**Title:**

Pulmonary endpoints in clinical trials for children with cystic fibrosis under two years of age.

**Lay Title:**

Can we measure effectiveness of new cystic fibrosis treatments in improving lung health in children with cystic fibrosis aged less than 2 years of age during clinical trials conducted for the approval of new medicines?

**Authors:**

Tim Lee, Kate Hill, Daan Caudri, Pierluigi Ciet, Gwyneth Davies, Jane C Davies, Anna-Maria Dittrich, Anders Lindblad, Paul McNally, Philippe Reix, Clare Saunders, Isabelle Sermet-Gaudelus, Mirjam Stahl, Harm A.W.M. Tiddens, Hettie M. Janssens.

**Affiliations:**

Leeds Children’s Hospital, United Kingdom; European Cystic Fibrosis Society – Clinical Trial Network, Denmark; Queen’s University, Belfast, N Ireland; Erasmus MC-Sophia Children’s Hospital, University Medical Center Rotterdam, the Netherlands; Department of Radiology, Policlinico Universitario, Cagliari, Italy; UCL Great Ormond Street Institute of Child Health, London, UK; NHLI, Imperial College, London, UK; Royal Brompton and Harefield Hospitals, Guy’s and St Thomas’ Trust, London, UK; ECFS CTN Central Overreading Centre for Lung Clearance Index; Hannover Medical University, Hannover, Germany; Queen Silvia Children’s Hospital, Gothenburg, Sweden; Children’s Health Ireland, Crumlin, Dublin, Ireland; RCSI University of Medicine and Health Sciences, Dublin, Ireland; Hospices Civils de Lyon, Bron, France; UMR CNRS 5558. Equipe EMET, UCBL1. Lyon, France ; INSERM, CNRS, Institut Necker Enfants Malades, Paris, France ; Université Paris-Cité, Paris, France ; Cystic Fibrosis National Paediatric Reference Center, Hôpital Necker Enfants Malades, Paris, France; ERN-Lung CF Network, Frankfurt, Germany; Charité – Universitätsmedizin Berlin,, Germany; German Center for Lung Research (DZL), Berlin, Germany; Thirona, Nijmegen, the Netherlands.

**What was your Research Question?**

Can we reliably measure improvements in lung health in children under 2 years old with cystic fibrosis (CF) during clinical trials of new treatments?

**Why is this important?**

CF is a serious, progressive disease that begins very early in life. Starting treatment in infancy could help slow the disease and protect long-term lung health. However, before new medicines can be approved for this age group, clinical trials must show that the treatments are both safe and effective. Measuring lung health in very young children is especially difficult, so we aimed to identify practical and reliable ways to do this in clinical trials.

**What did you do?**

The European Medicines Agency asked the European Cystic Fibrosis Society Clinical Trials Network (ECFS-CTN) to provide guidance on how to assess lung health in CF clinical trials involving children under 2 years of age. ECFS-CTN formed an expert panel and reviewed the scientific evidence for different lung function tests in this age group.

**What did you find?**

A few techniques can be used to assess lung health in infants and toddlers, including:

* **Multiple-breath washout (MBW)** or lung clearance index (LCI): a measure of lung health that measures how quickly a particular gas can be cleared out of the lungs when a person is breathing normally. It requires a mask and often sedation, for this age group.
* **Chest imaging**: CT or MRI scans can show changes in lung structure but may involve sedation or radiation.
* **Airway samples for infection and inflammation**: mucus from lung lavage or sputum can be tested for signs of infection or inflammation.

While these tests can give valuable information, none are accurate or practical enough to be used as the main way to judge if a new treatment works in children under 2. The differences in test results between treated and untreated children are often too small to detect clearly, which means trials would need to be very large and long—making them difficult to run.

This creates a challenge for developing and approving treatments for this age group.

**What does this mean and reasons for caution?**

For now, clinical trials in children under 2 with CF should focus on evaluating safety, how well the medicine is tolerated, getting the correct dose, and using simpler markers of treatment effect—such as the sweat test, which reflects how well the treatment is working. Lung function tests like MBW or imaging can still be included as secondary or exploratory outcomes.

**What’s next?**

Currently, none of the discussed lung health tests are reliable enough to be the main way of showing if a treatment works in children under 2 in clinical trials to get approval for a new medicine. The differences seen would be too small, meaning trials would need to be very large and long—making them impractical. Until better tests are developed, clinical trials should focus on safety, dosing, and indirect signs of benefit, like the sweat test. Lung health tests can still be included as secondary measures to suggest possible lung benefits. Long-term follow-up studies after approval will also be important to assess how treatments affect lung health over time.

**Original manuscript citation in PubMed:**

Tim Lee et al., Journal of Cystic Fibrosis, <https://doi.org/10.1016/j.jcf.2025.06.003>