Understanding how Baseline risk affects Treatment Outcomes in Clinical Trials: Exploring Key Factors

MSR84

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Conclusion

By incorporating baseline risk as a covariate in each trial, a significant decrease in the annualized relapse rate (ARR) was observed, indicating a favorable trajectory in treatment efficacy for patients with RRMS. These results underscore the importance of considering baseline risk in the initial analyses of trials to enhance comprehension of treatment effects and enhance therapeutic interventions for better patient outcomes.

Background

- Clinical trials are important for understanding how new treatments work and ensuring patients' safety. However, baseline risk is one of the important factors that affects trial results
- Baseline risk encapsulates the health status of patients before initiating treatment, embodying their pre-existing conditions or traits. Consequently, it plays a pivotal role in shaping treatment outcomes within the context of clinical trials
- Understanding how baseline risk and treatment benefits interact is crucial for fully understanding clinical trial analyses. To better understand this relationship, a method proposed by Thompson et al. is used in the analyses

Objective

- The objective of this research was to explore how baseline risk effects the outcomes of meta-analysis

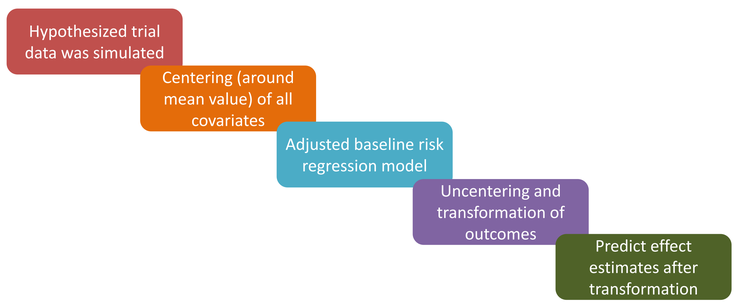
Methodology

- The methodology suggested by Thompson et al. was used to incorporate baseline risk (p_i) as a factor within each trial. In the model, p_i is treated as a random element, enabling its variation in every iteration of the Markov Chain Monte Carlo (MCMC) simulation
- This method effectively handles the natural correlation between the intercept and slope of the model. An aspect of this Bayesian approach is its inclusion of the "true" baseline, which the model estimates, as a factor. This inclusion automatically considers the uncertainty linked with baseline risk
- Instead of using a variable named x[i] for each study, p_i was used to represent the baseline risk for that study in the models (**Figure 1** provides an overview of the analysis flow)

Methodology (Cont'd)

- To assess the relative treatment effects on the annualized relapse rate (ARR), meta-regression models were used, and covariate values were centered on a common baseline risk value with a Poisson likelihood and a log link function
- The models were run using JAGS in the R software environment via the R2jags package.
- The choice of the preferred model was based on a comparison of the deviance information criterion (DIC) and residual deviance statistics
- Convergence diagnostics on the re-centered parameters were obtained using the coda R package
- The average baseline risk across studies was subtracted from the baseline risk estimated for each study in the network. Treatment effects from the model were interpreted as the effects for a cohort with the average baseline risk. These effects can be un-centered and transformed to produce effect estimates at any specified baseline risk
- Four regression analyses were utilized, including random and fixed effects models with common or exchangeable covariates
- Model convergence and chain mixing were assessed statistically and graphically using various diagnostics such as Brooks-Gelman-Rubin R hat, effective independent simulation draws, and trace plots

Figure 1: Analyses Flow diagram



Results

- The log-rate ratios were adjusted based on the mean baseline risk of the population. This adjustment allowed determining the relative treatment effects on the rate ratio scale
- The baseline risk regression results indicated significant overlap in the credible intervals for the rate ratios of ARR, suggesting that no therapy is statistically dominated in terms of efficacy **(Figure 2)**
- The deviance information criterion (DIC) and posterior means of the residual deviances for the four models did not indicate a clear preference for any single model
- However, after considering the influence of increasing complexity on model fit and the improvement in residual deviance, a random effect model with a common covariate effect was chosen as the preferred model **(Table 1)**

Figure 2: Forest plot showing relative risk across different treatments in comparison to treatment 1

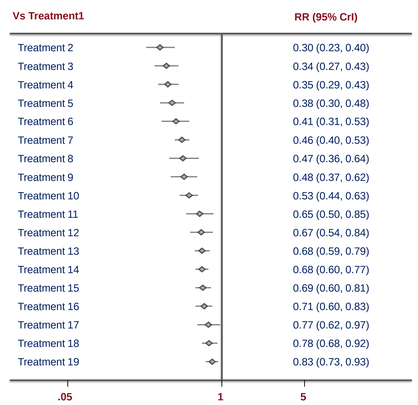


Table 1: Goodness of fit statistic for meta-regression models

	DIC	pD	Deviance
Fixed effect with common covariate	782.49	62.98	108.40
Fixed effect with exchangeable covariate	783.02	65.74	106.30
Random effect with common covariate	783.20	68.90	103.00
Random effect with exchangeable covariate	783.58	71.20	101.03

Disclosure

AS, SP and BS, the authors, declare that they have no conflict of interest

References

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Presented at ISPOR • ISPOR USA | Atlanta, GA, USA | May 5-8, 2024

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