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“Missing Data in Clinical Trials: Challenges and Recent Developments”

Health authorities are increasingly concerned about the impact of missing data on clinical trial results. In 2010, both US and European regulators released or commissioned documents that emphasize the prevention of missing data, request continued data collection after study treatment discontinuation and discuss the need for a clearly defined primary objective (‘estimand’) of the trial.

Indeed, defining the primary objective of a clinical trial in the presence of non-compliance or non-adherence to the assigned treatment is crucial for the choice of design, the statistical analyses - including the handling of missing data - and the interpretation of the results.

At first glance this seems obvious, however, primary objectives stated in clinical trial protocols often fail to give a precise definition of the measure of intervention effect. In particular, the impact of missing data is frequently not taken into account when defining the intervention effect of interest. However, different ways of dealing with missing data may well imply different measures of effect.

We will review these aspects and discuss why ‘missing at random’ based analyses may be unsuitable in certain clinical trial settings. We illustrate our ideas based on a case study and share recent health authority interactions on this topic.