Optimizing Parametric Model Selection: An Analysis Using Constructed IPD Extracted from Oncology Trials From 2014 to 2023?

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Introduction

In survival analysis, it's crucial to extrapolate survival estimates beyond clinical trial follow-up limits. Choosing the adequate model is crucial to address extrapolation uncertainty.

Objectives

1. To evaluate the goodness-of-fit (GoF) of various survival models, including direct GoF for single treatments and relative GoF between regimens.
2. To compare the performance Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC)
3. To evaluate the impact of minimal number-at-risk considerations (consideration-minnrisk) during individual patient data (IPD) reconstruction

Methods

1. Oncology trials approved by the FDA in the past 10-year were included. IPD were reconstructed from survival curves.
2. Standard Parametric Models (SPM), Fractional Polynomials (FP), Restricted Cubic Splines (RCS), Royston-Parmar models (RPM), Generalized Additive Models (GAM), and Parametric Mixture Models (PMM) were evaluated
3. Three GoF assessments (within-sample [GoF-f], extrapolation [GoF-e], and combined [GoF-fe]) were evaluated, measured mainly by Mean Absolute Error (MAE) and differences in Restricted Mean Survival Time between the parametrically extrapolated curves and updated Kaplan-Meier curves.
4. GoF were compared using Wilcoxon Signed-Rank test, subgroup analyses and linear regressions assessed result robustness. Using machine learning to build predictive models for optimal extrapolation.

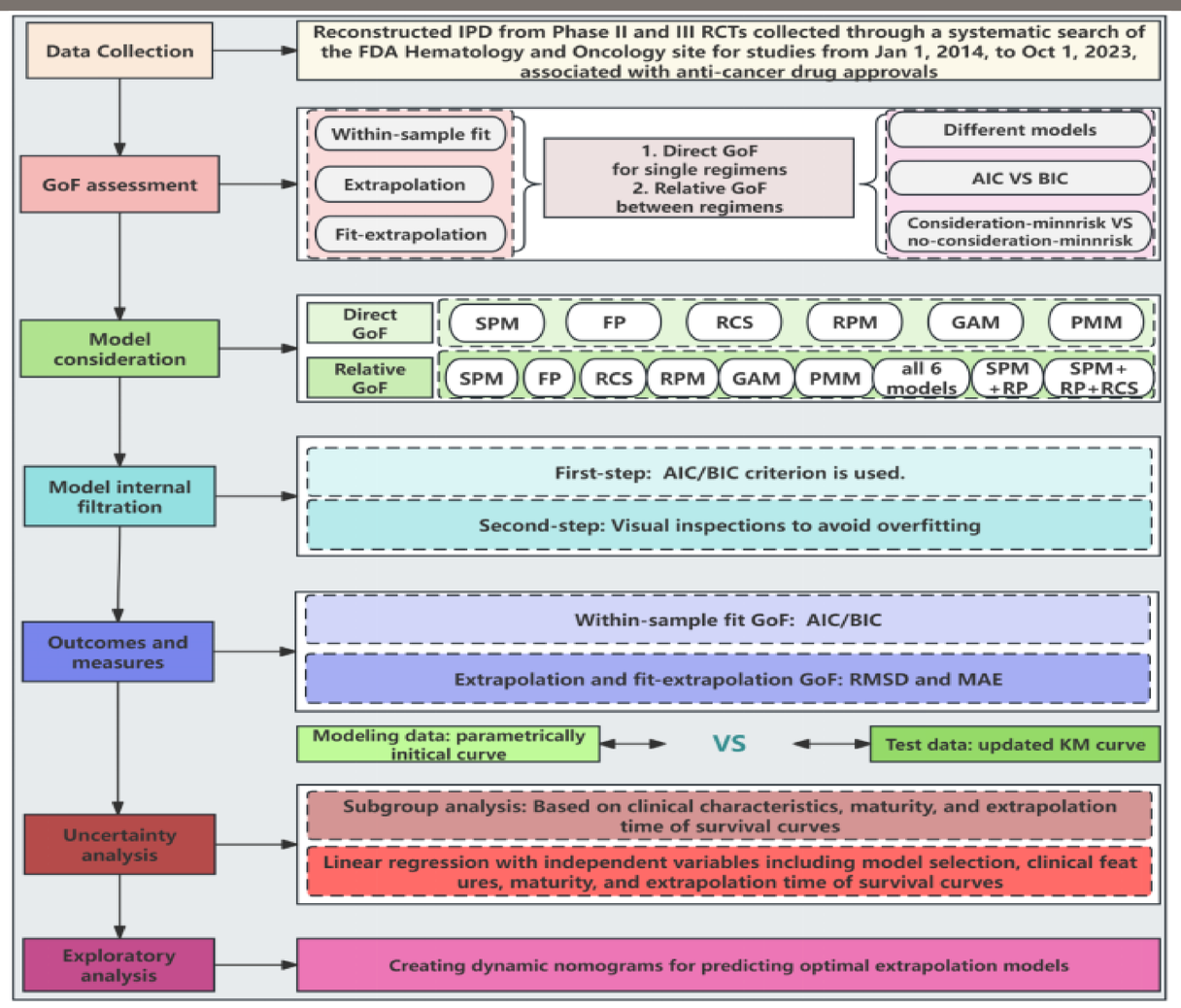

***Figure* 1 .** Flow chart of study process. AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion;.FP, fractional polynomials; GAM, generalized additive models; GoF, goodness-of-fit; MAE, mean absolute error; IPD, Individual patient data; PMM, parametric mixture models; RCS, restricted cubic splines; RMSD, Restricted Mean Survival Time; RPM, Royston-Parmar spline; SPM, standard parametric models.

Results

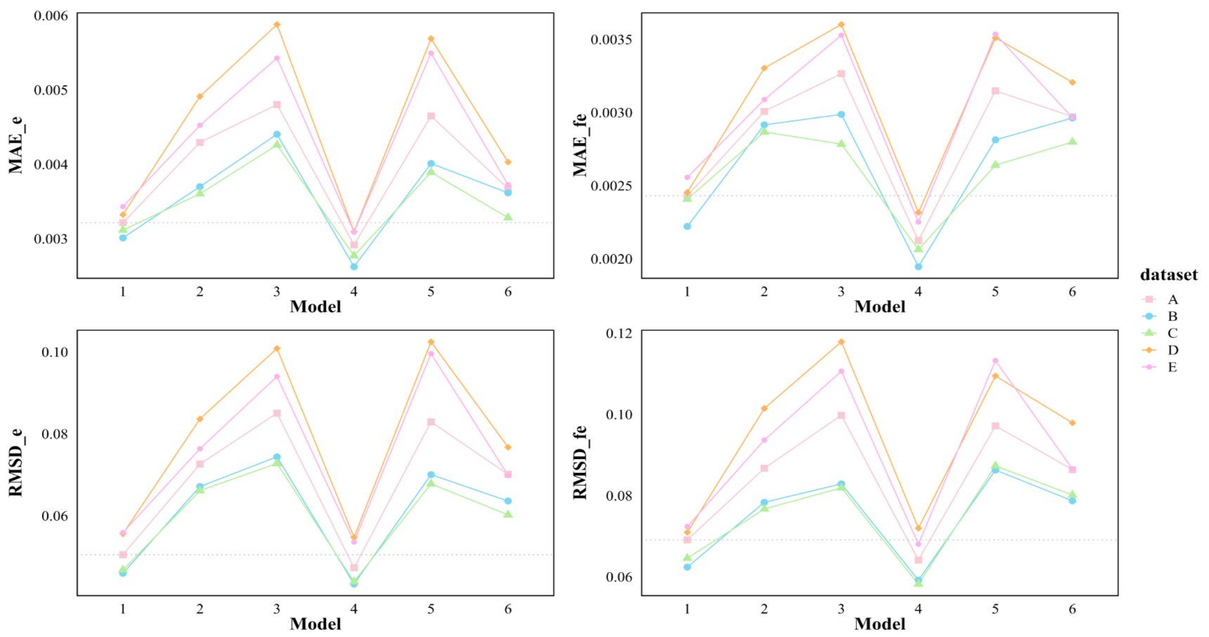

***Figure* 2 .** Direct goodness-of-fit for six models.
Dataset A-E: A, pooled analysis of AIC/BIC criterion and consideration/no consideration of minnrisk; B, consideration of AIC criterion and minnrisk; C, consideration of BIC criterion and minnrisk; D, consideration of AIC criterion and no consideration of minnrisk; E, consideration of BIC criterion and no consideration of minnrisk.
Model 1-6: 1, standard parametric models; 2, fractional polynomials; 3, restricted cubic splines; 4. Royston-Parmar spline; 5, generalized additive models; 6, parametric mixture models.
AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; e, extrapolation goodness-of-fit; fe, fitting-extrapolation goodness-of-fit; GoF-e, extrapolation goodness-of-fit; GoF-fe, goodness-of-fit concerning within-sample fit combined with extrapolation; minnrisk, minimal number-at-risk; MAE, mean absolute error; RMSD, Restricted Mean Survival Time

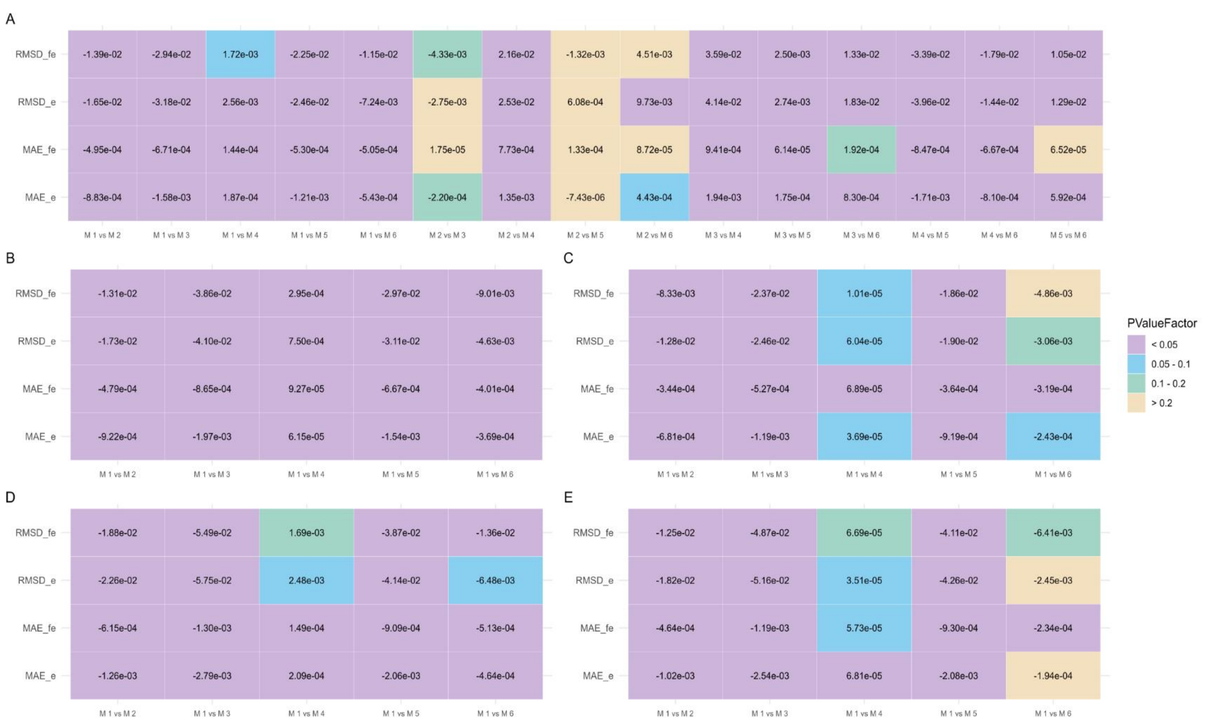

***Figure* 3 .** Comparative results of direct GoF-e/GoF-fe.
A-E: A, consideration of AIC criterion and minnrisk; B, pooled analysis of AIC/BIC criterion and consideration/no consideration of minnrisk; C, consideration of BIC criterion and minnrisk; D, consideration of AIC criterion and no consideration of minnrisk; E, consideration of BIC criterion and no consideration of minnrisk.
M 1-M 6: M 1, standard parametric models; M 2, fractional polynomials; M 3, restricted cubic splines; M 4. Royston-Parmar spline; M 5, generalized additive models; M 6, parametric mixture models.
e, extrapolation goodness-of-fit; fe, fitting-extrapolation goodness-of-fit; GoF-e, extrapolation goodness-of-fit; GoF-fe, goodness-of-fit concerning within-sample fit combined with extrapolation; MAE, mean absolute error; minnrisk, minimal number-at-risk; RMSD, Restricted Mean Survival Time
Note: For values in the cells in A-E: difference in GoF between two models (the value in the cell labeled "M 1 VS M 2, RMSD_fe" represents the difference in RMSD_fe between Model 2 and Model 1)

***Figure* 4 .** Direct goodness-of-fit for six models.
Dataset A-E: A, pooled analysis of AIC/BIC criterion and consideration/no consideration of minnrisk; B, consideration of AIC criterion and minnrisk; C, consideration of BIC criterion and minnrisk; D, consideration of AIC criterion and no consideration of minnrisk; E, consideration of BIC criterion and no consideration of minnrisk.
Model 1-6: 1, standard parametric models; 2, fractional polynomials; 3, restricted cubic splines; 4. Royston-Parmar spline; 5, generalized additive models; 6, parametric mixture models.
AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; e, extrapolation goodness-of-fit; fe, fitting-extrapolation goodness-of-fit; GoF-e, extrapolation goodness-of-fit; GoF-fe, goodness-of-fit concerning within-sample fit combined with extrapolation; minnrisk, minimal number-at-risk; MAE, mean absolute error; RMSD, Restricted Mean Survival Timev

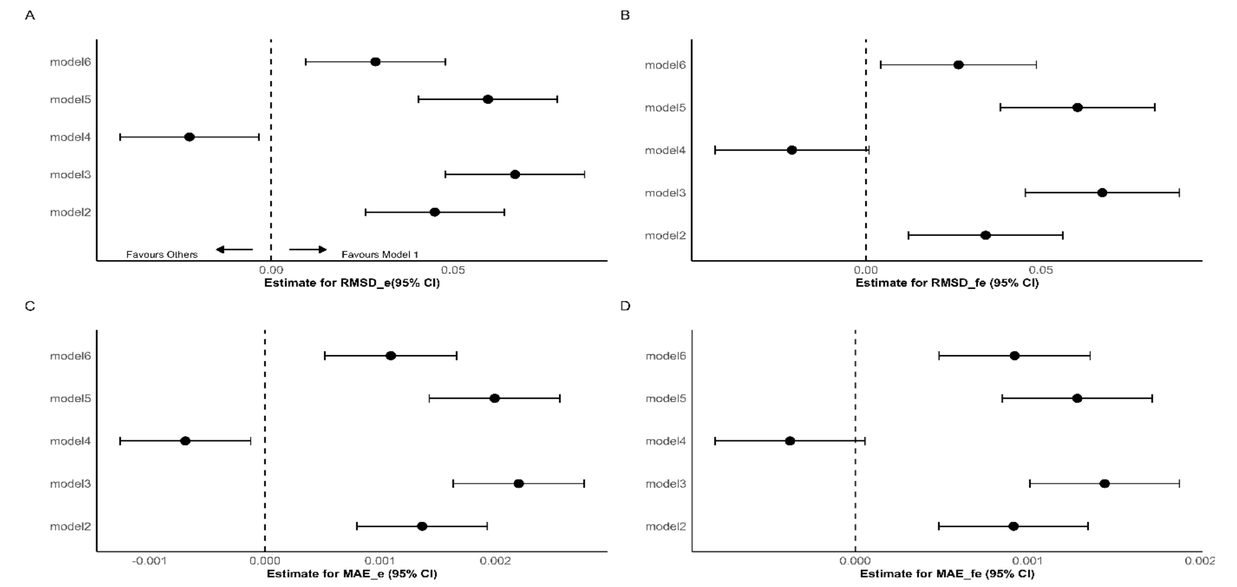

***Figure* 5 .** Regression-based analysis compared models' coefficients to standard parametric models and variable importance ranking for GoF.
Model 2-Model 6: 2, fractional polynomials; 3, restricted cubic splines; 4. Royston-Parmar spline; 5, generalized additive models; 6, parametric mixture models. A-E: A, MAE_e; B, MAE_fe; C, RMSD_e; D, RMSD_fe. e, extrapolation goodness-of-fit; fe, fitting-extrapolation goodness-of-fit; GoF, goodness-of-fit; MAE, mean absolute error; RMSD, Restricted Mean Survival Time

Conclusion

- Less-utilized RPM shows superior GoF-e/GoF-fe.
- Using machine learning for model selection may be promising and requires further study.