Identification of clinical effectiveness evidence in UK NICE single technology appraisal company submissions: databases, sources, and currency of searching

Kate Misso, Akvile Stoniute, Rhiannon Green, Nick Pooley

Maverex Limited, Newcastle upon Tyne, UK

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01 BACKGROUND

- Comprehensive systematic reviews (SRs) of clinical and cost-effectiveness evidence underpin company submissions to the UK National Institute for Health and Care Excellence (NICE) Single Technology Appraisal (STA) process for drug reimbursement. Independent Evidence Assessment groups (EAGs, previously called Evidence Review Groups: ERGs) critique company submissions and prepare EAG/ERG reports to aid NICE Appraisal Committees' consideration of each topic.
- NICE mandates up-to-date, well-conducted and robust methods,[1] however STA approaches vary greatly between submissions.

02 OBJECTIVES

- To survey the databases and sources used to identify clinical effectiveness in UK STA submissions to NICE;
- To examine the currency of search methods in relation to time to evidence submission;
- To assess application of language limits;
- To explore the transparency of clinical effectiveness evidence identification within STA submissions available in the public domain.[2]

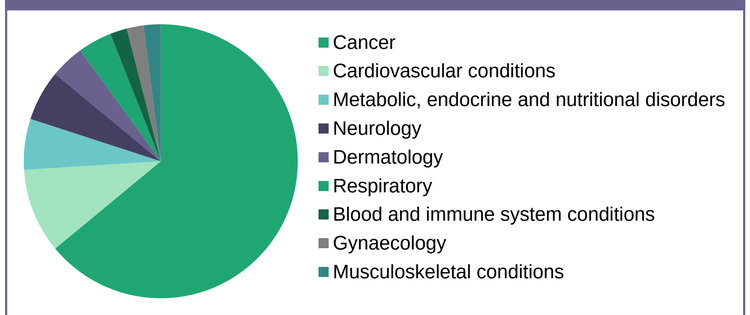
03 METHODS

- We conducted a survey of 50 randomly selected STA submissions included in committee papers for NICE STA submissions published between 10.1.2018 and 6.12.2023.
- As NICE limit the content of technology appraisal committee papers in the public domain,[2] available data were extracted from company submissions, clarification responses and EAG reports.
- Terminated appraisals, Fast Track Appraisal (FTA), Multiple Technology Appraisal (MTA) and Cancer Drugs Fund (CDF) submissions were excluded. For each STA submission included in our analysis, characteristics relating to the disease area, ERG/EAG, databases and grey literature searched, date of last search and submission date, and language restrictions, were extracted.

04 RESULTS

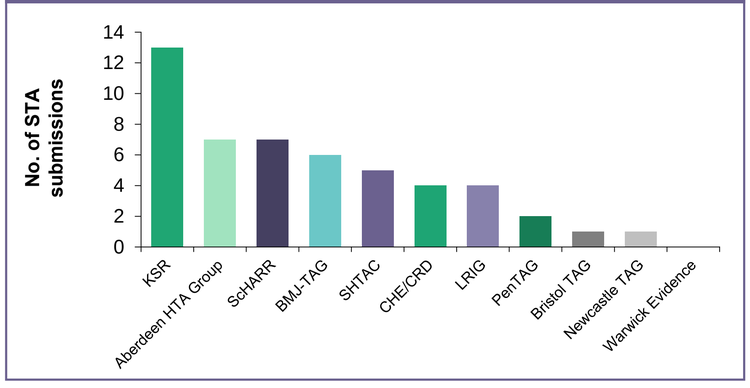
The majority of STAs in the sample (n=50) included indications in cancer (32), cardiovascular (5), neurology (3), and metabolic, endocrine and nutritional disorders (3).

Figure 1: Number of STAs in each disease area



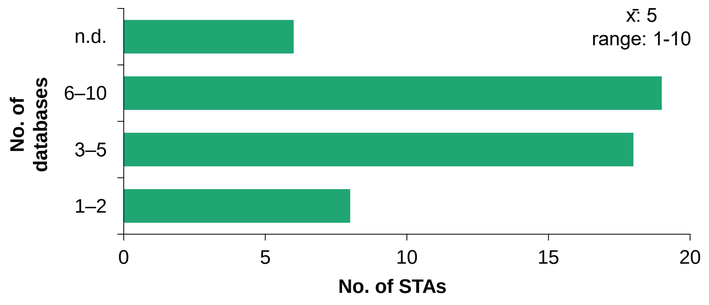
In our sample, the majority of STA assessments were carried out by the KSR ERG (26%, 13/50). None of the assessed STA critiques were prepared by Warwick Evidence.

Figure 2: Number of STAs from each EAG/ERG (n=50)



The mean number of databases searched per topic was 5 (range: 1-10).

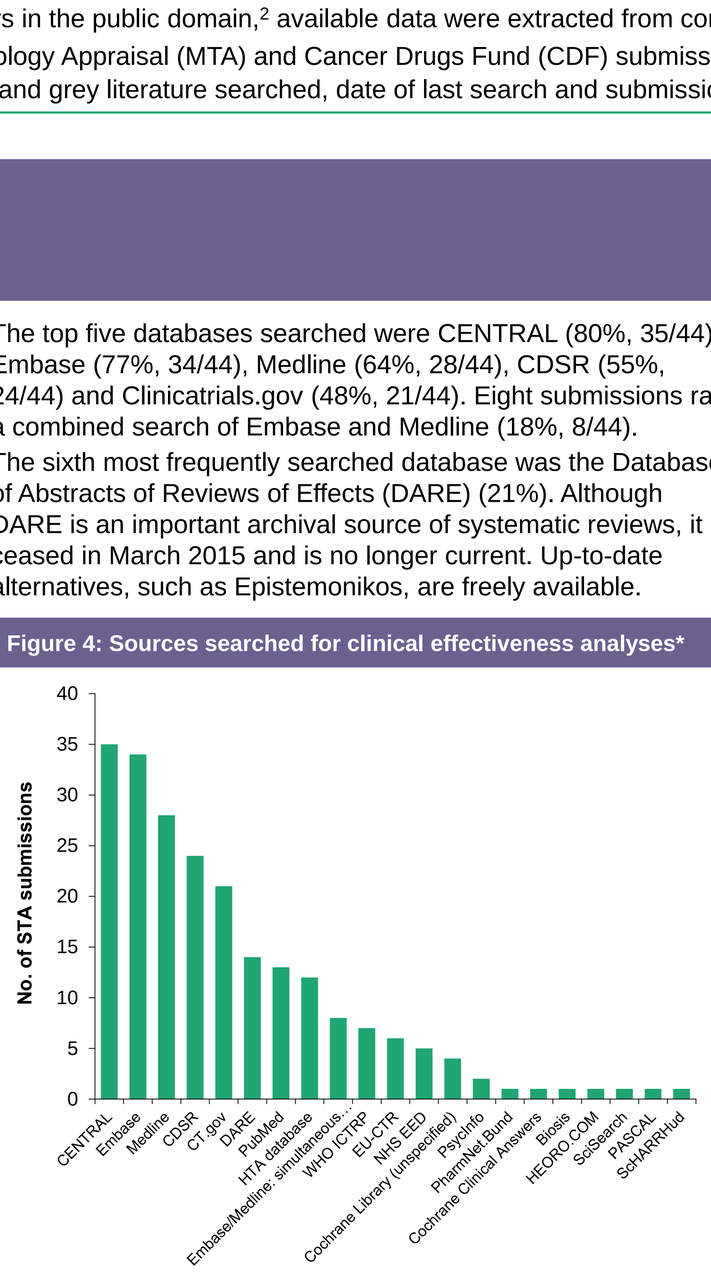
Figure 3: Number of databases searched by STAs in the sample



The top five databases searched were CENTRAL (80%, 35/44), Embase (77%, 34/44), Medline (64%, 28/44), CDSR (55%, 24/44) and Clinicatrials.gov (48%, 21/44). Eight submissions ran a combined search of Embase and Medline (18%, 8/44).

The sixth most frequently searched database was the Database of Abstracts of Reviews of Effects (DARE) (21%). Although DARE is an important archival source of systematic reviews, it ceased in March 2015 and is no longer current. Up-to-date alternatives, such as Epistemonikos, are freely available.

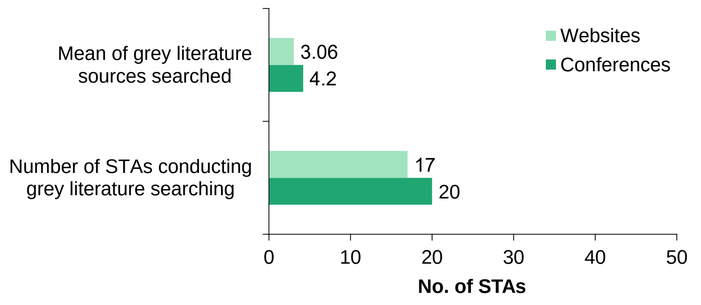
Figure 4: Sources searched for clinical effectiveness analyses*



*Most STAs searched more than one source.
6/50 STA presented no information about sources searched.

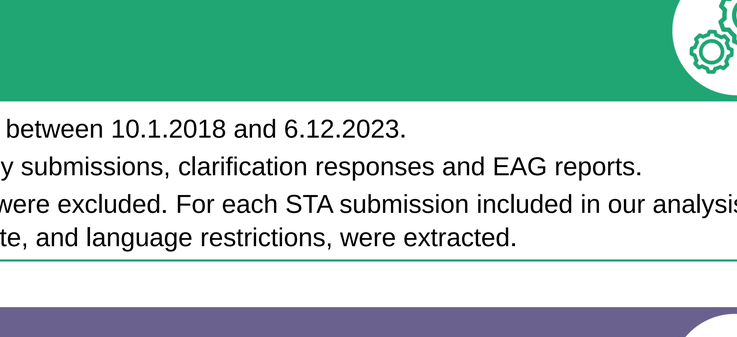
40% of submissions included conferences (20/44) and only 34% searched grey literature, such as regulatory body websites (17/44)

Figure 5: Grey literature inclusion



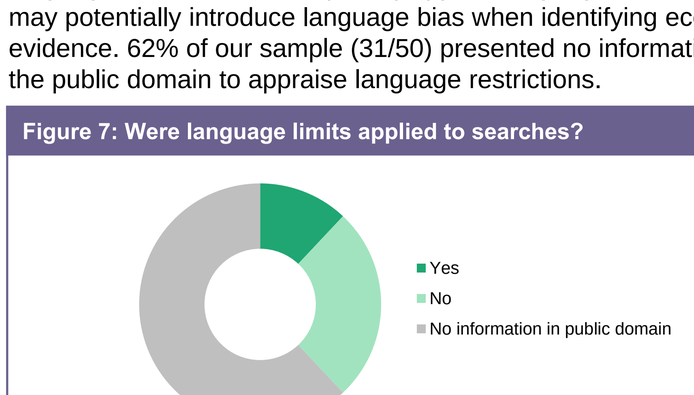
Currency of searching was an issue; the mean time elapsed between search date and STA submission was 6.65 months (range: 20-483 days). Searches for two submissions were completed over 15 months before submission, which suggested more current evidence may have been omitted from inclusion.

Figure 6: Currency: Time elapsed between date of last search & submission date



Of the 19 STAs that provided information about the application of language restrictions, 68% (13/19) applied language limits. This may potentially introduce language bias when identifying economic evidence. 62% of our sample (31/50) presented no information in the public domain to appraise language restrictions.

Figure 7: Were language limits applied to searches?



- Due to incomplete information available in STA committee papers in the public domain, it was not possible to conduct a meaningful analysis of how clinical effectiveness evidence was gathered for 6 STAs of our sample.
- For most of the selected STAs, information was provided about how the clinical effectiveness evidence was identified within the submission, clarification response and ERG report (44/50).
- Although NICE no longer renders submission appendices accessible in the public domain, we were able to access full appendices (redacted) and search strategies for three STAs on the NICE website.

05 DISCUSSION AND CONCLUSIONS

- **Application of language restrictions to clinical effectiveness searches may potentially introduce language bias.**
- **Currency of evidence searches could be improved, in line with best practice recommendations.[1, 3-4]**
- **Grey literature and conference abstracts are important sources to mitigate for publication bias,[3-4] however not all submissions include this type of supplementary searching.**
- **Due to the lack of completeness in STA committee papers in the public domain,[2] many of the SR and clinical effectiveness methods informing NICE reimbursement decisions lack detail, transparency and reproducibility.**
- **Our small study showed that transparency of the clinical effectiveness work within company submissions, and completeness of information provided by NICE in the public domain, could be much improved.**

References

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