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Estimands A multi- disciplinary partnership

 NOVARTIS

Framework to reimagine study designs and analyses through
Promotion of **E**stimand **T**hinking

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Disclaimer

The views and opinions expressed in this talk are those of the individual presenter and should not be construed to represent Novartis position

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Estimands implementation

A multi-disciplinary partnership

- 1. Challenges in the adoption of estimands beyond the statistical community**
- 2. Clinician's perspective**
- 3. Novartis experience – PoET – Promotion of Estimand Thinking**

Why do we still talk about estimands?

Adopting estimands beyond the stats community was and is challenging

-  **Estimand**
Technical term
-  **Language**
Takes time
-  **Rooted traditions**
Change takes time
-  **ICE**
Key topic with regulators
-  **Too far**
Too complex, too long
-  **Estimation**
Technical complexity
-  **Consistency**
Wanted & not possible
-  **Reporting**
Room for improvement



When to think about estimands?

- 1. My story – new indication / no guidelines, short course of treatment (1-2 wk), registrational endpoint at 6 months,**
- 2. Curiosity: opportunity to experiment in phase 2a, learn and consolidate estimand for phase 3**
- 3. ICE - importance to understand what may happen to patients over 6M**
 - Compliance – treatment policy, because duration of treatment needed to achieve patient cure was unknown (at the design of study ph2a study)
 - Clear distinction between disease-related symptoms (efficacy endpoint) vs disease-unrelated events (e.g. confounding symptoms from acute infections)
- 4. Clear distinction from ICE vs missing data**

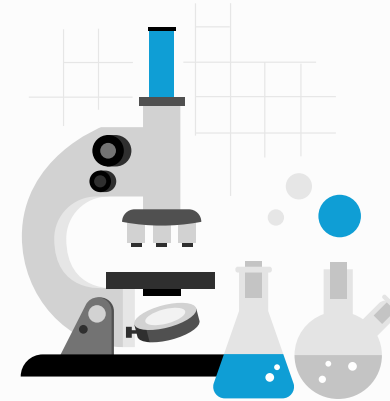
Estimate seen through Clinicians' eyes



Estimate



Laboratory result



Attributes: numerical value, units, reference range

Context: It depends on population (age, race, gender, region), analytical method, etc.

Clinician's perspective - Learnings



Solid understanding of patients' & investigators decisions is key:

- Same ICE (e.g. patients interrupting study medication) may have different meaning,
 - ICE should be interpreted in the context of **the specific disease and also health care system**, including considering alternate therapeutic options
 - Situational flexibility and transparent communication on the rationale & method chosen
- **ITT analyses (treatment policy strategy) as a base case may be an over-simplification of the clinical reality and complexity**

Clinician's perspective – reflection points




Difficulties in adoption: technical language, limited familiarity with statistical methods


- Technical language/jargon – statistical “literacy” – requires “translators”
 - Inconsistent definitions, inconsistent strategies for handling these events can bias treatment effect estimates and complicate cross-trial comparisons.
 - Best practices, statistical methods for estimation are still evolving
- Estimands enable deeper insights within a clearly defined clinical context (disease, condition, and health care system), leading to a more granular (and hopefully) more meaningful assessment of a novel medicine's value
- **Getting the estimand right matters because :**
- **allows to align study objective, data capture and analysis AND**
 - **ensures transparent & consistent communication among stakeholders - sponsor, clinical community, regulators, HTA.**


Promotion of Estimand Thinking (PoET) at Novartis


Cross-functional initiative launched in 2019 and now co-led by Statistics and Clinical to build awareness, education, and implementation of estimand thinking.


 **Templates**
Protocol, SAP, report, standard outputs


 **Trainings**
Education, on-demand and classroom


 **Knowledge Hub**
SharePoint: info, material, case studies

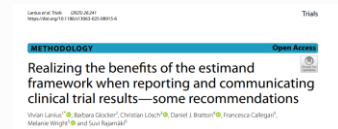
 **Estimand Clinic**
... and disease area ambassadors

 **Clinical Question**
Guidance how to write the Clinical Q of Interest

 **Estimation**
Treatment policy estimation guide

 **Seminars**
Journal club and learning series

 **Reporting**
External engagement via EIWG, publ. & webinar



Goal: Fit-for-purpose Estimands

Objectives

- Drive fit-for-purpose estimands and execution
- Estimand thinking as a default mindset
- Strengthen cross-functional ownership

Actions

- Awareness & knowledge through Trainings including Sci Rev Board
- State-of-the-Art perspectives through Seminars & Journal Club
- Further enhance reporting and communication

Thank you