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**ADMINISTRATIVE INFORMATION****Support** - OWN FINANCING.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202640024**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 April 2026 and was last updated on 7 April 2026.**INTRODUCTION**

**Review question / Objective** What is the effect of noninvasive ventilation, compared with conventional therapies such as oxygen therapy or usual care, on mortality and clinical outcomes in patients with acute pulmonary edema?

**Rationale** The high clinical impact of acute pulmonary edema and the increasing use of NIV in hospital settings highlight the urgency of establishing a solid evidence base to guide the use of this therapy. Although NIV is already included in clinical guidelines as a recommended ventilatory approach for cases of acute respiratory failure, the conflicting results between different systematic reviews and clinical trials indicate an important gap in the consolidation of its real benefit in terms of mortality and therapeutic efficacy. This uncertainty hinders the standardization of protocols and can lead to heterogeneous conducts in clinical practice. In view of this, an umbrella review presents itself as the ideal methodology to

integrate and critically evaluate the findings of systematic reviews already published, providing a comprehensive and hierarchical view of the scientific literature. The results of this synthesis can serve as a basis for clinical decision-making, support future updates of guidelines, and strengthen the quality of care provided to adult patients with pulmonary edema.

**Condition being studied** This condition is broadly categorized into two main subtypes: cardiogenic and noncardiogenic. Pulmonary edema of cardiogenic origin results from increased blood pressure in the pulmonary capillaries due to the increase in left ventricular end-diastolic pressure, a secondary mechanism to cardiac dysfunctions such as decompensated heart failure, chronic arterial hypertension, valvular heart diseases, and cardiomyopathies. Severe kidney disease can also contribute to this condition, mainly due to fluid retention and hemodynamic dysregulation. This type of pulmonary edema is directly associated with cardiovascular diseases and represents one of the main causes of hospital admission due to heart

failure decompensation. On the other hand, noncardiogenic pulmonary edema results from increased permeability of the alveolar-capillary membrane, allowing fluid to leak into the alveoli regardless of hydrostatic pressure. This mechanism occurs, for example, in ARDS, where inflammatory mediators such as cytokines and interleukins play a key role in the dysfunction of the alveolar-capillary barrier. This type of edema can be triggered by direct pulmonary aggressions, such as pneumonia, or by systemic factors, such as sepsis. In addition, other conditions, such as reduced plasma oncotic pressure, increased negative interstitial pressure after decompression of a pneumothorax, insufficiency of the lymphatic system, and lung transplantation, can also contribute to its manifestation.

## METHODS

**Search strategy** A comprehensive search was carried out in the following electronic databases: PubMed, BASE, Cochrane Database of Systematic Reviews, Epistemonikos and PEDro Search. The search was also carried out in a database of systematic reviews: PROSPERO (International Prospective Register of Systematic Reviews). In addition, a search was conducted in the references of the included studies using the Snowballing technique and the search for citations of the studies selected for synthesis using the Forward Citation Searching technique.

Terms:

("Pulmonary Edema"[ Mesh] OR "Pulmonary Edemas" OR "Acute Cardiogenic Pulmonary Edema" OR ACPE OR "Cardiogenic Pulmonary Edema" OR CPE OR "Acute Cardiogenic Pulmonary Oedema" OR ACPO OR "Wet Lung" OR "Wet Lungs") AND (CPAP OR "Continuous Positive Airway Pressure"[Mesh] OR BIPAP OR Bilevel OR "Bilevel Positive Airway Pressure" OR IPPB OR "Intermittent Positive Airway Pressure Breathing" OR "Intermittent Positive Pressure Breathing" OR "Non-invasive Positive Pressure" OR NIV OR "Noninvasive Positive Pressure" OR "Non Invasive Positive Pressure" OR "Non-invasive Ventilation" OR "Noninvasive Ventilation" OR "Non Invasive Ventilation" OR "Intermittent Positive Pressure" OR "Intermittent Positive Pressure Ventilation" OR "Intermittent Positive Pressure Hyperventilation") AND (Review OR "Systematic Review" OR "Systematic Literature Review" OR "root cause analysis"[Mesh] OR meta-analysis)).

**Participant or population** Adult patients with pulmonary edema.

**Intervention** Noninvasive ventilation (NIV): Continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP).

**Comparator** Oxygen therapy, standard medical therapy, or usual care.

**Study designs to be included** Systematic reviews.

**Eligibility criteria** Inclusion:

Outcomes evaluated: Mortality, Need for intubation, Need for mechanical ventilation, Acute myocardial infarction, Length of stay in the ICU, Length of hospital stay

Intervention: CPAP, BiPAP, VNI

Comparison: Oxygen therapy, standard medical therapy, or usual care

Method of analysis/synthesis: Meta-analysis, Narrative analysis, Tabbing.

**Information sources** A comprehensive search was carried out in the following electronic databases: PubMed, BASE, Cochrane Database of Systematic Reviews, Epistemonikos and PEDro Search. The search was also carried out in a database of systematic reviews: PROSPERO (International Prospective Register of Systematic Reviews). In addition, a search was conducted in the references of the included studies using the Snowballing technique and the search for citations of the studies selected for synthesis using the Forward Citation Searching technique.

**Main outcome(s)** Mortality, Need for intubation, Need for mechanical ventilation, Acute myocardial infarction, Length of stay in the ICU and Length of hospital stay.

**Quality assessment / Risk of bias analysis** Tools used for assessment such as Risk of Bias and PEDro Scale.

**Strategy of data synthesis** Considering the potential variations between the included studies, such as different inclusion criteria, synthesis methods and outcome measures, the findings of the umbrella review will also be presented in narrative format. In addition, the general outcome measures, together with the description of the characteristics and the evaluation of the quality of

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the reviews, will be summarized in tables. If the extracted data are sufficient to perform a meta-analysis, the pooled effect size will be estimated based on specific effect estimates (OR, RR, RD, MD, SMD or others), accompanied by uncertainty intervals (standard error or CI), in addition to the sample sizes of the meta-analyses included. To ensure the correct results, if it is possible to conduct meta-analysis, the data will be extracted directly from the primary studies.

Another approach will consist of the use of primary data extracted from the systematic reviews, including mean, standard deviation, and number of participants in the experimental and control groups for continuous variables, or number of events and total participants in each group for dichotomous variables. The heterogeneity of the studies will be assessed by the Higgins and Thompson ( $I^2$ ) inconsistency tests and the Cochrane Q test.  $I^2$  values greater than 50% or  $p > 0.1$  for the Q test will indicate significant heterogeneity. If identified, its possible causes will be investigated through subgroup and/or sensitivity analyses. In case each meta-analysis includes at least ten studies, the presence of publication bias will be investigated using funnel plots. For the statistical analysis, the RevMan 5.4 software will be used (RevMan ..., 2014). In studies that present multiple comparisons involving NIV (e.g., NIV vs usual care, NIV vs oxygen therapy, NIV vs CPAP, NIV vs BIPAP), only comparators that do not directly involve CPAP or BIPAP as a control group will be considered for this umbrella review. Therefore, inclusion will be restricted to comparisons between NIV and non-ventilatory interventions, in order to avoid overlapping effects and to ensure clarity in the analysis of the effects of NIV compared to conventional therapies.

**Subgroup analysis** Subgroup analyses will consider variables such as gender, type of edema, and intervention characteristics, including NIV modality, frequency, duration, and time of initiation of therapy.

**Sensitivity analysis** The sensitivity analysis will take into account factors such as no blinding or inadequate blinding of the evaluators, inadequate randomization methods, and a rate of losses to follow-up greater than 20%.

**Language restriction** Article published in any year.

**Country(ies) involved** Brazil.

**Keywords** Positive Airway Pressure Ventilation; Pulmonary Edema; Umbrella Review.

### Contributions of each author

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