

# How Do NICE Evidence Review Groups Perceive Single Technology Appraisals Presenting Limited Evidence of Comparative Treatment Efficacy?

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## Objectives

- This study aimed to establish how commonly NICE single technology appraisals lack a conventional treatment comparison, the manufacturer's rationale for not conducting a conventional comparison, and the prevalence of non-conventional techniques.
- A further aim of this review was to determine how Evidence Review Groups perceive these single technology appraisals in the absence of well-established methods.

## Background

- Methods such as meta-analysis (MA), network meta-analysis (NMA) and indirect treatment comparison (ITC) techniques are recommended to determine relative treatment effects, using data from several high-quality randomised controlled trials (RCTs).<sup>1,2</sup>
- Often, however, these conventional methods cannot be used due to limited evidence or between-study heterogeneity.
- It is unclear how Evidence Review Groups (ERGs) perceive NICE single technology appraisals (STAs) in the absence of these established methods.

## Methods

- Full STA manufacturer submissions from 2015 onwards, excluding terminated appraisals and reappraisals, were downloaded from the NICE website in May 2017.<sup>3</sup>
- STAs were included if a conventional comparison, defined as a MA, NMA or ITC using aggregate data, had not been conducted. Any STAs reporting a conventional comparison were excluded at the review stage.
- Information including the rationale for not using a conventional methodology, the use of any non-conventional techniques, the ERG critiques of these methodologies, and the ultimate outcome of the appraisal was extracted from all eligible STAs.

Figure 1 | PRISMA flow diagram

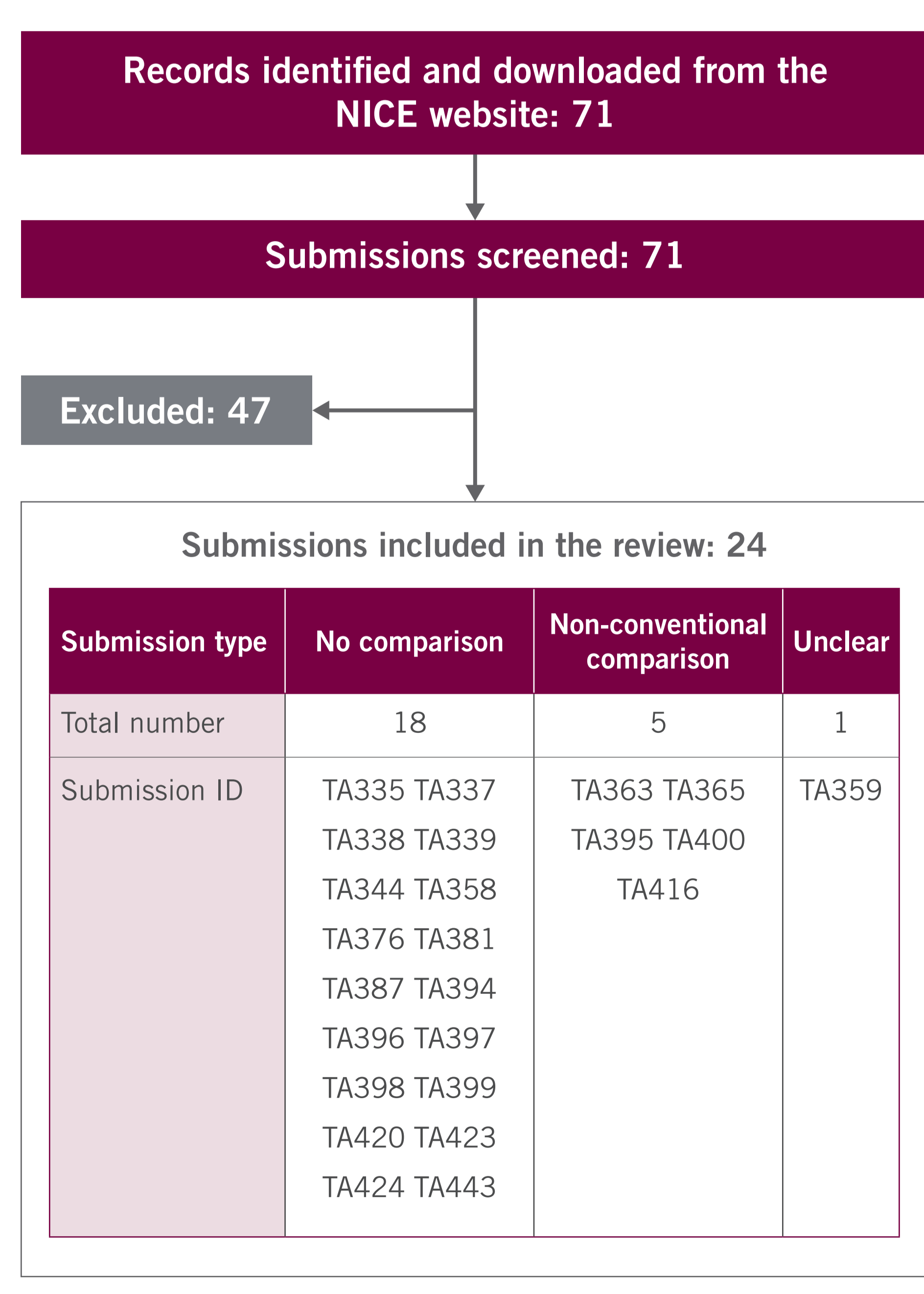
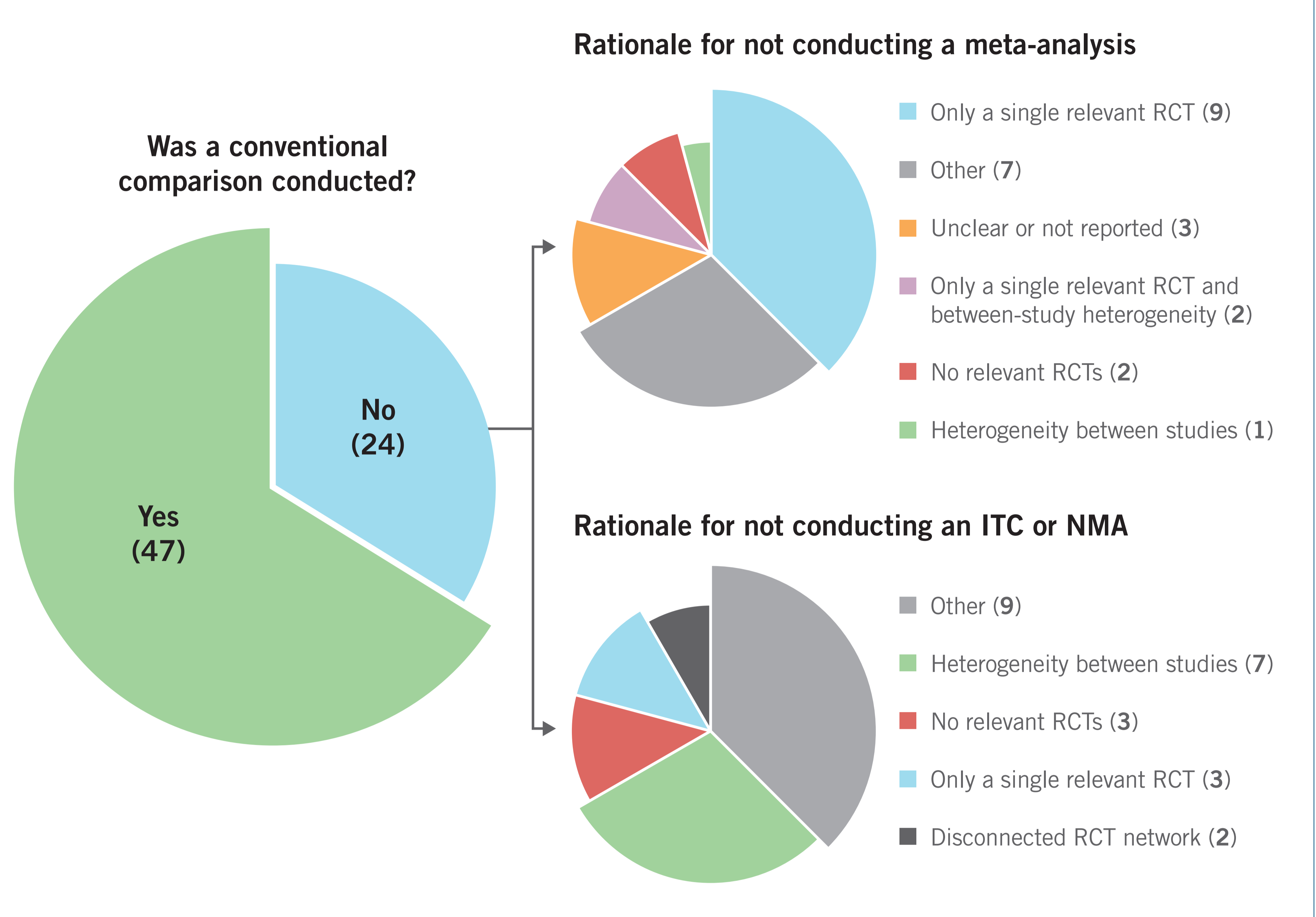


Figure 2 | Summary of rationale for not conducting a conventional comparison



- 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.

## Results

- Seventy-one STAs were screened and 24 were ultimately included in this review (Figure 1), of which 22 received a positive recommendation from NICE.
- In 11 of the 24 included STAs, the primary reason cited for not conducting a MA was because only a single relevant RCT was identified for the comparison of interest (Figure 2). Of these, two STAs also listed heterogeneity between studies as an additional factor.
- The remaining 13 STAs gave other reasons for not conducting a MA, or did not consider a MA. For two STAs, no MA was considered despite demonstrating sufficient evidence for this analysis and in one of these submissions (TA397) this was queried by the ERG.
- The primary reason for not conducting an ITC or NMA in seven of the 24 included STAs was between-study heterogeneity (Figure 2).
- In five of the 24 STAs assessed, the ERG concluded that conventional methodology could have been utilised and in one case conducted their own MA.
- Only six submissions used non-conventional methods which included:
  - Two naïve comparisons
  - Three adjusted comparison methods
  - One MA using single-arm trial data
- The ERGs were largely receptive of these non-conventional methods and acknowledged the data limitations; all six submissions were recommended. One ERG commended a manufacturer for their use of adjusted comparison techniques (TA416).

## Limitations and Future Work

- This analysis only considered STAs submitted from 2015 onwards, and did not consider reappraisals. These results may therefore have limited value when considering multiple technology appraisals, for example.
- As this work only considered STAs submitted to NICE, future work could assess how Health Technology Assessment bodies in different countries interpret submissions with limited evidence of relative treatment efficacy.

## Conclusions

- The primary reasons for a lack of conventional MA, NMA or ITC were limited data availability, availability of direct evidence from head-to-head trials, and between-study heterogeneity.
- ERGs were generally receptive of submissions that did not include a conventional comparison if a robust search strategy and full exploration of the evidence had been undertaken.
- Our research suggests that manufacturers unable to provide a conventional treatment comparison should fully assess the data available to inform a comparison and comprehensively report their findings.

## References

- Dias S. *et al.* "NICE DSU Technical Support Document 1: Introduction to evidence synthesis for decision making." University of Sheffield, Decision Support Unit 2011:1–24; 2. Dias S. *et al.* "NICE DSU Technical Support Document 2: A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials." University of Sheffield, Decision Support Unit 2011; 3. National Institute for Health and Care Excellence website. Available at: <https://www.nice.org.uk/> [Last accessed May 2017].

Appraisal documents for each of the 71 NICE appraisals were downloaded from the NICE website.

## Acknowledgements

The authors thank Mark Tassell, Costello Medical, for graphic design assistance.