

Summary – ISCTM Estimands and Missing Data WG in Collaboration with the Psychedelics WG Feb 21, 2025 – ISCTM Annual Meeting

This WG meeting focused on discussing different aspects related to psychedelics clinical trials that can be reframed using the estimand framework.

Some of the discussed aspects included:

- Functional unblinding & high expectancy bias
 - Unblinding can be considered as an intercurrent event (ICE)
 - Importance of using remote raters
 - Regulatory requirement for expectancy questionnaires pre and post treatment
 - Regulatory requirement to assess degree of unblinding
 - Important to consider target population, some participants might feel hopeless and see the trial as a last resort
 - Check if expectancy decreases over treatment sessions
 - Can stratify by level of expectancy
 - Check expectancy bias before and after 2021, when interest in psychedelic treatments increased
 - Causal inference analysis can use models in which treatment effect is mediated or not through expectancy
- Treatment definition and other aspects
 - When does treatment start (e.g. with pre-treatment prep session)
 - How to define end of treatment period, relevant to when to collect data
 - Psychological support/ psychotherapy in trials is usually “standard of care” clinical practice
 - Time to re-treat can be considered to assess durability of treatment
- Supplementary estimands can capture treatment effect from different angles

Other set-ups recommended to be discussed through the estimand framework include:

- Suicidality aspects for various treatments
- Long-term trials