ONCOSCOPE
REAL-TIME ONCOLOGY LIBRARY

Andrew Briggs[1], Alex Hill[1], Anna Forsythe[2]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom;
[2]Oncoscope, Miami, FL, USA

ISPOR Europe 2026
8-11 November 2026
Vienna, Austria

EE517

When the tail wags the dog – and when a population floor reins it in:

extrapolation transparency and relative survival across five oncology trials

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 framework at ISPOR Philadelphia this year called *When the tail wags the dog* [1], and in this series we apply it to five recent oncology trials, each representing a different survival pattern. This poster sets the five side by side. What it adds is not a sixth case but the pattern across them: how the extrapolated share of the benefit moves with the maturity of the data, and when placing general-population mortality underneath the extrapolation (relative survival [2]) changes the answer.

FIVE TRIALS, FROM LEAST TO MOST MATURE

HER2CLIMB-05 [6]

- HER2-positive metastatic breast cancer, maintenance.
- 51 deaths among 654 patients (8%).
- The persist-or-fade question asked of curves too immature to answer it.

Case study I – online

KEYNOTE-905 / EV-303 [7]

- Muscle-invasive bladder cancer, treated with curative intent.
- Deaths 22% and 39% of patients.
- Few deaths but long follow-up and a cure fraction: the population floor is decisive.

Poster MSR194

RASolute302 [8]

- Previously treated metastatic pancreatic cancer.
- Deaths 32% and 56% of patients.
- Maturity is asymmetric: the control arm has answered the persist-or-fade question and the treated arm has not.

Podium, Wednesday 11 November, 08:45

TROPION-Breast02 [9]

- Metastatic triple-negative breast cancer.
- Deaths 52% and 56% of patients.
- Both medians reached, both arms equally mature, and most of the gain still beyond the data.

Poster EE371

PANOVA-3 [10]

- Locally advanced pancreatic cancer.
- Deaths 71% and 80% of patients.
- Where the question stops mattering: almost no tail left to model.

Poster EE210

Deaths as published, experimental arm first.

METHODS

One framework, applied identically

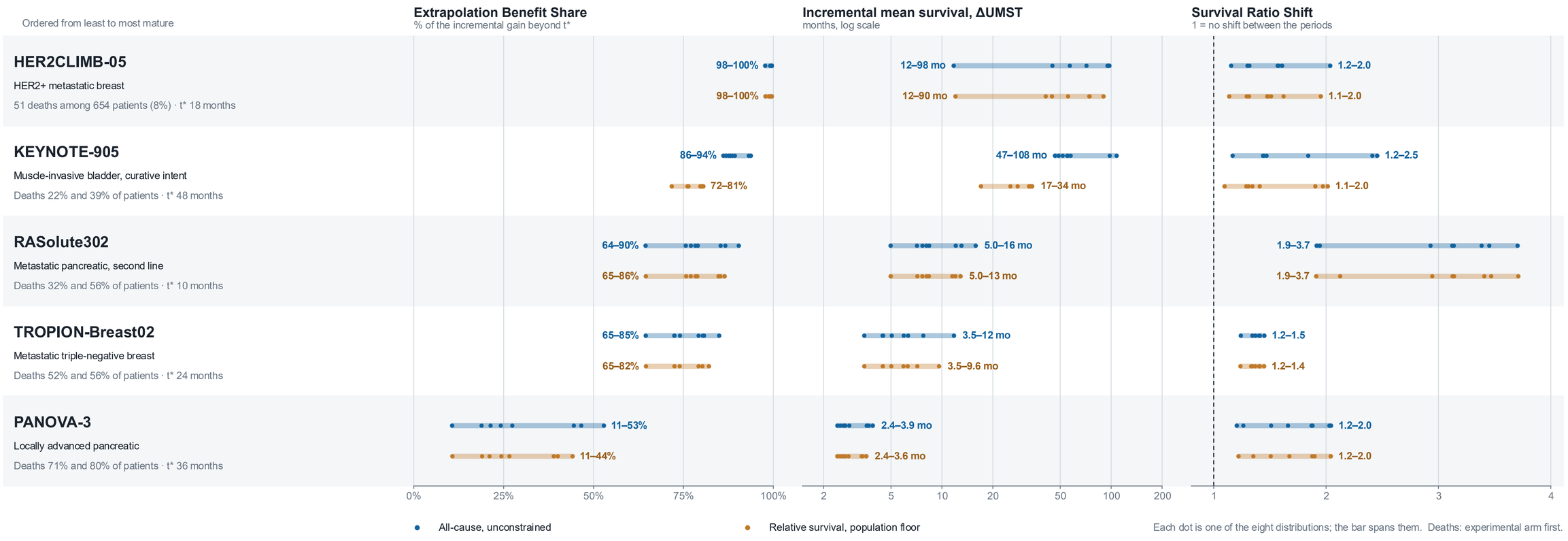
For each trial, pseudo-individual patient data were reconstructed from the published overall-survival Kaplan–Meier curves [3,4]. Eight distributions were fitted jointly – one shared distribution with a treatment covariate on the location parameter, so the two arms share a hazard shape and differ by a single treatment parameter – over a 40-year horizon. Each was fitted twice: all-cause, unconstrained; and as relative survival, modelling the excess hazard over ONS UK population mortality indexed to the trial's median age and sex [2,5]. All eight distributions are reported on both bases; nothing is selected.

The transparency statistics

t* marks the end of reliable follow-up, read from the reverse Kaplan–Meier curve for censoring [1]. The incremental mean survival (ΔUMST) splits into the part observed before t* (ΔRMST) and the part extrapolated after it (ΔEMST).

- **EBS** = ΔEMST / ΔUMST — the share of the incremental gain arising beyond the observed data.
- **SRS** = ($EMST_T$/$EMST_C$) / ($RMST_T$/$RMST_C$) — how much larger the treated-to-control ratio of mean survival is beyond the data than within them.

ACROSS THE FIVE TRIALS



WHAT THE FIVE SHOW TOGETHER

The extrapolated share tracks maturity, not significance

Every overall-survival effect in the series is statistically significant, yet the share of the gain arising beyond the data runs from 98–100% in HER2CLIMB-05 to 11–44% in PANOVA-3 (relative survival). It falls as the data mature: KEYNOTE-905 72–81%, RASolute302 65–86%, TROPION-Breast02 65–82%. Reaching the median is not enough. TROPION-Breast02 reached both medians and still placed 65–82% of its gain beyond the data. Only PANOVA-3, with 71% and 80% of patients dead, keeps most of a small gain inside the trial.

The population floor's value is conditional, and predictable

Where disease-specific mortality dominates, the floor changes little and costs nothing: TROPION-Breast02 3.5–12 months becomes 3.5–9.6, RASolute302 5.0–16 becomes 5.0–13, and PANOVA-3 2.4–3.9 becomes 2.4–3.6, the movement confined to the long-tailed fits. On immature data it trims the most optimistic tails without resolving the spread: HER2CLIMB-05 12–98 months becomes 12–90. Where a cure fraction exists it is decisive: KEYNOTE-905 47–108 months becomes 17–34, as the excess hazards converge on the population line. Whether the floor moves the answer tells you how the cancer's excess mortality behaves.

Read SRS by its size, not its sign

All 80 values of SRS in the series – five trials, eight distributions, two bases – exceed 1, from 1.10 to 3.71. That is a property of the model, not a finding: with both arms sharing one hazard shape and differing by a single parameter, the ratio of survival between arms grows over time for any beneficial treatment, so it is necessarily larger beyond the data than within them. The information is in the magnitude. RASolute302 stands apart at 1.9–3.7; elsewhere SRS sits at 1.1–2.5. A treatment effect that wanes beyond the data would put SRS below 1, and a joint fit cannot represent that – fitting each arm separately is where it could show.

CONCLUSION

Report how much of the benefit was seen, and put the population underneath what was not.

EBS alongside incremental survival makes plain how much of an overall-survival value claim rests on assumption, and the five trials show that this share follows maturity rather than statistical significance. A relative-survival floor is costless where excess mortality dominates and decisive where a cure fraction exists, so it should be applied as standard – the survival-extrapolation counterpart of the background mortality already routine in Markov models. Its action, or inaction, is itself diagnostic.

View all Oncoscope posters at ISPOR Europe 2026

REFERENCES

1. Briggs A, Lin Z, Hill A, Fenwick EA. When the tail wags the dog: rethinking partitioned survival modelling in oncology (MSR215). *Value in Health.* 2026;29(6 Suppl):S342. https://www.valueinhealthjournal.com/article/S1098-3015(26)01852-8/fulltext
2. Rutherford MJ, Lambert PC, Sweeting MJ, Pennington B, Crowther MJ, Abrams KR, Latimer NR. *NICE DSU Technical Support Document 21: Flexible methods for survival analysis.* Sheffield: NICE Decision Support Unit; 2020 (updated 2022). https://sheffield.ac.uk/nice-dsu/tsds/flexible-methods-survival-analysis
3. Zhang JZ, Rios JD, Pechlivanoglou T, et al. SurvdigitizeR: an algorithm for automated survival curve digitization. *BMC Med Res Methodol.* 2024;24:147. PMID 39003440. https://pubmed.ncbi.nlm.nih.gov/39003440/
4. Guyot P, Ades AE, Ouwens MJNM, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan–Meier survival curves. *BMC Med Res Methodol.* 2012;12:9. PMID 22297116. https://pubmed.ncbi.nlm.nih.gov/22297116/
5. Office for National Statistics. *National life tables – life expectancy in the UK: 2021 to 2023.* Newport: ONS; 18 March 2025. https://www.ons.gov.uk/releases/nationallifetablesuklifeexpectancyintheuk20212023
6. Diéras V, et al. *J Clin Oncol.* 2025;44(17):1597–1607. PMID 41369677. https://pubmed.ncbi.nlm.nih.gov/41369677/
7. Vulsteke C, et al. *N Engl J Med.* 2026. PMID 41707170. https://pubmed.ncbi.nlm.nih.gov/41707170/
8. O'Reilly EM, et al. *N Engl J Med.* 2026. PMID 42223072. https://pubmed.ncbi.nlm.nih.gov/42223072/
9. Dent R, et al. *Ann Oncol.* 2026;37(8):1066–1080. PMID 41937088. https://pubmed.ncbi.nlm.nih.gov/41937088/
10. Babiker HM, et al. *J Clin Oncol.* 2025. PMID 40448572. https://pubmed.ncbi.nlm.nih.gov/40448572/

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.