



Congress Review

Review of the American Thoracic Society (ATS) International Conference 2026

Location:	Orlando, Florida, USA
Date:	May 15–20, 2026
Citation:	Respir AMJ. 2026;4[1]:12-25. https://doi.org/10.33590/respiramj/R12O7F5B



THE American Thoracic Society (ATS) International Conference 2026, held in Orlando, Florida, USA, May 15–20, united the pulmonary medicine community for a week of discussion on the latest data, advances, and challenges in respiratory diseases. The meeting themes included the need for more individualized risk prediction, multidisciplinary care, and rehabilitation, which are explored in the following Congress Review.



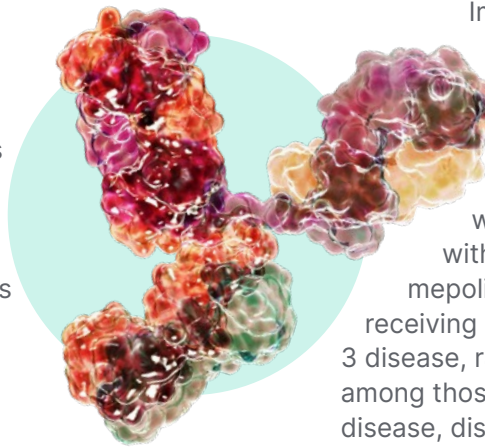
Mepolizumab Boosts Disease Stability in Severe COPD

ACCORDING to new research presented at ATS 2026, disease stability may be an achievable treatment goal for a broad range of patients with COPD receiving mepolizumab, even among those who remain poorly controlled despite triple therapy.¹

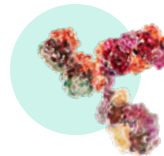
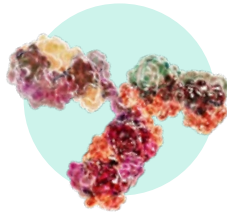
COPD is a progressive respiratory disease characterized by worsening symptoms, declining lung function, and recurrent exacerbations that accelerate disease progression. While reducing exacerbations has long been a key treatment objective, disease stability, defined as sustained low disease activity following optimization of treatment, is emerging as a more ambitious target. Researchers sought to determine whether mepolizumab, an approved add-on maintenance therapy for adults with eosinophilic COPD, could help more patients achieve this outcome.

The analysis pooled data from three Phase III RCTs: METREX, METREO, and MATINEE. A total of 1,146 patients with COPD, blood eosinophil counts of at least 300 cells/ μ L, a history of exacerbations, and ongoing triple therapy were included. Investigators assessed disease stability at Week 52 using a composite endpoint that required patients to experience no moderate or severe exacerbations, maintain or improve their COPD Assessment Test (CAT) score, and preserve or improve lung function compared with baseline.

Results showed that 18% of patients receiving mepolizumab achieved disease stability after 52 weeks, compared with 15% of those receiving placebo. The greatest contributor to this difference was a reduction in exacerbations. More than half of patients treated with mepolizumab met the exacerbation criterion for disease stability (52% versus 42% with placebo), while rates for maintaining health status and lung function were broadly similar between the groups.



Importantly, the benefits of mepolizumab were observed across all Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity categories. Disease stability was achieved by 26% of patients with GOLD 2 disease receiving mepolizumab compared with 23% receiving placebo. In patients with GOLD 3 disease, rates were 11% versus 9%, while among those with the most severe GOLD 4 disease, disease stability was achieved in 16% of patients receiving mepolizumab compared with just 6% of those receiving placebo.



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The findings suggest that disease stability is not only measurable in COPD but may also be attainable across a wide spectrum of disease severity. For patients with eosinophilic COPD who continue to experience symptoms and exacerbations despite triple therapy, mepolizumab may offer an opportunity to achieve more sustained disease control.

While the analysis was conducted post hoc and further prospective validation is needed, the results support the growing view that disease stability could become an important therapeutic target in COPD management.

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Twice-Yearly Depemokimab Maintains Asthma Control for 2 Years

NEW data presented at ATS 2026 showed that depemokimab, the first ultra-long-acting biologic for Type 2 asthma, delivered sustained reductions in exacerbations and maintained improvements in asthma control and quality of life over a 2-year treatment period.²

Depemokimab is designed to target IL-5, a key driver of eosinophilic inflammation in Type 2 asthma. Its extended half-life enables dosing just twice yearly, offering a potentially convenient treatment option for patients with inadequately controlled disease. While previous Phase III studies demonstrated efficacy over 52 weeks, the latest analysis assessed whether these benefits could be maintained over the longer term.

Researchers conducted an integrated post-hoc analysis of the Phase III SWIFT-1 and SWIFT-2 trials and the AGILE open-label extension study. In the original SWIFT studies, 762 patients with Type 2 asthma characterized by elevated blood eosinophil counts were randomized to receive either subcutaneous depemokimab 100 mg or placebo every 26 weeks for 1 year. Patients completing the trials were eligible to enter AGILE, where they either continued depemokimab treatment or switched from placebo to depemokimab, allowing assessment of outcomes across a total of 104 weeks.

The results demonstrated a substantial and durable reduction in asthma exacerbations. During the first year of treatment, depemokimab reduced the annualized

exacerbation rate by 54% compared with placebo, with rates of 0.51 versus 1.11, respectively. Among patients who received depemokimab continuously, this benefit was maintained throughout the full 2-year period, with an annualized exacerbation rate of 0.52.

Patient-reported outcomes also remained consistently improved. At Week 52, participants receiving depemokimab experienced a marked improvement in health-related quality of life, reflected by a 13.92-point reduction in St George's Respiratory Questionnaire score from baseline. This improvement was sustained through Week 104, reaching a 16.29-point reduction. Similarly, improvements in asthma control, measured using the Asthma Control Questionnaire-5 (ACQ-5), were maintained over the 2-year follow-up period, with scores improving from a reduction of 0.81 points at Week 52 to 0.89 points at Week 104.

Investigators also reported persistent suppression of Type 2 inflammation throughout treatment. Blood eosinophil counts remained consistently reduced over the 2 years among patients receiving continuous depemokimab therapy, indicating ongoing biological control of the inflammatory processes underlying disease activity.

Importantly, patients who switched from placebo to depemokimab after the first year experienced rapid and clinically meaningful improvements in clinical outcomes during their second year of treatment. These gains were sustained through the end of the study.

The findings suggest that depemokimab provides durable clinical benefits and long-term disease control in patients with Type 2 asthma, while supporting the potential value of a twice-yearly dosing schedule. Although the analysis was conducted post hoc and the extension study was open-label, the results provide encouraging evidence that the efficacy observed during the initial Phase III trials can be maintained over an extended treatment period.



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Brensocatic Improves Respiratory Symptoms in Bronchiectasis

BRENSOCATIC is a first-in-class oral, reversible dipeptidyl peptidase-1 inhibitor that targets neutrophil-driven inflammation in bronchiectasis. This post-hoc analysis of the Phase III ASPEN trial evaluated the impact of brensocatic on individual respiratory symptoms using the Quality of Life-Bronchiectasis Respiratory Symptoms Score (QOL-B RSS), as well as symptom outcomes according to on-study pulmonary exacerbation status.³

In ASPEN, adults with bronchiectasis and at least two pulmonary exacerbations in the preceding year were randomized to receive brensocatic 10 mg, brensocatic 25 mg, or placebo once daily for 52 weeks. QOL-B assessments were completed every 2 weeks throughout the study. The analysis focused on nine respiratory symptom items, including cough, congestion, sputum production and color, dyspnea, wheezing, chest pain, and nocturnal cough.

Overall, brensocatic treatment resulted in improvements across all respiratory symptom domains compared with placebo, with the greatest and most consistent benefits observed in the 25 mg treatment arm. At Week 52, the largest treatment differences versus placebo were seen for cough, congestion, dyspnea, and sputum color. Improvement in sputum color is of particular interest, as this parameter is a validated marker associated with neutrophilic airway inflammation.

Patients who experienced pulmonary exacerbations during the study reported a greater symptom burden than those who remained exacerbation-free. Nevertheless, symptom improvements with brensocatic were observed irrespective of whether patients experienced on-study exacerbations, including severe exacerbations, suggesting a treatment benefit beyond exacerbation prevention alone.

These findings complement the primary ASPEN results, in which brensocatic significantly reduced exacerbation frequency, while the 25 mg dose also slowed lung function decline and demonstrated improvements in patient-reported outcomes. Collectively, the data indicate that brensocatic provides clinically meaningful benefits across multiple dimensions of disease burden, including respiratory symptoms and exacerbation control. Further real-world studies are warranted to confirm the durability and generalizability of these symptom improvements in broader bronchiectasis populations.



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4 Brensocatib Shows Exposure-Dependent Benefits in Bronchiectasis Trials

NEW integrated data from the WILLOW and ASPEN clinical trials suggest that higher systemic exposure to brensocatib is associated with meaningful improvements in lung function and pulmonary exacerbation outcomes in patients with non-cystic fibrosis bronchiectasis, while maintaining a generally favorable safety profile.⁴

Brensocatib is a first-in-class, oral, reversible inhibitor of dipeptidyl peptidase 1, designed to reduce activation of neutrophil serine proteases and dampen neutrophil-driven airway inflammation. It is approved for use in patients aged 12 years and older with bronchiectasis.

The exposure–response analysis included 1,431 participants drawn from two pivotal studies: the Phase II WILLOW trial (NCT03218917) and the Phase III ASPEN trial (NCT04594369). Researchers evaluated relationships between steady-state drug exposure (AUC_τ) and key efficacy outcomes, including annualized pulmonary exacerbation rate, time to first exacerbation, and post-bronchodilator forced expiratory volume in 1 second (FEV₁), as well as safety events of special interest such as hyperkeratosis, periodontal disease, and pneumonia.

When exposure was analyzed as a continuous variable, no statistically significant relationship was observed for exacerbation rate or time to first exacerbation. However, threshold-based modelling identified clinically meaningful improvements at AUC_τ levels above 1,100 ng·h/mL. At this exposure, most patients receiving 25 mg (100%) and a majority receiving 10 mg (69%) achieved benefit in exacerbation-related outcomes.

A stronger relationship was observed for lung function. An AUC_τ threshold of 1,531 ng·h/mL was associated with preservation of FEV₁ over the treatment period. Above this threshold, nearly all patients on 25 mg (>99%) and almost half on 10 mg (46%) achieved exposures linked to stabilized lung function. In contrast, patients below this level or receiving placebo experienced comparable declines in FEV₁.

No exposure–response relationship was identified for pneumonia or periodontal disease. A modest exposure-dependent increase in hyperkeratosis was observed, although events were generally mild or moderate and absolute rates remained low, with modelled probabilities of approximately 1.5–3.4% on active treatment versus 0.5% with placebo.

Overall, the findings support the use of 10 mg and 25 mg brensocatib doses in bronchiectasis, demonstrating exposure-dependent efficacy across key clinical endpoints while maintaining an acceptable safety profile.



Home-Based Pulmonary Rehabilitation Matches Functional Gains While Improving Completion Rates

RESEARCH presented at ATS 2026 explored whether home-based pulmonary rehabilitation (PR) can provide comparable benefits while improving program completion. Investigators conducted a meta-analysis of RCTs directly comparing home-based and center-based approaches.⁵

Three randomized trials were included in the analysis, evaluating a total of 396 participants with chronic respiratory diseases. The primary outcome was change in 6-minute walk distance (6MWD), a widely used measure of functional exercise capacity. Using a predefined equivalence margin of ± 30 m, the pooled analysis demonstrated virtually no difference between home-based and center-based PR, with a mean difference of -0.42 m. Statistical testing confirmed equivalence under the standard random-effects model, indicating that home-based programs produced functional improvements comparable to those achieved in supervised center-based settings.

A more conservative sensitivity analysis using the Hartung-Knapp method widened the confidence intervals, resulting in an inconclusive equivalence assessment. Nevertheless, the findings did not suggest that home-based rehabilitation was inferior, highlighting the robustness of the overall functional outcomes despite some uncertainty.

Program completion emerged as a notable advantage of home-based rehabilitation. Across the included studies, participants assigned to home-based PR were



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approximately 45% more likely to complete their program than those enrolled in center-based services. Based on pooled estimates, home-based delivery increased completion rates by nearly 27%, corresponding to a number needed to treat of approximately four patients for one additional program completion. Although substantial heterogeneity was observed between studies, the overall trend consistently favored home-based approaches.

These findings suggest that structured home-based PR, including programs supported by telehealth or remote coaching, may offer a practical solution for expanding access to rehabilitation without sacrificing functional benefit. Given the ongoing challenges surrounding PR uptake worldwide, home-based pathways could help address longstanding barriers while maintaining clinical effectiveness. Future research should focus on standardizing definitions of program completion, evaluating responder outcomes, and identifying which implementation components, such as coaching intensity, digital support, or remote monitoring, most strongly influence adherence and long-term success.

6 Music-Facilitated Digital Pulmonary Rehabilitation Improves Exercise Capacity in COPD

RESEARCH presented at ATS 2026 evaluated a novel smartphone application-based rehabilitation program combining music-guided exercise and singing training in patients with moderate-to-severe COPD.⁶

In this multicenter RCT conducted across five centers in China, 70 patients with stable COPD were assigned to one of three groups: multicomponent training (MT), rhythm-guided walking (RW), or usual care (UC). The MT program combined tempo-guided walking, singing exercises, and educational content delivered through a dedicated smartphone application, while the RW group received only the walking component. Participants in the intervention arms completed a 12-week home-based program with individualized progression.

The primary outcome was exercise capacity, assessed using the Incremental Shuttle Walking Test (ISWT). At 12 weeks, patients in the MT group achieved significantly greater improvements in walking distance compared with those receiving usual care, with a mean increase of 56.35 m. This improvement exceeded the threshold generally considered clinically meaningful, demonstrating the potential of digitally delivered, music-supported rehabilitation to enhance physical performance in COPD.

The benefits of the multicomponent intervention extended beyond exercise capacity. Compared with usual care, participants in the MT group reported significant reductions in breathlessness, as measured by the modified Medical Research Council scale, alongside improvements in health status assessed by the COPD Assessment Test. Anxiety symptoms also decreased significantly, while inspiratory capacity showed meaningful physiological improvement. Notably, the multicomponent program outperformed rhythm-guided walking alone in reducing dyspnea, suggesting that the addition of singing

training may provide benefits beyond those achieved through exercise alone.

In contrast, rhythm-guided walking by itself did not produce significant differences compared with usual care across the measured outcomes, highlighting the importance of the program's combined approach. The findings suggest that integrating music, breathing control, vocal training, and exercise into a single digital platform may create a more engaging and effective rehabilitation experience.

This study demonstrates that a music-facilitated, smartphone-based pulmonary rehabilitation program can deliver clinically meaningful improvements in exercise capacity, symptoms, and psychological wellbeing in patients with COPD. As healthcare systems increasingly explore remote and hybrid models of care, such digitally enabled interventions may offer an innovative strategy for expanding access to pulmonary rehabilitation while enhancing patient engagement and adherence. Further studies involving larger populations and longer follow-up periods will help determine the sustainability of these benefits and identify the key components driving treatment success.

“At 12 weeks, patients in the MT group achieved significantly greater improvements in walking distance compared with those receiving usual care”



Air Pollution Tied to Higher Mortality in Acute Respiratory Failure

ACUTE respiratory failure outcomes were significantly worse among critically ill patients with higher cumulative air pollution exposure, according to a large multicenter study, presented at ATS 2026.⁷



Researchers conducted a retrospective cohort study across seven academic medical centers in the USA, participating in the Common Longitudinal ICU Format (CLIF) consortium between 2018–2024. The analysis included 128,808 adults admitted to intensive care who met clinical criteria for acute respiratory failure. Residential county data were linked to annual mean satellite derived estimates of fine particulate matter (PM_{2.5}) and nitrogen dioxide (NO₂) exposure prior to admission. Census tract sociodemographic variables were also incorporated into the analysis.

The cohort had a mean age of 62±15 years and was 59% male. Non-Hispanic Black patients accounted for 32% of the study population. In hospital mortality was 16.9±1.6%, while the mean duration of mechanical ventilation was 53.4±156.5 hours. Average annual exposure levels were 7.6±1.5 µg/m³ for PM_{2.5} and 6.0±2.9 ppb for NO₂, with notable regional variation.

The findings demonstrated a consistent association between greater air pollution exposure and poorer clinical outcomes. Each 10 ppb increase in cumulative NO₂ exposure was associated with a 5% higher risk of in hospital death: (95% CI: 1.03–1.08). It was also associated with a 2% longer duration of invasive ventilation (95% CI: 1.00–1.04).

Similarly, each 10 µg/m³ increase in cumulative PM_{2.5} exposure was associated with a 9% higher risk of in hospital death (95% CI: 1.03–1.16) and a 9% higher risk of death within 30 days (95% CI: 1.02–1.17).

Further analysis using competing risk models suggested that air pollution exposure may affect the likelihood of recovery relative to death. Greater cumulative NO₂ exposure was associated with a 51% higher subdistribution hazard ratio (SHR) of death relative to recovery (SHR: 1.51; 95% CI: 1.07–2.13). Higher PM_{2.5} exposure was linked to a 2.45-fold higher SHR of death relative to recovery (SHR: 2.45; 95% CI: 1.03–5.79).

The authors concluded that cumulative air pollution exposure was consistently associated with increased time on invasive ventilation and higher mortality among critically ill patients with acute respiratory failure. These findings suggest that long-term exposure to PM_{2.5} and NO₂ may hinder recovery even within controlled intensive care environments and could be relevant to clinical decision making.



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AD109 Significantly Reduces Snoring in Obstructive Sleep Apnea

A NEW analysis of two Phase III clinical trials has shown that AD109 significantly reduced snoring frequency compared with placebo in adults with obstructive sleep apnea (OSA), offering a potential new approach to addressing one of the condition’s most common and socially disruptive symptoms.⁸ The findings suggest that, alongside improving airway obstruction, oxygenation, and disease severity, AD109 may also provide meaningful benefits for patients affected by chronic snoring.

OSA is characterized by repeated upper airway collapse during sleep, leading to disrupted breathing, reduced oxygen levels, and fragmented sleep. Snoring is one of its most recognizable symptoms and can have a substantial impact on quality of life, affecting both patients and their bed partners. Despite its prevalence, snoring is often assessed subjectively, and objective measures of treatment response remain limited.

Researchers evaluated the effect of AD109, a once-daily oral combination of aroxycbutynin, a novel antimuscarinic, and atomoxetine, a selective norepinephrine reuptake inhibitor. The analysis included data from the randomized, placebo-controlled SynAIRgy and LunAIRo Phase III trials. Snoring was measured objectively during overnight polysomnography using a tracheal piezoelectric snore sensor, with snoring defined as breathing sounds exceeding 20 dB above background breathing noise.

Among participants with available baseline and Week 26 sleep study data, 189 individuals receiving AD109 and 281 receiving placebo met the predefined criteria for inclusion. Baseline snoring frequency was similar between groups, with snoring present

during approximately 42–45% of breaths during sleep.

By Week 26, AD109 reduced the proportion of breaths associated with snoring by 22.3% (95% CI: 19.1–25.5), compared with a 10.0% reduction in the placebo group (95% CI: 7.4–12.6). This represented a significant treatment difference of –12.3% (95% CI: –16.4––8.2; $p < 0.001$). In addition, 60.8% of participants receiving AD109 achieved at least a 50% reduction in snoring frequency, compared with 32.0% of those receiving placebo ($p < 0.001$).

Sensitivity analyses using stricter definitions of snoring, based on sound thresholds exceeding 25 dB and 30 dB above background breathing noise, produced similar findings, supporting the robustness of the results.

These findings indicate that AD109 may address an important symptom burden associated with OSA while complementing its previously demonstrated benefits on airway obstruction, oxygenation, and overall disease severity. Further research may help determine how reductions in snoring translate into improvements in patient-reported outcomes and quality of life.



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Biannual Depemokimab Shows Promise in Adolescents with Asthma

BREAKTHROUGH treatment evidence is emerging for adolescents with Type 2 asthma, according to an abstract presented at ATS 2026.⁹ Asthma is a chronic inflammatory airway disease with variable airflow obstruction and symptoms including wheeze and breathlessness. Severe Type 2 asthma is associated with eosinophilic inflammation and increased exacerbation risk. Depemokimab is an ultra-long-acting monoclonal antibody targeting IL-5 with high binding affinity and an extended half-life, enabling 26-week dosing.


In Phase III SWIFT-1/-2 trials, patients with Type 2 asthma characterized by elevated blood eosinophil counts and ≥ 2 exacerbations in the previous year were included. Participants were then randomized 2:1 to depemokimab 100 mg subcutaneously or placebo every 26 weeks in addition to standard therapy. This prespecified analysis assessed adolescents aged 12–17 years. The primary endpoint was set as the annualized clinically significant exacerbation (CSE) rate over 52 weeks. A Bayesian dynamic borrowing approach incorporated adult data due to low adolescent numbers.

The pooled SWIFT-1/-2 population included 30 adolescents, 15 of whom received depemokimab, and 732 adults. Annualized CSE rate reductions were generally consistent between adolescents and adults. In adolescents, depemokimab reduced annualized CSEs by 43% versus placebo, compared with 54% in adults, showing that reduction in CSEs was consistent across adolescent and adult populations. Bayesian analysis indicated a minimum prior weight of 0.6 to achieve statistical equivalence, with consistent point estimates across borrowing scenarios. This approach incorporated a proportion of adult data to improve estimate precision given the limited adolescent sample size. Adverse event incidence was similar between adolescents and adults (73% versus 72%).

Among adolescents, two treatment-related adverse events were reported and one serious adverse event (abdominal pain),

which resolved and was not considered treatment-related. No deaths or treatment-related discontinuations were reported. Overall, adverse event rates were comparable between adolescents and adults with no study withdrawal. Findings are limited by small adolescent participants, although adult data supported extrapolation using prespecified statistical methodology. Overall, results support a favorable benefit–risk profile of depemokimab in adolescents with Type 2 asthma.

“No deaths or treatment-related discontinuations were reported”


54%
In adolescents, depemokimab reduced annualized CSEs by 43% versus placebo, compared with 54% in adults



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Acute Respiratory Distress Syndrome Phenotypes Linked to Divergent Clinical Outcomes

IDENTIFYING two distinct acute respiratory distress syndrome (ARDS) subphenotypes from routine electronic health record data could support phenotype-guided risk stratification, according to research presented at ATS 2026.¹⁰

ARDS is a life-threatening condition where fluid builds up in the lungs, impairing oxygen exchange and leading to severe respiratory failure. As a heterogeneous condition, latent phenotypes identified in clinical trial populations have rarely been reproduced in electronic health record cohorts.

Researchers analyzed data from MIMIC-IV, a freely accessible electronic health record database, to determine whether latent profile analysis could identify clinically meaningful ARDS subphenotypes and whether these groups were associated with different outcomes. The retrospective study included 24,363 ARDS admissions and used 25 routinely collected clinical variables, including demographics, vital signs, laboratory results, ventilator parameters, and key diagnoses.

The analysis identified two ARDS subphenotypes: a hypoinflammatory group (61.9%) and a hyperinflammatory group (38.1%). Patients in the hyperinflammatory group were generally younger and were more likely to be women or Black patients. They also had poorer oxygenation and greater physiologic derangement at baseline.

Patients with the hyperinflammatory phenotype experienced substantially worse outcomes. Ninety-day mortality

reached 40.8%, compared with 19.1% in the hypoinflammatory group, and mean survival time over 90 days was 11.9 days shorter in the hyperinflammatory group.

Furthermore, the hyperinflammatory phenotype was associated with greater use of advanced organ support, with patients more likely to require invasive mechanical ventilation, vasopressor therapy, renal replacement therapy, and tracheostomy.

As a retrospective analysis of electronic health record data, the study cannot determine whether the identified phenotypes directly cause differences in outcomes. However, the findings demonstrate that clinically distinct ARDS subgroups can be reproduced at scale using routinely collected data.

The researchers suggest that phenotype-guided risk stratification could eventually be incorporated into clinical decision-support systems and used to identify candidates for future phenotype-directed clinical trials. They also noted that observed differences across sex and racial groups highlight the importance of equity safeguards as such approaches are developed. Future research could potentially explore how these subphenotypes perform prospectively and whether they can help guide treatment strategies in clinical practice.

The analysis identified two ARDS subphenotypes:



A hypoinflammatory group

61.9%

and a hyperinflammatory group

38.1%

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