SxP Trainee Award Presentation

Pharmacometrics Enhanced Bayesian Borrowing

Lucie Fayette

SxPM
Statistics & Pharmacometrics

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to learn more about it!

Pharmacometrics Enhanced Bayesian Borrowing

Lucie Fayette
Oliver Sailer
Alejandro Perez Pitarch

Boehringer Ingelheim

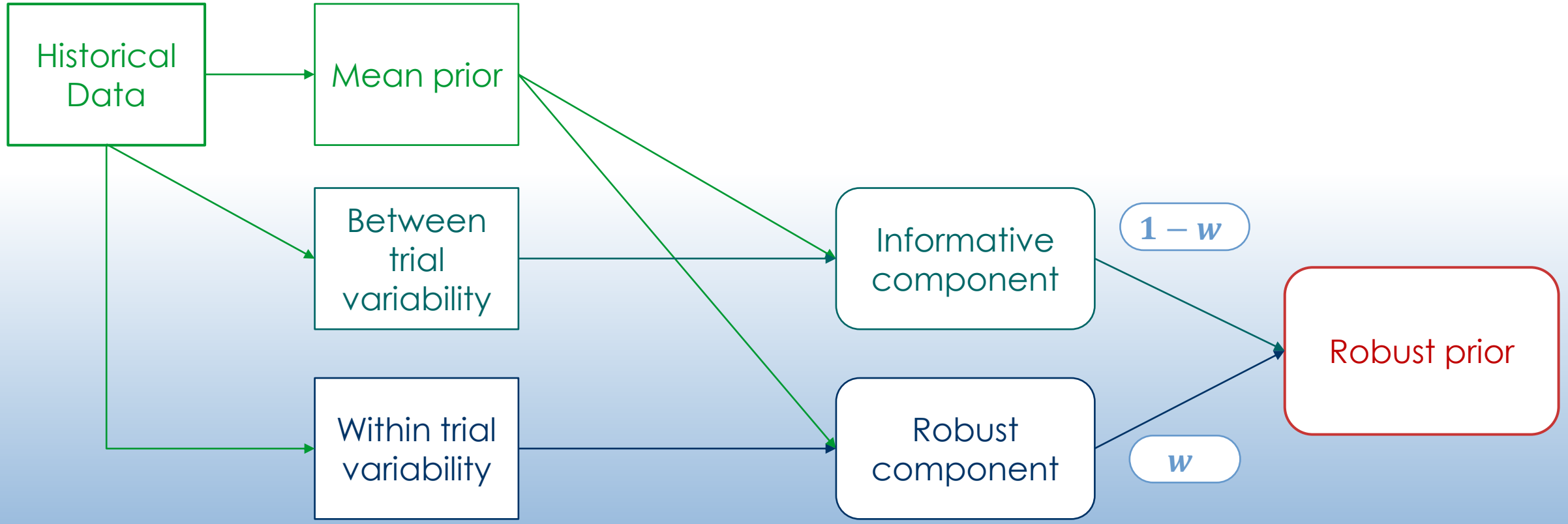
Bayesian Borrowing to supplement clinical trials

Two main approaches:

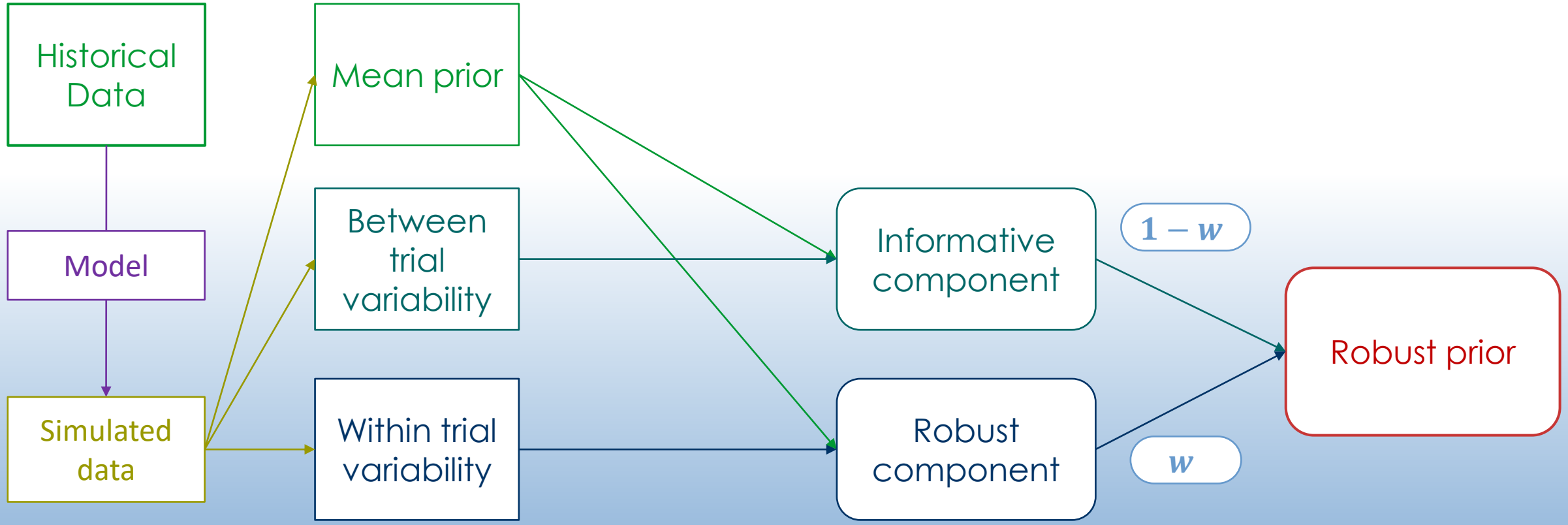
- **Meta-analytic predictive (MAP) priors with or without robustification**
  - Account for unexplained heterogeneity between historical data sources (e.g. between trials)
- **Propensity score matching**
  - Create "exchangeable" groups, assuming baseline covariates explain difference between historical data and target trial

Next generation: **Pharmacometrics Enhanced Bayesian Borrowing**
Use PK/PD models to create "exchangeable" data based on previous Pharmacokinetic and Pharmacodynamic knowledge, assuming baseline covariates can explain differences between historical data and target trial

Robustified prior



Robustified prior in PEBB



PEBB Workflow

Design Phase

1. With historical data, PK/PD model we simulate the outcome of K simulated TT with high number of patients per arm. Then, using the w we produce the **PRIOR**
2. To evaluate risk of type 1 error:
   a. Simulate TT results with drug which does not work→ "**Observed data**"
   b. **PRIOR** + **Observed data** = **Posterior** → depends on operating characteristic w

   Decide on reasonable w

Analysis phase

1. Generate **prior** based on recruited patients of TT
2. Combine this **prior** with **observed TT results** using chosen w to compute **posterior**
3. Answer whether we can conclude the drug works

Example

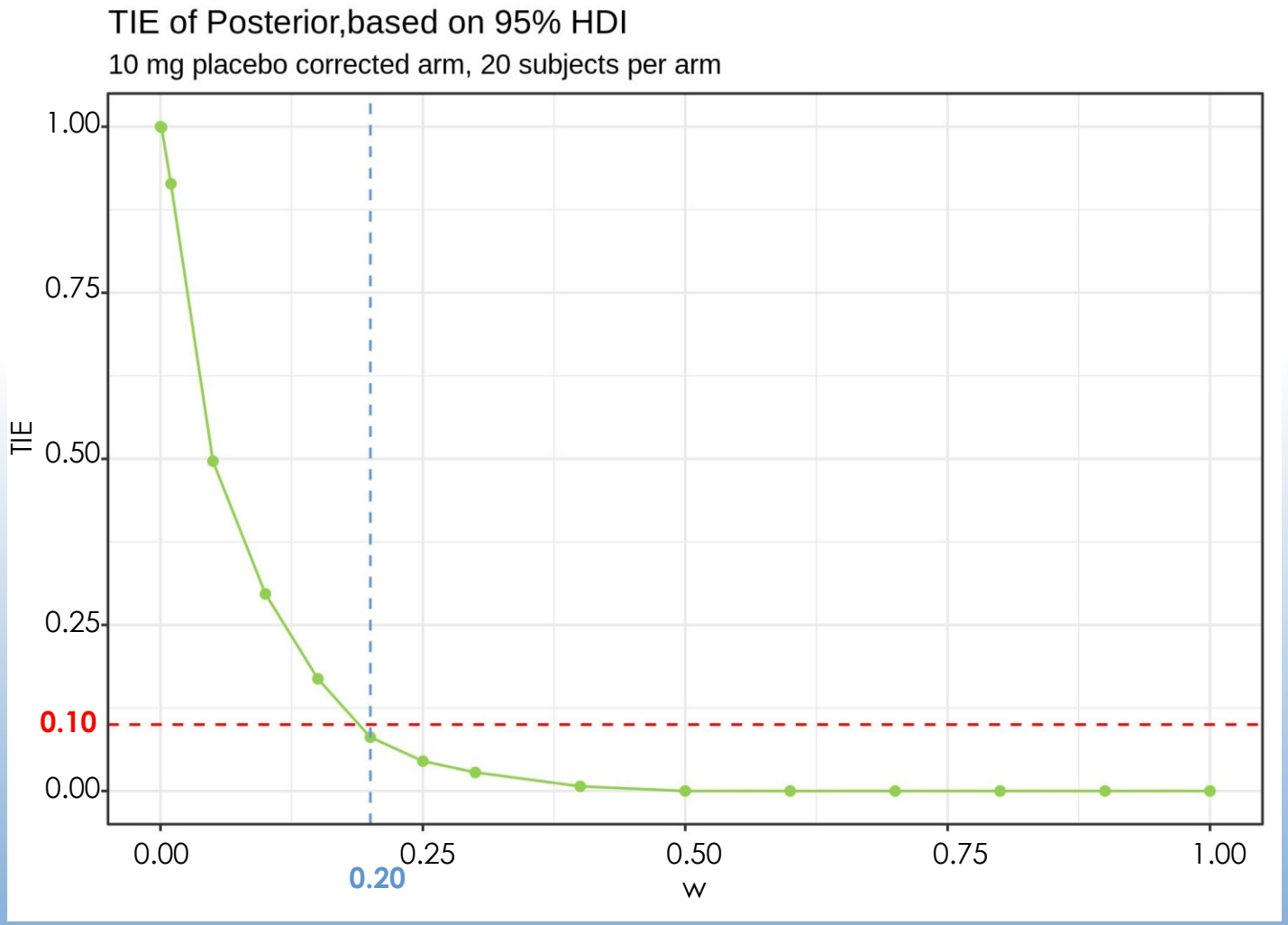
Target Trial – Hypothetical Phase III study built on real Phase III data:

- Assess the efficacy of a drug over a 24-week treatment
- Patients with T2DM
- Endpoint: change in HbA1c from baseline to week 24
- 2 Arms with N=20 patients each, testing placebo and 10mg of drug daily

Historical Data:

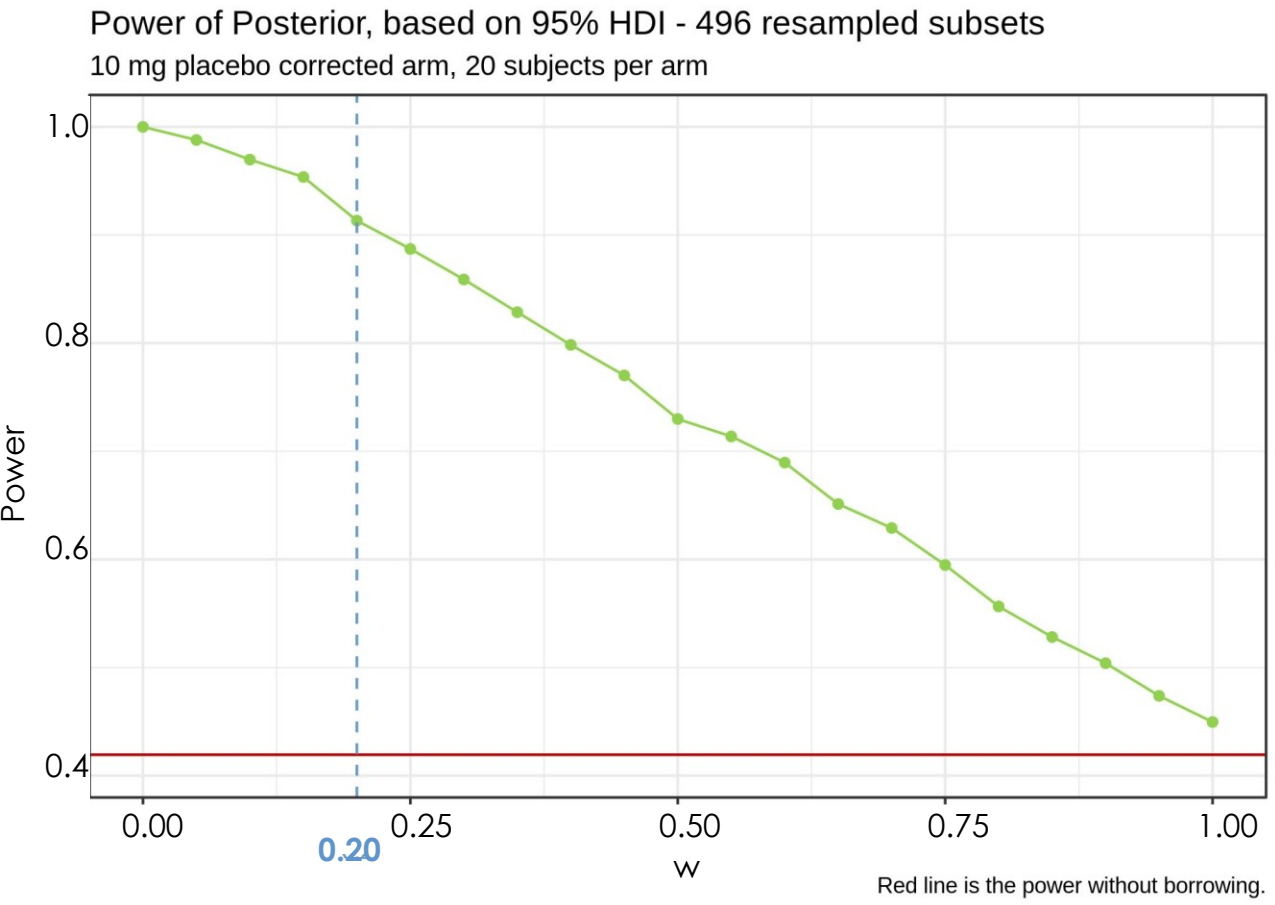
- Phase II studies
- Longer treatment being only 12 weeks
- Half of the patients meet inclusion and exclusion criteria from TT

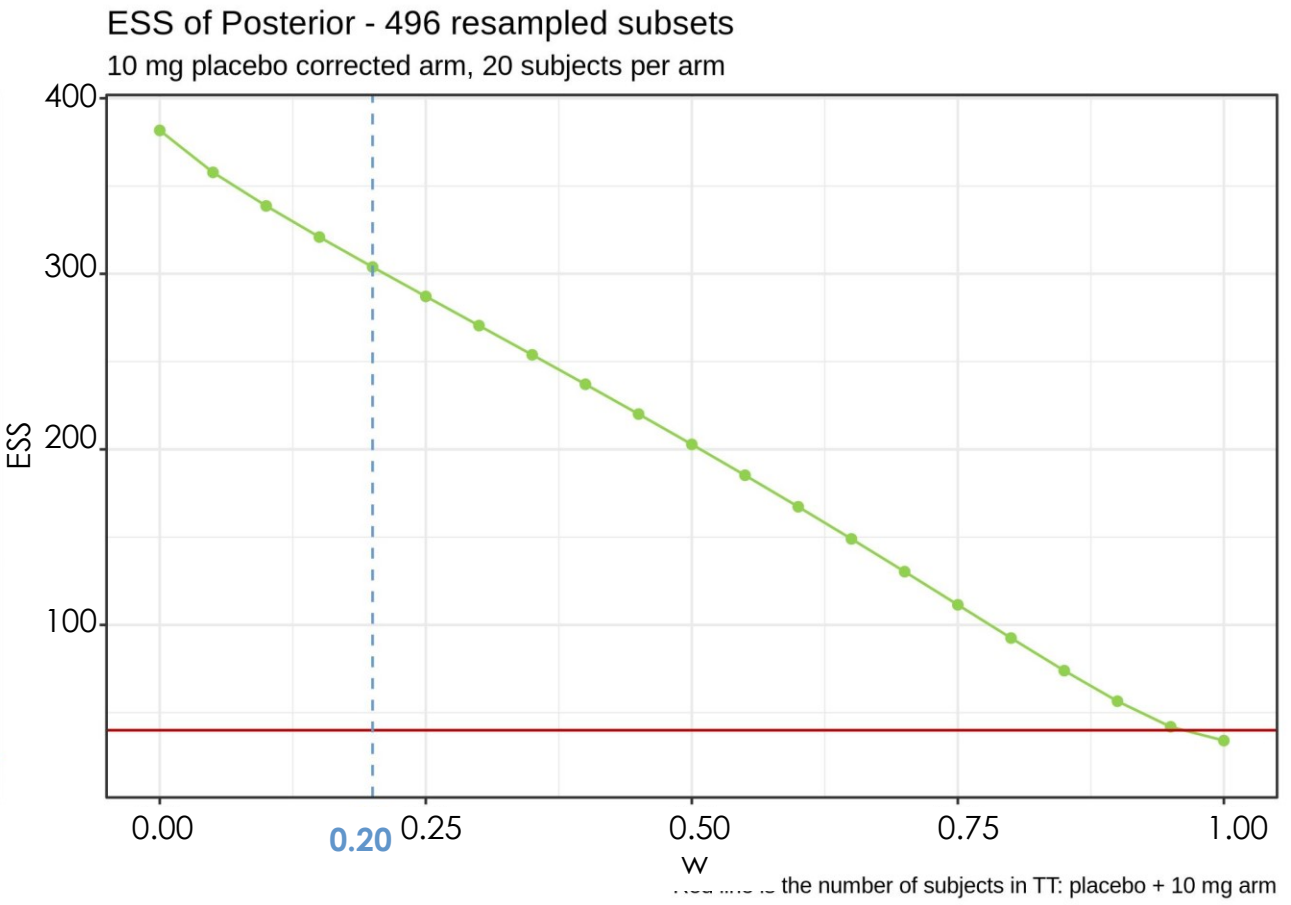
Design Phase: Type I error



$\longrightarrow w = 0.2$

Analysis Phase





⇒ Power at more than 90% whereas only 45% without borrowing
+ ESS more than 300 wheras only 40 without borrowing

Conclusion

The **PEBB** has the potential to **increase the power of clinical trials** while **controlling for type 1 error** by leveraging **the information from previous trials** through **population pharmacokinetic modelling and simulation**.

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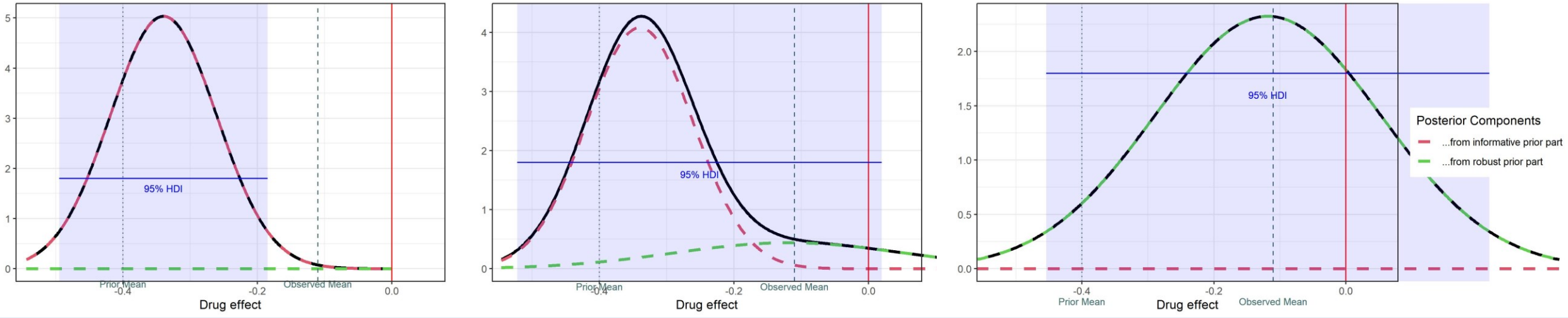
- Dr. Curtis Johnston
- Dr. Jim Rogers
- And many more colleagues at Boehringer supporting my work

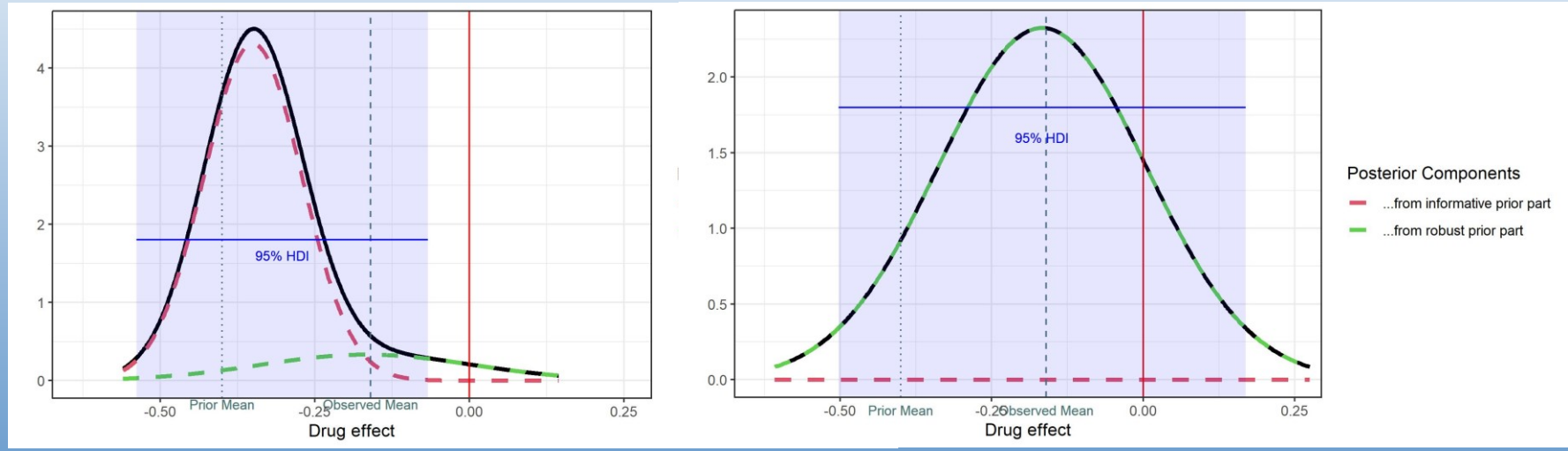
Case Drug does not work:



0 → 1

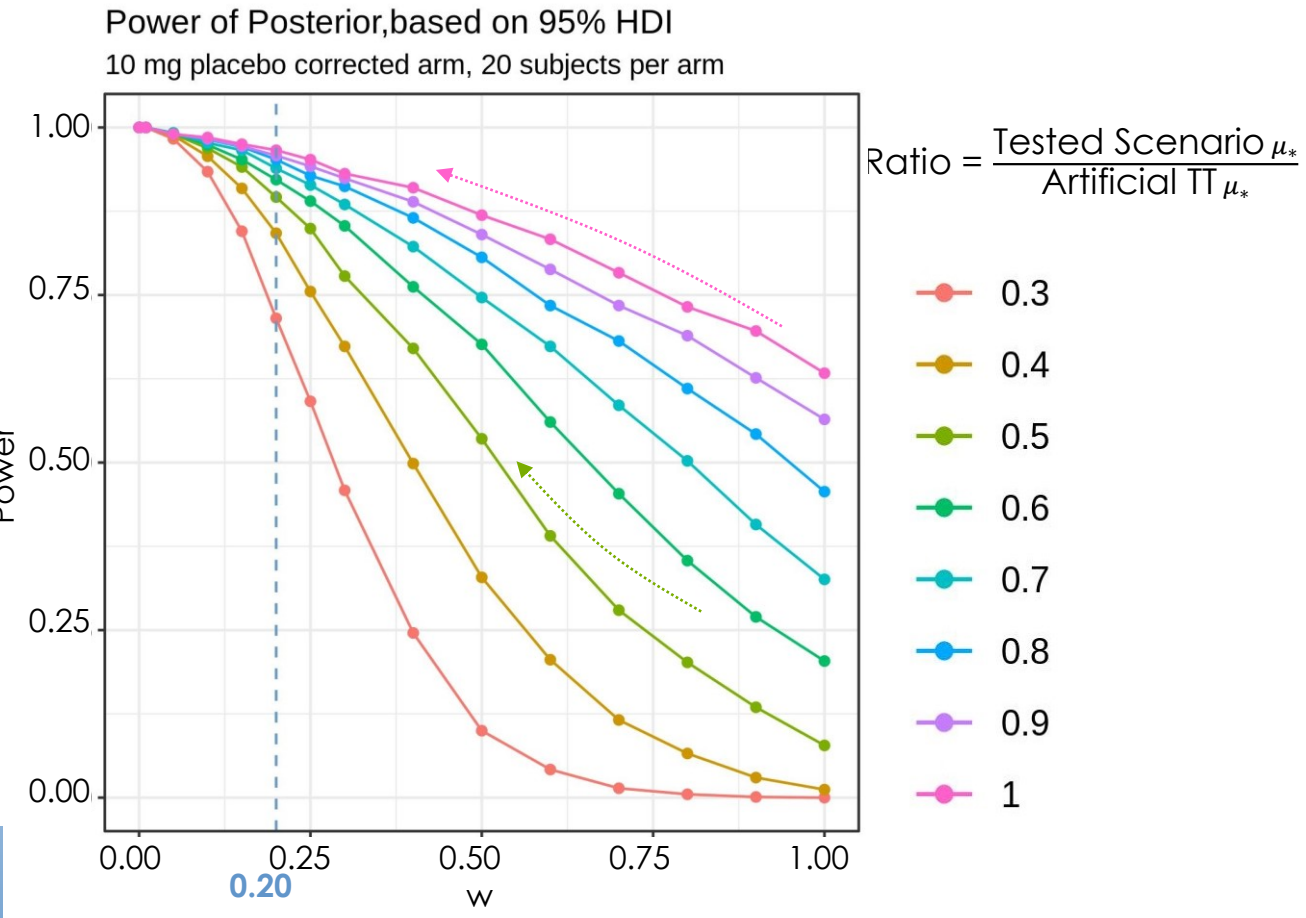
w

Case Drug does work:



Design Phase: Power

In case there is **no prior data conflict**, power without borrowing is **60%**



If trial results evidence that the drug works as we expected it to work (**Ratio = 1**), power can be increased **from ~60% to ~95%**

If the trial evidenced that the drug effect was only half of what we expected (**Ratio = 0.5**), power to conclude drug effect would be increased **from ~10% to ~90%**

Design Phase: ESS