Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺)

– An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Study Protocol

Version and Date: v.2.9-GENERAL dated 06 February 2024

Registry Identifier: DRKS00033262

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on behalf of the PROVEnet investigators

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Protocol signature page

The undersigned has received, read, and understood the PRoVENT 2+ study protocol in its version in force at the time of signature. The undersigned agreed to conduct this study in strict accordance with all stipulations of the protocol as well as in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice.

Chief investigator: Martin Scharffenberg

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(Place, date, signature)

Senior investigator: Marcelo Gama de Abreu

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(Place, date, signature)

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Role: ◯ SC member; ◯ National PI; ◯ Local PI; ◯ Investigator; ◯ Section coordinator

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(Name)

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(Local study centre)

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(Place, date, signature)

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Synopsis

Chief investigator / Senior investigator	Dr. med. Martin Scharffenberg / Prof. Dr. med. Marcelo Gama de Abreu
Title	Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet
Short title	PRoVENT 2⁺
Protocol version	V2.9-GENERAL
Registry identifier	DRKS00033262
Background and rationale	Mechanical ventilation (MV) is often life-saving, but may result in ventilator-induced lung injury (VILI), distal organ damage and death. Evidence about the current practice of MV in patients admitted to the intensive care unit (ICU), especially those without acute respiratory distress syndrome (ARDS), remains limited. Since the last large observational studies, evidence has grown and clinical routine and awareness for lung-protective ventilation may have changed. Nevertheless, MV practice may still be sub-optimal, while geo-economical and sex-related differences may still exist. Thus, this study aims to investigate the worldwide practice of MV, especially in adult non-ARDS ICU patients.
Primary objective	• To characterise the current practice of mechanical ventilation in adult non-ARDS ICU patients
Secondary objectives	Secondary objectives: • To describe the epidemiologic characteristics of this cohort; • To determine the proportion of patients at risk of ARDS; • To determine the rate of progression to ARDS; • To determine the rate of missed ARDS diagnosis; • To determine rate and types of complications; • To determine the mortality rate; • To identify risk factors associated with outcome; • To identify potentially modifiable risk factors associated with outcome; • To identify geo–economic variations; • To identify and compare ventilation practices reported in previous studies and in different phenotypes • To assess adjunctive diagnostics and therapies
Study subjects	Adult ICU patients undergoing high-flow nasal oxygen or invasive mechanical ventilation
Study design	Multi-centre prospective observational cohort study
Planned sample size	≥1151 patients
Inclusion criteria	• Patients admitted to intensive care unit within enrolment window • Initiation of high-flow nasal oxygen (HFNO, ≥30 l/min) or NIV/CPAP with at least 5 cmH_2O expiratory pressure or invasive mechanical ventilation within enrolment window
Exclusion criteria	• Age <18 years • Ventilated patients transferred from another hospital under ongoing invasive or non-invasive ventilation (incl. high flow oxygen therapy (≥30l/min))

	• (Inability to obtain written informed consent for participation and/or data usage, if locally mandated)
Exposure	Clinical routine care, not study-specific exposure
Primary endpoint	• Proportion of patients ventilated invasively within lung-protective limits, defined as tidal volume of ≤8 ml/kg predicted body weight and positive end-expiratory pressure of ≥5 cmH_2O (both must be met)
Secondary endpoints	• Demographics/Cohort characteristics (incl. medical history as well as reasons for ICU admission and MV), • Disease severity scores, Lung injury prediction score (LIPS), sedation scores • Ventilator modes and settings • Vital signs, incl. respiratory variables and haemodynamics • Proportion of patients at risk for ARDS (LIPS ≥4 points) • Rate of progression to ARDS • Incidence of Non-intubated ARDS • Incidence of missed ARDS diagnosis • Utilization of adjunctive therapies, i.e. neuro-muscular blockade, prone positioning, extra-corporeal techniques, inhalative NO, etc. • Utilization of adjunctive diagnostics, i.e. daily chest X-ray, lung ultrasound, electrical impedance tomography, and oesophageal pressure measurement (yes/no) • Rate of extra-/ pulmonary complications, • ICU Mortality rate, hospital mortality rate, mortality at day 28 and 90 • Length of ICU stay • Duration of invasive mechanical ventilation • Ventilator-free and ECMO-free days at day 28 and 90 • ICU- and hospital-free days at day 28 and 90 • Site-level organisational, staffing, and resource information will be collected via a one-time online survey.
Course of the clinical trial	Timepoints of data collection: • Day of initiation of invasive ventilation or HFNO (named “day 0”) • Days 1, 2, 3, 4, 5, 7±1, 14±2, and 21±2 • Day 28±2 • Day 90±2 • Day of ICU discharge or death
Trial specific procedures/ laboratory tests	• Collection of routine patient data • Questionnaire to the site staff • No study-specific testing, imaging, or blood sampling for the main protocol
Statistical considerations	Descriptive analysis, statistical comparisons between subgroups, correlations, logistic regression analysis.

Study timetable	• Funding/Endorsement received in 03/2022 • Enrolment window: Study centres are allowed to choose an enrolment window of 1-4 weeks depending on their expected patient volume. The enrolment window must be a coherent period of 1-4 weeks • The timing of this window is freely chosen by the study centre, but must be determined in advance and adhered to. • Planned end (LPLV): Max. 92 days after enrolling the last patient

List of abbreviations

APACHE II	Acute Physiology And Chronic Health Evaluation Score II
ARDS	Acute respiratory distress syndrome
CCS	Canadian Cardiovascular Society
COPD	Chronic obstructive pulmonary disease
COVID-19	Corona virus disease (Sars-CoV-II)
CRF	Case report form
EC	Ethics Committee
ECMO	Extra-corporeal membrane oxygenation
eCRF	Electronic case report form
ESAIC	European Society of Anaesthesiology and Intensive Care
GCP	Good clinical practice
GDPR	General data protection regulation
HCO_3^-	Bicarbonate
HFNO	High-flow nasal oxygen
HICs	High-income countries
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICU	Intensive care unit
IRB	Institutional Review Board
ISF	Investigator site file
LAR	Legally authorized representative
LIPS	Lung injury prediction score
Local PI	Local Principal investigator
LPLV	Last patient last visit
MICs	Middle-income countries
MP	Mechanical power
MV	Mechanical ventilation
NCI	National coordinating investigator
NIV	Non-invasive ventilation
NYHA	New York Heart Association
Pat-ID	Patient identifier
PEEP	Positive end-expiratory pressure
PT	Physiotherapist
RG	Research group
RM	Recruitment manoeuvre
RRT	Renal replacement therapy
RT	Respiratory therapist
SC	Steering committee
TBI	Traumatic brain injury
VILI	Ventilator-induced lung injury

1. Administrative structure

1.1 Chief investigator and senior investigator

Chief investigator of the PRoVENT 2⁺ study is Dr. med. Martin Scharffenberg, University Hospital Carl Gustav Carus at Technische Universität Dresden, Germany. Senior investigator is Prof. Dr. med. Marcelo Gama de Abreu, MD, PhD, MSc, DESA, Cleveland Clinic, Cleveland, Ohio, USA.

1.2 Steering and writing committee

The PRoVENT 2⁺ steering committee (SC) includes:

- Martin Scharffenberg, University Hospital Carl Gustav Carus at Technische Universität Dresden, Germany
- Marcelo Gama de Abreu, Cleveland Clinic, Cleveland, Ohio, USA
- Jakob Wittenstein, University Hospital Carl Gustav Carus at Technische Universität Dresden, Germany
- Robert Huhle, University Hospital Carl Gustav Carus at Technische Universität Dresden, Germany
- Andrea Kurz, University of Graz, Austria
- Marcus Schultz, UMC, University of Amsterdam, The Netherlands
- Sabrine Hemmes, het Antoni van Leeuwenhoek, The Netherlands Cancer Institute, Amsterdam, The Netherlands
- Lorenzo Ball, University of Genova, Genova, Italy; Policlinico San Martino Hospital, Genova, Italy
- Ary Serpa Neto, Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; Department of Intensive Care, Austin Hospital, Melbourne, Australia; Department of Critical Care, University of Melbourne, Melbourne, Australia; Hospital Israelita Albert Einstein, São Paulo, Brazil
- Patricia R. M. Rocco, Laboratory of Pulmonary Investigation, Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
- Luigi Pisani, Mahidol Oxford Tropical Research Unit, Bangkok, Thailand & Miulli Regional Hospital, Department of Anesthesia and Intensive Care, Acquaviva delle Fonti, Italy
- Frederique Paulus, Amsterdam UMC location University of Amsterdam, Department of Intensive Care, The Netherlands; Amsterdam University of Applied Sciences, faculty of Health, Center of Expertise Urban Vitality, Amsterdam, the Netherlands
- Christian Putensen, Department of Anesthesiology and Intensive Care Medicine, University Hospital Bonn, Bonn, Germany
- *Paolo Pelosi†, Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Genoa, Italy; Anesthesia and Critical Care, San Martino Policlinico Hospital, IRCCS for Oncology and Neurosciences, Genoa, Italy*

The following SC members constitute the core SC:

- Martin Scharffenberg
- Marcelo Gama de Abreu
- Marcus Schultz
- Ary Serpa Neto
- *Paolo Pelosi†*

Upon decision of the core SC, the steering committee can be further expanded, e.g. to include outstanding researchers or research coordinators with expertise in a certain field or specialty that is deemed beneficial or helpful for successfully conducting this study.

Statistician: Ary Serpa Neto

Writing committee: A writing committee will be constituted during the course of the study.

1.3 Sponsorship, coordinating centre, support

The PRoVENT 2⁺ study is an observational, non-interventional study, which does not require a formal sponsor. This study is conducted by the PROVEnet research group, represented by the chief investigator. Coordinating centre of this study is the University Hospital Carl Gustav Carus at Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany, where the chief investigator is affiliated to. The study is financially supported by the European Society of Anaesthesiology and Intensive Care (ESAIC) in terms of an ESAIC research group (also see 10. FUNDING AND SUPPORT).

2. BACKGROUND AND AIM OF THE STUDY

2.1 Background

Mechanical ventilation (MV) is essential and life-saving in intensive care units (ICU), but may initiate or aggravate lung injury, especially in presence of the acute respiratory distress syndrome (ARDS) (1–3). Thus, lung-protective MV, comprising limited tidal volume and distending pressures together with an adequate positive end-expiratory pressure (PEEP), is strongly recommended in international guidelines and paramount especially in critically ill patients requiring long-term MV (>24 h) (4,5). While not only ICU patients with ARDS benefit from pressure- and volume-limited MV strategies, studies suggest that also critically ill patients at risk of developing ARDS should receive protective ventilation to improve outcomes (6–9). A large observational trial revealed significant differences in respiratory variables between patients at risk for ARDS as compared to those not at risk, while being at risk significantly worsened clinical outcomes (10). However, data were obtained a considerable time ago. Since then, evidence has grown, clinical procedures and routine may have changed in the meanwhile, and awareness for ventilator-induced lung injury (VILI) may have risen over the last years. Nevertheless, clinical practice may still be sub-optimal and differ from guidelines and evidence, while geo-economical variations (11,12) and even sex-related differences (13) may still exist. Furthermore, new VILI risk factors and potential mechanisms have been suggested in recent years. In fact, the driving pressure (1,14) and mechanical power (MP) (15,16) were shown to be

associated with both experimental lung injury and worsened clinical outcomes. However, normal range of values as well as their respective association with ARDS development and mortality in non-ARDS patients remains elusive and should be determined using a broad pragmatic approach under current real-world clinical routine. In recent years, mechanical ventilation research was even more focused on ARDS due to the COVID-19-pandemic. However, we also need to ensure patient safety of mechanically ventilated non-ARDS patients as well to avoid progression to ARDS.

2.2 Rationale

Data on ventilatory management of non-ARDS ICU patients and modifiable factors associated with outcomes need to be updated. Possible differences between previous and contemporary cohorts regarding treatment concepts and outcomes should be investigated. With PRoVENT 2$^+$ we urge to assess whether the evidence and knowledge developed meanwhile has affected clinical practice and outcomes. Furthermore, there is a need to characterise recently proposed risk factors, i.e. driving pressure and mechanical power, during MV of non-ARDS patients and to investigate their association with progression to ARDS, other complications, and mortality. While research in recent years mainly focused on (COVID-19-)ARDS patients, we urge to redress the felt imbalance of evidence between the treatments and outcomes of patients with and without ARDS.

2.3 Research questions

Within the PRoVENT 2$^+$ study, the following main research questions should be answered:

- What are the epidemiological characteristics of patients at risk for ARDS?
- How is the current clinical practice of invasive mechanical ventilation characterized?
- Which modes of mechanical ventilation and settings are commonly used?
- How is PEEP selected in non-ARDS patients?
- Does MV practice vary widely between international centres?
- How many patients are at risk for ARDS and how many patients progress to ARDS?
- At which mechanical power and driving pressure are non-ARDS patients ventilated and is there a correlation with complications and, i.e., progression to ARDS and mortality?
- Which other modifiable factors affect complication rates and mortality?
- Do findings differ from the historic cohorts (PRoVENT-trial, PRoVENT-iMiC)?
- Does the MV practice in COVID-19, neuro-surgical, and thoracic-surgery patients differ from the broad cohort with diseases other than these?

Further research questions may be developed and addressed by performing sub-studies and/or post-hoc analysis of the PRoVENT 2$^+$ study. Contributing centres are encouraged to suggest additional research questions and sub-studies to the chief investigator, who will discuss proposals within the SC.

2.4 Preliminary data

Out of 935 patients enrolled in the PRoVENT trial, 30 % (95 % CI 27-33) were at risk for ARDS (10). There was significant geographical variation regarding being at risk for ARDS (Europe 29% (25–32); North America 18% (9–45); South America 43% (34–53); Australasia 27% (11–43)). Tidal volume was

>8 ml/kg predicted body weight in almost 30 % of patients regardless of ARDS risk and PEEP as well as respiratory rate, fraction of inspired oxygen, plateau pressure, and driving pressure were significantly higher in patients at risk for ARDS. Adjunctive therapies where used more frequently in patients at risk. ARDS developed mainly on day 2-3 and worsened likelihood of weaning, prolonged ICU and hospital stay, and increased the risk of mortality. These data were obtained between 2014 and 2015. This study was followed by one focusing on Asian middle income countries (2017-2018) (12). In this cohort, tidal volume was >8 ml/kg predicted body weight in 50 % of patients at risk for ARDS as well as significantly higher than in ARDS patients. Furthermore, generally accepted lung-protective MV settings were present in half of the non-ARDS patients and outcome was worse in patients at risk for ARDS as compared to those not at risk. Meanwhile, evidence and awareness on the relevance of MV for clinical outcomes have grown and new risk factors have been suggested, and, according to latest analyses, significant geo-economic as well as sex-related differences in treatments and outcomes persist but are not well explained. In 2020, within the recent COVID-19 pandemic, current MV practice was assessed again (17). However, this study was focused on invasive MV for COVID-19 ARDS and limited to centres in the Netherlands. Thus invasively ventilated patients without ARDS have not been assessed. This together with the relatively old data on MV practice justifies the planned PRoVENT 2$^+$ study.

3. OBJECTIVES AND OUTCOMES

3.1 Objectives

In invasively ventilated adult ICU patients, we aim to:

- Characterise the current practice of mechanical ventilation in adult non-ARDS ICU patients (Primary objective)

Secondary objectives include:

- To describe the epidemiologic characteristics of this cohort;
- To determine the proportion of patients at risk of ARDS;
- To determine the rate of progression to ARDS;
- To determine the incidence of non-intubated ARDS
- To determine the rate of missed ARDS diagnosis;
- To determine rate and types of complications;
- To determine the mortality rate;
- To identify risk factors associated with outcome;
- To identify potentially modifiable risk factors associated with outcome;
- To identify geo–economic variations;
- To identify and compare ventilation practices reported in previous studies and in different phenotypes/sub-cohorts (e.g., neuro-surgery, thoracic surgery, COVID-19)
- To assess adjunctive diagnostics and therapies

3.2 Primary endpoint

The following primary outcome will be assessed:

- Proportion of patients ventilated within lung-protective limits, defined as tidal volume of ≤8 ml/kg predicted body weight and positive end-expiratory pressure of ≥5 cmH_2O (both must be met) (18).

3.3 Secondary endpoints

The following secondary outcomes will be assessed:

- Demographics/Cohort characteristics (incl. medical history as well as reasons for ICU admission and MV),
- Disease severity scores, Lung injury prediction score (LIPS), sedation scores
- Ventilator modes and settings
- Vital signs, incl. respiratory variables and hemodynamics
- Proportion of patients at risk for ARDS (LIPS ≥4 points)
- Rate of progression to ARDS according to Berlin Definition*,
- Incidence of Non-intubated ARDS
- Incidence of missed ARDS diagnosis
- Utilization of adjunctive therapies, i.e. neuro-muscular blockade, prone positioning, extra-corporeal techniques, inhalative NO, etc.
- Utilization of adjunctive diagnostics, i.e. chest X-ray, lung ultrasound, electrical impedance tomography, and oesophageal pressure measurement (yes/no)
- Rate of extra-/ pulmonary complications,
- ICU Mortality rate, hospital mortality rate, mortality at day 28 and 90,
- Length of ICU stay
- Duration of invasive mechanical ventilation
- Ventilator-free and ECMO-free days at day 28 and 90,
- ICU- and hospital-free days at day 28 and 90
- Site-level organisational, staffing, and resource information will be collected via a one-time online survey.

*In resource-limited settings, the modified Kigali criteria (19) instead of the Berlin Definition (20) could be applied for ARDS diagnosis. However, Berlin Definition should take precedence if all necessary variables are available. Furthermore, the New Global Definition of ARDS will be applied and analysed separately (21).

3.4 Other variables

The complete list of variables to be collected can be found in Appendix 6 – Variables and timing of assessment.

4. STUDY COHORT

4.1 Study centre criteria

Hospital or institutions must meet the following conditions to qualify as a PRoVENT 2⁺ study centre:

- ICU with capability of invasive mechanical ventilation
- Personnel experienced in and dedicated to scientific research
- Personnel having the capacity for conducting the study and being capable of following the protocol, the Good Clinical Practice guidelines, and the Declaration of Helsinki
- Realistic chance of enrolling at least 10 patients (recommendation)
- Web access to the electronic case report forms/database
- Willingness to share collected data in a timely manner

- Absence of local regulations/laws prohibiting the sharing of pseudonymised data

4.2 Enrolment window

All patients fulfilling the inclusion criteria and not having exclusion criteria will be enrolled into the study within a certain enrolment window. Study centres are allowed to choose an enrolment window of 1-4 weeks depending on their expected patient volume. The enrolment window must be a coherent period of 1-4 weeks. The timing of this window, i.e. the time point of starting the enrolment, is freely chosen by the study centre, but must be determined in advance and adhered to. Thus, participating centres must select the duration and the timing of their enrolment window and report this to the PI before starting enrolment.

4.3 Subject inclusion criteria

- Patients admitted to intensive care unit within enrolment window
- Initiation of high-flow nasal oxygen (HFNO, ≥30 l/min) or NIV/CPAP with at least 5 cmH_2O expiratory pressure or invasive mechanical ventilation within enrolment window

4.4 Subject exclusion criteria

- Age <18 years
- Ventilated patients transferred from another hospital under ongoing invasive or non-invasive ventilation (incl. high flow oxygen therapy (≥30l/min))
- (Inability to obtain written informed consent for participation and/or data usage, if locally mandated by local law/IRB/EC review)

4.5 Criteria for withdrawal / discontinuation of participants

Due to the observational nature of the study, the protocol does not define any withdrawal/ discontinuation criteria. Patients electing to withdraw from the study may do so at any point. In this case, no further data will be collected, while already collected, encoded data will be pseudonymised and analysis may be performed up to the point of data collection (also see 8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION).

5. METHODS

5.1 Study design

PRoVENT 2+ is an investigator-initiated, international, multi-centre, prospective, observational cohort study collecting clinical routine data.

5.2 Setting and participants

PRoVENT 2+ will be conducted on intensive care units worldwide. Participants will be patients who are staying on or are admitted to an ICU of a participating centre and who have high-flow nasal oxygen therapy or invasive mechanical ventilation newly initiated within the defined enrolment window according to the above-mentioned inclusion and exclusion criteria.

5.3 Procedures

The time course of study-related procedures is shown in Appendix 8 – Time course of procedures.

5.3.1 Screening

Participating ICUs will be screened for eligible patients by the local PI or local investigator at least once daily, e.g. in the morning. In addition, new patients can be screened upon ICU admission, as appropriate. The local participating centres are requested to document the screening process using a screening log. A screening log template can be found in Appendix 9 – Screening log.

5.3.2 Enrolment

Following screening, eligible patients should be included into the study. In this case, the patient is enrolled in the moment of collecting first data.

If written informed consent was mandated by local law or IRB/EC review, the patient´s LAR or a consultant doctor should be approached as soon as possible after screening, as appropriate, with the relevant documents for a thorough explanation of the study. In this case, a patient is enrolled in the moment of signature of the ICF (by him-/herself, legally authorized representative or consultant doctor). If written informed consent was only mandated for the follow-up visits, the patient is already enrolled when recording the first data. For further details see 7. ETHICAL AND REGULATORY ASPECTS.

The local participating centres are requested to document the enrolment of patients using an enrolment log. An enrolment log template can be found in Appendix 10 – Enrolment log.

5.3.3 Visits

Data should be collected on the day of initiation of invasive mechanical ventilation or HFNO (day 0), daily between day 1 and 5 thereafter, as well as day 7±1, day 14±2, day 21±2, day 28±2, and day 90±2, as well as the day of ICU discharge or death on ICU (see Figure 1, Appendix 8 – Time course of procedures. After a patient was discharged alive from the hospital, only visits on day 28±2, and day 90±2 will be performed. The variables to be collected and the corresponding timing are described in detail in Appendix 6 – Variables and timing of assessment. The follow up log template helps to schedule visits, see Appendix 11 – Visit and follow up log. Data for visits beyond hospital stay (days 28±2, 90±2) should be obtained by telephone call by an investigator of the corresponding study centre.

5.4 Expected duration of subject participation

The subject´s participation begins with the fulfilment of eligibility criteria and consecutive collection of first data (or signature of ICF, if mandated). Participation automatically ends with death or completing the last follow-up, which is 90±2 calendar days after enrolment, whichever comes first.

5.5 Intervention

The PRoVENT 2+ is an observational study. There is no study-specific intervention to be performed. Medical interventions, measurements, examinations, sampling and analysis of specimens etc. are to be performed within clinical routine medical care. Participation in this study (or not participating) does not affect routine clinical care.

5.6 Participating centres and investigator roles

5.6.1 Participating centres and pre-study survey

Qualified centres worldwide are welcome to participate. To do so, centres must express their interest of participation to the chief investigator/coordinating centre. Site-level organisational, staffing, and resource information will be collected via a one-time online survey. The survey can be found in Appendix 18 – Pre-Study Centre Survey. The chief investigator together with the SC/core SC decides on the acceptance of an applicant as a study centre. Relevant information on the participating centres is stored at the coordinating centre. A local hospital/institution becomes a study centre in the moment a competent local PI signs the study protocol and thereby accepts all paragraphs included in the protocol.

5.6.2 National coordinating investigators (NCI)

National coordinating investigators (NCIs) are scientifically skilled and experienced anaesthesiologists, intensive care physicians, surgeons or other qualified medical/scientific professionals appointed by the core SC to lead the PRoVENT 2^{+} study within individual nations. Especially, they:

- Identify local participating centres and recruit local PIs in participating hospitals
- Assist in/perform the translation of study documents - upon needs; provide translated documents to the coordinating centre
- Ensure necessary country or regional regulatory approvals are in place prior to start of patient inclusion
- Assist and train the local PIs and monitor the conduct of the study according to good clinical practice (ICH-GCP guidelines)
- Ensure transparent and immediate communication with the chief investigator/the coordinating centre and the participating sites in their country, e.g. during data cleaning NCI will cascade the information/requests to the relevant sites and assist when necessary.

NCIs accept the content of the study protocol by signing the protocol signature page. Furthermore, NCIs confirm that they are willing to act as NCI by signing the NCI letter of intention (see Appendix 12 – NCI Letter of intention). No fee or financial compensation is given to NCIs or their institution for study-related actions.

5.6.3 Local principal investigators (Local PI)

Local principal investigators (local PIs) are scientifically skilled anaesthesiologists, intensive care physicians, surgeons or other qualified medical/scientific professionals in each participating institution who will have the following responsibilities:

- Provide scientific and structural leadership for the study in their institution
- Ensure all relevant regulatory/ethical approvals are in place for their institution
- Ensure adequate training of all relevant investigators/staff prior to data collection
- Ensure that all relevant investigators/staff act according to the principles of Good Clinical Practice and the Declaration of Helsinki
- Close supervision of daily data collection and assist with problem solving
- Ensure timely completion of eCRF and follow up data;
- Ensure and finally confirm integrity/validity of data collection

- Transparent and immediate communication with the corresponding NCI (and, as appropriate, the chief investigator/the coordinating centre)
- If necessary, provide direct and/or physical access to source data/documents/reports for study-related data checks to the persons assigned by the chief investigator

Local PIs accept the content of the study protocol by signing the protocol signature page. Furthermore, local PIs confirm that they are authorised to act as local PI at their institution and can and are willing to conduct the study at their centre by signing the local PI letter of intention (see Appendix 13 – Local PI Letter of intention), making the respective institution become a study centre of PRoVENT 2+. No fee or financial compensation is given to local PIs or their institution for study-related actions.

The organigram (see Appendix 14 – Organigram) summarises the organisational structure. Investigators are encouraged to submit and perform substudies which are related and beneficial to the main study goal.

5.6.4 Section coordinators

Dedicated section coordinators may be designated to ensure, organize, and monitor the inclusion of special patient populations, e.g. neuro-surgical patients, cardiac-surgical patients etc. Section coordinators will be invited/selected by the SC.

5.6.5 Fees, financial incentives

There will be no fees or any other financial incentives paid to committee members, NCIs, local PIs, investigators, other research staff, patients, relatives or other parties involved in this study. Deviating agreements can be made in justified cases for services provided and invoiced, e.g. provision and maintenance of the database, statistical evaluations, etc.

6. STATISTICAL METHODS

6.1 Sample size

This observational study aims at assessing the proportion of protectively ventilated adult ICU patients, while investigating the current practice of invasive mechanical ventilation. In order to calculate a sample size that is sufficient to estimate the population prevalence of protectively ventilated patients with a good precision, we used the following formula for calculation of sample sizes in prevalence studies (22):

$$n = Z^2 P (1 - P) / d^2,$$

where *n* stands for sample size, *Z* for confidence level (assumed as 1.96 for 95 % confidence intervals), *P* for expected prevalence and *d* for the margin of error, i.e. the precision. In a previous observational investigation in non-ARDS ICU patients, the proportion of patients ventilated within lung-protective settings, defined as tidal volume of ≤8 ml/kg and positive end-expiratory pressure of 5-8 cmH_2O, was 43.1 % (10). Assuming this 43.1 % as *P* and accepting a margin of error of 3 %, the sample size calculation resulted in 1047 patients. To compensate a potential drop-out/lost to follow-up rate of 10 %, at least, 1151 patients will be enrolled in this study.

6.2 Data processing

Source data will be collected at each centre and entered into a study-specific electronic case report form (eCRF) after pseudonymisation. Data from the eCRF/database are to be extracted by the coordinating centre.
The eCRF will be provided via REDCap, which will be hosted by the coordinating centre (or an institution within the coordinating centre that is authorised to do so).
In intervals, entered data will be checked for validity/plausibility by the coordinating centre (remote monitoring). However, onsite monitoring may apply. After the last enrolled patient has completed the study, the database will be closed. Prior to scientific analysis of the entered data, data cleaning will be performed.

6.3 Planned analyses

6.3.1 Main analysis

The detailed statistical analysis plan shall be published before analysing the collected data. In brief, analysis will include descriptive/explorative as well as comparative analysis. Continuous variables will be reported as mean and standard deviation or median and interquartile range, as appropriate. Categorical variables will be reported as numbers and proportions. Association between variables will be analysed using correlation/regression analyses. Between relevant sub-cohorts, continuous variables will be compared using t-test or Mann-Whitney U test (depending on distribution) or general linear model in case of repeated measurements. χ^2- or Fisher's exact tests will be used to compare categorical variables. Time-dependent data will be analysed using a proportional hazard model adjusted for possible imbalances of sub-cohort characteristics. To identify potential factors associated with adverse events/ARDS development, univariate analysis will be performed. Multivariate logistic regression model will be used to identify independent risk factor models. Time-to-event variables and survival to day 28/90 will be analysed using Cox regression/log-rank test and visualised by Kaplan-Meijer curves. P values will be two-sided. We will accept significance at $P<0.05$ (adjusted for multiple testing, if applicable).

Pulmonary complications reported in the first 24 hours of invasive ventilation may be analysed and reported separately, because these may simply represent the initial reason for initiation of invasive MV.

The main analysis will distinguish between patients who developed an ARDS and those who did not. Other subgroup analysis may be carried out, see below.

Lab values may be analysed if available. Blood sampling will be performed according to clinical routine care only, not related to the study.

Certain study endpoints will be compared between patients with LIPS 0-3 vs. LIPS ≥4 points. The LIPS criteria and points are shown in Appendix 20 – Scores.

6.3.2 Sub-study analyses

Secondary or post-hoc analyses will be performed, e.g. by grouping patient data according to certain characteristics. Amongst others, the following sub-groups will be analysed:

- Analysis between different geo-economic regions: middle-income countries (MICs) and high-income countries (HICs) as defined by 2016 World Bank classification (11)

- Analysis between and/or different disease entities (e.g., COVID-19, thoracic surgery, neuro-surgery etc.)
- Analysis between non-intubated and intubated ARDS

Investigators are encouraged to submit and perform substudies which are related and beneficial to the main study goal.

6.3.3 Datasets to be analysed

Variables of the main study and their timing of assessment are listed in Appendix 6 – Variables and timing of assessment. Data will be collected on day 0 and daily until day 5 inclusive, as well as on day 7±1, 14±2, 21±2, 28±2, and 90±2, and day of ICU discharge or death on ICU.

6.3.4 Handling of missing data

If the patient withdraws consent during the study, data until that time point will be pseudonymised and included in the analyses (also see 8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION). Patients will not be completely withdrawn from the study if some data points are missing. Instead, the data set will be analysed regarding the incidence and patterns of missing data. Accordingly, appropriate statistical methods and tests will be used.

6.3.5 Deviations from the original statistical analysis plan

Any deviations from the initial statistical analysis plan will be identified and explained in any reports. Additional analyses may be declared as post hoc analyses when reporting results.

6.3.6 Methods against bias

This study is observational. Thus, blinding and randomisation are not applicable. However, data integrity/validity/plausibility will be ensured by means of automatically and manually raised queries, and data monitoring. The database will be screened continuously for potential errors by automatically checking for outliers. A broad representative sample of adult patients of all ethnicities should be obtained without any selection bias. Reporting of results will follow the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for maximum transparency.

7. ETHICAL AND REGULATORY ASPECTS

7.1 Ethical conduct of the study

The research project will be carried out in accordance with the research plan and the principles stated in the current version of the Declaration of Helsinki (23) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines ICH-GCP E6 in its latest version (assessable via https://www.ich.org/). Specific national and local regulatory authorities' requirements will be followed as applicable. The principles of the "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies" will be followed (24). Everyone involved in this study is committed to adhering to and implementing best scientific practice.

7.2 Risk categorisation

The proposed study is an observational study. As such, there are no study-specific medical interventions to be performed with the participating patients. Invasive treatments, physiological measurements, analysis of blood samples etc. are performed within standard care and not study-related. Thus, there is no potential harm to be expected from participating or not participating in this study. When storing and processing sensitive data, there is the theoretical risk of data leakage or identification of individuals. However, these risks are reduced to a minimum by strong data protection regulations, strict confidentiality, and pseudonymisation (see 8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION).

7.3 Institutional review board, ethics committee or equivalent

Before starting patient enrolment, all participating centres must submit the study to their corresponding local Institutional Review Board (IRB) or ethics committee (EC) for ethical judgment, and obtain document of proof that the trial has been subject to IRB/EC review and given approval/favourable opinion. Relevant communication between participating centres and their local IRB/EC, especially the result of the IRB/EC consultation, must be submitted to the chief investigator for central storage before enrolling patients into the study (see Appendix 21 – EC/IRB approval documentation sheet).

Because 1) this study is strictly observational, 2) this study does not include the collection or analysis of bio-samples or specimens, 3) all data are collected completely within routine care/documentation, and 4) individuals cannot be identified by third parties due to effective pseudonymisation and data protection rules, written informed consent (for both study participation and data utilization) may not be required. In this case, an explicit, written exemption must be obtained from the IRB/EC to prove this (waiver of written informed consent).

According to local regulations, informed consent may be necessary 1) to obtain patient data in general, or 2) to obtain follow-up data for all time points beyond the discharge of the patient, although informed consent may not be necessary for study participation and data utilization (of routine clinical data) as long as the respective patient is in the respective hospital, i.e. as long as patient data is generated within the clinical routine, and/or 3) in order to transfer pseudonymised data into the eCRF/study database. In cases 1) and 3), where written informed consent is anyways required by local law or IRB/EC, written informed consent will be obtained from each patient or legal representative or consultant doctor prior to enrolment.
In case 2), where informed consent is not needed for the duration of the patient´s hospital stay but requried to obtain follow-up date beyond discharge by local law or IRB/EC, written informed consent will be obtained from each patient (or legal representative or consultant doctor) prior to discharge (latest).

Different scenarios and solutions that may apply in centres worldwide are described in the following sections and must be adapted by each study centre according to local regulations.

7.4 Participant information and informed consent, if mandated

Any waivers to obtain written informed consent issued by the corresponding EC/IRB must be confirmed or documented in writing and passed on to the coordinating centre.

However, in countries or regions where local law/regulations do require an informed consent (in general, for data transfer and/or for time points beyond discharge), informed consent forms (ICF) and any other written information to be provided to the patients as well as advertisement for subject recruitment (if used) should be subject to IRB/EC review and given approval/favourable opinion before starting enrolment.

If applicable, informed consent can be obtained as follows:

1) **Conscious patient:** The patients will be presented with the IRB/EC-approved Patient Information Sheet and Informed Consent Form (see Appendix) to make an informed decision about their participation in the study, i.e. explaining the nature of the study, its purpose, the general lack of any procedures involved, the expected duration, the potential risks and benefits. Each participant will be informed that their participation in the study is voluntary and that he/she may withdraw from the study at any time and without explanation, that withdrawal of consent will not affect his/her subsequent medical assistance and treatment and that no further data will be collected, while already collected, encoded data will be anonymised and analysis may be performed up to the point of data collection (8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION). The participant will be informed that his/her medical records will be examined by authorised individuals other than their treating physician. The participant will read the statement and will have the opportunity to ask questions and be given adequate time to reach a decision before signing and dating the informed consent form (ICF). The ICF must also be signed and dated by the investigator (or designee), when applicable, and it will be retained as part of study records. Patients will be given a copy of the signed document if he/she wants this or if this is a requirement of the local ethics committee or local law.
2) **Unconscious patient, with legally authorised representative:** Due to the expected cohort it is very likely that all patients are unable to give informed consent. If a legally authorised representative (LAR) has been appointed and can be reached, he or she decides on his or her own responsibility on behalf of the patient. The information and consent procedure is then carried out with the LAR in the same way as otherwise with the patient. Thereby, the same principles mentioned above also apply in this case, but a dedicated LAR information sheet and LAR ICF (see Appendix) will be used. As soon as the patient regains consciousness and understanding of the situation, he/she should be informed about his/her participation in the study. Of course, participation in the study can also be terminated without giving reasons at any time.
3) **Unconscious patient, independent consultant doctor:** In the circumstance that a patient is unable to give informed consent and there is no LAR appointed or the LAR cannot be reached (despite sufficient efforts), and there is no indication that the patient would generally refuse to participate, an experienced independent doctor (consultant/consilary doctor), who is not involved in the PRoVENT 2+ study, can be called in to give an expert opinion. In this case, the

consultant doctor checks the prerequisites for the patient's participation in the study in the sense of a second expert vote, which, however, neither binds the investigator nor relieves him of his responsibility. This is justified by the fact that the close monitoring and documentation associated with study participation may represent an individual benefit for the respective patient, while no significant risk for the patient arises from study participation due to the strictly observational study design without study-related interventions together with the high scientific need of conducting this study. For this consenting solution, a dedicated form should be used (see Appendix). As soon as the patient regains consciousness and understanding of the situation, i.e. capability of consenting, he/she should be informed about his/her participation in the study and informed consent must be obtained. Of course, participation in the study can also be terminated without giving reasons at any time.

4) **Unconscious patient in Germany, specific example for the State of Saxony:** According to paragraph 29 section (1) SächsKHG ("Sächsisches Krankenhausgesetz"), doctors and other scientific personnel may process patient data stored within their department or at universities within their medical facilities, in university hospitals or in other medical facilities for scientific research projects (25). According to paragraph 29 section (3) SächsKHG, this data may be passed on in pseudonymised form for analysis even without the patient's consent, provided that the purpose of a specific research project cannot be fulfilled in any other way and 1) the legitimate interest of the general public in carrying out the research project significantly outweighs the patient's interest in confidentiality or 2) it is not reasonable to obtain consent and other interests of the patient worthy of protection are not impaired. In fact, the scientific research objective of this study can only be achieved in terms of an international multi-centre observational study during the acute phase of an illness or medical course that requires mechanical ventilation, in which medical data must be obtained, pseudonymised, and merged for analysis. The investigation of the current clinical practice of intensive care mechanical ventilation for the acute phase of an disease or other urgent need of respiratory support, an invasive medical intervention which can significantly affect clinical outcomes, is of high scientific interest and its results have the potential to change and improve clinical routine worldwide, which may in fact outweigh the patient's interest in confidentiality – especially when taking into consideration that participating patients will not be practically identifiable by other centres or the participating statistician on the basis of the pseudonymized health data transmitted. In addition, it is actually unreasonable to obtain consent in light of the current legal situation in Germany, as the spousal emergency representation ("Ehegattennotvertretungsrecht") does not appear to be applicable to observational studies, but this will increasingly replace judicial care ("gerichtliche Notbetreuung") in acute situations and the consultant physician solution ("Konsiliararztlösung") is actually only specifically regulated for studies on drugs and medical/medicinal products ("Arzneimittel- und Medizinproduktegesetz"). In the acute medical situation, which necessitates the initiation of mechanical ventilation with sedation/anaesthesia and is the core of the scientific investigation here, there is therefore currently no satisfactory legal basis for the collection and pseudonymised transfer of routine data for the purpose of a multi-centre observational study in accordance with the Professional Code for Physicians ("Studie nach Berufsordnung für Ärzte") other than the

afore-mentioned §29 section (1) in combination with section (3). Other interests of patients worthy of protection are not impaired in this situation.
However, **for data collection beyond hospital stay**, informed consent must be obtained, ideally from the patient after regaining capability of giving informed consent (using dedicated documents, see Appendix 22 and 23) or from a legally authorised representative.

The coordinating centre provides the patient information sheet and patient ICF as well as the corresponding forms addressing the LAR and consultant doctor in English and German. The national coordinator is responsible for proper translation of all documents into the local language, if necessary. All translation and adaptation of the documents and appendices should be sent the coordinating centre for validation and central storage. Any guidance published by the coordinating centre should be followed in this regard.

Documents specifically developed for Germany, especially for the State of Saxony, are provided in the Appendix (see versions termed DE-SN). For other German centres who would opt for a consultant doctor solution, a corresponding template is provided as well.

7.5 Participant privacy

Every investigator affirms and upholds the principle of the participant's right to privacy and shall comply with applicable privacy laws. Specifically, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing in scientific journals. Identification of individuals from scientific communications/publications shall be impossible, because data shall be published in summarized form.

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by utilising subject identification code numbers (pseudonymisation) and only pseudonymised data will be recorded in the central database (see 8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION).

For data verification purposes, authorised representatives of the sponsor/coordinating centre may require direct access to parts of the medical records relevant to the study, including participants' medical history. However, authorised representatives are strictly obliged to confidentiality.

7.6 Early termination of project

An early termination of the project is not to be expected. Reasons for early termination of the study, as can occur in interventional studies, are not applicable here. However, in the unlikely event of unexpected, insurmountable problems can the project be terminated prematurely. Any necessary measures to prevent an early termination will be discussed and taken by the core SC, as appropriate.

7.7 Amendments and changes

Only the core SC or persons authorised by the core SC are entitled to amend the protocol. National coordinating investigators (NCIs) and local principal investigators (local PIs) will receive timely notification of changes and will be required to submit amendments locally. Written documentation of the amendments' approval will be provided to the coordinating centre and substantial

amendments of the protocol will be only implemented after approval of the responsible IRB/EC. In consideration of the observational nature of the study, the necessity of protocol deviations to protect the rights, safety and well-being of human subjects without prior approval of the sponsor and the IRB/EC appears remote. Such deviations must be documented and reported to the coordinating centre and the IRB/EC as soon as possible. All non-substantial amendments, like administrative changes, will be communicated to the IRB/EC as necessary by the local PI. It is the local PI's responsibility to communicate with their IRB/EC (also see 5.6 Participating centres and investigator roles).

8. DATA AND QUALITY MANAGEMENT, DATA PROTECTION

8.1 Data quality

The coordinating centre is responsible for implementing and maintaining quality assurance and quality control systems to ensure that the study is conducted, and data are generated, documented (recorded), and reported in compliance with the protocol, ICH-GCP, and the applicable regulatory requirements.

Quality control measures will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly for data collection and entry, automated consistency checks, and training of NCIs. It will be responsibility of the NCIs to train local PIs. Local PIs will ensure that the data in the eCRF are carefully entered in a timely manner and verified regularly. It will be the responsibility of local PIs to conduct periodic and random checks to ensure data quality in her/his centre. The coordinating centre will make random assessments of centres in order to confirm that there are no improper and incorrect data entered into the eCRF. On-site monitoring visits may occur as appropriate. By participating in this study, i.e. by signing the protocol signature page, local PIs agree to provide direct and, if necessary, physical access to source data/ documents/reports for study-related data checks to the persons assigned by the chief investigator to conduct data checks.

In the case of poor data quality (relevant amount of missing and/or implausible data, etc.), the local PI in charge will be requested to ensure appropriate rectification in a timely manner. If massive or insurmountable data deficiencies or a mode of operation that does not comply with the Good Clinical Practice guidelines and/or the Declaration of Helsinki become evident, the chief investigator is free to exclude the respective centre from the study. Such cases will be discussed in the Core SC.

8.2 Data handling and record keeping / archiving

Data will be handled strictly confidentially.

The hospital will be provided with log sheets for screening, enrolment, and follow ups (see corresponding appendices). The enrolment log that will contain the patient's name etc. will help sites to link patient with the unique study-specific patient identification number (Pat-ID), which is used for pseudonymisation. Patient´s names will remain at the local study centre and will not be shared with the coordinating centre or third parties.

The Pat-ID will consist of a numerical code for the corresponding study centre as well as the numerical code for the individual patient (format: XXX-YYYY), e.g. 005-0001 for the first patient of study centre #5. Study centre codes will be generated centrally and communicated to the study centres, while patients will be numbered consecutively.

Data will be then be collected at individual centres on printed case report forms (CRFs), see Appendix 15 – Case report forms for printing ("Worksheets"). CRFs are only identified through the Pat-ID and shall not include any patient names, initials or local hospital patient numbers/case numbers.

Local investigators will then transcribe all collected data from the CRFs into an internet-based electronic CRF (eCRF). Thus, data are collected first on paper CRF, then entered into the electronic database by the site staff using only the specific Pat-ID. Thereby, only pseudonymised data is transferred to the coordinating centre. Access to the eCRF/database is protected by a personalised and confidential username and password. Sharing of passwords/accounts is not allowed.

Printed and electronic CRF will be in English for all nations and centres involved in this study. Along with other relevant study-specific documents, CRFs for printing will be made available to all study centres for download. Study centres are responsible for printing the protocol, CRFs etc. in a sufficient amount at their own discretion. Each centre will maintain an investigator site file (ISF), including: Protocol, IRB/EC judgment/approval, local investigator delegation log (Appendix 16 – Delegation log), local translation of informed consent form (if applicable), signed informed consent forms (if applicable), etc. These study-related documents, especially those with sensitive data (log sheets, CRFs etc.) must be stored within a locked cabinet/office in accordance with local and national regulations until the coordinating centre has agreed to archive the study documents. After publication, source data have to be stored according to local regulations, e.g. for ten years in Germany.

Aggregated, pseudonymised data will be analysed at the study statistician's institution (Monash University, Melbourne, Australia). This institution will keep data until publication of the material. After completed publication, data must be sent for storage to the coordinating centre and be destroyed at the statistician's site, which will be documented in writing by the study statistician and the chief investigator. All parties involved in this study declare to respect the applicable data protection laws. All handling of personal data will comply with the GCP Guidelines. Coordinating centre and participating centres will maintain and update their ISF according to the recommendation of the ICH-GCP Guidelines E6 in its latest version.

8.3 Data transfer

By participating in the study, i.e. signing the protocol signature page and consecutively enrolling patients, local PIs commit to deliver the collected data in high quality and full integrity to the coordinating centre by entering data into the eCRF/database. Thereby, they agree to share the locally collected, pseudonymised data with the coordinating centre. This intention must be expressed using the respective LOI templates before starting patient recruitment.

8.4 Confidentiality, data protection

All persons involved in performing the study are obliged to confidentiality regarding study-related content. To safeguard patients' confidentiality, a patient identification code will be assigned to encode data. The confidential log linking patient identification code and identifiable patient data will be stored separately in a locked cabinet accessible to authorised personnel only and corresponding electronic files will be protected by personalised and confidential usernames and passwords. eCRF are identified through the patient identification code and will not include any names, initials, date of birth or local hospital patient numbers; therefore, no patient identifiable data will be directly accessible from the eCRF. Data protection will be guaranteed through encoding and the use of a secured database with restricted access by individual log-in and gradated user rights. Further, only encrypted (pseudonymised) data will be stored centrally. The database will be hosted on servers physically located in the European Union.

Open direct access to all relevant study information as well as source data/documents will be permitted for purposes of monitoring, audits or inspections to the coordinating centre, i.e. persons authorised by the chief investigator. All handling of personal data will comply with the GCP Guidelines and follow strictly the legal and national requirements of GDPR. For any additional questions the ESAIC Data Protection Officer at privacy@ESAIC.org or 24, Rue des comédiens 1000 Brussels, Belgium may be contacted.

As per GDPR (Articles 15-21), patients have the right of access to their personal data, rectification of data, erasure of data, restriction of data processing, and data portability. However, the right to erasure of data is limited by the GDPR Article 89(1) and (2): “Where personal data are processed for scientific (…) research purposes or statistical purposes pursuant to Article 89(1), the data subject, on grounds relating to his or her particular situation, shall have the right to object to processing of personal data concerning him or her, unless the processing is necessary for the performance of a task carried out for reasons of public interest.” Accordingly, if a patient or a patient´s LAR withdraws consent prematurely, his or her data can be anonymised and continued to be processed for the scientific purpose. Complete deletion of the data collected up to the point of withdrawal is not possible, as the deletion is likely to render impossible or seriously impair the achievement of the scientific purpose (GDPR Article 89 (2)). Patients are informed about their rights regarding their personal data as well as the limitation of rights within the patient/LAR information sheet.

9. PUBLICATION AND DISSEMINATION POLICY

9.1 Scientific publications

9.1.1 General aspects

Data collected from this project shall be used for publication of one or more studies in a peer-reviewed international journal of high quality as well as shall be presented at Euroanaesthesia conference and other national and international scientific meetings. The final main results will be published in a highly ranked, peer-reviewed scientific journal, which may be followed by publication of secondary/post hoc analysis/sub-studies. Only the writing committee may prepare results for the main publication. Any other arrangements, i.e. for secondary/post hoc analysis/sub-studies, must be agreed with the Core SC/ the Writing Committee and approved by the chief investigator.

Investigators of this study are not allowed to carry out their own uncoordinated sub-analyses or partial analyses or to publish results in any way prior to the main publication. Possible interim reports or other reports not intended for becoming publicly available, e.g. internal progress reports etc., must be reported to and approved by the chief investigator in advance. The PRoVENT 2+ and the PROVEnet Research Group, as well as the ESAIC must be acknowledged in all publications and presentations.

9.1.2 Writing committee

Selected members of the SC and other particularly committed investigators may be part of the writing committee.

9.1.3 Protocol publication

The study protocol, including a statistical analysis plan, will be published in an appropriate journal at the beginning or, at latest, prior to the analysis of the study.

9.1.4 Authorship rules

Transparent, fair rules for authorship and absence of financial incentives for participating centres shall emphasize and support pure scientific and unbiased interest.

The members of the writing committee and the "PRoVENT 2+ Investigators" will be authors of the publications derived from the PRoVENT 2+ study. When submitting a manuscript, the corresponding author will specify the group name as "PRoVENT 2+ Investigators". As recommended by the International Committee of Medical Journal Editors (ICMJE) (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html ; accessed July 12th 2020), authorship will be considered based on contributions to recruitment of patients, data acquisition and cleaning, analysis and interpretation of the data, manuscript writing, and submission of national/local grants AND final approval of the version to be published AND agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. According to the ICMJE recommendations, the byline of the article identifies who is directly responsible for the manuscript, and MEDLINE lists as authors whichever names appear on the byline. To ensure that MEDLINE will list the names of individual group members who are authors, there will be a note associated with the byline clearly stating that the individual names are elsewhere in the paper and that those names are authors. All collaborators will be detailed in the manuscript appendix and can be tracked via PubMed (in accordance with the Journal authorship policy). Local PIs will be asked to submit names of staff actively involved from their institution in the End of Study Reporting Form (Appendix 17 – End of the study reporting form). If the number of screened and/or recruited patients from a country/centre is too low to justify enough active involvement, the SC will decide on the legitimacy of authorship. The final decision will be left to the decision of the chief investigator in consultation with the core SC and in line with relevant journal policy.

Given a documented active participation, each participating centre can designate two investigators to be mentioned as collaborative authors in the main publication. In addition, one additional collaborative authorship will be granted per each ten screened patients after the first ten patients (irrespective of screening result, i.e. actual enrolment rate), also see Appendix 19 – Collaborative authorship calculation. Collaborators not fulfilling authorship criteria will be listed in the acknowledgement section, as appropriate.

9.1.5 Secondary analysis, sub-studies and data sharing

Duplicate data publication is not allowed. However, the pseudonymised pooled dataset may be available for secondary analyses/post-hoc analysis/sub-study upon specific request in form of a detailed study proposal (including authorship rules) to the SC. The final approval of these potential secondary analysis rests with the SC. Prior to journal submission, any paper originating from the pooled data will be reviewed by the SC that is also entitled to require revisions. Authorship of any publication derived from the pooled data set will include the group name "PRoVENT 2+ Investigators" and the names of the SC who have worked on the particular manuscript with a byline clearly stating that the individual names are elsewhere in the paper and specifying whose individual names refer to authors and to collaborators, respectively. For transparency, the original paper must be referenced to in all articles of secondary analyses. Requests for data sharing for individual-level meta-analyses are to be addressed to the core SC.

9.1.6 Scientific conferences

Presentation at international meetings will be restricted to the chief investigator and members of the core SC, or their delegates, as appropriate. NCIs will qualify for presentation at national meetings after approval by the core SC. The PRoVENT 2+ and the PROVEnet Research Group, as well as the ESAIC must be acknowledged in all publications and presentations.

9.2 Public dissemination

This study will be registered in a publicly assessable registry, which is WHO-approved as a primary study registry.

Furthermore, actions may be taken to communicate study-related content to the broad public, e.g. via press releases etc. All actions in this regard must be agreed with and approved by the chief investigator. The PRoVENT 2+ and the PROVEnet Research Group, as well as the ESAIC must be acknowledged in all communications.

10. FUNDING AND SUPPORT

PRoVENT 2+ is financially supported by the European Society of Anaesthesiology and Intensive Care (ESAIC) in terms of a dedicated research group (RG). The submission for national or local peer-reviewed grants to fund national or local implementation of the PRoVENT 2+ study is allowed conditional on prior written authorization from the chief investigator and the core SC. The core SC members transparently declare their potential conflicts of interest whenever necessary.

11. INSURANCE

Due the observational nature of the PRoVENT 2+ study, there is a no study-related risk for participants. In contrast to interventional studies, e.g. on medical products, medicinal products or drugs, there is no specific study-related insurance required. However, the public liability insurance of each participating centre may cover the liability risks of the respective centre. The local PI is responsible for checking, coordinating and ensuring compliance with local regulations regarding necessary insurances. In particular, the responsibility for any clinical negligence of its staff lies with

the respective local centre. The coordinating centre does not provide insurance for local centres. In case a written informed consent was mandated, it will be pointed out that there is no study-specific insurance for participants during the consenting process and in the patient information sheet.

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Appendix 1 – Patient information sheet, if mandated

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Patient information sheet

Dear Sir or Madam,

You are invited to participate in a research study of the Protective Ventilation Network (PROVEnet), supported by the European Society of Anaesthesiology and Intensive Care (ESAIC).

Before deciding whether or not to participate in this study, we would ask you to carefully read the following information which explains the study's objective and the implications of your possible participation.

Background and study objective

Mechanical ventilation is one of the most frequently used and life-saving intervention in the field of intensive care medicine. However, adherence to lung-protective ventilation strategies and evidence-based guidelines is paramount to favourable clinical outcomes. Scientific progress and updating of existing guidelines requires review of current clinical practice and, thus, recurring data collections. However, data on the practice of mechanical ventilation were obtained a considerable time ago and since then, evidence has grown, clinical procedures and routine may have changed in the meanwhile, and awareness for ventilator-induced lung injury (VILI) and associated risk factors may have risen over the last years. Therefore, the main objective is to investigate epidemiologic characteristics and practice of mechanical ventilation of adult intensive care unit patients undergoing invasive mechanical ventilation.

Study description

PRoVENT 2⁺ is an observational prospective clinical study, in which an investigator in your centre will collect information from your medical charts concerning previous illnesses, your health status, the applied mechanical ventilation strategy and other care during your stay on the intensive care unit.

What does your participation involve?

Whether you decide to participate or not will not affect the medical care you are going to receive, because this is an observational study. The treating doctors will not modify their decisions, neither during your hospital stay nor after your discharge, because you have participated or not. All medical diagnostics, interventions or treatments are performed within clinical routine care and not study-related. The medical data collected for scientific purpose of the study is limited to data generated in routine clinical care. Your medical data will be assessed at certain defined time points, i.e. at the day of enrolment, 1-5, 7±1, 14±2, 21±2, 28±2, and 90±2 days thereafter, if applicable. Data will be collected until discharge from the hospital. However, if you are discharged before day 28±2 or 90±2, the study team will be contacting you at those time points. Your participation automatically ends with the last time point available.

Risks and benefits

Due to its observational character, this study does not include any study-specific intervention. As such, there is no additional medical risk associated with your participation. The theoretical risk of data leakage or unintended identification of participants is prevented by strict data protection rules and efficient pseudonymisation. The close monitoring and documentation associated with study participation might represent an individual benefit for the respective patient. Furthermore, by participating you could help to advance medical/scientific knowledge, which may benefit other patients and/or future generations of patients.

Withdrawal from the study

Even though you have agreed to participate, you may leave the study whenever you wish and, moreover, without having to offer any kind of explanation. You will not have to justify your decision. Withdrawal from the study will not affect your medical treatments in any kind.

Results of the study

The results obtained in the present study will be published in a scientific/medical journal. Data included in this publication will be summarized and anonymized. Individual participants cannot be identified from scientific publications.

Insurance

There is no study-specific insurance for your participation in this study. However, the public liability insurance of each participating centre may cover the liability risks of the respective centre.

Do I receive financial compensation for my participation?

Participation in the study is free of charge for you. You will not be paid for your participation in this study.

Data privacy and data protection principles

In order to carry out the study it will be necessary to consult and make use of some of the information that appears in your medical record. Your acceptance will authorize us to consult, process, and store information in a computerized, secured, central study database. The stored data are pseudonymised, i.e. provided with a code instead of your name. Individual participants can only be identified at the local study centre by the doctors and scientists involved on site. Data will be stored for 10 years. Only pseudonymised data is passed on to the coordinating centre (Dept. of Anesthesiology and Intensive Care Medicine, University Hospital Carl Gustav Carus at TU Dresden, Dresden, Germany) and the involved statistician (Monash University, Melbourne, Australia) via the online database. No data concerning personal identification will be stored in the central study database. You cannot be identified from the data passed on. The data will only be passed on for the statistical evaluation of this study and never to third parties.

According to European Law (where applicable), you have the right to:

- withdraw consent regarding the processing of personal data.

- receive information about the personal data concerning you that are collected, processed or, if applicable, transferred in the context of the clinical study.
- have inaccurate personal data concerning you rectified.
- have personal data concerning you erased, e.g. if you end your participation in the study prematurely. However, medical data collected until the moment of withdrawal will be anonymized and may be further processed as scientifically intended.
- request restriction of processing under certain circumstances, i.e. the data may only be stored, not processed. However, this right may be restricted by conflicting legal regulations.
- obtain the personal data relating to you that you have provided to the clinical study/investigator, i.e. to request that this data be transferred either to you or, where technically feasible, to another body designated by you.
- object at any time to specific decisions or measures concerning the processing of personal data relating to you.
- lodge a complaint with the competent supervisory authority if your rights are not adequately taken into account.

In order to execute any of the above-mentioned rights, please immediately contact the local principle investigator of your centre. The responsible body for data processing is the University Hospital Carl Gustav Carus at the TU Dresden (Dept. of Anesthesiology and Intensive Care Medicine). The data protection officer at the University Hospital Carl Gustav Carus Dresden can be contacted as follows if you have any questions about data protection: dsv@ukdd.de.

The data protection officer responsible for your corresponding clinic is (if different from above):

_____

_____ (name and contact).

Who can I contact in case of any further questions?

Any inquiries concerning the study should be addressed to:

Local principle investigator: _____ Phone:_____

Thank you for taking time to read this information sheet.

Appendix 1-DE-SN – Patienteninformation (DE-SN)

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺

(Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Patienteninformation

Sehr geehrte Patientin, sehr geehrter Patient,

Sie kommen für die Teilnahme an einer wissenschaftlichen Studie zur aktuellen Praxis der maschinellen Beatmung auf Intensivstationen in Betracht. Die Studie wird von einer Gruppe von Wissenschaftlern (*Protective Ventilation Network*, PROVEnet) durchgeführt und von der Europäischen Gesellschaft für Anästhesiologie und Intensivmedizin (ESAIC) unterstützt.

Bevor Sie sich für oder gegen eine Teilnahme entscheiden, bitten wir Sie, diese Patienteninformation aufmerksam zu lesen. Hier gehen wir auf die Ziele der Studie ein und beleuchten, was eine Teilnahme für sie bedeutet.

Hintergründe und Ziel der Studie

Die maschinelle Beatmung ist eine lebensrettende Maßnahme und gehört zu den am häufigsten durchgeführten Therapien auf Intensivstationen weltweit. Dabei ist die Anwendung Lungen-schonender Beatmungsstrategien entsprechend evidenzbasierter Leitlinien von größter Bedeutung für bestmögliche Behandlungsergebnisse. Um wissenschaftlichen Fortschritt zu erreichen und existierende Leitlinien auf einem aktuellen Stand zu halten, ist es immer wieder vonnöten, die angewandten Strategien zu überprüfen und wiederholt Daten aus der klinischen Praxis zu sammeln. Die letzte große Datenerhebung zur klinischen Praxis von maschineller Beatmung liegt schon einige Zeit zurück. Seither wurden neue wissenschaftliche Erkenntnisse gewonnen. Zudem hat sich möglicherweise ein größeres Bewusstsein für Beatmungs-assoziierte Komplikationen (z.B. Beatmungs-assoziierte Lungenschädigungen) und deren Risikofaktoren entwickelt. Das alles könnte in der Zwischenzeit in veränderten klinischen Abläufen, Strategien und klinischen Standards resultiert haben. Aus diesem Grund zielen wir mit der Durchführung dieser Studie darauf ab, die epidemiologischen Eigenschaften der Patienten sowie die aktuelle Praxis der maschinellen Beatmung auf Intensivstationen abzubilden.

Studienbeschreibung

PRoVENT 2⁺ ist eine klinische prospektive Beobachtungsstudie, bei welcher ein Prüfarzt aus der Klinik, in der Sie sich in Behandlung befinden, Informationen aus Ihren medizinischen Unterlagen, z.B. Patientenakte, Fieberkurve und klinischem Informationssystem (KIS), erhebt. Diese Daten betreffen Ihren Gesundheitszustand, Vorerkrankungen, die Art und Weise der maschinellen Beatmung, sowie weiterer Behandlungen, welche Sie während Ihres Aufenthalts auf Intensivstation erhalten.

Was bedeutet eine Teilnahme für mich?

Die Teilnahme ist freiwillig. Ob Sie sich für oder gegen eine Teilnahme entscheiden, beeinflusst **nicht** die Behandlung und Pflege, welche Sie während Ihres Aufenthalts erhalten werden. Da es sich um

eine Beobachtungsstudie handelt, bei der keine Studien-spezifischen Maßnahmen erfolgen, werden die Entscheidungen der behandelnden Ärzte von Ihrer Studienteilnahme nicht beeinflusst. Durchgeführte Diagnostik, Behandlungen und/oder Eingriffe ergeben sich immer aus der klinischen Routine. Die für wissenschaftliche Zwecke erhobenen medizinischen Daten beschränken sich auf jene, welche durch die klinische Routineversorgung anfallen. Die Datenerhebung erfolgt zu definierten Zeitpunkten. Diese sind, sofern möglich, der Tag des Studieneinschlusses, sowie die Tage 1-5, 7±1, 14±2, 21±2, 28±2, und 90±2. Die Datenerhebung erfolgt bis zu dem Zeitpunkt des Verlassens des Krankenhauses. Sollte dies vor Tag 28±2 bzw. 90±2 passieren, werden Sie zu diesen zwei Zeitpunkten vom Studienteam kontaktiert. Die Studienteilnahme endet automatisch mit dem letzten erhobenen Zeitpunkt.

Individueller Nutzen und Risiko für den Patienten

Da es sich um eine Beobachtungsstudie handelt, kommt es zu keinen Studien-spezifischen Prozeduren. Daher sind Sie durch die Teilnahme keinem zusätzlichen medizinischen Risiko ausgesetzt. Dem theoretischen Risiko eines Datenlecks oder der ungewollten Identifikation von Teilnehmern begegnen wir durch Einhaltung strengster Datenschutzrichtlinien.
Da es sich um eine Beobachtungsstudie ohne Studien-spezifische Prozeduren handelt, ergibt sich für Sie durch die Teilnahme an dieser Studie kein unmittelbar greifbarer Nutzen. Allerdings erfolgt die Datenerhebung im Rahmen von Studien sehr detailliert und engmaschig, wobei der Studienarzt in engem Kontakt zu Ihren behandelnden Ärzten steht und diese auf etwaige besondere Befunde oder Auffälligkeiten hinweisen wird, was durchaus als Vorteil von Studienteilnahmen gewertet werden kann. Abgesehen davon können Sie durch Ihre Teilnahme wesentlich dazu beitragen, medizinisches Wissen zu erweitern, von dem zukünftige Patienten und/oder zukünftige Generationen profitieren können.

Widerruf der Einwilligung

Auch nachdem Sie bereits Ihre Einwilligung erteilt haben, können Sie die Teilnahme an der Studie zu jedem beliebigen Zeitpunkt widerrufen. Sie müssen diese Entscheidung weder erklären, noch müssen Sie sich dafür rechtfertigen. Der Widerruf Ihrer Teilnahme hat keinen Einfluss auf die medizinische Behandlung, die Sie erhalten.

Ergebnisse der Studie

Die Ergebnisse dieser Studie werden in einer medizinischen/wissenschaftlichen Fachzeitschrift veröffentlicht. Entsprechende Daten werden in diesem Zusammenhang ausschließlich zusammengefasst und anonymisiert veröffentlicht. Rückschlüsse auf die Identität einzelner Teilnehmer sind somit aus diesen Veröffentlichungen nicht möglich.

Versicherung

Eine studienspezifische Versicherung für ihre Teilnahme existiert nicht. Jedoch deckt die Haftpflichtversicherung jedes teilnehmenden Zentrums etwaige erwachsende Ansprüche.

Erhalte ich eine finanzielle Aufwandsentschädigung für die Teilnahme?

Durch die Studienteilnahme ergeben sich für Sie keine Kosten. Eine finanzielle Aufwandsentschädigung ist für die Studienteilnahme nicht vorgesehen.

Datenschutz

Im Rahmen der Durchführung dieser Studie ist es notwendig, Gesundheitsdaten, die sich in Ihren medizinischen Aufzeichnungen finden, zu erheben und zu nutzen. Ihre in der klinischen Routineversorgung erhobenen Daten können auch ohne Ihre Einwilligung auf Grundlage des §29 Absatz (1) und (3) Sächs. Krankenhausgesetz (SächsKHG) für wissenschaftliche Forschung genutzt werden. Dies bezieht sich auf den Zeitraum Ihres Krankenhausaufenthaltes, nicht aber auf nachfolgende Zeitpunkte. Da wir aber auch Informationen über Ihren Gesundheitszustand ca. einen und drei Monate nach Beginn Ihrer Teilnahme sammeln und auswerten wollen, bitten wir Sie hierfür um Einwilligung zur Teilnahme und Datenverarbeitung.

Die Speicherung Ihrer Daten erfolgt pseudonymisiert in einer gesicherten, elektronischen, zentralen Datenbank (bis zehn Jahre nach Abschluss der Studie). Das bedeutet, dass Ihre Daten nicht zusammen mit Ihrem Namen, Geburtstag oder anderen direkt identifizierenden Informationen, sondern lediglich mit einem Zahlencode verknüpft gespeichert werden. Die einzelnen Teilnehmer können dabei anhand des individuellen Zahlencodes lediglich durch die beteiligten Ärzte und Wissenschaftler der jeweiligen behandelnden Klinik identifiziert werden, nicht aber durch das koordinierende Studienzentrum, den Statistiker oder sonstige Dritte. Eine Weitergabe von Daten erfolgt ausschließlich zum Zwecke der statistischen Auswertung an das koordinierende Zentrum (Universitätsklinikum Carl Gustav Carus an der TU Dresden, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie) und den vom Studienleiter beauftragten Statistiker (Prof. Ary Serpa Neto, Monash University, Melbourne, Australien) auf Grundlage §29 (3) SächsKHG bzw. Ihrer Einwilligung. Für Australien gibt es derzeit keinen Angemessenheitsbeschluss der EU-Kommission, d.h. dort kann theoretisch ein niedrigeres Datenschutzniveau herrschen als in der EU.

Auf Grundlage der Europäischen Datenschutzgrundverordnung haben Sie folgende Rechte:

- Widerruf der Einwilligung zur Verarbeitung persönlicher Daten.
- Zu erfahren, welche persönlichen Daten gesammelt, verarbeitet oder im Rahmen der klinischen Studie weitergegeben werden.
- Korrektur von erhobenen, falschen persönlichen Daten.
- Löschung Ihrer persönlichen Daten, zum Beispiel nach vorzeitiger Beendigung der Studienteilnahme. Daten welche bis zum Zeitpunkt des Widerrufs erhoben wurden, werden anonymisiert und weiterverarbeitet, sofern für die Studie notwendig.
- Einschränkung der Verarbeitung von Daten unter bestimmten Umständen. Zum Beispiel erlauben Sie nur die Speicherung, nicht jedoch Verarbeitung von Daten. Dieses Recht kann jedoch aufgrund geltender Gesetze, welche damit in Konflikt stehen, eingeschränkt sein.
- Erhalt der persönlichen Daten, welche Sie dem Studienteam zur Verfügung gestellt haben. Diese Daten können dann zum Beispiel an Sie, oder falls technisch möglich, an eine von Ihnen bestellte Person übermittelt werden.
- Widerspruch gegen spezielle Entscheidungen oder Maßnahmen, die die Verarbeitung Ihrer persönlichen Daten betreffen.
- Beschwerde bei der zuständigen Aufsichtsbehörde, sollte Ihren Rechten nicht angemessen Rechnung getragen werden.

Sollten Sie von einem der oben genannten Rechte Gebrauch machen wollen, nehmen Sie bitte unverzüglich Kontakt zum lokalen Prüfer Ihres Zentrums auf. Für weitere Fragen bezüglich Datenschutz steht Ihnen ebenfalls die zuständige Datenschutzbeauftragte zur Verfügung.

Die verantwortliche Stelle für die Datenverarbeitung ist das Universitätsklinikum Carl Gustav Carus an der TU Dresden (Klinik und Poliklinik für Anästhesiologie und Intensivtherapie). Die Datenschutzbeauftragte am Universitätsklinikum Carl Gustav Carus Dresden kann bei Fragen zum Datenschutz wie folgt erreicht werden: dsv@ukdd.de.

Der/die für Ihre behandelnde Klinik zuständige Datenschutzbeauftragte ist (falls von o.g. abweichend):

_____

_____

An wen kann ich mich generell bei Fragen wenden?

Für Anliegen und Fragen bezüglich der Studie wenden Sie sich bitte an den Studienleiter:

Dr. med. Martin Scharffenberg, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universitätsklinikum Carl Gustav Carus Dresden, Fetscherstraße 74, 01307 Dresden. Telefon: 0351 458 4110, E-Mail: martin.scharffenberg@ukdd.de

oder Ihren lokalen Prüfarzt:_____ Telefon:_____

Vielen Dank, dass Sie sich die Zeit genommen haben, diese Patienteninformation durchzulesen.

Appendix 2 – Patient informed consent form, if mandated

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2+) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Patient informed consent form

I, _____ (first and last name), born on D D | M M | Y Y Y Y,

- have read the PRoVENT 2+ study information sheet for the patient,
- have been able to ask questions concerning the study, and
- have received sufficient information with respect to the study.

I have spoken to _____ (first and last name of the attending researcher), and understand

- that my participation in the study will not affect any medical care that I should receive from the hospital,
- that my participation is voluntary,
- that I can withdraw from the study whenever I wish, without having to give any explanations, and without suffering any repercussions with respect to my medical attention,
- my rights regarding data protection.

I freely give my consent to participate in the study and agree that my medical data will be processed for the scientific purpose of the study. If necessary, the collected data may be forwarded pseudonymized (encrypted) to the University Hospital Carl Gustav Carus at TU Dresden and Monash University, Melbourne, Australia for the purpose of scientific evaluation.

Place: _____, Date: _____

Signature of Participant: Signature of Researcher:

_____ _____

Appendix 2-DE-SN – Patienteneinwilligung (DE-SN)

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺

(Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Einwilligungserklärung für Patienten

Ich, _____ (Vor- und Nachname), geboren am T T | M M | J J J J ,

- habe die Patienteninformation der PRoVENT 2⁺ Studie gelesen und verstanden,
- hatte die Möglichkeit, Fragen bezüglich der Studie zu stellen und habe diese zufriedenstellend beantwortet bekommen.
- hatte ausreichend Bedenkzeit und habe bezüglich der Studie ausreichend Informationen erhalten.

Ich wurde in einem persönlichen Gespräch mit _____ (Vor- und Nachname des Prüfarztes) darüber aufgeklärt, dass

- die Teilnahme an der Studie keinen Einfluss auf die medizinische Behandlung während des Klinikaufenthalts hat,
- die Teilnahme freiwillig ist und
- ich jederzeit ohne Angabe von Gründen mein Einverständnis widerrufen kann. Dadurch entstehen mir keinerlei Nachteile bezüglich meiner medizinischen Behandlung.
- Ich wurde über meine Rechte bezüglich der Verarbeitung meiner Daten aufgeklärt.

Ich willige hiermit freiwillig in die Teilnahme an dieser Studie ein. Ich bin mit der Erhebung und Verarbeitung meiner medizinischen Daten zum Zwecke der Durchführung der PRoVENT 2⁺ Studie einverstanden. Soweit erforderlich, dürfen die erhobenen Daten pseudonymisiert (verschlüsselt) zum Zweck der wissenschaftlichen Auswertung weitergegeben werden an das Universitätsklinikum Carl Gustav Carus an der TU Dresden sowie die Monash University, Melbourne, Australien. Ein Exemplar der Patienteninformation sowie eine Kopie der Einwilligungserklärung habe ich erhalten.

Ort: _____, Datum: _____

Unterschrift Teilnehmer: Unterschrift Prüfarzt:

_____ _____

Appendix 3 – LAR information sheet, if mandated

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Information sheet for legally authorised representative (LAR) / independent consultant doctor

Dear Sir or Madam,

The person you represent is invited to participate in a research study of the Protective Ventilation Network (PROVEnet), supported by the European Society of Anaesthesiology and Intensive Care (ESAIC).

Before you decide for this person whether or not he/she should take part in the study, we ask you to read this document carefully. The following information explain the study's objective and the implications of his/her possible participation.

Background and study objective

Mechanical ventilation is one of the most frequently used and life-saving intervention in the field of intensive care medicine. However, adherence to lung-protective ventilation strategies and evidence-based guidelines is paramount to favourable clinical outcomes. Scientific progress and updating of existing guidelines requires review of current clinical practice and, thus, recurring data collections. However, data on the practice of mechanical ventilation were obtained a considerable time ago and since then, evidence has grown, clinical procedures and routine may have changed in the meanwhile, and awareness for ventilator-induced lung injury (VILI) and associated risk factors may have risen over the last years. Therefore, the main objective is to investigate epidemiologic characteristics and practice of mechanical ventilation of adult intensive care unit patients undergoing invasive mechanical ventilation.

Study description

PRoVENT 2⁺ is an observational prospective clinical study, in which an investigator of the hospital he/she is admitted to will collect information from the medical charts concerning previous illnesses, the health status, the applied mechanical ventilation strategy and other care of the person you represent during his/her stay on the intensive care unit.

What does a participation involve?

Whether you decide for the person you represent to participate or not will not affect the medical care he/she is going to receive, because this is an observational study. The treating doctors will not modify their decisions, neither during his/her hospital stay nor after his/her discharge, because he/she has participated or not. All medical diagnostics, interventions or treatments are performed within clinical routine care and not study-related. The medical data collected for scientific purpose of the study is limited to data generated in routine clinical care. His/her medical data will be assessed at certain defined time points, i.e. at the day of enrolment, 1-5, 7±1, 14±2, 21±2, 28±2, and 90±2 days thereafter, if applicable. Data will be collected until discharge from the hospital. However, if the

patient is discharged before day 28±2 or 90±2, he/she will be contacted by the study team at those time points. The patients participation automatically ends with the last time point available.

Risks and benefits

Due to its observational character, this study does not include any study-specific intervention. As such, there is no additional medical risk associated with participation of the person you represent. The theoretical risk of data leakage or unintended identification of participants is prevented by strict data protection rules and efficient pseudonymisation. The close monitoring and documentation associated with study participation might represent an individual benefit for the respective patient. Furthermore, by participating he/she could help to advance medical/scientific knowledge, which may benefit other patients and/or future generations of patients.

Withdrawal from the study

Even if you had agreed to participate on behalf of the person who is not capable of giving consent, he/she may leave the study at any time point and, moreover, without having to offer any kind of explanation or justification of the decision. Withdrawal from the study will not affect his/her medical treatments in any kind.

Results of the study

The results obtained in the present study will be published in a scientific/medical journal. Data included in this publication will be summarized and anonymized. Individual participants cannot be identified from scientific publications.

Insurance

There is no study-specific insurance for his/her participation in this study. However, the public liability insurance of each participating centre may cover the liability risks of the respective centre.

Is there a financial compensation for the study participation?

Participation in the study is free of charge for the person you represent. He/she will not be paid for his/her participation in this study.

Data privacy and data protection principles

In order to carry out the study it will be necessary to consult and make use of some of the information that appears in the medical record of the person you represent. Your acceptance on behalf of the person you represent will authorize us to consult, process, and store information in a computerized, secured, central study database. The stored data are pseudonymised, i.e. provided with a code instead of an actual name. Individual participants can only be identified at the local study centre by the doctors and scientists involved on site. Data will be stored for 10 years. Only pseudonymised data is passed on to the coordinating centre (Dept. of Anesthesiology and Intensive Care Medicine, University Hospital Carl Gustav Carus at TU Dresden, Dresden, Germany) and the involved statistician (Monash University, Melbourne, Australia) via the online database. No data concerning personal identification will be stored in the central study database. Participants cannot be identified from the data passed on. The data will only be passed on for the statistical evaluation of this study and never to third parties.

According to European Law (where applicable), participants have the right to:

- withdraw consent regarding the processing of their personal data.
- receive information about their personal data that are collected, processed or, if applicable, transferred in the context of the clinical study.
- have inaccurate personal data rectified.
- have their personal data erased, e.g. if participation in the study ends prematurely. However, medical data collected until the moment of withdrawal will be anonymized and may be further processed as scientifically intended.
- request restriction of processing under certain circumstances, i.e. the data may only be stored, not processed. However, this right may be restricted by conflicting legal regulations.
- obtain the their personal data that were provided to the clinical study/investigator, i.e. to request that this data be transferred either to them or, where technically feasible, to another body designated by the participant.
- object at any time to specific decisions or measures concerning the processing of their personal data.
- lodge a complaint with the competent supervisory authority if your rights are not adequately taken into account.

In order to execute any of the above-mentioned rights, please immediately contact the local principle investigator of your centre. The responsible body for data processing is the University Hospital Carl Gustav Carus at the TU Dresden (Dept. of Anesthesiology and Intensive Care Medicine). The data protection officer at the University Hospital Carl Gustav Carus Dresden can be contacted as follows if you have any questions about data protection: dsv@ukdd.de.

The data protection officer responsible for your corresponding clinic is (if different from above):
_____

_____ (name and contact).

Who can I contact in case of any further questions?

Any inquiries concerning the study should be addressed to:

Local principle investigator: _____ Phone:_____

Thank you for taking time to read this information sheet.

Appendix 3-DE-SN – Betreuer-Information (DE-SN)

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺

(Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Information für den Betreuer/Vorsorgebevollmächtigten

Sehr geehrte Dame, sehr geehrter Herr,

Der Patient, den Sie vertreten, kommt für eine wissenschaftliche Studie zur aktuellen Praxis der maschinellen Beatmung auf Intensivstationen in Betracht. Die Studie wird von einer Gruppe von Wissenschaftlern (*Protective Ventilation Network*, PROVEnet) durchgeführt und von der Europäischen Gesellschaft für Anästhesiologie und Intensivmedizin (ESAIC) unterstützt.

Bevor Sie sich, im Namen des Patienten, für oder gegen eine Teilnahme entscheiden, bitten wir Sie, diese Information aufmerksam zu lesen. Hier gehen wir auf die Ziele der Studie ein und beleuchten, was eine Teilnahme für den betreuten Patienten bedeutet.

Hintergründe und Ziel der Studie

Die maschinelle Beatmung ist eine lebensrettende Maßnahme und gehört zu den am häufigsten durchgeführten Therapien auf Intensivstationen weltweit. Dabei ist die Anwendung Lungen-schonender Beatmungsstrategien entsprechend evidenzbasierter Leitlinien von größter Bedeutung für bestmögliche Behandlungsergebnisse. Um wissenschaftlichen Fortschritt zu erreichen und existierende Leitlinien auf einem aktuellen Stand zu halten, ist es immer wieder vonnöten, die angewandten Strategien zu überprüfen und wiederholt Daten aus der klinischen Praxis zu sammeln. Die letzte große Datenerhebung zur klinischen Praxis von maschineller Beatmung liegt schon einige Zeit zurück. Seither wurden neue wissenschaftliche Erkenntnisse gewonnen. Zudem hat sich möglicherweise ein größeres Bewusstsein für Beatmungs-assoziierte Komplikationen (z.B. Beatmungs-assoziierte Lungenschädigungen) und deren Risikofaktoren entwickelt. Das alles könnte in der Zwischenzeit in veränderten klinischen Abläufen, Strategien und klinischen Standards resultiert haben. Aus diesem Grund zielen wir mit der Durchführung dieser Studie darauf ab, die epidemiologischen Eigenschaften der Patienten sowie die aktuelle Praxis der maschinellen Beatmung auf Intensivstationen abzubilden.

Studienbeschreibung

PRoVENT 2⁺ ist eine klinische prospektive Beobachtungsstudie, bei welcher ein Prüfarzt aus der Klinik, in der sich der Patientin Behandlung befindet, Informationen aus den medizinischen Unterlagen, z.B. Patientenakte, Fieberkurve und klinischem Informationssystem (KIS), erhebt. Diese Daten betreffen den Gesundheitszustand, Vorerkrankungen, die Art und Weise der maschinellen Beatmung, sowie weitere Behandlungen, welche der Patient während seines Aufenthalts auf Intensivstation erhält.

Was bedeutet eine Teilnahme für den Patienten?

Die Teilnahme ist freiwillig. Eine Entscheidung für oder gegen eine Teilnahme beeinflusst **nicht** die Behandlung und Pflege, welche die von Ihnen vertretene Person während des Aufenthalts erhalten wird, da es sich um eine Beobachtungsstudie handelt, bei der keine Studien-spezifischen Maßnahmen erfolgen. Diagnostik, Behandlungen und/oder Eingriffe ergeben sich immer aus der klinischen Routine und nicht Studien-bedingt. Die für wissenschaftliche Zwecke erhobenen medizinischen Daten beschränken sich auf jene, welche im Rahmen der klinischen Routineversorgung anfallen. Die Datenerhebung erfolgt zu definierten Zeitpunkten. Diese sind, sofern möglich, der Tag des Studieneinschlusses, sowie die Tage 1-5, 7±1, 14±2, 21±2, 28±2, und 90±2. Die Datenerhebung erfolgt bis zu dem Zeitpunkt des Verlassens des Krankenhauses. Sollte dies vor Tag 28±2 bzw. 90±2 passieren, wird der Patient zu diesen zwei Zeitpunkten vom Studienteam kontaktiert. Die Studienteilnahme endet automatisch mit dem letzten erhobenen Zeitpunkt.

Individueller Nutzen und Risiko für den Patienten

Da es sich um eine Beobachtungsstudie handelt, ist der Patient durch die Teilnahme keinem zusätzlichen medizinischen Risiko ausgesetzt. Dem theoretischen Risiko eines Datenlecks oder der ungewollten Identifikation von Teilnehmern begegnen wir durch Einhaltung strengster Datenschutzrichtlinien. Da es sich um eine Beobachtungsstudie ohne Studien-spezifische Prozeduren handelt, ergibt sich für den Patienten durch die Teilnahme an dieser Studie kein unmittelbar greifbarer Nutzen. Allerdings erfolgt die Datenerhebung im Rahmen von Studien sehr detailliert und engmaschig, wobei der Studienarzt in engem Kontakt zu den behandelnden Ärzten steht und diese auf etwaige besondere Befunde oder Auffälligkeiten hinweisen wird, was durchaus als Vorteil von Studienteilnahmen gewertet werden kann. Abgesehen davon kann der Patient durch seine Teilnahme wesentlich dazu beitragen, medizinisches Wissen zu erweitern, von dem zukünftige Patienten und/oder zukünftige Generationen profitieren können.

Widerruf der Einwilligung

Auch nachdem Sie im Namen des Patienten Ihre Einwilligung bereits erteilt haben, können Sie die Teilnahme an der Studie zu jedem beliebigen Zeitpunkt widerrufen. Sobald der Patient wieder geschäftsfähig ist, kann dieser natürlich in eigenem Namen die durch Sie gegebene Einwilligung widerrufen. Diese Entscheidungen müssen weder erklärt, noch in irgendeiner Form gerechtfertigt werden. Der Widerruf einer Teilnahme hat keinen Einfluss auf die medizinische Behandlung, die der Patient erhält.

Ergebnisse der Studie

Die Ergebnisse dieser Studie werden in einer medizinischen/wissenschaftlichen Fachzeitschrift veröffentlicht. Entsprechende Daten werden in diesem Zusammenhang ausschließlich zusammengefasst und anonymisiert veröffentlicht. Rückschlüsse auf die Identität einzelner Teilnehmer sind somit aus diesen Veröffentlichungen nicht möglich.

Versicherung

Eine studienspezifische Versicherung für die Teilnahme existiert nicht. Jedoch deckt die Haftpflichtversicherung jedes teilnehmenden Zentrums etwaig erwachsende Ansprüche.

Existiert eine finanzielle Aufwandsentschädigung für die Teilnahme?

Durch die Studienteilnahme ergeben sich für Sie oder die durch Sie vertretene Person keine Kosten. Eine finanzielle Aufwandsentschädigung für die Studienteilnahme ist nicht vorgesehen.

Datenschutz

Im Rahmen der Durchführung dieser Studie ist es notwendig, Gesundheitsdaten, die sich in den medizinischen Aufzeichnungen der von Ihnen betreuten Person finden, zu erheben und zu nutzen. Die in der klinischen Routineversorgung der von Ihnen betreuten Person erhobenen Daten können auch ohne Einwilligung auf Grundlage des §29 Absatz (1) und (3) Sächs. Krankenhausgesetz (SächsKHG) für wissenschaftliche Forschung genutzt werden. Dies bezieht sich auf den Zeitraum des Krankenhausaufenthaltes, nicht aber auf nachfolgende Zeitpunkte. Da wir aber auch Informationen über den Gesundheitszustand der von Ihnen betreuten Person ca. einen und drei Monate nach Beginn der Teilnahme sammeln und auswerten wollen, bitten wir Sie hierfür um Einwilligung zur Teilnahme und Datenverarbeitung.

Die Speicherung der Daten erfolgt pseudonymisiert in einer gesicherten, elektronischen, zentralen Datenbank (bis zehn Jahre nach Abschluss der Studie). Das bedeutet, dass die Daten nicht zusammen mit dem Namen, Geburtstag oder anderen direkt identifizierenden Informationen der von Ihnen betreuten Person, sondern lediglich mit einem Zahlencode verknüpft gespeichert werden. Die einzelnen Teilnehmer können dabei anhand des individuellen Zahlencodes lediglich durch die beteiligten Ärzte und Wissenschaftler der jeweiligen behandelnden Klinik identifiziert werden, nicht aber durch das koordinierende Studienzentrum, den Statistiker oder sonstige Dritte. Eine Weitergabe von Daten erfolgt ausschließlich zum Zwecke der statistischen Auswertung an das koordinierende Zentrum (Universitätsklinikum Carl Gustav Carus an der TU Dresden, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie) und den vom Studienleiter beauftragten Statistiker (Prof. Ary Serpa Neto, Monash University, Melbourne, Australien) auf Grundlage §29 (3) SächsKHG bzw. Ihrer Einwilligung. Für Australien gibt es derzeit keinen Angemessenheitsbeschluss der EU-Kommission, d.h. dort kann theoretisch ein niedrigeres Datenschutzniveau herrschen als in der EU.

Auf Grundlage der Europäischen Datenschutzgrundverordnung bestehen folgende Rechte:

- Widerruf der Einwilligung zur Verarbeitung persönlicher Daten.
- Zu erfahren, welche persönlichen Daten gesammelt, verarbeitet oder im Rahmen der klinischen Studie weitergegeben werden.
- Korrektur von erhobenen, falschen persönlichen Daten.
- Löschung Ihrer persönlichen Daten, zum Beispiel nach vorzeitiger Beendigung der Studienteilnahme. Daten welche bis zum Zeitpunkt des Widerrufs erhoben wurden, werden anonymisiert und weiterverarbeitet, sofern für die Studie notwendig.
- Einschränkung der Verarbeitung von Daten unter bestimmten Umständen. Zum Beispiel erlauben Sie nur die Speicherung, nicht jedoch Verarbeitung von Daten. Dieses Recht kann jedoch aufgrund geltender Gesetze, welche damit in Konflikt stehen, eingeschränkt sein.
- Erhalt der persönlichen Daten, welche Sie dem Studienteam zur Verfügung gestellt haben. Diese Daten können dann zum Beispiel an Sie, oder falls technisch möglich, an eine von Ihnen bestellte Person übermittelt werden.
- Widerspruch gegen spezielle Entscheidungen oder Maßnahmen, die die Verarbeitung Ihrer persönlichen Daten betreffen.

- Beschwerde bei der zuständigen Aufsichtsbehörde, sollte Ihren Rechten nicht angemessen Rechnung getragen werden.

Sollten Sie oder die von Ihnen betreute Person von einem der oben genannten Rechte Gebrauch machen wollen, nehmen Sie bzw. die von Ihnen betreute Person bitte unverzüglich Kontakt zum lokalen Prüfer des jeweiligen Zentrums auf. Für weitere Fragen bezüglich Datenschutz steht Ihnen ebenfalls die zuständige Datenschutzbeauftragte zur Verfügung.

Die verantwortliche Stelle für die Datenverarbeitung ist das Universitätsklinikum Carl Gustav Carus an der TU Dresden (Klinik und Poliklinik für Anästhesiologie und Intensivtherapie). Die Datenschutzbeauftragte am Universitätsklinikum Carl Gustav Carus Dresden kann bei Fragen zum Datenschutz wie folgt erreicht werden: dsv@ukdd.de.

Der/die für Ihre behandelnde Klinik zuständige Datenschutzbeauftragte ist (falls von o.g. abweichend):

_____

_____

An wen kann ich mich generell bei Fragen wenden?

Für Anliegen und Fragen bezüglich der Studie wenden Sie sich bitte an den Studienleiter:

Dr. med. Martin Scharffenberg, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universitätsklinikum Carl Gustav Carus Dresden, Fetscherstraße 74, 01307 Dresden. Telefon: 0351 458 4110, E-Mail: martin.scharffenberg@ukdd.de

oder Ihren lokalen Prüfarzt:_____ Telefon:_____

Vielen Dank, dass Sie sich die Zeit genommen haben, diese Informationen durchzulesen.

Appendix 4 – LAR informed consent form, if mandated

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Legally authorised representative (LAR) informed consent form

With respect to the proposal that _____ (patient´s first and last name), born on D D | M M | Y Y Y Y, participates in the above-mentioned study,

I, _____ (LAR´s first and last name),

as _____ (relationship with the patient)

declare that I

- have read the PRoVENT 2+ study information sheet for the LAR,
- have been able to ask questions concerning the study, and
- have received sufficient information with respect to the study.

I have spoken to _____ (first and last name of the attending researcher), and understand

- that participation in the study will not affect any medical care that the patient I am representing should receive from the hospital,
- that his/her participation is voluntary,
- that he/she can withdraw from the study whenever he/she wishes, without having to give any explanations, and without suffering any repercussions with respect to his/her medical attention,
- his/her rights regarding data protection.

I freely give my consent for the above-mentioned patient to participate in the study and agree that his/her medical data will be processed for the scientific purpose of the study. If necessary, the collected data may be forwarded pseudonymized (encrypted) to the University Hospital Carl Gustav Carus at TU Dresden and Monash University, Melbourne, Australia for the purpose of scientific evaluation.

Place: _____, Date: _____

Signature of LAR: Signature of Researcher:

_____ _____

Appendix 4-DE-SN – Betreuer-Einwilligung (DE-SN)

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺

(Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Einwilligungserklärung für den Betreuer/Vorsorgebevollmächtigten

Bezüglich der Teilnahme von_____ (Vor- und Nachname), geboren am T T | M M | J J J J , (nachfolgend „Patient“ genannt) an oben genannter Studie, erkläre

ich, _____ (Vor- und Nachname)

als _____ (Verhältnis zum o.g. Patienten), dass

- ich die Patienteninformation der PRoVENT 2⁺ Studie gelesen und verstanden habe,
- ich die Möglichkeit hatte, Fragen bezüglich der Studie zu stellen und diese zufriedenstellend beantwortet bekommen habe,
- ich ausreichend Bedenkzeit hatte und bezüglich der Studie ausreichend Informationen erhalten habe.

Ich wurde in einem persönlichen Gespräch mit _____ (Vor- und Nachname des Prüfarztes) darüber aufgeklärt, dass

- die Teilnahme an der Studie keinen Einfluss auf die medizinische Behandlung hat,
- die Teilnahme freiwillig ist und
- das Eiverständnis jederzeit ohne Angabe von Gründen durch mich, oder im weiteren Verlauf durch den Patienten selbst widerrufen werden kann. Dadurch entstehen dem Patienten keinerlei Nachteile bezüglich der medizinischen Behandlung.
- Ich wurde über die Rechte des Patienten bezüglich der Verarbeitung meiner Daten aufgeklärt.

Ich willige hiermit freiwillig in die Teilnahme des Patienten an dieser Studie ein. Ich bin mit der Erhebung und Verarbeitung seiner medizinischen Daten zum Zwecke der Durchführung der PRoVENT 2⁺ Studie einverstanden. Soweit erforderlich, dürfen die erhobenen Daten pseudonymisiert (verschlüsselt) zum Zweck der wissenschaftlichen Auswertung weitergegeben werden an das Universitätsklinikum Carl Gustav Carus an der TU Dresden sowie die Monash University, Melbourne, Australien. Ein Exemplar der Information sowie eine Kopie der Einwilligungserklärung habe ich erhalten.

Ort: _____, Datum: _____

Unterschrift Betreuer/Vorsorgebevollmächtigter: Unterschrift Prüfarzt:

_____ _____

Appendix 5 – Independent consultant doctor documents

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Information for the independent consultant doctor

Dear Sir or Madam,

You are invited to serve as an independent consultant doctor within the above-mentioned study. Please carefully read the following information.

Background and study objective

Mechanical ventilation is one of the most frequently used and life-saving intervention in the field of intensive care medicine. However, adherence to lung-protective ventilation strategies and evidence-based guidelines is paramount to favourable clinical outcomes. Scientific progress and updating of existing guidelines requires review of current clinical practice and, thus, recurring data collections. However, data on the practice of mechanical ventilation were obtained a considerable time ago and since then, evidence has grown, clinical procedures and routine may have changed in the meanwhile, and awareness for ventilator-induced lung injury (VILI) and associated risk factors may have risen over the last years. Therefore, the main objective is to investigate epidemiologic characteristics and practice of mechanical ventilation of adult intensive care unit patients undergoing invasive mechanical ventilation.

Study description

PRoVENT 2⁺ is an observational clinical study, in which routine medical data and clinical outcomes will be assessed, including medical history, health status, the applied mechanical ventilation strategy and other care.

What does the patient´s participation involve?

Participating or not participating in this study will not affect the medical care, because this is an observational study. The treating doctors will not modify their decisions. All medical diagnostics, interventions or treatments are performed within clinical routine care and not study-related. The medical data collected for scientific purpose of the study is limited to data generated in routine clinical care. These data will be assessed at certain defined time points, i.e. at the day of enrolment, 1-5, 7±1, 14±2, 21±2, 28±2, and 90±2 days thereafter, if applicable. Data will be collected until discharge from the hospital. However, if a patient is discharged before day 28±2 or 90±2, the study team will be contacting the patient at those two time points. The participation automatically ends with the last time point available.

Risks and benefits

Due to its observational character, this study does not include any study-specific intervention. As such, there is no additional medical risk associated with the participation. The theoretical risk of data leakage or unintended identification of participants is prevented by strict data protection rules and efficient pseudonymisation. The close monitoring and documentation associated with study participation might represent an individual benefit for the respective patient. Furthermore, the patient would help to advance medical/scientific knowledge, which may benefit other patients and/or future generations of patients.

Obtaining informed consent or withdrawal from the study

Once the patient regained the capability of giving informed consent, he or she must be approached with all relevant information. He or she must then decide whether or not to participate in this study. The patient may leave the study whenever he/she wishes and, moreover, without having to offer any kind of explanation. Withdrawal from the study will not affect medical treatments in any kind.

Results of the study

The results obtained in the present study will be published in a scientific/medical journal. Data included in this publication will be summarized and anonymized. Individual participants cannot be identified from scientific publications.

Insurance

There is no study-specific insurance for the participation in this study. However, the public liability insurance of each participating centre may cover the liability risks of the respective centre.

Financial compensation

Participation in the study is free of charge. The participant will not be paid for his/her participation in this study. Consultant doctors are also not paid for his/her efforts regarding this consenting process.

Data privacy and data protection principles

In order to carry out the study it will be necessary to consult and make use of some of the information that appears in the patient´s medical record. You may authorize the study team to consult, process, and store information in a computerized, secured, central study database. The stored data are pseudonymised, i.e. provided with a code instead of the patient´s name. Individual participants can only be identified at the local study centre by the doctors and scientists involved on site. Data will be stored for 10 years. Only pseudonymised data is passed on to the coordinating centre (Dept. of Anesthesiology and Intensive Care Medicine, University Hospital Carl Gustav Carus at TU Dresden, Dresden, Germany) and the involved statistician (Monash University, Melbourne, Australia) via the online database. No data concerning personal identification will be stored in the central study database. The individual patient cannot be identified from the data passed on. The data will only be passed on for the statistical evaluation of this study and never to third parties.

According to European Law (where applicable), participants have the right to:

- withdraw consent regarding the processing of personal data.
- receive information about the personal data concerning you that are collected, processed or, if applicable, transferred in the context of the clinical study.
- have inaccurate personal data concerning you rectified.
- have their personal data erased, e.g. if they end their participation in the study prematurely. However, medical data collected until the moment of withdrawal will be anonymized and may be further processed as scientifically intended.
- request restriction of processing under certain circumstances, i.e. the data may only be stored, not processed. However, this right may be restricted by conflicting legal regulations.
- obtain the personal data that the patient has provided to the clinical study/investigator, i.e. to request that this data be transferred either to the patient or, where technically feasible, to another body designated by the patient.

- object at any time to specific decisions or measures concerning the processing of personal data relating to the patient.
- lodge a complaint with the competent supervisory authority if the patient´s rights are not adequately taken into account.

In order to execute any of the above-mentioned rights, please immediately contact the local principle investigator of your centre. The responsible body for data processing is the University Hospital Carl Gustav Carus at the TU Dresden (Dept. of Anesthesiology and Intensive Care Medicine). The data protection officer at the University Hospital Carl Gustav Carus Dresden can be contacted as follows if you have any questions about data protection: dsv@ukdd.de.

The data protection officer responsible for your corresponding clinic is (if different from above):
_____

_____ (name and contact).

Who can I contact in case of any further questions?

Any inquiries concerning the study should be addressed to:

Local principle investigator: _____ Phone:_____

Thank you for taking time to read this information sheet.

Consenting process via independent consultant doctor

Title of the study: PRoVENT 2+

Name of the consultant doctor: _____

Mr./Mrs. _____, born on D D | M M | Y Y Y Y,

(Patient name)

suffers from _____

_____

_____.

The patient was examined by me to determine whether he or she is capable of recognising the nature, significance and consequences of his or her actions and participation in the study and of determining his or her will accordingly. The examination has shown that the patient

◯ is capable of giving consent. ◯ is NOT capable of giving consent.

The close monitoring and documentation associated with study participation may represent an individual benefit for the respective patient, while, in his or her individual current situation, an inclusion into the above-mentioned clinical study

◯ may represent an individual risk. ◯ may NOT represent an individual risk.

A declaration of informed consent could not be obtained. In particular, a legally authorised representative, who is responsible for the patient's health care, could not be consulted or appointed in time. Taking into account both the scientific need of the study and the conceivable risks of this observational, non-interventional clinical study, I consider the patient's participation in the clinical study

◯ to be justified. ◯ NOT to be justified.

I, the consultant doctor, am personally not involved in the respective clinical study.

Place: _____, date: D D | M M | Y Y Y Y, time: H H | M M,

_____

(Signature and stamp of the independent consultant doctor)

Date of this version: 11/2023

Appendix 5-DE – Konsiliararzt-Dokumente (DE)

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺

(Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Information für den Konsiliararzt

Sehr geehrte Kollegin, sehr geehrter Kollege,

Der Patient, den Sie konsiliarisch mitbeurteilen sollen, kommt für eine wissenschaftliche Studie zur aktuellen Praxis der maschinellen Beatmung auf Intensivstationen in Betracht. Die Studie wird durch eine Gruppe von Wissenschaftlern (*Protective Ventilation Network* (PROVEnet)) durchgeführt und von der Europäischen Gesellschaft für Anästhesiologie und Intensivmedizin (ESAIC) unterstützt.

Bitten lesen Sie sich die folgenden Informationen aufmerksam durch.

Hintergründe und Ziel der Studie

Die maschinelle Beatmung ist eine lebensrettende Maßnahme und gehört zu den am häufigsten durchgeführten Therapien auf Intensivstationen weltweit. Dabei ist die Anwendung Lungen-schonender Beatmungsstrategien entsprechend evidenzbasierter Leitlinien von größter Bedeutung für bestmögliche Behandlungsergebnisse. Um wissenschaftlichen Fortschritt zu erreichen und existierende Leitlinien auf einem aktuellen Stand zu halten, ist es immer wieder vonnöten, die angewandten Strategien zu überprüfen und wiederholt Daten aus der klinischen Praxis zu sammeln. Die letzte große Datenerhebung zur klinischen Praxis von maschineller Beatmung liegt schon einige Zeit zurück. Seither wurden neue wissenschaftliche Erkenntnisse gewonnen. Zudem hat sich möglicherweise ein größeres Bewusstsein für Beatmungs-assoziierte Komplikationen (z.B. Beatmungs-assoziierte Lungenschädigungen) und deren Risikofaktoren entwickelt. Das alles könnte in der Zwischenzeit in veränderten klinischen Abläufen, Strategien und klinischen Standards resultiert haben. Aus diesem Grund zielen wir mit der Durchführung dieser Studie darauf ab, die epidemiologischen Eigenschaften der Patienten sowie die aktuelle Praxis der maschinellen Beatmung auf Intensivstationen abzubilden.

Studienbeschreibung

PRoVENT 2⁺ ist eine klinische prospektive Beobachtungsstudie, bei welcher ein Prüfarzt aus der Klinik, in der sich der Patient in Behandlung befindet, Informationen aus dessen medizinischen Unterlagen, z.B. Patientenakte, Fieberkurve und klinischem Informationssystem (KIS), erhebt. Diese Daten betreffen Gesundheitszustand, Vorerkrankungen, die Art und Weise der maschinellen Beatmung, sowie weiterer Behandlungen.

Was bedeutet eine Teilnahme für den Patienten?

Die Teilnahme ist freiwillig. Eine Entscheidung für oder gegen eine Teilnahme, beeinflusst nicht die Behandlung und Pflege, welche der Patient während des Aufenthalts erhalten wird. Da es sich um eine Beobachtungsstudie handelt, bei der keine Studien-spezifischen Maßnahmen erfolgen, werden

die Entscheidungen der behandelnden Ärzte von der Studienteilnahme nicht beeinflusst. Durchgeführte Diagnostik, Behandlungen und/oder Eingriffe ergeben sich immer aus der klinischen Routine und werden nicht aufgrund der Studie durchgeführt. Die für wissenschaftliche Zwecke erhobenen medizinischen Daten beschränken sich auf jene, welche durch die klinische Routineversorgung anfallen. Die Datenerhebung erfolgt zu definierten Zeitpunkten. Diese sind, sofern möglich, der Tag des Studieneinschlusses, sowie die Tage 1-5, 7±1, 14±2, 21±2, 28±2, und 90±2. Die Datenerhebung erfolgt bis zu dem Zeitpunkt des Verlassens des Krankenhauses. Sollte dies vor Tag 28±2 bzw. 90±2 passieren, wird der Patient zu diesen zwei Zeitpunkten vom Studienteam kontaktiert. Die Studienteilnahme endet automatisch mit dem letzten erhobenen Zeitpunkt.

Individueller Nutzen und Risiko für den Patienten

Da es sich um eine Beobachtungsstudie handelt, kommt es zu keinen Studien-spezifischen Prozeduren. Daher ist der Patient durch die Teilnahme keinem zusätzlichen medizinischen Risiko ausgesetzt. Dem theoretischen Risiko eines Datenlecks oder der ungewollten Identifikation von Teilnehmern begegnen wir durch Einhaltung strengster Datenschutzrichtlinien.
Die mit der Studienteilnahme einhergehende sehr detaillierte Überwachung und Dokumentation könnte einen individuellen Vorteil darstellen, wobei der Studienarzt in engem Kontakt zu den behandelnden Ärzten steht und diese auf etwaige besondere Befunde oder Auffälligkeiten hinweisen wird. Abgesehen davon kann die klinische Studie wesentlich dazu beitragen, medizinisches Wissen zu erweitern, von dem zukünftige Patienten und/oder zukünftige Generationen profitieren können und zu dem der Patient mit seiner Teilnahme einen wesentlichen Beitrag leistet.

Nachholen bzw. Widerruf der Einwilligung

Sobald der Patient wieder einwilligungsfähig ist, muss dieser aufgeklärt werden und kann dann in eigenem Namen einwilligen oder die Teilnahme verweigern. Eine Verweigerung muss weder erklärt, noch in irgendeiner Form gerechtfertigt werden. Der Widerruf einer Teilnahme hat keinen Einfluss auf die medizinische Behandlung, die der Patient erhält.

Ergebnisse der Studie

Die Ergebnisse dieser Studie werden in einer medizinischen/wissenschaftlichen Fachzeitschrift veröffentlicht. Entsprechende Daten werden in diesem Zusammenhang ausschließlich zusammengefasst und anonymisiert veröffentlicht. Rückschlüsse auf die Identität einzelner Teilnehmer sind somit aus diesen Veröffentlichungen nicht möglich.

Versicherung

Eine studienspezifische Versicherung für die Teilnahme existiert nicht. Jedoch deckt die Haftpflichtversicherung jedes teilnehmenden Zentrums etwaig erwachsende Ansprüche.

Existiert eine finanzielle Aufwandsentschädigung für die Teilnahme?

Durch die Studienteilnahme ergeben sich für den Patienten keine Kosten. Eine finanzielle Aufwandsentschädigung ist für die Studienteilnahme nicht vorgesehen, auch nicht für den Konsiliararzt im Rahmen der Einwilligungsprozedur.

Datenschutz

Im Rahmen der Durchführung dieser Studie ist es notwendig, Gesundheitsdaten, die sich in medizinischen Aufzeichnungen finden, zu erheben und zu nutzen. Mit Ihrer Empfehlung zum

Studieneinschluss wird das Studienteam berechtigt, Daten zu erheben, zu verarbeiten und zu speichern. Die Speicherung erfolgt pseudonymisiert in einer gesicherten, elektronischen, zentralen Datenbank (für zehn Jahre nach Abschluss der Studie), d.h. es wird ein bestimmter Code anstelle des Klarnamens des Patienten verwendet. Die einzelnen Teilnehmer können nur durch die lokal beteiligten Ärzte und Wissenschaftler der behandelnden Klinik identifiziert werden. Die Übermittlung von Daten an das koordinierende Studienzentrum (Universitätsklinikum Carl Gustav Carus an der TU Dresden, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Deutschland) erfolgt pseudonymisiert mittels Online-Datenbank, sodass Teilnehmer anhand der dort gespeicherten Daten nicht identifiziert werden können. Diese Weitergabe von Daten erfolgt ausschließlich zum Zwecke der wissenschaftlichen Auswertung an o.g. Zentrum und zur statistischen Auswertung durch den vom Studienleiter beauftragten Statistiker (Prof. Ary Serpa Neto, Monash University, Melbourne, Australien). Für Australien gibt es derzeit keinen Angemessenheitsbeschluss der EU-Kommission, d.h. dort kann theoretisch ein niedrigeres Datenschutzniveau herrschen als in der EU.

Auf Grundlage der Europäischen Datenschutzgrundverordnung bestehen bezüglich der persönlichen Daten des Patienten die folgenden Rechte:

- Widerruf der Einwilligung zur Verarbeitung persönlicher Daten.
- Information darüber zu erhalten, welche persönlichen Daten gesammelt, verarbeitet oder im Rahmen der klinischen Studie weitergegeben werden.
- Korrektur von erhobenen, falschen persönlichen Daten.
- Löschung von persönlichen Daten, zum Beispiel nach vorzeitiger Beendigung der Studienteilnahme. Daten, welche bis zum Zeitpunkt des Widerrufs erhoben wurden, werden anonymisiert und weiterverarbeitet, sofern für die Studie notwendig.
- Einschränkung der Verarbeitung von Daten unter bestimmten Umständen. Zum Beispiel erlaubt der Patient nur die Speicherung, nicht jedoch Verarbeitung von Daten. Dieses Recht kann jedoch aufgrund geltender Gesetze, welche damit in Konflikt stehen, eingeschränkt sein.
- Erhalt der persönlichen Daten, welche dem Studienteam zur Verfügung gestellt wurden. Diese Daten können dann zum Beispiel an den Patienten, oder falls technisch möglich, an eine von ihm bestellte Person übermittelt werden.
- Widerspruch gegen spezielle Entscheidungen oder Maßnahmen, die die Verarbeitung der persönlichen Daten betreffen.
- Beschwerde bei einer zuständigen offiziellen Stelle, sollte den Datenschutzbestimmungen nicht adäquat Rechnung getragen werden.

Sollten Sie oder die von Ihnen betreute Person von einem der oben genannten Rechte Gebrauch machen wollen, nehmen Sie bzw. die von Ihnen betreute Person bitte unverzüglich Kontakt zum lokalen Prüfer des jeweiligen Zentrums auf. Für weitere Fragen bezüglich Datenschutz steht Ihnen ebenfalls die zuständige Datenschutzbeauftragte zur Verfügung.

Die verantwortliche Stelle für die Datenverarbeitung ist das Universitätsklinikum Carl Gustav Carus an der TU Dresden (Klinik und Poliklinik für Anästhesiologie und Intensivtherapie). Die Datenschutzbeauftragte am Universitätsklinikum Carl Gustav Carus Dresden kann bei Fragen zum Datenschutz wie folgt erreicht werden: dsv@ukdd.de.

Der/die für Ihre behandelnde Klinik zuständige Datenschutzbeauftragte ist (falls von o.g. abweichend):_____
_____

An wen kann ich mich generell bei Fragen wenden?

Für Anliegen und Fragen bezüglich der Studie wenden Sie sich bitte an den Studienleiter:

Dr. med. Martin Scharffenberg, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universitätsklinikum Carl Gustav Carus Dresden, Fetscherstraße 74, 01307 Dresden. Telefon: 0351 458 4110, E-Mail: martin.scharffenberg@ukdd.de

oder Ihren lokalen Prüfarzt:_____ Telefon:_____

Vielen Dank, dass Sie sich die Zeit genommen haben, diese Informationen durchzulesen.

Studieneinschluss mittels Konsiliararztverfahren

Name der Studie: ___PRoVENT 2+_____

Name des Konsiliararztes: _____

Herr/Frau _____, geboren am T T | M M | J J J J,

(Vor- und Zuname des Patienten)

in ärztlicher Behandlung aufgrund_____

_____

Die Untersuchung des Patienten erfolgte durch mich zur Klärung der Fragestellung, ob dieser in der Lage ist die Art, Tragweite und Konsequenzen seines Handelns vollumfänglich zu erfassen und ob auf dieser Grundlage Einwilligungsfähig bezüglich der Teilnahme an dieser klinischen Studie besteht. Im Weiteren wurde durch mich der mutmaßliche Willen des Patienten eruiert. Aufgrund meiner Untersuchung komme ich zu dem Schluss, dass der Patient

◯ einwilligungsfähig ist. ◯ NICHT einwilligungsfähig ist.

Die mit der Studienteilnahme einhergehende sehr detaillierte Überwachung und Dokumentation könnte einen individuellen Nutzen darstellen. Für den Patienten ergibt sich durch die Studienteilnahme in seiner aktuellen Situation darüber hinaus

◯ ein zusätzliches individuelles Risiko. ◯ KEIN zusätzliches individuelles Risiko.

Es konnte keine informierte Einwilligung vom Patienten erbracht werden. Des Weiteren konnte bis zum Zeitpunkt kein gesetzlicher Vertreter, verantwortlich für Fragen der Gesundheitsfürsorge, ausfindig gemacht oder bestellt werden. In Abwesenheit von Hinweisen darauf, dass der Patient eine Teilnahme generell ablehnen würde bzw. in der begründeten Annahme, dass eine Teilnahme dem mutmaßlichen Willen entspricht, und auf Basis der wissenschaftlichen Notwendigkeit der Studie, sowie des vernachlässigbaren Risikos, dem der Patient durch Teilnahme an dieser klinischen Beobachtungsstudie ausgesetzt ist, bewerte ich einen Einschluss des Patienten in diese klinische Studie als

◯ vertretbar. ◯ NICHT vertretbar.

Ich erkläre als Konsiliararzt nicht persönlich an der Durchführung der oben genannten Studie beteiligt zu sein.

Ort: _____, Datum: T T | M M | J J J J, Zeit: H H | M M,

_____

(Unterschrift und Dienststempel des unabhängigen Konsiliararztes)

Appendix 6 – Variables and timing of assessment

Variable	Unit	Day 0	Day 1-5	Day 7±1	Day 14±2	Day 21±2	Day 28±2	Day 90±2	ICU Discharge / Death on ICU †
DEMOGRAPHICS									
Date / time of assessment§	DD.MM.YYYY / hh:mm	X	X	X	X	X	X	X	X
Gender	Male, female, other	X							
Year of birth	YYYY	X							
Age	years	X							
Height	cm	X							
Weight	kg	X							
Ethnicity	Caucasian, Asian, Black, Other	X							
ADMISSION HISTORY									
Date / time of hospital admission	DD.MM.YYYY / hh:mm	X							
Date / time of ICU admission	DD.MM.YYYY / hh:mm	X							
Location before ICU admission	Study centre emergency dept., study centre operating theatre, study centre general ward, general ward of another hospital, ICU of another hospital, other (specify)	X							
Main reason for ICU admission	Rhythm disturbances; Hypovolemic hemorrhagic shock, Hypovolemic non-hemorrhagic shock; Septic shock; Anaphylactic shock, mixed and undefined shock; Liver failure; Severe pancreatitis; Acute abdomen; Intracranial mass effect; Focal neurologic deficit; Seizures; Coma; Stupor; Obtunded patient; Agitation; Vigilance disturbances; Confusion; Delirium; Other (specify)	X							
ICU admission planned or unplanned?	Planned / unplanned	X							

Surgical status at day 0	No surgery, after scheduled surgery, after emergency surgery	X							
If post-surgical, specify surgery	Abdominal, thoracic, vascular, neuro, transplantation (Liver, Kidney, Pancreas), cardiac, others	X							
PREDICTIVE SCORES									
APACHE II Score	See Appendix 20	X							
SAPS III Score	See Appendix 20	X							
LUNG INJURY PREDICTION SCORE (LIPS)									
Shock	Yes/no (Yes = 2)	X							
Aspiration	Yes/no (Yes = 2)	X							
Sepsis	Yes/no (Yes = 1)	X							
Pneumonia	Yes/no (Yes = 1.5)	X							
High-risk surgery: Check all that apply	Orthopedic spine (Yes = 1), acute abdomen (Yes = 2), cardiac (Yes = 2.5), aortic vascular (Yes = 3.5)	X							
Major / High-risk trauma: Check all that apply	TBI (Yes = 2), Smoke inhalation (Yes = 2), near drowning (Yes = 2), lung contusion (Yes = 1.5), multiple fractures (Yes = 1.5)	X							
Risk modifiers: Check all that apply	Alcohol abuse (Yes = 1), Obesity BMI >30 kg/m² (Yes = 1), Hypoalbuminaemia (Yes = 1), Chemotherapy (Yes = 1), FIO2 > 35% or O2 > 4l/min (Yes = 2), Tachypnea (>30/min) (Yes = 1.5), SpO_2 <95 (Yes = 1), Acidosis pH <7.35 (Yes = 1.5), Diabetes mellitus (Yes = -1)	X							
SOFA Score									
P/F ratio (mmHg)	See Appendix 20	X	X	X	X	X			X
Glasgow Coma Scale	See Appendix 20	X	X	X	X	X			X
Cardiovascular function	MAP>70 mmHg; MAP<70 mmHg; Dopamine ≤ 5 µg/kg/min or dobutamin (any dose); Dopamine > 5 µg/kg/min OR epinephrine ≤0.1 mg/kg/min OR norepinephrine ≤ 0.1	X	X	X	X	X			X

	µg/kg/min; Dopamine > 15 µg/kg/min OR epinephrine>0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min; See Appendix 20								
Bilirubin	See Appendix 20	X	X	X	X	X			X
Platelets	See Appendix 20	X	X	X	X	X			X
Kreatinine / urine output	See Appendix 20	X	X	X	X	X			X
MEDICAL HISTORY / RISK FACTORS									
Smoking	never, former, currently	X							
Functional status	non-, partially, totally dependent	X							
Clinical ARDS diagnosis at day 0	Yes/no	X							
If yes: date/time	DD.MM.YYYY / hh:mm	X							
If ARDS yes: Specify definition #	Berlin Definition, Kigali Modification, New Global Definition 2023	X							
If ARDS yes: Specify severity	Mild, moderate, severe	X							
Current confirmed COVID-19 infection	Yes/no	X							
Previous Covid-19 infection?	Yes/no	X							
Extra-pulmonary infection	Yes/no	X							
COPD	Yes/no	X							
If yes: use of inhalation therapy and/or steroids	Yes/no	X							
Active cancer/neoplasm	Yes/no	X							
If yes: Specify type		X							
Chronic heart failure	Yes/no	X							
If yes: Specify severity (NYHA/CCS)		X							
Diabetes mellitus	Yes/no	X							
If yes: Specify type	Type 1, 2, 3	X							
Chronic kidney failure	Yes/no	X							
If yes: Specify stadium		X							
If yes: Specify with or without RRT		X							
Liver cirrhosis	Yes/no	X							

If yes: Specify Child stadium		X							
Immunosuppression	Yes/no	X							
If yes: Specify		X							
Arterial hypertension	Yes/no	X							
Home ventilation	Yes/no	X							
Inhalational trauma	Yes/no	X							
Pulmonary vasculitis	Yes/no	X							
Drowning	Yes/no	X							
Pancreatitis	Yes/no	X							
Severe burns	Yes/no	X							
Drug overdose	Yes/no	X							
Blood transfusion	Yes/no	X							
If yes: Specify	Single transfusion, multiple transfusions	X							
Transfusion-associated acute lung injury (TRALI)	Yes/no	X							
Any of the following medication (check all that apply)	Amiodarone; Methotrexate; Hydrochlorothiazide; Tyrosine kinase inhibitors; Chemotherapy agents; other pneumotoxic	X							
MECHANICAL VENTILATION									
Current non-invasive oxygen insufflation >4 l/min	Yes/no	X	X	X	X	X	X	X	X
Current HFNO with flow >30 l/min *	Yes/no	X	X	X	X	X	X	X	X
If yes: Specify start date / time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X	X	X
If yes: Specify flow	l/min	X	X	X	X	X	X	X	X
Current NIV/CPAP with PEEP ≥5 cmH_2O *	Yes/no	X	X	X	X	X	X	X	X
If yes: Specify start date / time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X	X	X
Current other NIV mode *	Yes/no	X	X	X	X	X	X	X	X
If yes: Specify start date / time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X	X	X
If yes: Specify mode		X	X	X	X	X	X	X	X
If yes: Specify interface	Cannula, Prongs, Mask, Helmet, other	X	X	X	X	X	X	X	X

Currently on invasive MV?*	Yes/no	X	X	X	X	X	X	X	X
If yes: Specify start date / time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X	X	X
If yes: Specify device	Endotracheal tube, tracheostomy	X	X	X	X	X	X	X	X
If yes: Main reason for initiating invasive MV		X	X	X	X	X	X	X	X
Ventilation mode	Volume A/CM; PC/BIPAP/APRV; SIMV; PRVC; PSV; NAVA; HFO; CPAP; T-piece; Other	X	X	X	X	X	X	X	X
Presence of spontaneous breathing activity	Yes/no	X	X	X	X	X	X		X
Planned extubation performed	Yes/no	X	X	X	X	X	X		X
If yes: Specify date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X		X
Unplanned extubation performed	Yes/no	X	X	X	X	X	X		X
If yes: Specify date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X		X
If yes: Select related consequence	Re-intubation, NIV, oxygen insufflation, none, other	X	X	X	X	X	X		X
Tracheostomy performed	Yes/no	X	X	X	X	X	X		X
If yes: Specify date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X	X		X
Tidal volume (total)	ml	X	X	X	X	X			X
Tidal volume (spontaneous)	ml	X	X	X	X	X			X
Respiratory rate (total)	1/min	X	X	X	X	X			X
Respiratory rate (spontaneous/triggered)	1/min	X	X	X	X	X			X
Inspiratory to expiratory time ratio (I:E)		X	X	X	X	X			X
Peak airway pressure	cmH_2O, mbar	X	X	X	X	X			X
Plateau airway pressure	cmH_2O, mbar	X	X	X	X	X			X
Positive end-expiratory pressure	cmH_2O, mbar	X	X	X	X	X			X
Inspiratory oxygen fraction (F_IO_2)	[0.21-1.0]	X	X	X	X	X			X
Estimated FiO_2 = Ambient FiO_2 (e.g. 0.21) + 0.03 * O_2 flow rate (l/min)	[0.21-1.0]	X	X	X	X	X			X
End-tidal CO_2	mmHg, kPa	X	X	X	X	X			X
Compliance	ml/mbar, ml/cmH_2O	X	X	X	X	X			X
Resistance	kPa*s*l^{-1}, cmH_2O*s^{*-1}	X	X	X	X	X			X

Inspiratory flow	l/min	X	X	X	X	X			X
VITAL SIGNS									
Peripheral oxygen saturation, SpO_2	%	X	X	X	X	X			X
Heart rate	1/min	X	X	X	X	X			X
Cardiac rythm	[SR, AF, blocks, others…]	X	X	X	X	X			X
Systolic arterial blood pressure	mmHg	X	X	X	X	X			X
Diastolic arterial blood pressure	mmHg	X	X	X	X	X			X
Mean arterial blood pressure	mmHg	X	X	X	X	X			X
Central venous pressure	mmHg	X	X	X	X	X			X
Body core tempterature	°C, F	X							
FLUIDS and TRANSFUSIONS									
Daily fluid balance	ml	X	X	X	X	X			X
Use of vasopressors (since last visit)	Yes/no	X	X	X	X	X			X
Transfusion performed (since last visit)	Yes/no	X	X	X	X	X			X
If yes: Specify	red blood cell, fresh frozen plasma, platelets	X	X	X	X	X			X
SEDATION									
Richmond Agitation Sedation Scale (RASS)	[-5 … +4]	X	X	X	X	X			X
Glasgow Coma Scale	[3-15]	X	X	X	X	X			X
BLOOD GASES and LAB VALUES (last available at visit)									
Arterial partial pressure of oxygen, PaO_2	mmHg, kPa	X	X	X	X	X			X
Arterial partial pressure of carbon dioxide, $PaCO_2$	mmHg, kPa	X	X	X	X	X			X
Arterial pH		X	X	X	X	X			X
HCO3	mmol/l	X							
Arterial lactate	mmol/l	X	X	X	X	X			X
Arterial base excess	mmol/l	X	X	X	X	X			X
Hemoglobine concentration	mmol/l, mg/dl	X	X	X	X	X			X
Hematocrit	%	X	X	X	X	X			X
Leucocytes	10^9/l, G/l, Cells x10^3/mm^3	X	X	X	X	X			X
Platelets	G/l, Cells x10^3/mm^3	X	X	X	X	X			X

Creatinine in serum	mg/dl, µmol/l	X	X	X	X	X			X
Albumin in serum	mmol/L, µmol/L, g/L, g/dL, g/100mL, mg/mL	X	X	X	X	X			X
C-Reactive Protein	mg/dl	X	X	X	X	X			X
Na+	mmol/L	X	X	X	X	X			X
K+	mmol/l	X	X	X	X	X			X
Bilirubine	mg/dl, µmol/l	X	X	X	X	X			X
ADJUNCTIVE THERAPIES									
Currently on ECMO?	Yes/no	X	X	X	X	X			X
If yes: Specify mode	Veno-arterial, veno-venous, other	X	X	X	X	X			X
If yes: Blood flow	l/min	X	X	X	X	X			X
If yes: Sweep gas flow	l/min	X	X	X	X	X			X
Any recruitment manoeuvres (RM) performed?	Yes/no	X	X	X	X	X			X
If yes: How many since the last visit?		X	X	X	X	X			X
If yes: Specify mode of RM	VT-strategy, PEEP-strategy, CPAP, others	X	X	X	X	X			X
Application of inhaled nitric oxide?	Yes/no	X	X	X	X	X			X
If yes: highest dose since last visit	ppm	X	X	X	X	X			X
Prone positioning	Yes/no	X	X	X	X	X			X
If yes: Cumulative time in prone position since last visit	Hours or minutes	X	X	X	X	X			X
Use of neuromuscular blockers	Yes/no	X	X	X	X	X			X
Use of high dose corticosteroids	Yes/no	X	X	X	X	X			X
ADJUNCTIVE DIAGNOSTICS									
Measurement of plateau pressure	Yes/no	X	X	X	X	X			X
Swan-Ganz-Catheter and MPAP?	Yes/no	X	X	X	X	X			X
Electrical impedance tomography (EIT)	Yes/no	X	X	X	X	X			X
Oesophageal pressure measurement	Yes/no	X	X	X	X	X			X
If yes: Indicate reason for Peso measurement	To measure chest wall elastance; PEEP titration, assess work of breathing; assess asynchrony; other	X	X	X	X	X			X

Chest-X-ray / CT scan	Yes/no	X	X	X	X	X			X
If yes: Bilateral opacities on chest radiograph and computed tomography, not fully explained by effusions, atelectasis, or nodules/masses.	Yes/no	X	X	X	X	X			X
Lung ultrasound	Yes/no	X	X	X	X	X			X
If yes: or bilateral B lines and/or consolidations by ultrasound, not fully explained by effusions, atelectasis, or nodules/masses.	Yes/no	X	X	X	X	X			X
Broncho-alveolar lavage	Yes/no	X	X	X	X	X			X
THERAPEUTIC CONCEPT									
Therapy limitation / palliative situation?	Yes/no	X	X	X	X	X	X	X	X
Currently aiming at weaning? **	Yes/no	X	X	X	X	X	X	X	X
CLINICAL OUTCOME									
Mortality	Yes/no						X	X	X
If yes: Specify date/time	DD.MM.YYYY / hh:mm						X	X	X
If yes: Specify main cause of death							X	X	X
ICU discharge (alive)	Yes/no								X
If yes: date/time	DD.MM.YYYY / hh:mm								X
If yes: Discharge with continued invasive MV?	Yes/no								X
If yes: Discharge to	Other ICU, normal ward, rehab, home, other								X
If discharge alive: Respiratory status at ICU discharge	Tracheostomy; Tube; Invasive ventilation; Non-invasive ventilation; Oxygen therapy; none								X
Day of hospital discharge (alive)	DD.MM.YYYY						X	X	X
PULMONARY COMPLICATIONS (New)									
Hypoxemia? (P/F <300 mmHg or <40 kPa)	Yes/no	X	X	X	X	X			X
If yes: Can hypoxemia be entirely explained by cardiac failure?	Yes/no	X	X	X	X	X			X
If yes: Did you use any of these method to rule out the cardiac origin?	Echo; Swan-Ganz-Catheter; PiCCO; other (specify); none	X	X	X	X	X			X

Acute onset or worsening of hypoxemic respiratory failure (within 1 week of the onset of the predisposing risk factor or of new or worsening respiratory symptoms	Yes/no	X	X	X	X	X			X
Acute onset or worsening of hypoxemic respiratory failure and pulmonary edema not exclusively or primarily attributable to cardiogenic pulmonary edema or fluid overload, atelectasis or lung collapse, pleural effusion, or pulmonary embolism	Yes/no	X	X	X	X	X			X
New clinical ARDS diagnosis (if not already present at day 0)	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
If ARDS yes: Specify definition #	Berlin Definition, Kigali Modification, New Global Definition 2023	X	X	X	X	X			X
If ARDS yes: Specify severity	Mild, moderate, severe	X	X	X	X	X			X
Pulmonary Infection / pneumonia[1]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Cardiogenic pulmonary oedema[2]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
New pulmonary infiltrates[3]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Atelectasis[4]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Pleural effusion[5]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Barotrauma/Pneumothorax[6]	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
EXTA-PULMONARY COMPLICATIONS (New)									
SIRS	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Sepsis	Yes/no	X	X	X	X	X			X

If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Severe Sepsis	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Septic Shock	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Extrapulmonary infection	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
Acute kidney failure	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X
New renal replacement therapy	Yes/no	X	X	X	X	X			X
If yes: date/time	DD.MM.YYYY / hh:mm	X	X	X	X	X			X

APACHE II: Acute Physiology And Chronic Health Evaluation Score; ARDS: Acute respiratory distress syndrome; COPD: Chronic obstructive pulmonary disease; CCS: Canadian Cardiovascular Society; ECMO: Extra-corporeal membrane oxygenation; HCO_3^-: Bicarbonate: ICU: Intensive care unit; LIPS: Lung injury prediction score; MV: Mechanical ventilation; NYHA: New York Heart Association; RM: Recruitment manoeuvre; RRT: Renal replacement therapy; TBI: Traumatic brain injury

† whichever comes first

§ Patients should be assessed everyday at the same time, i.e. at 8:00 am.

In resource-limited settings, the ARDS criteria according to the Kigali modification (19) could be applied. Berlin Definition should take precedence if all necessary variables are available

* Every day a patient needs ventilation counts, irrespectively of MV duration during this day, irrespectively of mode of airway (tube, tracheostomy), duration of IMV and NIV will be assessed separately

** According to local weaning criteria/protocols

[1] Need of new antibiotics in the presence of new or changed lung opacities on chest X-ray and/or new or changed sputum plus at least one of the following criteria: 1) temperature >38.3ºC; or 2) WBC count >12,000; [2] Defined as pulmonary edema due to cardiac failure; [3] Defined as infiltrates on the CXR without other clinical signs; [4] Suggested by lung opacification with shift of the mediastinum, hilum, or hemidiaphragm towards the affected area, and compensatory overinflation in the adjacent nonatelectatic lung; [5] Suggested by lung opacification with shift of the mediastinum, hilum, or hemidiaphragm towards the non-affected area; [6] Air in mediastinum or in the pleural space with no vascular bed surrounding the visceral pleura;

Appendix 7 – Calculated variables

The following variables will be calculated from the recorded variables mentioned in Appendix 6.

Variable	Unit	Comments
Body mass index	kg/m²	Bodyweight [kg] / height [m]²
Obesity	Yes/no	Yes, if body mass index >30 kg/m²
LIPS	Points	See Appendix 20
SOFA Score	Points	See Appendix 20
Predicted body weight (PBW)	kg	Males: PBW=50+0.91x(height[cm] – 152.4) Females: PBW=45.5+0.91x(height[cm] – 152.4)
Tidal volume per measured body weight	ml/kg	= tidal volume (total) / bodyweight
Tidal volume per predicted body weight	ml/kg	= tidal volume (total) / PBW
Elastance	mbar/ml, cmH_2O/ml	Elastance = 1/Compliance
Driving pressure	cmH_2O, mbar	dP = Plateau - PEEP
Minute volume ventilation (total)	l/min	Tidal volume (total) * Respiratory rate (total)
Minute volume ventilation (spontaneous)	l/min	Tidal volume (spont) * Respiratory rate (spont)
Mechanical power (2016 formula)	J/min	= RR* (VT^2 * (1/2*Elastance + RR * ((1+IE) / 60*IE) * Resistance) + VT*PEEP)
Mechanical power (simplified formula)	J/min	= VT*(Ppeak-((Pplat-PEEP)/2))*RR*0,098
Mechanical power (Dresden formula)	J/min	= RR* (VT^2 * (1/2*Elastance + RR * ((1+IE) / 60*IE) * Resistance))
Mechanical power (elastic)	J/min	= VT^2*E/2*RR*0,098
Horovitz index	mmHg	PaO_2/F_IO_2
Modified Horovitz index		SpO_2/F_IO_2
ICU length of stay	Days	
Hospital length of stay	Days	
Hospital-free days on d28 and d90	Days	
ICU-free days on d28 and d90	Days	
Ventilator-free days on d28 and d90	Days	
ECMO-free days on d28 and d90	Days	
ARDS diagnosis 2012 definition	Yes/no	fulfillment of Berlin criteria (20)
ARDS diagnosis 2023 definition	Yes/no	fulfillment of New Global Definition 2023 criteria (21)
Non-intubated ARDS	Yes/no	Yes = if: Non-intubated patient, PaO_2/FiO_2 ≤300 mmHg or SpO_2/FiO_2 ≤315 (if SpO_2 ≤97%) on HFNO with flow ≥30 l/min or NIV/CPAP with ≥5 cmH_2O expiratory pressure

Intubated ARDS: Mild	Yes/no	Yes = if: Intubated patient, PEEP ≥ 5 cmH_2O and 200 < PaO_2/FiO_2 ≤ 300 or 235 ≤ SpO_2/FiO_2 ≤ 315 (if SpO_2 ≤ 97%)
Intubated ARDS: Moderate	Yes/no	Yes = if: Intubated patient, PEEP ≥ 5 cmH_2O and 100 < PaO_2/FiO_2 ≤ 200 or 148 < SpO_2/FiO_2 ≤ 235 (if SpO_2 ≤ 97%)
Intubated ARDS: Severe	Yes/no	Yes = if: Intubated patient, PEEP ≥ 5 cmH_2O and PaO_2/FiO_2 ≤ 100 or SpO_2/FiO_2 ≤ 148 (if SpO_2 ≤97%)
ARDS worsening	Yes/no	Any change in the prior classification
Probability of death according to SAPS III		Logit = 32.6659 +ln(SAPS 3 score +20.5958) 7.3068 Probability of death = elogit/(1+elogit). *Ref.* (26)

Appendix 8 – Time course of procedures

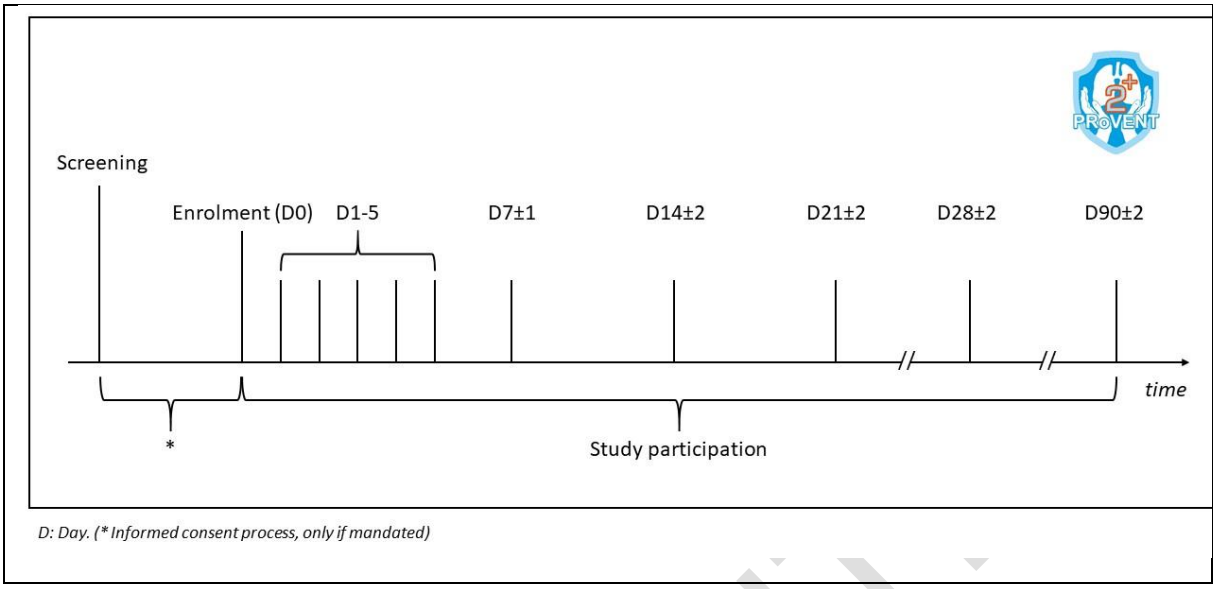

Figure 1: Time course of study-related procedures. Data will be collected on day 0 and daily until day 5 inclusive, as well as on day 7±1, 14±2, 21±2, 28±2, 90±2, and day of ICU discharge or death on ICU– whichever comes first.

Appendix 9 – Screening log

Consecutive number	Year of birth	Eligible? Yes | No	If not eligible, main reason:
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	
		○ | ○	

Page ___ of ___

Appendix 10 – Enrolment log

Pat. identification number	Name	Date of birth	Date of informed consent	Remarks
|_|_|_|_|_|_|				
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|_|_|_|_|_|_|				

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Appendix 11 – Visit and follow up log

Pat. ID	Date D0	Date D1	Date D2	Date D3	Date D4	Date D5	Date D7±1	Date D14±2	Date D21±2	Date D28±2	Date D90±2	Remarks (incl. information about follow-up phone calls, if applicable)
|_|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	
|_|_|_|_|_|_|_| Visit done? (tick if yes)	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	Done ◯	

Page ___ of ___

Appendix 12 – NCI Letter of intention

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Letter of intention for the role of a National coordinating investigator (NCI)

Hereby I, _____ (full name), express my intention to take the role of a National coordinating investigator for the PRoVENT 2⁺ study in the following country: _____.

By signing this form, I accept the content of the study protocol and acknowledge the responsibilities associated with the NCI role, as described in this protocol. I confirm that I am able and willing to act as NCI for the above-mentioned country. I acknowledge that there is no fee or financial compensation given to me or my institution for study-related actions.

National coordinating investigator:

_____

(Name)

_____

(Affiliation)

_____

(Place, date, signature)

Appendix 13 – Local PI Letter of intention

Update on the practice of mechanical ventilation in non-ARDS ICU patients (PRoVENT 2⁺) – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet

Letter of intention for the role of a Local principle investigator (Local PI)

Hereby I, _____ (full name), express my intention to take the role of a Local principle investigator for the PRoVENT 2⁺ study in the following study centre (Hospital name, place, country):_____

_____

_____.

By signing this form, I accept the content of the study protocol and acknowledge the responsibilities associated with the Local PI role, as described in this protocol. I confirm that I am authorised to act as local PI at my institution and that I am able and willing to conduct the study at my centre. I acknowledge that there is no fee or financial compensation given to me or my institution for study-related actions.

At my centre, the planned enrolment window is: ◯ 1 week; ◯ 2 weeks; ◯ 3 weeks; ◯ 4 weeks

Planned start of enrolment window: D D | M M | Y Y Y Y

Local principle investigator:

_____

(Name)

_____

(Affiliation)

_____

(Place, date, signature)

Appendix 14 – Organigram

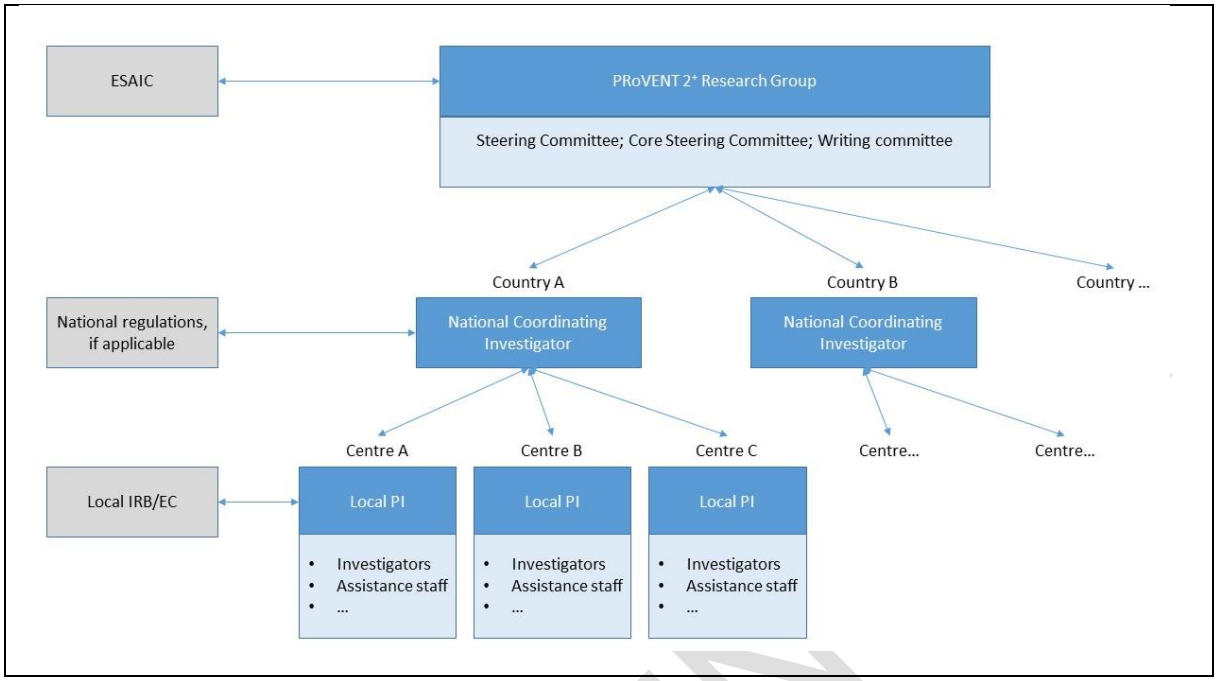

Figure 2: Organigram of the organisational structure of PRoVENT 2+. ESAIC, European Society of Anaesthesiology and Intensive Care; IRB, Institutional review board; EC: Ethics committee; PI: Principle investigator.

Appendix 15 – Case report forms for printing ("Worksheets")

CRFs for printing are developed based on Appendix 6 and provided separately.

Appendix 16 – Delegation log

Nr.	Print name	Role[1]	Responsibilities[2]	Signature	Participation start and end dates	

Page ___ of ___

[1] Roles: **NCI**=National coordinating investigator, **LPI**=Local principle investigator, **I**=Investigator, **A**=Study assistant, **SeCo**=Section coordinator. [2] Responsibilites: **1**=Coordinating study nationally; **2**=Coordinating study locally; **3**=Correspond with IRB/EC; **4**=Maintain regulatory documents; **5**=Screening; **6**=Obtain informed consent; **7**=Collect data; **8**=Enter data into eCRF; **9**=Respond to/resolve queries

Appendix 17 – End of the study reporting form

Centre name: _____

Local PI: _____; Date of obtaining IRB/EC approval: DD | MM | YYYY

Duration of enrolment window: ◯ 1 week; ◯ 2 weeks; ◯ 3 weeks; ◯ 4 weeks

Start date of enrolment window: DD | MM | YYYY;

Date of first enrolment: DD | MM | YYYY; Date of last enrolment: DD | MM | YYYY

Number of screened patients: _____; Number of enrolled patients: _____

Collaborator names for to be included in the main publication:

Surname(s)	Family name

(Please see the rules for authorship in the study protocol)

Appendix 18 – Pre-Study Centre Survey

Centre name: _____

Local PI: _____; **Continent/Country:** _____

Type of hospital: ◯ University Hospital, ◯ Academic hospital, ◯ Heart centre, ◯ Tertiary care hospital, ◯ Secondary care hospital, ◯ Public hospital, ◯ Private hospital, ◯ General hospital,
◯ Other, please specify:_____ _____

Total nr. of beds: ◯ ≥1500, ◯ 1000-1499, ◯ 800-999, ◯ 600-799, ◯ 400-599, ◯ 200-399, ◯ ≤199

Total nr. of ICUs in the hospital: _____; **Is your hospital >1000 m above sea level?** ◯ yes, ◯ no

Total nr. of ICU beds: ◯ ≥200, ◯ 150-199, ◯ 100-149, ◯ 75-99, ◯ 50-74, ◯ 25-49, ◯ ≤24

Please answer the following items for each participating ICU if there are more than one in your hospital.

Type of the ICU: ◯ Surgical; ◯ Internal medicine; ◯ Neuro; ◯ Anaesthesiological; ◯ Other: _____

Nr. of beds on your ICU: _____ **Doctor/patient ratio day:** _____ **Doctor/patient ratio night:** _____

Nurse/patient ratio day: _____ **Nurse/patient ratio night:** _____

Do you regularly assess patient-ventilator-asynchrony? ◯ Yes, ◯ No

if yes, how: ◯ Ventilator waveforms, ◯ specific software, ◯ clinically

How do you set PEEP regularly: ◯ ARDSnet tables, ◯ individual titration ◯ no standard procedure

if individually: which primary variable do you use for titration?_____

Are ARDSnet PEEP/FIO_2 tables available at the bedside, i.e. as printed cards etc.? ◯ Yes, ◯ No

Is the actual height of patients measured regularly? ◯ Yes, ◯ No

Do you calculate the exact predicted body weight regularly? ◯ Yes, ◯ No, ◯ We estimate it (height[cm]-100)

Do you use lung recruitment manoeuvres (RM)? ◯ Yes, ◯ No

if yes: ◯ routinely, ◯ as rescue strategy, ◯ for PEEP titration

if yes, how are RM performed? ◯ increase of VT, ◯ increase of PEEP with fixed driving pressure, ◯ sustained inflation via CPAP, ◯ other: _____

Do you regularly assess driving pressure in order to set ventilation? ◯ Yes, ◯ No

Do you regularly assess mechanical power in order to set ventilation? ◯ Yes, ◯ No

Do you distinguish between ARDS and non-ARDS patients regarding mechanical ventilation (MV) concepts or MV settings by any means? ◯ Yes, ◯ No

How often is MV checked for appropriateness? ◯ 1/d, ◯ 2/d, ◯ 3/d, ◯ 4/d, ◯ more often

Do you have respiratory therapists/physiotherapists taking care of MV settings? ◯ Yes, ◯ No

Who regularly sets/adjusts ventilation: ◯ Doctor, ◯ Nurse, ◯ Respiratory/physio therapist, ◯ all of them, ◯ Other: _____

I hereby confirm that I am authorised to pass on these data to the coordinating centre and that these data are correct.

Place: _____ Date: DD | MM | YYYY Signature: _____

Appendix 19 – Collaborative authorship calculation

Number of investigators named as collaborative authors in the main publication according to number of patients screened: After the first ten patients, one collaborative author can be mentioned per each ten screened patients.

Number of patients screened	Number of collaborative authors from that centre
0-10	2
11-20	2+1
21-30	2+2
31-40	2+3
Etc…	Etc…

Appendix 20 – Scores (LIPS, APACHE II, SOFA)

Lung Injury Prediction Score

TABLE 3. LUNG INJURY PREDICTION SCORE CALCULATION WORKSHEET

	LIPS Points	Examples
Predisposing Conditions		
Shock	2	
Aspiration	2	
Sepsis	1	(*1*) Patient with history of alcohol abuse
Pneumonia	1.5	with septic shock from pneumonia
High-risk surgery*		requiring $F_{IO_2} > 0.35$ in the
Orthopedic spine	1	emergency room: Sepsis + shock +
Acute abdomen	2	pneumonia + alcohol abuse +
Cardiac	2.5	$F_{IO_2} > 0.35$
Aortic vascular	3.5	1 + 2 + 1.5 + 1 + 2 = 7.5
High-risk trauma		(*2*) Motor vehicle accident with
Traumatic brain injury	2	traumatic brain injury, lung contusion,
Smoke inhalation	2	and shock requiring $F_{IO_2} > 0.35$
Near drowning	2	Traumatic brain injury + lung
Lung contusion	1.5	contusion + shock+ $F_{IO_2} > 0.35$
Multiple fractures	1.5	2 + 1.5 + 2 + 2 = 7.5
Risk modifiers		
Alcohol abuse	1	
Obesity (BMI > 30)	1	(*3*) Patient with history of diabetes
Hypoalbuminemia	1	mellitus and urosepsis with shock
Chemotherapy	1	Sepsis + shock + diabetes
$F_{IO_2} > 0.35$ (> 4 L/min)	2	1 + 2 − 1 = 2
Tachypnea (RR > 30)	1.5	
$Sp_{O_2} < 95\%$	1	
Acidosis (pH < 7.35)	1.5	
Diabetes mellitus†	−1	

Definition of abbreviations: BMI = body mass index; RR = respiratory rate; Sp_{O_2} = oxygen saturation by pulse oximetry.

* Add 1.5 points if emergency surgery.

† Only if sepsis.

From (27)

APACHE II Score

Age (y)	**Points**
≤ 44	0
45 – 54	2
55 – 64	3
65 – 74	5
≥ 75	6
Acute Physiology Score	
Temperature (°C [°F])	Points
≤ 29.9 [≤ 85.9]	4
30-31.9 [86.0-89.5]	3
32-33.9 [89.6-93.1]	2
34-35.9 [93.2-96.7]	1
36-38.4 [96.8-101.2]	0
38.5-38.9 [101.3-102.1]	1
39-40.9 [102.2-105.7]	3
≥ 41 [≥ 105.8]	4
Heart rate (bpm)	
≤ 39	4
40-54	3
55-69	2
70-109	0
110-139	2
140-179	3
≥ 180	4
Mean arterial pressure (mmHg)	
≤ 49	4
50-69	2
70-109	0
110-129	2
130-159	3
≥ 160	4
Respiratory rate (/min)	
≤ 5	4
6-9	2
10-11	1
12-24	0
25-34	1
35-49	3
≥ 50	4
Oxygenation	
A-a Gradient (if FiO_2 ≥ 0.5):	
<200	0
200-349	2
350-499	3
≥ 500	4
PaO_2 (if FiO_2 <0.5):	
≤ 54	4
55-60	3
61-70	1
>70	0
Na^+ (mmol/L)	
≤ 110	4
111-119	3
120-129	2
130-139	0
150-154	1
155-159	2

160-179	3
≥ 180	4
K^+ (mmol/L)	
≤ 2.4	4
2.5-2.9	2
3.0-3.4	1
3.5-5.4	0
5.5-5.9	1
6.0-6.9	3
≥ 7.0	4
Creatinine (mg/dL)	
<0.6	2
0.6-1.4	0
1.5-1.9	2
2.0-3.4	3
≥ 3.5	4
Arterial pH	
≤ 7.14	4
7.15-7.24	3
7.25-7.32	2
7.33-7.49	0
7.5-7.59	1
7.6-7.69	3
≥ 7.7	4
Serum HCO_3 (mmol/L): use only if no ABG	
≤ 14	4
15-17.9	3
18-21.9	2
22-31.9	0
32-40.9	1
41-51.9	3
≥ 52	4
Leukocytes ($x10^3$/L)	
≤ 1.0	4
1.0-2.9	2
3.0-14.9	0
15-19.9	1
20-39.9	2
≥ 40	4
Hct (%)	
≤ 20	4
20-29.9	2
30-45.9	0
46-49.9	1
50-59.9	2
≥ 60	4
Glasgow Coma Scale	Score = 15 - actual GCS
Chronic health points (patients with immunocompromise or history of severe organ insufficiency)	
Elective postoperative patient	2
Nonoperative or emergency postoperative patient	5

From (28)

SAPS III - Simplified Acute Physiology Score

BOX I	
Age (years)	
<40	0
≥ 40 < 60	5
≥ 60 < 70	9
≥ 70 < 75	13
≥ 75 < 80	15
≥ 80	18
Length of stay before ICU admission (days)	
<14	0
≥ 14 < 28	6
≥ 28	7
Intra-hospital location before ICU admission	
Operative room	0
Emergency room	5
Other ICU	7
Other	8
Co-Morbidities	
Cancer therapy	3
Cancer	11
Haematological cancer	6
Chron. Heart failure (NYHA IV)	6
Cirrhosis	8
AIDS	8
Use of major therapeutic options before ICU admission	
Vasoactive drugs	3
BOX II	
ICU admission	16
ICU admission: Planned or Unplanned	
Planned	0
Unplanned	3
Reasons for ICU admission (*:If both reasons are present, only the worse value (-4) is scored)	
Cardiovascular:	
Rhythm disturbances*	-5
Hypovolemic hemorrhagic shock, Hypovolemic non-hemorrhagic shock	3
Septic shock	5
Anaphylactic shock, mixed and undefined shock	5
Hepatic:	
Liver failure	6
Digestive:	
Severe pancreatitis	9
Acute abdomen, other	3
Neurologic:	
Intracranial mass effect	10
Focal neurologic deficit	7
Seizures*	-4
Coma, Stupor, Obtuned patient, Agitation, Vigilance disturbances, Confusion, Delirium	4
All other	0
Surgical status at ICU admission	
Scheduled surgery	0
Emergency surgery	6
No surgery	5
Anatomical site of surgery	

Transplantation surgery: Liver, Kidney, Pancreas, Kidney and pancreas, other	-11
Trauma-other, isolated: includes Thorax, Abdomen, limb; Trauma-Multiple	-8
Cardiac surgery: CABG without valvular repair	-6
Neurosurgery: Cerebrovascular accident	5
All others	0
Acute infection at ICU admission	
Nosocomial	4
Respiratory	5
BOX III	
Estimated GCS (lowest)	
3-4	15
5	10
6	7
7-12	2
≥ 13	0
Total bilirubine (highest) (mg/dl [µmol/L])	
< 2mg/dl [< 34.2µmol/L]	0
≥ 2 < 6 mg/dl [≥ 34.2 < 102.6µmol/L]	4
≥ 6mg/dl [≥ 102.6 µmol/L]	5
Body temperature (highest) (°C)	
< 35	7
≥ 35	0
Creatinine (highest) (mg/dl [µmol/L])	
< 1.2 mg/dL [< 106.1 µmol/L]	0
≥ 1.2<2 mg/dl [≥ 106.1 < 176.8 µmol/L]	2
≥ 2 <3.5 mg/dL [≥ 176.8 < 309.4 µmol/L]	7
≥ 3.5 mg/dL [≥ 309.4 µmol/L]	8
Heart rate (highest) (1/min)	
< 120	0
≥ 120 < 160	5
≥ 160	7
Leukocytes (lowest) (G/L; Cells x10³ / mm³)	
<15	0
≥ 15	2
Hydrogen ion concentration (lowest) (pH)	
≤ 7.25	3
> 7.25	0
Platelets (lowest) (G/L; Cells x10³ / mm³)	
<20	13
≥ 20 < 50	8
≥ 50 < 100	5
≥ 100	0
Systolic blood pressure (lowest) (mmHg)	
< 40	11
≥ 40 < 70	8
≥ 70 < 120	3
≥ 120	0
Oxygenation (mmHg)	
PaO_2/FiO_2 < 100 and MV	11
PaO_2/FiO_2 ≥ 100 and MV	7
PaO_2/FiO_2 < 60 and no MV	5
PaO_2/FiO_2 ≥ 60 and no MV	0

From (26)

SOFA Score

Respiratory system	
PaO_2/FiO_2 (mmHg)	
> 400	0
< 400	1
< 300	2
< 200 with respiratory support	3
< 100 with respiratory support	4
Nervous system	
Glasgow Coma Scale	
15	0
13-14	1
10-12	2
6-9	3
<6	4
Cardiovascular system	
Mean arterial pressure (MAP) *OR* administration of vasopressors required	
MAP>70 mmHg	0
MAP<70 mmHg	1
Dopamine ≤ 5 µg/kg/min or dobutamin (any dose)	2
Dopamine > 5 µg/kg/min OR epinephrine ≤0.1 mg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	3
Dopamine > 15 µg/kg/min OR epinephrine>0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	4
Liver	
Bilirubin (mg/dl) [µmol/L]	
<1.2 [<20]	0
1.2-1.9 [20-32]	1
2.0-5.9 [33-101]	2
6.0-11.9 [102-204]	3
>12.0 [>204]	4
Coagulation	
Platelets ($x10^3$/ml)	
>150	0
<150	1
<100	2
<50	3
<20	4
Kidneys	
Creatinine (mg/dl) [µmol/L]; urine output	
<1.2 [<110]	0
1.2-1.9 [110-170]	1
2.0-3.4 [171-299]	2
3.5-4.9 [300-440]; (or urine output <500 ml/day)	3
>5.0 [>440]; urine output <200ml/day	4

From (29)

Appendix 21 – EC/IRB approval documentation sheet

PRoVENT 2⁺ - EC/IRB Documentation Sheet

Please return this form to the PRoVENT 2⁺ PI before the study starts in your centre (martin.scharffenberg@ukdd.de)

Local PI first and last name: _____

Institution Name: _____

Country: _____ Centre #: _____

Total number of pages incl. attachments: _____

Ethics Committee (EC)/Institutional Review Board (IRB) Submission details:

Submission to: ◯ Country EC; ◯ Regional EC; ◯ Local EC; ◯ Local IRB; ◯ Other:_____

Detailed name of EC/IRB: _____

_____

Head of this EC/IRB: _____

- Date of first submission to EC/IRB: D D|M M| Y Y Y Y
- Acknowledgement of receipt by EC/IRB: D D|M M| Y Y Y Y
- Date of decision by EC/IRB: D D|M M| Y Y Y Y

EC/IRB consultation result:

- Ethics approval mandatory for this centre? Yes ◯; No ◯
- Successful EC/IRB approval of PRoVENT 2+? Yes ◯; No ◯
- Written informed consent mandatory for this centre? Yes ◯; No ◯

I have attached the following documents to this approval documentation sheet:

- ◯ EC/IRB acknowledgement of receipt
- ◯ EC/IRB approval letter
- ◯ EC/IRB waiver of subject information sheet and written informed consent
- ◯ EC/IRB member list
- ◯ Other documents: _____

Space for further notes:

_____

(Date / Name / Signature)

Appendix 22 – DE-SN-**Follow Up** Patienteninformation

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺ [Follow Up]

(Update on the practice of mechanical ventilation in non-ARDS ICU patients – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Patienteninformation (Follow Up)

Sehr geehrte Patientin, sehr geehrter Patient,

Sie brauchten im Rahmen Ihrer aktuellen Erkrankung eine maschinelle Beatmung und kamen bzw. kommen daher für die Teilnahme an einer wissenschaftlichen Studie zur aktuellen Praxis der maschinellen Beatmung auf Intensivstationen in Betracht. Diese Studie wird von einer Gruppe von Wissenschaftlern (*Protective Ventilation Network*, PROVEnet) durchgeführt und von der Europäischen Gesellschaft für Anästhesiologie und Intensivmedizin (ESAIC) unterstützt.

Wir möchten Sie bitten, sich diese Patienteninformation aufmerksam durchzulesen. Hier gehen wir auf die Ziele der Studie ein und beleuchten, was eine Teilnahme für sie bedeutet.

Hintergründe und Ziel der Studie

Die maschinelle Beatmung ist eine lebensrettende Maßnahme und gehört zu den am häufigsten durchgeführten Therapien auf Intensivstationen weltweit. Dabei ist die Anwendung Lungen-schonender Beatmungsstrategien entsprechend aktueller Leitlinien von größter Bedeutung für bestmögliche Behandlungsergebnisse. Um wissenschaftlichen Fortschritt zu erreichen und Leitlinien auf einem aktuellen Stand zu halten, ist es immer wieder vonnöten, die angewandten Strategien zu überprüfen und hierfür wiederholt Daten aus der klinischen Praxis zu sammeln. Die letzte große Datenerhebung zur klinischen Praxis von maschineller Beatmung liegt schon einige Zeit zurück. Seither wurden neue wissenschaftliche Erkenntnisse gewonnen. Zudem hat sich möglicherweise ein größeres Bewusstsein für Beatmungs-assoziierte Komplikationen (z.B. Beatmungs-assoziierte Lungenschädigungen) und deren Risikofaktoren entwickelt. Das alles könnte in der Zwischenzeit in veränderten klinischen Abläufen, Strategien und klinischen Standards resultiert haben. Aus diesem Grund zielen wir mit der Durchführung dieser Studie darauf ab, die epidemiologischen Eigenschaften der Patienten sowie die aktuelle Praxis der maschinellen Beatmung auf Intensivstationen abzubilden.

Studienbeschreibung

PRoVENT 2⁺ ist eine klinische Beobachtungsstudie, bei welcher ein Prüfarzt aus der Klinik, in der Sie sich in Behandlung befinden, Informationen aus Ihren medizinischen Unterlagen, z.B. Patientenakte, Fieberkurve und klinischem Informationssystem (KIS), erhebt. Diese Daten betreffen Ihren Gesundheitszustand, Vorerkrankungen, die Art und Weise der maschinellen Beatmung, sowie weiterer Behandlungen, welche Sie während Ihres Aufenthalts auf Intensivstation erhalten. **Daten aus dem**

Zeitraum Ihres Krankenhausaufenthaltes können zum Zwecke der wissenschaftlichen Forschung auf Grundlage des §29 Absatz (1) und (3) Sächs. Krankenhausgesetz (SächsKHG) ohne Ihre Einwilligung erhoben und pseudonymisiert (d.h. ohne direkten Rückschluss auf Ihre Person) ausgewertet werden, was bereits geschehen ist bzw. derzeit geschieht, bis Sie das Krankenhaus verlassen. In dieser Studie ist zusätzlich auch vorgesehen, Daten an zwei späteren Zeitpunkten zu erheben, die möglicherweise nach Ihrer Entlassung liegen. Für diese Datenerhebung und –auswertung benötigen wir Ihre schriftliche Einwilligung.

Was bedeutet eine Teilnahme für mich?

Die Teilnahme ist freiwillig. Ob Sie sich für oder gegen eine Teilnahme entscheiden, beeinflusst **nicht** die Behandlung und Pflege, welche Sie während Ihres Aufenthalts erhalten haben bzw. werden. Da es sich um eine Beobachtungsstudie handelt, bei der keine Studien-spezifischen Maßnahmen erfolgen, werden die Entscheidungen der behandelnden Ärzte von Ihrer Studienteilnahme nicht beeinflusst. Durchgeführte Diagnostik, Behandlungen und/oder Eingriffe ergeben sich immer aus der klinischen Routine. Es werden nur Daten erhoben, die in der klinischen Routineversorgung sowieso anfallen. Die Datenerhebung erfolgt zu definierten Zeitpunkten. Diese sind, sofern möglich, der Tag des Studieneinschlusses, sowie die Tage 1-5, 7±1, 14±2, 21±2, 28±2, und 90±2. Die Datenerhebung erfolgt bis zu dem Zeitpunkt des Verlassens des Krankenhauses, wobei Ihre Einwilligung bis zu diesem Zeitpunkt aufgrund der o.g. Gesetzeslage nicht notwendig ist. Sollten Sie vor Tag 28±2 bzw. 90±2 entlassen werden, werden Sie zu diesen zwei Zeitpunkten vom Studienteam kontaktiert. Hierfür bitten wir Sie um Einwilligung zur Datensammlung und –auswertung. Die Studienteilnahme endet automatisch mit dem letzten erhobenen Zeitpunkt.

Individueller Nutzen und Risiko für den Patienten

Da es sich um eine Beobachtungsstudie handelt, kommt es zu keinen Studien-spezifischen Prozeduren. Daher sind Sie durch die Teilnahme keinem zusätzlichen medizinischen Risiko ausgesetzt. Dem theoretischen Risiko eines Datenlecks oder der ungewollten Identifikation von Teilnehmern begegnen wir durch Einhaltung strengster Datenschutzrichtlinien. Da es sich um eine Beobachtungsstudie ohne Studien-spezifische Prozeduren handelt, ergibt sich für Sie durch die Teilnahme an dieser Studie kein unmittelbar greifbarer Nutzen. Allerdings erfolgt die Datenerhebung im Rahmen von Studien sehr detailliert und engmaschig, wobei der Studienarzt in engem Kontakt zu Ihren behandelnden Ärzten steht und diese auf etwaige besondere Befunde oder Auffälligkeiten hinweisen wird, was durchaus als Vorteil von Studienteilnahmen gewertet werden kann. Abgesehen davon können Sie durch Ihre Teilnahme wesentlich dazu beitragen, medizinisches Wissen zu erweitern, von dem zukünftige Patienten und/oder zukünftige Generationen profitieren können.

Widerruf der Einwilligung

Auch nachdem Sie bereits Ihre Einwilligung erteilt haben, können Sie die Teilnahme an der Studie zu jedem beliebigen Zeitpunkt widerrufen. Sie müssen diese Entscheidung weder erklären, noch müssen Sie sich dafür rechtfertigen. Der Widerruf Ihrer Teilnahme hat keinen Einfluss auf die medizinische Behandlung oder Pflege, die Sie erhalten.

Ergebnisse der Studie

Die Ergebnisse dieser Studie werden in einer medizinischen/wissenschaftlichen Fachzeitschrift veröffentlicht. Entsprechende Daten werden in diesem Zusammenhang ausschließlich

zusammengefasst und anonymisiert veröffentlicht. Rückschlüsse auf die Identität einzelner Teilnehmer sind somit aus diesen Veröffentlichungen nicht möglich.

Versicherung

Eine studienspezifische Versicherung für ihre Teilnahme existiert nicht. Jedoch deckt die Haftpflichtversicherung jedes teilnehmenden Zentrums etwaige erwachsende Ansprüche.

Erhalte ich eine finanzielle Aufwandsentschädigung für die Teilnahme?

Durch die Studienteilnahme ergeben sich für Sie keine Kosten. Eine finanzielle Aufwandsentschädigung ist für die Studienteilnahme nicht vorgesehen.

Datenschutz

Im Rahmen der Durchführung dieser Studie ist es notwendig, Gesundheitsdaten, die sich in Ihren medizinischen Aufzeichnungen finden, zu erheben und zu nutzen. Ihre in der klinischen Routineversorgung erhobenen Daten können auch ohne Ihre Einwilligung auf Grundlage des §29 Absatz (1) und (3) Sächs. Krankenhausgesetz (SächsKHG) für wissenschaftliche Forschung genutzt werden. Dies bezieht sich auf den Zeitraum Ihres Krankenhausaufenthaltes, nicht aber auf nachfolgende Zeitpunkte. Da wir aber auch Informationen über Ihren Gesundheitszustand ca. einen und drei Monate nach Beginn Ihrer Teilnahme sammeln und auswerten wollen, bitten wir Sie hierfür um Einwilligung zur Teilnahme und Datenverarbeitung.

Die Speicherung Ihrer Daten erfolgt pseudonymisiert in einer gesicherten, elektronischen, zentralen Datenbank (bis zehn Jahre nach Abschluss der Studie). Das bedeutet, dass Ihre Daten nicht zusammen mit Ihrem Namen, Geburtstag oder anderen direkt identifizierenden Informationen, sondern lediglich mit einem Zahlencode verknüpft gespeichert werden. Die einzelnen Teilnehmer können dabei anhand des individuellen Zahlencodes lediglich durch die beteiligten Ärzte und Wissenschaftler der jeweiligen behandelnden Klinik identifiziert werden, nicht aber durch das koordinierende Studienzentrum, den Statistiker oder sonstige Dritte. Eine Weitergabe von Daten erfolgt ausschließlich zum Zwecke der statistischen Auswertung an das koordinierende Zentrum (Universitätsklinikum Carl Gustav Carus an der TU Dresden, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie) und den vom Studienleiter beauftragten Statistiker (Prof. Ary Serpa Neto, Monash University, Melbourne, Australien) auf Grundlage §29 (3) SächsKHG bzw. Ihrer Einwilligung. Für Australien gibt es derzeit keinen Angemessenheitsbeschluss der EU-Kommission, d.h. dort kann theoretisch ein niedrigeres Datenschutzniveau herrschen als in der EU.

Auf Grundlage der Europäischen Datenschutzgrundverordnung haben Sie folgende Rechte:

- Widerruf der Einwilligung zur Verarbeitung persönlicher Daten.
- Zu erfahren, welche persönlichen Daten gesammelt, verarbeitet oder im Rahmen der klinischen Studie weitergegeben werden.
- Korrektur von erhobenen, falschen persönlichen Daten.
- Löschung Ihrer persönlichen Daten, zum Beispiel nach vorzeitiger Beendigung der Studienteilnahme. Daten welche bis zum Zeitpunkt des Widerrufs erhoben wurden, werden anonymisiert und weiterverarbeitet, sofern für die Studie notwendig.
- Einschränkung der Verarbeitung von Daten unter bestimmten Umständen. Zum Beispiel erlauben Sie nur die Speicherung, nicht jedoch Verarbeitung von Daten. Dieses Recht kann jedoch aufgrund geltender Gesetze, welche damit in Konflikt stehen, eingeschränkt sein.

- Erhalt der persönlichen Daten, welche Sie dem Studienteam zur Verfügung gestellt haben. Diese Daten können dann zum Beispiel an Sie, oder falls technisch möglich, an eine von Ihnen bestellte Person übermittelt werden.
- Widerspruch gegen spezielle Entscheidungen oder Maßnahmen, die die Verarbeitung Ihrer persönlichen Daten betreffen.
- Beschwerde bei der zuständigen Aufsichtsbehörde, sollte Ihren Rechten nicht angemessen Rechnung getragen werden.

Sollten Sie von einem der oben genannten Rechte Gebrauch machen wollen, nehmen Sie bitte unverzüglich Kontakt zum lokalen Prüfer Ihres Zentrums auf. Für weitere Fragen bezüglich Datenschutz steht Ihnen ebenfalls die zuständige Datenschutzbeauftragte zur Verfügung.

Die verantwortliche Stelle für die Datenverarbeitung ist das Universitätsklinikum Carl Gustav Carus an der TU Dresden (Klinik und Poliklinik für Anästhesiologie und Intensivtherapie). Die Datenschutzbeauftragte am Universitätsklinikum Carl Gustav Carus Dresden kann bei Fragen zum Datenschutz wie folgt erreicht werden: dsv@ukdd.de.

Der/die für Ihre behandelnde Klinik zuständige Datenschutzbeauftragte ist (falls von o.g. abweichend):

_____

_____

An wen kann ich mich generell bei Fragen wenden?

Für Anliegen und Fragen bezüglich der Studie wenden Sie sich bitte an den Studienleiter:

Dr. med. Martin Scharffenberg, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universitätsklinikum Carl Gustav Carus Dresden, Fetscherstraße 74, 01307 Dresden. Telefon: 0351 458 4110, E-Mail: martin.scharffenberg@ukdd.de.

Vielen Dank, dass Sie sich die Zeit genommen haben, diese Patienten-information durchzulesen.

Appendix 23 – DE-SN-**Follow Up** Patienteneinwilligung

Erhebung zur aktuellen klinischen Praxis der intensivmedizinischen Beatmung – PRoVENT 2⁺ [Follow Up]

(Update on the practice of mechanical ventilation in non-ARDS ICU patients – An international, multi-centre, prospective, observational ICU cohort study of the PROVEnet)

Hinweis: Aus Gründen der besseren Lesbarkeit wird im Folgenden auf die gleichzeitige Verwendung der Sprachformen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen gelten gleichermaßen für alle Geschlechter.

Einwilligungserklärung für Patienten (Follow Up)

Ich, _____
(Vor- und Nachname), geboren am T T | M M | J J J J ,

- habe die Patienteninformation der PRoVENT 2⁺ Studie gelesen und verstanden,
- hatte die Möglichkeit, Fragen bezüglich der Studie zu stellen und habe diese zufriedenstellend beantwortet bekommen.
- hatte ausreichend Bedenkzeit und habe bezüglich der Studie ausreichend Informationen erhalten.

Ich wurde in einem persönlichen Gespräch mit _____

(Vor- und Nachname des Prüfarztes) darüber aufgeklärt, dass

- die Teilnahme an der Studie keinen Einfluss auf die medizinische Behandlung während des Klinikaufenthalts hat,
- die Teilnahme freiwillig ist und
- ich jederzeit ohne Angabe von Gründen mein Einverständnis widerrufen kann. Dadurch entstehen mir keinerlei Nachteile bezüglich meiner medizinischen Behandlung.
- Ich wurde über meine Rechte bezüglich der Verarbeitung meiner Daten aufgeklärt.

Ich willige hiermit freiwillig in die Teilnahme an dieser Studie ein. Ich bin mit der Erhebung und Verarbeitung meiner medizinischen Daten zum Zwecke der Durchführung der PRoVENT 2⁺ Studie einverstanden. Soweit erforderlich, dürfen die erhobenen Daten pseudonymisiert (verschlüsselt) zum Zweck der wissenschaftlichen Auswertung weitergegeben werden an das Universitätsklinikum Carl Gustav Carus an der TU Dresden sowie die Monash University, Melbourne, Australien. Ein Exemplar der Patienteninformation sowie eine Kopie der Einwilligungserklärung habe ich erhalten.

Ort: _____, Datum: _____

Unterschrift Teilnehmer: Unterschrift Prüfarzt:

_____ _____