



# Cystic Fibrosis Research News

## **Title:**

Evaluating assumptions of definition-based pulmonary exacerbation endpoints in cystic fibrosis clinical trials

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## **What was your research question?**

Counting the number of pulmonary exacerbations or chest infections that happen during a clinical trial can show if a new CF drug improves health. We wanted to learn if the way that exacerbations are counted by staff in CF clinics is similar to the way that exacerbations are counted in CF clinical trials.

## **Why is this important?**

Treatments that reduce the number of CF pulmonary exacerbations can improve the health of people with CF. The ways that CF exacerbations are identified during routine care and during clinical trials are different. No one has compared these different methods to see if they give similar results. If the two ways of counting exacerbations give similar results, then results seen in clinical trials are more likely to be experienced by people with CF after trials are completed. If they give different results, we need to think about changing how we define exacerbations in CF clinical trials.

## **What did you do?**

Using information collected from an earlier one-year clinical trial of the drug ataluren completed in 2017, we studied "respiratory events" where doctors and/or patients reported problems related to their lungs or airways. We asked whether these events would have been counted as exacerbations by definitions used in previous clinical trials, and then compared those answers to whether the physician treating the patients thought those same events were exacerbations. We also looked to see how often at each event there was enough



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information, to determine if the event was an exacerbation according to clinical trial definitions.

## **What did you find?**

We studied 751 respiratory events that occurred among 244 patients during the ataluren study. Exacerbation counts using definitions from earlier clinical trials did not agree well with opinions of treating CF clinicians. More than one third of the time, exacerbations counted by clinical trial definitions were not considered to be exacerbations by clinicians, while about half of events counted as exacerbations by clinicians were not counted as exacerbations when using clinical trial definitions. About 90% of respiratory events were missing all the different information needed to use clinical trial definitions correctly.

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

Our results suggest that events counted as exacerbations in clinical trials and in the clinic are different, which could mean that how effectively a CF drug reduces exacerbations in real life may be different than what was found in clinical trials. If trial exacerbation definitions were changed to agree better with clinician opinions, then trial results might better show how drugs will work after approval. We need to be cautious because regulators will need to agree with new ways to identify exacerbations in clinical trials, and we will need to confirm that results using new definitions are correct.

## **What's next?**

Drug developers need to work with regulators to find ways of counting exacerbations in clinical trials that include opinions of both clinicians and people with CF.

## **Original manuscript citation in PubMed**

<https://pubmed.ncbi.nlm.nih.gov/32682670/>