21st Annual Scientific Meeting

Estimands and Missing Data Working Group

Co-Chairs:
Elena Polverejan, PhD
Lorenzo Guizzaro, MD, PhD

Disclosures

- Elena Polverejan, PhD is an employee of Johnson & Johnson Innovative Medicine

- Lorenzo Guizarro, MD, PhD is an employee off Office for Therapies for Neurological and Psychiatric Disorders, European Medicines Agency

Outline

- Introductions
- Background on previous work and current progress of this working group (ISCTM Estimand WG)
- Update on collaboration with the Psychedelics WG
- Discussion

ISCTM Estimands and Missing Data WG

Initial Main Objective: Develop an approach to the process of applying the estimand framework that is relevant to many types of studies across clinical areas and illustrate the approach with examples of specific Central Nervous System (CNS) studies.

Members:

Clinical, Statistical, FDA/EMA Regulatory

First Output

Published paper: https://link.springer.com/article/10.1007/s43441-023-00524-2

Published Paper

Acknowledgements

The authors would like to thank Zimri S. Yaseen, MD (FDA) and Lorenzo Guizzaro, MD, PhD (EMA) for significant contributions to this paper.

Paper available open access due to ISCTM sponsorship

Collaboration with the ISCTM Psychedelics WG

Untangling the specific methodological issues of psychedelics' trials using the estimand framework:

- Potential for functional unblinding
- High expectancy bias
- Lack of appropriate comparator
- Use of psychological support/ psychotherapy along with study drug
- Intermittent (few) treatment vs daily dosing, including implications for demonstrating durability of effect and long-term study designs

Estimand Related Topics of Interest?

Back-Up

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

ADDENDUM ON ESTIMANDS AND SENSITIVITY ANALYSIS IN CLINICAL TRIALS

TO THE GUIDELINE ON STATISTICAL PRINCIPLES FOR CLINICAL TRIALS

E9(R1)

Final version

Adopted on 20 November 2019

https://database.ich.org/sites/default/files/E9-R1_Step4_Guideline_2019_1203.pdf

Implementation status:

ANMAT, Argentina - Not yet implemented;

ANVISA, Brazil - In the process of implementation; Date: 1 December 2023;

COFEPRIS, Mexico - Not yet implemented;

EC, Europe - Implemented; Date: 30 July 2020; Reference: EMA/CHMP/ICH/436221/2017

EDA, Egypt - Implemented; Date: 1 January 2019; Reference: Regulatory Guide for mechanisms, procedures and rules of implementing the Decree of Egyptian Drug Authority No.343 of 2021

FDA, United States - Implemented; Date: 11 May 2021; Reference: FDA, United States website

HSA, Singapore - Implemented; Date: 1 November 2019; Reference: HSA, Singapore webpage: Guidance documents for clinical trials

Health Canada, Canada - Implemented; Date: 21 July 2020; Reference: File #: 20-109237-45

JFDA, Jordan - Not yet implemented;

MFDS, Republic of Korea - Implemented; Date: 15 December 2023; Reference: Guideline on the Estimands and Sensitivity Analysis in Clinical Trials [Guideline-1335-01]

MHLW/PMDA, Japan - Implemented; Date: 20 June 2024; Reference: PSB/PED Notification No. 0620-1

MHRA, UK - Implemented; Date: 1 July 2020;

NMPA, China - Implemented; Date: 25 January 2022; Reference: NMPA, China Announcement No. 16 (2021)

SFDA, Saudi Arabia - Implemented; Date: 10 August 2023;

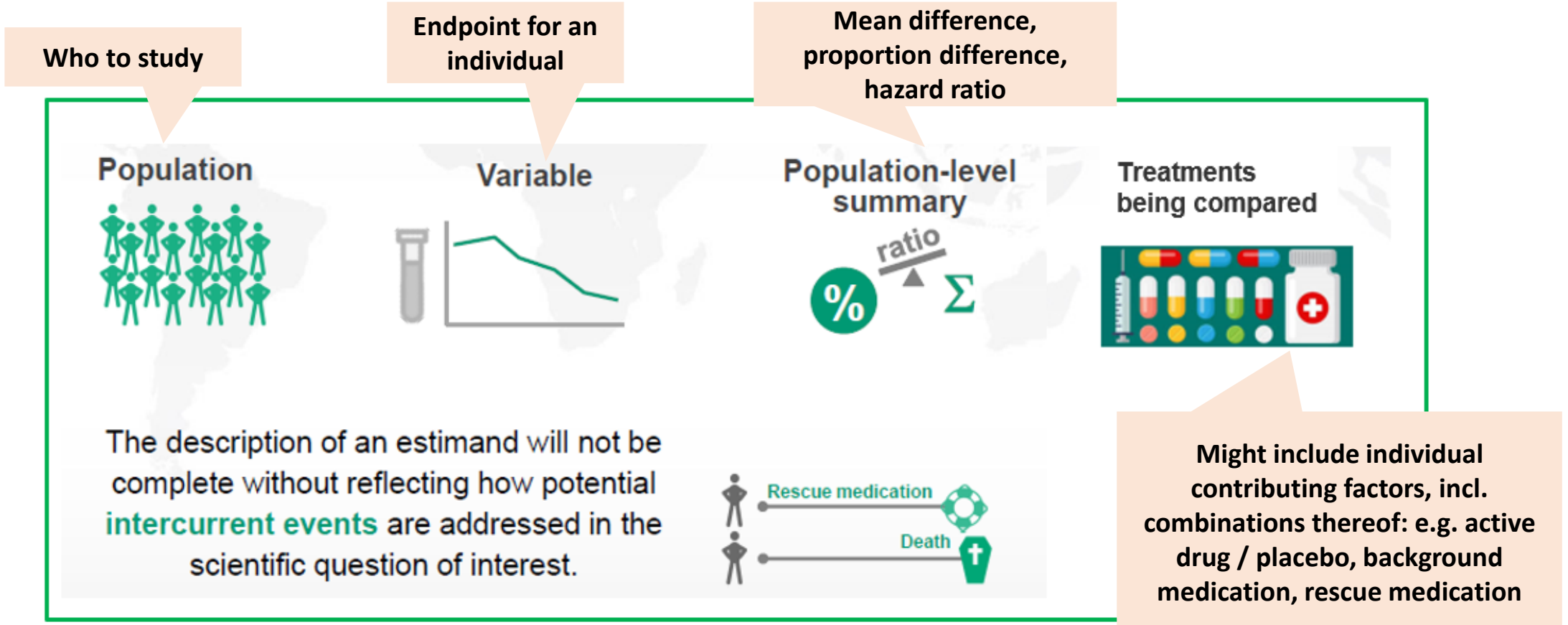
Swissmedic, Switzerland - Implemented; Date: 30 November 2019;

TFDA, Chinese Taipei - Implemented; Date: 9 February 2021; Reference: Updated-Announcement for ICH Guidelines Recognition List

TITCK, Türkiye - Not yet implemented;

Estimand - Five Attributes

An estimand is a precise description of the treatment effect reflecting the clinical question posed by a given clinical trial objective.



ISCTM WG
Recommended Steps in Applying the Estimand Framework

- Identify the stakeholder(s) for whom the estimand is being defined
- State decision(s) to be made by each stakeholder
- Define objective(s)
- Under each objective supporting main decision making:
  - Formulate the clinical question of interest:
    - Consider the clinical context
    - Consider potential intercurrent events (ICEs) and how they relate to the question
  - Define the corresponding estimand
  - Justify the utility of the selected question and corresponding estimand to the specific stakeholder(s).