# CLINICAL TRIAL PROTOCOL (FINAL VERSION)

## Protocol Identification

Title: Feasibility and Clinical Effects of an Oscillatory Negative-Pressure Device (Simeox®) in Patients Hospitalized with Acute Exacerbation of COPD

Study Type: Interventional (Randomized Controlled Trial)
Design: Parallel-group, double-blind
Estimated Duration: April 2024 – December 2026
Primary Completion: December 2026

## Sponsor and Investigators

Sponsor: Investigator-initiated (no external funding)

Principal Investigator:
Manuel João Oliveira Fernandes
Hospital Senhora da Oliveira, Guimarães, Portugal

Collaborators:
María Luz González Doníz (University of A Coruña)
Cátia Caneiras

## Background and Rationale

Acute exacerbations of COPD are associated with impaired mucus clearance, worsening airflow limitation, and increased morbidity. Airway clearance techniques are commonly used, but their clinical impact remains modest. Oscillatory negative-pressure devices such as Simeox® act on distal airways and may improve secretion mobilization. Evidence in hospitalized exacerbations is limited, justifying this randomized controlled trial.

## Objectives

Primary Objective:
To evaluate the effect of the intervention on COPD impact (change in CAT score).

Secondary Objectives:
- To assess secretion mobilization (sputum weight)
- To evaluate cough-related quality of life (LCQ-acute)

- To assess length of hospital stay
- To evaluate feasibility and tolerability

## Study Design

Randomized, controlled, parallel-group, double-blind clinical trial.

Participants are randomized (1:1) to:
- Intervention: Physiotherapy + Simeox®
- Control: Physiotherapy + sham device

Blinding:
Participants and outcome assessors are blinded. The treating therapist is not blinded.

## Eligibility Criteria

Inclusion:
- Hospitalized with acute COPD exacerbation
- Increased sputum production
- Referred for respiratory physiotherapy

Exclusion:
- Hemodynamic instability requiring vasopressors
- Severe respiratory failure ($PaO_2/FiO_2$ <100 or $FiO_2$ >60%)
- Altered consciousness or inability to cooperate
- Pneumothorax (untreated)
- Massive hemoptysis
- Unstable cardiovascular disease

## Intervention Description

Both groups receive standard respiratory physiotherapy including breathing exercises, airway clearance techniques, and cough facilitation.

Intervention group:
Physiotherapy + Simeox® device applied during passive expiration.

Control group:
Physiotherapy + sham device (inactive).

Treatment frequency:
Once daily until discharge or discontinuation.

## Outcomes

Primary Outcome:
Change in COPD Assessment Test (CAT) score from baseline to final assessment.

Secondary Outcomes:
- Sputum weight (grams within 1 hour post-treatment)
- LCQ-acute score
- Length of hospital stay
- Adverse events and tolerability

## Randomization and Allocation

Randomization performed using computer-generated sequence (Randomizer®).
Allocation concealment ensured via software-based assignment.

## Blinding

Participants and outcome assessors are blinded.
Therapist delivering intervention is aware of allocation.
Unblinding only permitted in case of medical necessity.

## Safety Monitoring

Adverse events will be recorded and monitored.
Serious adverse events will be reported to the Ethics Committee.

Stopping rules:
- Participant deterioration
- Withdrawal of consent
- Clinical contraindication to intervention

## Follow-up

Participants are followed during hospitalization.
Reasons for discontinuation and outcomes at discharge are recorded.

## Data Management

Data are anonymized and stored in secure institutional systems.
Access restricted to research team.
Data retained for 4 years and then destroyed.

## Statistical Analysis

Analysis performed using JASP software.

Significance level: $p < 0.05$

## Quality Assurance

Standardized procedures and trained investigators.
Data verification performed periodically.
Protocol adherence monitored by principal investigator.

## Ethical Considerations

Approved by institutional Ethics Committee.
Written informed consent obtained.

Study complies with Declaration of Helsinki and GDPR regulations.

## Dissemination

Results will be published in peer-reviewed journals and presented at scientific meetings.

Participants will not be individually identified in any publication.

## Timeline

Project design: 2023–2024
Data collection: 2024–2026
Analysis: 2027
Publication: 2027

## Limitations

Small sample size and single-center design.

## Conclusion

This trial will provide important data on feasibility and physiological effects of oscillatory negative-pressure devices in acute COPD exacerbations and inform future large-scale studies.