Population Adjusted-Indirect Comparisons in Health Technology Assessment: A Methodological Systematic Review

HTA20

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INTRODUCTION

In health technology assessment (HTA), population-adjusted indirect comparisons (PAICs) are increasingly considered to adjust for the difference in the target population between studies. We aim to assess the conduct and reporting of PAICs in recent HTA practice.

METHODS

Methodological systematic review of all papers that reported the use of a population-adjusted indirect comparison method to account for the difference between study populations prior to assessing the treatment effectiveness. Articles were retrieved from PubMed, EMBASE Classic, Embase/Ovid Medline All, and Cochrane databases from 01/01/2010 to 02/13/2023. We extracted: (i) general characteristics, (ii) methodological characteristics of the conducted PAIC analysis and (iii) reporting and discussions of the PAIC results.

RESULTS

- ❑ Of 3990 identified records, 162 eligible articles were included.
- ❑ General characteristics: More than half of these records are in oncology (58.0%, n=94). Most PAICs were conducted to assess the effectiveness or safety of pharmacological interventions (96.3%, n=156) on a binary (46.9%, n=76) or time-to-event outcome (40.7%, n=66). Most of the eligible records (96.9%, n=157) were conducted by, or received funding from pharmaceutical companies.
- ❑ Methodological characteristics of the PAIC analysis and reporting of the PAIC results were summarized in Table 1 and Table 2.
- ❑ We also proposed in some practical recommendations to assist applied researchers in avoiding the pitfalls encountered in this review (**See Additional Information – QR code**).

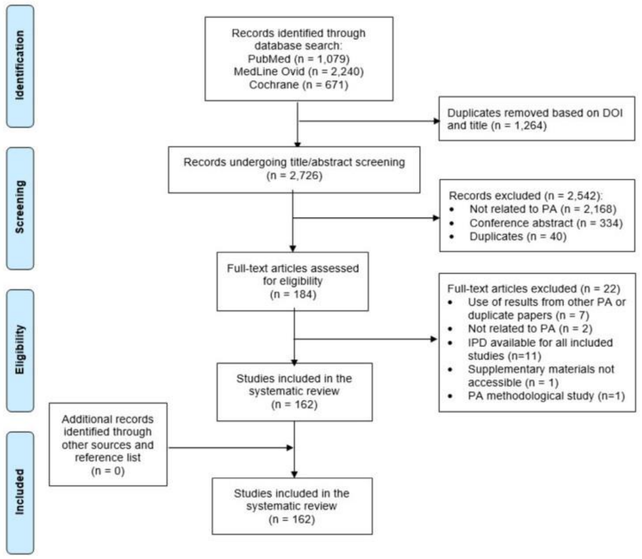

Figure 1. PRISMA flowchart

REFERENCES AND ADDITIONAL INFO

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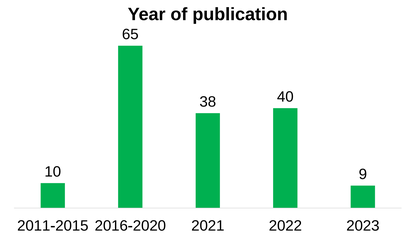

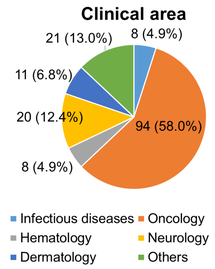

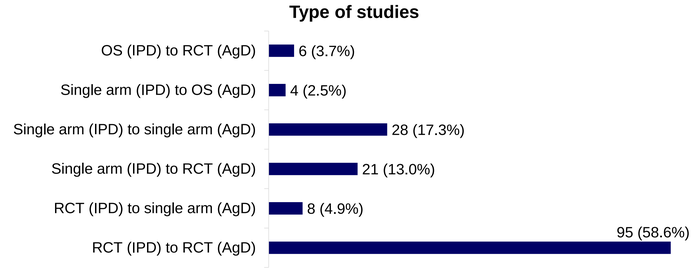

Figure 2. Characteristics of eligible studies

Table 1. Methodological characteristics of the PAIC analysis across studies

Characteristics	Statistics
Population adjustment methods, N(%)	
▪ Matching-Adjusted Indirect Comparison (MAIC)	144 (88.9)
▪ Simulated Treatment Comparison (STC)	11 (6.8)
▪ Both MAIC and STC	6 (3.7)
▪ Multilevel Network Meta Regression (ML-NMR)	1 (0.6)
Type of comparison, N(%)	
▪ Anchored	57 (35.2)
▪ Unanchored	105 (64.8)
Handling multiple treatments (>2 for unanchored and >3 for anchored comparisons), N(%)	50 (30.9)
▪ Separate PAIC analysis for each pair (or each group of three) of treatments	48 (29.6)
▪ One common analysis for the entire treatment network (e.g., by using ML-NMR)	2 (1.2)
Handling multiple studies (>2) with IPD, N(%)	42 (25.9)
▪ Studies with IPD merged	41 (25.3)
▪ Studies with IPD kept apart (by using ML-NMR)	1 (0.6)
Handling multiple studies (>2) with AgD, N(%)	37 (22.8)
▪ Studies with AgD pooled	34 (21.0)
▪ Separate PAIC analysis for each AgD study	3 (1.8)
Before adjustment, the eligibility criteria of one study (i.e. the one with AgD) were used to refine the patient sample of other studies (with IPD), N(%)	
▪ No	90 (55.5)
▪ Partially	33 (20.4)
▪ Fully	39 (24.1)
Bias/quality assessment of each study included in the PAIC analysis	
▪ Yes	15 (9.3)
▪ No	147 (90.7)
Heterogeneity assessment, N(%)	
▪ No description/discussion	18 (11.1)
▪ Informal assessment	40 (24.7)
▪ Partially/fully formal assessment	104 (64.2)
Covariates	
Number of adjusted covariates, Med (IQR)	7 (5-9)
Covariates selection based on, N(%):	
▪ Availability of covariates across eligible studies	67 (41.4)
▪ Experts' opinions	77 (47.5)
▪ Statistical methods	47 (29.0)
▪ Literature reviews	45 (27.8)
Evaluation of case-mix overlap between populations (MAIC-specific), N(%)	
▪ No evaluation	24 (16.0)
▪ By effective sample size	117 (78.0)
▪ By checking the presence of extreme weights	15 (10.0)
▪ Others	20 (13.3)
Sensitivity analysis to assess the robustness of PAIC results	
▪ No sensitivity analysis	77 (47.5)
▪ Adjusting for different sets of covariates	55 (34.0)
▪ Applying additional inclusion/exclusion criteria to the IPD study	19 (11.7)
▪ Using different outcome definitions	7 (4.3)
▪ Using different follow-up time	11 (6.8)
▪ Others	12 (7.4)

Med, Median. IQR, Interquartile range. MAIC, Matching-adjusted indirect comparison. STC, Simulated treatment comparison. IPD, Individual patient data. AgD, Aggregate data. PAIC, Population-adjusted indirect comparison.

Table 2. Reporting and discussions of PAIC results

Characteristics	Statistics
Covariate distribution in each study before adjustment reported, N(%):	
▪ Not described	11 (6.8)
▪ Partially described*	42 (25.9)
▪ Fully described**	109 (67.3)
Covariate distribution in each study after adjustment reported (MAIC-specific), N(%): (N=150)	
▪ Not described	15 (10.0)
▪ Partially described*	40 (26.7)
▪ Fully described**	95 (63.3)
Results of the model fitting procedure reported (i.e., coefficient estimates and uncertainty measures, STC-specific), N (%): (N=18)	
▪ Not reported	15 (83.3)
▪ Fully reported (both coefficient estimates and uncertainty measures)	3 (16.7)
Comparison of results before and after population adjustment	
▪ No	48 (29.6)
▪ Yes	114 (70.4)
Discussion about whether the change of results after population adjustment is clinically relevant (N=114)	
▪ No	88 (77.2)
▪ Yes	26 (22.8)
Limitations acknowledged by authors:	
▪ No acknowledgement	5 (3.1)
▪ Unmeasured covariates	136 (84.0)
○ Unmeasured covariates explicitly mentioned	33 (20.4)
▪ Important covariates not reported in one of the included studies	60 (37.0)
▪ Limited sample size	31 (19.1)
▪ Heterogeneity across studies	139 (85.8)
▪ Small ESS/little overlap between populations	35 (21.6)
▪ Lack of a common comparator	23 (14.2)
▪ Others	7 (4.3)

MAIC, Matching-adjusted Indirect Comparison. SE, Standard Error. CI, confidence interval. ESS, Effective Sample Size. *Either (i) a measure of central tendency (e.g. mean, median) or (ii) a measure of dispersion (e.g. standard deviation, interquatile range) was not reported for each covariate. **Both (i) and (ii) were reported for each covariate.

CONCLUSION

The conduct and reporting of PAICs are remarkably heterogeneous and suboptimal in current practice. More recommendations and guidelines on PAICs are thus warranted to enhance the quality of these analyses in the future.