Historical Data
A PSI / EFSPI Special Interest Group

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EFSPI EUROPEAN FEDERATION OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY
Representing Statistical Associations in Europe

SIG purpose and activities

- Scientific cross-industry exchange forum with 30+ statisticians from 15+ companies
- How to incorporate historical / external data into the design and analysis of clinical trials?

Collaborate with experts to refine and extend available methods

Review of methods, data sources and case studies

Interact with regulators to understand their requirements

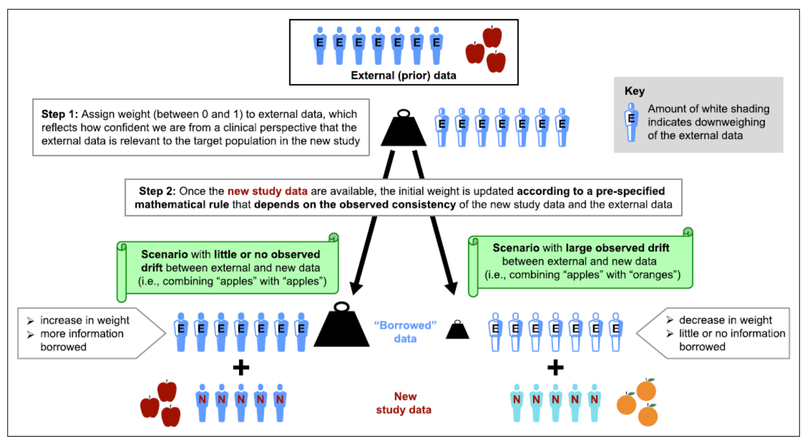
SIG activities

Provide trainings, workshops and talks

Promote good practice through templates

Bayesian dynamic borrowing (BDB)

- Borrow from existing data to reduce the sample size or increase the power of a new study
- Select relevant data from historical clinical trials / other sources
- Generate prior information about control arm or treatment difference
- Bayesian analysis: update information with new study data
- Robust analysis: Dynamically down-weight historical data in case of prior – data conflict (drift)



Edwards et al. (2024): Ther Innov Regul Sci 58:1-10

Metrics for BDB: beyond type I error

- The more prior information is available, the higher the maximum type I error probability (T1E) in BDB
- No power gains possible under max. T1E control (Kopp-Schneider et al. 2020)

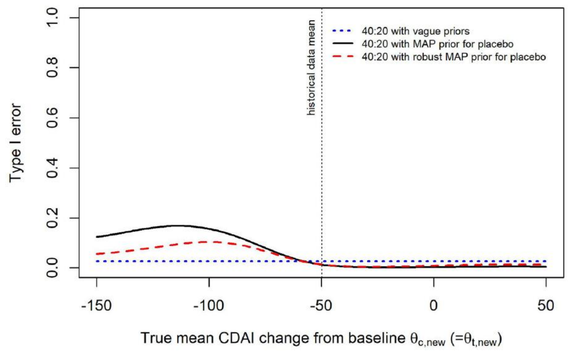
Best et al. (2025) propose to go beyond classical T1E and distinguish two cases:

1) borrowing of historical data on control arm **vs.**

2) borrowing of historical data on treatment difference.

Case 1):

- T1E as a function of drift or prior-data conflict (difference historical and new data)
- Pronounced T1E inflation may occur in region of low biological plausibility
- True drift unknown: use average T1E with respect to a design prior to reflect probability weighted error
- Average T1E controlled if design prior = analysis prior



More details in: *Best et al. (2025)*

Collaboration with EFSPI Methods Leaders for EMA workshop Bayes

- Historical Data SIG substantially contributed to EMA workshop on the use of Bayesian statistics in clinical development (17 June 2025)
- Engage with EMA on when the use of Bayesian statistics is most appropriate
- Feedback will be considered in a future reflection paper
- 6 industry presentations showcasing broad spectrum of Bayesian use cases throughout clinical development (4 of which driven by or with SIG members involved)

Bayesian methods without borrowing in ultrarare diseases

Bayesian modelling to facilitate interim decision making

Bayesian borrowing for pediatric extrapolation

Leveraging information for a key secondary endpoint across adjacent populations

Bayesian shrinkage for routine estimation of subgroup effects

ICH M15 for Bayesian modelling

EMA qualification request

- Limited regulatory guidance and acceptability of historical data borrowing so far
- Case-by-case discussions on methodology
- No widely accepted framework for evaluation of BDB designs
- Interest to use BDB generally beyond hybrid control arms or pediatric extrapolation if suitable historical data exists
- SIG approached EMA innovation task force (ITF) in 2021
- Based on ITF recommendation, SIG prepared a proposal for BDB using the robust meta-analytic prior methodology:
  - Statistical approach for confirmatory RCT analysis
  - Framework to evaluate & report BDB designs
- Formal request for qualification of BDB submitted in 2024 – ongoing process

Joint continuous learning & exchange

- One important element of our monthly meetings is joint continuous learning and exchange via presentations on SIG-related topics by SIG members or external speakers.
- In the past year (since Sep 2024) we had on the agenda:
  - Implementing Bayesian augmented control designs into business practice (SIG member)
  - Investigating the impact of data monitoring committee recommendations on the probability of trial success (external: Luca Rondano)
  - Sharing experiences discussing Bayesian topics with cardiovascular KOLs (SIG member)
  - Pre-posterior distributions in drug development and their properties (external: Andy Grieve)
  - Practicalities of longitudinal models with informative priors (external: Christian Stock)
  - Sharing experiences with building an inhouse tool to support Bayesian (internal) decision making (SIG member)

Would **YOU** like to be our next external speaker? Then reach out to Monika Jelizarow: Monika.Jelizarow@ucb.com

On our future agenda

In our monthly discussions throughout the past year two topics have repeatedly come up which we are planning to invest more thought into in the near future:

- Communicating Bayesian concepts to non-statisticians: what is needed to get ideas across successfully?
- Wouldn't it be great to have open source software that allows the community to put the content of the EMA qualification request into action? We think so too.

Where you can meet us (face-to-face)

Our SIG members are regularly attending & contributing to statistics conferences, e.g.

- PSI annual meeting
- PSI webinars
- ISCB
- EFSPI Regulatory Statistics workshop
- ASA Biop Regulatory-Industry workshop
- Bayes Pharma (BAYES2025 in Leiden, NL, 10-12 Oct)
- and more.

Get in contact

For more information and materials check out our website:

Interested to join us? Get in touch with the SIG leads Nicky Best nicky.x.best@gsk.com and Simon Wandel simon.wandel@novartis.com