

Background

- ❖ Algorithms for the digitisation of survival curves by Hoyle et al. in 2011¹ and Guyot et al. in 2012² have helped make health technology assessment of cancer treatments one of the most published types of economic evaluations, with more than 16,000 peer-reviewed papers published over the last 15 years.
- ❖ These types of analyses are complex, and it can be a challenge for non-technical reviewers to assess whether the data is correct.

Objectives

- ❖ This case study aims to present a discrepancy arising from what appears to be a misalignment of the initial coordination of the digitisation algorithm.

Methods

- ❖ The overall survival (OS) curves from a pivotal trial for a next-wave PD-1 inhibitor called serplulimab were reconstructed from the pivotal phase III trial (ASTRUM-005)³ and compared to a recently published cost-effectiveness analysis by Zheng et al. 2024 (Zheng)⁴.
- ❖ The difference between the original ASTRUM-005 OS data and the reconstructed data in Zheng was examined.

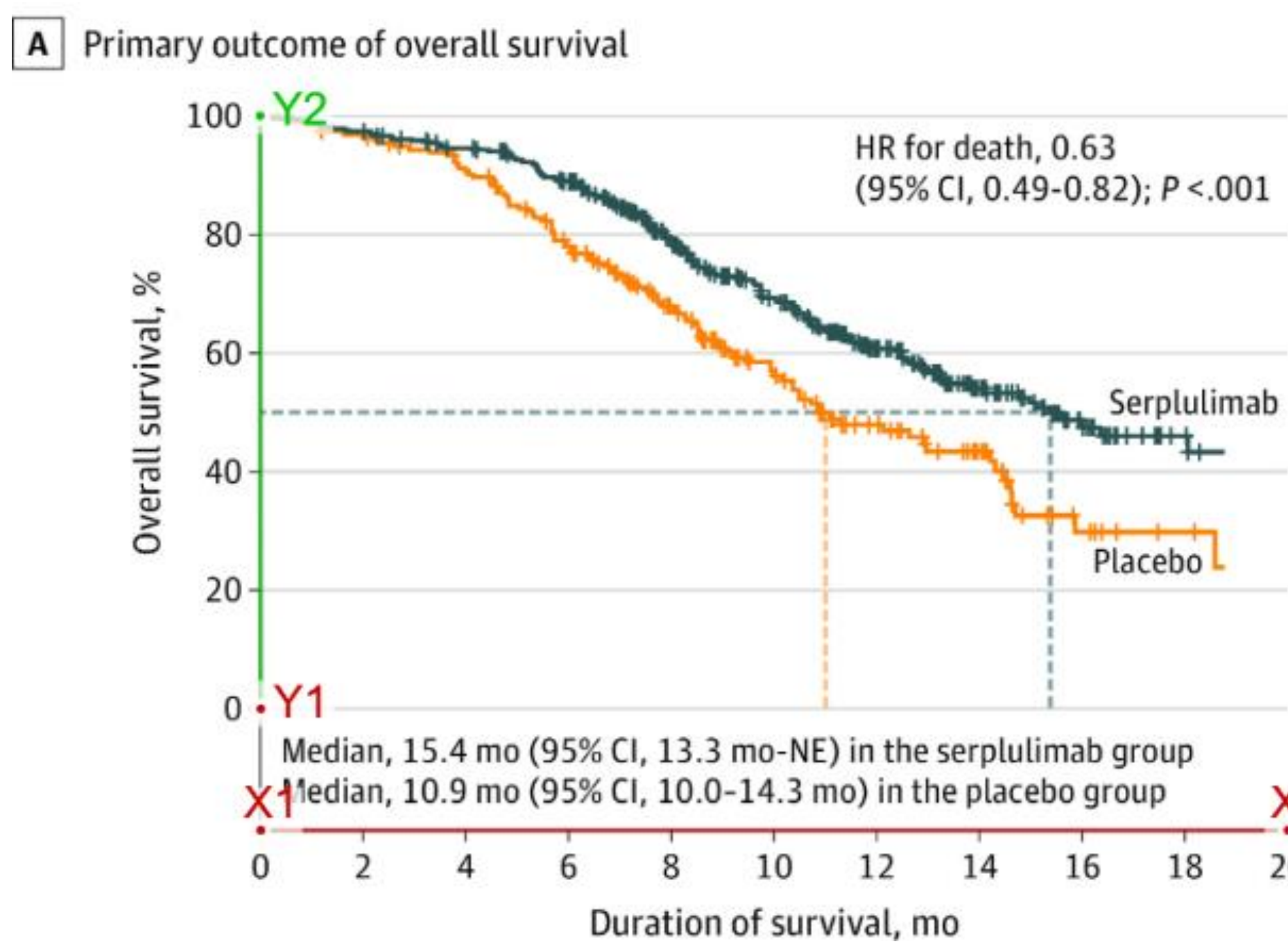


Figure 1. Axis calibration used for digitising the overall survival Kaplan–Meier curve from the ASTRUM-005 study. Source: ASTRUM-005³

Results

- ❖ There was a difference in the median OS reported by Zheng (not reached) vs ASTRUM-005 trials (15.4mth).
- ❖ The hazard ratio between the Zheng OS curve and the Astrum-005 curve was 0.974 [95% CI 0.845, 1.122] (see figure 2).

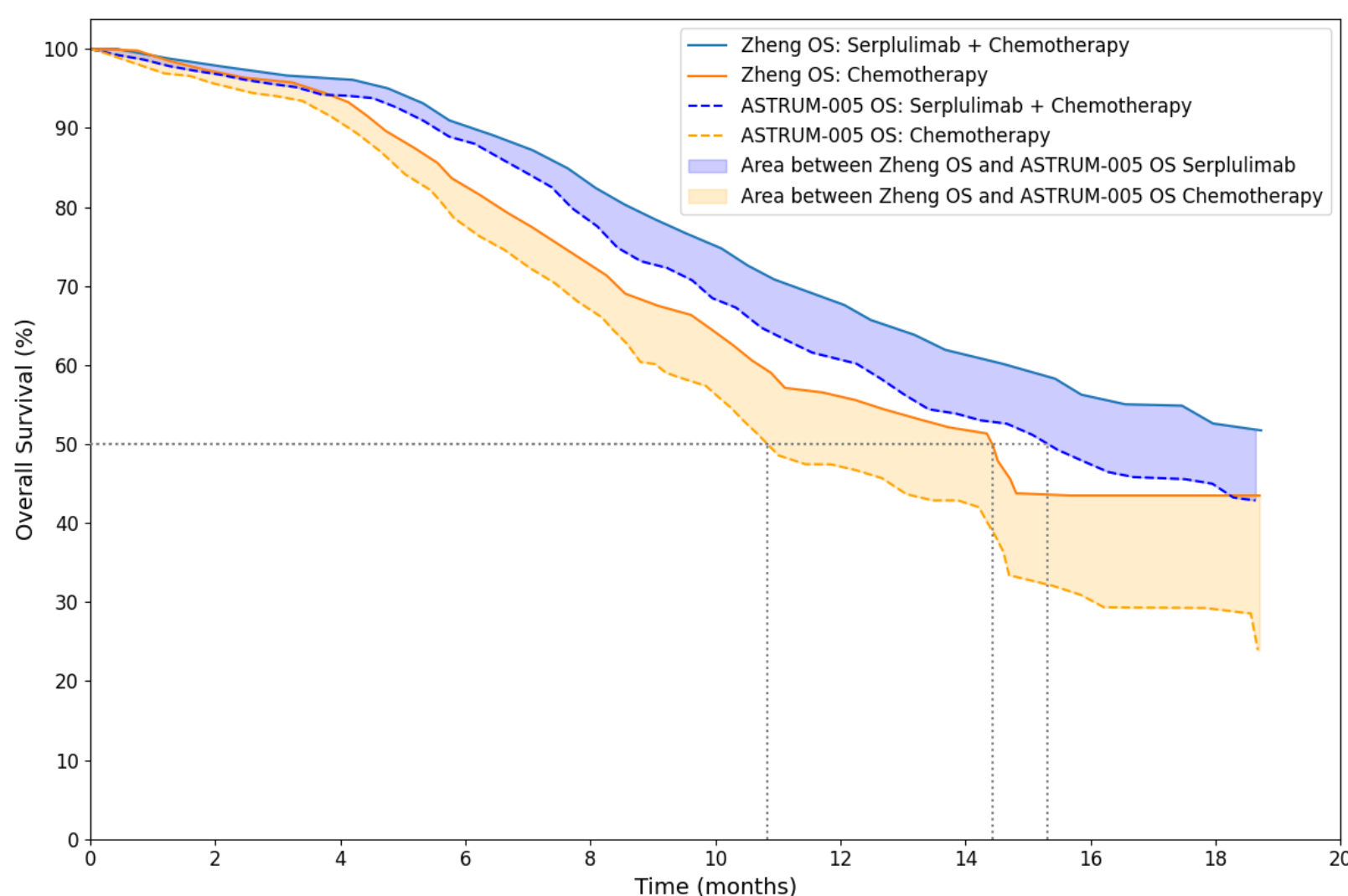


Figure 2. Overall survival curves comparison between the original ASTRUM-005 and the reconstructed data in Zheng

- ❖ The fitted hazard rate over time peaked at around 0.06 at 8 months for the Zheng data vs 0.09 at 11 months for the ASTRUM-005 data.

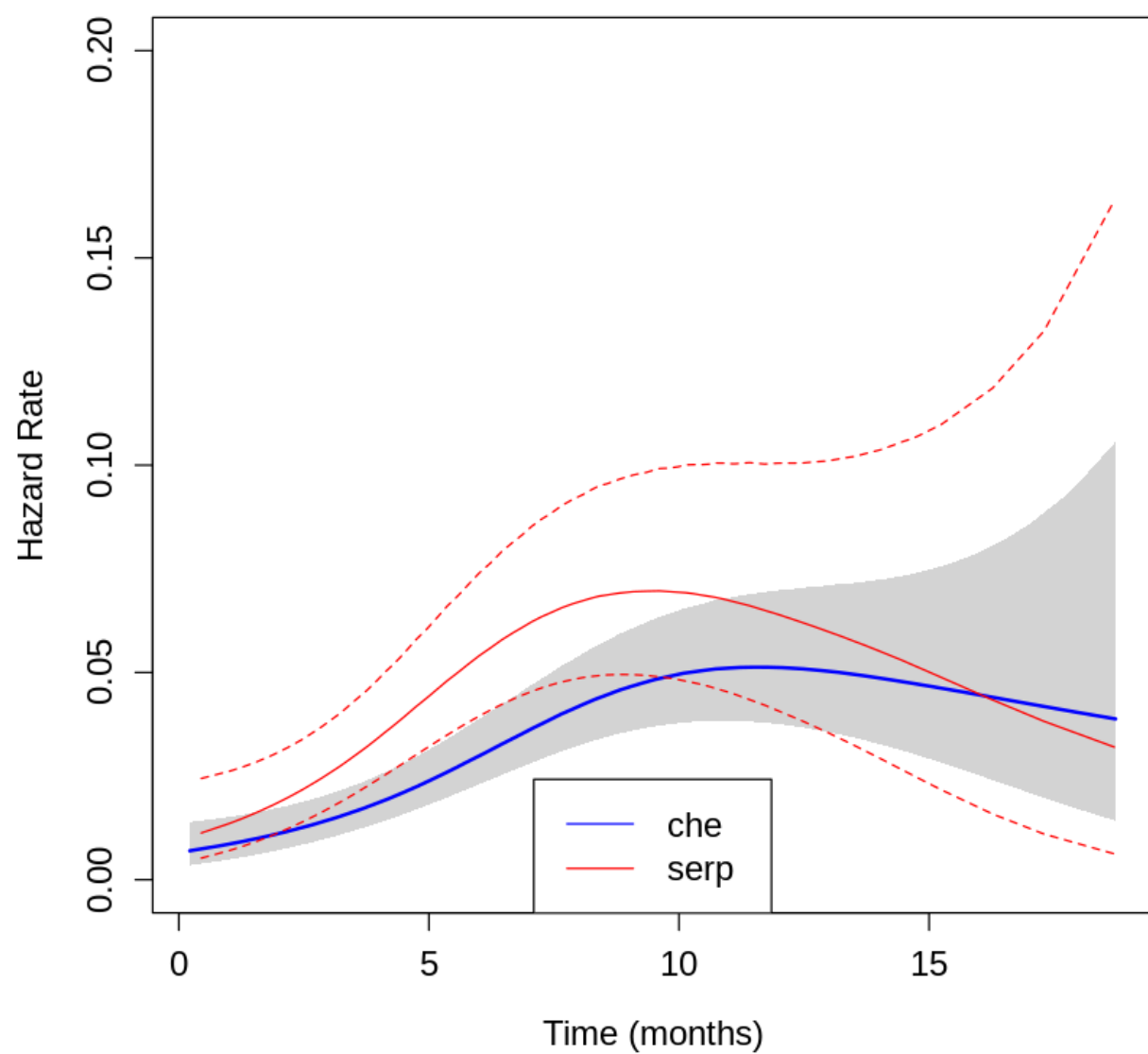


Figure 3. Estimated hazard function (smoothed) for overall survival using Zheng reconstructed Kaplan-Meier data

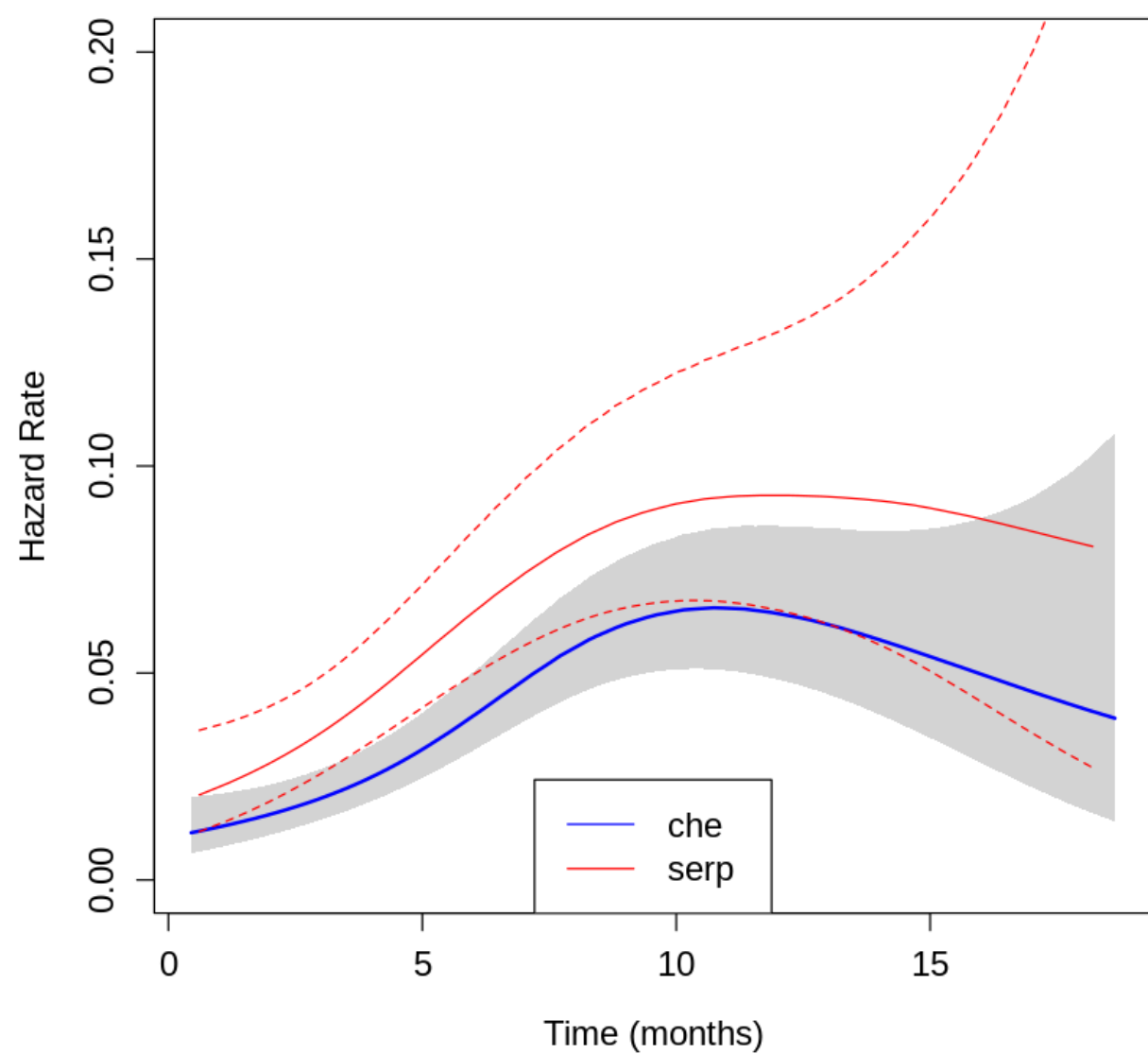


Figure 4. Estimated hazard function (smoothed) for overall survival using ASTRUM-005 Kaplan-Meier data

- ❖ For both datasets, AIC/BIC statistics favoured the log-logistic distribution for extrapolation (see Table 1).

Table 1. Goodness-of-fit criteria (Akaike information criterion (AIC)/ Bayesian information criterion (BIC)) of the extrapolated curves for serplulimab plus chemotherapy

	Zheng et al., 2024		ASTRUM-005	
Distributions	AIC	BIC	AIC	BIC
Exponential	954.05	958.01	1191.47	1195.44
Weibull	915.78	923.70	1154.15	1162.08
Loglogistic	913.63	921.55	1154.05	1161.97
Gompertz	928.09	936.02	1162.74	1170.67
Lognormal	917.37	925.30	1169.77	1177.69
Gengamma	916.45	928.34	1156.15	1168.04

- ❖ Over a 10-year time period, this resulted in a 9% overestimation of survival when using Zheng compared to ASTRUM-005.

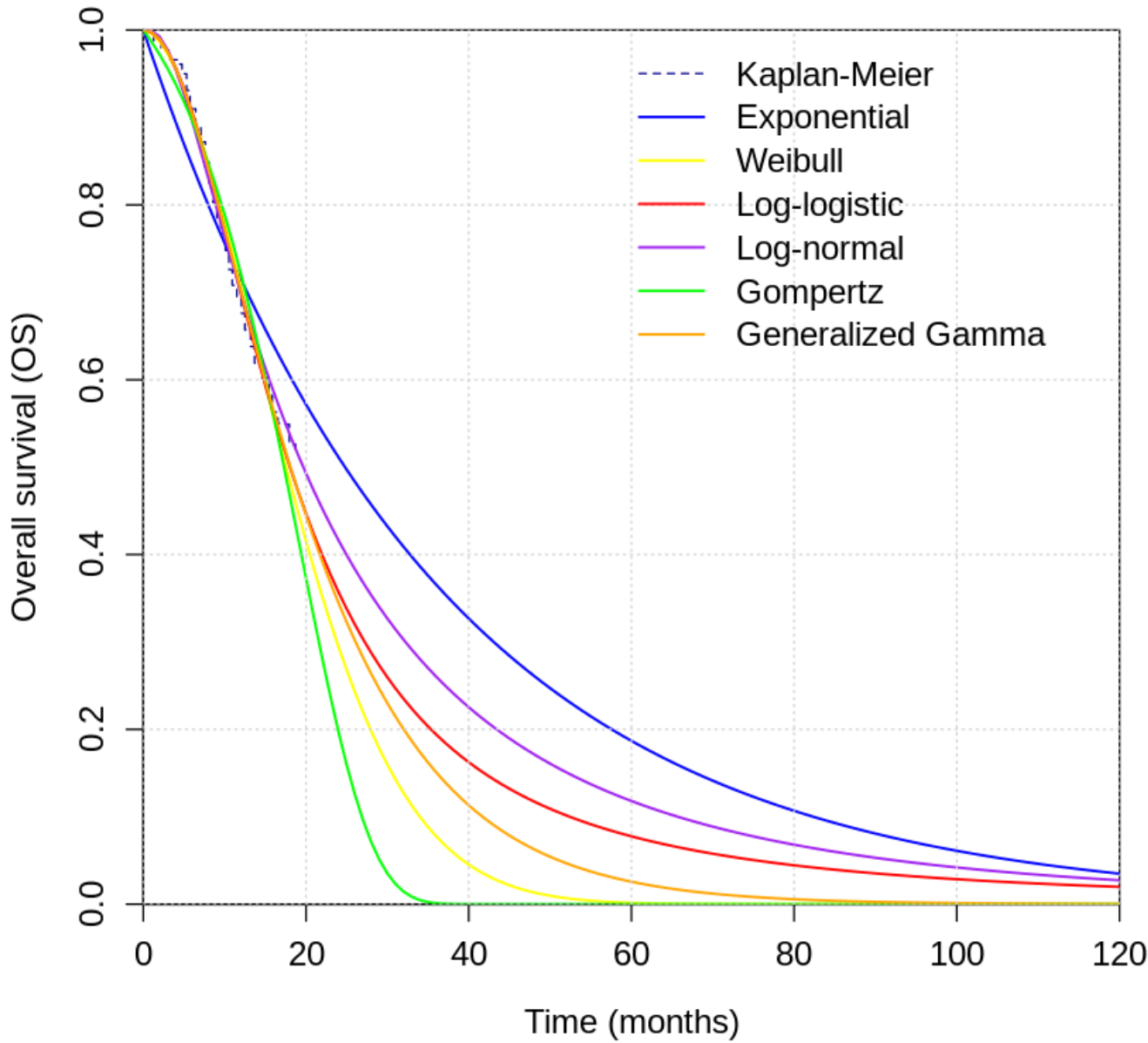


Figure 5. Overall survival curve extrapolation for serplulimab plus chemotherapy using Kaplan-Meier data reconstructed by Zheng

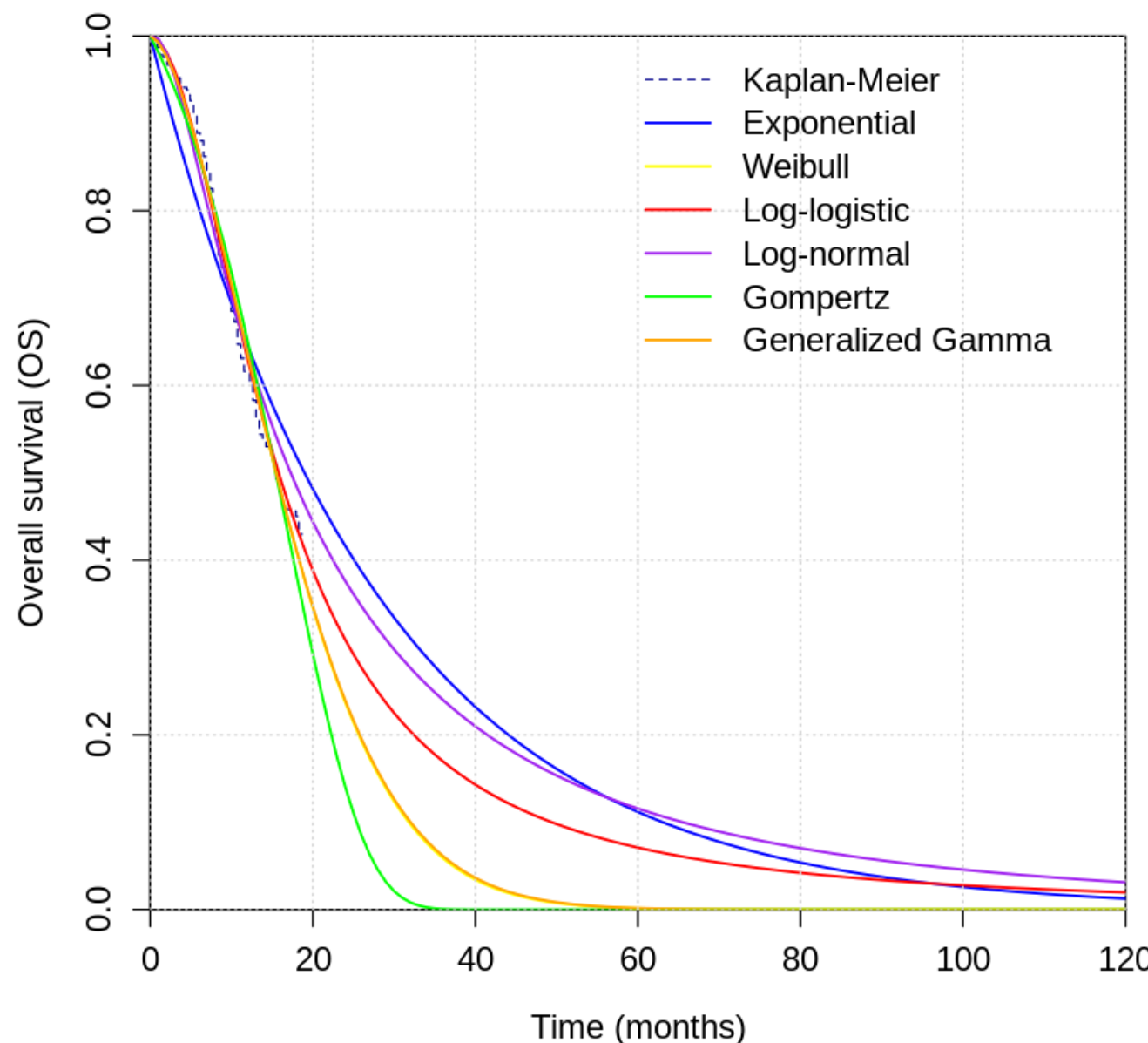


Figure 6. Overall survival curve extrapolation for serplulimab plus chemotherapy using Kaplan-Meier data from ASTRUM-005

Conclusions

- ❖ It is recommended that validation of the digitisation is performed by replicating the statistics reported for the original clinical data (median survival, hazard ratio, survival at different time points etc).
- ❖ Moreover, it is recommended that journals enlist reviewers with appropriate expertise when considering manuscripts containing cancer modelling.

References

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3. Cheng Y, Han L, Wu L, Chen J, Sun H, Wen G, Ji Y, Dvorkin M, Shi J, Pan Z, Shi J, Wang X, Bai Y, Melkadze T, Pan Y, Min X, Viguro M, Li X, Zhao Y, Yang J, Makharadze T, Arkania E, Kang W, Wang Q, Zhu J; ASTRUM-005 Study Group. Effect of First-Line Serplulimab vs Placebo Added to Chemotherapy on Survival in Patients With Extensive-Stage Small Cell Lung Cancer: The ASTRUM-005 Randomized Clinical Trial. JAMA. 2022 Sep 27;328(12):1223-1232. doi: 10.1001/jama.2022.16464. PMID: 36166026; PMCID: PMC9516323.
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