How prognostic factors are identified for population matching analysis

MSR125

Juliette C Thompson, Eric Manalastas, David A Scott || Visible Analytics Ltd

Juliette.Thompson@VisibleAnalytics.co.uk || Eric.Manalastas@VisibleAnalytics.co.uk || David.Scott@VisibleAnalytics.co.uk

INTRODUCTION

- Indirect treatment comparisons in health technology assessment (HTA) submissions are increasingly using uncontrolled phase 2 data or real-world studies requiring the use of population matching techniques to compare to relevant comparators
- Prognostic factors (PFs) and treatment effect modifiers are fundamental to the conduct of meaningful population matching analyses (matching adjusted indirect comparisons [MAIC], simulated trial comparisons [STC]) yet there are no formal recommendations or consensus for their identification
- We conducted a review of analyses in 'musculoskeletal diseases' (excluding oncology) that used population matching to determine how each analysis identified relevant PFs to be adjusted for

METHODS

- A systematic literature review was conducted using the following eligibility criteria:

Population	Adults with a musculoskeletal disease
Intervention/comparator	Any
Outcome	Any
Study design	Population matching adjusted analysis (MAIC, STC, ML-NMR)
Other	Conference abstracts were excluded due to their limited reporting

- Searches were conducted in Medline and Embase (via Embase.com)
- Abstracts and full papers were assessed by two reviewers and data was extracted as per Table 1

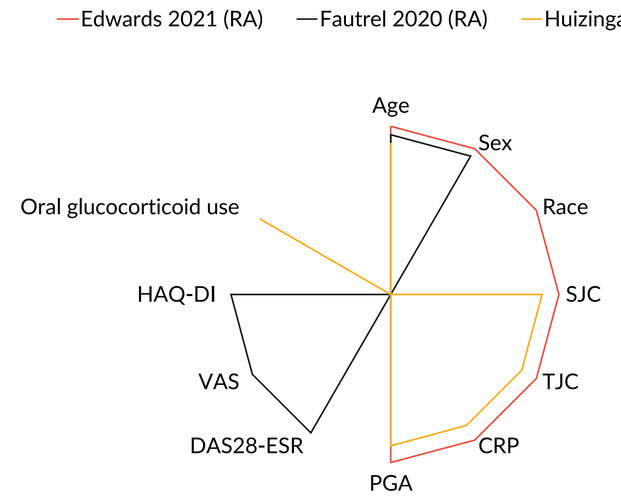
RESULTS

- Searches were conducted on 26-May-2023; 52 abstracts were reviewed and 11 population matching analyses included (Table 2)

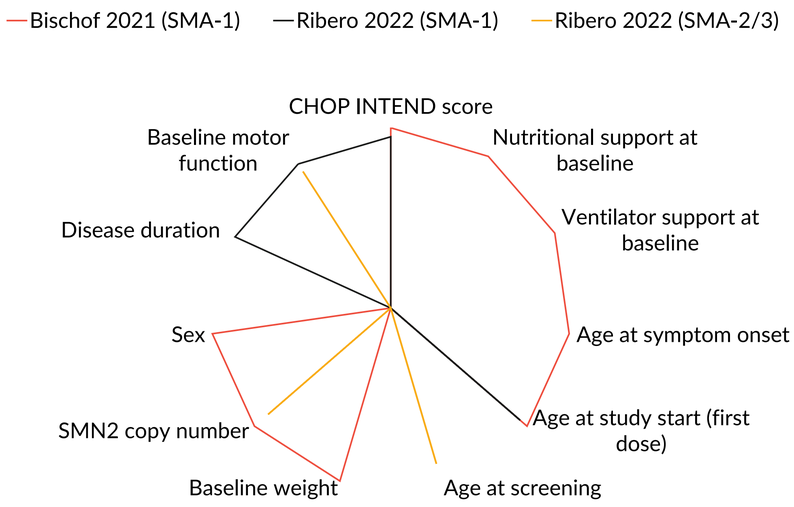
Author	Indication	Population matching technique	Identification of prognostic factors & treatment effect modifiers				
			Clinical trial	Clinical/ statistical experts	Prior MAIC/STC or literature	Published SLR of prognostic factors	Not specified
Bischof (2021)	SMA Type 1	MAIC		✓			
Edwards (2021)	RA	MAIC	✓				
Fautrel (2020)	RA	MAIC					✓
Huizinga (2023)	RA	MAIC and STC	✓	✓			
Kirson (2013)	PsA	MAIC	✓	✓			
Klamroth (2021)	Haemophilia A	MAIC	✓				
Nash (2018)	PsA	MAIC	✓				
Ribero (2022)	SMA type 1, 2/3	MAIC				✓	
Strand (2019)	PsA	MAIC			✓		
Tremblay (2021)	GVHD	STC		✓	✓		
Wahono (2023)	Ankylosing spondylitis	MAIC					✓

Abbreviations: GVHD: graft-versus-host disease; MAIC: matching adjusted indirect comparison; PsA; psoriatic arthritis; RA: rheumatoid arthritis; SLR: systematic literature review; SMA: spinal muscular atrophy; STC: simulated trial comparison

- The two most frequently used methods to identify PFs were:
  - **Clinical trials →** analyses adjusted for all baseline characteristics which were reported in both trials
  - **Clinical/statistical experts →** analyses adjusted for baseline characteristics which were determined as most important by clinical or statistical experts
- The PFs identified from those used in prior MAICs included an earlier analysis conducted by the same authors (Strand 2017), and Nash 2018, which adjusted based on clinical trial baseline characteristic cross-over
- In the three analyses in RA, the only PF used across all analyses was age; sex, SCJ, TJC, CRP and PGA were used in two analyses:



- Ribero 2022 was the only set of analyses to specify the methodological identification of prognostic factors, using data from a recent systematic literature review of prognostic factors in SMA (Baranello 2021)
- In the two analyses in SMA Type 1, there were only two PFs which were adjusted for in both analyses: CHOP INTEND score and age at study start



CONCLUSIONS

- A key facet of evidence-based medicine is the comprehensive, unbiased identification of data, typically by the conduct of systematic literature reviews
- Whilst population matching techniques constitute an advancement in evidence-based medicine, greater consideration should be given to the identification of PFs and treatment effect modifiers in order to increase the validity of findings
- Clinical opinion, which is placed on the lowest evidence level on the hierarchy of evidence, featured in PF identification across the majority of the analyses we identified
- Only one analysis cited a recent systematic review used to inform PFs included in their analysis
- Our review highlights inconsistent prognostic factors featured in analysis of the same indications, which could be attributed to less than reliable methods of elicitation
- Ideally a systematic review should be commissioned to support the choice of prognostic factors and treatment effect modifiers in population matching

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