

Controlled Multiple Imputation:

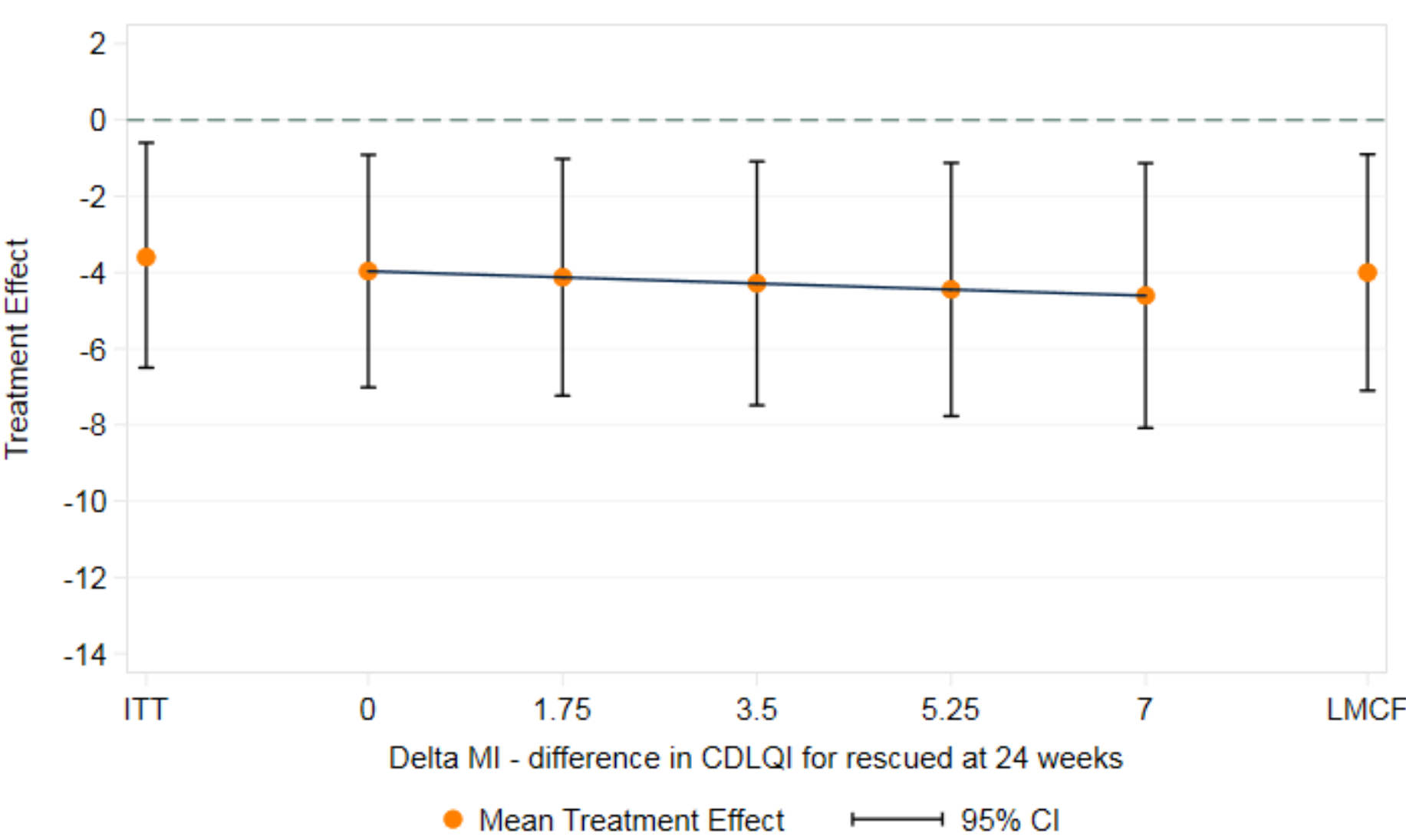
An accessible tool for estimating hypothetical estimands in clinical trials

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Introduction

- Intercurrent events in trials, such as use of rescue medication, are often unavoidable
- An Intention-to-treat analysis estimates the effect of the assigned treatment
- Estimating the treatment effect that would have been obtained if rescue medication had not been used may also be of value
- The ICH-E9 addendum discusses such ‘hypothetical’ estimands but does not provide guidance on estimation
- We demonstrate the use of controlled multiple imputation for estimating hypothetical estimands

Results



- In all analyses a clinically significant treatment effect is obtained

Methods

- An analysis of quality of life data (CDLQI) from the Atopic Dermatitis Anti-IgE Paediatric Trial
- Data post rescue is set missing and imputed using:

Controlled Multiple Imputation	Assumption
Delta-based	Rescued have mean outcome ranging from 0 to 7 points worse
Last mean carried forward	Rescued have mean of randomised arm at last time point prior to rescue

- Imputation performed using Stata command `mimix`
- Analysis model: Linear regression of 24 week CDLQI on treatment, baseline CDLQI, age and IgE
- Results are compared to an ITT analysis including all observed data post rescue initiation

Discussion

- Anti-IgE is an effective treatment for severe atopic dermatitis in the absence of rescue medication
- Controlled multiple imputation provides a flexible accessible tool for estimating hypothetical estimands
- For more information on the mimix command see: <https://journals.sagepub.com/doi/10.1177/1536867X1601600211> or scan the QR code:

