Study shows survival benefit of augmentation therapy for people with the genetic lung condition AATD

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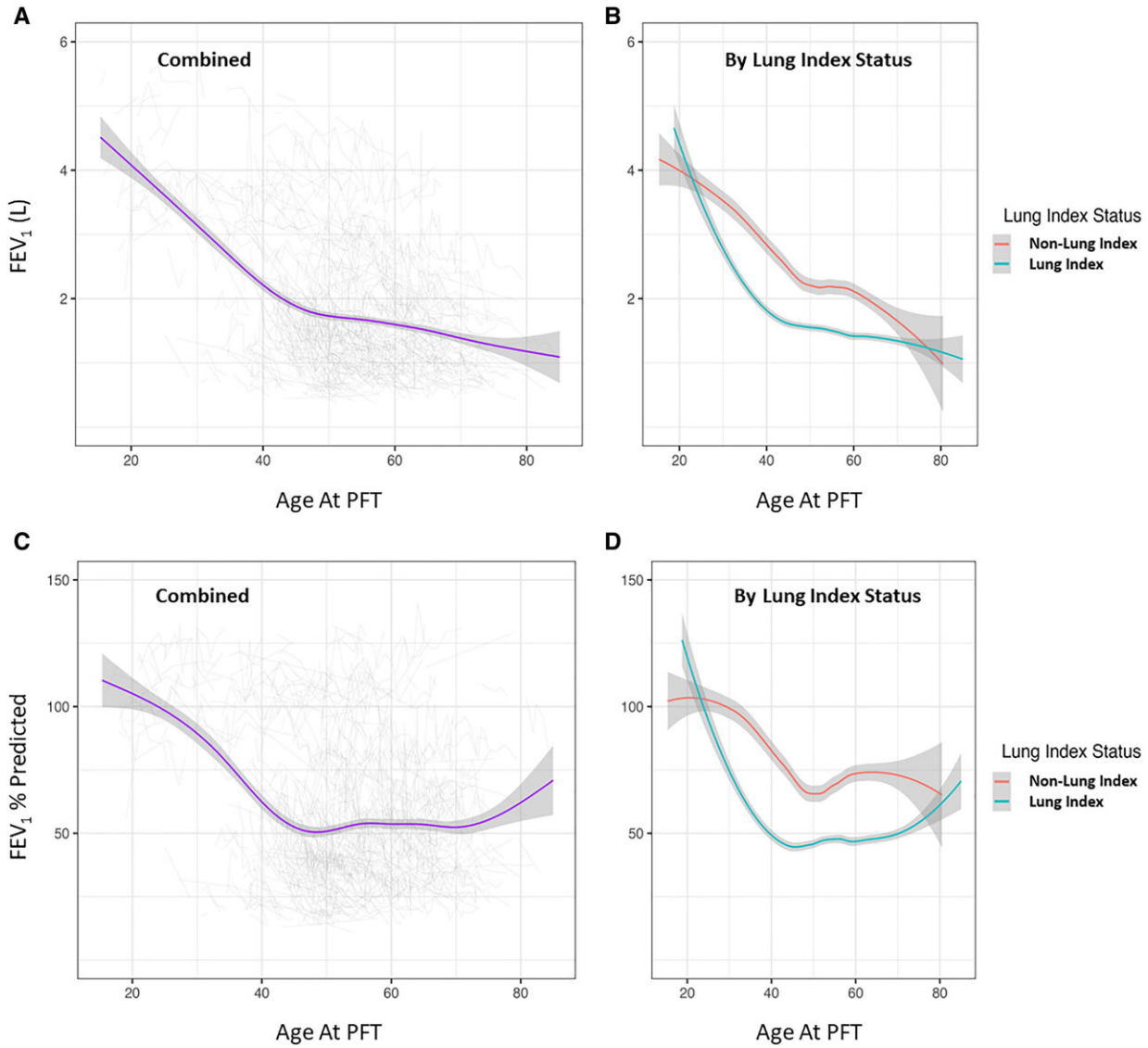

(*A*) FEV_1 (in liters; L) at age of pulmonary function testing (PFT) in all study participants. (*B*) FEV_1 (L) at age of PFT stratified by lung index status. (*C*) FEV_1 percent predicted at age of PFT in all study participants. (*D*) FEV_1 percent predicted at age of PFT stratified by lung index status. Gray shading represents 95% confidence interval of the mean. Credit: *American Journal of Respiratory and Critical Care Medicine* (2023). DOI: 10.1164/rccm.202305-0863OC

Boosting levels of a deficient protein has clear survival benefits for people with the genetic condition alpha-1 antitrypsin deficiency (AATD), according to new research led by RCSI University of Medicine and Health Sciences. The findings underscore a call to make augmentation therapy accessible to patients with AATD in Ireland and more widely across Europe.

People with severe AATD are born with very low levels of a protective protein called alpha-1 antitrypsin, and they can develop serious lung and liver disease. Previous studies of augmentation therapy in AATD showed it can slow the rate of lung damage that leads to emphysema and COPD, but they did not show a long-term benefit on survival. A weakness of these studies was that they included patients with AATD who already had serious lung disease.

The new study gathered a real-word perspective from patients with severe AATD who were not as seriously ill to start with. The researchers examined health data from 615 patients with severe AATD and the lung condition emphysema, tracking their progress over a period of about 10 years by looking at patient registries in Ireland, Switzerland and Austria.

The results, published Nov. 1 in the *American Journal of Respiratory and Critical Care Medicine*, showed that boosting levels of alpha-1 antitrypsin in these patients improved survival rates.

"We showed that by boosting this protein in people who are born with very little of it, it is possible to protect them against early death caused by lung disease," says the study's first author Dr. Daniel Fraughen, from the Irish Center for Genetic Lung Disease, based at RCSI's Department of Medicine.

The countries in the study were chosen carefully, he explains. "We looked at three countries where access to standard medical care is equal, but access to augmentation therapy is not. In Switzerland and Austria, augmentation therapy is reimbursed but in Ireland it is not," says Dr. Fraughen. "This situation allowed us to test the effects of augmentation therapy on lung function decline and mortality."

The research showed that the people with AATD in Switzerland and Austria benefitted from a clear survival advantage due to augmentation therapy that people with AATD in Ireland do not.

"This study provides real world evidence for a survival benefit to augmentation therapy for emphysema caused by severe alpha-1 antitrypsin deficiency. From the data we could see that augmentation with alpha-1 antitrypsin confers a clear survival benefit in this real-world setting," says study co-author Dr. Tomás Carroll, a Senior Lecturer at RCSI and Chief Scientist at the patient advocate organization Alpha-1 Foundation Ireland.

The study, which involved collaborators in the U.S., Austria and Switzerland and was co-authored by Geraldine Kelly, CEO of Alpha-1 Foundation Ireland, now provides evidence to support reimbursement of augmentation therapy for patients in Ireland and more widely across Europe.

"As this therapy is not currently reimbursed in Ireland or in several other European countries, this international collaboration generates further

evidence of efficacy for the only specific treatment for the lung disease caused by this condition," she said.

The findings also point to the need for early detection of AATD and to include younger and healthier patients in studies of augmentation therapy, notes study senior co-author Professor Gerry McElvaney, RCSI Professor of Medicine.

"Future studies of augmentation therapy should recruit younger patients with less severe lung disease," says Professor McElvaney. "We also show that a majority of people with AATD are being diagnosed too late, by which time severe lung disease has already occurred. Detecting people with severe AATD as early as possible and intervening before the establishment of lung disease should be the goal to improve survival. This may require newborn screening for AATD."

More information: Daniel D Fraughen et al, Augmentation Therapy for Severe Alpha-1 Antitrypsin Deficiency Improves Survival and Is Decoupled from Spirometric Decline—A Multi-National Registry Analysis, *American Journal of Respiratory and Critical Care Medicine* (2023). DOI: 10.1164/rccm.202305-0863OC

Provided by RCSI University of Medicine and Health Sciences