

VARIABLE PROTOCOL- Local researchers

List of variables to collect, format of each variable in brackets

I. VARIABLES RELATED TO THE PATIENT

(Eligibility & Demographical data form)

1) Number ID (general)

Consecutive number of any patient admitted to PICU ongoing invasive mechanical ventilation

2) Center/ Clinic (text)

Research Center (Hospital), according to the corporate acronyms commonly used by each center.

Example: VHH: Vall d'Hebron Hospital

3) Local Code (text)

The code of each patient will consist of each center code plus the consecutive registration number-entry into the study from each center.

Example: Vall d'Hebron Hospital.

Example: VHH-001
 VHH-002 ...

Each researcher must keep a document relating the medical record number of the patient and the study code.

4) Eligibility and Exclusion criteria

1. Invasive mechanical ventilation < 48 hours
2. Age > 30 days or infants with a corrected age < 44 weeks
3. Age >18 years
4. Previous tracheostomy/any kind of domiciliary ventilation or other PICU previous ventilation*
5. Cyanotic congenital heart disease, right-to-left shunt (including ECMO), or pulmonary hypertension

6. MV \geq 48h and NONE of the above

*Patients from another PICU ventilated for >24h will be excluded unless both PICUs participate in the PROMETHEUS Study

5) PICU admission date (date)

Date of admission to the pediatric ICU, format: dd / mm / yyyy

6) GENDER (general, categorical)

Patient sex/gender

1. Male
2. Female

7) Date of Birth (date)

Date of birth, format: dd / mm /yyyy

8) Age (months) calculated (numerical)

Automatically calculated, with one decimal place. Example: 81.2.

9) Age (years) calculated (numerical)

Automatically calculated, with one decimal place. Example:6.7

10)Age (months) (numerical)

Patient age expressed in months, with NO decimal place.

11) Weight (numerical)

Patient weight in kilograms (kg), with one decimal place. Ex. 5.3 kg, 5.0 kg

12) Hospital admission date (date)

Date of hospital admission, format: dd / mm / yyyy

13) Organ failure/dysfunction as principal reason for admission (general, categorical)

1. Respiratory failure
2. Heart failure or post-CPR/arrhythmias
3. Neurological disturbance/failure
4. Sepsis/septic shock
5. Hydroelectrolytic disturbances/renal failure

6. Acute liver failure
7. Hemorrhage
8. Post-surgery/procedure
9. Other

14) Specific diagnosis / reason for admission (free text format)

It refers to the patient condition that demands the PICU admission, the primary clinical reason for admission but not the organ failure/dysfunction responsible for his/her admission to the PICU

Examples: Bronchiolitis (not respiratory failure)
 Postoperative cardiac surgery (not cardiogenic shock)
 Cardiac decompensation (not heart failure)

15) Pre-existing conditions (numbered, dichotomous)

Other current active problems / diseases at the beginning of the episode of mechanical ventilation and that they do not correspond to the principal diagnosis.

1. Yes
0. No

16) Pre-existing conditions_type (general, categorical)

EXCEPTION: If there are some active issues related to prematurity, this diagnosis also will be added as pre-existing conditions, despite a full-term corrected age.

1. Lung disease
2. Heart disease
3. Neurological disease
4. Kidney disease
5. Gastrointestinal / Liver disease
6. Solid cancer
7. Hematological malignant disease
8. SCT (Stem Cell Transplant)
9. Solid Transplant
10. Other immunocompromised
11. Prematurity
12. Other conditions

NOTES:

- Assumption 6 refers to solid tumors undergoing chemotherapy, being treated at the time of the onset of the mechanical ventilation episode.
- Assumption 10 refers to states of primary / secondary or pharmacological immunosuppression different from those related to the treatments and / or pathologies of items 6-9. Examples: human immunodeficiency virus infection, primary immunodeficiencies, cytotoxic / biological therapies in the context of autoimmune diseases.

17) Type of patient (general, categorical):

1. Medical
2. Surgical
3. Trauma-burn

18) Status at UCIP discharge (number, dichotomous)

Patient condition at discharge from PICU.

0. Alive
1. Dead

19) Status at hospital discharge (number, dichotomous)

Patient condition at discharge from the hospital.

0. Alive
1. Dead

20) COMMENTS (free text format)

Other comments to understand the patient's conditions i.e. other infections or culture results than respiratory

21) PICU discharge date (date)

Date of PICU discharge, dd / mm /yyyy format

22) Hospital admission date (date)

Date of hospital discharge, dd / mm / yyyy format

23) Hospital discharge date (date)

Date of hospital discharge, dd / mm / yyyy format

II. VARIABLES RELATED TO THE MECHANICAL VENTILATION EPISODE

(Variables related to the MV 1, 2 and 3 forms)

An EPISODE of mechanical ventilation is defined as the number of consecutive (calendar) days during which the patient is ventilated.

NOTES:

- In case of requiring re-initiation of mechanical ventilation after a period of at least one calendar day without invasive respiratory support (at least one calendar day off the ventilator) it will be classified as NEW EPISODE of the same patient during that period of admission.
- Each PICU admission following inclusion criteria must have completed a minimum of two forms (Eligibility & Demographical data, Variables related to MV episode 1) by the local researcher or more, in case of presenting several episodes of mechanical ventilation during that admission period. The Study Coordinator form will be filled out by Elias Iosifidis or Yolanda Peña-López.

1) PRISM24h at the onset of MV EPISODE (numeric)

PRISM III score of the patient in the first 24 hours of the beginning of the episode of mechanical ventilation.

NOTE: If the first 24 hours of mechanical ventilation coincide with the day of admission, it will also coincide with the PRISM III score at the patient's admission. Numerical Format Document is attached for easy calculation.

2) Reason for mechanical ventilation (MV) (general, categorical)

Primary/underlying cause for mechanical ventilation.

1. Surgery / other procedures
2. Respiratory failure
3. Cardiogenic shock-cardiorespiratory arrest. NOTE: Retrograde heart failure that occurs with pulmonary edema will be counted as respiratory failure (2).
4. Alteration of the level of consciousness
5. Septic shock

3) Intubation place (general, categorical)

Place where intubation and beginning of mechanical ventilation is performed.

1. Operating room.

This variable will also include those places where intubation is performed in a controlled way for a procedure (ie interventional radiology procedures).

2. PICU

3. Outpatient

4. Emergency / Hospitalization ward

4) Episode onset date

Date of episode onset, format: dd / mm / yyyy

NOTE: An EPISODE of mechanical ventilation is defined as the number of consecutive (calendar) days during which the patient is ventilated. In case of requiring re-initiation of mechanical ventilation **after a period of at least one calendar day** without invasive respiratory support (at least one calendar day off the ventilator) it will be classified as NEW episode of the same patient during that period of admission.

5) Tracheostomy during the EPISODE (number, dichotomous)

Tracheostomy procedure performed during the mechanical ventilation episode. Previously tracheostomized patients will be excluded from the study.

1. Yes

0. No

6) Tracheostomy date (date)

Start date of mechanical ventilation through tracheostomy tube, format: dd / mm / yyyy

7) PELOD episode (numerical)

Value of this score of multi-organ failure of the patient during the episode of mechanical ventilation. Numerical Format Document is attached for easy calculation.

8) Episode ending date (date)

Date of mechanical ventilation completion: endotracheal tube removal date or date of disconnection from invasive mechanical ventilation through tracheostomy tube for more than 1 calendar day.

Final date of the mechanical ventilation episode, format: dd / mm /yyyy

9) Episode ending STATUS (number, dichotomous)

Condition of the patient at the end of the episode of mechanical ventilation, NOT to be confused with patient condition at PICU discharge.

- 0. Alive
- 1. Death

III. DAILY RECORDS OF VARIABLES

(Variables related to the MV 1, 2 and 3 forms)

1) Date (daily record)

Day 1 corresponds to day of invasive mechanical ventilation onset. Format: dd / mm / yyyy

2) Neuromuscular blocking agents (NMBAs) (general, categorical)

- 0. No
- 1. Continuous intravenous infusion
- 2. Discontinuous administration

3) FiO₂min (percentage)

Daily minimum FIO₂: This is the lowest fraction of oxygen in inspired gas (FiO₂) value that is set on the ventilator during a calendar day and maintained for > 1 hour, format: percentage.

NOTE:

In the event that ventilator settings are monitored and recorded less frequently than once per hour, the daily minimum FiO₂ is simply the lowest value of FiO₂ set on the ventilator during the calendar day. Similarly, in circumstances where there is no value that has been maintained for > 1

hour (for example, the lowest value of FiO_2 is set late in the calendar day, mechanical ventilation is discontinued early in the calendar day, FiO_2 settings are changed very frequently throughout the calendar day) the daily minimum FiO_2 is the lowest value of FiO_2 set on the ventilator during the calendar day (regardless of how long that setting was maintained). For example, a patient who is intubated and started on mechanical ventilation at 11:30 pm on June 1, with a FiO_2 setting of 0.30 from 11:30 pm to midnight, would have a daily minimum FiO_2 of 0.30 on June 1 for the purposes of PedVAE surveillance.

4) PEEP_{min} (numerical)

Daily minimum PEEP: This is the lowest positive pressure at the end of the expiration (PEEP) value documented during a calendar day and that was maintained for > 1 hour, format: numeric.

5) MAP_{min} (numerical)

Daily minimum MAP: This is the lowest mean airway pressure (MAP) value documented during a calendar day and maintained for > 1 hour, format: numeric.

6) Short endovenous continuous sedative-analgesic drugs (number, dichotomous)

The patient during that day has received any of the following drugs in continuous infusion EV:

1. Remifentanil, and/or dexmedetomidine, and/or propofol.
0. None of them

7) Long endovenous continuous sedative-analgesic drugs (general, categorical)

The patient during that day has received any of the following drugs in continuous infusion

1. Benzodiazepines and/or fentanyl/morphine and / or ketamine
2. None of them

If the patient is receiving other long half life drugs ie. barbiturates in continuous infusion, please specify in comments (form one)

8) Patient temperature (general, categorical)

In temperature measurements of that day the patient presents one or more temperature measurements higher than 38 ° C.

1. >38 °C
2. 36-38 °C

3. <36°C
4. Induced hypothermia or temperature regulated by an external device

9) White cell count/Leucocytes (general, categorical)

Leucocyte count <4,000 or ≥12,000 / mm³ on that day. If no blood test has been performed that calendar day,

- 1.<4000
- 2.4000-12000
- 3.>12000
- 4.Not performed

10) Purulent secretions (number, dichotomous)

New onset of secretions from the lungs, bronchi, or trachea that contain ≥ 25 neutrophils and ≤10 squamous epithelial cells per low power field [lpf, x100].

1. Yes
02. No
03. Not stated

NOTE 1: The isolated appearance of a purulent sputum or a non-maintained change in its characteristics will not be considered in this regard.

NOTE2: Some clinical laboratories may use different results reporting formats for direct examinations of respiratory secretions. Additional instructions for using the purulent respiratory secretions criterion are provided in [Table 1](#).

Table 1: Instructions for using the purulent respiratory secretions criterion, based on laboratory reporting of respiratory secretion direct examination results.

How do I use the purulent respiratory secretion criterion if...	Instruction
My laboratory reports counts of “white blood cells” or “polymorphonuclear leukocytes” or “leukocytes” rather than counts of “neutrophils”	Assume that counts of cells identified by these other descriptors (for example, “white blood cells”) are equivalent to counts of neutrophils, unless the laboratory tells you this is not the case.
My laboratory reports semi-quantitative results (not quantitative results) for numbers of neutrophils and squamous epithelial cells?	Check with the laboratory to get information about what quantitative ranges the semiquantitative reports correspond to.

My laboratory cannot provide additional information on how its semi-quantitative reporting corresponds to quantitative reporting ranges for neutrophils and squamous epithelial cells?	Use the following direct examination results to meet the purulent respiratory secretions criterion: many, heavy, numerous, 4+, or ≥ 25 neutrophils per low power field (lpf) [x100], AND no, rare, occasional, few, 1+ or 2+, or ≤ 10 squamous epithelial cells per lpf [x100].
My laboratory reports <u>only</u> the numbers of neutrophils present, without reporting the number of squamous epithelial cells?	In this situation, the purulent secretions criterion may be met using the specified quantitative and semi-quantitative thresholds for neutrophils alone (specifically many, heavy, numerous, 4+, or ≥ 25 neutrophils per lpf [x100]).
My laboratory uses different reporting thresholds for neutrophils and squamous epithelial cells (for example, maximum report of ≥ 20 neutrophils per low power field [x100], or minimum report of ≤ 15 squamous epithelial cells per low power field [x100])?	In this situation, the purulent secretions criterion may be met using the laboratory's specified maximum quantitative threshold for neutrophils, and/or minimum quantitative threshold for squamous epithelial cells.
My laboratory processes respiratory specimens such as bronchoalveolar lavage fluid using a centrifugation procedure (for example, "cytospin"), and there is no quantitation or semi-quantitation of neutrophils or white blood cells in the direct examination report?	In this situation, a report indicating the presence of white blood cells, without quantitation, is sufficient to meet the purulent secretions criterion.

Ventilator-associated Event. CDC Definitions. January 2022
https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf

11) Clinical respiratory worsening (number, dichotomous)

Respiratory worsening appearing or increasing during that calendar day compared to previous day and identified by clinical criteria (eg. Increased sustained oxygen therapy needs)

1. Yes
0. No

NOTES:

- In case of respiratory worsening with an increase in the value of FiO₂ / PEEP, note that on that day the most favorable FiO₂ and PEEP records will be computed if they were maintained for more than one hour. Therefore, apparently in the FiO₂ min and PEEP min boxes there will be no change except for the clinical respiratory worsening variable.

- In case of problem resolution and recovery of oxygenation and FiO₂ or PEEP needs in a few hours, it is possible that in the FiO₂ / PEEP min boxes will show no changes. Only this incident will be pointed out by the clinical worsening of respiratory worsening.

12) Chest X ray (general, categorical)

Variable referred to the interpretation of the chest radiograph performed that day by the attending physician/radiologist.

0. Not performed
1. No changes from baseline
2. No changes from the previous one
3. Better compared to the previous one
4. Condensation
5. Atelectasis
6. ARDS (Acute Respiratory Distress Syndrome)
7. Pulmonary edema-positive fluid balance-Pleural effusion
8. Other

13) Antibiotic / Antimicrobial treatment (general, categorical)

Variable referred to the prescription of an antibiotic or antimicrobial therapy that is initiated on that day as empirical or targeted treatment of an infection (confirmed or not subsequently). ***Antimicrobials prescribed as usual prophylaxis because of the patient condition (i.e. immunosuppression, ureteral reflux, secondary prophylaxis) are excluded.***

0. No
1. Yes (same treatment as previous day)
2. Yes (new or change of pattern)

NOTE: When the antimicrobial therapy is stopped, the day of the last antimicrobial dose will be recorded as 1 (Yes, the same as the previous day) and the next day will appear as 0 (No).

14) Reason for initiating an antibiotic/antimicrobial (ATB / AM) regimen (general, categorical)

Variable referring to antimicrobial prescription cause.

0. Prophylaxys procedure
1. Increase in acute phase reactants (only)
2. Clinical sepsis
3. Respiratory infection
4. Other focal infection without sepsis
5. Empiric antimicrobial escalation
6. Antimicrobial de-escalation/adjustment

15) Type of respiratory sample (general, categorical)

Variable referred to the type of respiratory sample sent to the microbiology laboratory for culture. If more than one is available, the results referring to the respiratory sample with the highest microbiological value will be recorded.

0. Not performed
1. Lung tissue
2. BAL: Bronchoalveolar lavage
3. PSB: Protected specimen brush
4. Endotracheal aspirate (ETA) grade 3 or not assessable
5. Endotraqueal aspirate (ETA) grade 4
6. Endotracheal aspirate (ETSA) grade 5

Table 2. Murray&Washington gradation system to assess the quality of the respiratory sample applied to endotracheal aspirate

GRADE	Number of squamous epithelial cells per 10x objective (low power)	Number of leukocytes per 10x objective (low power)
1	>25	<10
2	>25	10-25
3	>25	>25
4	10-25	>25
5	<10	>25

16) Culture results 1 (general, categorical)

Variable in relation to culture identification.

0. Qualitative negative
1. Qualitative positive
2. Quantitative / semi-quantitative WITH significant growth
3. Quantitative / semi-quantitative WITHOUT significant growth

Table 3. Threshold values for cultured specimens used in VAE definition by specimen collection/technique

Specimen collection/technique	Values
Lung tissue	$\geq 10^4$ CFU/g tissue*
Bronchoscopically (B) obtained specimens <i>Bronchoalveolar lavage (B-BAL)</i> <i>Protected BAL (B-PBAL)</i> <i>Protected specimen brushing (B-PSB)</i>	$\geq 10^4$ CFU/ml* $\geq 10^4$ CFU/ml* $\geq 10^3$ CFU/ml*
Nonbronchoscopically (NB) obtained (blind) specimens <i>NB-BAL</i> <i>NB-PSB</i>	$\geq 10^4$ CFU/ml* $\geq 10^3$ CFU/ml*
Endotracheal aspirate (ETA)	$\geq 10^5$ CFU/ml*

CFU = colony forming units, g = gram, ml = milliliter *Or corresponding semi-quantitative result if your laboratory only performs semi-quantitative cultures of lower respiratory tract specimens

CORRESPONDING SEMI-QUANTITATIVE RESULTS

For the purposes of this surveillance, and in the absence of additional information available from your laboratory, a semi-quantitative result of “moderate” “many numerous” or “heavy” growth, or 2+, 3+ or 4+ growth is considered to meet positive criteria.

NOTES:

- A qualitative culture result will be provided when it has not been interpreted as contamination, colonization or any microorganism without clinical value.
- A semi-quantitative result of “few” will be considered WITHOUT significant growth.

17) Microorganism (text)

Isolated pathogenic microorganisms from the respiratory tract sample. Free text format.

18) Polymicrobial growth? (general, dichotomous)

More than one microorganism is isolated in the respiratory sample

1. Yes
0. No

19) Culture results2 (general, categorical) (see variable 16)

20) Microorganism2 (text) (see variable 17)

21) Culture results3 (general, categorical) (see variable 16)

22) Microorganism3 (text) (see variable 17)

23) Mechanical ventilation > 10 days? (general, dichotomous)

This question is referring to the actual mechanical ventilation episode (this specific form)

1. Yes

0. No

24) Mechanical ventilation > 20 days? (general, dichotomous)

This question is referring to the actual mechanical ventilation episode (this specific form)

1. Yes

0. No

25) Mechanical ventilation > 40 days? (general, dichotomous)

This question is referring to the actual mechanical ventilation episode (this specific form)

1. Yes

0. No

26) Date definitive MV withdrawal? ()

This question only will pop up when the actual mechanical ventilation episode lasts more than 40 days. If this is the case, no more days of MV during this episode or other MV episodes will be recorded. Only the date of the definitive MV withdrawal must be recorded.