

**INTRODUCTION**

The validity of the proportional hazards assumption is critical for the interpretation of meta-analysis results, especially when summarizing survival data from different trials. The assumption of proportional hazards (PH) is a key component of the Cox proportional hazards model, which is widely used in the meta-analysis of time-to-event data. The PH assumption states that the hazard ratio comparing two treatments is constant over time. If this assumption is violated, the results of the meta-analysis may be misleading. However, the PH assumption can be restrictive, as violations can occur in various scenarios, such as differing baseline risks, time-varying treatment effects, or non-proportional hazards.

**RESULTS**

**Searches of NICE website**

**META-ANALYSIS OF TIME-TO-EVENT DATA**

- Time-to-event data are commonly used to evaluate the effectiveness of interventions. The Cox proportional hazards model is a popular tool for analyzing such data, as it allows for the estimation of the hazard ratio (HR) and the corresponding 95% confidence interval (CI).

**SEARCHES OF HTA BODY GUIDELINES**

| HTA Body | NICE TA Number | Summary of TAS Reporting Time-to-Event Meta-analyses: Evidence Synthesis Submitted to/Published by NICE | Comments on PH Assumption
| --- | --- | --- | --- |
| NICE | TA192 | • NMA of OS using summary statistics and IPD (TA192) | No comments relating to the PH assumption. The appraisal committee concluded that the results of the indirect comparisons and the meta-analysis of time-to-event data were presented in a way that was transparent and understandable.

**CONCLUSIONS**

- The validation of the proportional hazards assumption is essential for the accuracy of the results of time-to-event meta-analyses.

**REFERENCES**

2. META-ANALYSIS OF TIME-TO-EVENT DATA TO SUPPORT THE VALIDITY OF THE PROPORTIONAL HAZARDS ASSUMPTION. Batson S1, Webb N1, Greenall G1, Hudson P1. 1Abacus International, Bicester, Oxfordshire, UK. 
3. The PH assumption can be crudely assessed when reviewing publications. The investigator needs to be aware of the limitations of such an approach, but if individual trials are sufficiently powered to detect deviations from the PH assumption, the study results should be interpreted with caution, as the assumption might not hold.

**TABLE 1: SUMMARY OF TAS REPORTING TIME-TO-EVENT META-ANALYSES: EVIDENCE SYNTHESIS SUBMITTED TO/PUBLISHED BY NICE**

- **PBAC** “Where the analysis is based on a Cox proportional hazards model, present the hazard ratios, together with their 95% confidence intervals.
- **NICE TA296** Afatinib for treating advanced or metastatic breast cancer that is receptor-positive, associated with an HER2 mutation: the first-line treatment for HER2-positive, locally advanced or metastatic breast cancer (TA296). No comments relating to the PH assumption. The appraisal committee concluded that the results of the indirect comparisons and the meta-analysis of time-to-event data were presented in a way that was transparent and understandable.
- **NICE PBAC** No comments No comments relating to the PH assumption. Therefore, a most plausible ICER could not be estimated.

**TABLE 2: SUMMARY OF ADVICE ON TIME-TO-EVENT DATA AND THEIR ASSUMPTION IN THE CONTENT OF EVIDENCE SYNTHESIS**

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