Demonstrating Similar or Greater Health Benefits Based on Indirect Evidence: A Review of NICE Evaluations that Included a Cost-Comparison Approach

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Objective

To understand the indirect evidence accepted by NICE to demonstrate similar/greater health benefits between an intervention and the relevant comparator(s) and meet the NICE cost-comparison pathway criteria.

Background

- The National Institute for Health and Care Excellence (NICE) cost-comparison pathway (formerly fast-track appraisal [FTA] pathway) is an expedited reimbursement route that aims to grant faster access to new interventions than the conventional single technology appraisal (STA) pathway.[1,2]
- Suitable interventions for consideration via the cost-comparison pathway are those that can demonstrate similar/greater health benefits, at similar/lower costs, than technologies already recommended in the same indication.[1] Where this is demonstrated, a cost-comparison analysis (also referred to as a cost-minimisation analysis) is sufficient in lieu of a cost-utility analysis that is typically required for the STA pathway.
- As head-to-head evidence is often not available between an intervention and the relevant comparator(s), indirect treatment comparisons (ITCs) are frequently used to demonstrate similar/greater health benefits in these evaluations. However, the interpretation of ITC results can often be associated with high uncertainty and it is unclear what indirect evidence is accepted by NICE to meet the criteria for a cost-comparison analysis.

Methods

- The Committee papers for NICE evaluations with final guidance published between 1 April 2017 (when the cost-comparison pathway was launched) and 1 May 2023 were searched for relevant terms relating to cost-comparison and cost-minimisation analyses.
- Evaluations that included a cost-comparison analysis were added to a pre-formatted extraction grid into which details of the evidence used to demonstrate similar/greater health benefits were extracted, including the methodology of any ITC used and the volume of indirect evidence presented.
- Data extraction was undertaken by two reviewers and a third reviewer independently verified the extracted information.

Results

- A total of 30 NICE evaluations were identified which included a cost-comparison analysis, of which 19 fell under the NICE cost-comparison pathway and 11 were STA evaluations that included a cost-comparison analysis; all 30 interventions evaluated received a positive recommendation in at least one population.
- The vast majority of evaluations (26/30; 86.7%) demonstrated similar/greater health benefits using an ITC, of which 20/26 (76.9%) used a network meta-analysis (NMA; **Figure 1**). The remaining evaluations (4/30; 13.3%) demonstrated similar/greater health benefits through randomised control trial data or bioequivalence.
- Considering the ITC results for the primary clinical efficacy endpoint, 3/26 (11.5%) evaluations demonstrated statistically significant superiority for the intervention versus comparator(s), 9/26 (34.6%) demonstrated no statistically significant difference and 5/26 (19.2%) described 'comparable' results (**Table 1**). Results were fully redacted for the remaining evaluations (9/26 [34.6%]).
- In 2/26 (7.7%) evaluations, similar/greater health benefits were demonstrated based on ITC results for one clinical efficacy endpoint; the majority of evaluations (16/26; 61.5%) presented ITC results for four or more efficacy endpoints (**Figure 2**).
- In addition, 18/26 (69.2%) and 2/26 (7.7%) evaluations used ITC results to demonstrate similar/greater health benefits in terms of safety and health-related quality of life, respectively.
- Lastly, 18/26 (69.2%) evaluations cited clinical expert feedback to support the demonstration of similar/greater health benefits for the intervention.

Conclusions

In the vast majority of NICE evaluations which included a cost-comparison analysis, ITCs (most commonly NMAs) were used to demonstrate similar/greater health benefits between the intervention and the relevant comparator(s). However, there was considerable variation in the ITC results presented by the manufacturer and subsequently accepted by NICE, particularly in terms of statistical significance and the number of endpoints presented. Where only one or two ITC endpoints were presented, it may be useful in future research to understand if there were additional contributing factors to the acceptance of the cost-comparison analysis, such as whether the intervention had the same mechanism of action as the relevant comparator(s).

All evaluations analysed had a positive recommendation from NICE in at least one population, but some had rejections in some of the considered populations. Further research is therefore warranted to analyse the reasons why a cost-comparison analysis may not have been accepted in a particular population.

Finally, a limitation of this research is that over one third (9/26 [34.6%]) of the evaluations had redacted ITC results. This may be improved following NICE's recent update to confidentiality marking, which should lead to less redacted data in future evaluations.

TABLE 1

Summary of NICE evaluations that used an ITC to demonstrate similar/greater health benefits (N=26)

TA number	Title	Type of evaluations	ITC primary clinical endpoint result: Statistically superior	Not statistically different	Comparable	Fully redacted	Demonstrated similar/greater safety	Demonstrated similar/greater HRQoL	Support obtained from clinical experts
TA871	Eptinezumab for preventing migraine	STA → FTA (scenario cost-comp)		✓					✓
TA868	Vutrisiran for hereditary transthyretin-related amyloidosis	FTA			✓				✓
TA861	Upadacitinib for active non-radiographic axial spondyloarthritis	FTA		✓					✓
TA829	Upadacitinib for active ankylosing spondylitis	FTA			✓				✓
TA820	Brolucizumab for diabetic macular oedema	FTA			✓		✓		✓
TA803	Risankizumab for previously treated active psoriatic arthritis	FTA				✓	✓		✓
TA799	Faricimab for diabetic macular oedema	FTA			✓		✓		✓
TA800	Faricimab for wet age-related macular degeneration	FTA				✓	✓		✓
TA773	Empagliflozin for chronic heart failure with reduced ejection fraction	STA → FTA (scenario cost-comp)				✓	✓		
TA735	Tofacitinib for juvenile idiopathic arthritis	FTA				✓	✓		✓
TA723	Bimekizumab for moderate to severe plaque psoriasis	FTA				✓	✓		
TA705	Atezolizumab monotherapy for untreated advanced non-small cell lung cancer	STA → FTA (scenario cost-comp)				✓			✓
TA689	Acalabrutinib for chronic lymphocytic leukaemia	STA → FTA (scenario cost-comp)		✓			✓		✓
TA685	Anakinra for Still's disease	Other*		✓			✓		✓
TA671	Mepolizumab for severe eosinophilic asthma	FTA	✓				✓		
TA672	Brolucizumab for wet age-related macular degeneration	FTA			✓		✓		
TA670	Brigatinib for ALK-positive advanced non-small cell lung cancer that has not been previously treated with an ALK inhibitor	STA (base case cost-comp)		✓					✓
TA596	Risankizumab for moderate to severe plaque psoriasis	FTA				✓	✓	✓	
TA583	Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for type 2 diabetes	STA (base case cost-comp)		✓			✓		✓
TA572	Ertugliflozin monotherapy and dual therapy for type 2 diabetes mellitus	FTA	✓				✓		
TA563	Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer	STA → FTA (scenario cost-comp)				✓			✓
TA561	Venetoclax in combination with rituximab for relapsed or refractory chronic lymphocytic leukaemia	STA → FTA (scenario cost-comp)				✓			✓
TA562	Encorafenib with binimetinib for unresectable or metastatic BRAF V600 mutation-positive melanoma	STA → FTA (scenario cost-comp)		✓			✓	✓	✓
TA521	Guselkumab for moderate to severe plaque psoriasis	FTA	✓				✓		
TA497	Golimumab for non-radiographic axial spondyloarthritis	FTA		✓			✓		
TA486	Aflibercept for choroidal neovascularisation	FTA		✓			✓		✓

*The External Assessment Group (EAG) provided a cost-minimisation analysis which was concluded to be sufficient for decision making by NICE.

FIGURE 1

Type of ITC used to demonstrated similar/greater health benefits (N=26)

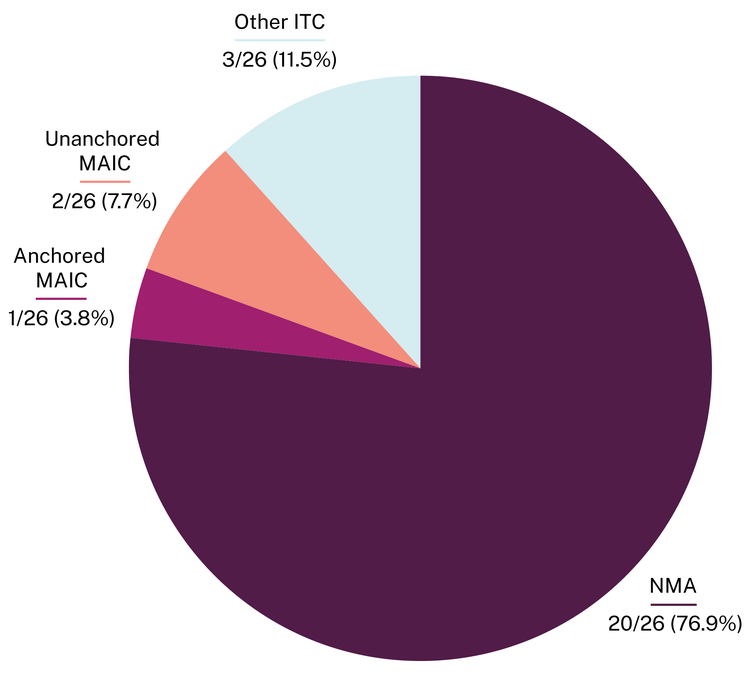
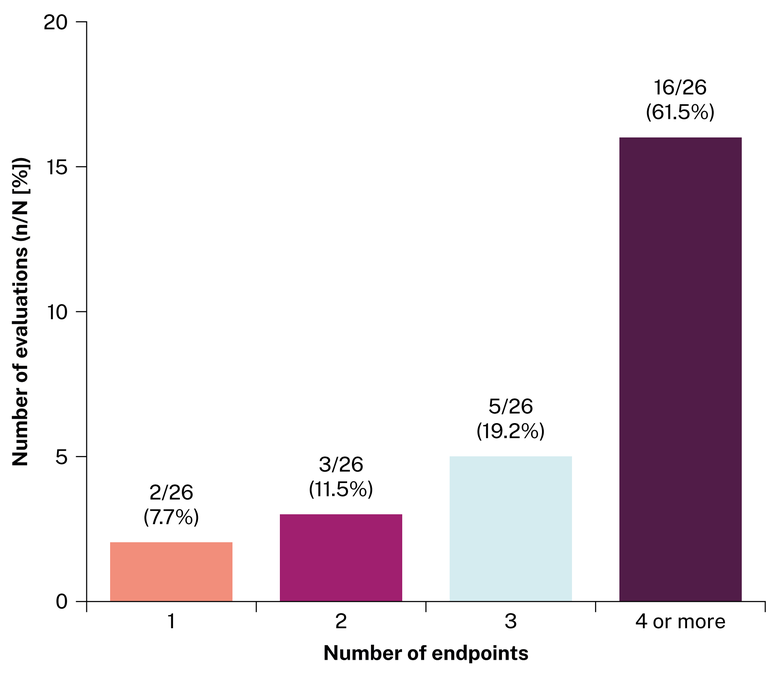


FIGURE 2

Number of ITC clinical efficacy endpoints used to demonstrate similar/greater health benefits (N=26)



Abbreviations: Cost-comp: cost-comparison; **EAG:** Evidence Assessment Group; **FTA:** fast-track appraisal; **HRQoL:** health-related quality of life; **ITC:** indirect treatment comparison; **MAIC:** matching-adjusted indirect comparison; **NICE:** National Institute for Health and Care Excellence; **TA:** technology appraisal; **STA:** single technology appraisal.

References: [1]National Institute for Health and Care Excellence. Health technology evaluations: interim methods and process guide for the proportionate approach to technology appraisals. Available at: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/process [Last accessed: 06.10.23]; [2]Thiam A *et al*. Presented at ISPOR Europe 2022. Vienna, Austria. HTA151; [3]National Institute for Health and Care Excellence. Principles for marking and redacting confidential information in technology appraisals and highly specialised technologies evaluations. Available at: https://www.nice.org.uk/process/pmg40/chapter/developing-guidance [Last accessed: 22.09.23]. **Acknowledgements:** The authors thank Emma White, Costello Medical, for graphic design assistance.

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