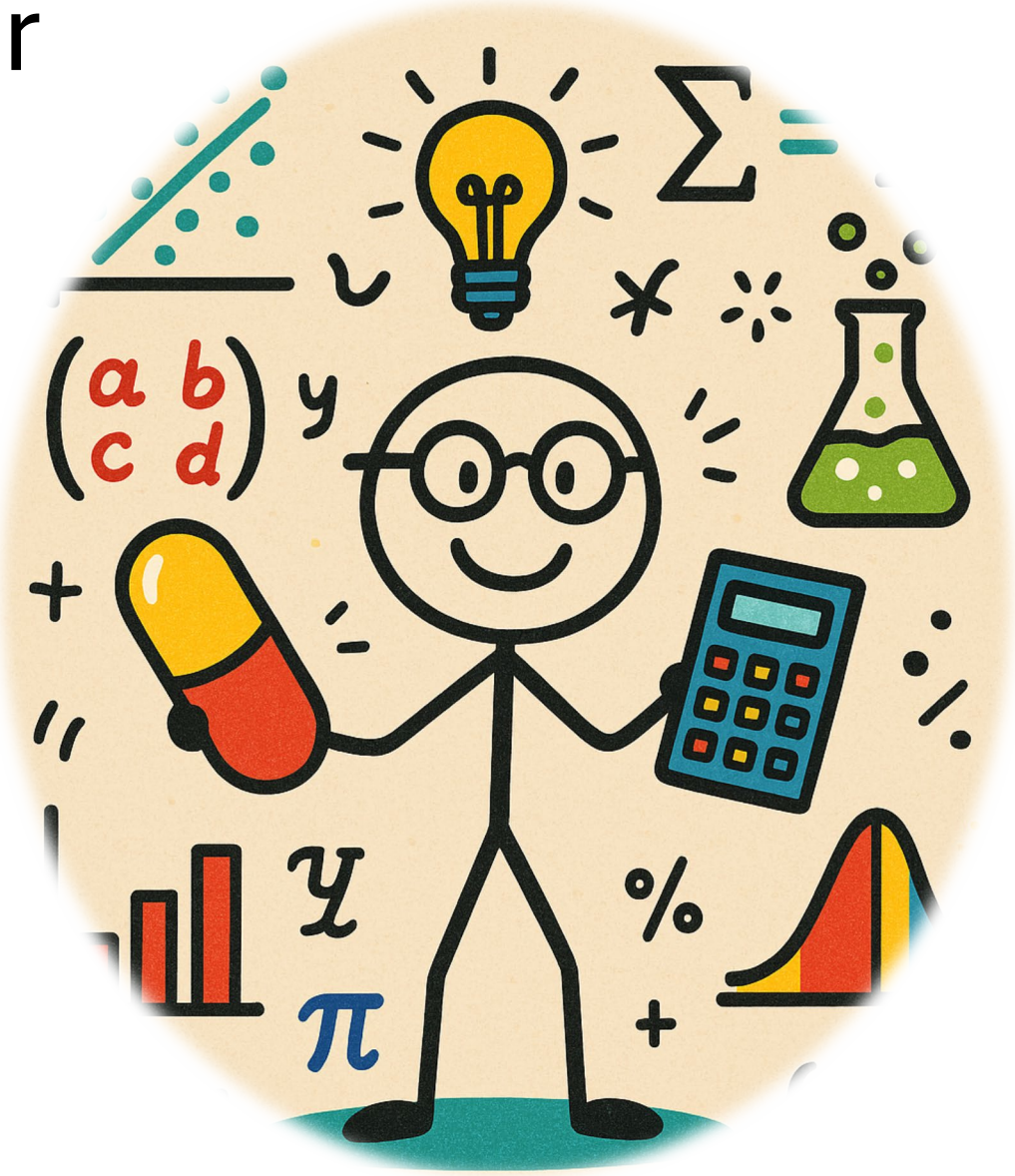
Strategic Priorities in Pharmaceutical Statistics - A Quantitative Drug Developer's Perspective

Mouna Akacha, Cornelia Kunz, Kaspar Rufibach
(On behalf of the EFSPI Statistical Methodology Leaders)

10th EFSPI Regulatory Statistics Workshop
10th September 2025 – Basel, Switzerland

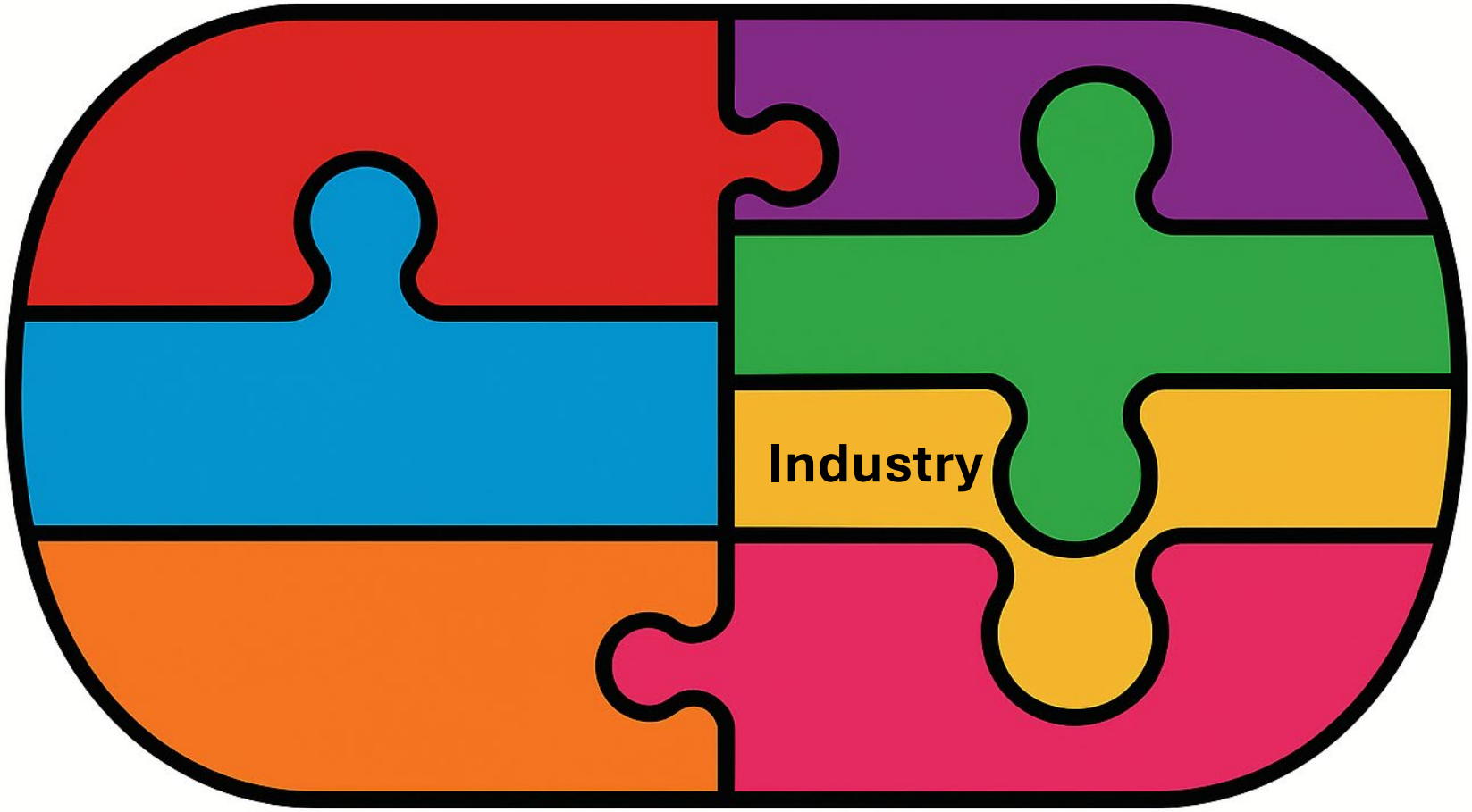
Quantitative drug developer

- Enable evidence-based medicine
- Facilitate faster, ethical and safe access to treatments
- Innovate for impact
- Collaborate for meaningful outcome



Quantitative drug developer in industry

We are just a small piece of the puzzle



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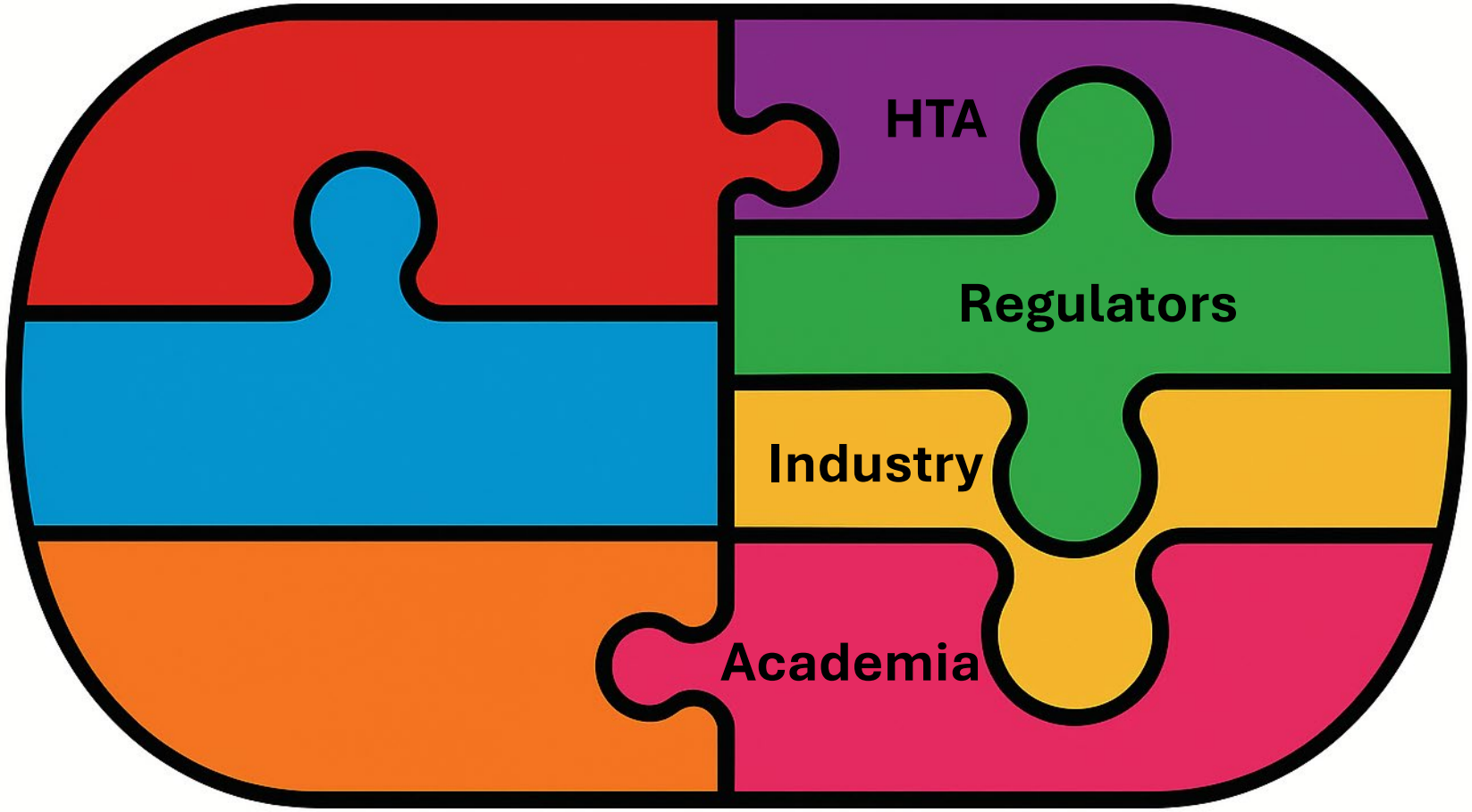

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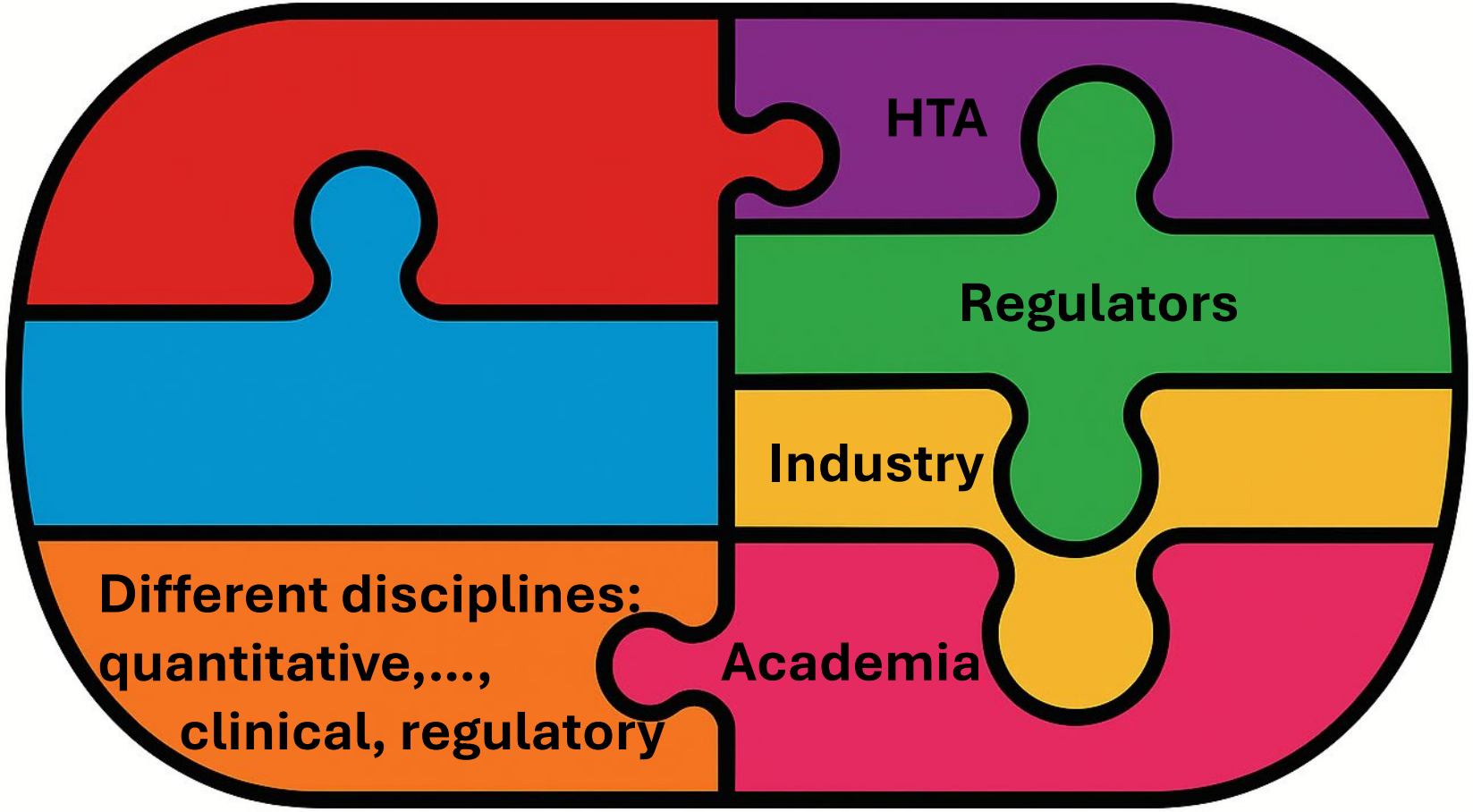

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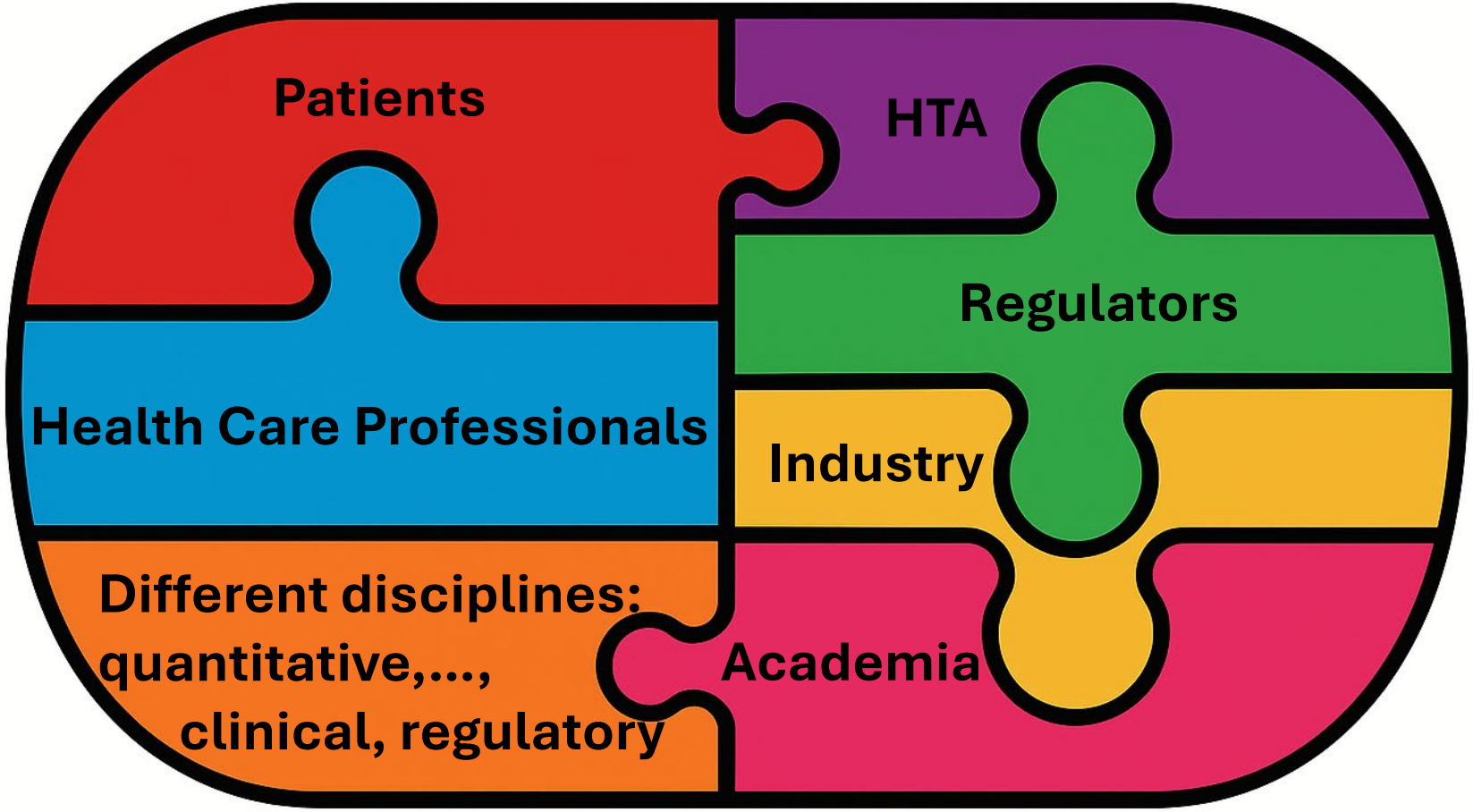

EFSPI Statistical Methodology Leaders

Check out our web page

- Formed in September 2023
- Aims to capitalize on opportunities for synergies
  - Pre-competitive collaborations, e.g. on trainings and policy matters
  - Co-develop and scale innovation
  - Anticipate and shape future trends
  - Support career development of methodologists

Strategic priorities for 2025

Four priorities defined through:

- Needs and opportunities in modern drug development
- Regulatory landscape and priorities

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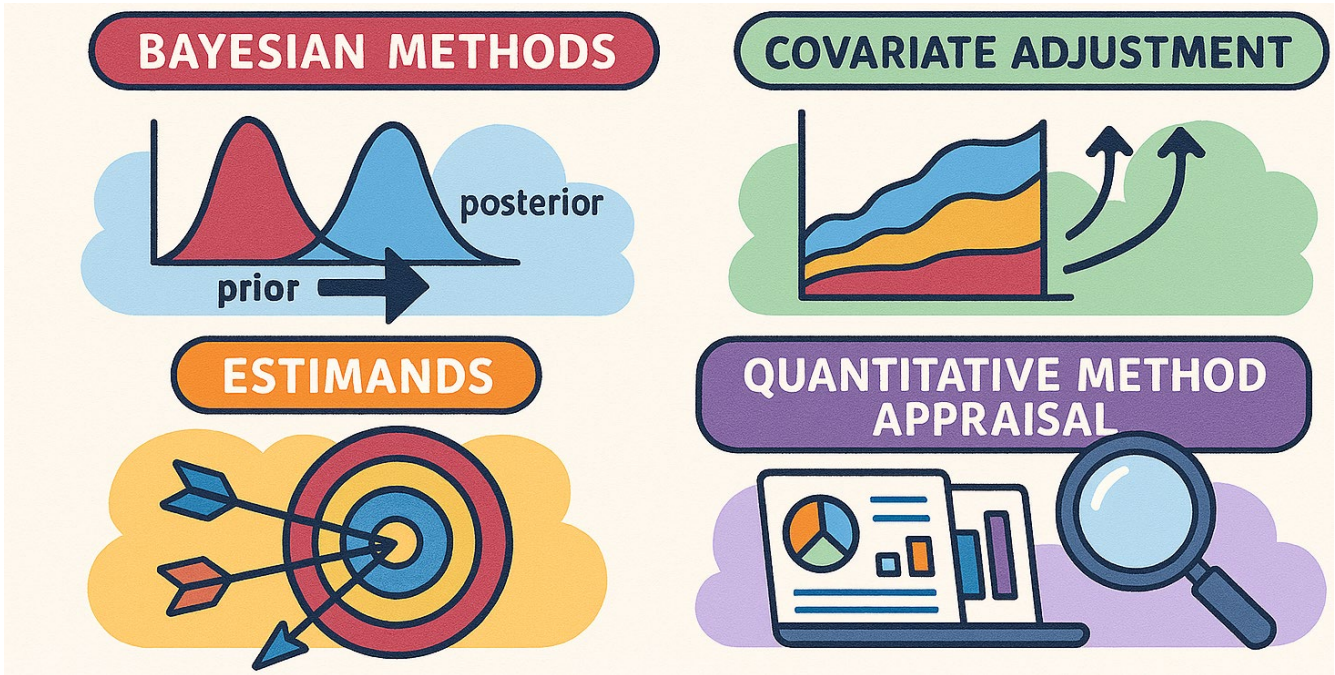

Bayesian methods

- Several regulatory agencies are working on guidance documents

FDA

Bayesian Statistical Analysis (BSA) Demonstration Project

CDER Center for Clinical Trial Innovation (C3TI)

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【国家】关于公开征求《药物临床试验中应用贝叶斯外部信息借用方法的指导原则（征求意见稿）》意见的通知

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2025.08.14 Drug Evaluation Center of the State Medical Products Administration

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ICH harmonisation for better health

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

ICH HARMONISED GUIDELINE

ADAPTIVE DESIGNS FOR CLINICAL TRIALS
E20

[1] This section on Bayesian methods for adaptive designs is not fully harmonized. The broad use of Bayesian methods may not be justified in all situations for regulatory decision-making. As noted in ICH E9 and in this draft guideline, the use of Bayesian methods in clinical trials may be considered when the reasons for their use are clear and when the resulting conclusions are sufficiently robust. Public consultation comments are sought on the topic, and on situations in which Bayesian methods satisfy the core adaptive design principles, and in which the use of Bayesian methods could be considered.

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- Bayesian methods are valuable in various drug development settings:
  - stabilize estimation; predict unobserved data; borrow trial-external data
- For which confirmatory settings, beyond paediatric/rare diseases, is there a strong rationale for adopting a Bayesian approaches?
- What are best practices for the design and analysis of clinical trials using Bayesian methods?

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e) What are best practices for defining estimands and estimating these in the presence of terminal events?

Covariate adjustment

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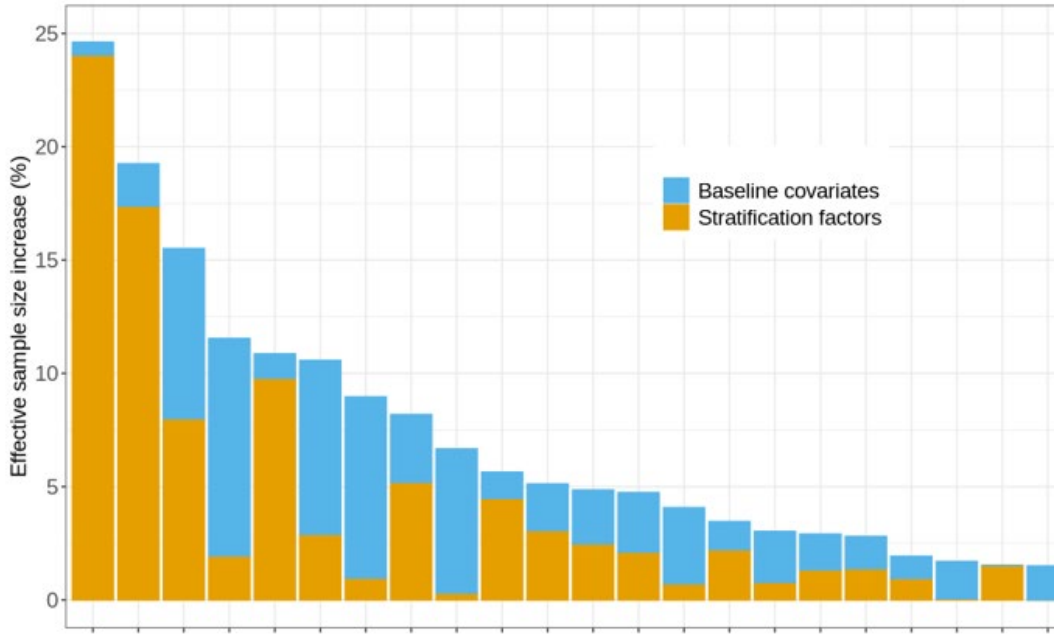
Covariate adjustment over 22 historical Oncology Phase III studies



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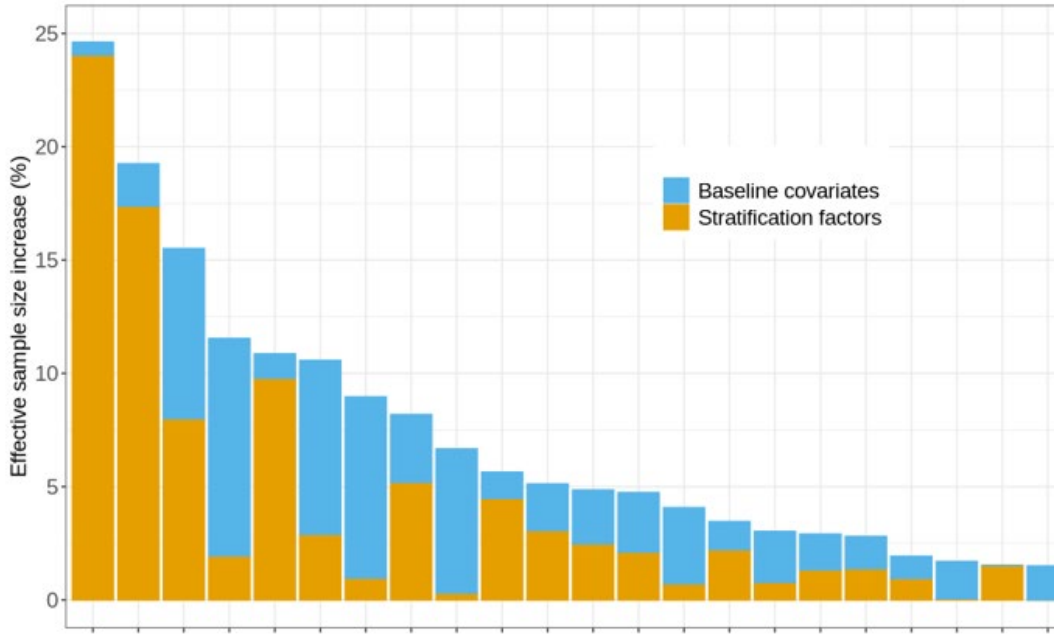
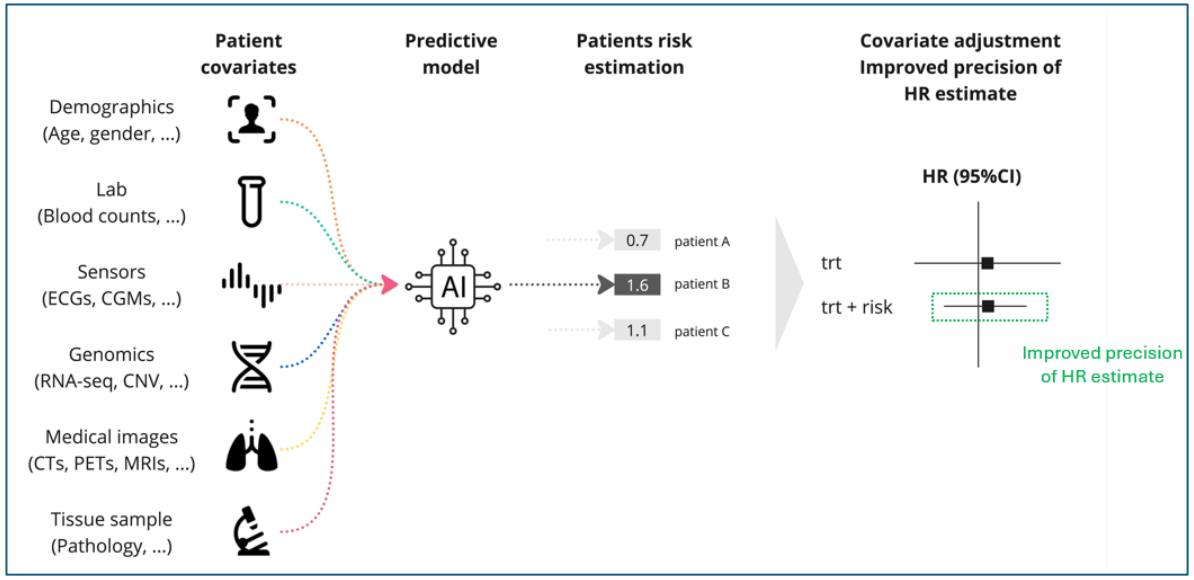
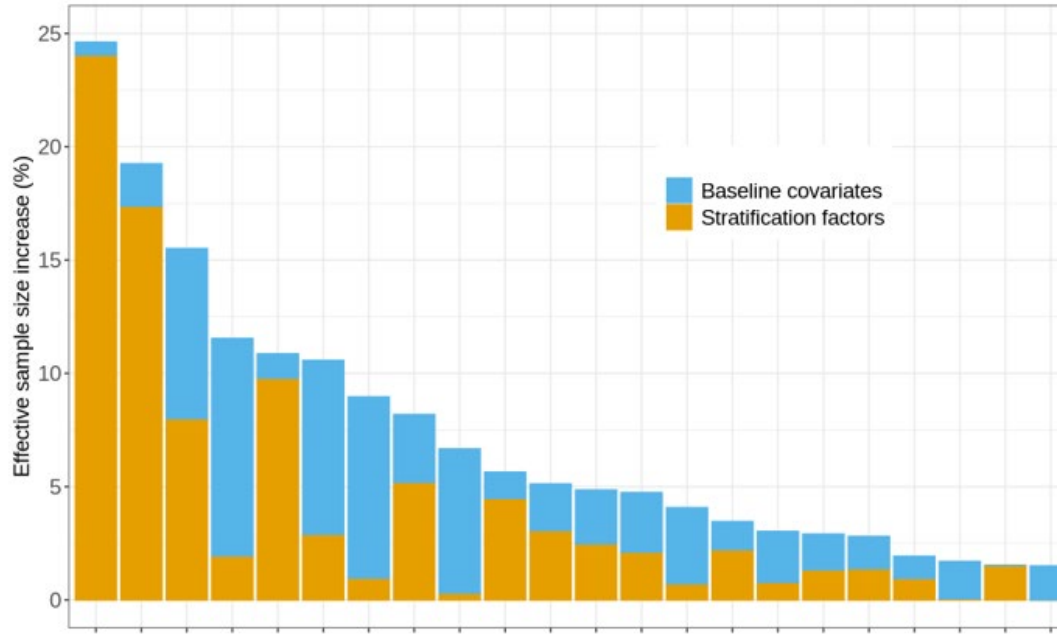


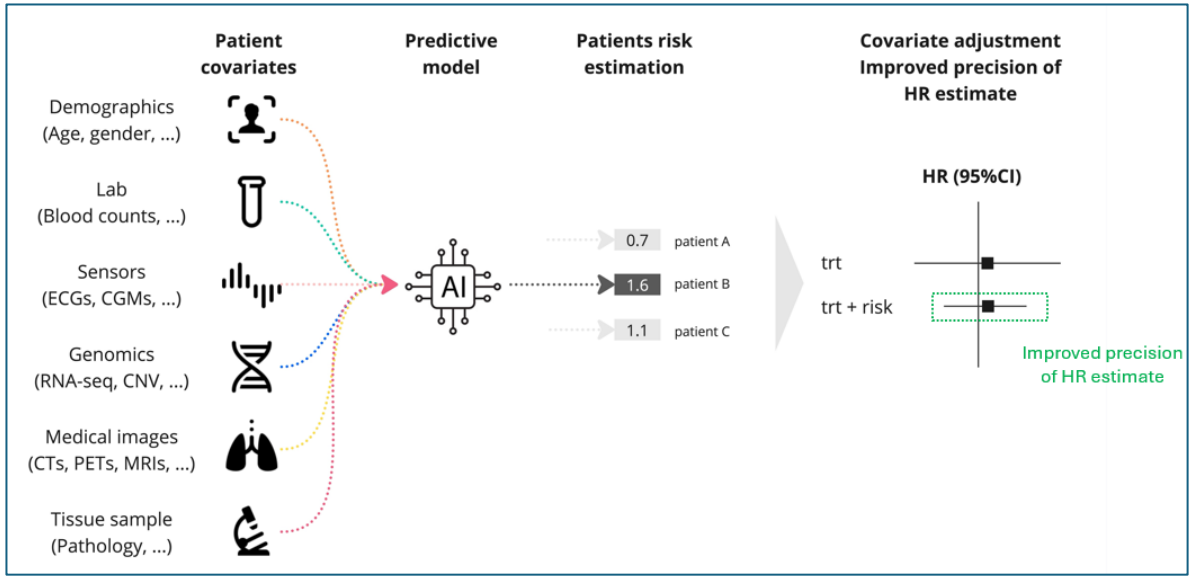


Covariate adjustment

- Recent FDA guidance and EMA qualification have increased focus on using prognostic covariates to improve trial efficiency
- ICH E9(R1) raised awareness of marginal vs. conditional effects
- Causal inference methods and semi-parametric theory have helped to further understand the interplay between efficiency gains and robustness
- How can we take advantage of these developments (incl. supercovariates)?

Covariate adjustment over 22 historical Oncology Phase III studies





Quantitative method appraisal

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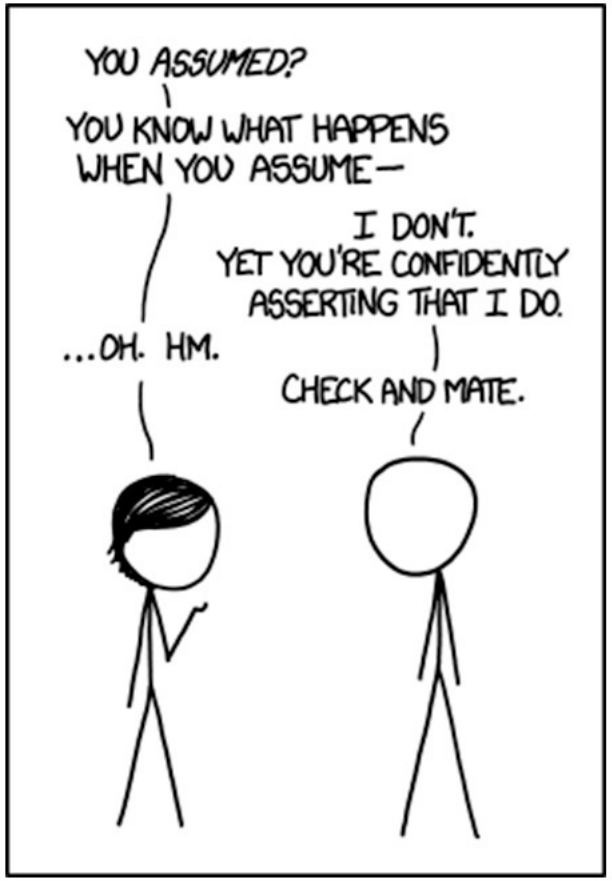
  - Reluctance to rely on methods with ‘strong assumptions’
  - Applies to RCTs and non-randomized trials



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a cartoon from xkcd
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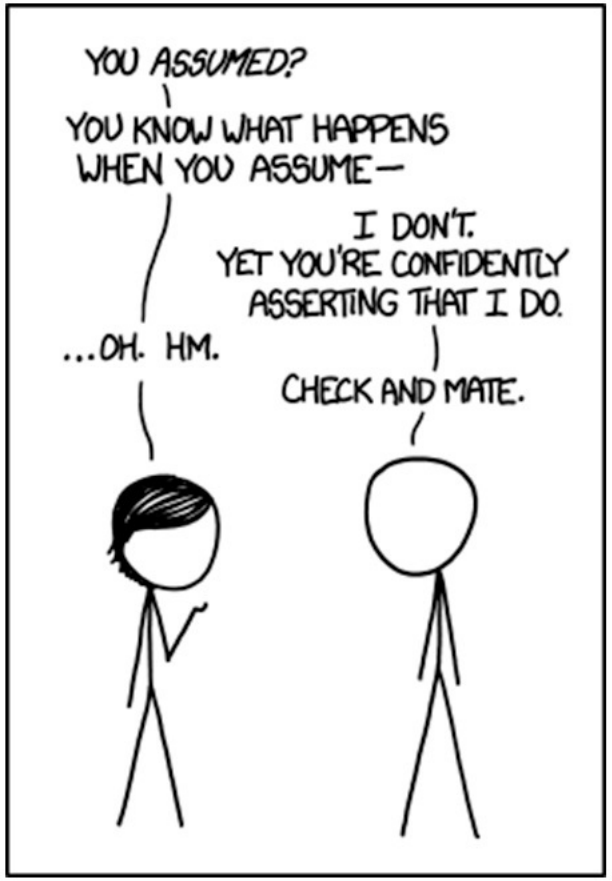

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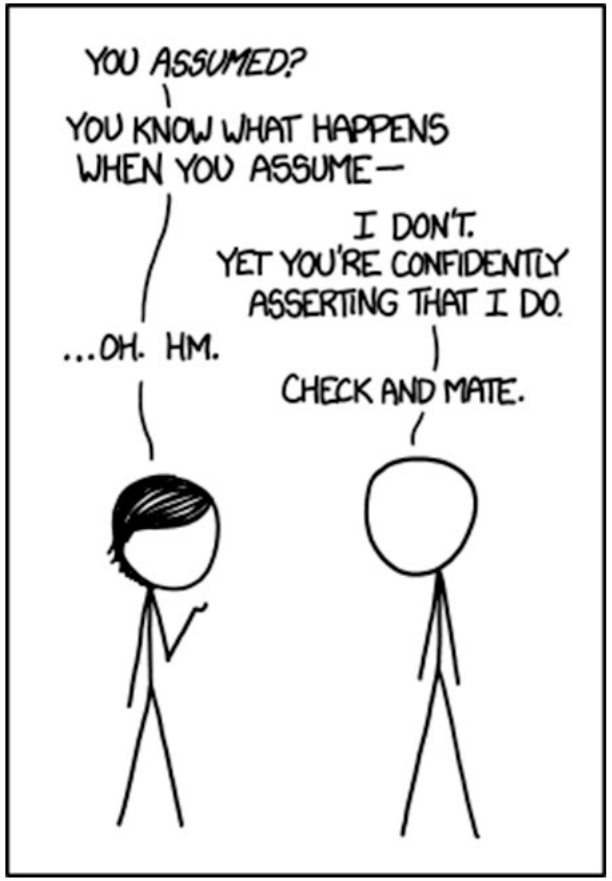
- Can we develop an overarching framework?
- Can the ICH M15 MIDD credibility framework serve as basis?



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What is next?

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It's about making ideas happen.
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What is next?

- **Dissemination of ideas and positions:** conferences, webinars, trainings, Q&A documents, peer-reviewed publications
- **Formal regulatory pathways if suitable:** commenting on regulatory guidance documents, pilots, qualification procedures
- **Collaboration**

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  - Does not imply other topics are not important
  - Efforts will extend beyond 2025

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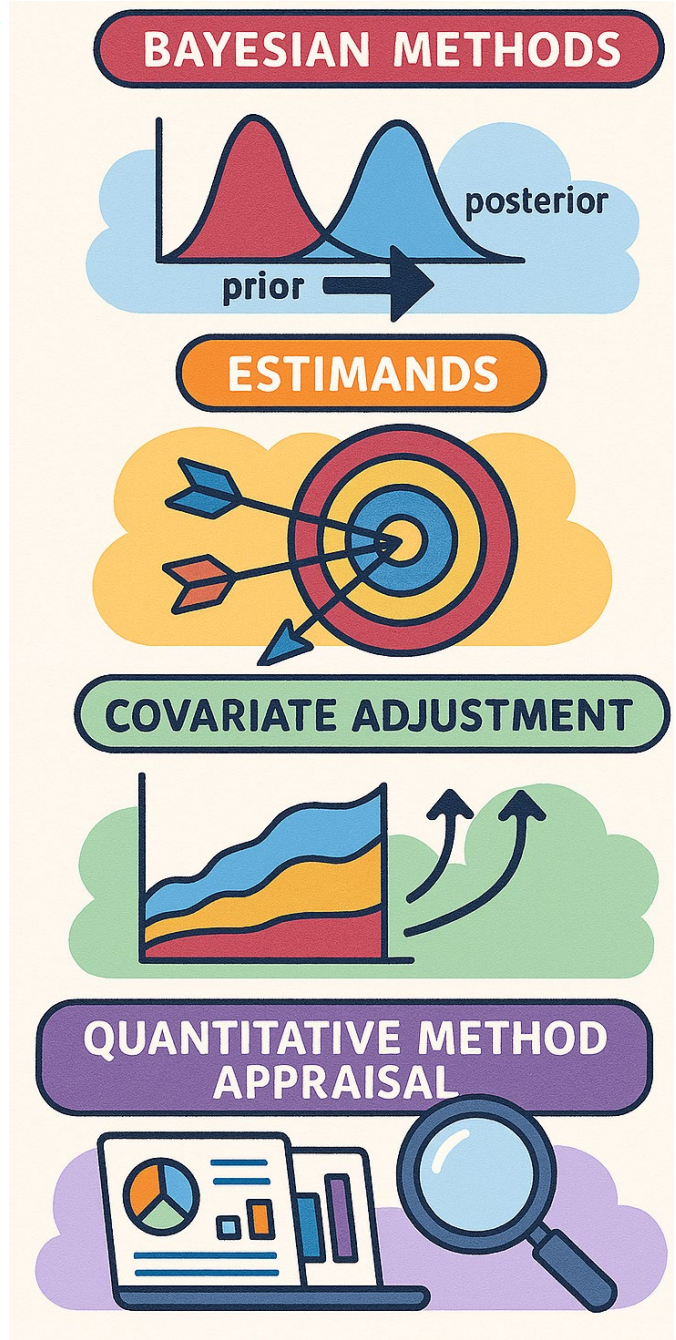

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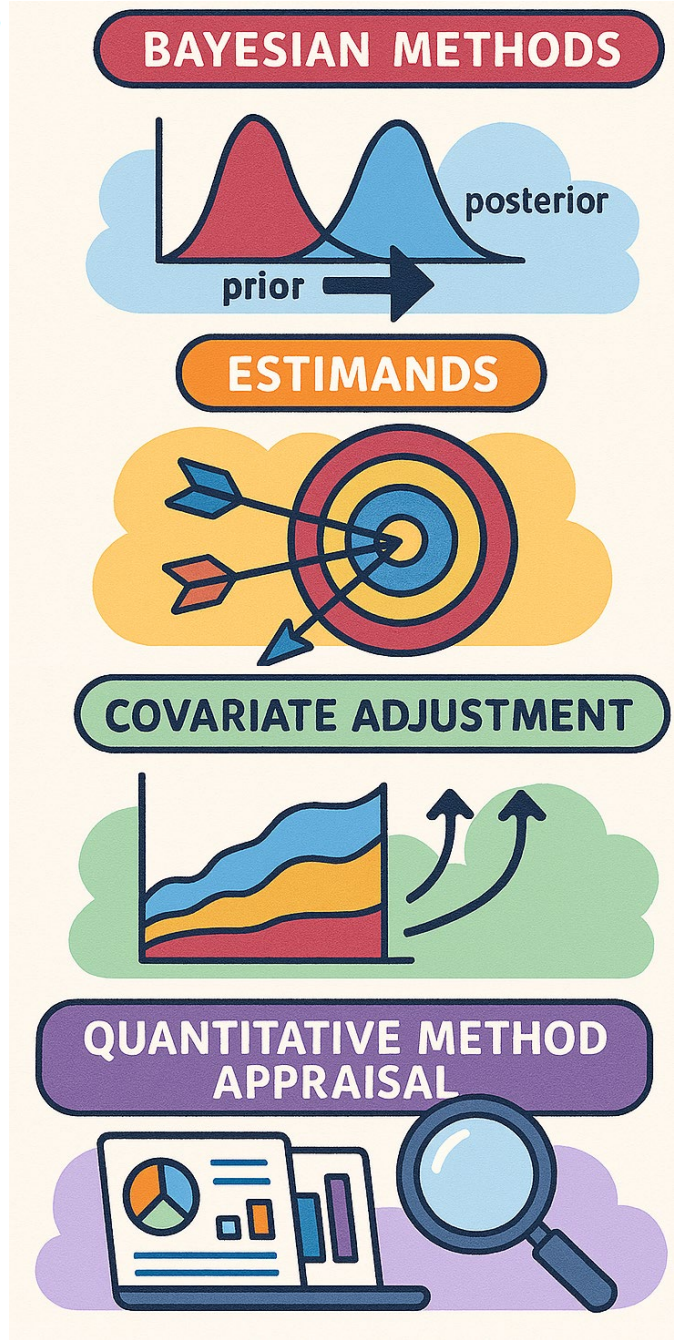

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