MSR109

Multi-indication Evidence Synthesis In Oncology Health Technology Assessment: Case-study On Bevacizumab

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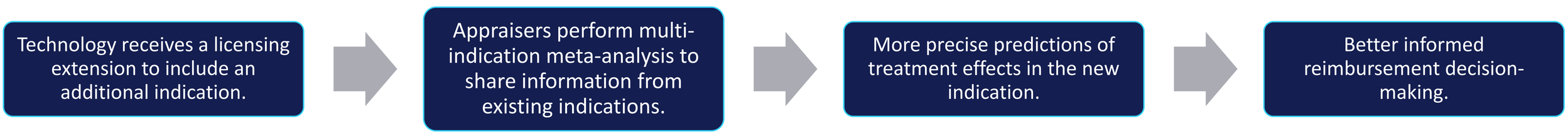
Figure 1: Our proposed pathway for health technology assessment of technologies licensed across multiple indications, based on the application of multi-indication evidence synthesis methods.



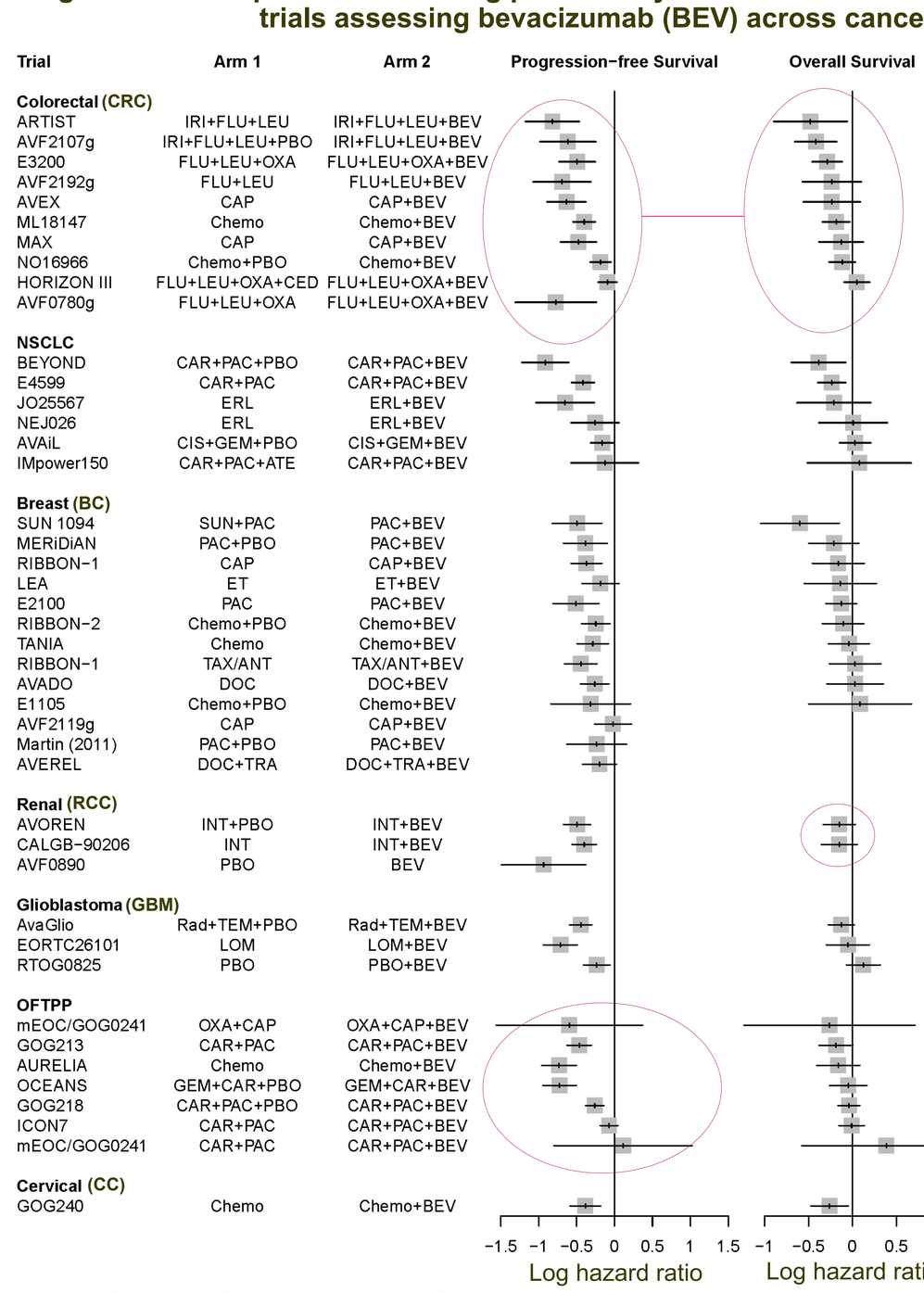
Background

- Increasingly, cancer drugs receive licensing extensions to include additional indications (patient populations) as trial evidence on a treatment effect, in terms of overall survival (OS) or progression-free survival (PFS) (where OS data are limited), accumulates over time.
- Health technology assessments (HTAs) typically restrict the scope of the evidence considered to a single target indication, leading to uncertainty surrounding the treatment effect on OS.
- Alternatively, sharing information across multiple indications on the OS effect, and on the surrogate relationship between PFS and OS effects, could provide more precise predicted OS effect estimates for the target indication.

Methods

- We apply meta-analysis methods which allow for different levels of sharing across indications; on PFS and OS effects individually, and on the surrogate relationship between PFS and OS effects.
- We predict the OS effect for a particular indication by entering the corresponding PFS effect into the model describing the surrogate relationship, where sharing across indications is imposed on either the surrogate relationship alone (OS – Predicted (IP)), or on the PFS effects in additional to the surrogate relationship (OS – Predicted (Matched)).
- We use summary data from trials assessing the effectiveness of bevacizumab (**Figure 2, right**), a drug that is licensed by the European Medicines Agency across seven cancer indications, to demonstrate the methods.

Figure 2: Forest plots summarising present-day data on PFS and OS from randomised controlled trials assessing bevacizumab (BEV) across cancer indications.



Evidence of a surrogate relationship, with a larger PFS effect associated with a larger OS effect.

The strength of the surrogate relationship seems to vary between indications.

Indications with limited evidence on the final outcome motivate sharing from indications with more abundant data.

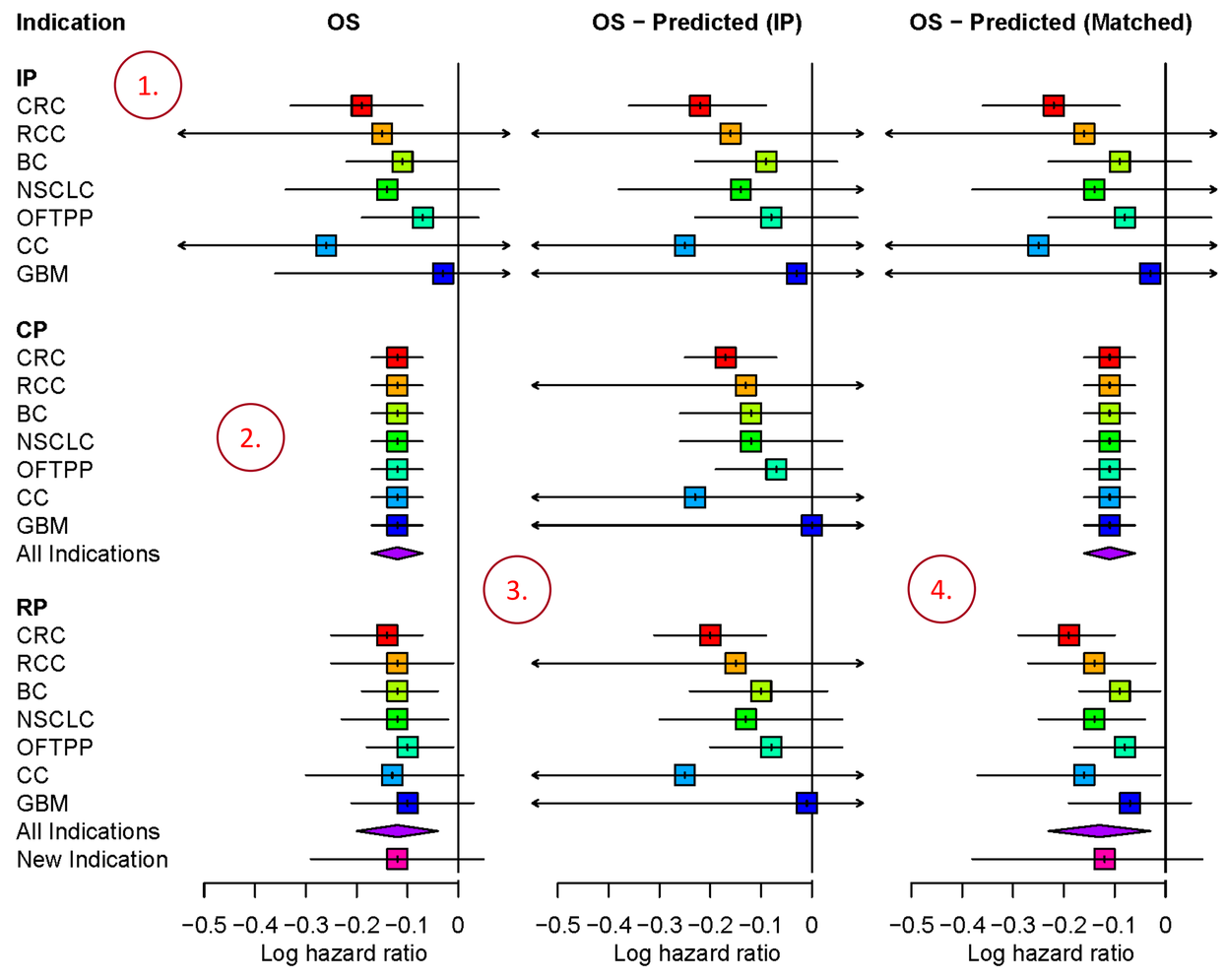
Evidence of between-studies heterogeneity within indications.

Figure 3: Forest plots depicting indication-specific pooled, and predicted, treatment effect estimates on OS, from performing multi-indication meta-analysis using data available at present-day.

Independent parameters (**IP**): no sharing across indications.

Common parameter (**CP**): maximal sharing, by assuming a common parameter, across indications.

Random parameters (**RP**): intermediate sharing, by assuming similar parameter values across indications.



CRC – colorectal cancer; RCC – renal cell carcinoma; BC – breast cancer; NSCLC – non-small cell lung cancer; OFTPP – ovarian, fallopian tube, and primary peritoneal; CC – cervical cancer; GBM - glioblastoma

Results

1. When pooling OS effects within each indication (no sharing across indications), a statistically meaningful effect was only evident for CRC (nine trials).
2. Precision was gained when sharing across indications was allowed, with the most precise estimates provided by assuming a common OS effect.
3. When sharing was imposed on the surrogate relationship alone, predicted OS effect estimates had a similar level of uncertainty to estimates from pooling within each indication.
4. Uncertainty in the predicted OS effects was notably reduced when sharing was imposed on both the surrogate relationship and the PFS effects.

Conclusions

- Multi-indication meta-analysis can be usefully applied in HTA by borrowing strength across indications to better predict OS effects within a target indication (**Figure 1**).
- Using the surrogate relationship to predict an OS effect is applicable where there is strong evidence on the corresponding PFS effect.
- These findings are generalizable to other multi-indication technologies, but further research is required to understand the evidential scenarios where the methods would be most beneficial.

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