EFSPI Stats Leaders Meeting

Innovative clinical trial methodologies and their adoption - Priorities and Opportunities

EFSPI statistical methodology leaders

May, 13th 2025 - Copenhagen

EFPSI Stats Methods Leaders – Since Q4 2023

webpage

Achievements

- Forming of team.
- LinkedIn and poster presentations at different conferences (PSI, RISW, EFSPI).
- 2 F2F meetings so far.
- Active participations in EMA workshops:
  - ACT EU Methodology workshop in Nov 2023
  - EMA MWP workshop in June 2024
- Fostering thinking about invention, innovation, adoption and impact (podcast, round tables, panel discussions, presentations, webinar)
- Creating links and collaborations with EFSPI Stats Leaders, EFPIA, EMA
- Identification of priorities for fit-for-purpose clinical trial methodologies – collaboration with EFPIA

Why are we here today?

- Present EFSPI Statistical Methodology Leaders **list of priority topics** and **WHY** we chose those.
- Define list of **tangible actions** how EFSPI Statistical Leaders can support these priorities (based on pre-meeting survey).
- Seek your input on how our group can be (even more) **useful** for our community and you.

Priority topics

1. Application of Bayesian methods in drug development.
2. Covariate adjustment.
3. A framework to appraise quantitative methods and their underlying assumptions building on ICH M15.
4. Specific topics related to estimands.

Defined through:

- majority vote in the group,
- regulatory landscape,
- biggest need for interaction with regulators and / or commercialization.

Why did we chose these topics?

Application of Bayesian methods in drug development

- FDA, EMA, NMPA, (ICH?) are all working on guidance documents.
- ICH E20 working group discussions around ‘Bayesian Statistics’ seem to have been challenging
- Bayesian methods are valuable in various drug development settings:
  - predict unobserved data; stabilize parameter estimation; borrowing trial external data
  - Potentially easier interpretability of results
- What arguments, whether statistical or clinical, are needed to justify the use of Bayesian statistics for inference in confirmatory trials (beyond paediatric trials or rare diseases)?
- If strict T1E control is impossible: what are considerations for deviating from minimising bias / maximum type I error rate control in a confirmatory setting?

Covariate adjustment

- Adjusting for prognostic covariates can increase the power of RCTs but efficiency gains are often not realized
- Some technical questions still unsolved
- EMA workplan rather narrow – plan is to initiate discussion on further open questions

A framework to appraise quantitative methods and their underlying assumptions building on ICH M15

- Inferences for a trial where we depart from a “vanilla RCT approach” requires assumptions
  - NPH, leveraging trial-external data, hypothetical estimands, principal stratification, …
- Regulatory reluctance to assumptions
- Currently scenario-specific frameworks are available to enable understanding and assessment of assumptions, e.g. MIDD credibility framework (see ICH M15)
- Can we develop an overarching framework? Could the MIDD credibility framework serve as basis?

Estimands

While the estimand framework has allowed our community to transparently discuss scientific questions of interest in view of intercurrent events, some important questions remain:

- Do we approve a drug or a treatment strategy?
- What influences the choice of treatment-policy estimands in most situations?
- What are best practices when testing and estimating treatment-policy estimands?
- How can we leverage designs to fully reap the potential of the estimand framework?
- Best practices for defining estimands in the presence of terminal events (+ estimation strategy)

Your task for the breakouts

- Collate a list of concrete actions YOU can take to help advance / commercialize these four topics, within your company and in our ecosystem at large
- Discuss where our two groups can intensify collaboration / support each other

Summary of concrete actions

Action	Target audience	Responsible	Deadline

How can Methods leaders better support Stats leaders?

How can Stats leaders better support Methods leaders?

Session 2 Breakout Groups

Group 1: 00-35

- Lucy De Costa
- Mikala Fiig Jarner
- Florence Casset-semanaz
- Anna Huusom
- Janice Branson (P)
- Torsten Westermeier (L)
- Farzaneh Safavimanesh
- David Wright

Group 2: 00-24

- Simon Cleall
- Pantelis Vlachos
- Jennifer Visser-Rogers
- Simon Wilcock
- Jenny Devenport (L)
- Richardus Vonk (P)
- Frank Langer
- Emmanual Zuber
- Signe Møgelmose
- Bjarke Klein

Group 3: 00-39

- Rene Kubiak
- Lilla Di Scala (P)
- Guillaume Desachy
- Julia Igel
- Shahrul Mt-Isa (L)
- Josephine Wolfram
- Aaron Mitchell
- Aksel Kaastrup
- Rene dePont Christensen

Group 4: 00-42

- Estelle lambert (P)
- Per Soerensen (L)
- Kate Peacock
- Simon Wilcock
- Kyle Raymond
- Chrissie Fletcher
- Julie Funch
- Christian Bjerregård
- Emma Jones (V)