

Performance of MAIC under covariate imbalance: Insights from real-world data and simulation

BACKGROUND

Single-arm trials are increasingly used to assess new therapies, often without direct comparative evidence. Robust analytical methods are therefore needed to support indirect comparisons using heterogeneous data sources. Among them, the matched-adjusted indirect comparison (MAIC) allows comparison of individual-level data from a single-arm study with aggregated data from an external comparator.

OBJECTIVES

The objective is to illustrate the use of MAIC on treatment comparison and to evaluate the impact of variables selected for MAIC adjustment.

METHODS

Database and study population

Individual-level National Health Data System (SNDS) data were used to compare treatment A and B for 2,486 patients enrolled from 2018 to 2022 and followed until 2023. The treatment effect on overall survival (OS) was assessed using the weighted Kaplan-Meier method and the weighted Cox model.

Comparison with a gold-standard method

To obtain a gold-standard estimate, an IPTW was computed to the full individual-level dataset and compared with an unanchored MAIC using individual data for treatment A and aggregated data for treatment B. Adjustment variables included age, sex, comorbidities and emergency room or ICU history.

Simulation framework

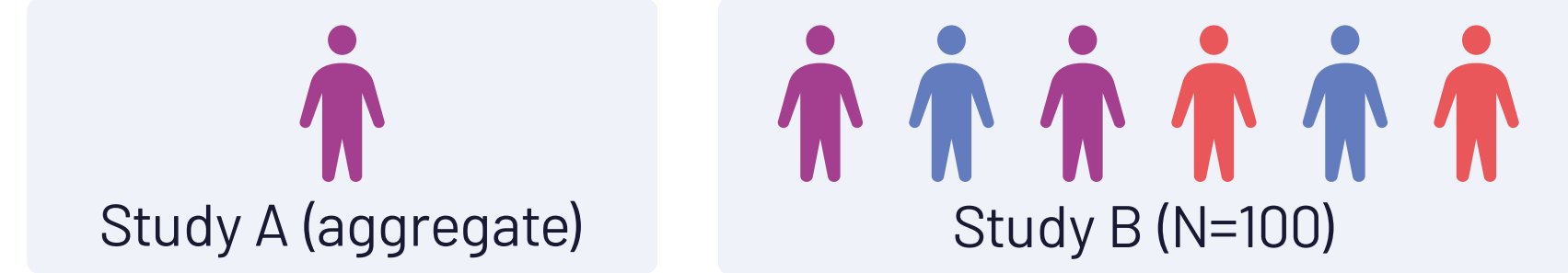
A simulation framework was developed to evaluate MAIC performance under controlled conditions. Survival times were generated from a Weibull distribution incorporating adjustment variables and treatment, yielding HRs of treatment from 0.5 to 1.5. Variables were added incrementally to the MAIC weighting to evaluate impact on effective sample size (ESS), bias (HR ratio), confidence-interval width (CI) and coverage rate (CR) of HRs.

METHODOLOGY OVERVIEW

1 Population and variables

Similar study population in the two studies
Selection of variables to use in matching
⇒ Validation with experts

2 Available data

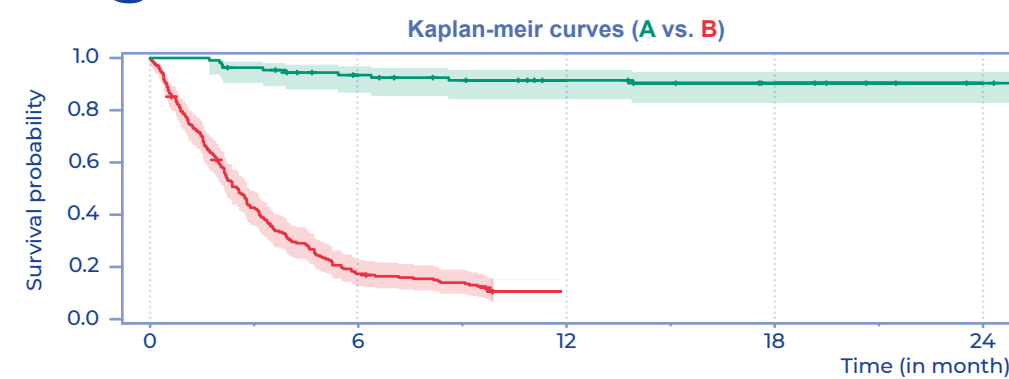


3 Calculation of weight and ESS



4 Calculation of weighted outcome

Example :
Overall survival



CONCLUSION

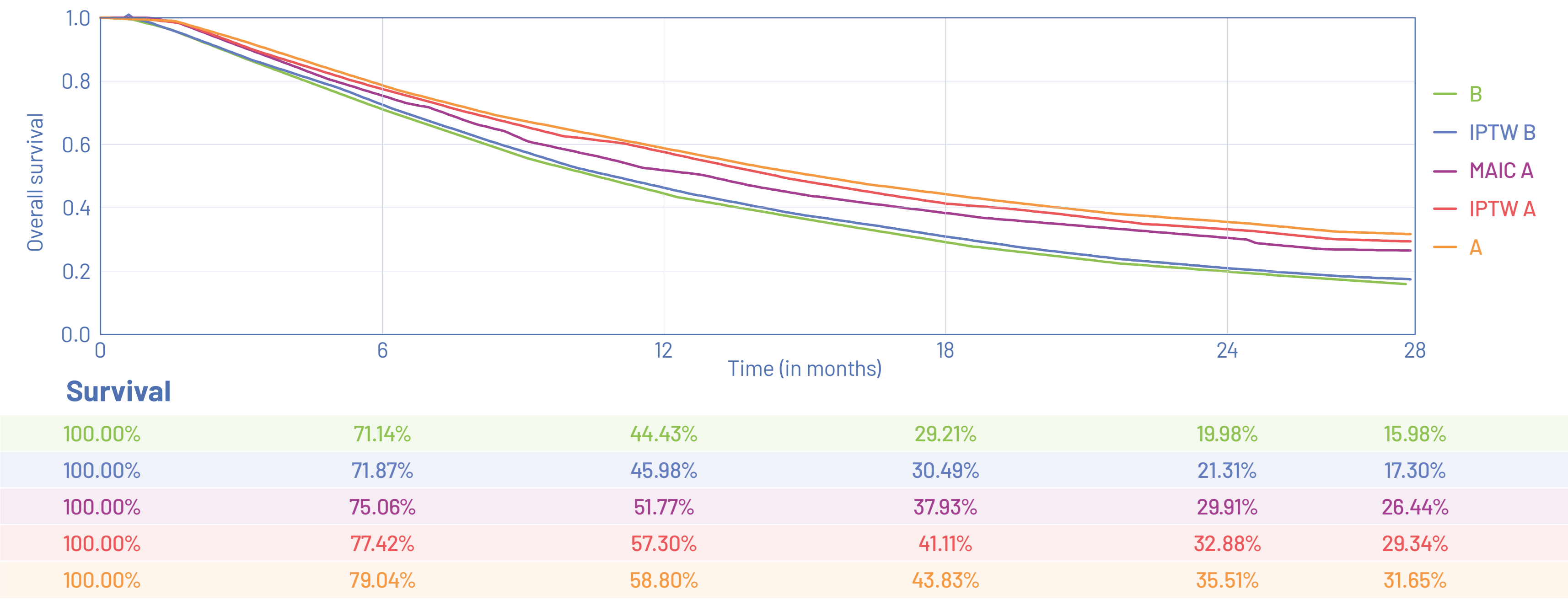
MAIC enables indirect comparisons using individual and aggregated data, but including variables with large treatment imbalances markedly reduces ESS and may lead to overestimation of treatment effects, reduced precision, and poorer HR coverage. When key variables show large imbalance, alternative external data source or designs should be considered.

RESULTS

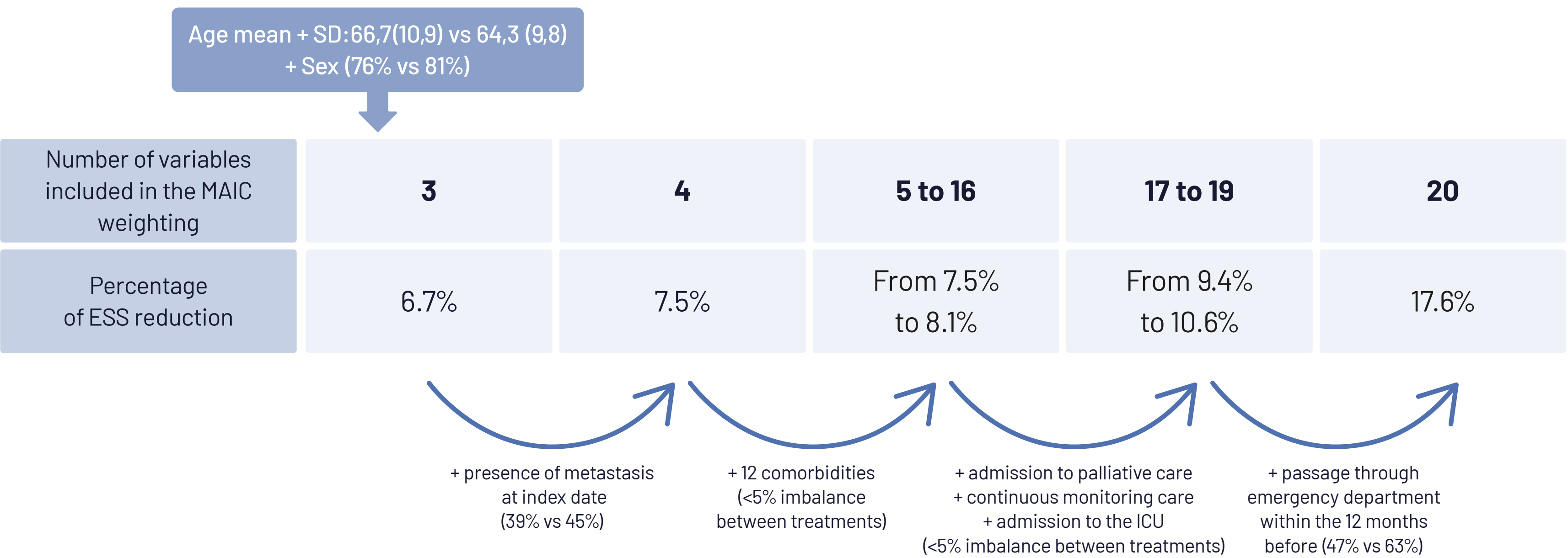
Comparison with a gold-standard method

The restricted mean survival time (RMST) and the median time of treatment A were similar across methods (IPTW : 15.89 and 14.49 months; MAIC : 15.02 and 12.81 months). The hazard ratio (HR) between MAIC and IPTW methods were close (IPTW: 0.73 [0.68 ; 0.78] ; MAIC: 0.78 [0.72 ; 0.84]).

Case	RMST	Median	Median	HR A vs. B	P-value
B	13,04	10,48	Non-adjusted	0,65 [0,62 ; 0,69]	<0.0001
IPTW B	13,36	10,87	IPTW	0,73 [0,68 ; 0,78]	<0.0001
A	16,45	15,18	MAIC	0,78 [0,72 ; 0,84]	<0.0001
IPTW A	15,89	14,49			
MAIC A	15,02	12,81			



Impact of variables on effective sample size

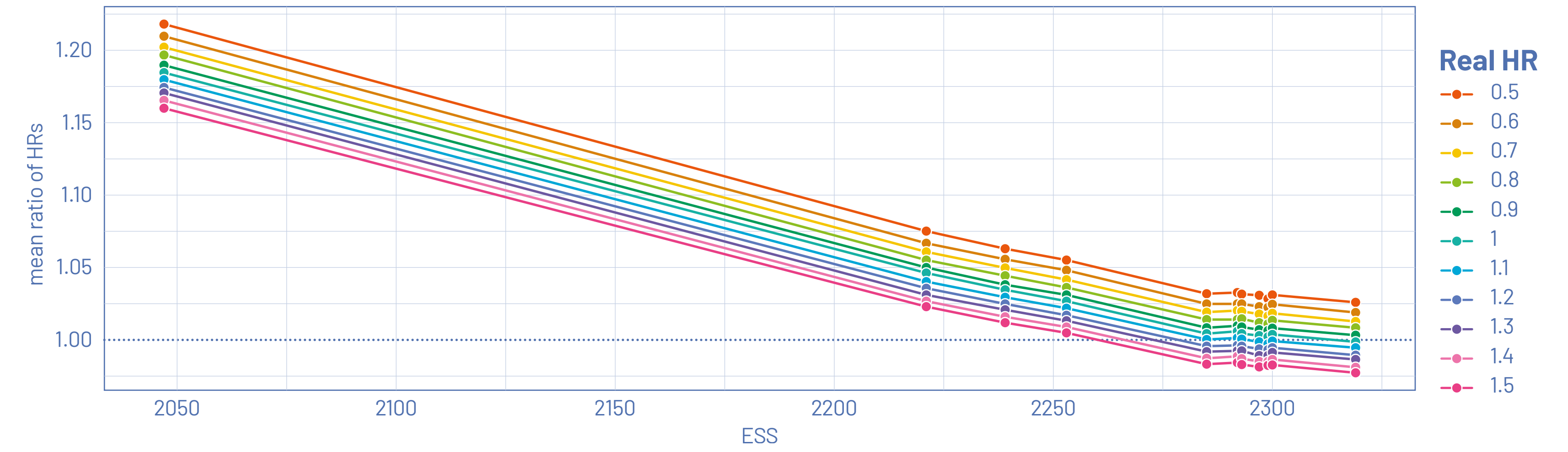


Simulation Results

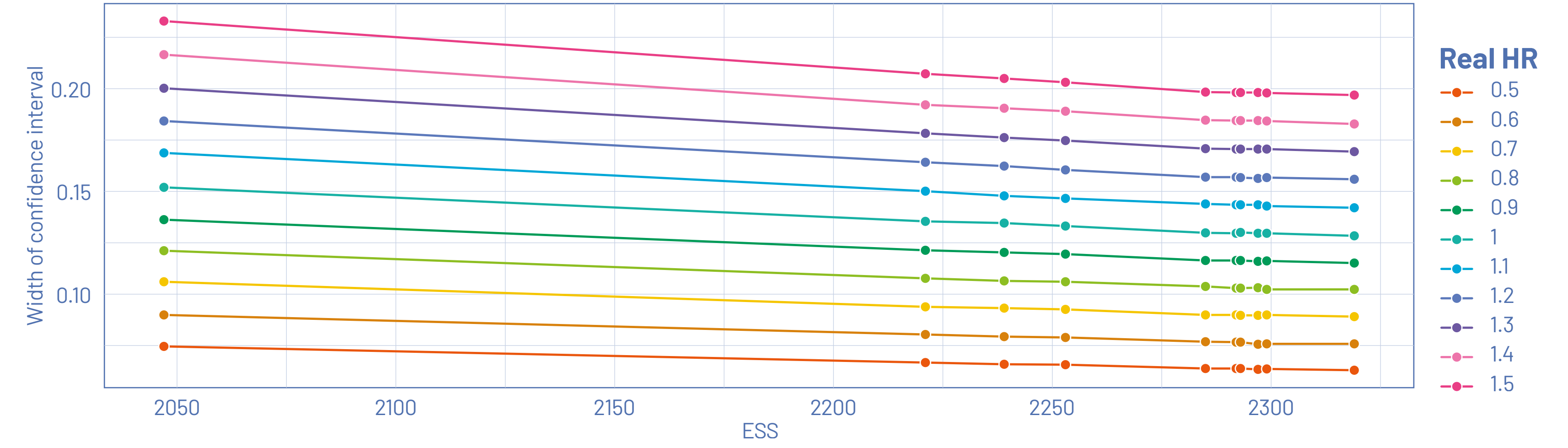
MAIC consistently concludes that the protective effects are smaller (HR < 0.9), and CI width increased as ESS decreased.

CR worsened with increasing protective effect (CR 98% at HR 0.9; 77% at HR 0.7; 18% at HR 0.5). Adding the variable with a 10% difference causes a sharp drop in the CR.

Changes in the ratio between the real HR based on individual data and the HR obtained using MAIC



Changes in the width of the confidence interval performed with MAIC



MAIC coverage rate

