

Augmented controls in the confirmatory setting

- Substantial experience has accumulated with augmented controls in non-confirmatory phases (e.g. PoC). What role, if any, could it play in a confirmatory setting?¹

RCT as gold-standard
when feasible

Is there a place for
augmented controls?

Approvals have been granted²
based on **single-arm trials** in
special situations (esp. rare
diseases with high burden)

¹ [ACT-EU PA08 MST report.pdf](#) (page 6). ² Goring et al., 2019.

Augmented controls in the confirmatory setting

- Under which circumstances may augmented controls be accepted for:
 - Market authorization?
 - Additional efficacy claims?
 - Safety (e.g. rare events)?
- In terms of methodology, are there any specific concerns regarding well-established approaches such as propensity-score matching or Bayesian dynamic borrowing?
- Type I error can be slightly inflated.¹
 - Under which circumstances could this be acceptable?
 - Can it be complemented by alternative metrics?²

¹ Kopp-Schneider et al. 2020. ² Best et al. 2024.

Augmented controls in the confirmatory setting

- What documentation should sponsors provide to facilitate regulatory review at different stages (scientific advice, submission...)?
 - Possibility of early interaction before investing in large simulation studies?
- What technical requirements should the source of augmentation fulfil?
 - Summary-level information (e.g. from literature) vs. access to raw data?
 - Data standards?
 - Access to ICF? ...
- Additional considerations if the source of augmentation is not a CT but:
 - RWD?
 - Synthetic data?