Assessing Literature Reviews in NICE Single and Multiple Technology Appraisals

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INTRODUCTION & OBJECTIVES

- NICE Evidence Review Groups (ERGs) review and critically appraise manufacturers' evidence submissions as part of technology appraisal processes, to recommend whether technologies would represent an effective use of NHS resources in England and Wales.[1]
- NICE has detailed requirements for clinical systematic reviews for reimbursement submissions,[2] and the quality of clinical systematic review methods and reporting submitted by the manufacturer may affect the outcome of submissions.
- We therefore conducted a review of submissions to:
  - Assess the limitations of companies' clinical review methodologies as critiqued by NICE ERGs in recent appraisals
  - Provide guidance to manufacturers on clinical literature review practices to assist in future submissions

METHODS

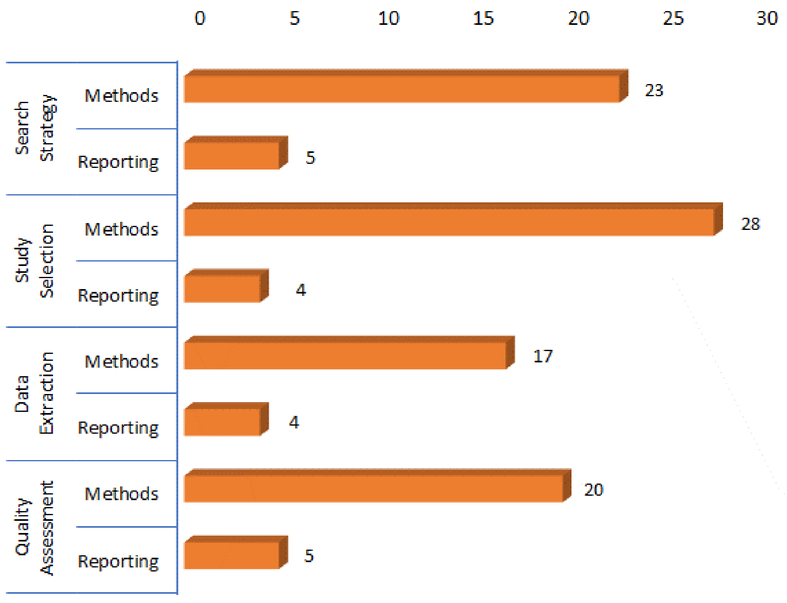
- ERG reports available on the NICE website were retrieved by searching manufacturer submissions published between year 2019 to 2021.
- The manufacturer's approach to the clinical systematic literature review (SLR) in terms of methodology/ reporting and the critiques highlighted by ERG was extracted.
- A mapping spreadsheet was developed to collect data on 31 predefined variables related to search strategy, study selection, data extraction, and quality assessment (QA).
- We used descriptive statistics using MS Excel® to analyze the data.

RESULTS

EVIDENCE IDENTIFICATION AND SUBMISSION CHARACTERISTICS

- Ninety-six submissions were identified with associated ERG reports: 33, 33, and 30 in 2019, 2020, and 2021, respectively.
- Of the included 96 submissions, half were for therapies to treat indications in oncology (48), followed by neurology (12), rheumatology (7), cardiology, immunology, respirology, metabolism & endocrinology (4 each), urology, dermatology, gastroenterology, hematology (3 each), and ophthalmology (1).
- The ERG noted limitations related to the clinical systematic literature review in 58% of submissions. Submissions were most often critiqued for issues in study selection methodology or reporting (28 reports), search strategies (26 reports), QA (21), and data extraction (17) (Figure 1).

Figure 1. Number of submissions in which clinical systematic literature reviews were critiqued



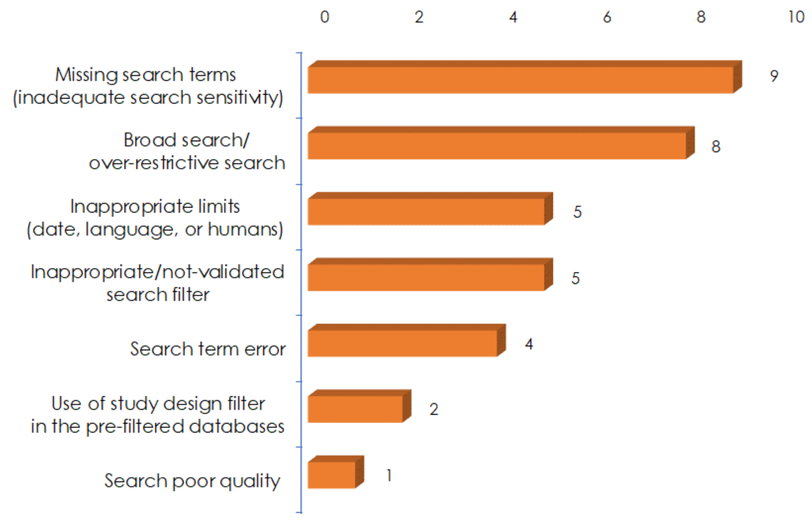
SEARCH STRATEGIES

- The ERG provided comments or critiques on search strategy conduct and/or reporting in 26 submissions.
- The main issues included missing indexed or free-text terms (9 submissions), use of over-restrictive search terms or the use of too broad search terms (8) (Figure 2)

RESULTS (*continued..*)

- Reporting issues included search terms for conference proceedings not being properly documented (2 submissions) and missing line(s) in the search strategy (1)

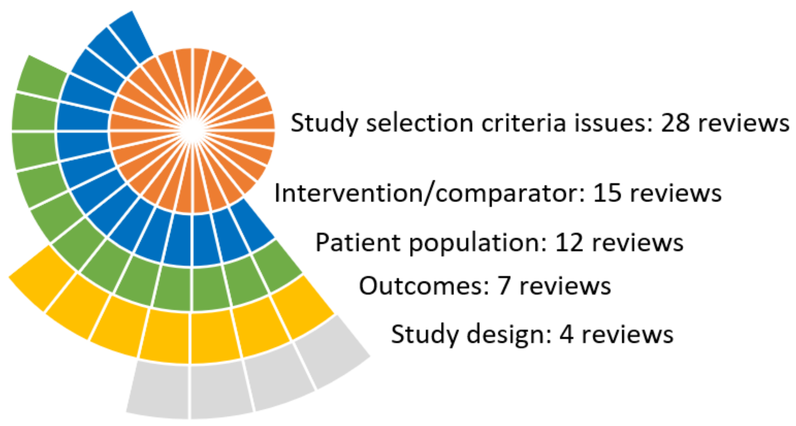
Figure 2. Number of submissions critiqued on conduct of search strategy



STUDY SELECTION

The ERG noted limitations in the study selection methodology or reporting in 28 submissions. Figure 3 presents the issues related to study selection criteria used.

Figure 3. Number of submissions critiqued on inclusion/exclusion criteria



- Nine submission reviews were critiqued on a broader/narrower population than specified in the NICE scope. Three reviews focused on a population not fully representative as defined in the scope.
- For intervention/comparators, the main issues were inclusion of limited comparators or exclusion of valid comparators based on clinical practice (7 submissions).
- Reviews in three submissions had inappropriate selection of outcomes.
- For study design, one submission was critiqued for not including non-RCTs, which may have led to missing potentially eligible studies.
- In three submissions, an English language restriction was applied, possibly leading to missing relevant publications.
- For review process, only one reviewer was involved in three submissions, which was considered as a potential source of bias by the ERG.

Reporting:

- The number of reviewers involved in the study selection process was not reported for 20 submissions.
- ERG noted inconsistencies in PRISMA reporting in terms of numbers not following a logical progression (2 submissions), mismatch in search numbers (1), or no exclusion reasons reported for full-text articles (2).

DATA EXTRACTION

The ERG provided critiques on the data extraction methodology and/or reporting for 14 submissions.

Methodology:

- Data quality was considered inappropriate in four submissions due to data extraction errors, data extracted being unsuitable for comparison, or data extracted for network meta-analysis only.
- Thirteen submissions were critiqued for data extraction being conducted by a single reviewer only.

Reporting: Noted to be appropriate in most submissions (60 submissions). Four reviews provided incomplete data or did not provide a copy of the data extraction sheet. For the remaining submissions, the ERG did not comment on this reporting issue.

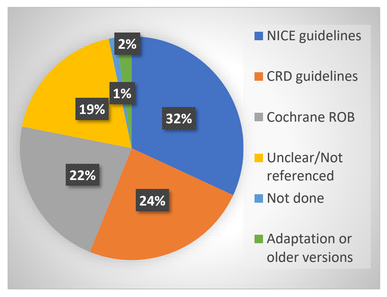
RESULTS (*continued..*)

QUALITY ASSESSMENT

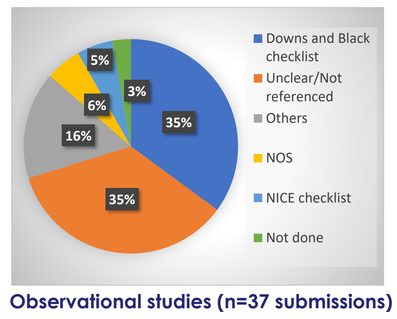
Seventy-four submissions reported use of a quality assessment tool.

- For appraisal of RCTs in 91 submissions, the NICE checklist was used in 29, followed by the tool in the Centre for Review and Dissemination guidance in 22, and Cochrane Risk of Bias tool in 20 submissions.
- Observational studies were included in 37 submissions, of which 13 used the Downs and Black checklist was used to appraise studies (Figure 4).

Figure 4. Quality assessment tools used in the included submissions



RCTs (n=91 submissions)



Observational studies (n=37 submissions)

Abbreviations: CRD: Centre for Review and Dissemination; NOS: Newcastle Ottawa Scale; ROB: risk of bias
Note: Other tools for observational studies; Cochrane ROBINS-I, Quality Assessment Tool for Quantitative Studies as part of the Effective Public Health Practice Project (EPHPP), STROBE checklist, and Institute of Health Economics (IHE) Quality Assessment Checklist, and Critical Appraisal Skills Programme (CASP) quality assessment tool.

The ERG noted limitations in the QA methodology and reporting for 21/96 submissions.

Methodology:

- ERG critiqued the use of an older, modified version of the Cochrane risk of bias tool (not adaptable to single arm trials) in one submission. The ERG also noted incorrect assessments in four submissions, and two in which all included studies were not critically appraised with the help of a QA tool.
- QA of included studies was performed by a single reviewer in 14 submissions.

Reporting: Limitations in QA reporting was highlighted by ERG in five submissions, specifically: not reporting the name of the tool (3 submissions) or not providing details of the assessment (2).

DISCUSSION AND CONCLUSION

- In recent HTA submissions, the ERG noted issues related to methodology and reporting of clinical systematic reviews, particularly study selection. Weaknesses in search strategies, data extraction, and quality assessment were also noted.
  - These issues may lead to delays in assessments, additional work and may also affect the outcome of submissions.
- Overall quality of clinical SLRs will be improved if manufacturers carefully address the following issues:
  - Adopt appropriate methodology for study selection and provide a rationale or justification for differences in inclusion/exclusion criteria with those of the NICE scope
  - Search strategies should be carefully designed with a combination of indexed and free-text terms and properly documented according to recognized standards[3,4]
  - Data extraction should be conducted by two independent reviewers and checked for quality
  - Quality assessment methods and findings should be transparently reported, with appropriate selection of tools used for the assessment.
- In summary, shortcomings in review methodology and reporting in submissions are frequently noted by the ERG, which contribute to uncertainty in the evidence and require additional clarifications from the manufacturer. Meeting the SLR requirements of NICE ERGs would improve efficiency of the HTA process.

REFERENCES

1. NICE. April 2018. Available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/technology-appraisal-processes-guide-apr-2018.pdf
2. NICE. 10 Feb 2022. Available at: https://www.nice.org.uk/process/pmg24/resources/single-technology-appraisal-and-highly-specialised-technologies-evaluation-user-guide-for-company-evidence-submission-appendices-10956190861/chapter/instructions-for-companies
3. Page *et al.* Sys revs. 2021;10(1):1-1.
4. Rethlefsen *et al.* Sys rev. 2021;10(1):1-9.

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