# Estimands in Safety Analytics

PHUSE Safety Analytics Education Working Group in cooperation with EIWG

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## Problem Statement

The importance of clearly defined safety estimands is not widely recognised and has not been effectively communicated to safety scientists and the broader research community.

## Objective

To get a better understanding /consistent application of the estimand framework in the analysis of safety data. This would drive clarity on both the specific question that an analysis addresses, as well as the associated outcome of the analysis.

## Aim

To create a modular safety education platform (Videos, Slides, and Webinars) for a cross-functional (safety scientists, clinicians, statisticians) audience together with an annotated bibliography of estimands in safety analytics. A long-term plan is to write a white paper.

**It's to have a one stop place where everything is combined.**

### *1. Fundamentals of Estimands in Safety Analytics*

***A. Basic Concepts***

- ***Define*** *what an estimand is and* ***explain*** *its importance in clinical research, referencing ICH E9(R1).*
- ***Articulate*** *the motivation behind using estimands in clinical trials, especially for safety.*
- ***Distinguish*** *between an estimand, an estimator, and an estimate.*
- ***Describe*** *basic concepts relevant to estimands using relatable analogies.*

***B. Application in Safety***

- ***Differentiate*** *between efficacy and safety objectives in clinical trials and explain how this impacts the estimand definition.*
- ***Describe*** *typical questions asked in safety analyses and how they influence the choice of estimands.*
- ***List*** *key questions typically asked in safety analysis and* ***explain*** *how estimands help answer them.*
- ***List*** *typical safety endpoints and* ***explain*** *how they influence the choice of estimands.*

### *2. Managing Intercurrent Events (ICEs)*

- ***Define*** *intercurrent events and identify common examples in safety studies (e.g. rescue medication, treatment discontinuation).*
- ***Compare and contrast*** *various ICE handling strategies (e.g., treatment policy, hypothetical, composite).*
- ***Explain*** *why multiple estimands may be needed to reflect different clinical questions.*
- ***Match*** *appropriate ICE handling strategies to specific clinical questions or trial contexts.*

### *3. From Estimands to Estimators*

- ***Explain*** *the relationship between an estimand and the statistical estimator used to analyze it.*
- ***Describe*** *the implications of various ICE handling strategies on how these events are handled in the analysis*
- ***Identify*** *key estimators used in safety analysis (e.g., incidence proportion, EAIR, 1-KM, AJE) and* ***describe*** *the advantages and disadvantages of each*
- ***Evaluate*** *which estimators are appropriate based on how ICEs are handled.*
- ***Demonstrate*** *how to align the choice of estimator with the defined estimand in a given context.*

### *4. Communication & Practical Implementation*

- ***Write*** *clear and well-structured estimand statements for safety objectives.*
- ***Recognize*** *common pitfalls in defining or applying estimands and* ***suggest*** *ways to avoid them.*
- ***Apply*** *regulatory and industry best practices in estimand formulation and analysis.*
- ***Critically assess*** *estimand statements in real-world examples and* ***evaluate*** *whether the analysis answers the question posed.*
- ***Effectively communicate*** *estimand-related concepts to cross-functional stakeholders, including non-technical audiences like safety scientists.*
- ***Explain*** *the role of high-quality data collection in supporting robust estimand-based analysis.*