The application of the estimand framework: A Neuroscience perspective

Joint seminar of EFSPi and BBS
Outline of today

13:00-13:10 Welcome. Introduction to the estimand framework
   Hans Ulrich Burger, BBS president

13:10-13:30 Outline of an estimand strategy in MS
   Nikolaos Sfikas, Novartis

13:30-13:50 Outline of an estimand proposal in migraine prevention and neuropathic pain
   Mette Krog Josiassen, Lundbeck and Peter Quarg, Novartis

13:50-14:10 Using the Estimand Framework to address challenges in AD clinical trial with a closer look at the hypothetical strategy
   Paul Delmar, Hoffmann-La Roche AG

14:10-14:30 Estimands in Huntington’s disease
   Carrie Li, Hoffmann-La Roche AG

14:30-14:45 Break

14:45-15:05 Impact of Covid-19 on studies in Neuroscience
   Andrew Hartley, PPDI

15:05-15:45 Regulatory aspects of the estimand framework: Clinical and statistical perspectives
   Joel Raffel, MHRA and Khadija Rantell, MHRA

15:45-16:30 Panel discussion including all speakers and Anja Schiel, Norwegian agency and Chair of Scientific advise working party SAWP

16:30 End of the meeting
ICH E9 (R1) addendum

Estimand Framework
The estimand framework is a multidimensional concept used to align planning, design, conduct, analysis, and interpretation of a clinical trial

Principles of the framework
The estimand framework attributes

Always keep in mind the Scientific Questions of interest
# Estimand attributes definitions

<table>
<thead>
<tr>
<th><strong>Population</strong></th>
<th>Underlying study population suitable for the targeted question</th>
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<tr>
<td><strong>Treatment</strong></td>
<td>e.g. patients will be randomised to receive either test or placebo, plus any existing stable medication.</td>
</tr>
<tr>
<td><strong>Variable or endpoint</strong></td>
<td>The variable measured for each patient that is required to address the clinical question e.g. overall response, progression free survival</td>
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<tr>
<td><strong>Intercurrent events</strong></td>
<td>Events occurring after treatment initiation that affect the interpretation of measurements associated with the clinical question e.g. discontinuation from treatment due to adverse events, or death, use of rescue medication</td>
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<tr>
<td><strong>Population summary measures</strong></td>
<td>Provides the basis for comparison between treatment conditions, e.g. mean change from baseline, proportion of responders.</td>
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Strategies for handling post-randomisation events

<table>
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<tr>
<th>Treatment policy strategy</th>
<th>Hypothetical strategy</th>
<th>Composite variable strategy</th>
<th>While on treatment strategy</th>
<th>Principal stratum strategy</th>
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<tr>
<td>The occurrence of the intercurrent effect <strong>is irrelevant</strong> for the evaluation of the treatment effect and can be ignored</td>
<td>Evaluation of the treatment effect in the hypothetical scenario in which the intercurrent event does not occur</td>
<td>Intercurrent event in itself is <strong>informative about patient’s outcome</strong> and is therefore incorporated into the definition of the variable</td>
<td>For this strategy, response to treatment prior to the occurrence of the intercurrent event is of interest</td>
<td>Target population to be the “principal stratum” in which an intercurrent event would (not) occur</td>
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Some house keeping

• Keep yourself muted and do not switch on the camera to save bandwidth

• Use the Chat to pose questions

• There should be time for one questions for clarification after each talk. Content discussion should take place at the end in the panel discussion

• We have a 15 min break. For that we opened two more lines that we can meet in smaller chats. Speakers and panelist will also be available there

• How to do this?
  • Get out of this WebEx and join the one you like
  • Get out there after 15 min to join the plenum again
  • Hope this will be a more entertaining break
  • Of course you can also take a proper break
312 participants by country
Profession of participants

Count of Background

- Regulatory: 4.5%
- Statistics, Clinical: 2.3%
- Statistics, Regulatory: 1.0%
- Clinical: 10.4%
- Statistics: 77.0%
Institutional backgrounds of participants

Count of Type of institution

- Regulator: 1.6%
- Academia: 7.0%
- CRO: 12.4%
- Pharma, Biotech: 1.0%
- Pharma: 75.2%