

Bayesian dynamic borrowing for clinical trials

EMA – Methodology Working Party Interested Parties Meeting

7 June 2024

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Acknowledging input from industry colleagues

BACKGROUND AND CHALLENGES

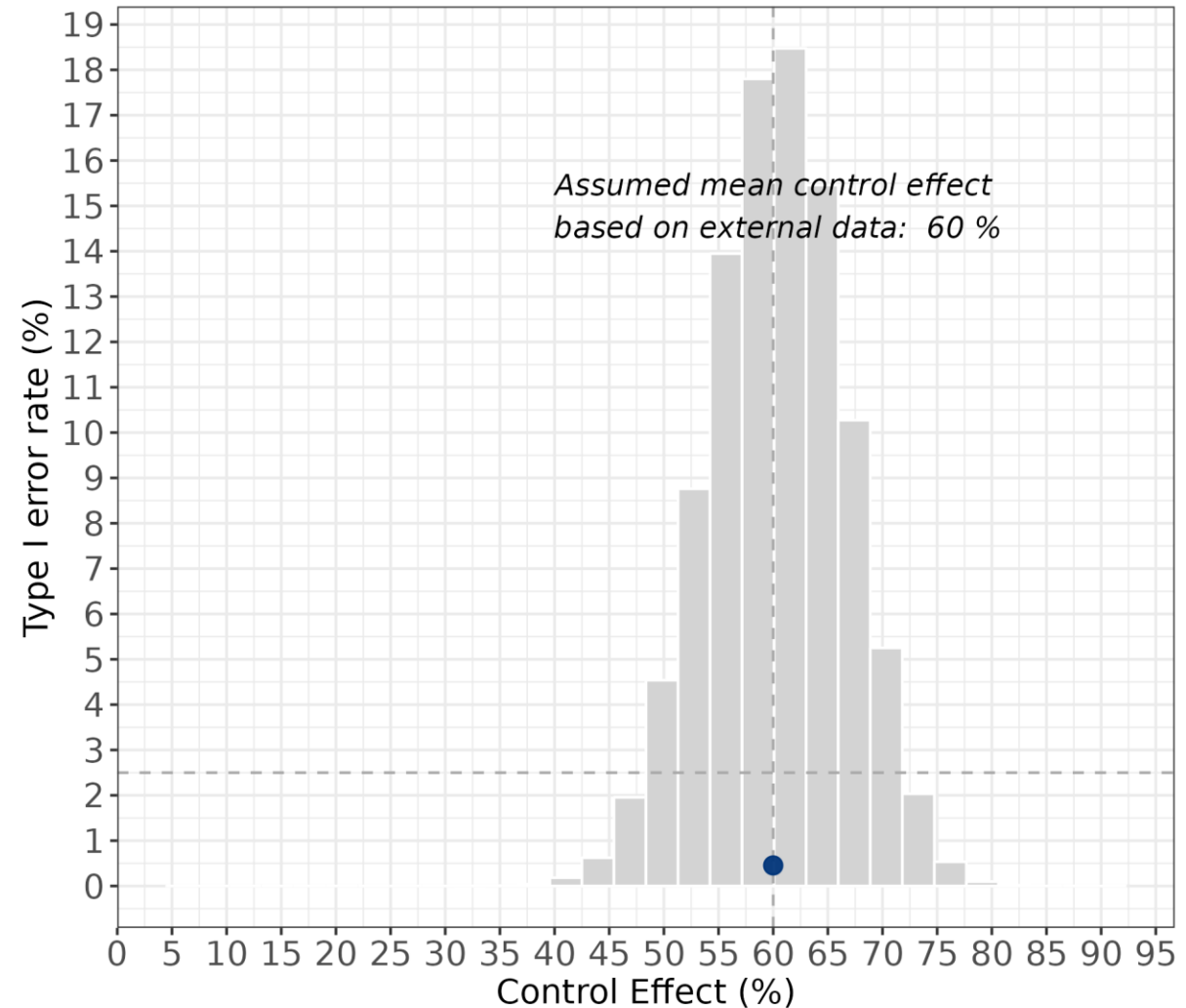
- Background:
 - **Out of scope: when or when not** to apply a Bayesian Dynamic Borrowing (BDB) approach
 - We want to address **how** to implement a BDB design and analysis to augment **control** data in a confirmatory RCT used for submission.
- Challenges we want to discuss:
 - How to appropriately address **Type I error rate** of the design/analysis?
 - How to increase the chance of **exchangeability** and what information needed to make the assumption of exchangeability appropriate?

POTENTIAL SOLUTIONS

- How to appropriately address concerns on **Type I error** rate of the design/analysis?
 - Focus on trial outcomes of interest
 - Propose metric based on relevant range iso single point metrics (i.e. Max Type I)

POTENTIAL SOLUTIONS

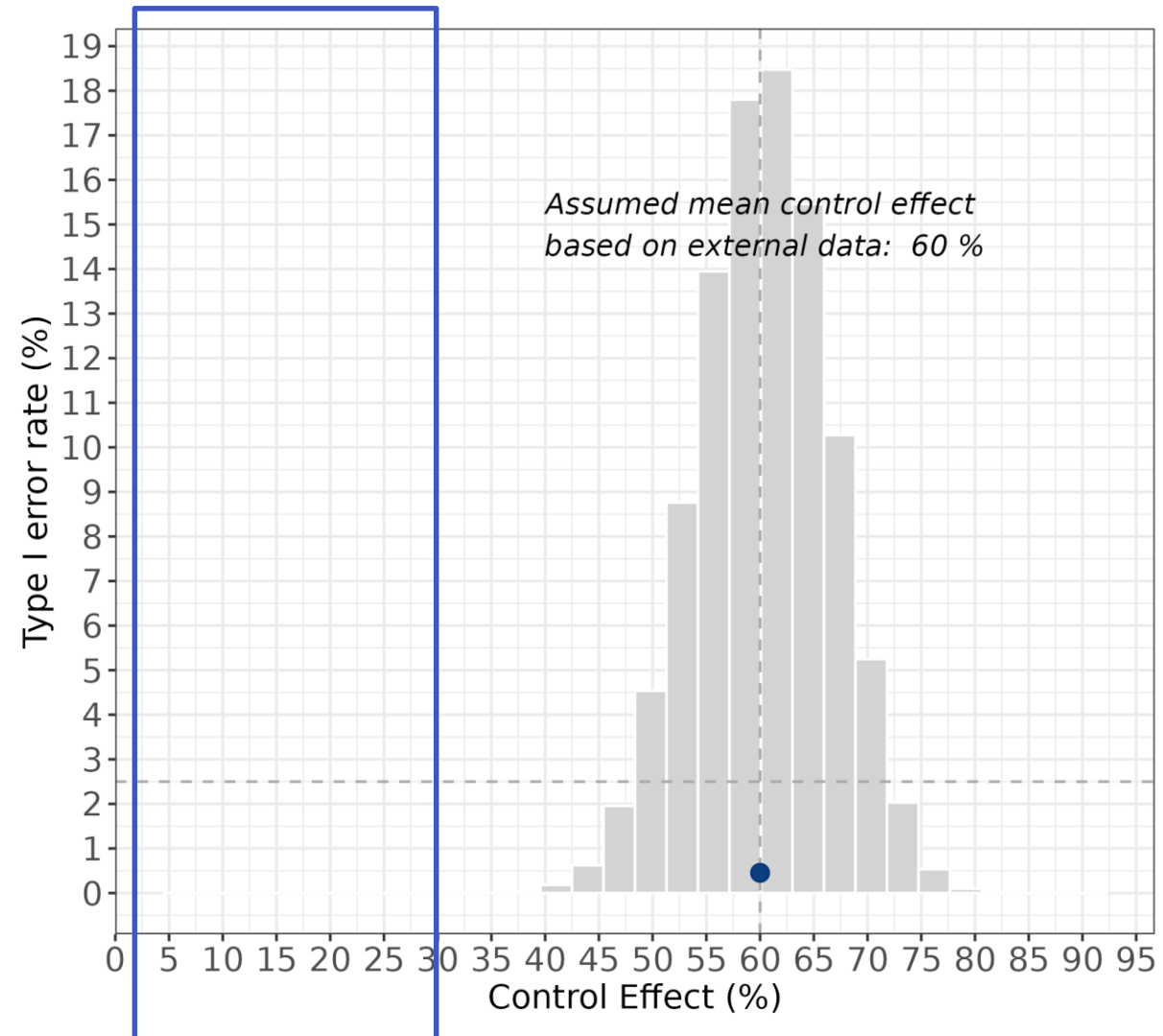
- How to appropriately address concerns on **Type I error** rate of the design/analysis?



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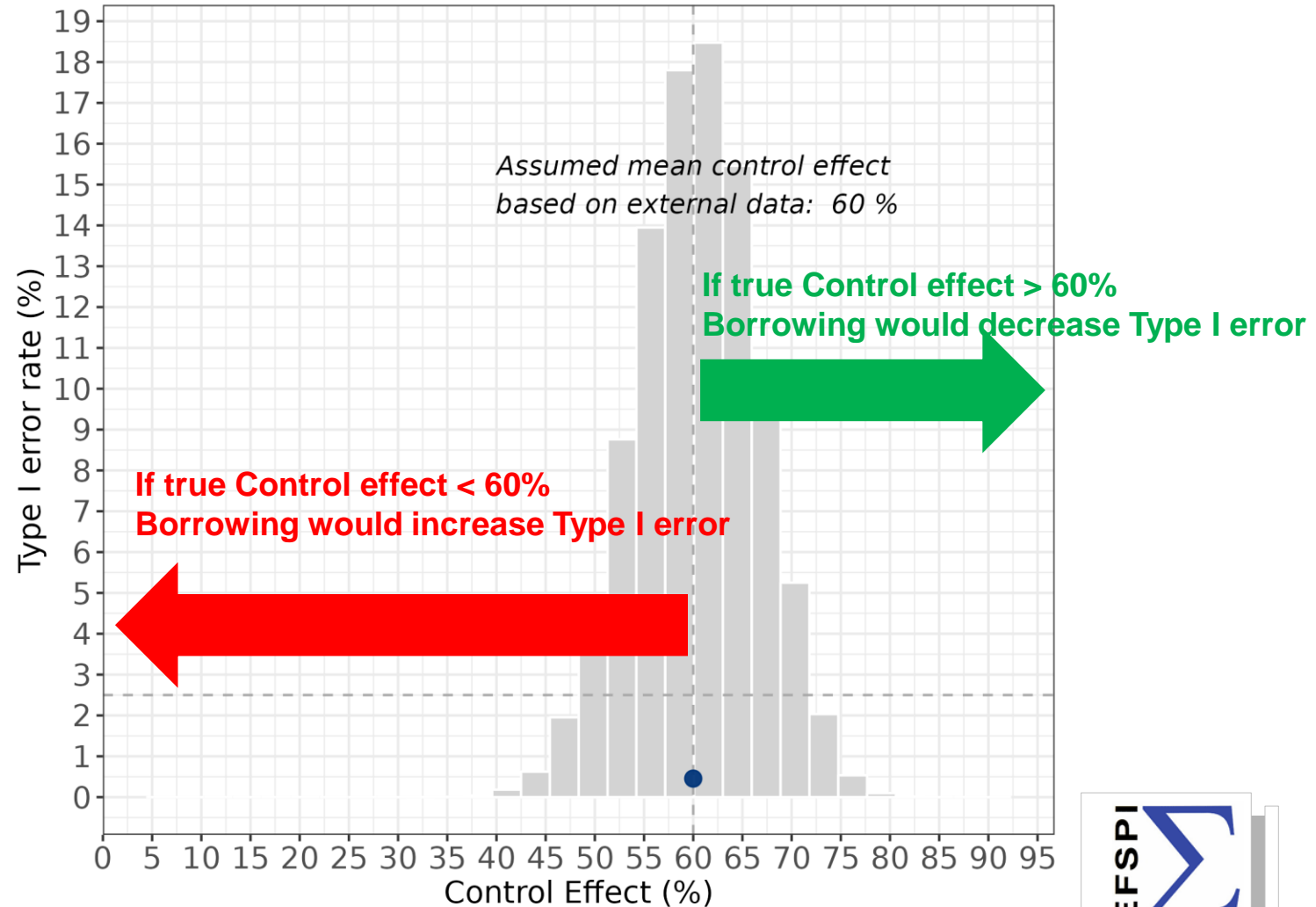
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Unlikely to be interested in this region



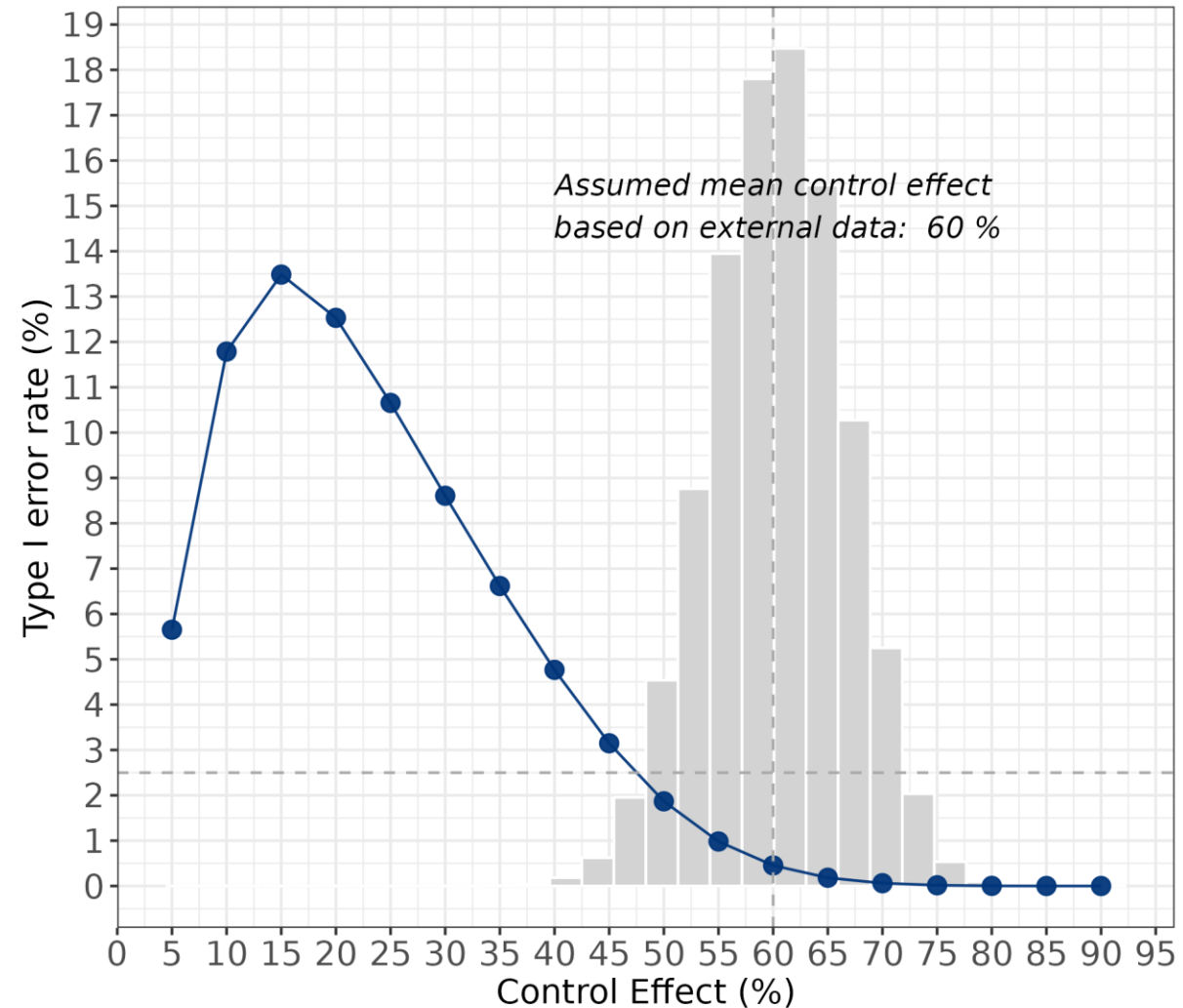
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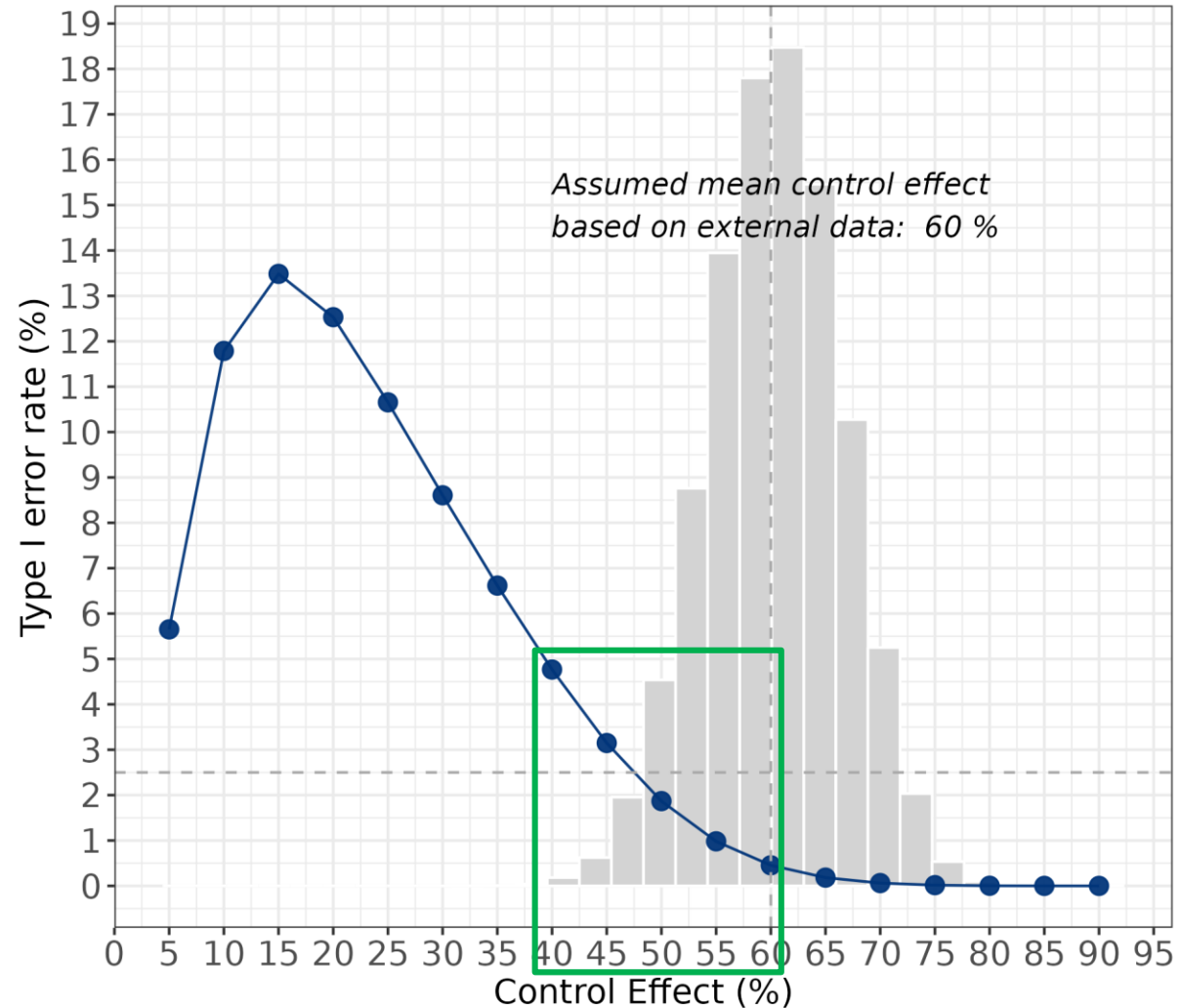


POTENTIAL SOLUTIONS

- How to appropriately address concerns on **Type I error** rate of the design/analysis?

Quantify Type I under range of relevant deviations:

- How to define the range?
- Potential Metrics:
 - “Averaged” Type I error
 - Maximum Type I error with corresponding probability of occurrence



POTENTIAL SOLUTIONS

- How to increase the chance of **exchangeability** and what information needed to make the assumption of exchangeability appropriate?
 - increase the chance of exchangeability
 - ❖ Applying appropriate statistical methodology, eg Propensity scoring
 - ❖ Design new study as close as possible to the external data
 - What information needed to make assumption of exchangeability appropriate?
 - ❖ Do not have a proposed solution – Hope to address this in discussion

NEXT STEPS - DISCUSSIONS

- Would Type I error metrics linked to a relevant range be considered as appropriate?
- How to quantify the relevant range for which to calculate Type I error metrics?
- What information would be needed for the agency to make assumption of exchangeability appropriate?