Novel Statistical Approaches for Leveraging Real-World Data to Support Regulatory Decisions

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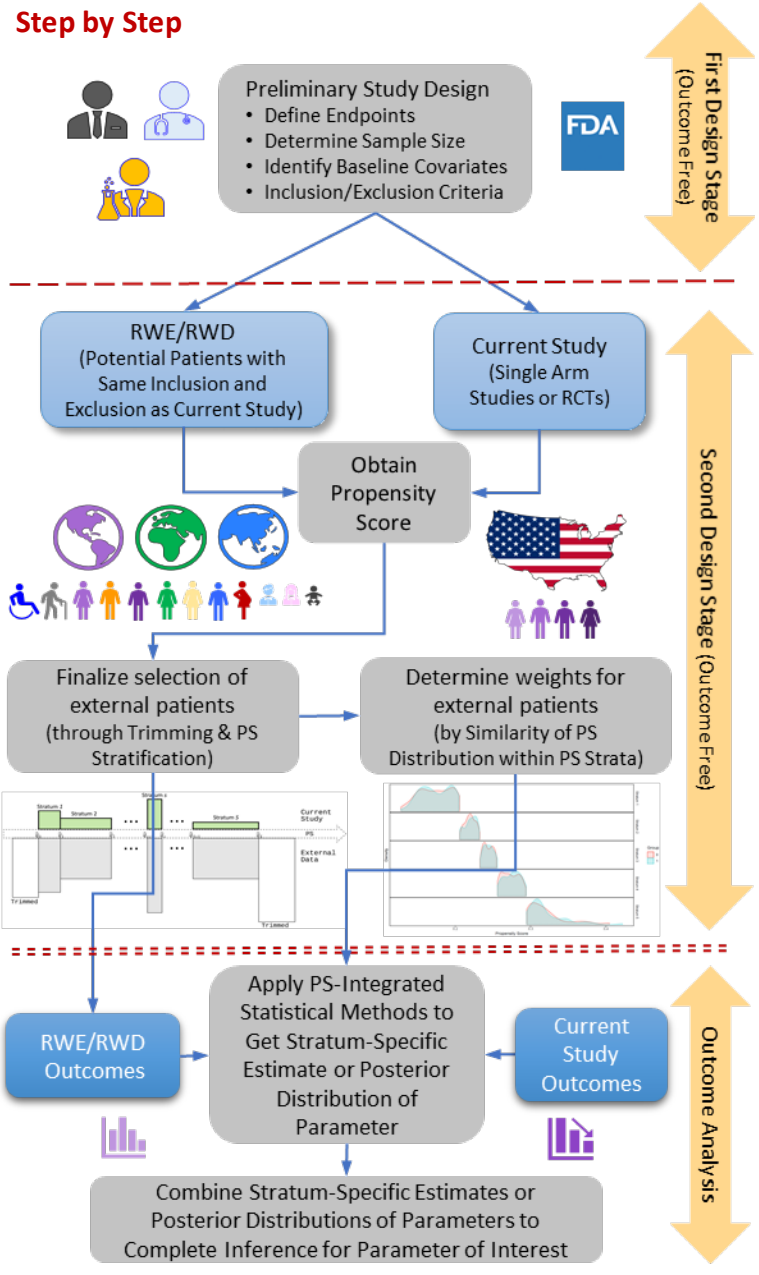
Introduction

Propensity score-integrated approaches (PS) are developed for incorporating patients from a real-world data (RWD) source to augment a single-arm or prospectively randomized (RCT) investigational clinical study. The approaches leverage real-world patients who are similar to those that are prospectively enrolled into the investigational clinical study, and then either Frequentist or Bayesian methods can be applied to outcome data analysis.

Methods

- Apply *two-stage study design* [1-3] and the *PS-integrated statistical methods* (Power Prior (PP) [1] or Composite Likelihood (CL) [2,3]) to augment:
  - Patient cohort enrolled in a single-arm investigational study [1,2]
  - Control arm of a randomized controlled trial [3]
- Two-stage study design (*outcome free*):
  - *1st stage:* preliminary study planning
  - *2nd stage:* using propensity score methodology
    - Select comparable patients from external data source
    - Determine the weights used to down-weight information of external patients
    - Finalize study design
- Outcome analysis:
  - Using PP [1] (*Bayesian*) or CL [2,3] (*Frequentist*) for statistical inference, while leveraging RWE/RWD

Step by Step



Results

Through simulation studies, the procedure shows that the bias and mean squared error for the parameter of interest (e.g., safety event rate in a single arm study or treatment effect in an RCT) can be reduced.

Conclusions

The implementation of PS-integrated approaches ensure the outcome free principle in clinical trials and properly utilize the RWE/RWD to augment the single arm studies and the RCTs for regulatory decision marking.

References

[1] Wang, C., Li, H., Chen, W.-C., Lu, N., Tiwari, R., Xu, Y., Yue, L. (2019), Propensity Score-Integrated Power Prior Approach for Incorporating Real-World Evidence in Single-Arm Clinical Studies. *Journal of Biopharmaceutical Statistics*, **29**(5), 731—748.

[2] Wang, C., Lu, N., Chen, W.-C., Li, H., Tiwari, R., Xu, Y., Yue, L., Propensity Score-Integrated Composite Likelihood Approach for Incorporating Real-World Evidence in Single-Arm Clinical Studies. *Journal of Biopharmaceutical Statistics*, **30**(3), 495—507.

[3] Chen, W.-C., Wang, C., Li, H., Lu, N., Tiwari, R., Xu, Y., and Yue, L. (2020), "Propensity Score-Integrated Composite Likelihood Approach for Augmenting the Control Arm of a Randomized Controlled Trial by Incorporating Real-World Data," *Journal of Biopharmaceutical Statistics*, **30**(3), 508—520.