🌎 Congress Highlights

NEW research presented at the American Thoracic Society (ATS) International Conference, held in San Francisco, California, USA, highlights the rapid advances in respiratory health. The six featured studies provide a snapshot of the research highlights from the extensive meeting, and span a range of topics, including improved outcomes in lung transplant allocation and the long-term effects of air pollution and pediatric pulmonary conditions.
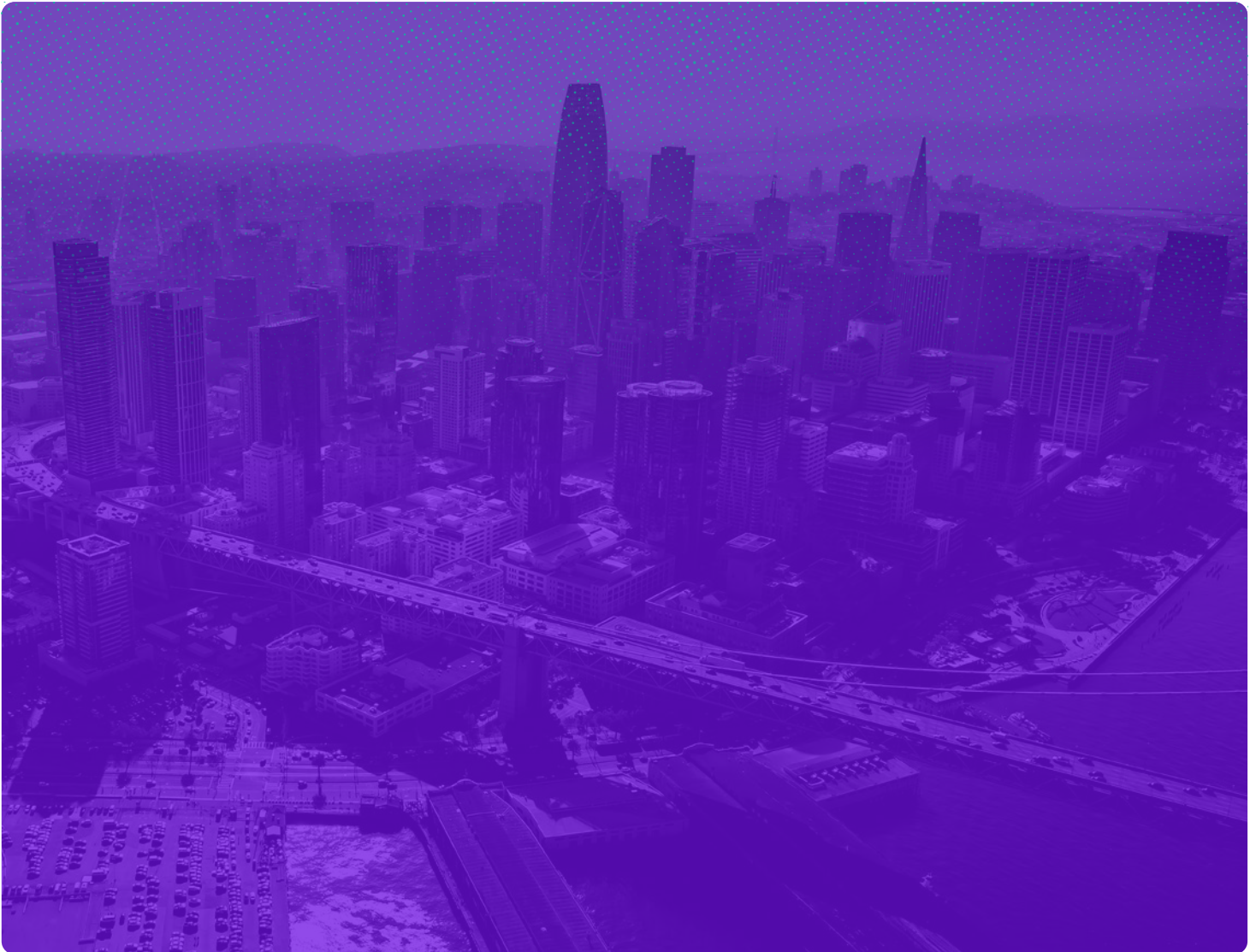
Lung Transplant Waitlist Deaths Halved Under New Allocation System

THE LATEST research presented at the ATS International Conference 2025 revealed that the Composite Allocation Score (CAS) system significantly reduced lung transplant waitlist deaths, particularly among patients who are critically ill.[1]

Lung donor allocation in the USA has undergone major changes over the past decade, transitioning from a geographically based model to one focused on medical urgency. Following a 2017 lawsuit that led to broader sharing within a 250-nautical-mile radius, the United Network for Organ Sharing (UNOS [Virginia, USA]) implemented the CAS system in March 2023. CAS combines multiple clinical and logistical factors into a single score to prioritize patients more equitably. Researchers conducted a retrospective cohort study of 24,368 patients listed for transplant since February 2015, dividing them into three eras: pre-2017 local allocation, post-2017 regional sharing, and the CAS era.

Results show that 11.2% of waitlisted patients died or were delisted in the pre-2017 era, which declined to 8.4% after the geographic expansion in 2017 and fell sharply to 4.1% following CAS implementation. Patients who were critically ill benefited most: among those in the top 5% of waitlist urgency scores, mortality or delisting dropped from 34.5% before 2017 to just 6.5% under CAS.

Adjusted models confirmed these trends, with pre- and post-2017 patients having a 3.3-fold and 2.1-fold greater risk of death or delisting compared to those in the CAS era, respectively. For the highest-risk group, the risk was up to eight times higher before CAS was introduced. Patients receiving high-flow nasal cannula oxygen at listing also saw significantly improved outcomes under CAS.

> **CAS combines multiple clinical and logistical factors into a single score to prioritize patients more equitably**

These findings confirm that prioritizing medical urgency through CAS is improving survival chances for the most vulnerable patients awaiting lung transplants. Researchers should perform further analysis to determine whether individual components of CAS are driving these improvements and how best to continue refining the system.

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Pulmonary Sarcoidosis: Methotrexate Matches Prednisone Efficacy, with Milder Side Effects

IN THE SEARCH for better-tolerated treatments for pulmonary sarcoidosis, a new study presented at the ATS International Conference 2025 found methotrexate as effective as prednisone, with a potentially more favorable side effect profile.[2]

Prednisone remains the standard first-line treatment for pulmonary sarcoidosis, but its adverse effects can significantly reduce patient quality of life. Methotrexate, a long-standing immunosuppressant, is considered to have fewer side effects, but it has not previously been studied as an initial therapy for this condition. The PREDMETH trial, a clinician- and patient-designed, randomized non-inferiority study conducted across 17 Dutch hospitals, compared the efficacy and safety of methotrexate to prednisone in treatment-naïve patients. Participants were randomized 1:1 to receive either drug, with forced vital capacity (FVC) at 24 weeks as the primary endpoint. Adverse events (AE) and patient-reported outcomes were monitored throughout.

Out of 138 enrolled patients, 70 were assigned to prednisone (with one exclusion) and 68 to methotrexate. The cohort was predominantly male (73.7%) with a mean age of 46.6 years. Baseline FVC (%) was predicted to be 79.8% (SD: 15.44) in the prednisone group and 74.8% (SD: 12.68) in the methotrexate group. After 24 weeks, methotrexate demonstrated non-inferiority, with a mean between-group difference in FVC change of –1.8% (90% CI: –4.40–0.76). Protocol adherence was high (83% prednisone, 81% methotrexate). While the total number of AEs was similar between groups, ongoing AEs at 24 weeks were notably fewer in the methotrexate arm (104 versus 171). Prednisone was more often associated with weight gain, insomnia, increased appetite, and cushingoid appearance, whereas methotrexate more frequently caused nausea, fatigue, elevated liver enzymes, abdominal discomfort, and respiratory infections.

> **While the total number of AEs was similar between groups, ongoing AEs at 24 weeks were notably fewer in the methotrexate arm**

The PREDMETH trial is the first to demonstrate that methotrexate is as effective as prednisone as an initial therapy for pulmonary sarcoidosis. The total AEs were comparable; however, their differing profiles, and the fewer persistent side effects with methotrexate, highlight its potential as a viable first-line option.

Maternal Air Pollution Exposure Alters Offspring Asthma Risk

A RECENT study, presented at the ATS International Conference 2025, has shed light on how maternal exposure to particulate air pollution may contribute to increased asthma risk in adult offspring, even when the offspring themselves are never directly exposed.[3]

The researchers focused on understanding the epigenetic mechanisms that underlie this transgenerational effect using a well-established mouse model of allergic airway disease. They exposed female mice to particulate pollution before conception and throughout pregnancy and lactation. The adult offspring of these mice displayed significantly heightened airway hyperreactivity, as confirmed by flexiVent™ (SCIREQ; Montreal, Canada) lung function testing. Interestingly, this was accompanied by a blunted lung transcriptomic response to allergen challenge.

RNA sequencing revealed the differential expression of over 2,800 genes related to pathways such as SMAD and TGFβR, regardless of maternal exposure. However, unique transcriptomic patterns emerged in offspring depending on whether their mothers had been exposed to air pollution (2,792 unique genes in controls and 374 in pollution-exposed progeny). This indicates a divergence in gene expression profiles likely shaped by the maternal environment.

Gene set enrichment analysis further showed a notable loss of pathway activity in offspring of exposed mothers. Whole-genome methylation analysis supported these findings, revealing a reduction and skew toward hypomethylation in differentially methylated DNA regions in the pollution group, particularly in intronic regions and transposons.

The findings suggest that the maternal environment alters epigenetic programming in the lungs of offspring, leading to suppressed gene expression and heightened allergic airway disease. These insights highlight the potential of targeting epigenetic mechanisms to prevent or treat asthma and related respiratory conditions rooted in prenatal environmental exposure.

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Two Distinct Recovery Paths for Individuals Impacted by Critical Illness

A NEW study, presented at the ATS International Conference 2025, has identified two distinct recovery trajectories in individuals who have experienced critical illness, shedding light on the long-term challenges faced by many patients and highlighting key risk factors for poor outcomes.[4]

Researchers analyzed data from 804 adult patients enrolled in the BRAIN-ICU and MIND-ICU prospective cohort studies, all of whom had previously been hospitalized for respiratory failure or shock. The study aimed to better understand how patients recover in the year following discharge from intensive care, with a particular focus on cognitive function and the ability to perform daily activities.

Post-intensive care syndrome is a well-documented but poorly understood condition affecting a significant proportion of patients coming from the ICU. It encompasses a constellation of long-term impairments in cognitive, physical, and psychological function. However, the patterns of recovery and factors that influence them have remained unclear.

Using advanced statistical modeling techniques, the researchers identified two classes of patients based on recovery trajectories over a 12-month period. Patients in Class 1 (620 individuals; median age: 61.5 years) experienced better cognitive recovery and fewer impairments in basic and instrumental activities of daily living. In contrast, Class 2 (184 individuals; median age: 66.0 years) demonstrated persistently worse cognitive function and increasing dependence on others for daily tasks. These

characteristics are consistent with post-intensive care syndrome.

The survival outlook also differed markedly between the two groups. At 12 months, 78.0% of Class 1 patients were still alive, compared with just 51.3% in Class 2.

The study identified older age, worse baseline cognitive function, and greater frailty at the time of ICU admission as significant predictors of Class 2 membership. Interestingly, the severity of illness and the duration of delirium during the ICU stay were not found to be associated with long-term recovery trajectory.

The authors called for the development of a predictive tool to help clinicians identify high-risk patients and explore targeted rehabilitation strategies, including cognitive, physical, and occupational therapies.

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Prospective Study Challenges Rarity of Pediatric Pulmonary Embolism

A STEP forward has been made by the BEEPER study, presented at the ATS International Conference 2025, which has offered the first prospective analysis of pulmonary embolism (PE) diagnosis in children, drawing from a large, multicenter cohort.[5]

PE in children has traditionally been viewed as a rare condition, with existing estimates suggesting it affects fewer than 1 in 100,000 children annually; however, these estimates are primarily based on administrative databases.

Conducted between 2020–2024 at 21 pediatric emergency departments across the US, BEEPER enrolled 4,103 children aged 4–17 years who presented with symptoms warranting a PE workup. Each participant was followed for 45 days, and PE diagnosis was confirmed through a rigorous adjudication process, using imaging criteria for both PE and deep vein thrombosis (DVT).

As of November 1st, 2024, adjudication was complete for 3,663 patients. Among these, 156 children (4.2%) were diagnosed with PE, with 2.1% having isolated PE, 1.1% isolated DVT, and 1.0% both PE and DVT. The mean age of children with confirmed PE was 15 years, slightly older than the overall cohort average of 14 years. Notably, 64.4% of those tested were female, and 57.7% identified as White.

Diagnostic testing showed that D-dimer was used in nearly 80% of cases. CT pulmonary angiography was performed in about one-third of patients, yielding a 10.4% positive rate. Ventilation-perfusion scans and MRI had a 16.7% positivity rate, while venous ultrasound detected DVT in 17.8% of cases.

This landmark prospective study challenges the long-held assumption of PE rarity in children, revealing rates and diagnostic patterns similar to those observed in adult populations. These findings emphasize the importance of heightened clinical awareness and refined diagnostic strategies in pediatric emergency care.

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Cilia Analysis Provides New Perspective on Chronic Neonatal Lung Injury

A STUDY presented at the ATS International Conference 2025 revealed new evidence that impaired ciliary motion may play a role in the pathophysiology of bronchopulmonary dysplasia (BPD), particularly in its more severe forms.[6]

> **The severity of BPD may be associated with altered ciliary biomechanics, which could impair pulmonary defense and contribute to disease progression**

Researchers analyzed nasal cilia dynamics in preterm infants with moderate and severe BPD using high-speed video microscopy and manual image analysis techniques. The study revealed that infants with severe BPD showed significantly reduced net angle and amplitude of ciliary beating compared to those with moderate disease, findings that may indicate disrupted mucociliary clearance in this vulnerable population.

BPD, a chronic lung condition resulting from barotrauma and oxygen toxicity in premature neonates, has traditionally been studied through the lens of lung structure and vascular involvement. However, this investigation shifts the focus toward the functional integrity of the airway epithelium, specifically the respiratory cilia essential for mucus and pathogen clearance.

Using nasal brushings from infants classified by the Jensen criteria (N=9), the team recorded 36 high-speed videos and evaluated multiple ciliary metrics, including length, angle, orientation vector, and bending index. While no significant differences were noted in ciliary length or orientation, reductions in both net angle (p=0.045) and amplitude (p=0.028) were seen in those with severe BPD. These findings suggest that the severity of BPD may be associated with altered ciliary biomechanics, which could impair pulmonary defense and contribute to disease progression.

The authors call for further research with larger cohorts and advanced imaging technologies to validate these findings and explore potential therapeutic targets aimed at improving mucociliary clearance in infants with BPD.

References

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