of:

- Mechanical ventilation (intubation or tracheostomy)
- Oxygen administration > 8 L/min,

- Oxygen administration via non-rebreather mask

Presence in the last 8 hours of:

- Non-invasive ventilation

- Tracheobroncheal toilet > 2 times

Cardiovascular support

The heart icon will be displayed in bold if the patient is dependent on inotropy or vasopressors in the last 2 hours:

- (Nor)adrenaline

- Dobutamine

- Dopamine

- Enoximone (Perfan)

Renal support

The kidney icon will be displayed in bold if the patient has been dependent on CVVH(D) in the last 2 hours

Appendix B – Software user interface information

Department monitor

1. **Bednr.**
   The patient's bed number is shown here. The patients can be sorted by bed number by clicking on 'bednr.' or the arrow next to 'bednr.'.

2. **Patiëntgegevens**
   Here the identifying patient data is displayed. Specifically name, gender, age, MRN number and the admission duration.

3. **Heropname/mortaliteitsrisico**
   Here the probability of readmission or mortality within 7 days is shown if the patient were to be discharged to the ward right now. Patients can be sorted by risk by clicking on 'heropname/mortaliteitsrisico' or the arrow next to 'heropname/mortaliteitsrisico'.

4. **Ondersteuning**
   The lung, heart, and kidney icons show whether the patient is receiving organ support. When exactly an icon lights up, is specified in appendix A.

5. **Geen voorspelling**
   When a patient is not considered ready for discharge, due to specific support, or when the patient's data appears unreliable, no prediction is shown (displayed with "-"). When exactly this exactly happens is specified in appendix A.

6. **Toon enkel patiënten met voorspelling**
   If this checkbox is selected, only the patients for whom a prediction can be shown are displayed.

7. **Meer patiënten**
   If the screen is zoomed in so far that not all patients are visible, this button can be clicked to display the other patients as well.

8. **Handleiding**
   The instructions for use can be downloaded as a PDF by clicking on 'handleiding'.

9. **Label**
   The product label can be shown by clicking 'Label'.

10. **Feedback**
    Feedback on the use of the software, complaints, problems, questions, suggestions for improvements and compliments, can be given to Pacmed by filling in the feedback form

11. **Verander wachtwoord**
    The password can be changed by clicking on 'Verander wachtwoord'.

12. **Log uit**
    The user can log out by clicking on 'Log uit'.

13. **Version number**
    The version number of the software is visible on the top left part of the screen.

Patient Detail Screen
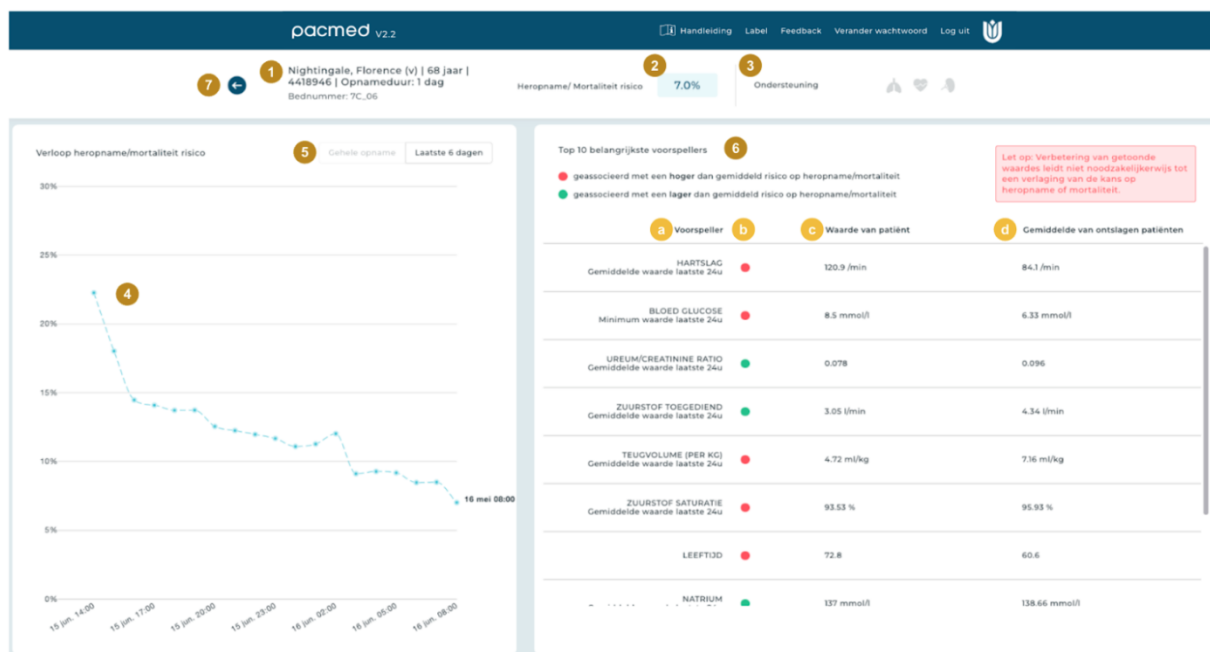
1. **Patiëntgegevens**
   Here the identifying patient data is displayed. Specifically name, gender, age, MRN number and the admission duration.

2. **Heropname/mortaliteitsrisico**
   Here the probability of readmission or mortality within 7 days is shown if the patient were to be discharged to the ward right now.

3. **Ondersteuning**
   The lung, heart, and kidney icons show whether the patient is receiving organ support. When exactly an icon lights up, is specified in appendix A.

4. **Graph**
   The graph shows the evolution of the patient's readmission/mortality risk during admission. No prediction is shown for times when the patient did not appear to be ready for discharge. The x-axis shows the date and time, the y-axis shows the predicted risk. If the mouse is hovered over a dot, the exact percentage and time of the prediction is displayed. The time of the last prediction is displayed to the right of the graph.

5. **Gehele opname / laatste 6 dagen**
   By default, the chart does not show predictions made more than 6 days ago. The user can see predictions for the entire admission by clicking on 'Gehele opname'.

6. **Table**
   The right side of the screen shows the predictors that had the most impact on this patient's

prediction. The table is sorted by importance, the predictors with the greatest impact are at the top. The text in the red box warns the user that there is no causality here; medical intervention merely to improve the values of the predictors does not necessarily lead to a reduction in the risk of readmission or mortality

   a. **Voorspeller**
   For the 10 most important predictors the name of the parameter is shown (e.g. heart rate) and the aggregation used is shown (e.g. average last 24 hours).

   b. **Red/green dot**
   A red or green dot shows whether the predictor value for this patient is associated with an increase (red) or decrease (green) in the risk of readmission or mortality.

   c. **Waarde van patiënt**
   This shows the exact value of the predictor used in the most recent prediction for this patient.

   d. **Gemiddelde van ontslagen patiënten**
   As a reference number, the average value that this predictor had at the time of discharge, for the discharged patients in the historical data.

7. **Back arrow**
   Clicking on the arrow will lead to returning to the department monitor.

Error message

Example of the error message

Er ging iets mis, er werd geen data ontvangen. Probeer het later opnieuw.

Login screen

Example of the login screen

pacmed

Vul onderstaande gegevens in om in te loggen

Gebruikersnaam / e-mailadres

Wachtwoord

Inloggen

Appendix C – Feature list VUmc

The features below are used by the prediction model

Variable	Aggregate	First Imputation technique[9]	Second Imputation technique
activated partial thromboplastin time	average last 24 hours	last measured value	impute with 35
age			
alanine transaminase	average last 24 hours	last measured value	impute with 45

albumin	average last 24 hours	last measured value	
alkaline phosphatase	average last 24 hours	last measured value	impute with 80
amylase	average last 24 hours	last measured value	impute with 107
arterial blood pressure diastolic	average last 24 hours	last measured value	
arterial blood pressure diastolic	trend (delta per hour) last 24 hours		
arterial blood pressure systolic	average last 24 hours	last measured value	
aspartate transaminase	average last 24 hours	last measured value	impute with 35
base excess	average last 24 hours	last measured value	
bicarbonate arterial	average last 24 hours	last measured value	
bilirubin total	average last 24 hours	last measured value	impute with 10
body mass index	average last 24 hours	last measured value	
c reactive protein	average last 24 hours	last measured value	impute with 4
c reactive protein	trend (delta per hour) last 24 hours		
calcium ionised	average last 24 hours	last measured value	
cardiac output	highest last 24 hrs	last measured value	
cardiac output	lowest value last 24 hrs	last measured value	
cardiac output	measured last 24 hrs?		
chloride	average last 24 hours	last measured value	
cough stimulus ('absent'/ 'normal' / 'reasonable' / 'weak')	most frequent in last 24 hours		
creatinine kinase mb mass	is it measured in the last 24 hours?		
creatinine	last measurement (max 4 days old)		

fio2	average of last 24 hours	impute with 21	
fluid out urine	total volume last 24 hrs	impute with 0	
gamma glutamyl transferase	average of last 24 hours	last measured value	impute with 55
glasgow coma scale total	highest value last 24 hrs	impute with 15	
glasgow coma scale total	lowest value last 24 hrs	impute with 15	
glucose	lowest value last 24 hrs	last measured value	
heart rate	average of last 24 hours	last measured value	
heart rate	trend (delta per hour) last 24 hours		
haemoglobin	average of last 24 hours	last measured value	
lactate dehydrogenase	average of last 24 hours	last measured value	impute with 248
lactate unspecified	last measurement	impute with 1.1	
length of stay in hours			
leukocytes	average of last 24 hours	last measured value	impute with 10
magnesium	average of last 24 hours	last measured value	impute with 0.85
neutrophils	average of last 24 hours	last measured value	impute with 4
o2 flow	average of last 24 hours	impute with 0	
o2 flow	trend (delta per hour) last 24 hours		
o2 saturation	average of last 24 hours	last measured value	
o2 saturation	trend (delta per hour) last 24 hours		
pao2 over fio2	last measurement	last measured value	
pco2 arterial	average last 24 hours	last measured value	
peep	maximum last 24 hours	last measured value	impute with 0

ph arterial	last measurement	last measured value	
phosphate	average last 24 hours	last measured value	
potassium	average last 24 hours	last measured value	impute with 4
prothrombin time (INR)	average last 24 hours	last measured value	
Absolute difference between left and right pupil diameter	average last 24 hours	last measured value	
Maximum of left and right pupil diameter	average last 24 hours	last measured value	
respiratory rate measured	last measurement	last measured value	
richmond agitation sedation scale score	highest last 24 hrs	last measured value	impute with 0
richmond agitation sedation scale score	lowest last 24 hrs	last measured value	impute with 0
sex (male)			
sex (female)			
sodium	average last 24 hours	last measured value	impute with 141
temperature blood	average last 24 hours	last measured value	
temperature internal	highest value last 24 hours	last measured value	
temperature internal	lowest value last 24 hours	last measured value	
temperature skin	average last 24 hours	last measured value	
temperature skin	trend (delta per hour) last 24 hours		
thrombocytes	average last 24 hours	last measured value	
tidal volume per kg	average last 24 hours	last measured value	

tracheobronchial toilet	number of times last 24 hrs	impute with 0	
troponin t	measured last 24 hours		
troponin t	highest last 24 hours	impute with 14	
ureum	average last 24 hours	last measured value	
ureum over creatinine	average last 24 hours	last measured value	

[9] If the imputation technique is "last measured value", we use the last available value in an amount of hours prior to the moment of prediction, up to a maximum of 4 days old. If we do not find one, a second imputation technique is used.
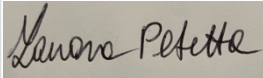
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Audit trail

Document version	Change description	Author	Change date
01	initial release - IFU VUmc	Brian Tielrooij	2024/01/03

signatures

Signature Meaning	Name	Title	Date	Signature
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Reviewer	Leon Derks	Technical Product Manager	2024/01/03 17:25:37	**sign-p22-i12107-b20240103162537927**
Approver	Tamara Petetta	Regulatory Affairs Manager	2024/01/03 17:19:04	**sign-p22-i12107-b20240103161904643**