Improving Indirect Treatment Comparisons via an Alternative Patient Weighting Scheme

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Introduction

Indirect treatment comparisons (ITCs) estimate the effectiveness of treatments not directly compared in head-to-head trials. When trial populations differ, unadjusted ITCs can be biased due to differences in baseline characteristics. Matching-adjusted indirect comparison (MAIC) addresses this bias by reweighting individual patient data (IPD) to match the baseline characteristics of a target trial.

The effective sample size (ESS) reflects the amount of information retained after reweighting; higher ESS reduces variability in treatment estimates. The approach introduced by Signorovitch et al. 2010 [1] is the industry standard when estimating patient weights (PWs) in MAICs (SignMAIC). Though alternatives exist, none have usurped this method. The PolyMAIC approach, introduced by Alsop and Pont 2016 [2], has shown potential to retain more information.

Methods

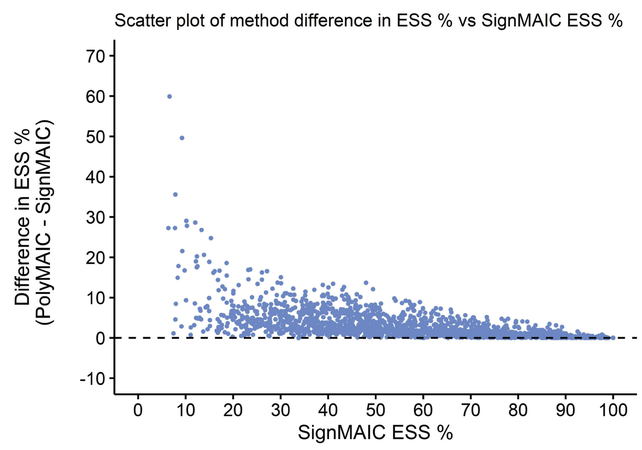
To compare PolyMAIC against SignMAIC, IPD and target aggregate-level data (ALD) were simulated for 2000 scenarios. The design factors of the data generation process included:

- Number of characteristics to match on (1,2,3,4,5)
- Characteristic distribution types (binary, normal, log–normal)
- IPD sample size (50, 100, 250, 500)
- Correlation of baseline characteristics (Multivariate normal Spearman r=0, 0.2, 0.4)
- Difference in baseline distributions between (unweighted) IPD and target data

PWs for SignMAIC were estimated in R using code provided in NICE's TSD [3]. The PolyMAIC method was implemented in R using the gradient-based SLSQP algorithm via the NLOPTR package [4, 5]. PolyMAIC allows for user-specified tolerances (acceptable differences between weighted and target statistics). These were set to ensure that PolyMAIC matched target statistics as well as, or better than, SignMAIC.

Performance of the weighting methods was assessed using the ESS as a percentage of the original IPD sample size (ESS %), and the maximum estimated PW.

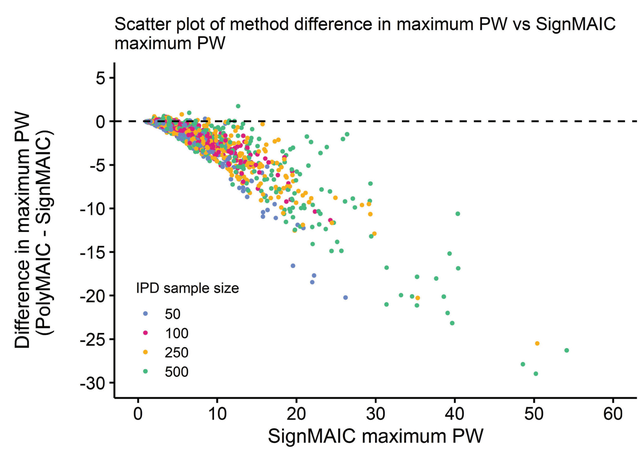
Figure 1



Results

In all scenarios, PolyMAIC matched the target summary statistics as well as, or better than, SignMAIC. The ESS %s obtained from SignMAIC reflected the broad range of overlap between the IPD and their respective ALD targets across the scenarios. PolyMAIC was able to retain a higher proportion of IPD information during the matching process. On average, ESS % was 2.8% higher for PolyMAIC compared to SignMAIC. The difference in ESS % was most notable when ESS % for SignMAIC was low (Figure 1). Lower IPD sample sizes and higher number of matching variables were also associated with a greater improvement in performance for PolyMAIC versus SignMAIC. The maximum PW was on average 1.8 lower with PolyMAIC compared to SignMAIC (Figure 2).

Figure 2

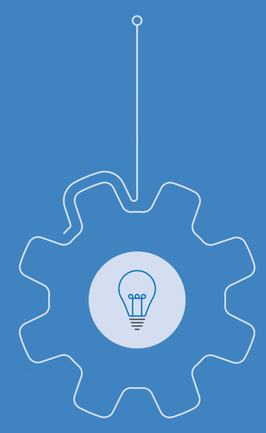


Conclusion

PolyMAIC consistently outperformed the industry standard Signorovitch method to estimate PWs.

Our new approach achieved a more statistically efficient set of PWs across a broad range of scenarios whilst matching baseline characteristics. The performance gain was greater in more complex scenarios where SignMAIC could not retain a high proportion of information.

For more information, please contact us at polymaic@numerus.com.



References

[1] **J Signorovitch, et al.** "*Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept.*" Pharmacoeconomics 28 (2010): 935-945.
[2] **J Alsop, L Pont.** "*Matching-adjusted indirect comparison via a polynomial-based non-linear optimization method.*" Journal of Comparative Effectiveness Research 11.8 (2022): 551-561.
[3] **D Phillippo, et al.** "*NICE DSU technical support document 18: methods for population-adjusted indirect comparisons in submissions to NICE.*" (2016).
[4] **S Johnson.** The NLopt nonlinear-optimization package. https://nlopt.readthedocs.io/en/latest/.
[5] **https://github.com/Numerus-Ltd/polyMAIC**

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