The Dynamic Nature of Network Meta-Analysis: How Data Updates Could Influence Health Technology Assessment

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Background and Aim

- In HTA, ITCs are required when direct head-to-head trials between treatments that are relevant to the decision problem are unavailable
- ITCs can estimate the relative effectiveness of interventions when a common comparator (e.g., placebo) is available. When a common comparator is not available, an unanchored approach can be used, though this requires stronger assumptions about the comparability of patient populations
- NMAs extend ITCs by synthesizing evidence from multiple clinical trials to estimate relative efficacy across a network of treatments
- At the point of HTA submission, clinical trial data are often immature or incomplete, particularly for newer treatments. This can lead to uncertainty in estimating relative efficacy, affecting decision making. Additional data from ongoing or new trials may alter conclusions drawn from an initial NMA
- This study replicated a previously conducted NMA from a past HTA submission (1). It examined how the inclusion of more recent and mature data affects the estimated treatment effects. The goal was to understand whether updated evidence changes the conclusions of the original analysis, which could influence decision making in HTA

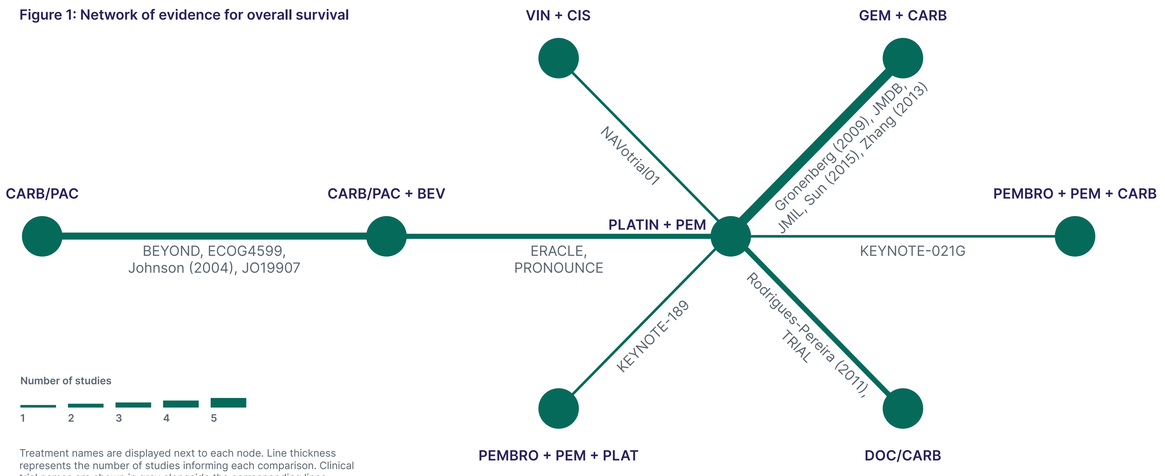
Methods

- A Bayesian NMA of overall survival in NSCLC was replicated, encompassing eight treatments, using publicly available documentation from NICE TA557. An illustration of the treatment network is depicted in Figure 1
- Some point estimates were not included in the publicly available committee papers, so, where necessary, the analysis was supplemented by estimating redacted values from published data. Given that the TA was published in 2019, key values were identified within the literature via relevant clinical trial publications
- Searches were conducted to identify updated data cuts from relevant clinical trials in the network, evaluating the impact of new evidence that was unavailable during the original appraisal
- In line with the NICE submission, both fixed- and random-effects NMAs were conducted assuming constant HRs. Random effects were ultimately used in the economic model within the NICE submission and are therefore presented here
- All analyses were conducted in R (Version 4.4.1) using the *multinma* package (2)

Results

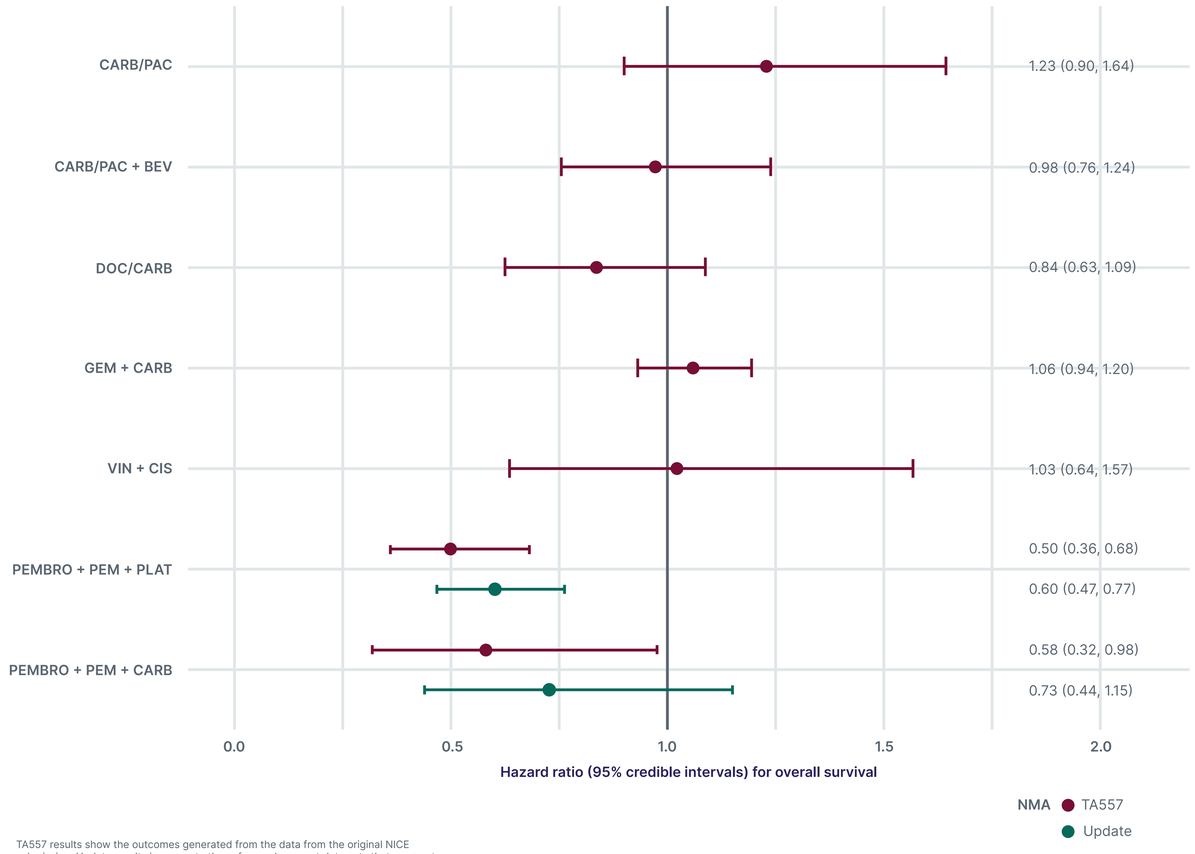
- Not all results were publicly available within the TA557 documents published on the NICE website. Using information from the literature, results were produced that were comparable to those presented in TA557
- Newer data cuts were identified in the literature for two treatments within the network: pembrolizumab plus pemetrexed and platinum (3) and pembrolizumab plus pemetrexed and carboplatin (4)
- After incorporating results from the most recently published data cuts, outcomes for both treatments relative to carbo(cis)platin plus pemetrexed attenuated towards the null (Figure 2). The HR and 95% credible interval for pembrolizumab plus pemetrexed and platinum versus placebo plus pemetrexed and platinum increased from 0.50 (0.36, 0.68), using the data cut available at the time of the NICE submission, to 0.60 (0.47, 0.77), with newly published data. Similarly, results for pembrolizumab plus pemetrexed and carboplatin changed from 0.58 (0.32, 0.98) to 0.73 (0.44, 1.15)
- The posterior distribution for pembrolizumab plus pemetrexed and carboplatin shifted, with the 95% credible interval now including 1 (Figure 2). This change may have important implications for how HTA bodies interpret the treatment's effectiveness

Figure 1: Network of evidence for overall survival



Treatment names are displayed next to each node. Line thickness represents the number of studies informing each comparison. Clinical trial names are shown in grey alongside the corresponding lines.

Figure 2: Forest plot of results from random-effects NMAs for each treatment relative to carbo(cis)platin plus pemetrexed



TA557 results show the outcomes generated from the data from the original NICE submission. Update results incorporate those from subsequent data cuts that were not available at the time of NICE submission.

Conclusion

The results of the current study demonstrate that incorporating more recent data can lead to meaningful changes in results, highlighting the dynamic nature of NMAs in HTAs. Seemingly small changes in point estimates of HRs can have a profound impact on cost-effectiveness results, and thus, decision making. Additionally, publicly available information can be limited, hindering reproducibility. These findings emphasize the need for updating NMAs when new data are made available, greater transparency in reporting, and improved access to complete data to ensure health policy recommendations reflect the most current evidence.

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Abbreviations

BEV, bevacizumab
CARB, carboplatin
CIS, cisplatin
DOC, docetaxel
GEM, gemcitabine
HR, hazard ratio
HTA, health technology assessment
ITC, indirect treatment comparison
NICE, National Institute for Health and Care Excellence
NMA, network meta-analysis
NSCLC, non-small cell lung cancer
PAC, paclitaxel
PEM, pemetrexed
PEMBRO, pembrolizumab
PLAT, platinum
PLATIN, carbo(cis)platin
TA, technology appraisal
VIN, vinorelbine