

# Cystic Fibrosis Research News

**Title:**

INVESTIGATING THE EFFECTS OF LONG-TERM DORNASE ALFA USE ON LUNG FUNCTION USING REGISTRY DATA

**Authors:**

Newsome SJ<sup>1</sup>, Daniel RM<sup>2</sup>, Carr SB<sup>3</sup>, Bilton D<sup>4</sup> and Keogh RH<sup>1</sup>

**Affiliations:**

<sup>1</sup>Department of Medical Statistics, London School of Hygiene & Tropical Medicine, London, UK

<sup>2</sup>Division of Population Medicine, Cardiff University, Cardiff, UK

<sup>3</sup>Department of Paediatric Respiratory Medicine, Royal Brompton & Harefield NHS Foundation Trust, London, UK

<sup>4</sup>Faculty of Medicine, National Heart & Lung Institute, Imperial College London, London, UK

**What was your research question?**

What are the long-term effects of dornase alfa (DNase) use on lung function in people with cystic fibrosis (CF)? For example, what would we expect someone's lung function to be if they used DNase for five years continuously compared to if they never used DNase. We aimed to investigate this question using data from the UK CF Registry.

**Why is this important?**

DNase is an enzyme that cuts up DNA. DNA is found in the mucus in the lungs and contributes to the mucus being thick and sticky. Clinical trials have shown that using DNase improves lung function for as long as two years, but, in general, people with CF will continue to use DNase for longer than this. Therefore, it is important to estimate how DNase might affect lung function over the long-term. Ideally, we hope that DNase treatment not only improves lung function in the short-term but can also slow down the rate of lung function decline long-term.

**What did you do?**

We looked at data from 4198 people enrolled in the UK CF Registry between 2007 and 2016. The first visit for all 4198 people was during a year when they were not taking DNase. The majority of these people (57%) started taking DNase at some point during follow-up and we compared lung function measures taken when people were receiving DNase to measures taken when people were not receiving the treatment. However, on average, people who start

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to use DNase already have a lower lung function than people who are not taking it. To take this into account, we used a statistical analysis method known as 'g-estimation', which enabled us to estimate what effect DNase has had on lung function.

## What did you find?

Our results suggest that DNase improves lung function in people with lower lung function (<70 ppFEV<sub>1</sub>). In people who started DNase with a lower lung function, we observed an increase in lung function over the first year of treatment. Our findings were similar over five years: people who started treatment with a low lung function and continued to take treatment were estimated to have a higher lung function at five years than if they had never taken DNase. However, the difference between the two groups at one year was similar to the difference between the two groups at five years, suggesting that treatment did not change the rate of lung function decline.

## What does this mean and reasons for caution?

For people with lower lung function, treatment is beneficial long-term, but does not alter the underlying decline in lung function. We did not find evidence that DNase improves lung function in those who already have high lung function, perhaps because the treatment cannot further improve lung function in these people.

The statistical methods used aim to correct for any systematic differences between people using and not using DNase, however we cannot be sure whether these differences have been fully accounted for. We must interpret our results with caution, because the study is not a randomised clinical trial.

## What's next?

Our work has shown how appropriate statistical methods can estimate the long-term effects of treatments using national registries. We hope that similar work can therefore be carried out looking at other common CF treatments.

## Original manuscript citation in PubMed

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