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# When the tail wags the dog IV:

## a marginal survival benefit where the transparency statistics give the all-clear and a population floor correctly does nothing (PANOVA-3)

## WHY THIS CASE STUDY

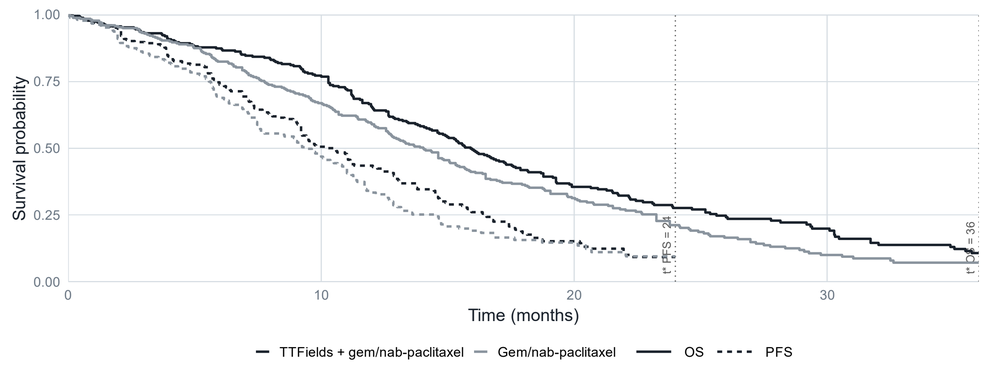
PANOVA-3 is the case that returns an all-clear. It has the most complete curves in the series: by 36 months 71.6% and 82.2% of patients had died and the curves stood at 0.11 and 0.07, with almost no tail left to model. A series made only of problem cases would say nothing about how often extrapolation matters; PANOVA-3 is the trial where it barely does.

## BACKGROUND

Cost-effectiveness models in oncology are driven by extrapolated survival curves, and almost nobody reports how much of the modelled lifetime benefit was seen in the trial and how much was assumed beyond it. We introduced a new framework at ISPOR Philadelphia this year we called *When the tail wags the dog* [1] and in this series we apply the framework to five recent oncology trials each representing a different survival pattern. For each case study we report the share of the incremental gain arising after the data end, where in time that gain sits, and what changes when general-population mortality is placed underneath the extrapolation (relative survival [2]).

## PANOVA-3

- Unresectable locally advanced pancreatic adenocarcinoma; median age 67 years, 52% female.
- **Tumour Treating Fields** added to **gemcitabine and nab-paclitaxel**, against the same chemotherapy alone.
- **Overall survival** — published hazard ratio 0.82 (95% CI 0.68–0.99), p = 0.039, medians 16.2 against 14.2 months. 201 and 230 deaths by study end among 285 and 286 patients.
- **Progression-free survival** — published hazard ratio 0.85 (95% CI 0.68–1.05), medians 10.6 against 9.3 months. Per-arm event counts are not published.
- The contrast is the whole case study: a marginal benefit on the most mature follow-up in the series — the opposite corner from HER2CLIMB-05.
- Babiker HM, et al. *J Clin Oncol* 2025. PMID 40448572.




*Kaplan–Meier curves are reconstructed from the published figures [3,4]; all trial results quoted are as reported.*

## METHODS

### Extrapolation

Pseudo-individual patient data were reconstructed from the published Kaplan–Meier curves [3,4]. Eight distributions were fitted jointly — one shared distribution with a treatment covariate on the location parameter and ancillary parameters common to both arms, so the two arms share a hazard shape and differ by a single treatment parameter — over a 40-year horizon [1]. All-cause fits are unconstrained; relative-survival fits model the excess hazard over ONS UK population mortality [2,5]. The median age and sex of the trial population, given in the case study above, index that life table, so the extrapolation sits above the mortality a general-population cohort of the same age and sex would experience.

**t*** separates the observed period from the extrapolated one and is not simply the maximum trial follow-up. Instead it is a judgement call, made from a reading of the reverse Kaplan–Meier curve for censoring [1]: it marks the end of reliable follow-up, before the risk sets are spent and before the two arms' censoring patterns diverge. t* is marked on the reconstructed Kaplan–Meier curves above.

Fits are compared on the Akaike and Bayesian information criteria (AIC and BIC), the standard fit statistics for choosing between parametric survival models. Both are reported for all eight distributions on each basis.

### Transparency statistics

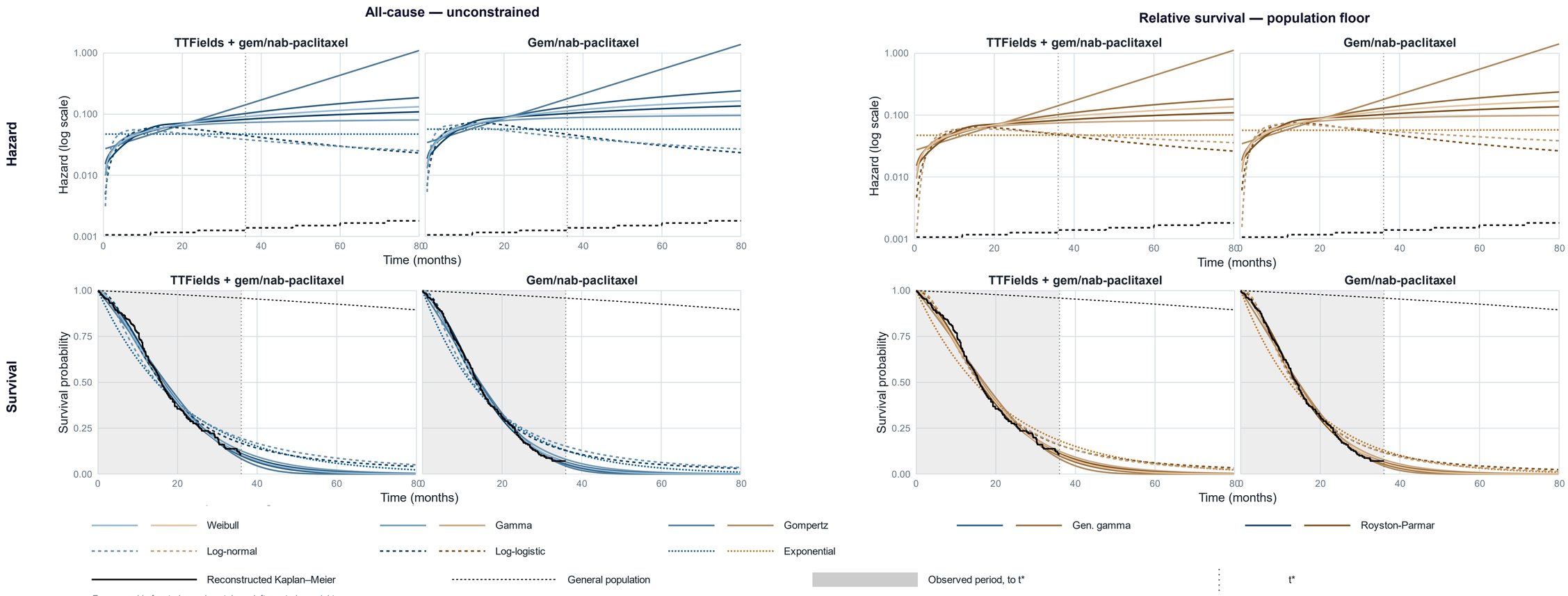
The area under each survival curve up to t* is the Restricted Mean Survival Time (RMST) and the period beyond t* is the Extrapolated Mean Survival Time (EMST). Added together they give the Unrestricted Mean Survival Time (UMST), which is the quantity that is compared between arms in an HTA / cost-effectiveness analysis:

- **ΔUMST** = ΔRMST + ΔEMST

From these quantities we form two transparency statistics [1]:

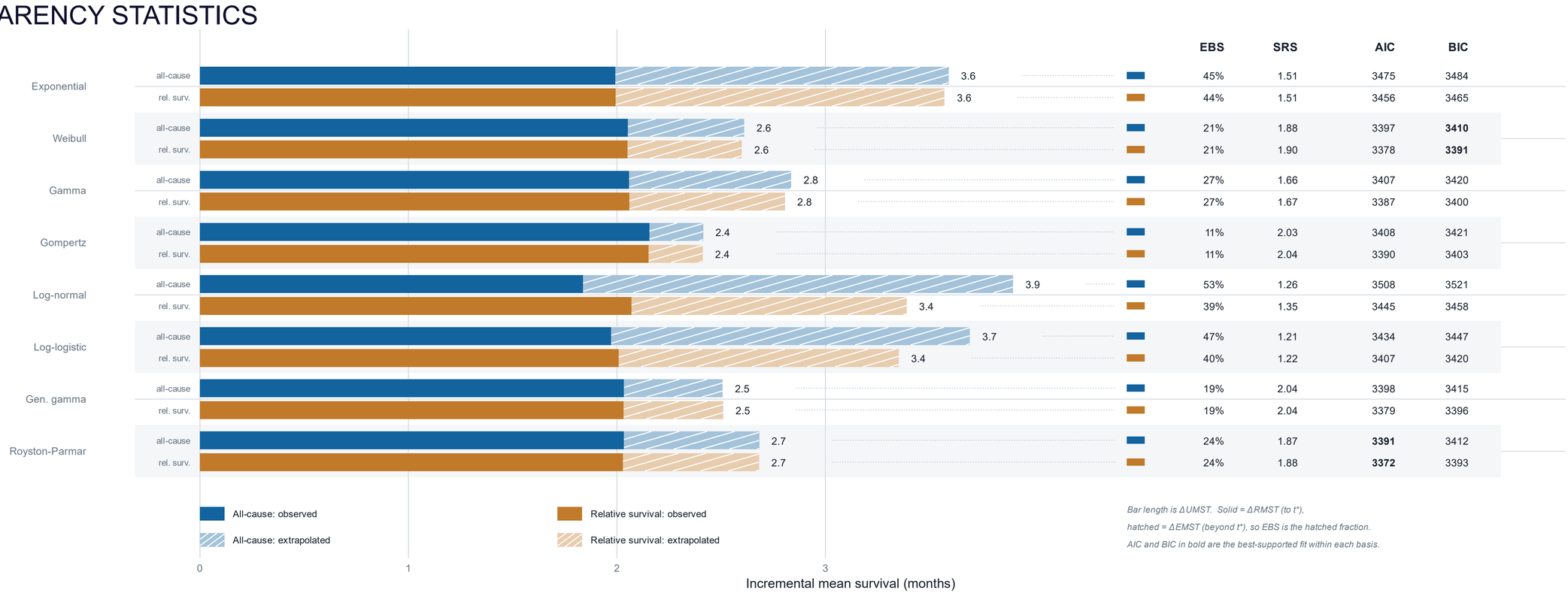
- **EBS** = ΔEMST / ΔUMST — the share of the incremental gain arising beyond the observed data.
- **SRS** = $(EMST_T/EMST_C) / (RMST_T/RMST_C)$ — above 1, the gain is concentrated in the extrapolated tail.

## THE EXTRAPOLATION




*Every panel is faceted experimental arm left, control arm right.*

## TRANSPARENCY STATISTICS




*Bar length is ΔUMST. Solid = ΔRMST (to t*),*
*hatched = ΔEMST (beyond t*), so EBS is the hatched fraction.*
*AIC and BIC in bold are the best-supported fit within each basis.*

## CONCLUSION

### A small gain, mostly observed — the transparency statistics return an all-clear.

AIC selects the Royston-Parmar spline and BIC the Weibull. Their lifetime gains are 2.7 months and 2.6. All eight put 2.0–2.2 months of that gain inside the observed period and differ only in what follows, which ranges 0.3–1.6 months, so EBS runs 11–44% — the lowest in the series — and SRS 1.2–2.0. The disagreement between the criteria costs a tenth of a month, and the fit that tracks the observed curves most closely is the Royston-Parmar spline, at 2.7 months. The population-mortality floor moves nothing beyond a few weeks on the two long-tailed fits, because follow-up is mature and disease-specific mortality dominates — the value question here is the size of the benefit and the price of the device, not how long the benefit is presumed to persist.

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## DISCLOSURES

The analysis was conducted by Occam Research Ltd as relationship investment; no trial-sponsor funding. Public data only. AI-assisted content disclosable per ISPOR policy: scaffolding and drafting assistance were used, and all analysis and outputs were validated by the authors.