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Capturing real-world evidence alongside trial evidence in HTA-specified systematic literature review: optimizing search strategies across the totality of evidence required

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Objectives

- There is increasing use of real-world evidence (RWE) in health technology assessment (HTA) with treatment effect estimates from real-world, non-randomized studies potentially being considered in relative efficacy assessments.
- This is changing the way we search for evidence, with systematic literature review (SLR) extending from randomized controlled trials (and single-arm trials) to RWE with similar methodological rigour.
- SLRs are a time-consuming aspect of HTA and, to our knowledge, there is no guidance about how to combine searches for clinical evidence, including trial and RWE, alongside other evidence requirements.
- Other HTA requirements include quality of life and health-state utility values, which can overlap clinical RWE, alongside cost, resource use and economic evaluations (**Box 1**).
- We aimed to test overall efficiency of search strategies for HTA.

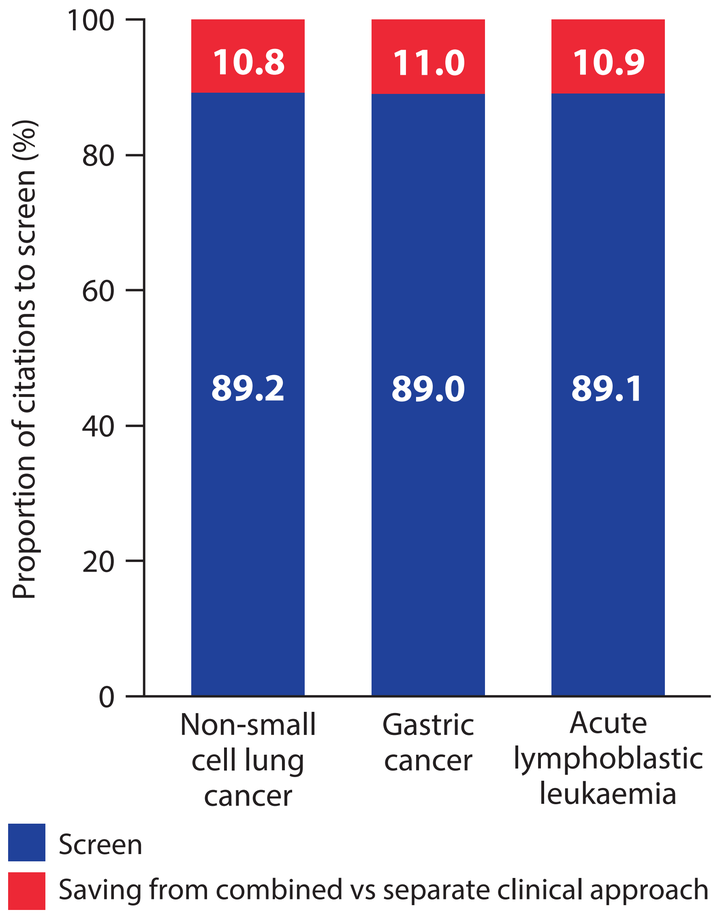
Methods

- We tested how different combinations affected the total number of citations retrieved from Embase by constructing pairs of search strings.
- These were conducted across three oncology indications and for each pair of search strings, by indication, the overall Patient, Intervention, Comparator, Outcome, Study design (PICOS) terms and limitations were identical.
- Each pair included the totality of evidence required for HTA and RWE treatment effects but differed in how the evidence was partitioned:
  - **separate clinical** (clinical trials + all other)
  - **combined clinical** (clinical RWE/clinical trials + all other).
- Differences in citations retrieved were due to duplication between searches.

Results

- Total numbers of citations retrieved ranged from 2086 to 13 541 across the three indications.
- There were consistently fewer overall citations, showing lower duplication, for the combined clinical versus the separate clinical approach: mean 10.9% fewer citations (standard deviation, 0.10%) (**Figure 1**). This means that the **combined clinical** approach is more efficient for screening.

Figure 1. Citations to screen following the combined clinical approach shown as a proportion of the total from the separate clinical approach.



Box 1. Designing search strategies for HTA – considerations from Cochrane, NICE and PRISMA.[1–3]

Study type	Efficacy and safety	Quality of life and health-state utility values	Cost, resource use and economic evaluations
Patient	Restricted, sensitivity versus specificity according to need		
Intervention, comparator	Usually not restricted		
Study design	Restricted to RCT + SAT +/– RWE	Not restricted Quality of life restricted to RCT + SAT + RWE	
Outcome	Not restricted	Restricted	
Timing	Not restricted	Restricted	

Combining searches

Combined clinical	This search can retrieve other evidence for HTA if the inclusion/exclusion criteria are adjusted, including: • treatment effect modifiers and prognostic factors • epidemiology and treatment sequence and treatment patterns	
Separate clinical		An advantage of this approach is being able to use single-person screening for some evidence that does not require the full level of stringency

HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial; RWE, real-world evidence; SAT, single-arm trial.

Conclusions

- Our results show that when RWE of treatment effects is considered alongside clinical trial evidence it is more efficient to combine the searches across study type than to keep them separate. These RWE studies can then follow the same review process as trials.

References

1. Higgins JPT *et al*., editors. Cochrane Handbook for Systematic Reviews of Interventions. Version 6.4. Cochrane, 2023. Available from: https://training.cochrane.org/handbook (Accessed 26 October 2023).
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3. Page MJ *et al*. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71.

Disclosures

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