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ORIGINAL RESEARCH

Early management of out-of-hospital respiratory distress: an interdisciplinary consensus guidance

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Abstract

Background: Respiratory distress represents one of the most prevalent clinical presentations in out-of-hospital emergency medicine. Despite its frequency, optimal out-of-hospital management remains variable, and evidence-based guidance is lacking. **Methods**: An interdisciplinary panel of sixteen experts employed the RAND Corporation/University of California Los Angeles (RAND/UCLA) Appropriateness Method to evaluate 56 statements on the assessment and treatment of out-of-hospital respiratory distress. These statements were developed through a scoping review of the literature and expert clinical judgment. Appropriateness ratings were performed over two rounds. Non-voting observers from patient associations participated in the discussions to represent the patient perspective. **Results**: The scoping review identified the available evidence on out-of-hospital respiratory distress and informed the development of 56 candidate statements subsequently evaluated by the panel. After the two-round RAND/UCLA consensus process, 27 statements (49%) were rated as appropriate, 13 (23%) as uncertain, and 16 (29%) as inappropriate. Oxygen therapy was rated appropriate both to improve symptoms (median 8, interquartile range (IQR) 8–9; disagreement index (DI) −0.20) and to prevent clinical deterioration (median 8, IQR 7.75–9; DI −0.20). Non-invasive ventilation received similarly high appropriateness ratings for improving symptoms (median 8, IQR 8–9; DI −0.34) and preventing deterioration (median 8.5, IQR 8–9; DI −0.34). The panel agreed on the need for early treatment, with oxygen therapy initiated within 10 minutes judged appropriate (median 8, IQR 8–9; DI −0.34). Advanced respiratory support was preferred over oxygen alone in moderate-to-severe respiratory distress (median 8, IQR 8–8.25; DI 0.00). **Conclusions**: This consensus provides practical, expert-driven recommendations to standardize early management of out-of-hospital respiratory distress. While many recommendations reached strong agreement, areas of uncertainty remain, underscoring the need for further clinical research.

Keywords

Respiratory distress; Out-of-hospital management; Non-invasive ventilation; Emergency medical services; RAND/UCLA appropriateness method

1. Background

Respiratory distress is among the most common and serious presentation in out-of-hospital settings, accounting for a substantial proportion of encounters globally. In one large Australian study, nearly 14% of all emergency medical service (EMS) activations were related to respiratory distress, and such cases were associated with high rates of hospitalization, increased need for ventilatory support, and elevated mortality [1]. Over the past decade, EMS calls for patients presenting with respiratory distress have shown a steady increase, reflecting the growing burden of chronic respiratory and cardiovascular diseases in the community [2]. Among patients transported for acute dyspnea, approximately 76% required hospital admission, with 5–6% needing intensive care, and in-hospital mortality among admitted patients being about 6–7% [3].

Paramedic field assessments of dyspnea were highly concordant with emergency department diagnoses, highlighting the reliability of out-of-hospital evaluation in this population [4, 5]. Importantly, strategies aimed at strengthening out-of-hospital treatment of respiratory distress—such as early recognition, optimized single oxygen therapy, and timely use of non-invasive ventilation—are associated with reductions in clinical deterioration and mortality [6].

Despite the critical importance of early recognition and management, there exist deep and persistent gaps in both evidence and practice. Evidence from the literature reveals substantial variability in how EMS systems assess and treat respiratory distress: in many studies, key monitoring tools (*e.g.*, blood gas analysis) and treatment (*e.g.*, non-invasive ventilation) are often underused or delayed; protocols differ considerably across systems; and the quality of data from out-of-hospital research is often limited by observational designs, small sample sizes, and lack of randomized comparisons [7, 8]. Unlike myocardial infarction, stroke, or cardiac arrest, where explicit time targets guide intervention, no comparable recommendations exist for respiratory distress [9, 10]. In addition, in the development of prehospital emergency care guidelines, patients are seldom involved, and their perspective is rarely represented in the decision-making process. These gaps and variability highlight the necessity for a structured methodology to evaluate and standardize practice.

The Delphi RAND/UCLA Appropriateness Method is a robust tool for systematically evaluating medical procedures by combining the best available evidence with the collective judgment of expert panels. The Delphi RAND/UCLA method employs a structured approach, allowing experts to rate appropriateness across various clinical scenarios [11]. This method is particularly valuable where direct evidence may be limited, and clinical decision-making requires context-specific insights. An interdisciplinary, national task force was established by the NAVIGATE steering committee consisting of experts from various field. This consensus-based guidance, developed using the Delphi RAND/UCLA method, aimed to identify optimal strategies and enhance decision-making frameworks for early management of out-of-hospital respiratory distress in adult patients.

2. Methods

2.1 Study design

This consensus study used the RAND/UCLA Appropriateness Method, a modified Delphi technique that integrates evidence synthesis with expert opinion, to evaluate the appropriateness of early management strategies for out-of-hospital respiratory distress. A multidisciplinary expert panel rated predefined statements across two rounds, with a discussion between rounds to clarify perspectives without attempting to force consensus.

2.2 Panel formation

The expert panel was convened following a meeting of the NAVIGATE steering committee, which defined the framework and methodology for the consensus process in accordance with the RAND/UCLA Appropriateness Method. The NAVIGATE Steering Committee is the scientific board of the NAVIGATE study and is composed of senior physicians and allied health professionals. The committee is responsible for overseeing the study design, ensuring methodological rigor, supervising the scoping review, and coordinating the development and refinement of the statements evaluated by the panel [12]. Panelists were selected to ensure multidisciplinary, recognized expertise in their field, absence of conflicts of interest, and diversity in practice setting and geography. Although all experts were based in Italy, they were deliberately recruited from multiple regions (Northern, Central, and Southern Italy) to ensure broad geographic representation. A multidisciplinary expert panel was convened including experts in intensive care, physiotherapy, nursing, emergency medicine, and prehospital providers with extensive experience in the early management of out-of-hospital respiratory distress. The expert panel was composed of sixteen members formally nominated by NAVIGATE steering committees. Twelve were both intensivists and anesthesiologists, two were nurses, one was a physiotherapist, and one was a surgeon with experience in emergency departments and prehospital care. Members were selected based on expertise and contributions to clinical practice or research in the field. Conflicts of interest were transparently disclosed. In addition to the voting members, non-voting observers from patient associations participated in the discussions, ensuring that the patient perspective was represented, although they did not take part in the final voting.

2.3 Literature review

A systematic search of PubMed, Cochrane Library, and EMBASE databases was conducted from inception to 01 September 2025 by two reviewers (PP, RL), to identify studies relevant to management of out-of-hospital respiratory distress. Inclusion criteria focused on randomized controlled trials and quasi-randomized trials, and relevant guidelines addressing early management of out-of-hospital respiratory distress in adult patients. Data extraction was independently performed by two reviewers, collecting information on study design, methodology, sample size, interventions, and outcomes. Evidence was synthesized into an evidence report by two reviewers including tables summarizing study characteristics, key outcomes and identified knowledge gaps (**Supplementary materials 1 and 2**). This report was distributed to panel members to guide their ratings and inform the consensus-building process. The panelists received the complete scoping review (including all supporting references used to inform the consensus process) (**Supplementary material 3**).

2.4 Statement generation

The development of candidate statements followed the RAND/UCLA Appropriateness Method. Statements were generated through a scoping review of the published literature combined with expert clinical judgment. According to the RAND/UCLA manual, candidate interventions were selected if they represented procedures or strategies commonly used in practice, if there was evidence of variation in use across regions, or if their use was associated with substantial risk or uncertainty regarding clinical benefit.

Each statement was required to be specific enough to allow panelists to make a rating, while sufficiently broad to encompass the range of relevant clinical scenarios. Statements were written in a clear, concise, and clinically meaningful format, avoiding ambiguity and redundancy. Draft statements were reviewed by the coordinating team, refined through iterative feedback from the panel, and organized into three thematic sections: (1) assessment tools in respiratory distress, (2) respiratory support strategies, and (3) indications for non-invasive ventilation (NIV) and oxygen therapy.

2.5 Consensus process

The first Round was conducted via e-mail. The panelist received the literature review, list of clinical scenarios (indications), definitions of terms, and instructions for rating. For each indication, the panel members rated the benefit-to-harm ratio of the procedure on a scale of 1 to 9, where 1 means that the expected harms greatly outweigh the expected benefits, and 9 means that the expected benefits greatly outweigh the expected harms. A middle rating of 5 may indicate either that the expected benefits and potential harms of the procedure are approximately balanced, or that the rater could not determine the appropriateness of the intervention for the specific patient scenario described [11]. In accordance with the RAND/UCLA guidelines, intermediate median values (*e.g.*, 3.5 and 6.5) were rounded up and assigned to the higher appropriateness category. In line with the RAND/UCLA Appropriateness Method, “appropriate” indicated that the expected health benefits of an intervention clearly outweighed its potential harms, without consideration of costs or logistical feasibility.

During the second round, panelists participated in an in-person meeting and were invited to discuss their ratings in light of aggregated group results and individual responses. This round allowed for structured discussion and refinement of ratings, using updated forms that included the frequency of responses and each panelists prior ratings. Indications were then classified into three levels of appropriateness (appropriate, uncertain or inappropriate) based on the panelists median ratings and level of agreement (Fig. 1).

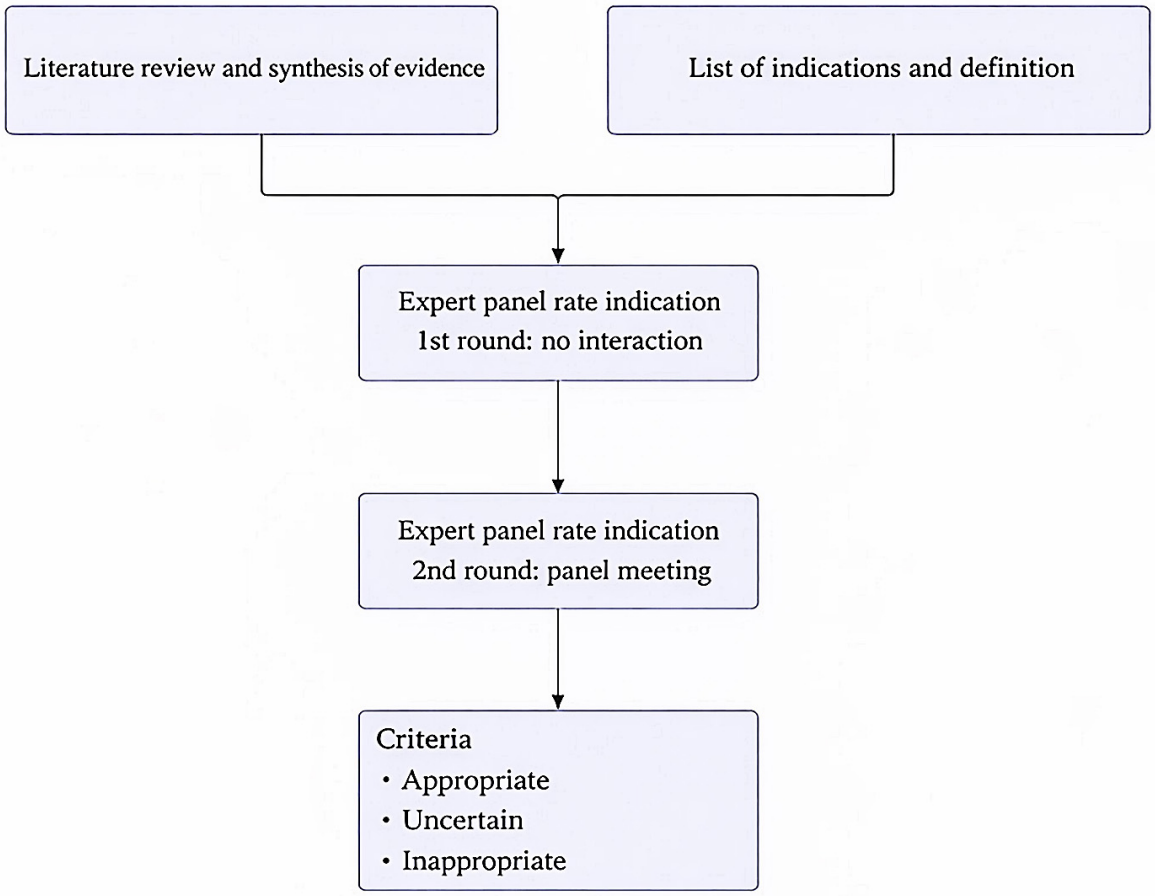

FIGURE 1. Flowchart of consensus guidance for the early management of out-of-hospital respiratory distress valve implantation.

2.6 Statistical analysis

The median appropriateness rating for each statement and rating distribution, as expressed by the interquartile range (IQR), were calculated. Indications with a median rating of 7–9 and no disagreement were classified as appropriate. Those with a median rating of 4–6 and those with any median accompanied by disagreement were categorized as uncertain. Indications with a median rating of 1–3 and no disagreement were deemed inappropriate [11].

The level of agreement is expressed as the disagreement index (DI) that is based on the inter-percentile range (difference between the 66th and 33rd centiles appropriateness score) with a correction factor for asymmetry. To ensure equitable participation, all 16 panelists had equal voting rights, irrespective of their specialty. The potential impact of asymmetry in panel composition was addressed using the RAND/UCLA Appropriateness Method's formal procedure for detecting disagreement. Specifically, disagreement was evaluated by calculating the DI, defined as the ratio between the Interpercentile Range (IPR) and the Interpercentile Range Adjusted for Symmetry (IPRAS). The IPRAS was derived by adjusting a reference interpercentile range (IPRr) according to the degree of asymmetry in the ratings, using the Asymmetry Index (AI) and a correction factor for asymmetry (CFA), as outlined in the RAND/UCLA Appropriateness Method manual. A DI greater than one indicated the presence of disagreement among panelists. In such cases, regardless of the median score, the intervention was not classified as appropriate. The writing group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) network classification for strength of recommendation (I = strong; II = weak) and for quality of evidence (a = high; b = moderate; c = low). The maximum achievable quality of evidence was "c" if the results were solely based on the consensus process. A median appropriateness score of >7.9 and DI <0.5 indicated a strong recommendation (GRADE IC). Disagreement was identified if DI was >1 [13, 14].

3. Results

The round one survey consisted of 41 initial statements in different clinical scenarios. In total, 20 (49%) of statements were rated as appropriate, 9 (22%) as inappropriate, and 12 (29%) as uncertain. Following the group discussion, 16 new statements were added to the survey. Thus, a total of 56 statements were included in round two of the survey. After the second round of voting, 27 (48%) of statements were rated as appropriate, 16 (29%) as inappropriate, and 13 (23%) as uncertain (Table 1). All recommendations were informed by the structured literature review. This evidence was reviewed by all panelists and integrated into the appropriateness ratings, alongside clinical expertise, using the RAND/UCLA Appropriateness Method. Key clinical indications are reported in Table 2.

TABLE 1. Consensus based recommendations for the early management of out-of-hospital respiratory distress valve implantation.

Number	Statement	Appropriateness	GRADE
1	The use of pulsoxymeter as additional tool for management respiratory distress in the out-of-hospital setting	Appropriate	IC
2	The use of venous blood gas analysis as additional tool to improve the management respiratory distress in the out-of-hospital setting	Appropriate	IC
3	Intervene when respiratory distress/acute respiratory failure is identified out-of-hospital, even if the underlying cause is not yet diagnosed	Appropriate	IC
4	NIV therapy alone is sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Appropriate	IC
5	Provide advanced respiratory support (*e.g.*, NIV, CPAP) rather than only oxygen therapy in out-of-hospital patients with moderate to severe respiratory distress	Appropriate	IC
6	Start NIV as soon as possible (*e.g.*, <10 min) in severe respiratory distress	Appropriate	IC
7	Start oxygen therapy as soon as possible (*e.g.*, <10 min) in severe respiratory distress	Appropriate	IC
8	Is it appropriate to use oxygen therapy in order to improve the patient's symptoms?	Appropriate	IC
9	Simple oxygen therapy on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Appropriate	IC
10	NIV therapy on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Appropriate	IC
11	Oxygen therapy prevents clinical deterioration	Appropriate	IC
12	Non-invasive ventilation improves the patient's symptoms	Appropriate	IC
13	Non-invasive ventilation prevents clinical deterioration	Appropriate	IC
14	The use of out-of-hospital NIV for patients with suspected acute exacerbation of COPD presenting with respiratory failure	Appropriate	IC
15	The use of out-of-hospital NIV for patients with acute cardiogenic pulmonary oedema	Appropriate	IC
16	The use of out-of-hospital oxygen for patients with acute cardiogenic pulmonary oedema	Appropriate	IC
17	The use of out-of-hospital NIV for patients with respiratory distress due to pneumonia	Appropriate	IC
18	The use of out-of-hospital oxygen for patients with respiratory distress due to pneumonia	Appropriate	IC
19	The use of out-of-hospital oxygen for patients with respiratory distress due to asthma	Appropriate	IC
20	The use of out-of-hospital NIV for patients with respiratory distress due to neuromuscular diseases	Appropriate	IC
21	The use of out-of-hospital oxygen for patients with suspected respiratory distress due to pulmonary embolism	Appropriate	IC
22	The use of non-invasive ventilation in out-of-hospital settings for patients with acute respiratory failure	Appropriate	IC
23	Initiate NIV before patient transport to the hospital rather than waiting until arrival at the emergency department	Appropriate	IC
24	Initiate out-of-hospital non-invasive ventilation in patients with acute respiratory distress who are already on chronic home NIV (*e.g.*, using their own device)	Appropriate	IC
25	Continue NIV during ambulance transport	Appropriate	IC
26	Consider HFNC in the management of out-of-hospital respiratory distress	Appropriate	IC
27	When oxygen therapy is indicated, titrate oxygen to target oxygen saturation levels rather than routinely administering high-flow oxygen	Appropriate	IC
28	The use nasal capnography as additional tool to improve the management respiratory distress in the out-of-hospital setting	Uncertain	
29	Simple oxygen therapy alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
30	Bronchodilators alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
31	Nebulized adrenaline alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
32	Diuretics alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	

TABLE 1. Continued.

Number	Statement	Appropriateness	GRADE
33	Corticosteroids therapy on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
34	Pain killer on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
35	Bronchodilators on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
36	Nebulized adrenaline on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
37	Diuretics on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Uncertain	
38	The use of out-of-hospital oxygen for patients with suspected acute exacerbation of COPD presenting with respiratory failure	Uncertain	
39	The out-of-hospital NIV for patients with respiratory distress due to asthma	Uncertain	
40	The use of out-of-hospital NIV for patients with suspected respiratory distress due to pulmonary embolism	Uncertain	
41	The use arterial blood gas analysis as additional tool to improve the management respiratory distress in the out-of-hospital setting	Inappropriate	IC
42	Corticosteroids therapy alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
43	Physiotherapy alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
44	NSAIDs alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
45	Anticoagulant alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
46	Pain killer alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
47	Autogenic training alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
48	Sedatives alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
49	Magnesium sulphate alone may be sufficient to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
50	Physiotherapy alone on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
51	NSAIDs on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
52	Anticoagulant on top of standard medical therapy may be useful to postpone clinical deterioration?	Inappropriate	IC
53	Autogenic training on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
54	Sedatives on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
55	Magnesium sulfate on top of standard medical therapy may be useful to postpone clinical deterioration in patients with out-of-hospital respiratory distress	Inappropriate	IC
56	Prefer oxygen therapy over NIV in order to improve the patient's symptoms	Inappropriate	IC

1–27: Appropriate; 28–40: Uncertain; 41–56: Inappropriate.
Appropriate: Indications with a median rating of 7–9 and no disagreement. Uncertain: Indications with a median rating of 4–6 or any median accompanied by disagreement. Inappropriate: Indications with a median rating of 1–3 and no disagreement.
NIV, Non-Invasive Ventilation; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; CPAP, Continuous Positive Airway Pressure; COPD, Chronic Obstructive Pulmonary Disease; HFNC, High-Flow Nasal Cannula; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

TABLE 2. Key practice recommendations for out-of-hospital respiratory distress.

Clinical domain	Key recommendation	Appropriateness	GRADE
Early intervention	Initiate treatment for respiratory distress even before a definitive diagnosis is established	Appropriate	IC
Disease-indipendent approach	Apply respiratory support strategies in undifferentiated respiratory distress regardless of etiology	Appropriate	IC
Timing of care	Start oxygen therapy or NIV within 10 min	Appropriate	IC
Respiratory support	Prefer NIV over oxygen alone in moderate-to-severe respiratory distress	Appropriate	IC
Symptom control	Non-invasive ventilation improves symptoms and prevents clinical deterioration	Appropriate	IC
Transport	Continue NIV during ambulance transport when indicated	Appropriate	IC
Diagnostic tools	Avoid routine arterial blood gas analysis in the out-of-hospital setting	Appropriate	IC

NIV, non-invasive ventilation; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

3.1 Diagnostic tool for out-of-hospital respiratory distress

The use of pulse oximetry and venous blood gas analysis as additional tools in the out-of-hospital management of respiratory distress was judged appropriate with a strong recommendation (GRADE IC). The use of nasal capnography was rated uncertain. Routine arterial blood gas analysis was considered inappropriate with a strong recommendation against its use (GRADE IC). Detailed results are reported in Table 1, Fig. 2, **Supplementary Tables 1 and 2**.

Fig. 2 was constructed by translating the appropriateness ratings from the expert panel into a stepwise decision-making algorithm. Items with a median score $\geq$7 and no disagreement (DI $<$1) were incorporated as recommended ("appropriate") actions, whereas items with median scores $\leq$3 or disagreement indicating lack of support were included in the "avoid before diagnosis" section. The figure, therefore, provides a visual synthesis of the consensus-based management pathway for undifferentiated out-of-hospital respiratory distress.

3.2 Respiratory support in respiratory distress

Early intervention when respiratory distress/acute respiratory failure is identified in the out-of-hospital setting, even in the absence of a defined underlying diagnosis, was judged appropriate (GRADE IC). Among therapeutic strategies, NIV alone was the only intervention judged appropriate to be sufficient in postponing clinical deterioration (strong recommendation, GRADE IC). In patients with moderate to severe respiratory distress, it was considered appropriate to prefer NIV over oxygen therapy (strong recommendation, GRADE IC). The following interventions were all rated appropriate (GRADE IC): initiating oxygen or NIV within 10 minutes of presentation, using either modality to improve symptoms or prevent clinical deterioration, and adding oxygen or NIV to standard therapy.

Several interventions were rated uncertain: bronchodilators, nebulized adrenaline, and diuretics; the isolated use of oxygen therapy; and the addition of corticosteroids or analgesics to standard therapy. Conversely, the isolated use of corticosteroids and painkillers was considered inappropriate (strong recommendation, GRADE IC), as was the use of physiotherapy, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), anticoagulants, autogenic training, sedatives, or magnesium sulphate to standard medical therapy. Preferring oxygen therapy over NIV to control symptoms was also deemed inappropriate (strong recommendation, GRADE IC).

Full consensus results for this chapter are reported in Table 1, Fig. 2, **Supplementary Tables 3 and 4**.

3.3 Indication for non-invasive ventilation and oxygen therapy

Out-of-hospital NIV was considered appropriate (GRADE IC) in patients with suspected acute exacerbation of chronic obstructive pulmonary disease (COPD), acute cardiogenic pulmonary oedema, respiratory distress due to pneumonia or neuromuscular disease, and in patients with acute respiratory failure in general. Initiating NIV before hospital transport, continuing NIV during transport, and starting NIV in patients already on chronic home NIV were all judged appropriate (GRADE IC). Oxygen therapy was also deemed appropriate in acute cardiogenic pulmonary oedema, asthma, pulmonary embolism, and pneumonia (GRADE IC). The use of High flow nasal cannula (HFNC) with titrated oxygen therapy to reach target saturations, instead of routine high-flow oxygen, were also considered appropriate (GRADE IC).

Uncertainty was expressed regarding the use of oxygen in COPD exacerbations and the appropriateness of NIV in asthma or suspected pulmonary embolism.

Detailed results for this chapter are reported in Table 1, Fig. 3, **Supplementary Tables 5 and 6**.

4. Discussion

This consensus document, developed using the RAND/UCLA Appropriateness Method, provides the first comprehensive evaluation of early management of out-of-hospital respiratory distress. The panel reached strong consensus on several key issues. Most notably, oxygen therapy and non-invasive ventilation were the only interventions consistently judged

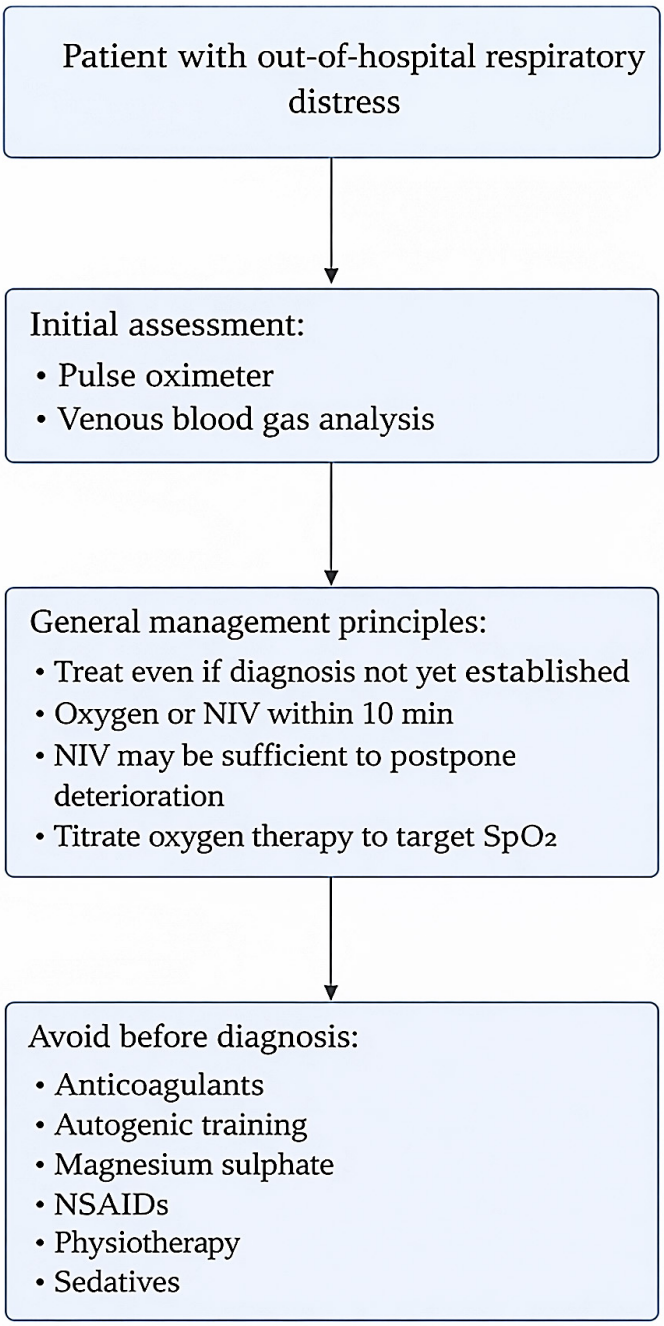

FIGURE 2. Algorithm for general management of out-of-hospital respiratory distress. NIV, non-invasive ventilation; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; SpO_2, Peripheral Capillary Oxygen Saturation.

appropriate both to relieve symptoms and to prevent clinical deterioration. This finding underscores the central role of respiratory support in the out-of-hospital management of undifferentiated respiratory distress, in contrast to the uncertainty or inappropriateness assigned to most pharmacological or supportive interventions when used in isolation.

In addition, treatment should be initiated within 10 minutes of presentation, with oxygen therapy or NIV. Also, in the mixed population of patients with acute respiratory distress—where diagnosis is often unclear in the out-of-hospital setting—NIV should be preferred over oxygen therapy. This recommendation highlights the importance of an early, non-diagnosis-dependent approach, recognizing NIV as the intervention most likely to support patients at the highest risk of rapid deterioration. The endorsement of very early treatment and its continuation during transport acquires particular significance across diverse health systems. In urban settings, early intervention may primarily bridge patients to definitive care, whereas in regions where hospitals are geographically distant, therapy initiated within minutes and maintained en route may effectively constitute the first hours of treatment. Although the recommendation to initiate treatment rapidly seemed intuitive, no previous consensus statement explicitly defined this approach, nor did any prior guideline specify the critical 10-minute threshold identified by our panel. While several interventions were rated inappropriate or uncertain in undifferentiated patients with respiratory distress, the panel recognized that such therapies may be

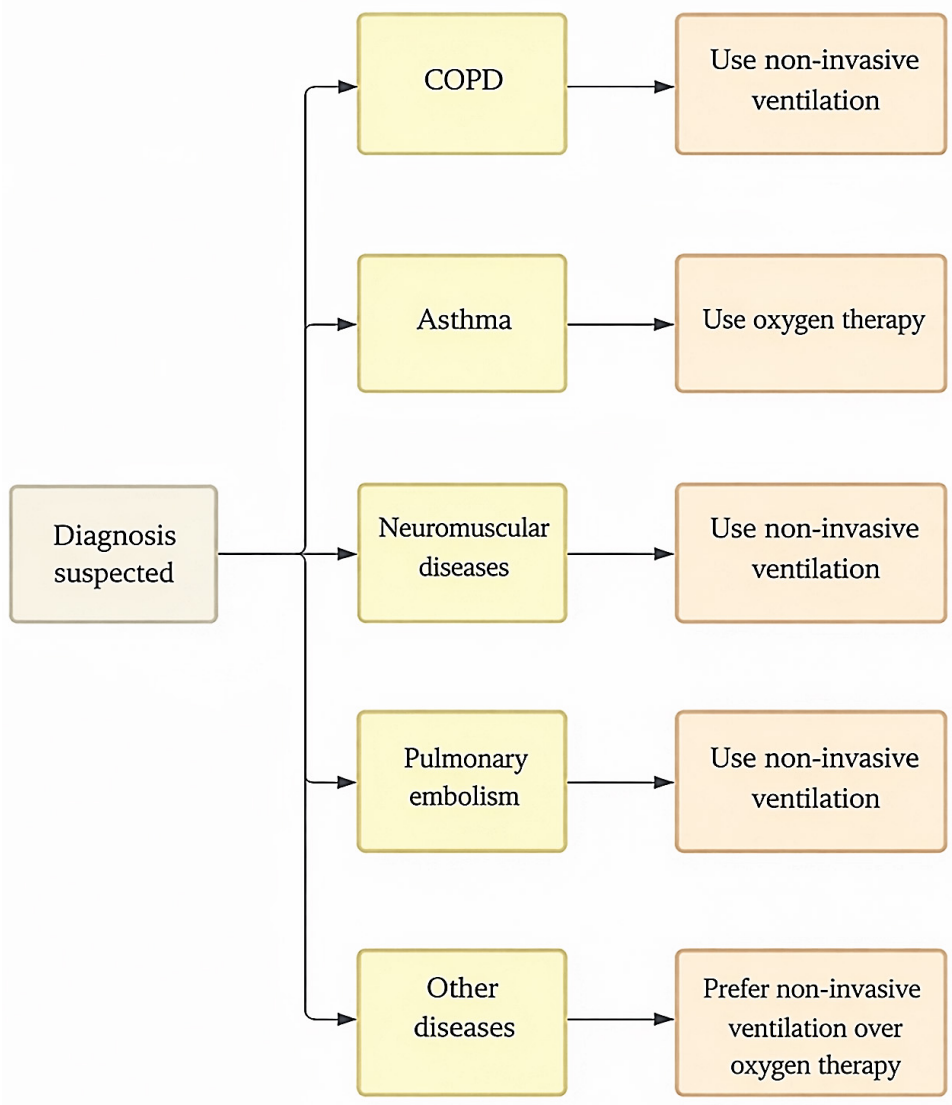

FIGURE 3. Algorithm for disease-specific management of out-of-hospital respiratory distress. COPD, Chronic Obstructive Pulmonary Disease.

highly appropriate in disease-specific contexts. For instance, bronchodilators in acute asthma or diuretics in cardiogenic pulmonary edema remain cornerstones of management once a presumptive diagnosis has been established. This underscores the distinction between guidance for the initial presentation of acute respiratory distress in the field and recommendations tailored to defined disease entities.

The consensus also identifies important gaps for future research. Over one-fifth of statements in the second round were rated uncertain, reflecting areas where evidence is absent or conflicting. These include the role of NIV in asthma or pulmonary embolism, the utility of nasal capnography, and the effectiveness of pharmacological agents when used in isolation or on top of standard therapy in the out-of-hospital setting. Addressing these gaps will require prospective multicenter studies or randomized trials, ideally embedded within EMS systems.

Previous efforts focused primarily on disease-specific management of respiratory distress, addressing interventions such as oxygen titration, bronchodilators, systemic corticosteroids, nitrates, diuretics, and non-invasive ventilation in conditions like COPD, asthma, and acute pulmonary edema, and were not specifically focused on the out-of-hospital setting [15–17]. These recommendations provided guidance for the treatment of defined diagnostic categories, and their purpose was largely to harmonize protocols across local EMS agencies. By contrast, the present consensus is disease-agnostic and addresses the broader clinical challenge of patients presenting with acute respiratory distress in the out-of-hospital setting, where a precise diagnosis is often not immediately available. Rather than defining treatment pathways for individual conditions, our panel evaluated the appropriateness of interventions in undifferentiated patients presenting with acute shortness of breath distress, reflecting the diagnostic uncertainty and time-critical nature of out-of-hospital care. This distinction is critical: while disease-specific consensus statements guide treatment once a working diagnosis has been made, our approach aims to support decision-making at the very first point of patient contact, when early interventions may influence outcomes, but diagnostic clarity is limited. The apparent overlap among certain statements reflects the need to separately address different clinical goals in the out-of-hospital setting,

where interventions may be used to relieve symptoms, prevent deterioration, or complement standard therapy; each of these dimensions was therefore assessed independently within the consensus process [18, 19]. A central implication of this consensus is its potential to support clinical decision-making in the presence of diagnostic uncertainty, which is a defining feature of out-of-hospital care. In the prehospital setting, treatment is often required before a definitive diagnosis can be established, relying on limited clinical information and time-sensitive assessments. By adopting a disease-agnostic framework and prioritizing early respiratory support strategies that were consistently judged appropriate, this consensus provides a pragmatic approach to initial management that emphasizes physiological stabilization over diagnostic precision. Such an approach may reduce delays in care and mitigate the risk of early clinical deterioration while preserving flexibility for subsequent, diagnosis-specific interventions once additional information becomes available. Importantly, the identification of interventions rated as inappropriate or uncertain in undifferentiated patients also offers actionable guidance, helping clinicians to avoid potentially ineffective or harmful treatments before a working diagnosis is established. This structured navigation of uncertainty reflects real-world prehospital practice and represents a key contribution of the present consensus.

This consensus document was developed using a modified Delphi methodology, specifically the RAND/UCLA Appropriateness Method, a well-recognized approach that has been successfully applied in hundreds of consensus projects across multiple clinical domains and supported by a rigorously developed methodological manual. Its strengths include the integration of scoping evidence review (**Supplementary material 3**) with structured expert judgment and the ability to distinguish agreement from persistent uncertainty or disagreement. An important strength of this work is the involvement of patient association representatives in the consensus process, which is rarely incorporated in prehospital emergency care guidance and aligns with the principles of patient-centered decision-making promoted by the RAND/UCLA Appropriateness Method. Unlike classical Delphi techniques, the method does not force consensus, allowing unresolved areas to remain explicitly identified. A limitation of the RAND/UCLA method is that all statements must be formulated as questions of "appropriateness", a structure that does not always fit every clinical or organizational issue and may restrict the way certain complex topics can be explored. By integrating targeted literature review with multidisciplinary expert input, the aim was to generate practical guidance in areas where clinical uncertainty remains. In line with the RAND/UCLA Appropriateness Method, representatives from patient associations were included as non-voting participants; while they did not meet the criteria for expert panel membership, their input was central to shaping the statements and ensuring that the patient perspective informed the consensus process.

Although the Delphi RAND/UCLA method ensures a rigorous and transparent process, the consensus is inherently influenced by expert opinion. The limited number of panelists, despite their recognized expertise, may not fully capture the diversity of clinical practice. A limitation of this consensus is the predominant representation of intensivists and anesthesiologists on the panel, with a relative underrepresentation of EMS physicians, paramedics/advanced care practitioners, and emergency physicians. An important limitation of this work is that all recommendations received a GRADE IC rating, indicating very low certainty evidence, and reflecting the heavy reliance on expert opinion necessitated by the limited availability of high-quality randomized studies in the prehospital setting. We focused particularly on non-invasive ventilation, as it represented the only area supported by randomized trials in the prehospital setting. Given the limited and heterogeneous nature of the available data, all statements were conservatively rated as level of evidence "C". While this reflects a limitation in terms of the underlying evidence base, it also represents a strength of the consensus process, The RAND/UCLA Appropriateness Method was applied specifically to address areas of uncertainty and variability, allowing integration of this evidence with multidisciplinary expert judgment. Although the panel consisted exclusively of Italian experts, which we acknowledge as a limitation, as it may not fully reflect variations in EMS organization and practice in other countries, the practice environment is characterized by high out-of-hospital caseloads: emergency medical services handled approximately ~14,000 per 100,000 inhabitants [20]. The participating centers represent a spectrum of institutional models and procedural volumes, thereby mirroring elements common to high-performing international programs. Additionally, the protocol of the qualitative scoping review was not prospectively registered and no formal risk-of-bias assessment was performed, as the review was designed to inform the RAND/UCLA consensus process, rather than to function as a standalone systematic synthesis. Moreover, the RAND/UCLA methodology emphasizes the evaluation of appropriateness in relation to clinical contexts, rather than institutional norms, making the resulting recommendations broadly adaptable. The use of a structured, scenario-based RAND/UCLA methodology supports generalizability and offers a reproducible framework for application in diverse healthcare systems with varying levels of anesthesiology involvement. The panel consisted of only sixteen members, which, despite their recognized expertise, may not fully capture the breadth of nationwide clinical practice. However, this aligns with RAND/UCLA methodology, which is specifically designed for structured consensus among small, multidisciplinary groups of experts. The panel did not evaluate the management of patients with a tracheostomy, nor did it address the role of invasive mechanical ventilation in the out-of-hospital setting. Similarly, issues related to humidification devices and the palliative care for patients with advanced respiratory disease were not included in the scope of this work. These areas remain clinically important and warrant dedicated evaluation in future studies and consensus efforts.

A formal grading system for the strength of evidence was employed, and the recommendations reflects the group's collective assessment of the underlying evidence. Areas with limited evidence or ongoing debate have been explicitly identified and addressed throughout the document.

This consensus provides a practical foundation for national and institutional protocols aimed at optimizing early management of out-of-hospital respiratory distress. Further re-

search should prioritize the uncertain or controversial areas identified by the panel, ideally through randomized controlled trial, to generate definitive guidance in the future. Given the predominance of expert consensus-based recommendations (evidence level C), this document also serves to identify important gaps in current knowledge. Future prospective or randomized studies are particularly warranted to clarify the optimal early management of out-of-hospital respiratory distress in patients with high-risk comorbidities, the role of caregivers in home-initiated respiratory support, the best advanced monitoring modalities, how clinical phenotypes should guide prehospital management, how standardized protocol can impact patient outcomes, and the impact of out-of-hospital strategies—such as high flow nasal cannula—on clinical outcomes (**Supplementary Table 7**).

5. Conclusions

This consensus offers practical, expert-driven recommendations aimed at standardizing the early management of out-of-hospital respiratory distress. Although strong agreement was achieved for several key statements, relevant areas of uncertainty persist. Further well-designed clinical studies are, therefore, needed to refine and validate these recommendations.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

KD, PP, FL, FDA, VR, RL, ABB, FCo, GP, FMO, AL, GG, VA, AB, RV, MBR, FCa, PB, SB, AR, GS, GF and GMo—conceived the study. AB, RV, MBR, GMo, FCo, PB, SB, AR, GS, GF and GMa—designed the search strategy and did the literature search. KD, PP, FL, FDA, VR, RL, ABB, FCo, GP, FMO, AL, GG and VA—did the statistical analysis. FCa, GP, FMO, AL, GG, VA, AR, GS, GF and GMo—wrote the initial protocol. KD, PP, FL, FDA, VR, RL, ABB, AB, RV, MBR, GMa, FCo, PB and SB—wrote the manuscript. All authors shared the study data, gave a critical appraisal of the protocol, provided crucial revisions, and approved the final manuscript. All authors approved the final version of the manuscript. They agree to be accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Alessandro Belletti, Martina Baiardo Redaelli and Giacomo Monti are serving as the Editorial Board members of this journal. We declare that Alessandro Belletti, Martina Baiardo Redaelli and Giacomo Monti had no involvement in the peer review of this article and have no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to VL.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/2038855707904622592/attachment/Supplementary%20material.docx.

REFERENCES

[1] Zhou J, Nehme E, Dawson L, Bloom J, Nehme Z, Okyere D, *et al*. Epidemiology, outcomes and predictors of mortality in patients transported by ambulance for dyspnoea: a population-based cohort study. Emergency Medicine Australasia. 2023; 35: 48–55.

[2] Pittet V, Burnand B, Yersin B, Carron PN. Trends of pre-hospital emergency medical services activity over 10 years: a population-based registry analysis. BMC Health Services Research. 2014; 14: 380.

[3] Kelly AM, Holdgate A, Keijzers G, Klim S, Graham CA, Craig S, *et al*.; AANZDEM Study Group. Epidemiology, prehospital care and outcomes of patients arriving by ambulance with dyspnoea: an observational study. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine. 2016; 24: 113.

[4] Del Pozo Vegas C, Sanz-García A, Dueñas-Ruiz A, de Santos Castro P, Gil Contreras A, Blanco González M, *et al*. Prehospital oxygen-therapy and mortality in patients treated by emergency medical services: a prospective, observational multicenter study. World Journal of Emergency Medicine. 2025; 16: 357–366.

[5] Spörl P, Beckers SK, Rossaint R, Felzen M, Schröder H. Shedding light into the black box of out-of-hospital respiratory distress—a retrospective cohort analysis of discharge diagnoses, prehospital diagnostic accuracy, and predictors of mortality. PLOS ONE. 2022; 17: e0271982.

[6] Balen F, Lamy S, Fraisse S, Trinari J, Bounes V, Dubucs X, *et al*. Predictive factors for early requirement of respiratory support through phone call to Emergency Medical Call Centre for dyspnoea: a retrospective cohort study. European Journal of Emergency Medicine. 2023; 30: 432–437.

[7] Bakke SA, Botker MT, Riddervold IS, Kirkegaard H, Christensen EF. Continuous positive airway pressure and noninvasive ventilation in prehospital treatment of patients with acute respiratory failure: a systematic review of controlled studies. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine. 2014; 22: 69.

[8] Scquizzato T, Imbriaco G, Moro F, Losiggio R, Cabrini L, Consolo F, *et al*. Non-invasive ventilation in the prehospital emergency setting: a systematic review and meta-analysis. Prehospital Emergency Care. 2023; 27: 566–574.

[9] Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH, *et al*. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of

the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. Circulation. 2025; 151: e771–e862.

[10] Fonarow GC, Smith EE, Saver JL, Reeves MJ, Hernandez AF, Peterson ED, *et al*. Improving door-to-needle times in acute ischemic stroke: the design and rationale for the American Heart Association/American Stroke Association's Target: stroke initiative. Stroke. 2011; 42: 2983–2989.

[11] Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lázaro P, *et al*. The RAND/UCLA appropriateness method user's manual. 2001. Available at: https://www.rand.org/pubs/monograph_reports/MR1269.html (Accessed: 29 January 2026).

[12] Monti G, Cabrini L, Kotani Y, Brusasco C, Kadralinova A, Giardina G, *et al*.; NAVIGATE Study Group. Early noninvasive ventilation in general wards for acute respiratory failure: an international, multicentre, open-label, randomised trial. British Journal of Anaesthesia. 2025; 134: 382–391.

[13] Glahn KPE, Bendixen D, Girard T, Hopkins PM, Johannsen S, Rüffert H, *et al*.; European Malignant Hyperthermia Group. Availability of dantrolene for the management of malignant hyperthermia crises: European Malignant Hyperthermia Group guidelines. British Journal of Anaesthesia. 2020; 125: 133–140.

[14] Rüffert H, Bastian B, Bendixen D, Girard T, Heiderich S, Hellblom A, *et al*.; European Malignant Hyperthermia Group. Consensus guidelines on perioperative management of malignant hyperthermia suspected or susceptible patients from the European Malignant Hyperthermia Group. British Journal of Anaesthesia. 2021; 126: 120–130.

[15] Hodroge SS, Glenn M, Breyre A, Lee B, Aldridge NR, Sporer KA, *et al*. Adult patients with respiratory distress: current evidence-based recommendations for prehospital care. The Western Journal of Emergency Medicine. 2020; 21: 849–857.

[16] Baugh CW, Neuenschwander JF, Lenox J, Hoh J, Ward K, Muramoto S, *et al*. Acute care of patients with moderate respiratory distress: recommendations from an American College of Emergency Physicians expert panel. The Western Journal of Emergency Medicine. 2025; 26: 1485–1494.

[17] Holland AE, Spathis A, Marsaa K, Bausewein C, Ahmadi Z, Burge AT, *et al*. European Respiratory Society clinical practice guideline on symptom management for adults with serious respiratory illness. European Respiratory Journal. 2024; 63: 2400335.

[18] Scquizzato T, D'Amico F, Rocchi M, Saracino M, Stella F, Landoni G, *et al*. Impact of COVID-19 pandemic on out-of-hospital cardiac arrest system-of-care: a systematic review and meta-analysis. Prehospital Emergency Care. 2022; 26: 30–41.

[19] Scquizzato T, Landoni G, Scandroglio AM, Franco A, Calabrò MG, Paoli A, *et al*. Outcomes of out-of-hospital cardiac arrest in patients with SARS-CoV-2 infection: a systematic review and meta-analysis. European Journal of Emergency Medicine. 2021; 28: 423–431.

[20] Regione Emilia Romagna. Emergency Medical Service (118): over 1,400 patients assisted per day (rapidly increasing), with an average response time of 15 minutes (4 minutes faster than the national average). 2025. Available at: https://www.regione.emilia-romagna.it/notizie/2025/luglio/118-dati2024?utm (Accessed: 29 January 2026).

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