

The use of exploratory analyses within the National Institute for Health and Care Excellence single technology appraisal process: an evaluation and qualitative analysis

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Scientific summary

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Background

The National Institute for Health and Care Excellence (NICE) single technology appraisal (STA) process is undertaken for a technology for a single indication. The process includes the production of a submission by the manufacturer of the technology. One of the nine independent Evidence Review Groups (ERGs) undertakes a critical appraisal of this submission. As part of the critical appraisal process the ERG may undertake exploratory analyses to explore uncertainties around the company's model and their implications for decision-making. The number and type of exploratory analyses undertaken varies between appraisals. The ERG reports are a central component of the evidence considered by the NICE Technology Appraisal Committees (ACs) in their deliberations. The findings of the committee are used to produce the appraisal consultation document (ACD) and, after further considerations and a consultation period, a final appraisal determination (FAD) is produced, which results in NICE guidance.

Objectives

The aim of this research was to develop an understanding of the number and type of exploratory analyses undertaken by the ERGs within the NICE STA process and to understand how these analyses are used by the NICE ACs in their decision-making process. For the purpose of this research, an exploratory analysis was defined as any additional analysis generating an incremental cost-effectiveness ratio (ICER) and included in the ERG report section 'Exploratory and sensitivity analyses undertaken by the ERG'. This is most commonly reported as Section 6 of an ERG report, based on the suggested ERG report template. The study aimed to address the following objectives:

1. to identify ERG reports that contain exploratory analyses conducted by the ERG, as defined above
2. to identify ERG approaches to exploratory analyses of economic evidence submitted by companies for NICE STAs and to categorise these approaches by type of analysis performed
3. to identify data sources used for exploratory analyses undertaken by ERGs
4. to identify factors that influence or predict the extent of ERG exploratory analyses
5. to identify whether or not companies were provided with the opportunity to provide the analyses as part of the clarification stage
6. to identify situations in which a committee requested the ERG to conduct additional analyses
7. to make an assessment of the degree to which the exploratory analyses influenced a committee's considerations and recommendations.

Methods

The 100 most recently completed STAs (from 2009) for which guidance has been published were selected for inclusion in the analysis. The documents associated with the 100 STAs and used in data extraction were:

- ERG reports (unredacted versions, including confidential information used by the ACs)
- clarification letters and responses
- the first ACD issued (subsequent ACDs were not considered)
- the last FAD issued (where more than one FAD has been produced).

More than 400 documents were assessed in this study. Information on the number of AC meetings for each STA was provided directly by NICE.

A data extraction tool was developed and piloted to ensure usability and to standardise extraction. The final categories of exploratory analyses were based on discussions with the project team and used an existing relevant published taxonomy; the categories of types of exploratory analyses included (i) fixing errors, (ii) fixing violations, (iii) addressing matters of judgement and (iv) the ERG-preferred base case. All data extractions were double-checked. A narrative synthesis of the extracted data was performed, summarising key data through text and tables to address the objectives. The mean number of exploratory analyses per ERG report was calculated as well as the median. The key data used in the synthesis were then reduced to whether a STA conducted more or fewer than the overall mean number of exploratory analyses.

Results

The level and type of detail in ERG reports and clarification letters varied considerably. The principal disease areas covered by the STAs were cancer (44%), blood and the immune system conditions (11%), cardiovascular conditions (10%) and musculoskeletal conditions (8%). Of the 100 STAs, 21% were assessed by the AC using end-of-life criteria. The vast majority (93%) of ERG reports reported one or more exploratory analyses with a range from 1 to 29 per report with an approximate mean of 8.5 analyses per report and a median of 7 analyses per report. The most frequently reported type of analysis in the 93 ERG reports that generated at least one exploratory analysis related to the category 'matters of judgement', which was reported in 83 (89%) of reports. The category 'ERG base-case/preferred analysis' was reported in 45 (48%), the category 'fixing errors' was reported in 33 (35%) and the category 'fixing violations' was reported in 17 (18%). ERG reports often included more than one type of exploratory analysis. The principal source of data used by the ERG was published literature.

The likelihood of an ERG performing eight or more exploratory analyses was not affected by the company's base-case ICER or disease area covered by the STA. The proportion of ERG reports with eight or more analyses appears to be relatively stable over time, although the number of exploratory analyses did vary by ERG.

Of the 93 STAs with at least one exploratory analysis, 65 (70%) ERG reports included at least one exploratory analysis that was covered in the clarification letter to the company. Overall, 36% (287/798) of the total exploratory analyses within the 93 reports were issues highlighted at the clarification stage. Almost all exploratory analyses performed were the result of any issue raised by an ERG in its critique of the submitted economic evidence, usually in the chapter in the ERG report preceding the section in which the exploratory analyses were presented.

Appraisal consultation document recommendations were clearly influenced by one or more of the mentioned ERG exploratory analyses in 55 out of the 76 STAs with ACDs (72%). This was reduced for FADs, as FAD recommendations were clearly influenced by one or more of the mentioned ERG exploratory analyses in 44 out of the 93 STAs with FADs (47%). The preferred ICERs reported in ACDs were 36% from ERGs and 11% from companies, while in 9% of ACDs, ICERs from both ERGs and companies were included or the ICERs from both were the same. This changed at FAD, where the preferred ICERs were 27% from ERGs and 23% from companies, with 17% of FADs using some ICERs from ERGs and some from companies.

Discussion

An ERG's judgement relating to perceived uncertainties or possible variation in the evidence base and model was the type of exploratory analysis appearing in the largest proportion of ERG reports. Rather than simply generating a single alternative ICER, exploratory analyses were conducted to present a number of scenario analyses.

As the most recent 100 STAs with guidance issued were included in this analysis, current practice is reflected. Extensive piloting and double-checking of data by experienced modellers helped to reduce inconsistencies and inaccuracies in the data extraction. By using a descriptive synthesis method, the likelihood of overstating relationships in the data was reduced.

Data extraction was difficult owing to the differences in the level and type of detail provided in the ERG reports and clarification letters so that data extractors had to exercise interpretation of some of the data. When grouping reports by indication, ICER or numbers of exploratory analyses, the numbers were too small to evaluate relationships in the data using basic statistical tests in a meaningful manner.

Conclusions

Evidence Review Groups frequently conduct exploratory analyses to test or improve the economic evaluations submitted by companies as part of the STA process. ERG exploratory analyses appear to often influence the recommendations produced in the ACDs and FADs issued within the NICE STA process. The influence appears to be greatest for ACDs and this influence is reduced by subsequent work between the ACD and the FAD. For the 79% of STAs with no ACD, the company ICER was < £20,000 per quality-adjusted life-year gained and the impact of the analyses was reduced. Caution should be used when drawing conclusions from the evidence, especially concerning the generalisability of the findings.

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