

# Cystic Fibrosis Research News

**Title:**

Dose adjustments of Elexacaftor/Tezacaftor/Ivacaftor in response to mental health side effects in adults with cystic fibrosis

**Lay Title:**

Adjusting the dose of triple therapy (Elexacaftor/Tezacaftor/Ivacaftor) to reduce mental health side effects

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**What was your research question?**

A small number of people with cystic fibrosis (CF) on combined triple therapy, elexacaftor, tezacaftor and ivacaftor, can develop significant mental health side effects such as depression, difficulty sleeping, anxiety and mental foginess. We wanted to know if we could minimise these side effects by reducing the drug dose, using the level of chloride in a sweat test as an indirect marker of how well the drug was working.

**Why is this important?**

Triple therapy has proved life changing for many people with CF with treatment significantly reducing the number of chest infections, increase lung function and improving quality of life. In view of the clinical significance of triple therapy, every effort should be made to continue treatment while resolving or minimising any side effects.

**What did you do?**

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We report our real world experience of adjusting the dose of triple therapy to try to minimise symptoms, in people experiencing significant mental health problems. Dose adjustments took place under close medical supervision and using the level of sweat chloride to guide dose adjustments. All cases were discussed at a weekly, triple therapy multi-disciplinary meeting.

## What did you find?

Thirteen adults, of whom nine (69.2%) had previous history of mental health problems, underwent dose reduction of triple therapy with monitoring of their sweat test and lung function. Four preferred to stop treatment, and two decided to continue with full dose of treatment while starting psychological support.

Dose adjustment resulted in normal and borderline sweat chloride levels in six (46.2%) and seven (53.2%) cases respectively and the majority of individual remained clinically stable. A further dose adjustment was required in three cases. A rapid resolution or improvement in mental health adverse events occurred in 10 out of 13 cases. In the remaining three cases, symptoms only resolved after discontinuing treatment (two cases) and in one person, switching back to their original ivacaftor therapy.

## What does this mean and reasons for caution?

In a minority of subjects, triple therapy is associated with significant deterioration in mental health, which may improve by supervised dose adjustment without significantly affecting physical health. It seems that sweat chloride concentration can be used as an indirect marker of how well the drug is working to guide dose adjustment when and if required. We do not know what the long term effect of reducing dose will be and some of the emotional issues seen may have been exacerbated by the introduction of this life changing treatment as well as the COVID-19 pandemic. Dose alterations should always be supervised by the clinical team and avoided if at all possible.

## What's next?

Further studies on mental health, using standardized questionnaire are needed.

## Original manuscript citation in PubMed

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