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Cystic Fibrosis Research News

Title:
A New Path for CF Clinical Trials through the use of Historical Controls

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A New Path for CF Clinical Trials through the use of Historical Controls

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What was your research question?
We wanted to test whether new cystic fibrosis therapies, such as modulators, could be evaluated more quickly or with fewer persons. We wondered whether we could assess response to a new therapy by comparing persons taking the therapy to persons who participated in previous studies.

Why is this important?
Many research studies involve assigning some persons to receive an experimental drug and assigning others to receive no drug at all, such as a placebo. These studies can require many participants to make a definitive comparison. The number of participants needed may be increasing as pulmonary exacerbations become less frequent, due to increasing modulator use.

Instead, we wanted to try a study where most (if not all) enrolled participants receive the new therapy. This approach may reduce the number of persons needed to be studied, and may provide more of them with a potentially beneficial treatment.

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What did you do?

We considered EPIC (2004-2009) and OPTIMIZE (2014-2017), two completed studies on children with early *Pseudomonas aeruginosa* infection. The EPIC study (older) compared two types of antibiotics and two schedules for providing the antibiotics; and participants had a similar number of exacerbations no matter which treatment they received. The OPTIMIZE study (newer) added azithromycin for some participants, randomizing others to a similar treatment as was given in the older study; and those who got the azithromycin had fewer exacerbations. We combined both completed studies in several ways, taking care to consider how participants might differ, and looked again to see if azithromycin still appeared beneficial.

What did you find?

Participants in the two studies were largely alike, with those in the newer study more likely to use emerging therapies. Originally, the newer study had found that azithromycin reduced exacerbations by about half (45%). When we combined new and old studies together, and accounted for differences between participants, we found azithromycin reduced exacerbations by a similar amount (37% to 40%). The reduction was similar whether we combined all participants together, or whether we left out some (or all) of the non-azithromycin participants in the newer study. When we *did not account for differences* between participants, our findings did not match the original results.

What does this mean and reasons for caution?

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What's next?

We will continue to try and find the best approach for combining old and new data, with the goals of 1) making the best use of past studies, and 2) keeping future study participants as safe as possible. We hope this research will helps advance new therapies.

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