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Protocol for the development of a guideline on post-extubation respiratory support for mechanically ventilated patients in ICU

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**Protocol for the development of a guideline on post-extubation
respiratory support for mechanically ventilated patients in ICU**

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Background: Prophylactic respiratory support for patients after extubation is effective in improving their outcomes and prognosis. However, the optimal post-extubation respiratory support for different populations and different disease types of mechanically ventilated patients is still controversial, and there is a lack of detailed, multidisciplinary, evidence-based recommendations for clinical application.

Methods: This guideline strictly follows the development process of the WHO handbook for guideline development and Guidelines 2.0 and the guidelines for the development of relevant methodological standards. Key steps in developing the guideline include the following: (i) establishing the guideline working groups; (ii) defining the scope of guideline application; (iii) selecting the priority clinical questions; (iv) evidence retrieval and screening; (v) grading the quality of evidence; (vi) forming recommendations; and (vii) external review.

Discussion: This guideline will provide guidance on choosing the best form of respiratory support after extubation for mechanically ventilated patients in different populations (adults, children, neonates) and different disease types, thereby reducing the rate of reintubation and mortality and improving prognosis of patients. The

protocol will guarantee the standardization of the development method as well as the openness and transparency of the development process.

Ethics and dissemination: Ethical approval has been granted by Changzhi People's Hospital(2023K023). Findings from this study will be disseminated through peer-review publications.

Guideline registration: PREPARE-2023CN418.

Keywords: respiratory support; mechanical ventilation; guideline; Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

Strengths and limitations of this study

1. The strengths of this study lie in the diversity of our working groups: clinical and nursing scientists from different fields (ICU, Pediatric ICU and Neonatal ICU), Methodologists, epidemiologists, policy-makers.
2. This is a post-extubation respiratory support guideline developed specifically for different populations and different disease types of mechanically ventilated patients.
3. We developed this guideline protocol and formal guideline document in strict accordance with the guidelines 2.0 and the RIGHT.
4. The limitation of this study is that only literature in Chinese and English will be included.

Introduction

About 30% of patients in ICU rely on mechanical ventilation for assisted breathing^[1,2]. However, long-term mechanical ventilation leads to a significantly higher incidence of complications related to Intensive Care Unit-Acquired Weakness (ICU-AW), Pulmonary Atelectasis, Pneumothorax, Ventilator-associated pneumonia (VAP), etc, which seriously impairs physical function, delays recovery, and also increases the cost of treatment^[3-5]. Therefore, during the course of treatment, when the patient's primary illness is under control and ventilation and oxygenation are corrected, the ventilator should be disconnected and the artificial airway should be

removed as soon as possible (extubation)^[6].

However, there are some patients (about 10%-30%) with complex and critical conditions (high risk of extubation failure) in the ICU, who after extubation again experience respiratory distress, decreased oxygenation, and inability to maintain spontaneous breathing, i.e., extubation failure, requiring secondary intubation. Secondary intubation not only leads to prolonged mechanical ventilation, but even death in up to 25-50% of patients^[7,8].

Respiratory support technique is an important tool to maintain the relative stability of respiratory function in critically ill patients. Several studies found that post-extubation respiratory support for patients at high risk of extubation failure is effective in improving clinical symptoms, lung function, prognosis, and reducing the rate of reintubation and mortality^[9]. In recent years, common respiratory support techniques for patients include Conventional oxygen therapy (COT), Nasal continuous positive airway pressure (NCPAP), Noninvasive positive pressure ventilation (NIPPV) and High-flow nasal cannula (HFNC), etc^[10,11]. However, the optimal post-extubation respiratory support for mechanically ventilated patients in different populations (adults, children, neonates) and different diseases is controversial, and there is no guideline to provide guidance on the optimal post-extubation respiratory support for mechanically ventilated patients. In other words, there is a lack of detailed, multidisciplinary, evidence-based recommendations for clinical application. Therefore, it is necessary to develop a high-quality, evidence-based guideline for post-extubation respiratory support in mechanically ventilated patients.

Therefore, we aimed to develop a guideline for respiratory support after extubation for mechanically ventilated patients in ICU to improve their outcomes and prognosis, based on the methodology of the WHO Manual for Guideline Development (2nd edition, 2014)^[12].

Methods

Guidance of Guideline

We will develop the guideline in accordance with the American Academy of Medical Sciences (Institution of Medicine, IOM) ^[13] clinical practice guideline concept, the develop processes and relevant methodological standards of WHO handbook for guideline development^[14], and use guideline research and evaluation tool(Appraisal of

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Guidelines for Research and Evaluation II , AGREE II)^[15]. Develop this protocol and the formal guideline according to the guidelines 2.0 and the Reporting Items for practice Guidelines in Healthcare (RIGHT)^[16]. This study of guideline development begins in May 2023 and ends in July 2024. The key steps and timeline of the guideline is shown in the Gantt chart (Figure 1).

Key steps	20 23 /05	20 23 /06	20 23 /07	20 23 /08	20 23 /09	20 23 /10	20 23 /11	20 23 /12	20 24 /01	20 24/ 02	20 24/ 03	20 24/ 04	20 24/ 05	20 24/ 06	20 24/ 07
Launch the guideline															
Establish the guideline working groups															
Guideline registration and plan writing															
Formulate clinical questions (PICO questions)															
Evidence retrieval, evaluation, and synthesis															
Grade the quality of the body of evidence															
Draft the recommendations															
Formulate the final recommendations															
Draft full guideline															
Send to external reviewers															
Revise the guideline															
Submit to medical journal															

Figure 1 Gantt Chart: the key steps and timeline of guideline development. PICO, patient/population, intervention, comparison, and outcomes.

Guidance sponsorship and support units

This guide is jointly initiated by Changzhi Nursing Association and Changzhi People's Hospital. The methodology and evidence will be supported by the Evidence-Based Medicine Center of Lanzhou University and the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation.

Guideline registration

Establishment of guideline working groups

Table 1 The composition and responsibilities of the guideline working groups

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Group	Composition	Responsibility
		(III) assess conflicts of interest and deal with conflicts as needed
		(IV) chaired the guide work meeting
		(V) review and approval plan
		(VI) approved recommendations and full guidelines
		(VII) suination and update of the guide
consensus expert group	consists of 25 to 30 experts in the fields of critical care, respiratory, pediatrics, neonatology, and respiratory therapists.	(I) Priority topics and outcome indicators of evaluation guidelines
		(II) formed recommendations on some issues
		(III) reached consensus on recommendations
		(IV) modified the full text of the guidelines and gave feedback
		(V) published and promoted guidelines
secretarial group	consists of 3 to 5 staff members of the lead unit.	(I) Complete the guide registration and draft the guide plan
		(II) investigate the clinical problems of the guidelines, design the questionnaire according to the initially formed clinical problem list, collect clinical problems and ranked the importance of clinical problems
		(III) coordinate the work of other working groups
		(IV) organize recommendation consensus meeting
		(V) complete the coordination of external review of the whole process of the guide
		(VI) recorded the whole process of the detailed guide
		(VII) draft the draft guide

Group	Composition	Responsibility
evidence evaluation group	consists of 3 to 10 people with evidence-based medicine background and experienced evidence retrieval.	(VIII)guide submission
		(I) completed the guide literature search, screening, evidence extraction, risk of bias evaluation and GRADE evidence rating
		(II) completed the quality evaluation of the published systematic evaluation / Meta analysis related to the guide topic
		(III) completed the update and production of meta analysis
external audit expert group	composed of 5 to 10 experts engaged in related fields who do not directly participate in the formulation of the guidelines.	(IV) made the evidence summary table and recommendation opinion decision table
		(I) evaluate and review the problems and scope of the clinical practice guidelines
		(II) review the final recommendations
		(III) provides specific amendments for the full text of the guidelines

Scope of the guideline

The guideline focuses on the key issues in the post-extubation respiratory support treatment for patients with mechanical ventilation in ICU. The users of the guideline are ICU clinicians, nurses, respiratory therapists and other medical workers. The guideline apply to all levels of medical institutions including adults, children, and neonates, and the target population is all patients post-extubation of mechanical ventilation in ICU.

Interest statement and fund grants

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All members of the Guide Steering Committee, Guide Consensus Expert Group, External Audit Expert Group, Guide Secretary Group and Evidence Evaluation Group are required to fill in the conflict of interest declaration form and manage possible conflicts of interest. This guideline does not receive any pharmaceutical enterprise fund funding.

Identification of clinical problems and evaluation of their importance

Preliminary clinical questions by searching relevant domestic and international guidelines and conducting questionnaires to clinicians, nurses and respiratory therapists. The secretarial group will be responsible for sorting out the collected clinical problems, and by eliminating duplication and merger, the related problems that need emergency guidance after extubation in mechanically ventilated ICU are summarized and sorted out. After the initial list of clinical questions is developed, it will be discussed by the Steering Committee, which will convene a panel of experts to discuss the list of clinical questions. Two rounds of Delphi method to determine the final clinical problems of the guideline. In the second round meeting, the team members will evaluate the importance of all issues (using 5-point system, the highest score, the lowest score, the clinical problem is not important). Finally construct specific clinical problems according to P (population), I (intervention), C (control), O (outcome) elements. After that, the top 10 to 20 clinical questions will be selected in the order of the highest score. After being approved by the expert committee, the clinical problems to be solved in this guideline will be determined.

Evidence retrieval, screening, and data extraction

The following electronic databases will be searched for eligible studies: Pubmed, Medline, Embase, The Cochrane Library, Epistemonikos, Up To Date, BMJ Best Practice, Clinical Key, DynaMed Plus, the China Biology Medicine disc (CBM), ClinicalTrials.gov, the International Clinical Trial Registry Platform (ICTRP) and other Chinese and English databases. At the same time, we will supplement the retrieval of clinical trial registration platform and trace the references included in the literature. Subject headings and free terms will be used to form the search strategy. The search is limited to the period from construction of the library to October 2023.

The limited language is English or Chinese. The search terms include “Airway Extubation*”, “Tracheal Extubation*”, “Intratracheal Extubation*”, “Endotracheal Extubation*”, “post-extubation”, “high flow nasal cannula”, “high flow nasal oxygen”, “HFNC”, “HHFNC”, “HHFN”, “NHF*”, “high flow”, “Cannula”, “Nasal Cannula*”, “oxygen inhalation therap*”, “Positive Pressure Respiration”, “Non-Invasive Ventilation*”, “Noninvasive Ventilation*”, “non-invasive positive pressure ventilation*”, “noninvasive positive pressure ventilation*”, “NIPPV”, “NPPV”, “conventional oxygen therapy”, “COT”, “standard oxygen therapy”, “SOT”, “venturi mask”, “face mask”, “bag valve mask”. The search strategy for the PubMed database is presented in the Supplementary.

The study types include: relevant domestic and foreign guidelines, systematic review or meta-analysis and randomized controlled trials, diagnostic tests, cohort studies, case-control studies, case series and case reports, etc. First we will include secondary research literature such as clinical practice guidelines, expert consensus, reticulated Meta-analysis, systematic review or Meta-analysis, health technology assessment. If the quality of the literature of secondary research can't solve the clinical problems that need to be answered in the guideline, there is no relevant secondary evidence and it needs to be updated (the publication year is more than 2 years and the original research is published within 2 years), we will systematically search RCT, non-randomized controlled studies, case reports and other studies.

The guideline development team will search independently in groups of two, and screen the literature according to the order of title, abstract and full text, extract the literature information, and record the literatures obtained from the initial search and the number of literatures finally included. Any disagreements will be resolved by joint discussion or consultation with a third-party, evidence-based methodologist.

Evaluation of the quality of the literature

We will use the Clinical Guidelines Research and Evaluation Scale(AGREE II)^[17] , the Methodological Quality of Systematic Reviews (AMSTAR)^[18], the Cochrane Collaboration's tool for assessing risk of bias in randomized trials^[19],and the Newcastle-Ottawa Scale (NOS)^[20]to evaluate the methodological quality of the

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included literature. The evaluation process will be completed independently by two researchers, and any disagreements will be resolved by joint discussion or consultation with an evidence-based methodologist who consult a third party.

Grading the quality of evidence and recommendation strength

The quality of evidence and the strength of recommendation will be grade using the GRADE grading criteria. Classification of evidence quality: high (A), very sure, the observed value is close to the real value; medium (B), medium sure of the observed value, the observed value may be close to the real value, or very different; low (C), the observed value is limited, the observed value may be very different from the real value; very low (D), the observed value may be very different from the real value. Four recommendation levels will be given to the recommendations supported by evidence: strong, weak, strong against, and weak against (Table 2).

Table 2 GRADE strength level of recommendation

Strength level	Definition
Strong (I)	Support the use of an intervention where the benefits clearly outweigh the risks
Weak (II)	Support the use of an intervention where the benefits may outweigh the risks
Strong against (I)	Oppose the use of an intervention where the risks clearly outweigh the benefits
Weak against (II)	Oppose the use of an intervention where the risks may outweigh the benefits or the balance of benefits and risks is unclear

GRADE, Grading of Recommendations Assessment.

Forming recommendations and reaching consensus

For each clinical problem, the members of the evidence evaluation group sort out all the evidence, clearly present the study type and quality of evidence, form a detailed evidence summary table, and form a preliminary recommendation and recommendation basis based on patients' values and preferences, economic costs and balance of advantages and disadvantages. Then the consensus panel will be invited to participate in two rounds of modified Delphi questionnaires to reach consensus on the recommendations. For recommendations without consensus, the next round of Delphi

questionnaire survey will be revised based on expert opinion. The consensus recommendation should be met: at least 3/4 of the voting experts agree with the recommendation; for the recommendation without consensus, the second Delphi questionnaire is modified based on the expert opinion. In this process, the secretarial group will give feedback to the experts one by one, and modify the recommendations accordingly. The final recommendation after the expert consensus shall be submitted to the guidance committee for review. If the contents are modified and improved, the guideline steering Committee shall obtain the consent of at least two-thirds of the members of the consensus expert group, and the secretarial group shall truthfully record the entire revision process.

Writing of the guideline and external review of recommendations

The secretarial group will write the first draft of the guide according to the RIGHT entries, and submit the first draft to the experts of the external audit expert group for review and feedback. The external audit expert group is composed of clinical medical experts, nursing experts, methodology experts and other multidisciplinary personnel. They will examine and approve from the aspects of approval degree, expression clarity and clinical feasibility, and fill in the improvement opinions. The secretarial group and the evidence evaluation group will revise the first draft of the opinions of external audit experts and form the final draft of the guideline.

Guideline approval, release, and update

The final draft of the guideline will be reviewed, determined, and approved by the expert committee. With the agreement of 2/3 of the experts in the consensus group, the expert committee can modify and improve the important issues in the proposal, and the secretary group should record the whole modification process faithfully.

Guideline dissemination, implementation, and evaluation

After the release of the guideline, the project team will disseminate and promote the guideline mainly in the following ways: (I) introduce in relevant academic conferences; (II) organize special guide promotion sessions in some provinces and cities in China to ensure that clinicians, respiratory therapists and nurses can fully understand and correctly apply the guideline; (III) push the guideline interpretation on

medical websites, APP and short video platforms commonly used in China. Two to three years after the publication and implementation of the full text of the guideline, the current status of post-extubation respiratory support modalities for mechanically ventilated patients in ICU in China and abroad will be evaluated to understand the dissemination of the guideline, the recognition of the recommendations in clinical practice and the impact on treatment decisions. At the same time, it is beneficial to improve and perfect the guideline when it is updated.

Discussion

Due to physiological differences in adults, children and neonates (e.g., preterm neonates are more prone to complications and even death after extubation due to immature organ function, especially respiratory function^[21].) as well as different characteristics of different diseases (e.g., in patients with respiratory failure, severe impairment of pulmonary ventilation and/or air exchange is likely to cause a series of pathophysiological changes and corresponding clinical manifestations of the syndrome^[22].), it is clear that it is not reasonable to give the same type of respiratory support to all extubated patients, but rather to provide respiratory support tailored to their needs in order to maintain normal respiratory function and thus improve their prognosis.

With the progress and development of medical technology, there are various ways of post-extubation with respiratory support in mechanically ventilated patients. Non-invasive ventilation (NIV) maintains airway defenses while re-dilating the bronchi and restoring respiratory mechanics, but it has a high complication rate^[23]. NCPAP and NIPPV are two common forms of non-invasive ventilation. NCPAP improves alveolar compliance, reduces airway resistance, and improves pulmonary ventilation and air exchange; however, it is relatively poorly tolerated and adherent^[24]. NIPPV provides positive end-expiratory pressure and positive airway pressure and improves cardiopulmonary function and oxygenation index, but it may increase the risk of ventilator-associated lung injury^[25]. NHFOV is an emerging non-invasive ventilation modality that adds pressure oscillation to NCPAP, giving it greater advantages in maintaining alveolar stability, improving oxygenation, and

promoting carbon dioxide expulsion^[26]. HFNC is also a new form of respiratory support that provides patients with a high flow of heated and humidified gas with a stable concentration of inhaled oxygen, which can significantly improves their comfort and tolerability with good clinical outcomes.^[27,28] However, current guidelines only provide recommendations for the prophylactic use of respiratory support in post-extubation patients, but still do not explicitly provide specific recommendations for different populations and different diseases^[29], so users are often unable to obtain useful information on respiratory support modalities from these guidelines.

Therefore, in order to recommend the best respiratory support modalities for patients, we will form a multidisciplinary team to develop a guideline for post-extubation respiratory support in mechanically ventilated patients, and strictly follow the WHO guideline development manual^[14] and a comprehensive checklist for guideline development^[30], using this protocol as the basis and framework for guideline development, thus guaranteeing standardization of the development process and methodology. Based on the results of the literature review and questionnaire survey, the guideline development working group will fully understand the key clinical issues that need to be addressed in post-extubation respiratory support, after which the best available clinical evidence will be systematically searched, evaluated and graded, and the experience of clinical experts will be combined with various factors to develop high-quality post-extubation respiratory support guidelines, with the aim of scientifically guiding evidence-based clinical practice and improving clinical outcomes for patients.

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Search Strategy for PubMed

#1 "Airway Extubation"[Mesh] OR "Airway Extubation*"[Title/Abstract] OR "Tracheal Extubation*"[Title/Abstract] OR "High-Frequency Ventilation"[Title/Abstract] OR "Endotracheal Extubation*"[Title/Abstract] OR "post-extubation"[Title/Abstract] OR "Ventilator Weaning"[Mesh] OR "Weaning, Ventilator"[Title/Abstract] OR "Respirator Weaning"[Title/Abstract] OR "Mechanical Ventilator Weaning"[Title/Abstract]

#2 "Respiratory Support"[Title/Abstract] OR "high flow nasal cannula"[Title/Abstract] OR "high flow nasal oxygen"[Title/Abstract] OR "HFNC"[Title/Abstract] OR "HHFNC"[Title/Abstract] OR "HHFN"[Title/Abstract] OR "NHF*"[Title/Abstract]

#3 ("high flow"[Title/Abstract] AND ("Cannula"[Mesh] OR "Nasal Cannula*"[Title/Abstract])) OR ("high flow"[Title/Abstract] AND ("oxygen inhalation therapy"[MeSH] OR "oxygen inhalation therap*"[Title/Abstract]))

#4 "Positive Pressure Respiration"[Mesh] OR "Noninvasive Ventilation"[Mesh] OR "Noninvasive Ventilation*"[Title/Abstract] OR "Non-Invasive Ventilation*"[Title/Abstract] OR "non-invasive positive pressure ventilation*"[Title/Abstract] OR "noninvasive positive pressure ventilation*"[Title/Abstract] OR "NIPPV"[Title/Abstract] OR "NPPV"[Title/Abstract] OR "conventional oxygen therapy"[Title/Abstract] OR "COT"[Title/Abstract] OR "standard oxygen therapy"[Title/Abstract] OR "SOT"[Title/Abstract] OR "venturi mask"[Title/Abstract] OR "face mask"[Title/Abstract] OR "bag valve mask"[Title/Abstract]

#5 #1 AND (#2 OR #3 OR #4)

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Background: Prophylactic respiratory support for patients after extubation is effective in improving their outcomes and prognosis. However, the optimal post-extubation respiratory support for different populations and different disease types of mechanically ventilated patients is still controversial, and there is a lack of detailed, multidisciplinary, evidence-based recommendations for clinical application.

Methods: This guideline strictly follows the development process of the WHO handbook for guideline development and Guidelines 2.0 and the guidelines for the development of relevant methodological standards. Key steps in developing the guideline include the following: (i) establishing the guideline working groups; (ii) defining the scope of guideline application; (iii) selecting the priority clinical questions; (iv) evidence retrieval and screening; (v) grading the quality of evidence; (vi) forming recommendations; and (vii) external review.

Discussion: This guideline will provide guidance on choosing the best form of respiratory support after extubation for mechanically ventilated patients in different populations (adults, children, neonates) and different disease types, thereby reducing the rate of reintubation and mortality and improving prognosis of patients. The protocol will guarantee the standardization of the development method as well as the openness and transparency of the development process.

Ethics and dissemination: Ethical approval has been granted by Changzhi People's Hospital(2023K023). Findings from this study will be disseminated through peer-review publications.

Guideline registration: PREPARE-2023CN418.

Keywords: respiratory support; mechanical ventilation; guideline; Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

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Strengths and limitations of this study

1. The strengths of this study lie in the diversity of our working groups: clinical and nursing scientists from different fields (ICU, Pediatric ICU and Neonatal ICU), Methodologists, epidemiologists, policy-makers.
2. This is a post-extubation respiratory support guideline developed specifically for different populations and different disease types of mechanically ventilated patients.
3. We developed this guideline protocol and formal guideline document in strict accordance with the guidelines 2.0 and the RIGHT.
4. The limitation of this study is that only literature in Chinese and English will be included.

Introduction

Approximately 30% of patients in intensive care unit (ICU) rely on mechanical ventilation for respiratory support^{1,2}. However, prolonged mechanical ventilation significantly increases the incidence of complications associated with ICU-acquired weakness (ICU-AW), atelectasis, pneumothorax, ventilator-associated pneumonia (VAP), and other conditions, severely impairing physical functions, delaying recovery, and increasing treatment cost of³⁻⁵. Therefore, during the course of treatment, when the patient's primary condition is under control and ventilation and oxygenation are corrected, the ventilator and the artificial airway (extubation) should be removed as soon as possible⁶. However, some patients in the ICU (about 10%-30%) present complex and critical conditions (high risk of extubation failure), experiencing respiratory distress, reduced oxygenation, and inability to maintain spontaneous breathing after extubation, necessitating re-intubation. Re-intubation not only prolongs the duration of mechanical ventilation, but also results in mortality rates as high as 25-50% in these patients^{7,8}.

Respiratory support is crucial for critically ill patients to maintain relatively stable respiratory function. Several studies have found that providing respiratory support post-extubation to patients at high risk of extubation failure (e.g., due to underlying comorbidities such as heart failure, severe obesity, or chronic obstructive pulmonary disease)⁹ can effectively improve clinical symptoms, lung function, prognosis, and reducing the rates of re-intubation and mortality^{10,11}. However, some studies have found that prophylactic use of respiratory support after extubation in patients with brain injury does not reduce the rate of reintubation and length of hospitalisation^{12,13}.

In recent years, respiratory support for these patients includes conventional oxygen therapy (COT), nasal continuous positive airway pressure (NCPAP), non-invasive positive pressure ventilation (NIPPV) and high-flow nasal cannula (HFNC), etc^{14,15}. Regarding the choice of respiratory support, a guideline recommends using HFNC in high-risk and/or obese patients undergoing cardiac or thoracic surgery to prevent immediate respiratory failure¹⁶. Similarly, the ACP

guideline recommends the use of HFNC in hospitalized adults with acute hypoxaemic respiratory failure after extubation^{16,17}; however, some studies have found that NFNC after extubation does not prevent re-intubation¹⁸, for example, HFNC may be less effective than NIPPV in preventing re-intubation in patients receiving prolonged mechanical ventilation (PMV) for at least 2 weeks¹⁹.

In summary, the effectiveness and optimal respiratory support post-extubation in different populations (adults, children, neonates) and various disease types (such as respiratory failure, post-cardiac surgery, hypercapnia, etc.) remain controversial, and there is no clinical guideline that provides guidance for the best respiratory support after extubation of all types of mechanically ventilated patients²⁰, lacking detailed, multidisciplinary, and evidence-based support. Therefore, it is necessary to develop a high-quality, evidence-based guideline for post-extubation respiratory support in mechanically ventilated patients. Thus, it is necessary to develop a high-quality, evidence-based guideline for respiratory support after extubation for mechanically ventilated patients in ICU, based on the methodology of the WHO Handbook for Guideline Development (2nd edition, 2014)²¹.

Methods

Guiding principles of the guideline We developed the guideline based on the concept of clinical practice guidelines by the US Institution of Medicine (IOM), the National Academy of Medicine²² concept, the guideline development process and methodological standards outlined in WHO Handbook for Guideline Development²³, using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool²⁴. The guideline was formulated in accordance with the guidelines 2.0 and the Reporting items for practice Guidelines in HealThcare (RIGHT)²⁵. We provide a detailed overview of the working groups' directions and their roles in this guideline in Supplementary Table.. This guideline development study began in May 2023 and will end in April 2025. The key steps and timeline of the guideline are shown in a Gantt chart (Figure 1).

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Sponsors and supporting organizations of the guideline This guideline is jointly sponsored by Changzhi Nursing Association and Changzhi People's Hospital. The methodology and evidence are supported by the Evidence-Based Medicine Center of Lanzhou University and the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation.

Patient and Public Involvement

None

Guideline registration

This guideline was registered on the International Practice Guide Registration Platform (international practice guidelines registry platform, IPGRP) in both Chinese and English. The registration number is PREPARE-2023CN418.

Establishment of guideline working groups

The guideline development group consists of the guideline steering committee, the consensus expert panel, secretariat, the evidence evaluation group and the external audit expert group. Furthermore, the study will be conducted in accordance with the Declaration of Helsinki (revised in 2013). To be selected for the guideline groups, members must be (I) experts in clinical medicine, nursing, guideline development, bioethics, health economics, and other fields related to critical care medicine; (II) representative of different regions, with balanced age and gender; and (III) providers for informed consent. All members of the guideline working groups must declare conflicts of interest. These declarations will be published as an appendix to the final guideline document. Table 1 shows the composition and responsibilities of the guideline working groups.

Scope of the guideline

The guideline focuses on the key issues related to respiratory support treatment post-extubation for ICU patients receiving mechanical ventilation. The intended

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users of the guideline include ICU clinicians, nurses, respiratory therapists and other healthcare workers. This guideline is intended for healthcare professionals, including those in pediatrics, critical care, respiratory medicine, and other related clinical fields. The target population affected includes all patients undergoing mechanical ventilation extubation in the ICU.

Conflict of interest and funding

All members of the guideline steering committee, guide consensus expert panel, external audit expert group, secretariat and evidence evaluation group are required to complete a conflict of interest declaration form and manage potential conflicts of interest. This guideline does not receive any funding from pharmaceutical companies.

Identification of clinical questions and evaluation of their importance

Preliminary clinical questions are raised through the review of relevant guidelines both domestically and internationally, and by conducting questionnaires to clinicians, nurses and respiratory therapists. The secretariat will be responsible for organizing the collected clinical questions, eliminating duplicates, and consolidating urgent guidance-related problems post-mechanical ventilation in the ICU. After the initial list of clinical questions is established, it will be discussed by the steering committee, which will convene an expert panel to discuss the list. The final clinical questions for the guideline are determined through two rounds of the Delphi method. In the second-round meeting, the team members will evaluate the importance of all issues on a scale of 1 to 5 (with 5 being the most important, 1 the least, indicating clinical insignificance). Finally, specific clinical questions will be conducted according to the elements of P (population), I (intervention), C (comparison), O (outcome) elements. Subsequently, the top 10 to 20 clinical questions will be selected according to the highest score. After approval by the expert committee, the clinical questions to be addressed in this guideline will be determined.

Evidence retrieval, screening, and data extraction

Eligible studies will be identified through searches in databases including Pubmed, Medline, Embase, the Cochrane Library, Epistemonikos, Up To Date, BMJ Best Practice, Clinical Key, DynaMed Plus, the China Biology Medicine disc (CBM), ClinicalTrials.gov, the International Clinical Trial Registry Platform (ICTRP) and other Chinese and English databases. Searches will also be supplemented by clinical trial registries and tracing the references of included articles. Subject headings and free terms will be used to form the search strategy. Both MeSH terms and free text will be used to form the search strategy, limited to publications from the inception of the databases until October 2023. Searches will be conducted in English or Chinese. The search terms include “Airway Extubation*”, “Tracheal Extubation*”, “Intratracheal Extubation*”, “Endotracheal Extubation*”, “post-extubation”, “high flow nasal cannula”, “high flow nasal oxygen”, “HFNC”, “HHFNC”, “HHFN”, “NHF*”, “high flow”, “Cannula”, “Nasal Cannula*”, “oxygen inhalation therap*”, “Positive Pressure Respiration”, “Non-Invasive Ventilation*”, “Noninvasive Ventilation*”, “non-invasive positive pressure ventilation*”, “noninvasive positive pressure ventilation*”, “NIPPV”, “NPPV”, “conventional oxygen therapy”, “COT”, “standard oxygen therapy”, “SOT”, “venturi mask”, “face mask”, “bag valve mask”. The search strategy for the PubMed database is presented in the Supplementary file.

Literature inclusion criteria: (1) The subjects of the study were patients undergoing mechanical ventilation and extubation of any age; (2) The types of studies included China and international guidelines, systematic reviews or meta-analyses, randomized controlled trials, diagnostic tests, cohort studies, case-control studies, case series, and case reports. Exclusion criteria: We excluded articles not written in Chinese or English; articles with incomplete or missing research data; articles for which we were unable to obtain original data; and duplicate articles.

If the literature from secondary research can't address the clinical questions required in the guideline, lacks relevant secondary evidence, or needs updating (publications older than 2 years and the original studies published within 2 years), a systematical search for randomized controlled trial (RCT), non-randomized controlled studies, case reports and other studies will be conducted.

The guideline development team will work in pairs to independently search and screen the literature by title, abstract and full text. They will extract data from the literature, and record the number of articles initially retrieved and finally included. Any disagreements will be resolved by discussion or consultation with a third-party expert in evidence-based methodology.

Evaluation of the quality of the literature

We will use the Appraisal of Guidelines for Research and Evaluation II (AGREE II)²⁶, A Measurement Tool to Assess systematic Reviews (AMSTAR)²⁷, the Cochrane Collaboration's tool for assessing risk of bias in randomized trials²⁸, and the Newcastle-Ottawa Scale (NOS)²⁹ to evaluate the methodological quality of the included literature. Table 2 provides a detailed description of the assessment tools used for various study types in the assessment process. The assessment will be completed independently by two researchers, and any disagreements will be resolved through discussion or consultation with a third-party expert in evidence-based methodology.

Grading evidence quality and recommendation strength

The quality of evidence and the strength of recommendations will be grade using the GRADE grading system. The quality of evidence will be classified as follows: High (A), very certain that the observed value is close to the true effect; Moderate (B), moderate certain that the observed value probably close to the true effect, but there is a possibility that they are substantially different; Low (C), limited observational values which may be substantially different from the true effect; very low (D), observational values are likely to be substantially different from the true effect.. Recommendations supported by evidence will be divided into four levels:: strong, weak, strong against, and weak against (Table 3).

Forming recommendations and reaching consensus

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For each clinical question, the members of the evidence evaluation group collate all evidence, clearly present the types and quality of evidence in a detailed evidence summary table, and form a preliminary recommendation and rationales based on patients values and preferences, economic costs and balance of benefits and risks.

Based on existing literature and practical experience, the initial questionnaire was designed to cover all critical issues in the protocol. It includes both qualitative and quantitative questions to gather detailed feedback and ratings from the experts. After each round of feedback, we summarized and analyzed the expert opinions, revised the questionnaire content, and provided feedback to the expert panel. We proposed to conduct three rounds of questionnaire surveys, with each round's improvements based on the feedback and analysis from the previous one.

If over 50% of the experts chose "2", and over 70% chose "2" or "1", the recommendation reached a consensus with a "Strong" recommendation strength. If more than 50% of the experts chose "2" or "1" and fewer than 20% chose "-2" or "-1", the recommendation also reached a consensus but with a "weak" recommendation strength. Other scenarios were considered as no consensus reached, and the recommendation proceeded to the next round of voting. For guideline issues where no consensus was reached and a recommendation must be made, the guideline steering committee further discussed and determined the final recommendation based on the voting analysis. When all issues reached a consensus or a non-consensus threshold, and no new significant opinions arose, we considered the Delphi process complete.

For recommendations where consensus is not reached, the next round of Delphi questionnaire survey will be adjusted based on expert opinions. During this process, the secretariat will individually feedback to the expert and accordingly modify the recommendations. The final recommendation, agreed upon by should be submitted to the guideline steering committee for review. To finalize any content modifications, the guideline steering committee must obtain the agreement of at least two-thirds of the members of the consensus expert panel, and the secretariat must accurately record the entire modification process.

Guideline drafting and external review of recommendations

The secretariat will draft the initial version of the guideline according to the RIGHT entries, and submit the draft to the external audit expert group for review and feedback. The external audit expert group consists of clinical medical experts, nursing experts, methodology experts and other multidisciplinary personnel. They will evaluate the draft from the aspects of acceptability, expression clarity and clinical feasibility, and provide suggestions for improvement. The secretariat and the evidence evaluation group will revise the draft based on feedback from external audit experts and form the final version of the guideline.

Guideline approval, release, and update

The final draft of the guideline will be reviewed, finalized, and approved by the expert committee. With the agreement of 2/3 of the consensus group experts, the expert committee can modify and refine the important issues in the proposal. The secretariat is responsible for accurately documenting the entire modification process. We have developed a comprehensive program for regular review and updates, including a systematic process for monitoring new evidence, reviewing guideline content, and incorporating necessary changes. Guideline updates will be based on the following criteria: (1) the recommendations remain unchanged, but there is with a larger sample size or higher quality than before; (2) the recommendations have changed, new high-quality evidence does not support the existing recommendations, or there have been changes in the safety or target population of the existing recommendations.

We plan to formally review and update the guidelines every two to three years. This schedule allows us to incorporate important new evidence and to ensure that our recommendations reflect the latest clinical study and practice standards.

Guideline dissemination, implementation, and evaluation

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After the guideline is released, the project team will promote and disseminate the guideline mainly through the following methods: (I) presentations at relevant academic conferences; (II) organization dedicated guideline promotion meetings in some provinces and cities in China to ensure that clinicians, respiratory therapists, and nurses fully understand and correctly apply the guideline; (III) distribution of guideline interpretations through commonly used medical websites, APPs, and short video platforms in China; (IV) Organization of guideline training sessions in different provinces for clinicians, pharmacists and nurses to familiarize them with the guideline; (V) members of the guideline steering committee and guideline development expert panel will write articles related to the guideline and publish them in journals; (VI) Evaluation of the impact of this guideline on clinical decision-making. We aim to provide evidence-based recommendations to enhance the decision-making process of clinicians, reduce variability in treatment practices and ensure consistent application of best practices. Two to three years after the publication and implementation of the full text of the guideline, the current status of post-extubation respiratory support modalities for mechanically ventilated patients in ICU in China and abroad will be evaluated to understand the dissemination of the guideline, the recognition of the recommendations in clinical practice and the impact on treatment decisions. At the same time, it is beneficial to improve and perfect the guideline when it is updated.

Discussion

Due to physiological differences among adults, children and neonates (such as preterm infants who are more prone to complications and even death post-extubation due to immature organ function, particularly respiratory function³⁰.) and the distinct characteristics of various diseases (for example, in patients with respiratory failure, severe impairment of pulmonary ventilation and/or gas exchange can lead to a series of pathophysiological changes and corresponding clinical syndromes³¹.), it is clear that providing the same type of respiratory support to all extubated patients is

unreasonable. Instead, tailored respiratory support should be provided according to their needs to maintain normal respiratory function and thus improve their prognosis. With the advancement of medical technology, there are various methods of respiratory support post extubation in mechanically ventilated patients. Non-invasive ventilation (NIV) maintains airway defenses while aiding in bronchial re-expansion and restoring respiratory mechanics, but it has a high complication rate³². NCPAP and NIPPV are two common modes of NIV. NCPAP enhances alveolar compliance, reduces airway resistance, and improves pulmonary ventilation and gas exchange; however, its tolerance and adherence are relatively poor³³. NIPPV provides positive end-expiratory pressure and airway pressure, improving cardiopulmonary function and oxygenation indices, but it may increase the risk of ventilator-associated lung injury³⁴. NHFOV is an emerging mode of NIV that adds pressure oscillations to NCPAP, providing greater benefits in maintaining alveolar stability, improving oxygenation, and promoting carbon dioxide elimination³⁵. HFNC is also a novel form of respiratory support that provides patients with a high-flow heated and humidified gases with stable inspired oxygen concentrations, significantly enhancing their comfort and tolerance, and showing clinical outcomes.^{36,37}. However, current guidelines only offer recommendations for the prophylactic use of respiratory support after extubation but do not provide specific guidance for different populations and different diseases³⁸, leaving users often unable to obtain useful information on respiratory support modes from these guidelines.

Therefore, to recommend the best respiratory support methods for patients, we will establish a multidisciplinary team to develop a guideline for respiratory support after mechanical ventilation extubation , strictly following the WHO guideline development handbook²³ and the guideline development checklist³⁹. This protocol serves as the foundation and framework for guideline development process, ensuring standardization of the process and methods. The guideline development working group will conduct a thorough review of the literature and surveys to fully understand the key clinical issues in post-extubation respiratory support. Subsequently, they will systematically search, evaluate, and grade the existing best clinical evidence,

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combining this with clinical expert experience and various factors to develop high-quality guidelines for post-extubation respiratory support, aimed at scientifically guiding evidence-based clinical practice and improving patient outcomes.

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Supplementary Information

Supplementary Table. List of international representative guidelines working groups
Supplementary file. Search Strategy for PubMed.

Contributors

All listed authors meet authorship criteria and that no others meeting the criteria have been omitted. XFH conceived the idea for the project. All authors (JC, JLH, MZ, YH, and JHT) contributed to the design of the study. XFH wrote the first draft of the manuscript. JC, JLH, and JHT contributed to the refinement of the study methods and critical revision of the manuscript. All authors read and approved the final version of the manuscript. The guarantor of the study is XFH, accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests

None declared.

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Figure 1. Gantt chart. the key steps and timeline of guideline development. PICO, patient/population, intervention, comparison, and outcomes.

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Table 1 The composition and responsibilities of the guideline working groups

Group	Composition	Responsibility
Steering group	one clinical chairman, one methodology chairman, one government representative, two nursing specialists with rich experience in ICU, two clinical specialists with rich experience in ICU, and two respiratory therapists with rich respiratory work experience.	(I) determine the theme and scope of the guide and construct key issues according to PICO format (II) establish the guide consensus expert group, guide secretary group, evidence evaluation group, external audit expert group (III) assess conflicts of interest and deal with conflicts as needed (IV) chaired the guide work meeting (V) review and approval plan (VI) approve recommendations and full guidelines (VII) revise and update the guidelines
Consensus expert panel	consists of 25 to 30 experts in the fields of critical care, respiratory, pediatrics, neonatology, and respiratory therapists.	(I) Priority topics and outcome indicators of evaluation guidelines (II) formulate recommendations on some issues (III) reach consensus on recommendations (IV) modify the full text of the guidelines and provide feedback (V) publish and promote guidelines

Group	Composition	Responsibility
secretariat	3 to 5 staff members of sponsors and supporting organizations.	(I) complete the guide registration and draft the guide plan (II) investigate the clinical problems of the guidelines, design the questionnaire according to the initially formed clinical problem list, collect clinical problems and ranked the importance of clinical problems (III) coordinate the work of other working groups (IV) organize recommendation consensus meeting (V) complete the coordination of external review of the whole process of the guide (VI) record the whole process of the detailed guide (VII) draft the draft guide (VIII) guide submission
Evidence evaluation group	3 to 10 people with a background in evidence-based medicine and experience in evidence retrieval.	(I) completed the guide literature search, screening, evidence extraction, risk of bias evaluation and GRADE evidence rating (II) complete the quality evaluation of the published systematic evaluation / Meta analysis related to the guide topic (III) complete the update and production of meta analysis (IV) make the evidence summary table and recommendation opinion decision table
External audit expert group	5 to 10 experts engaged in related fields who do not directly participate in the formulation of the guidelines.	(I) evaluate and review the problems and scope of the clinical practice guidelines

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Group	Composition	Responsibility
		(II) review the final recommendations
		(III) provide specific amendments for the full text of the guidelines

Note: "Rich experience in ICU work" means: (1) Years of work experience: at least five years of full-time experience working in an ICU. (2) Education level: a bachelor's degree or higher. (3) Professional title: intermediate or senior.

Table 2 Document types and evaluations tools

Steps	Research type	Methodological assessment tools	Quality
Evidence production	Randomized controlled trial (RCT)	Cochrane risk of bias assessment tool	
	Non-randomized experimental study	MINORS items	
	Cohort study	NOS scale	
	Case-control study	NOS scale	
	Animal experiment	STAIR list	
Evidence synthesis	Systematic review/Meta-analysis	AMSTAR 2 tool	
		OQAQ scale	
		SQAC scale	
	Overviews of systematic reviews	AMSTAR 2 tool	
Creating guidelines and conducting health	Clinical practice guidelines	AGREEII tool	
		Checklist for HTA report	
	Health technology assessment	Experimental study: Cochrane EPOC evaluation method	
		Observational research: quality evaluation criteria for Hilton's effective public health policy project development	
Dissemination of evidence	Clinical practice guidelines	AGREEII tool	
	Health technology assessment	Checklist for HTA report	
Applied evidence	Decision support system		
Assessment and improvement practices	Real-world study		

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Table 3 GRADE strength level of recommendation

Strength level	Definition
Strong (I)	Support for the use of an intervention where the benefits clearly outweigh the risks
Weak (II)	Support for the use of an intervention where the benefits may outweigh the risks
Strong against (I)	Opposition to the use of an intervention where the risks clearly outweigh the benefits
Weak against (II)	Opposition to the use of an intervention where the risks may outweigh the benefits or the balance of benefits and risks is unclear

GRADE, Grading of Recommendations Assessment.

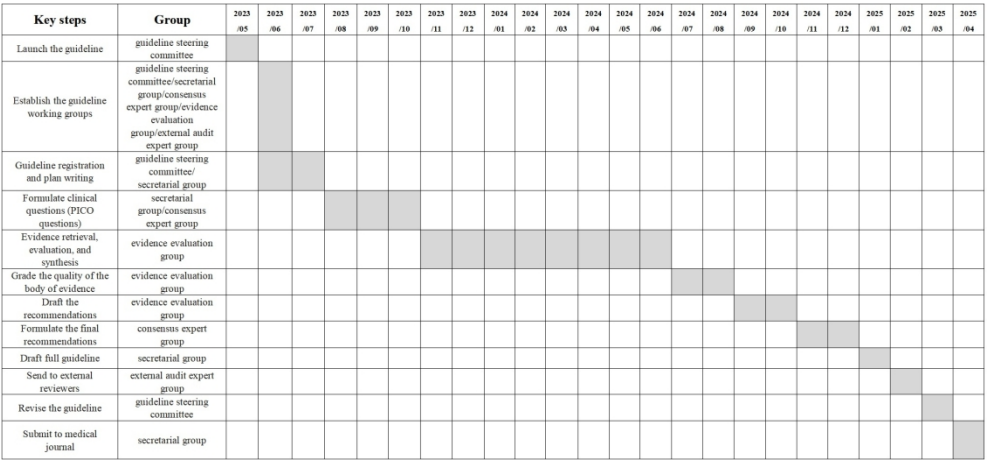


Figure 1. Gantt chart. the key steps and timeline of guideline development. PICO, patient/population, intervention, comparison, and outcomes.

275x129mm (192 x 192 DPI)

Supplementary Table.

List of international representative guidelines working groups

Methodology	Working group direction	The specific role in the development of
Working Group		this guideline
WHO handbook for guideline development	Guideline formulation	Provide a systematic approach and framework for developing high-quality guidelines.
RIGHT	Guideline report	Provide a structured checklist for a systematic and comprehensive reporting guide, and the development of the guide with reference to the RIGHT reporting norms ensures greater regularity and transparency in reporting.
Guideline 2.0	Guideline formulation	A comprehensive checklist systematically developed for the successful development of guidelines. Careful consideration of the entries in the checklist will assist in the development, implementation and evaluation of the guidelines.
AGREE II	Evaluation of the methodological quality of the guidelines	AGREE II serves as a methodological quality assessment tool for guidelines, with results reflecting the rigor and scientific validity of the development process. To ensure that the guidelines we reference and develop meet high standards of development and reporting.
GRADE	Grading the quality of guideline evidence and strength of recommendation	Provides a clear, comprehensive grading and summarization methodology for quality grading the evidence on which it relies to support its recommendations.

Supplementary file

Search Strategy for PubMed

#1 "Airway Extubation"[Mesh] OR "Airway Extubation*"[Title/Abstract] OR "Tracheal Extubation*"[Title/Abstract] OR "High-Frequency Ventilation"[Title/Abstract] OR "Endotracheal Extubation*"[Title/Abstract] OR "post-extubation"[Title/Abstract] OR "Ventilator Weaning"[Mesh] OR "Weaning, Ventilator"[Title/Abstract] OR "Respirator Weaning"[Title/Abstract] OR "Mechanical Ventilator Weaning"[Title/Abstract]

#2 "Respiratory Support"[Title/Abstract] OR "high flow nasal cannula"[Title/Abstract] OR "high flow nasal oxygen"[Title/Abstract] OR "HFNC"[Title/Abstract] OR "HHFNC"[Title/Abstract] OR "HHFN"[Title/Abstract] OR "NHF*"[Title/Abstract]

#3 ("high flow"[Title/Abstract] AND ("Cannula"[Mesh] OR "Nasal Cannula*"[Title/Abstract])) OR ("high flow"[Title/Abstract] AND ("oxygen inhalation therapy"[MeSH] OR "oxygen inhalation therap*"[Title/Abstract]))

#4 "Positive Pressure Respiration"[Mesh] OR "Noninvasive Ventilation"[Mesh] OR "Noninvasive Ventilation*"[Title/Abstract] OR "Non-Invasive Ventilation*"[Title/Abstract] OR "non-invasive positive pressure ventilation*"[Title/Abstract] OR "noninvasive positive pressure ventilation*"[Title/Abstract] OR "NIPPV"[Title/Abstract] OR "NPPV"[Title/Abstract] OR "conventional oxygen therapy"[Title/Abstract] OR "COT"[Title/Abstract] OR "standard oxygen therapy"[Title/Abstract] OR "SOT"[Title/Abstract] OR "venturi mask"[Title/Abstract] OR "face mask"[Title/Abstract] OR "bag valve mask"[Title/Abstract]

#5 #1 AND (#2 OR #3 OR #4)

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BMJ Open

Protocol for the development of a guideline on post-extubation respiratory support for mechanically ventilated patients in ICU

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Manuscript ID	bmjopen-2023-078271.R2
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Date Submitted by the Author:	14-Oct-2024
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Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Evidence based practice, Intensive care, Respiratory medicine
Keywords:	Adult intensive & critical care < INTENSIVE & CRITICAL CARE, Neonatal intensive & critical care < INTENSIVE & CRITICAL CARE, Paediatric intensive & critical care < INTENSIVE & CRITICAL CARE, Adult intensive & critical care < INTENSIVE & CRITICAL CARE, Respiratory Therapy

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Manuscripts

**Protocol for the development of a guideline on post-extubation
respiratory support for mechanically ventilated patients in the ICU**

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Background: Prophylactic respiratory support for patients after extubation is effective in improving their outcomes and prognosis. However, the optimal post-extubation respiratory support for different populations and disease types of mechanically ventilated patients remains controversial, and there is a lack of detailed, multidisciplinary, evidence-based recommendations for clinical application.

Methods: This guideline strictly follows the development process outlined in the World Health Organization (WHO) handbook for guideline development and Guidelines 2.0, as well as the guidelines for the development of relevant methodological standards. Key steps in developing the guideline include: (I) establishing the guideline working groups; (II) defining the scope of guideline application; (III) selecting the priority clinical questions; (IV) retrieving and screening evidence; (V) grading the quality of evidence; (VI) forming recommendations; and (VII) conducting an external review.

Ethics and dissemination: Ethical approval has been granted by Changzhi People's Hospital (2023K023). Findings from this study will be disseminated through peer-review publications.

Guideline registration: PREPARE-2023CN418.

Keywords: respiratory support; mechanical ventilation; guideline; Grading of Recommendations Assessment, Development, and Evaluation.

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Strengths and limitations of this study

1. The strength of this study lies in the diversity of the composition of our working group: Firstly, the group includes clinical (ICU clinicians, respiratory therapists and other healthcare workers) and nursing experts from different specialties (ICU, pediatric ICU, and neonatal ICU) with extensive clinical experience in critical care; Secondly, methodological experts, including experts in evidence-based methodology and epidemiology, whose guidance on the methodology of guideline development will make the guideline more scientific and rigorous; Finally, the involvement of Changzhi Health Commission and Changzhi Nursing Association as policymakers will further enhance the implementability of the guideline.
2. This is a post-extubation respiratory support guideline in the development specifically for different populations and disease types of mechanically ventilated patients.
3. We are in the development of this guideline protocol and formal guideline document in strict accordance with the Guidelines 2.0 and the Reporting Items for Practice Guidelines in Healthcare (RIGHT).
4. The limitation of this study is that only literature in Chinese and English will be included.

INTRODUCTION

Diseases such as acute respiratory distress syndrome (ARDS) and sepsis are often triggered by infections, trauma, inhalation injuries, leading to activation of the pulmonary immune system.¹ Neutrophils are rapidly recruited to the lungs, releasing a variety of inflammatory mediators, such as tumor necrosis factor alpha (TNF- α), interleukin (IL)-1 and IL-6, which further exacerbate alveolar injury. Lymphocytes play a crucial role in regulating the appropriate inflammatory response, and a reduction in circulating lymphocytes may perpetuate a harmful inflammatory state.² As the lungs fail to effectively provide oxygen to other parts of the body or remove carbon dioxide, these patients require mechanical ventilation support to assist with breathing. Approximately 30% of patients in the intensive care unit (ICU) rely on mechanical ventilation for respiratory support.^{3 4} However, routine and prolonged mechanical ventilation (PMV) significantly increases the incidence of complications associated with ICU-acquired weakness (ICU-AW), atelectasis, pneumothorax, ventilator-associated pneumonia (VAP), and other conditions, severely impairing physical functions, delaying recovery, and increasing length of stay in hospital and treatment costs.⁵⁻⁷

Therefore, during the course of treatment, when the patient's primary condition is under control and ventilation and oxygenation are corrected, the ventilator and the artificial airway (extubation) should be removed as soon as possible.⁸ However, some patients in the ICU (about 10%-30%) present complex and critical conditions (high risk of extubation failure), experiencing respiratory distress, reduced oxygenation, and inability to maintain spontaneous breathing after extubation, necessitating reintubation. Reintubation not only prolongs the duration of mechanical ventilation, but also results in mortality rates as high as 25%-50% in these patients.^{9 10}

The benefits of providing post-extubation respiratory support to ICU patients are still under discussion.¹¹ Several studies have found that providing post-extubation respiratory support to patients at high risk of extubation failure (e.g., due to

underlying comorbidities such as heart failure, severe obesity, or chronic obstructive pulmonary disease)¹² can effectively improve clinical symptoms, lung function, prognosis, and reduce the rates of reintubation and mortality.¹³⁻¹⁵ However, some studies have found that prophylactic use of respiratory support after extubation in patients with brain injury does not reduce the rate of reintubation and length of hospitalisation.^{16 17}

In recent years, respiratory support options include conventional oxygen therapy (COT), nasal continuous positive airway pressure (NCPAP), non-invasive positive pressure ventilation (NIPPV) and high-flow nasal cannula (HFNC), among other modalities.^{18 19} Given the wide range of respiratory support treatment options available, existing guidelines do not provide adequate guidance regarding appropriate treatments for different populations and disease types. Consider the following examples of various ill-defined post-extubation respiratory support treatment options. Regarding the choice of respiratory support, a guideline recommends using HFNC in high-risk and/or obese patients undergoing cardiac or thoracic surgery to prevent immediate respiratory failure.²⁰ Similarly, the American College of Physicians (ACP) guideline recommends the use of HFNC in hospitalized adults with acute hypoxemic respiratory failure after extubation.^{20 21} However, some studies have found that NFNC after extubation does not prevent reintubation.²² For example, HFNC may be less effective than NIPPV in preventing reintubation in patients receiving PMV for at least 2 weeks.²³

In summary, the effectiveness and optimal post-extubation respiratory support in different populations (adult, pediatric, and neonatal patients) and various disease types (such as respiratory failure, post-cardiac surgery, hypercapnia) remain controversial, and no clinical guideline currently provide guidance for the best post-extubation respiratory support for all types of mechanically ventilated patients.²⁴ There is a lack of detailed, multidisciplinary, and evidence-based support. Therefore, it is necessary to develop a high-quality, evidence-based support. Therefore, it is necessary to

develop a high-quality, evidence-based guideline for post-extubation respiratory support in mechanically ventilated patients in the ICU. This development should be based on the methodology outlined in the World Health Organization (WHO) Handbook for Guideline Development (2nd edition, 2014).²⁵

METHODS

Guiding principles of the guideline

We are in the development of the guideline based on the concept of clinical practice guidelines from the US Institution of Medicine (IOM), the National Academy of Medicine.²⁶ The guideline development process and methodological standards outlined in the WHO Handbook for Guideline Development are utilized,²⁷ along with the Appraisal of Guidelines for Research and Evaluation II (AGREE II).²⁸ The guideline is formulated in accordance with the Guidelines 2.0 and the Reporting Items for Practice Guidelines in Healthcare (RIGHT).²⁹ A detailed overview of the working groups' directives and their roles in this guideline is provided in Supplementary Table 1. This guideline development study began in May 2023 and is scheduled to conclude in April 2025. The key steps and timeline of the guideline are shown in a Gantt chart (Figure 1).

Sponsors and supporting organizations of the guideline

This guideline is jointly sponsored by Changzhi Nursing Association and Changzhi People's Hospital. The methodology and evidence are supported by the Evidence-Based Medicine Center of Lanzhou University and the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation.

Patient and public involvement

None.

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Guideline registration

This guideline was registered on the International Practice Guide Registration Platform (IPGRP) in both Chinese and English. The registration number is PREPARE-2023CN418.

Establishment of guideline working groups

The guideline development group consists of the guideline steering committee, the consensus expert group, the secretary group, the evidence evaluation group and the external audit expert group. They are responsible for identifying guideline topics, formulating clinical questions, conducting evidence searches, synthesizing and evaluating evidence, developing recommendations, drafting guideline, and completing external reviews. Supplementary Table 2 provides a detailed overview of the composition and responsibilities of the guideline working groups. Furthermore, the study will be conducted in accordance with the Declaration of Helsinki (revised in 2013), ensuring that the dignity, rights, safety, and health of participants are upheld throughout the research. To be selected for the guideline groups, members must be (I) experts in clinical medicine, nursing, guideline development, bioethics, health economics, and other fields related to critical care medicine; (II) representative of different regions, with a balanced age and gender distribution; and (III) providers for informed consent. All members of the guideline working groups are required to declare any conflicts of interest and these declarations will be published as an appendix to the final guideline document.

Scope of the guideline

The guideline focuses on the key issues related to post-extubation respiratory support treatment for ICU patients, including adult, pediatric and neonatal patients who are receiving mechanical ventilation. It is intended for healthcare professionals, including ICU clinicians, nurses, respiratory therapists, and those in related fields such as

pediatrics and critical care. The target population includes all patients undergoing mechanical ventilation extubation in the ICU.

Conflict of interest and funding

All members of the guideline steering committee, consensus expert panel, external audit expert group, secretariat and evidence evaluation group are required to complete a conflict of interest declaration form and manage any potential conflicts of interest. This guideline has not received any funding from pharmaceutical companies.

Identification of clinical questions and evaluation of their importance

Preliminary clinical questions related to post-extubation respiratory support for mechanically ventilated patients in the ICU are generated through the review of relevant guidelines both domestically and internationally, as well as by conducting questionnaires to clinicians, nurses and respiratory therapists. The secretariat will be responsible for organizing the collected clinical questions, eliminating duplicates, and consolidating remaining questions. The final clinical questions for the guideline will be determined through two rounds of the Delphi method, where a panel of experts rates and provides feedback on each question to reach consensus on their importance and scope. In the second-round meeting, team members will evaluate the importance of all issues on a scale of 1 to 5 (with 5 being the most important and 1 the least, indicating clinical insignificance). Specific clinical questions will be formulated according to the PICO elements: P (population), I (intervention), C (comparison), and O (outcome). Subsequently, the top 10 to 20 clinical questions will be selected according to the highest scores. After approval by the expert committee, the clinical questions to be addressed in this guideline will be finalized.

Evidence retrieval, screening, and data extraction

Eligible studies will be identified through searches in databases including Pubmed, Medline, Embase, the Cochrane Library, Epistemonikos, UpToDate, BMJ Best Practice, Clinical Key, DynaMed Plus, the China Biology Medicine disc (CBM), ClinicalTrials.gov, the International Clinical Trial Registry Platform (ICTRP) and other Chinese and English databases. Searches will also be supplemented by clinical trial registries and by tracing the references of included articles. Both Medical Subject Headings (MeSH) terms and free words will be used to form the search strategy, limited to publications from the inception of the databases until January 2024. Searches will be conducted in English or Chinese. The search terms include “Airway Extubation*”, “Tracheal Extubation*”, “Intratracheal Extubation*”, “Endotracheal Extubation*”, “post-extubation”, “high flow nasal cannula”, “high flow nasal oxygen”, “HFNC”, “HHFNC”, “HHFN”, “NHF*”, “high flow”, “Cannula”, “Nasal Cannula*”, “oxygen inhalation therap*”, “Positive Pressure Respiration”, “Non-Invasive Ventilation*”, “Noninvasive Ventilation*”, “non-invasive positive pressure ventilation*”, “noninvasive positive pressure ventilation*”, “NIPPV”, “NPPV”, “conventional oxygen therapy”, “COT”, “standard oxygen therapy”, “SOT”, “venturi mask”, “face mask”, “bag valve mask”, “entrainment mask”. The search strategy for the PubMed database is presented in the Supplementary file.

Literature inclusion criteria: (1) The subjects of the study were patients of any age undergoing mechanical ventilation and extubation; (2) The types of studies included China and international guidelines, systematic reviews or meta-analyses, randomized controlled trials (RCTs), diagnostic tests, cohort studies, case-control studies, case series, and case reports. Exclusion criteria: we excluded articles not written in Chinese or English. However, journal articles with formal translations in Chinese or English will not be excluded. Additionally, we excluded articles with incomplete or missing research data, articles for which we were unable to obtain original data, and duplicate articles.

If the literature from secondary research (defined as analyses or systematic assessments based on existing primary data or published research findings, such as systematic reviews and meta-analyses) fails to address the clinical questions required for the guideline, lacks relevant secondary evidence, or needs updating (publications older than 2 years and the original studies published within 2 years), a systematic search will be conducted for RCT, non-randomized controlled studies, case reports and other relevant studies.

The guideline development team will work in pairs to independently search and screen the literature by title, abstract and full text. They will extract data from the literature and record the number of articles initially retrieved and those finally included. Any disagreements will be resolved by discussion or consultation with a third-party expert in evidence-based methodology.

Evaluation of the quality of the literature

We will use the AGREE II)³⁰, A Measurement Tool to Assess systematic Reviews (AMSTAR)³¹, the Cochrane Collaboration's tool for assessing risk of bias in randomized trials³², and the Newcastle-Ottawa Scale (NOS)³³ to evaluate the methodological quality of the included literature. Supplementary Table 3 provides a detailed description of the assessment tools used for various study types in the assessment process. The assessment will be conducted independently by two researchers using the research instrument. If there is a disagreement between their findings, it will be resolved through discussion or negotiation with a third-party expert to reach a final consensus.

Grading the quality of evidence

Evidence quality grading was conducted for the pooled evidence corresponding to each guideline question's outcome indicator. The guideline questions included in the original research evidence were assessed using the Grading of Recommendations

Assessment, Development, and Evaluation (GRADE) system. This assessment considered 5 downgrading factors: limitations (risk of bias), imprecision, inconsistency, indirectness, and publication bias, as well as 3 escalating factors: large effect, dose-response, and the presence of all plausible residual confounding.. The quality of evidence will be classified as follows: High (A): very certain that the observed value is close to the true effect; Moderate (B): moderately certain that the observed value is probably close to the true effect, but there is a possibility of substantial differences; Low (C): limited observational values which may be substantially different from the true effect; Very low (D), observational values are likely to be substantially different from the true effect. The evidence quality was graded according to these evaluations, and a summary table of the evidence was compiled.

Forming recommendations and reaching consensus

Recommendations supported by evidence will be categorized into 4 levels according to the GRADE system: strong, weak, strong against, and weak against (Table 1). The consensus expert group assessed factors such as the quality of evidence, values, economic analysis, balance of advantages and disadvantages to form a preliminary recommendation. All the recommendations were compiled into a recommendation letter questionnaire, which was distributed to the consensus group experts for evaluation and suggested modifications. The consensus expert group reached a consensus on the recommendation after conducting 2-3 rounds of Delphi method. A flowchart depicting each stage of the Delphi process is shown in Figure 2.

The rules for reaching a consensus are as follows: If over 50% of the experts chose "2", and over 70% chose "2" or "1", the recommendation achieved consensus with a "Strong" recommendation strength. If more than 50% of the experts chose "2" or "1", and fewer than 20% chose " -2" or "-1", the recommendation also reached consensus but with a "weak" recommendation strength. Other scenarios were considered as

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lacking consensus, and the recommendation moved forward to the next round of voting. For guideline issues where no consensus was reached but a recommendation is needed, the guideline steering committee further discussed and determined the final recommendation based on the voting analysis. When all issues reached either a consensus or a non-consensus threshold, and no new significant opinions emerged, the Delphi process was deemed complete.

Guideline drafting and external review of recommendations

The RIGHT checklist, which consists of 22 items, can assist guideline developers in effectively reporting their guidelines.²⁹ The secretariat will draft the initial version of the guideline according to the RIGHT entries, and submit it to the external audit expert group for review and feedback. This group consists of clinical medicine, nursing, methodology and other multidisciplinary experts. They will evaluate the draft from the perspectives of acceptability, clarity of expression and clinical feasibility, and provide suggestions for improvement. The secretariat and the evidence evaluation group will revise the draft based on feedback from external audit experts to create the final version of the guideline.

Guideline approval, release, and update

The final draft of the guideline will be reviewed, finalized, and approved by the expert committee. With the agreement of 2/3 of the consensus group experts, the expert committee can modify and refine the important issues in the proposal. The secretariat is responsible for accurately documenting the entire modification process. We are in the development of a comprehensive program for regular review and updates, which includes a systematic process for monitoring new evidence, reviewing guideline content, and incorporating necessary changes. Guideline updates will be based on the following criteria: (1) the recommendations remain unchanged, but new evidence is available based on a larger sample size or higher quality than previously considered;

(2) the recommendations have changed due to new high-quality evidence that does not support the existing recommendations, or there have been changes in the safety or target population of the existing recommendations.

We plan to formally review and update the guidelines every two to three years. This schedule allows us to incorporate important new evidence and ensures that our recommendations align with the latest clinical research and practice standards.

Guideline dissemination, implementation, and evaluation

After the guideline is released, the project team will promote and disseminate it primarily through the following methods: (I) presentations at relevant academic conferences; (II) organization dedicated guideline promotion meetings in some provinces and cities in China to ensure that clinicians, respiratory therapists, and nurses fully understand and correctly apply the guideline; (III) distribution of guideline interpretations through commonly used medical websites, applications (APPs), and short video platforms in China; (IV) organization of guideline training sessions in different provinces for clinicians, pharmacists and nurses to familiarize them with the guideline; (V) members of the guideline steering committee and guideline development expert panel will write articles related to the guideline for publication in journals; and (VI) evaluation of the guideline’s impact on clinical decision-making. We aim to provide evidence-based recommendations to enhance clinicians’ decision-making process , reduce variability in treatment practices and ensure consistent application of best practices. Two to three years after the publication and implementation of the full text of the guideline, we will evaluate the current status of post-extubation respiratory support modalities for mechanically ventilated patients in the ICU in China and abroad. This evaluation will help us understand the dissemination of the guideline, the recognition of its recommendations in clinical practice, and its impact on treatment decisions. Additionally, it will be beneficial for improving and refining the guideline during its next update.

DISCUSSION

Due to the physiological and pathophysiological differences among adults, children and neonates (such as preterm infants who are more susceptible to complications and even death post-extubation due to immature organ function, particularly respiratory function³⁴) and the distinct characteristics of various diseases (for example, in patients with respiratory failure, severe impairment of pulmonary ventilation and/or gas exchange can lead to a series of pathophysiological changes and corresponding clinical syndromes³⁵), it is clear that providing the same type of respiratory support to all extubated patients is unreasonable. Instead, tailored respiratory support should be provided according to their individual needs to maintain normal respiratory function and improve their prognosis.

With advancements of medical technology, various methods of post-extubation respiratory support are available for mechanically ventilated patients. Non-invasive ventilation (NIV) helps maintain airway defenses while aiding in bronchial re-expansion and restoring respiratory mechanics, but it has a high complication rate.³⁶ Two common modes of NIV are NCPAP and NIPPV. NCPAP enhances alveolar compliance, reduces airway resistance, and improves pulmonary ventilation and gas exchange; however, its tolerance and adherence are relatively poor.³⁷ NIPPV provides positive end-expiratory pressure and airway pressure, improving cardiopulmonary function and oxygenation indices, but it may increase the risk of ventilator-associated lung injury.³⁸ NHFOV is an emerging mode of NIV that adds pressure oscillations to NCPAP, providing greater benefits in maintaining alveolar stability, improving oxygenation, and promoting carbon dioxide elimination.³⁹ HFNC is also a novel form of respiratory support that delivers patients with high-flow heated and humidified gases with stable inspired oxygen concentrations, significantly enhancing patient comfort and tolerance while demonstrating improved clinical outcomes.^{40 41} However, current guidelines only recommend the prophylactic use of

post-extubation respiratory support without providing specific guidance for different populations and diseases,⁴² leaving users often unable to obtain useful information on respiratory support modes from these guidelines.

To recommend the best respiratory support methods for patients, we will establish a multidisciplinary team to develop a guideline for respiratory support after mechanical ventilation extubation. This process will strictly adhere to the WHO guideline development handbook²⁷ and the guideline development checklist.⁴³ This protocol will serve as the foundation and framework for the guideline development process, ensuring standardization in both procedures and methods. The guideline development working group will conduct a thorough review of the literature and surveys to fully understand the key clinical issues in post-extubation respiratory support. They will systematically search for, evaluate, and grade existing best clinical evidence, integrating this with clinical expert experience and various other factors to develop high-quality guideline. This guideline will aim to scientifically guide evidence-based clinical practice and ultimately improve patient outcomes.

Supplementary Information

Supplementary Table 1. Internationally representative guidance guidelines.

Supplementary Table 2. The composition and responsibilities of the guideline working groups

Supplementary Table 3. Document types and evaluations tools

Supplementary file. Search Strategy for PubMed.

Contributors

All listed authors meet authorship criteria and that no others meeting the criteria have been omitted. XFH conceived the idea for the project. All authors (JC, JLH, MZ, YH, and JHT) contributed to the design of the study. XFH wrote the first draft of the manuscript. JC, JLH, and JHT contributed to the refinement of the study methods and critical revision of the manuscript. All authors read and approved the final version of the manuscript. The guarantor of the study is XFH, accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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None

Competing interests

None declared.

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Figure 1. Gantt chart. The key steps and timeline of guideline development. PICO, patient/population, intervention, comparison, and outcomes.

Figure 2. The flowchart showing each stage of the Delphi process.

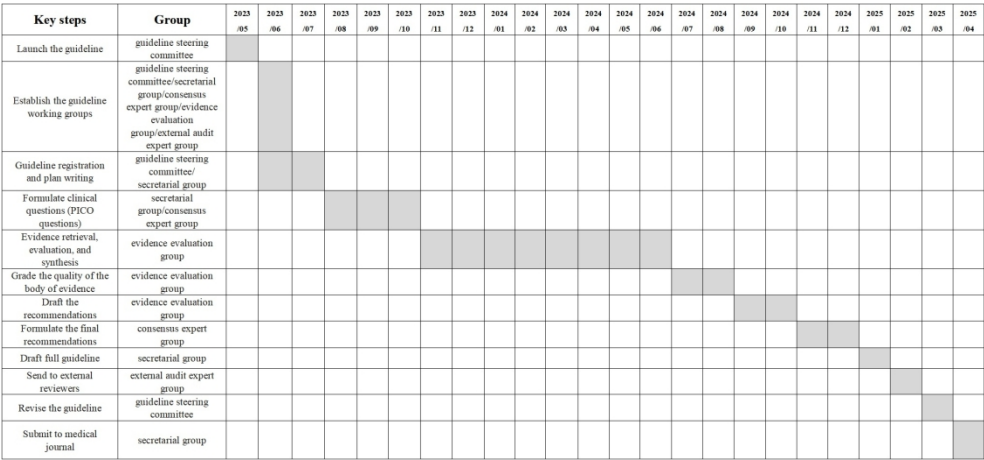
For peer review only

Table 1. GRADE strength level of recommendation

Strength level	Definition
Strong (I)	Support for the use of an intervention where the benefits clearly outweigh the risks
Weak (II)	Support for the use of an intervention where the benefits may outweigh the risks
Strong against (I)	Opposition to the use of an intervention where the risks clearly outweigh the benefits
Weak against (II)	Opposition to the use of an intervention where the risks may outweigh the benefits or the balance of benefits and risks is unclear

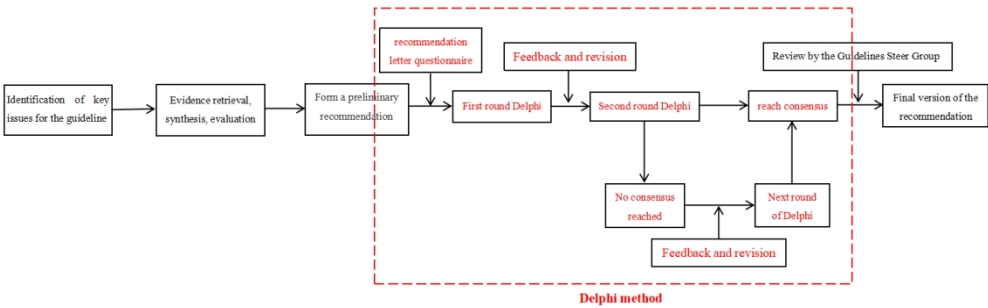
GRADE, Grading of Recommendations Assessment, Development and Evaluation.

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Gantt chart

275x129mm (192 x 192 DPI)



A flowchart depicting each stage of the Delphi process

519x161mm (76 x 76 DPI)

Supplementary Table 1.

Internationally representative guidance guidelines

Methodology	Working group direction	The specific role in the development of this guideline
Working Group		
WHO handbook for guideline development	Guideline formulation	Provide a systematic approach and framework for developing high-quality guidelines.
RIGHT	Guideline report	Provide a structured checklist for a systematic and comprehensive reporting guide, and the development of the guide with reference to the RIGHT reporting norms ensures greater regularity and transparency in reporting.
Guideline 2.0	Guideline formulation	A comprehensive checklist systematically developed for the successful development of guidelines. Careful consideration of the entries in the checklist will assist in the development, implementation and evaluation of the guidelines.
AGREE II	Evaluation of the methodological quality of the guidelines	AGREE II serves as a methodological quality assessment tool for guidelines, with results reflecting the rigor and scientific validity of the development process. To ensure that the guidelines we reference and develop meet high standards of development and reporting.
GRADE	Grading the quality of guideline evidence and strength of recommendation	Provides a clear, comprehensive grading and summarization methodology for quality grading the evidence on which it relies to support its recommendations.

Supplementary Table 2.

The composition and responsibilities of the guideline working groups

Group	Composition	Responsibility
Steering committee	one clinical chairman, one methodology chairman, one government representative, two experienced ICU nursing specialists, two experienced ICU clinical specialists, and two respiratory therapists with rich respiratory care experience.	(I) determine the theme and scope of the guideline and construct key issues according to PICO format (II) establish the guideline consensus expert group, guideline secretariat, evidence evaluation group, and external audit expert group (III) assess conflicts of interest and address any conflicts as needed (IV) chair the guideline working meetings (V) review and approval the plan (VI) approve recommendations and the full guideline (VII) revise and update the guideline
Consensus expert group	consists of 25 to 30 experts in the fields of critical care, respiratory, pediatrics, neonatology, and respiratory therapists.	(I) identify key issues for the guideline and prioritize topics for assessment (II) formulate recommendations on some issues (III) reach consensus on the recommendations (IV) modify the full text of the guideline based on feedback (V) publish and promote the guideline

Group	Composition	Responsibility
Secretary Group	3 to 5 staff members from sponsors and supporting organizations.	(I) complete the guideline registration and draft the guideline plan (II) investigate the clinical questions related to the guideline, design a questionnaire according to the initial clinical question list, collect questions and rank the importance of these questions (III) coordinate the work of other working groups (IV) organize the recommendation consensus meeting (V) facilitate the external review process for the entire guideline (VI) record the entire guideline development process in detail (VII) draft the guideline (VIII) submit the guideline for approval
Evidence evaluation group	3 to 10 individuals with a background in evidence-based medicine and experience in evidence retrieval.	(I) complete the literature search, screening, evidence extraction, risk of bias evaluation, and GRADE evidence rating for the guideline (II) complete the quality evaluation of the published systematic evaluation/meta analysis related to the guideline topic (III) update and produce meta-analysis (IV) create the evidence summary table and the recommendation decision table
External audit expert	5 to 10 experts in related fields who do not directly participate in the formulation of the guideline.	(I) evaluate and review the questions and scope of the clinical practice guidelines

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Group	Composition	Responsibility
group		(II) review the final recommendations (III) provide specific amendments for the full text of the guideline

Note: "Rich experience in the ICU work" is defined: (1) Years of working experience: at least five years of full-time work in an ICU. (2) Education level: a bachelor's degree or higher. (3) Professional title: intermediate or senior level.

Supplementary Table 3

Document types and evaluations tools			
Steps	Research type	Methodological assessment tools	quality
Evidence production	Randomized controlled trial	Cochrane risk of bias assessment tool	
	Non-randomized experimental study	MINORS items	
	Cohort study	NOS scale	
	Case-control study	NOS scale	
	Animal experiment	STAIR list	
Evidence synthesis	Systematic review/Meta-analysis	AMSTAR 2 tool	
		OQAQ scale	
		SQAC scale	
	Overviews of systematic reviews	AMSTAR 2 tool	
		OQAQ scale	
Creating guidelines and conducting health	Clinical practice guidelines	AGREEII tool	
	Health technology assessment	Checklist for HTA report	
		Experimental study: Cochrane EPOC evaluation method	
	Health policy research	Observational research: quality evaluation criteria for Hilton's effective public health policy project development	
Dissemination of evidence	Clinical practice guidelines	AGREEII tool	
	Health technology assessment	Checklist for HTA report	
Applied evidence	Decision support system		
Assessment and improvement practices	Real-world study		

Supplementary file

Search Strategy for PubMed

#1 "Airway Extubation"[Mesh] OR "Airway Extubation*"[Title/Abstract] OR "Tracheal Extubation*"[Title/Abstract] OR "High-Frequency Ventilation"[Title/Abstract] OR "Endotracheal Extubation*"[Title/Abstract] OR "post-extubation"[Title/Abstract] OR "Ventilator Weaning"[Mesh] OR "Weaning, Ventilator"[Title/Abstract] OR "Respirator Weaning"[Title/Abstract] OR "Mechanical Ventilator Weaning"[Title/Abstract]

#2 "Respiratory Support"[Title/Abstract] OR "high flow nasal cannula"[Title/Abstract] OR "high flow nasal oxygen"[Title/Abstract] OR "HFNC"[Title/Abstract] OR "HHFNC"[Title/Abstract] OR "HHFN"[Title/Abstract] OR "NHF*"[Title/Abstract]

#3 ("high flow"[Title/Abstract] AND ("Cannula"[Mesh] OR "Nasal Cannula*"[Title/Abstract])) OR ("high flow"[Title/Abstract] AND ("oxygen inhalation therapy"[MeSH] OR "oxygen inhalation therap*"[Title/Abstract]))

#4 "Positive Pressure Respiration"[Mesh] OR "Noninvasive Ventilation"[Mesh] OR "Noninvasive Ventilation*"[Title/Abstract] OR "Non-Invasive Ventilation*"[Title/Abstract] OR "non-invasive positive pressure ventilation*"[Title/Abstract] OR "noninvasive positive pressure ventilation*"[Title/Abstract] OR "NIPPV"[Title/Abstract] OR "NPPV"[Title/Abstract] OR "conventional oxygen therapy"[Title/Abstract] OR "COT"[Title/Abstract] OR "standard oxygen therapy"[Title/Abstract] OR "SOT"[Title/Abstract] OR "venturi mask"[Title/Abstract] OR "face mask"[Title/Abstract] OR "bag valve mask"[Title/Abstract]

#5 #1 AND (#2 OR #3 OR #4)

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BMJ Open

Protocol for the development of a guideline on post-extubation respiratory support for mechanically ventilated patients in ICU

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Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Evidence based practice, Intensive care, Respiratory medicine
Keywords:	Adult intensive & critical care < INTENSIVE & CRITICAL CARE, Neonatal intensive & critical care < INTENSIVE & CRITICAL CARE, Paediatric intensive & critical care < INTENSIVE & CRITICAL CARE, Adult intensive & critical care < INTENSIVE & CRITICAL CARE, Respiratory Therapy

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**Protocol for the development of a guideline on post-extubation
respiratory support for mechanically ventilated patients in the ICU**

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ABSTRACT

Background: Prophylactic respiratory support for patients after extubation is effective in improving their outcomes and prognosis. However, the optimal post-extubation respiratory support for different populations and disease types of mechanically ventilated patients remains controversial, and there is a lack of detailed, multidisciplinary, evidence-based recommendations for clinical application.

Methods: This guideline strictly follows the development process outlined in the World Health Organization (WHO) handbook for guideline development and Guidelines 2.0, as well as the guidelines for the development of relevant methodological standards. Key steps in developing the guideline include: (I) establishing the guideline working groups; (II) defining the scope of guideline application; (III) selecting the priority clinical questions; (IV) retrieving and screening evidence; (V) grading the quality of evidence; (VI) forming recommendations; and (VII) conducting an external review.

Ethics and dissemination: Ethical approval has been granted by Changzhi People's Hospital (2023K023). Findings from this study will be disseminated through peer-review publications.

Guideline registration: PREPARE-2023CN418.

Keywords: respiratory support; mechanical ventilation; guideline; Grading of Recommendations Assessment, Development, and Evaluation.

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Strengths and limitations of this study

1. The strength of this study lies in our working group's diverse composition, which includes clinical and nursing experts with extensive critical care experience, alongside methodologists and policymakers, ensuring the guideline's development is professional, scientific, and feasible.
2. This is a post-extubation respiratory support guideline in the development specifically for different populations and disease types of mechanically ventilated patients.
3. We are developing this guideline protocol and formal guideline document in strict accordance with the Guidelines 2.0 and the Reporting Items for Practice Guidelines in Healthcare (RIGHT).
4. The limitation of this study is that only literature in Chinese and English will be included.

INTRODUCTION

Diseases such as acute respiratory distress syndrome (ARDS) and sepsis are often triggered by infections, trauma, inhalation injuries, leading to activation of the pulmonary immune system.¹ Neutrophils are rapidly recruited to the lungs, releasing a variety of inflammatory mediators, such as tumor necrosis factor alpha (TNF- α), interleukin (IL)-1 and IL-6, which further exacerbate alveolar injury. Lymphocytes play a crucial role in regulating the appropriate inflammatory response, and a reduction in circulating lymphocytes may perpetuate a harmful inflammatory state.² As the lungs fail to effectively provide oxygen to other parts of the body or remove carbon dioxide, these patients require mechanical ventilation support to assist with breathing. Approximately 30% of patients in the intensive care unit (ICU) rely on mechanical ventilation for respiratory support.^{3 4} However, routine and prolonged mechanical ventilation (PMV) significantly increases the incidence of complications associated with ICU-acquired weakness (ICU-AW), atelectasis, pneumothorax, ventilator-associated pneumonia (VAP), and other conditions, severely impairing physical functions, delaying recovery, and increasing length of stay in hospital and treatment costs.⁵⁻⁷

Therefore, during the course of treatment, when the patient's primary condition is under control and ventilation and oxygenation are corrected, the ventilator and the artificial airway (extubation) should be removed as soon as possible.⁸ However, some patients in the ICU (about 10%-30%) present complex and critical conditions (high risk of extubation failure), experiencing respiratory distress, reduced oxygenation, and inability to maintain spontaneous breathing after extubation, necessitating reintubation. Reintubation not only prolongs the duration of mechanical ventilation, but also results in mortality rates as high as 25%-50% in these patients.^{9 10}

The benefits of providing post-extubation respiratory support to ICU patients are still under discussion.¹¹ Several studies have found that providing post-extubation respiratory support to patients at high risk of extubation failure (e.g., due to

underlying comorbidities such as heart failure, severe obesity, or chronic obstructive pulmonary disease)¹² can effectively improve clinical symptoms, lung function, prognosis, and reduce the rates of reintubation and mortality.¹³⁻¹⁵ However, some studies have found that prophylactic use of respiratory support after extubation in patients with brain injury does not reduce the rate of reintubation and length of hospitalisation.^{16 17}

In recent years, respiratory support options include conventional oxygen therapy (COT), nasal continuous positive airway pressure (NCPAP), non-invasive positive pressure ventilation (NIPPV) and high-flow nasal cannula (HFNC), among other modalities.^{18 19} Given the wide range of respiratory support treatment options available, existing guidelines do not provide adequate guidance regarding appropriate treatments for different populations and disease types. Consider the following examples of various ill-defined post-extubation respiratory support treatment options. Regarding the choice of respiratory support, a guideline recommends using HFNC in high-risk and/or obese patients undergoing cardiac or thoracic surgery to prevent immediate respiratory failure.²⁰ Similarly, the American College of Physicians (ACP) guideline recommends the use of HFNC in hospitalized adults with acute hypoxemic respiratory failure after extubation.^{20 21} However, some studies have found that NFNC after extubation does not prevent reintubation.²² For example, HFNC may be less effective than NIPPV in preventing reintubation in patients receiving PMV for at least 2 weeks.²³

In summary, the effectiveness and optimal post-extubation respiratory support in different populations (adult, pediatric, and neonatal patients) and various disease types (such as respiratory failure, post-cardiac surgery, hypercapnia) remain controversial, and no clinical guideline currently provide guidance for the best post-extubation respiratory support for all types of mechanically ventilated patients.²⁴ There is a lack of detailed, multidisciplinary, and evidence-based support. Therefore, it is necessary to develop high-quality, evidence-based support. Therefore, it is necessary to develop

a high-quality, evidence-based guideline for post-extubation respiratory support in mechanically ventilated patients in the ICU. This development should be based on the methodology outlined in the World Health Organization (WHO) Handbook for Guideline Development (2nd edition, 2014).²⁵

METHODS

Guiding principles of the guideline

We will develop this guideline based on the concept of clinical practice guidelines from the US Institution of Medicine (IOM) and the National Academy of Medicine.²⁶ The guideline development process and methodological standards outlined in the WHO Handbook for Guideline Development are utilized,²⁷ along with the Appraisal of Guidelines for Research and Evaluation II (AGREE II).²⁸ The guideline is formulated in accordance with the Guidelines 2.0 and the Reporting Items for Practice Guidelines in Healthcare (RIGHT).²⁹ A detailed overview of the working groups' directives and their roles in this guideline is provided in Supplementary Table 1. This guideline development study began in May 2023 and is scheduled to conclude in April 2025. The key steps and timeline of the guideline are shown in a Gantt chart (Figure 1).

Sponsors and supporting organizations of the guideline

This guideline is jointly sponsored by Changzhi Nursing Association and Changzhi People's Hospital. The methodology and evidence are supported by the Evidence-Based Medicine Center of Lanzhou University and the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation.

Patient and public involvement

None.

Guideline registration

This guideline was registered on the International Practice Guide Registration Platform (IPGRP) in both Chinese and English. The registration number is PREPARE-2023CN418.

Establishment of guideline working groups

The guideline development group consists of the guideline steering committee, the consensus expert group, the secretary group, the evidence evaluation group and the external audit expert group. They are responsible for identifying guideline topics, formulating clinical questions, conducting evidence searches, synthesizing and evaluating evidence, developing recommendations, drafting this guideline, and completing external reviews. Supplementary Table 2 provides a detailed overview of the composition and responsibilities of the guideline working groups. Furthermore, the study will be conducted in accordance with the Declaration of Helsinki (revised in 2013), ensuring that the dignity, rights, safety, and health of participants are upheld throughout the research. To be selected for the guideline groups, members must be (I) experts in clinical medicine, nursing, guideline development, bioethics, health economics, and other fields related to critical care medicine; (II) representative of different regions, with a balanced age and gender distribution; and (III) providers for informed consent. All members of the guideline working groups are required to declare any conflicts of interest and these declarations will be published as an appendix to the final guideline document.

Scope of the guideline

The guideline focuses on the key issues related to post-extubation respiratory support treatment for ICU patients, including adult, pediatric and neonatal patients who are receiving mechanical ventilation. It is intended for healthcare professionals, including ICU clinicians, nurses, respiratory therapists, and those in related fields such as

pediatrics and critical care. The target population includes all patients undergoing mechanical ventilation extubation in the ICU.

Conflict of interest and funding

All members of the guideline steering committee, consensus expert panel, external audit expert group, secretariat and evidence evaluation group are required to complete a conflict-of-interest declaration form and manage any potential conflicts of interest. This guideline has not received any funding from pharmaceutical companies.

Identification of clinical questions and evaluation of their importance

Preliminary clinical questions related to post-extubation respiratory support for mechanically ventilated patients in the ICU are generated through the review of relevant guidelines both domestically and internationally, as well as by conducting questionnaires to clinicians, nurses and respiratory therapists. The secretariat will be responsible for organizing the collected clinical questions, eliminating duplicates, and consolidating remaining questions. The final clinical questions for the guideline will be determined through two rounds of the Delphi method, where a panel of experts rates and provides feedback on each question to reach consensus on their importance and scope. In the second-round meeting, team members will evaluate the importance of all issues on a scale of 1 to 5 (with 5 being the most important and 1 the least, indicating clinical insignificance). Specific clinical questions will be formulated according to the PICO elements: P (population), I (intervention), C (comparison), and O (outcome). Subsequently, the top 10 to 20 clinical questions will be selected according to the highest scores. After approval by the expert committee, the clinical questions to be addressed in this guideline will be finalized.

Evidence retrieval, screening, and data extraction

Eligible studies will be identified through searches in databases including Pubmed, Medline, Embase, the Cochrane Library, Epistemonikos, UpToDate, BMJ Best Practice, Clinical Key, DynaMed Plus, the China Biology Medicine disc (CBM), ClinicalTrials.gov, the International Clinical Trial Registry Platform (ICTRP) and other Chinese and English databases. Searches will also be supplemented by clinical trial registries and by tracing the references of included articles. Both Medical Subject Headings (MeSH) terms and free words will be used to form the search strategy, limited to publications from the inception of the databases until January 2024. Searches will be conducted in English or Chinese. The search terms include “Airway Extubation*”, “Tracheal Extubation*”, “Intratracheal Extubation*”, “Endotracheal Extubation*”, “post-extubation”, “high flow nasal cannula”, “high flow nasal oxygen”, “HFNC”, “HHFNC”, “HHFN”, “NHF*”, “high flow”, “Cannula”, “Nasal Cannula*”, “oxygen inhalation therap*”, “Positive Pressure Respiration”, “Non-Invasive Ventilation*”, “Noninvasive Ventilation*”, “non-invasive positive pressure ventilation*”, “noninvasive positive pressure ventilation*”, “NIPPV”, “NPPV”, “conventional oxygen therapy”, “COT”, “standard oxygen therapy”, “SOT”, “venturi mask”, “face mask”, “bag valve mask”, “entrainment mask”. The search strategy for the PubMed database is presented in the Supplementary file.

Literature inclusion criteria: (1) The subjects of the study were patients of any age undergoing mechanical ventilation and extubation; (2) The types of studies included China and international guidelines, systematic reviews or meta-analyses, randomized controlled trials (RCTs), diagnostic tests, cohort studies, case-control studies, case series, and case reports. Exclusion criteria: we excluded articles not written in Chinese or English. However, journal articles with formal translations in Chinese or English will not be excluded. Additionally, we excluded articles with incomplete or missing research data, articles for which we were unable to obtain original data, and duplicate articles.

If the literature from secondary research (defined as analyses or systematic assessments based on existing primary data or published research findings, such as systematic reviews and meta-analyses) fails to address the clinical questions required for the guideline, lacks relevant secondary evidence, or needs updating (publications older than 2 years and the original studies published within 2 years), a systematic search will be conducted for RCT, non-randomized controlled studies, case reports and other relevant studies.

The guideline development team will work in pairs to independently search and screen the literature by title, abstract and full text. They will extract data from the literature and record the number of articles initially retrieved and those finally included. Any disagreements will be resolved by discussion or consultation with a third-party expert in evidence-based methodology.

Evaluation of the quality of literature

We will use the AGREE II)³⁰, A MeaSurement Tool to Assess systematic Reviews (AMSTAR)³¹, the Cochrane Collaboration's tool for assessing risk of bias in randomized trials³², and the Newcastle-Ottawa Scale (NOS)³³ to evaluate the methodological quality of the included literature. Supplementary Table 3 provides a detailed description of the assessment tools used for various study types in the assessment process. The assessment will be conducted independently by two researchers using the research instrument. If there is a disagreement between their findings, it will be resolved through discussion or negotiation with a third-party expert to reach a final consensus.

Grading the quality of evidence

Evidence quality grading was conducted for the pooled evidence corresponding to each guideline question's outcome indicator. The guideline questions included in the original research evidence were assessed using the Grading of Recommendations

Assessment, Development, and Evaluation (GRADE) system. This assessment considered 5 downgrading factors: limitations (risk of bias), imprecision, inconsistency, indirectness, and publication bias, as well as 3 escalating factors: large effect, dose-response, and the presence of all plausible residual confounding. The quality of evidence will be classified as follows: High (A): very certain that the observed value is close to the true effect; Moderate (B): moderately certain that the observed value is probably close to the true effect, but there is a possibility of substantial differences; Low (C): limited observational values which may be substantially different from the true effect; Very low (D), observational values are likely to be substantially different from the true effect. The evidence quality was graded according to these evaluations, and a summary table of the evidence was compiled.

Forming recommendations and reaching consensus

Recommendations supported by evidence will be categorized into 4 levels according to the GRADE system: strong, weak, strong against, and weak against (Table 1). The consensus expert group assessed factors such as the quality of evidence, values, economic analysis, balance of advantages and disadvantages to form a preliminary recommendation. All the recommendations were compiled into a recommendation letter questionnaire, which was distributed to the consensus group experts for evaluation and suggested modifications. The consensus expert group reached a consensus on the recommendation after conducting 2-3 rounds of Delphi method. A flowchart depicting each stage of the Delphi process is shown in Figure 2.

The rules for reaching a consensus are as follows: If over 50% of the experts chose "2", and over 70% chose "2" or "1", the recommendation achieved consensus with a "Strong" recommendation strength. If more than 50% of the experts chose "2" or "1", and fewer than 20% chose " -2" or "-1", the recommendation also reached consensus but with a "weak" recommendation strength. Other scenarios were considered as

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lacking consensus, and the recommendation moved forward to the next round of voting. For guideline issues where no consensus was reached but a recommendation is needed, the guideline steering committee further discussed and determined the final recommendation based on the voting analysis. When all issues reached either a consensus or a non-consensus threshold, and no new significant opinions emerged, the Delphi process was deemed complete.

Guideline drafting and external review of recommendations

The RIGHT checklist, which consists of 22 items, can assist guideline developers in effectively reporting their guidelines.²⁹ The secretariat will draft the initial version of the guideline according to the RIGHT entries, and submit it to the external audit expert group for review and feedback. This group consists of clinical medicine, nursing, methodology and other multidisciplinary experts. They will evaluate the draft from the perspectives of acceptability, clarity of expression and clinical feasibility, and provide suggestions for improvement. The secretariat and the evidence evaluation group will revise the draft based on feedback from external audit experts to create the final version of the guideline.

Guideline approval, release, and update

The final draft of the guideline will be reviewed, finalized, and approved by the expert committee. With the agreement of 2/3 of the consensus group experts, the expert committee can modify and refine the important issues in the proposal. The secretariat is responsible for accurately documenting the entire modification process. We are in the development of a comprehensive program for regular review and updates, which includes a systematic process for monitoring new evidence, reviewing guideline content, and incorporating necessary changes. Guideline updates will be based on the following criteria: (1) the recommendations remain unchanged, but new evidence is available based on a larger sample size or higher quality than previously considered;

(2) the recommendations have changed due to new high-quality evidence that does not support the existing recommendations, or there have been changes in the safety or target population of the existing recommendations.

We plan to formally review and update the guidelines every two to three years. This schedule allows us to incorporate important new evidence and ensures that our recommendations align with the latest clinical research and practice standards.

Guideline dissemination, implementation, and evaluation

After the guideline is released, the project team will promote and disseminate it primarily through the following methods: (I) presentations at relevant academic conferences; (II) organization dedicated guideline promotion meetings in some provinces and cities in China to ensure that clinicians, respiratory therapists, and nurses fully understand and correctly apply the guideline; (III) distribution of guideline interpretations through commonly used medical websites, applications (APPs), and short video platforms in China; (IV) organization of guideline training sessions in different provinces for clinicians, pharmacists and nurses to familiarize them with the guideline; (V) members of the guideline steering committee and guideline development expert panel will write articles related to the guideline for publication in journals; and (VI) evaluation of the guideline’s impact on clinical decision-making. We aim to provide evidence-based recommendations to enhance clinicians’ decision-making process, reduce variability in treatment practices and ensure consistent application of best practices. Two to three years after the publication and implementation of the full text of the guideline, we will evaluate the current status of post-extubation respiratory support modalities for mechanically ventilated patients in the ICU in China and abroad. This evaluation will help us understand the dissemination of the guideline, the recognition of its recommendations in clinical practice, and its impact on treatment decisions. Additionally, it will be beneficial for improving and refining the guideline during its next update.

ETHICS AND DISSEMINATION

Ethical approval has been granted by Changzhi People's Hospital (2023K023). Findings from this study will be disseminated through peer-review publications.

DISCUSSION

Due to the physiological and pathophysiological differences among adults, children and neonates (such as preterm infants who are more susceptible to complications and even death post-extubation due to immature organ function, particularly respiratory function³⁴) and the distinct characteristics of various diseases (for example, in patients with respiratory failure, severe impairment of pulmonary ventilation and/or gas exchange can lead to a series of pathophysiological changes and corresponding clinical syndromes³⁵), it is clear that providing the same type of respiratory support to all extubated patients is unreasonable. Instead, tailored respiratory support should be provided according to their individual needs to maintain normal respiratory function and improve their prognosis.

With advancements of medical technology, various methods of post-extubation respiratory support are available for mechanically ventilated patients. Non-invasive ventilation (NIV) helps maintain airway defenses while aiding bronchial re-expansion and restoring respiratory mechanics, but it has a high complication rate.³⁶ Two common modes of NIV are NCPAP and NIPPV. NCPAP enhances alveolar compliance, reduces airway resistance, and improves pulmonary ventilation and gas exchange; however, its tolerance and adherence are relatively poor.³⁷ NIPPV provides positive end-expiratory pressure and airway pressure, improving cardiopulmonary function and oxygenation indices, but it may increase the risk of ventilator-associated lung injury.³⁸ NHFOV is an emerging mode of NIV that adds pressure oscillations to NCPAP, providing greater benefits in maintaining alveolar stability, improving oxygenation, and promoting carbon dioxide elimination.³⁹ HFNC is also a novel form of respiratory support that delivers patients with high-flow heated and humidified

gases with stable inspired oxygen concentrations, significantly enhancing patient comfort and tolerance while demonstrating improved clinical outcomes.^{40 41} However, current guidelines only recommend the prophylactic use of post-extubation respiratory support without providing specific guidance for different populations and diseases,⁴² leaving users often unable to obtain useful information on respiratory support modes from these guidelines.

To recommend the best respiratory support methods for patients, we will establish a multidisciplinary team to develop a guideline for respiratory support after mechanical ventilation extubation. This process will strictly adhere to the WHO guideline development handbook²⁷ and the guideline development checklist.⁴³ This protocol will serve as the foundation and framework for the guideline development process, ensuring standardization in both procedures and methods. The guideline development working group will conduct a thorough review of the literature and surveys to fully understand the key clinical issues in post-extubation respiratory support. They will systematically search for, evaluate, and grade existing best clinical evidence, integrating this with clinical expert experience and various other factors to develop high-quality guideline. This guideline will aim to scientifically guide evidence-based clinical practice and ultimately improve patient outcomes.

Supplementary Information

Supplementary Table 1. Internationally representative guidance guidelines.

Supplementary Table 2. The composition and responsibilities of the guideline working groups.

Supplementary Table 3. Document types and evaluations tools.

Supplementary file. Search Strategy for PubMed.

Contributors

All listed authors meet authorship criteria and that no others meeting the criteria have been omitted. XFH conceived the idea for the project. All authors (JC, JLH, MZ, YH, and JHT) contributed to the design of the study. XFH wrote the first draft of the manuscript. JC, JLH, and JHT contributed to the refinement of the study methods and critical revision of the manuscript. All authors read and approved the final version of the manuscript. The guarantor of the study is XFH, accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests

None declared.

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Figure 1. Gantt chart. The key steps and timeline of guideline development. PICO, patient/population, intervention, comparison, and outcomes.

Figure 2. The flowchart showing each stage of the Delphi process.

For peer review only

Table 1. GRADE strength level of recommendation

Strength level	Definition
Strong (I)	Support for the use of an intervention where the benefits clearly outweigh the risks
Weak (II)	Support for the use of an intervention where the benefits may outweigh the risks
Strong against (I)	Opposition to the use of an intervention where the risks clearly outweigh the benefits
Weak against (II)	Opposition to the use of an intervention where the risks may outweigh the benefits or the balance of benefits and risks is unclear

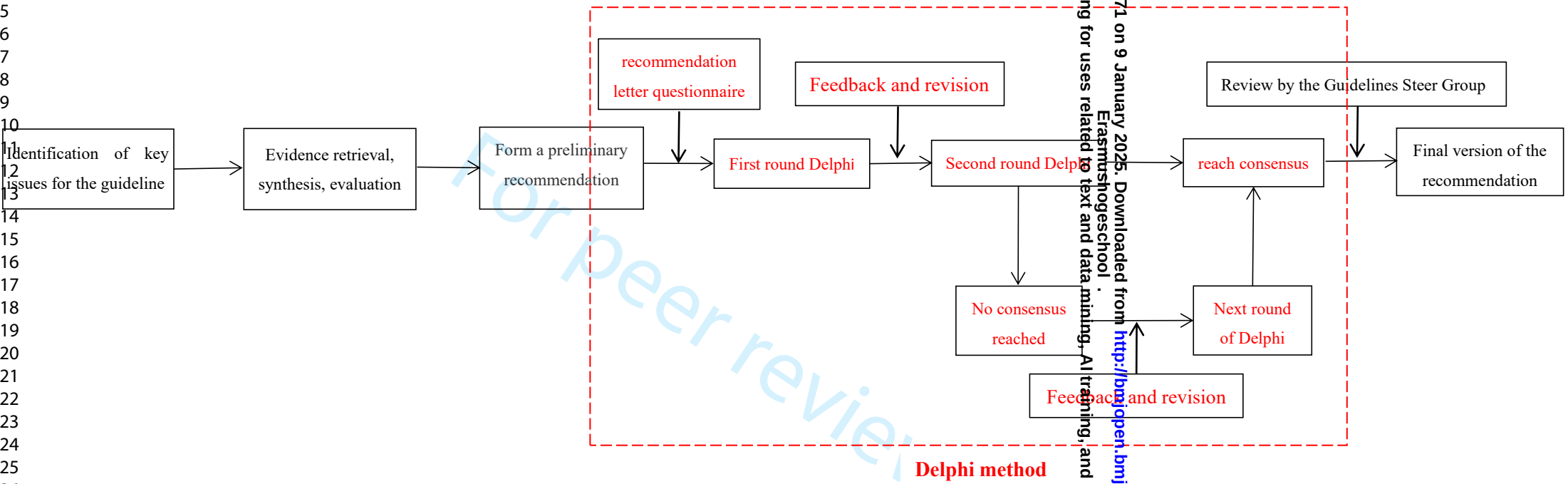
GRADE, Grading of Recommendations Assessment, Development and Evaluation.

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Key steps	Group	2023 /05	2023 /06	2023/07	2023 /08	2023 /09	2023 /10	2023 /11	2023 /12	2024 /01	2024 /02	2024 /03	2024 /04	2024 /05	2024 /06	2024/07	2024 /08	2024 /09	2024 /10	2024 /11	2024 /12	2025 /01	2025/02	2025 /03	2025 /04
Launch the guideline	Guideline steering committee																								
Establish the guideline working groups	Guideline steering committee/ Secretarial group/ Consensus expeit group/ Evidence evaluationgroup/ External audit expeit group																								
Guideline registration and plan writing	Guideline steering Committee/ Secretarial group																								
Formulate clinical questions (PICO questions)	Secretarial group/ Consensus expeit group																								
Evidence retrieval, evaluation, and synthesis	Evidence evaluation group																								
Grade the quality of the body of evidence	Evidence evaluation group																								
Draft the recommendations	Evidence evaluation group																								
Formulate the final recommendations	Consensus expeit group																								
Draft full guideline	Secretarial group																								
Send to external reviewers	External audit expeit group																								
Revise the guideline	Guideline steering committee																								
Submit to medical journal	Secretarial group																								

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Supplementary Table 1.

Internationally representative guidance guidelines

Methodology	Working group direction	The specific role in the development of this guideline
Working Group		
WHO handbook for guideline development	Guideline formulation	Provide a systematic approach and framework for developing high-quality guidelines.
RIGHT	Guideline report	Provide a structured checklist for a systematic and comprehensive reporting guide, and the development of the guide with reference to the RIGHT reporting norms ensures greater regularity and transparency in reporting.
Guideline 2.0	Guideline formulation	A comprehensive checklist systematically developed for the successful development of guidelines. Careful consideration of the entries in the checklist will assist in the development, implementation and evaluation of the guidelines.
AGREE II	Evaluation of the methodological quality of the guidelines	AGREE II serves as a methodological quality assessment tool for guidelines, with results reflecting the rigor and scientific validity of the development process. To ensure that the guidelines we reference and develop meet high standards of development and reporting.
GRADE	Grading the quality of guideline evidence and strength of recommendation	Provides a clear, comprehensive grading and summarization methodology for quality grading the evidence on which it relies to support its recommendations.

Supplementary Table 2.

The composition and responsibilities of the guideline working groups

Group	Composition	Responsibility
Steering committee	one clinical chairman, one methodology chairman, one government representative, two experienced ICU nursing specialists, two experienced ICU clinical specialists, and two respiratory therapists with rich respiratory care experience.	(I) determine the theme and scope of the guideline and construct key issues according to PICO format (II) establish the guideline consensus expert group, guideline secretariat, evidence evaluation group, and external audit expert group (III) assess conflicts of interest and address any conflicts as needed (IV) chair the guideline working meetings (V) review and approval the plan (VI) approve recommendations and the full guideline (VII) revise and update the guideline
Consensus expert group	consists of 25 to 30 experts in the fields of critical care, respiratory, pediatrics, neonatology, and respiratory therapists.	(I) identify key issues for the guideline and prioritize topics for assessment (II) formulate recommendations on some issues (III) reach consensus on the recommendations (IV) modify the full text of the guideline based on feedback (V) publish and promote the guideline

Group	Composition	Responsibility
Secretary Group	3 to 5 staff members from sponsors and supporting organizations.	(I) complete the guideline registration and draft the guideline plan (II) investigate the clinical questions related to the guideline, design a questionnaire according to the initial clinical question list, collect questions and rank the importance of these questions (III) coordinate the work of other working groups (IV) organize the recommendation consensus meeting (V) facilitate the external review process for the entire guideline (VI) record the entire guideline development process in detail (VII) draft the guideline (VIII) submit the guideline for approval
Evidence evaluation group	3 to 10 individuals with a background in evidence-based medicine and experience in evidence retrieval.	(I) complete the literature search, screening, evidence extraction, risk of bias evaluation, and GRADE evidence rating for the guideline (II) complete the quality evaluation of the published systematic evaluation/meta analysis related to the guideline topic (III) update and produce meta-analysis (IV) create the evidence summary table and the recommendation decision table
External audit expert	5 to 10 experts in related fields who do not directly participate in the formulation of the guideline.	(I) evaluate and review the questions and scope of the clinical practice guidelines

Group	Composition	Responsibility
group		(II) review the final recommendations
		(III) provide specific amendments for the full text of the guideline

Note: "Rich experience in the ICU work" is defined: (1) Years of working experience: at least five years of full-time work in an ICU. (2) Education level: a bachelor's degree or higher. (3) Professional title: intermediate or senior level.

Supplementary Table 3

Document types and evaluations tools			
Steps	Research type	Methodological assessment tools	quality
Evidence production	Randomized controlled trial	Cochrane risk of bias assessment tool	
	Non-randomized experimental study	MINORS items	
	Cohort study	NOS scale	
	Case-control study	NOS scale	
	Animal experiment	STAIR list	
Evidence synthesis	Systematic review/Meta-analysis	AMSTAR 2 tool	
		OQAQ scale	
		SQAC scale	
	Overviews of systematic reviews	AMSTAR 2 tool	
Creating guidelines and conducting health	Clinical practice guidelines	AGREEII tool	
		Checklist for HTA report	
		Experimental study: Cochrane EPOC evaluation method	
	Health policy research	Observational research: quality evaluation criteria for Hilton's effective public health policy project development	
Dissemination of evidence	Clinical practice guidelines	AGREEII tool	
	Health technology assessment	Checklist for HTA report	
Applied evidence	Decision support system		
Assessment and improvement practices	Real-world study		

Supplementary file

Search Strategy for PubMed

#1 "Airway Extubation"[Mesh] OR "Airway Extubation*"[Title/Abstract] OR "Tracheal Extubation*"[Title/Abstract] OR "High-Frequency Ventilation"[Title/Abstract] OR "Endotracheal Extubation*"[Title/Abstract] OR "post-extubation"[Title/Abstract] OR "Ventilator Weaning"[Mesh] OR "Weaning, Ventilator"[Title/Abstract] OR "Respirator Weaning"[Title/Abstract] OR "Mechanical Ventilator Weaning"[Title/Abstract]

#2 "Respiratory Support"[Title/Abstract] OR "high flow nasal cannula"[Title/Abstract] OR "high flow nasal oxygen"[Title/Abstract] OR "HFNC"[Title/Abstract] OR "HHFNC"[Title/Abstract] OR "HHFN"[Title/Abstract] OR "NHF*"[Title/Abstract]

#3 ("high flow"[Title/Abstract] AND ("Cannula"[Mesh] OR "Nasal Cannula*"[Title/Abstract])) OR ("high flow"[Title/Abstract] AND ("oxygen inhalation therapy"[MeSH] OR "oxygen inhalation therap*"[Title/Abstract]))

#4 "Positive Pressure Respiration"[Mesh] OR "Noninvasive Ventilation"[Mesh] OR "Noninvasive Ventilation*"[Title/Abstract] OR "Non-Invasive Ventilation*"[Title/Abstract] OR "non-invasive positive pressure ventilation*"[Title/Abstract] OR "noninvasive positive pressure ventilation*"[Title/Abstract] OR "NIPPV"[Title/Abstract] OR "NPPV"[Title/Abstract] OR "conventional oxygen therapy"[Title/Abstract] OR "COT"[Title/Abstract] OR "standard oxygen therapy"[Title/Abstract] OR "SOT"[Title/Abstract] OR "venturi mask"[Title/Abstract] OR "face mask"[Title/Abstract] OR "bag valve mask"[Title/Abstract]

#5 #1 AND (#2 OR #3 OR #4)

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