EUROPEAN FEDERATION OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY
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Target trial emulation and incorporation of observational data into clinical trials from an HTA perspective

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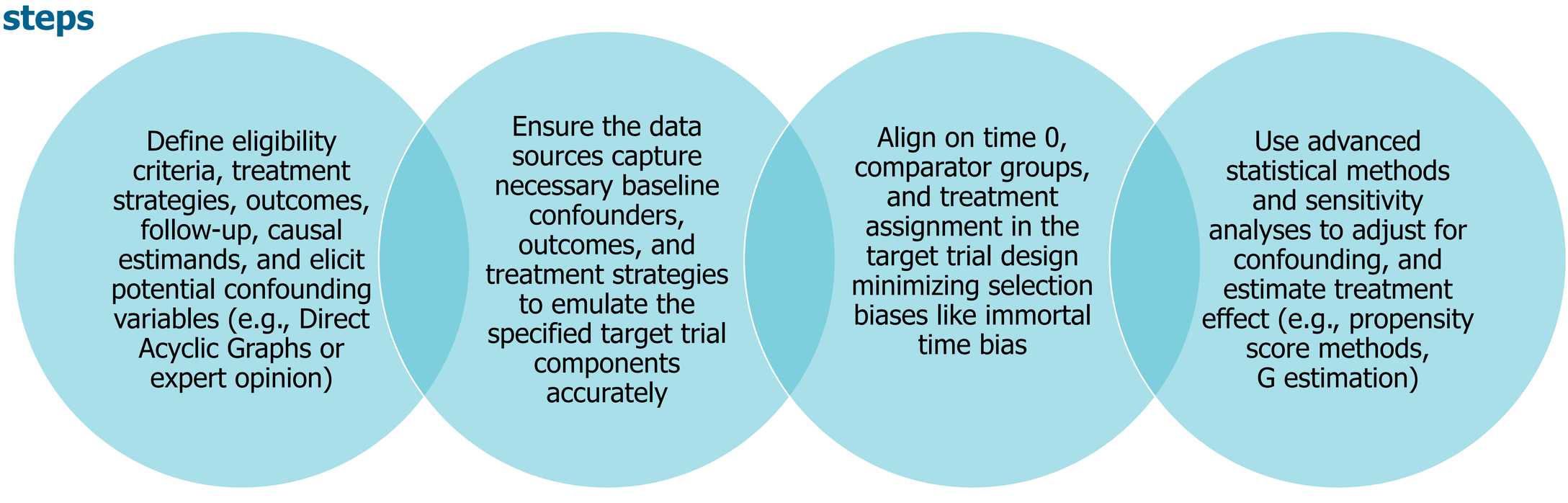
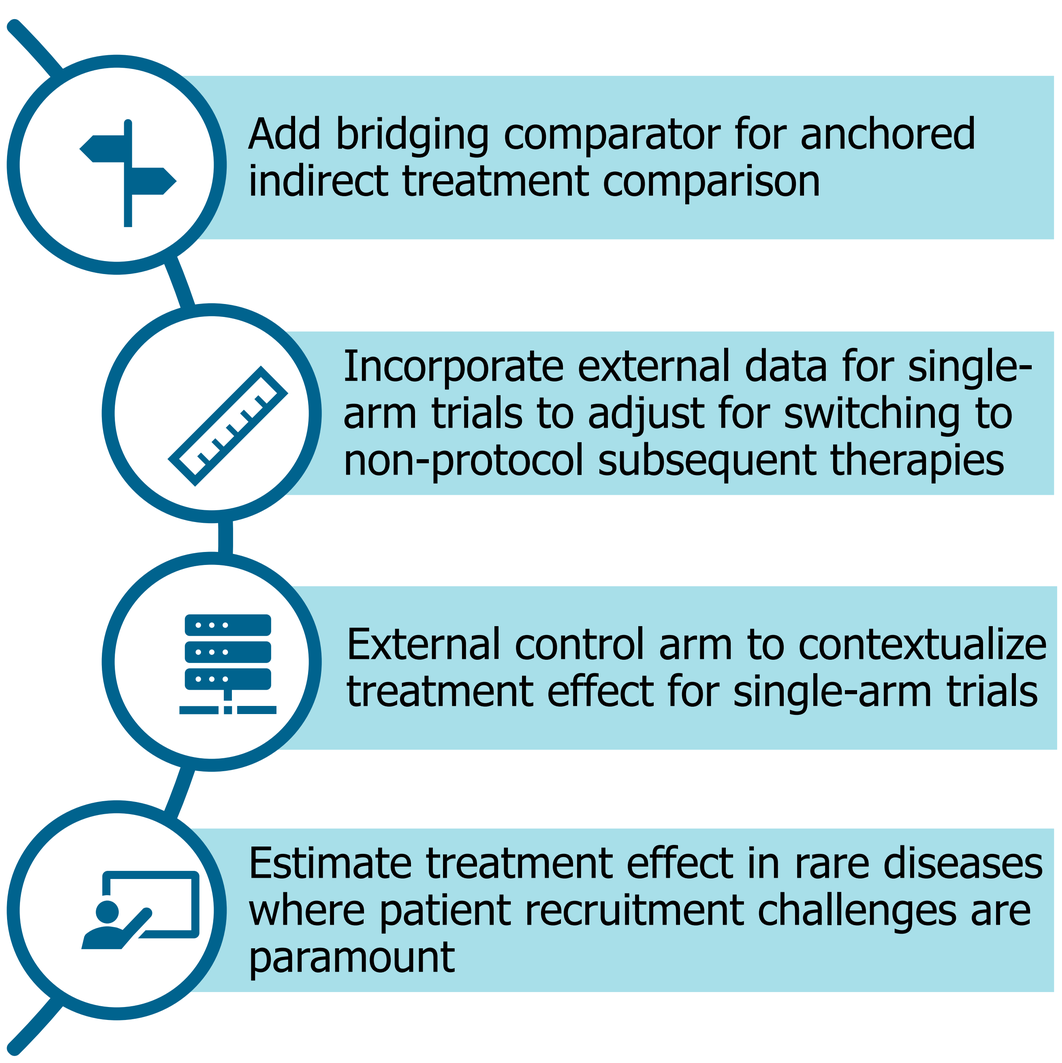
What is target trial emulation?

Target trial emulation (TTE)[1] is a method used in observational research to address common sources of bias when answering causal inference questions. This method first elicits the main design attributes of the target trial that would answer the causal question of interest (eligibility criteria, treatment strategies, outcomes, follow-up, causal estimands, and statistical methods). Then, this target trial is mimicked or emulated in an observational data source. This method is useful in multiple HTA applications combining clinical trial sources with external data.

Key steps



Possible TTE Applications in HTA



What are the challenges?

- **Limited adoption**: TTE remains underutilized in HTA due to lack of expertise, limited methodological guidance, and insufficient reporting standards despite being central to NICE's RWE framework[2].
- **Data limitations**: RWD may fail to capture the depth and breadth required, limiting the ability to emulate key trial components such as eligibility criteria, confounders, and treatment strategies. Historical data may lack easily accessed individual patient-level data.
- **Confounding and bias**: Challenges include addressing unmeasured confounding, selection bias, and residual bias, which makes robust causal inference from observational studies more complex.
- **Access and harmonization**: Gaining access to high-quality data is expensive, time-consuming, and requires harmonization across different sources for consistent analyses.

Conclusions

- Answering causal treatment effect questions with real-world data or historical data is challenging, and conclusions are often difficult to draw
- TTE is a method that can minimize bias by design to enhance certainty in all decision making, including HTA
- TTE can be extended to applications leveraging multiple sources of information
- TTE attributes are aligned and complementary to attributes of the estimand, causal roadmap or PICO frameworks
- **Rigorous use of TTE by statisticians can foster acceptance by regulatory agencies and HTA bodies.**

References:
[1] Hernán, Miguel A., and James M. Robins. "Using big data to emulate a target trial when a randomized trial is not available." American journal of epidemiology 183.8 (2016): 758-764.
[2] NICE RWE framework: https://www.nice.org.uk/corporate/ecd9/chapter/overview

Acronyms: TTE: Target trial emulation RWD: Real-world data, RWE: Real-world evidence, HTA: Health Technology Assessment

Want to learn more?

Join the PSI HTA ESIG and PSI RWD SIG!

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