

DOPE-ICU feasibility trial synopsis

Title	Drainage of pleural effusions in the intensive care unit – a feasibility trial
Short title	DOPE-ICU feasibility trial
Objectives	To assess the feasibility of a randomised evaluation of performing versus withholding therapeutic pleural drainage in adult patients with pleural effusion and respiratory failure in the intensive care unit (ICU)
Population	Adults acutely admitted to the ICU with pleural effusion and respiratory failure
Intervention	Ultrasonography-guided therapeutic pleural drainage with insertion of a small-bore catheter in the pleural cavity with effusion ≥ 2 cm (uni- or bilaterally)
Comparator	No therapeutic pleural drainage in ICU, except if escape criteria are present, which are defined similarly as exclusion criteria 2,3,4,5 and 7 (see below).
Outcomes	<p>Primary (feasibility) Proportion of patients receiving pleural drainage during ICU admission, within 90 days from randomisation</p> <p>Secondary feasibility outcomes</p> <ol style="list-style-type: none"> 1. Proportion of patients with one or more protocol violations 2. Proportion of included patients out of number of eligible patients 3. Proportion of randomised patients with consent withdrawn for use of data <p>Secondary clinical outcomes</p> <ol style="list-style-type: none"> 1. All-cause 90-day mortality 2. Proportion of patients with one or more serious adverse events (SAEs) within 90 days after randomisation; SAEs are defined as new pneumothorax requiring invasive treatment (drainage or surgery), new haemothorax requiring red blood cell transfusion, new blood stream infection defined as any cultured microorganism from any blood sample except microorganisms clearly specified to be contaminants or likely contaminants by the microbiological department, and new episode of invasive mechanical ventilation defined as endotracheal intubation or re-intubation after extubation or tracheal decannulation 3. Absolute number of days alive without the use of mechanical ventilation, renal replacement therapy or circulatory support in the 90-day period 4. Days alive and out of hospital in the 90-day period <p>The specific elements of the composite outcomes will also be reported.</p> <p>Secondary process outcomes</p> <ol style="list-style-type: none"> 1. Proportion of patients with new pleural infection after 24 hours from randomisation defined as any positive pleural fluid culture of any fungi or bacteria except contaminants within the 90-day follow-up period. 2. PaO₂/FiO₂ ratio in ICU in the arterial blood gas analysis closest to 24- and 72-hours post-randomisation 3. pH in ICU in the arterial blood gas analysis closest to 24- and 72-hours post-randomisation 4. PaCO₂ in ICU in the arterial blood gas analysis closest to 24- and 72-hours post-randomisation <p>Differences (Δ) from individual baseline registrations will be reported supplementally.</p>
Eligibility	<p>Inclusion criteria</p> <ol style="list-style-type: none"> 1. Acute admission to the ICU and 2. Age ≥ 18 years and 3. Pleural effusion ≥ 2 cm in either pleural cavity assessed by ultrasonography, CT, or MRI (measured between pleurae parietale and viscerae perpendicularly to the chest wall at the largest-separation point) and

	<p>4. Respiratory failure defined as any of the following: any oxygen supplementation in an open system, invasive or non-invasive mechanical ventilation (including non-intermittent mask CPAP), or most recent arterial blood gas analysis with $\text{PaCO}_2 > 6.0$ kPa and $\text{pH} < 7.35$</p> <p>Exclusion criteria</p> <ol style="list-style-type: none"> 1. Mediastinal drain or pleural drain in situ on either side 2. Suspected or confirmed haemothorax (e.g., due to recent thoracic trauma or intrathoracic surgery) 3. Suspected or confirmed pneumothorax (e.g., by anamnesis, on radiographic or ultrasonographic assessment, or due to presence of subcutaneous emphysema) 4. Suspected or confirmed pleural empyema (e.g., by anamnesis or clinical presentation, or on CT, MRI or ultrasonographic assessment) 5. Pleural malignancy (suspected or confirmed pleural lymphoma, pleural metastases or direct pleural invasion, or malignant mesothelioma) 6. Antithrombotic treatment or coagulation deficiency incompatible with conducting pleural drainage as by local recommendations, and contraindications to reversal of this (clinical assessment) 7. Clinically assessed absolute indication for pleural drainage and: <ol style="list-style-type: none"> a. Invasive or non-invasive mechanical ventilation or mask CPAP with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 13.3 kPa in the most recent arterial blood gas analysis b. High-flow humidified oxygen therapy with a flow ≥ 50 L/min and a $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 13.3 kPa in the most recent arterial blood gas analysis c. Persistent respiratory acidosis with a $\text{pH} < 7.25$ and a $\text{PaCO}_2 > 6.0$ kPa in the most recent arterial blood gas analysis in spite of non-invasive ventilation for > 1 hour 8. Withdrawal from active therapy or brain death deemed imminent 9. Expected ICU stay < 24 hours from randomisation. 10. Pregnancy 11. Under coercive measures (i.e., ongoing involuntary hospital admission or under correctional authorities' jurisdiction) 12. Consent not obtainable as per the model approved for the specific site 13. Previously randomised in the DOPE-ICU feasibility trial
Sample size	<p>A total of 88 patients will be included to detect or reject an expected minimal 75% relative increase (an absolute increase of 30 %-points) in the primary feasibility outcome of patients receiving pleural drainage in the intervention group, assuming a maximal incidence of pleural drainage in the ICU within 90 days of 40% in the control group (two-sided $\alpha=0.05$ and $\beta=0.2$), and an added 4 patients due to an expected dropout rate of maximum 5%.</p>
Study duration	<p>The trial intervention will continue for maximum of 90 days post randomisation; follow-up will be done at 90 days. Estimated recruitment period is 1 year.</p>