

REVIEW OF RECENT NICE TECHNOLOGY APPRAISALS USING SIMULATED TREATMENT COMPARISONS

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Objectives

- This study aimed to establish how commonly used simulated treatment comparisons are in NICE single technology appraisals.
- A further aim of this review was to determine how Evidence Review Groups and the appraisal committee view this methodology.

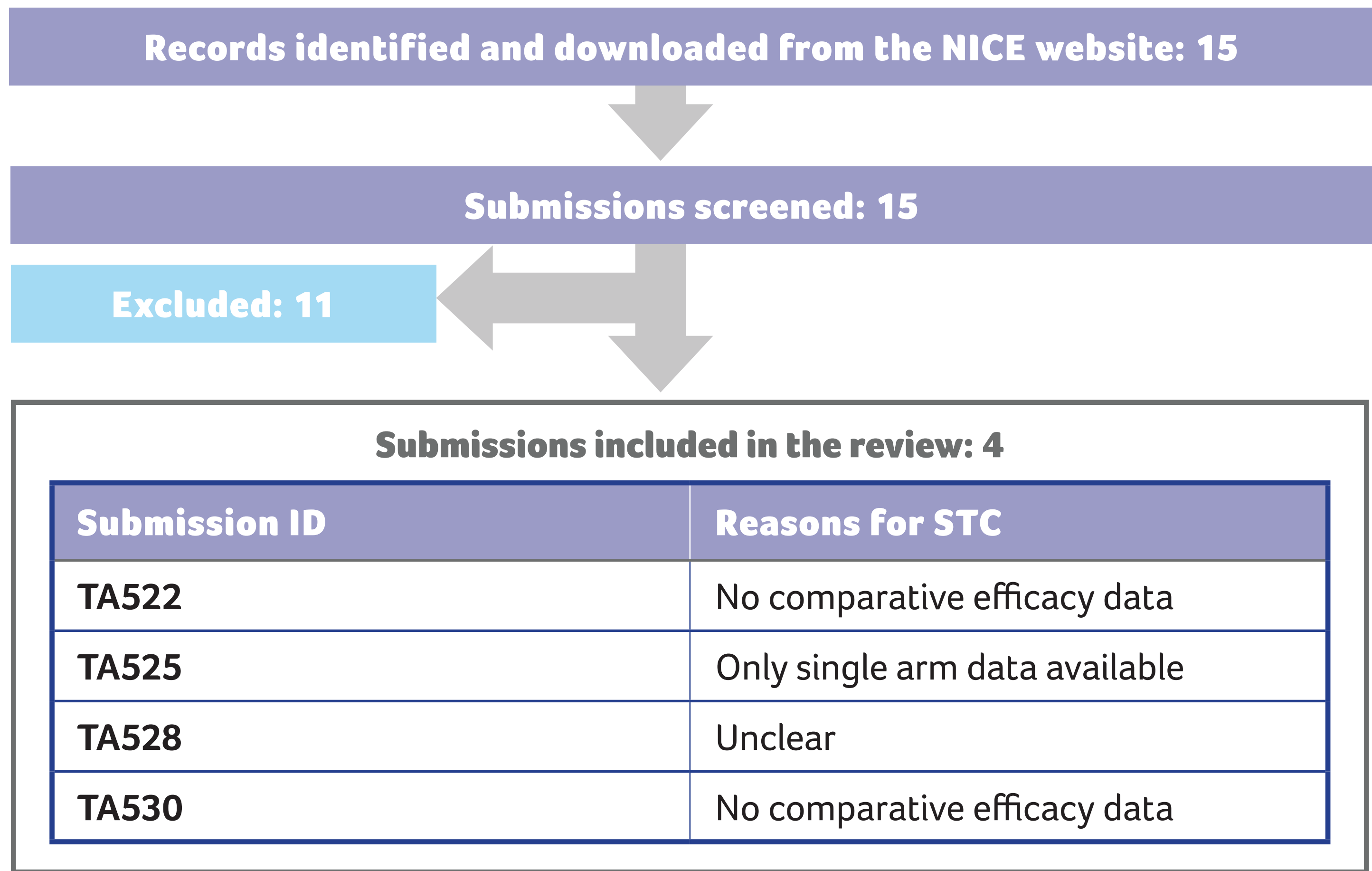
Background

- Population-adjusted indirect comparisons such as matching-adjusted indirect comparisons (MAICs) and simulated treatment comparisons (STCs) are becoming increasingly common in health technology assessments when conventional treatment comparisons are not feasible.
- Despite current National Institute for Health and Care Excellence (NICE) guidelines¹ not displaying a preference for conducting a MAIC over an STC, MAICs are more commonly used.
- This study evaluated recent NICE single technology appraisals (STAs) that used STCs to determine how their use is perceived by the Evidence Review Group (ERG) and the appraisal committee.

Methods

- The NICE website was searched using the key words “simulated treatment comparison” and “STC”. Full STA manufacturer submissions published after the release of NICE Decision Support Unit Technical Support Document 18 (December 2016)¹ were downloaded from the NICE website.
- STAs were included if the submission or response from the ERG included an STC analysis. All documents unrelated to STAs identified from the search were excluded.
- Details of the STA, rationale for performing an STC, methodology implemented, and the ERG and appraisal committee’s critiques of these methodologies were extracted from all eligible STAs.
- Records were screened by one reviewer. All extractions were performed by a single reviewer and checked by a second, independent reviewer. Any discrepancies were resolved by discussion or by a third independent reviewer if necessary.

Figure 1: PRISMA flow diagram



Results

- Fifteen STAs were screened and four were included in this review (**Figure 1**), all of which were published in 2018.
- All four STAs were oncology submissions where the manufacturer used STC methodology to analyse overall survival, progression-free survival or overall response rate outcomes.
- The main rationale for conducting STCs were no comparative efficacy data, only single arm data available for the intervention of interest or no rationale stated (**Figure 1**).
- Two STAs (TA525 and TA528) also conducted a MAIC.
- Mixed responses were given by the ERG, with the main negative feedback being lack of validity and omission of important prognostic variables and effect modifiers (**Table 1**).
- The appraisal committee mainly agreed with the responses provided by the ERG (**Table 1**).

Table 1: Submission IDs with ERG and appraisal committee comments

ERG comments	Appraisal committee comments
TA522	
The ERG disagrees with the company’s choice of STC instead of MAIC”	“The committee concluded that the results of the company’s simulated treatment comparison lack validity .”
“ Unlikely all effect modifiers and prognostic variables identified. ”	“The committee will consider both the company’s and the ERG’s indirect comparisons in its decision-making.”
TA525	
“ ...following concerns regarding the simulated treatment comparison: it is based on a very small set of covariates, some aspects of the analysis are unclear, including how the company accounted for missing covariate values and the cumulative impact of small errors and inconsistencies in the data is unclear.”	“The committee considered that it was unlikely that all of the important prognostic factors had been accounted for in the simulated treatment comparison and that the results of the simulated treatment comparison were very uncertain .”
“The ERG agrees that STC is the most suitable approach for the available data structure...”	
TA530	
“ ...the STC was limited by the following issues: the method used for the prediction models lacked transparency and there was a lack of information from the comparator studies on possible effect modifiers or prognostic variables...”	“The results of the simulated treatment comparison need to be treated with caution because the analysis was unanchored.”
“ Multiple limitations in the STC were identified and a judgment of the influence of the adjustment due to the STC cannot be evaluated because the company did not present an unadjusted (naïve) analysis.”	“The committee was aware that bias is introduced into a simulated treatment comparison if all important prognostic factors are not accounted for. It considered that it is unlikely that all of the important prognostic factors had been accounted for in the simulated treatment comparison, therefore affecting the robustness of the results”

TA528 conducted an STC although did not display the results as the models did not converge. Therefore, there was little/no feedback available from the ERG or appraisal committee.

Limitations and Further Work

- Investigation into STAs submitted to NICE which conducted MAICs over STCs may be part of future research to provide further insight into why STCs are not as commonly used.
- As this review only considered STAs submitted to NICE, results are not generalisable and future work could also assess how other health technology assessment bodies in other countries perceive the use of STCs.

Conclusions

- Despite current guidance, STCs are rarely used in NICE STAs and are generally not well received by the ERG and the appraisal committee.
- Many criticisms were not unique to STC methodology and therefore further research into why MAICs are more commonly implemented than STCs is warranted.
- Our research suggests that manufacturers unable to provide a conventional treatment comparison should fully assess the data available to ensure appropriate methodology is implemented to derive treatment comparison estimates.

References

¹ Phillipo D, Ades A, Dias S et al. Methods for population-adjusted indirect comparisons in health technology appraisal (2016). Medical Decision Making. 38(2): 200-211.