How to Implement the Estimand Framework…

What are we learning?

Michael O'Kelly, IQVIA

Michael O’Kelly Disclosures

- Employee of IQVIA.
- No content about products of IQVIA or of its customers
- The opinions expressed here are my own.

We are learning…

- Estimands allow us to see more clearly **the constraints of the experimental process**
  - especially when the process is over a significant amount of time.
- Take any approach, for example…
  - Treatment policy approach
  - Principal stratum approach, e.g. effect in those who would adhere
  - Composite approach

Estimand framework allows us to see (1)…

- Treatment policy approach – use outcomes of all randomized subjects
  - Encourages designs with lower treatment discontinuation.
  - Can argue: "**prespecifies the outcomes** used to assess a new treatment".
  - Can sometimes argue: "any advantage to the experimental arm (e.g. extra rescue vs. control group) is likely to be small".
  - In fact, outcomes can never be prespecified because **some subjects will withdraw from the study**.
  - **Little control over what treatment** is administered.
  - **Does not prevent an intercurrent event from making the experimental treatment "look good".**

Estimand framework allows us to see (2)…

- Principal stratum approach – e.g., use outcomes of subjects who would adhere, irrespective of treatment to which randomized
  - Who are these subjects? What are we proving in a principal stratum analysis?
    - Doctor in their surgery: "Would the patient in front of me be in the principal stratum?"
    - **Is the model of the principal stratum good enough** to provide "causal inference"?

  - **We *can* provide a stratum balanced with respect to known baseline predictors of, say, adherence**

Estimand framework allows us to see (3)…

- Composite approach – impose penalty on a treatment group when an event judged unfavourable occurs
  - How satisfactory is the preplanned penalty?
  - Can be used to **prevent events from advantaging the experimental arm**.
  - **How real for the clinician is the resulting penalised estimate** of treatment effect?