SA44

Exploring Approaches to Search Strategy Optimisation in Systematic Literature Reviews for Metastatic Breast Cancer

Tom Macmillan,[1] Neil Webb,[1] Pauline Herscu,[2] Evelina Bertranou.[3]
1. Source Health Economics, Oxford, Oxfordshire, UK
2. Daiichi Sankyo Europe GmbH, Munich, Bayern, Germany
3. AstraZeneca, Cambridge, Cambridgeshire, UK

Background

- In December 2022, a systematic literature review (SLR) was conducted to identify clinical trials on adults with human epidermal growth factor receptor (HER2) negative, hormone receptor (HR) positive, inoperable or metastatic breast cancer.
- In total, 22,218 publications were identified through the electronic database searches, of which 10,855 were from Embase alone.
- Following screening, despite the large number of hits from the search strategy, only 26 multi-arm trials involving two or more relevant treatments, or pooled analyses of trials, were included in the SLR.

Objective

- To explore ways in which the broad search strategy utilised for the SLR could be refined to be made more efficient, in terms of reducing the screening burden, without excluding relevant studies.

Methods

- Our methodology followed a standard approach to creating and testing search filters, for example, those used to identify specific study types (e.g. randomised controlled trials [RCTs]).
- The performance of a search filter is measured in a similar way to diagnostic accuracy studies [1-3]. For search filters, the focus is on sensitivity, precision, and number needed to read (NNR).
- Sensitivity relates to the number of relevant studies correctly retrieved in a search. Thus, the numerator is the number of relevant studies retrieved by a search strategy (from our gold standard reference set), and the denominator is all the relevant studies discoverable in the database (our gold standard reference set) [4]. This is usually expressed as a percentage.
- Precision relates to the efficiency or 'hit rate' of a search strategy; it is a measure of the ability of the search strategy to retrieve records that are genuinely relevant, such that they can be included in an SLR [5]. This is calculated as the number of relevant studies retrieved in a search strategy (from our gold standard reference set), relative to all the studies (both relevant and irrelevant) retrieved by a search strategy [4]. This is expressed either as a percentage or as NNR.
- NNR refers to the number of references that have to be checked to find one relevant study [5]. Typically, in an SLR, this would be the number of titles or abstracts retrieved from the electronic search that would have to be manually checked and considered to pick up one additional relevant article from the set of retrieved citations.
- **In terms of optimising a search strategy, the preference is for a higher precision and a lower NNR.**

$$\textbf{Sensitivity (\%)} = \frac{\text{Relevant articles retrieved by search strategy}}{\text{All relevant articles (our gold standard reference set)}} \times 100$$

$$\textbf{Precision (\%)} = \frac{\text{Relevant articles retrieved by search strategy}}{\text{All relevant articles reference set}} \times 100$$

$$\textbf{NNR} = \frac{1}{\text{Precision}}$$

- The original search strategy was developed to maximise sensitivity. The population terms comprised terms for breast cancer combined with terms for advanced, metastatic, and non-resectable disease.
- We applied stepwise alterations to the existing population search terms (Table 1), measuring sensitivity and precision after each change. Each alteration was designed to try to increase precision, without decreasing sensitivity.
- As some of the included publications were conference abstracts, and Medline does not index conference abstract, alterations were made to the Embase and Cochrane searches only.
- Of particular interest was how the search strategy performed when limited by terms for HER2 and/or HR status.
- The final set of included studies from the SLR was used as the reference set (n=26 papers [14 unique trials]; n=24 indexed in Embase at time of search).

Results

- The precision of the original search was 0.22%, 0.35% and 0.39% for Embase, Medline and CENTRAL. The total number of hits were 10,880, 5,385 and 5,767 (Table 2).
- In Embase, the highest precision (0.42%) and lowest NNR (236 hits) was seen combining HR/HER2 terms with the population terms using the AND Boolean operator (2,124 hits); however, this resulted in a sensitivity of 37.5% (9/24 of the relevant studies identified) [Figure 1, Table 2].
- For the Embase search, the best balance between precision (0.34%) and sensitivity (79%) was seen combining HR/HER2 terms (with Emtree terms) with the population terms using the AND Boolean operator; this resulted in 5 papers (2 unique trials) being excluded [Figure 1, Table 2].
- In CENTRAL, the highest precision (0.59%) and lowest NNR (168) was seen using HR/HER2 MeSH terms only (1,009 hits); however, this resulted in a sensitivity of 23.1% (6/26 of the relevant studies identified) [Figure 2, Table 2]. Precision for this search is likely skewed by the relatively low number of hits which is why it is important to measure both sensitivity and precision when assessing the performance of a search filter.
- With the aim of reducing screening burden whilst maintaining sensitivity, the best compromise between sensitivity (65.3%), precision (0.54%) and NNR (185 hits) was judged to be a CENTRAL search that combined the original terms with HR/HER2 terms, with MeSH terms (3,146 hits); however, 9 papers (5 unique trials) were excluded (Figure 2, Table 2).

Conclusion

- Limiting searches using disease subtype-specific population filters may reduce the screening burden in large topics, albeit at the expense of reductions in sensitivity.
- If using disease subtype-specific population filters, these should be used in combination with population terms for stage of disease ('advanced' or 'metastatic'), as disease subtype-specific population filters ('HR' or 'HER2') on their own resulted in reduced sensitivity in all cases.
- In order to improve efficiency for researchers and the sensitivity of search strings, electronic databases should consistently and accurately use controlled vocabulary terms (EMTREE and MeSH terms) to capture important clinical criteria (e.g. staging and biomarkers).
- In general, greater precision was obtained by searching in CENTRAL alone, although at reduced sensitivity. Whilst this approach may not meet the stringent requirements of a health technology assessment (HTA) submission, depending. on the research objective (e.g. early scoping for potential network meta-analysis or a targeted review to assess the clinical trial landscape for mBC), the review could be limited to CENTRAL to reduce screening burden.

Table 1: Search terms used in Embase and CENTRAL

Description	Terms
Original population limit	(stage 3 or stage 3c or stage iiic or stage 3b or stage iiib or stage 4 or stage iv or metasta* or advanc* or unresect* or ((late* or last) adj2 stag*) or nonresect* or (non adj1 resect*) or inoperable or un resect* or unresect* or non resect* or nonresect* or ('not' adj2 (amenabl* or suit*) adj2 (surg* or opera*))).tw.
HR OR HER2 terms (or)	(luminal A or luminal type A or luminal subtype A or HR or hormone receptor* or ER or PR or Hrpositive or ?estrogen receptor* or progesterone receptor* or Erpositive or Prpositive or human epidermal growth factor receptor or HER2* or HER 2* or ERBB2 or CD340 or "HER-2/neu" or MLN 19 or NEU or NGL or TKR1 or ERBB2 or erb-b2 receptor or tyrosine kinase 2).tw.
HR OR HER2 terms (or)- simplified	(luminal A or luminal type A or luminal subtype A or hormon* or Hrpositive or ?estrogen* or progesteron* or Erpositive or Prpositive or human epidermal growth factor receptor or HER2* or HER 2* or CD340 or "HER-2/neu" or MLN 19 or NEU or NGL or TKR1 or ERBB2 or erb-b2 receptor or tyrosine kinase 2).tw.
HR AND HER2 terms	(luminal A or luminal type A or luminal subtype A or ((HR or hormone receptor* or ER or PR or Hrpositive or ?estrogen receptor* or progesterone receptor* or Erpositive or Prpositive) and (human epidermal growth factor receptor or HER2* or HER 2* or ERBB2 or CD340 or "HER-2/neu" or MLN 19 or NEU or NGL or TKR1 or ERBB2 or erb-b2 receptor or tyrosine kinase 2))).tw.
HR/HER2 EMTREE terms	exp luminal A breast cancer/ or exp hormone receptor/ or exp epidermal growth factor receptor 2/ or exp estrogen receptor-positive, HER2-negative breast cancer/ or exp estrogen receptor positive breast cancer/ or exp hormone receptor positive breast cancer/ or exp human epidermal growth factor receptor 2 negative breast cancer/ or exp breast cancer molecular subtype/ or exp progesterone receptor positive breast cancer/
HR/HER2 MeSH terms	exp Receptors, Estrogen/ or exp Receptors, Progesterone/ or exp Receptor, ErbB-2/ or exp Neoplasms, Hormone-Dependent/ or exp Genes, erbB-2/

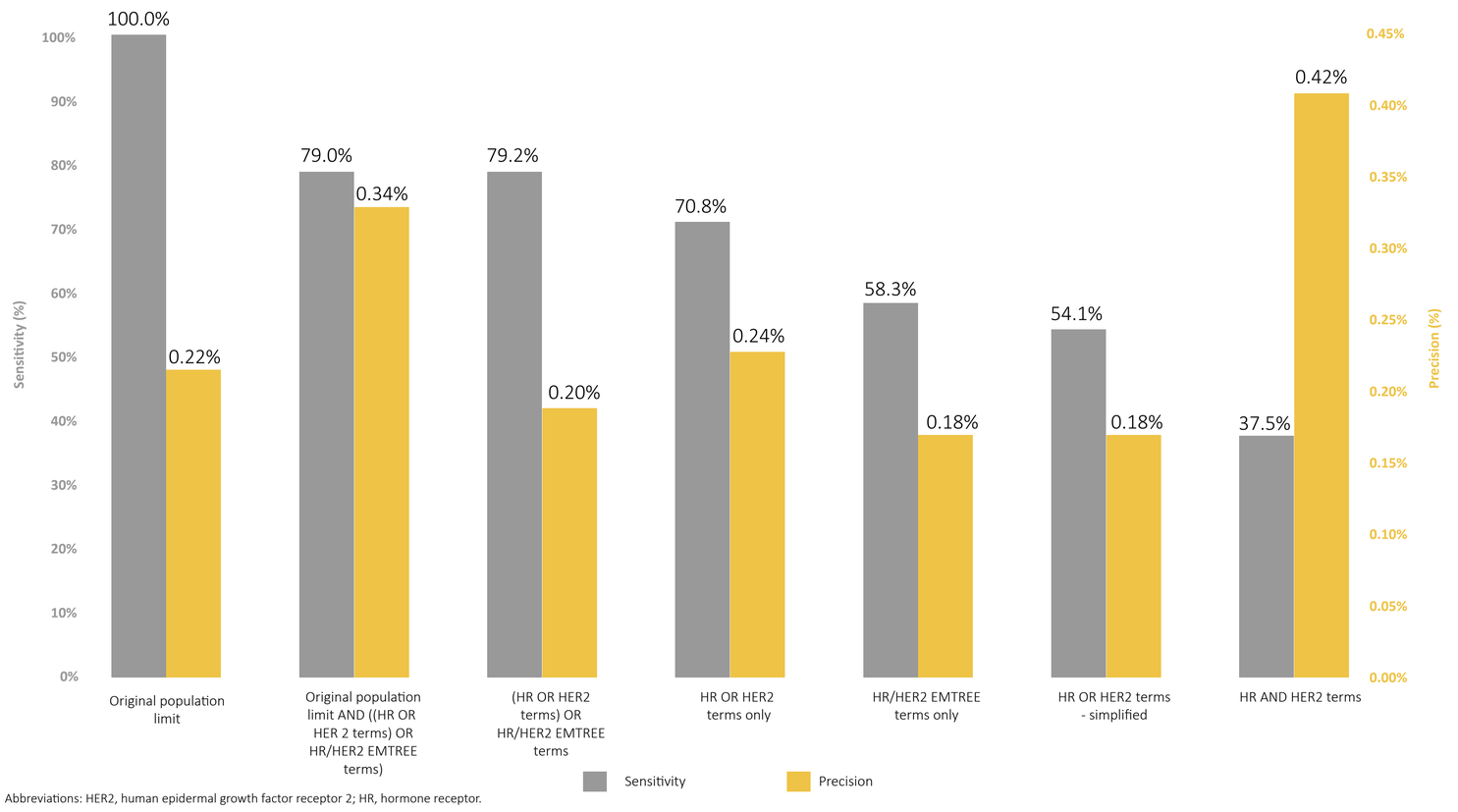
Abbreviations: HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MeSH, medical subject headings

Table 2: Performance of different sets of terms used in Embase and CENTRAL

Description	Database	Overall hits	NNR	Number of publications excluded
Original population limit	Embase	10,880	453	-
	CENTRAL	5,767	251	3 [6-8]
Original population limit AND ((HR OR HER2 terms) OR HR/HER2 controlled vocabulary terms [EMTREE or MeSH terms])	Embase	5,658	298	5 [6,9-12]
	CENTRAL	**3,146**	**185**	**9 [6-14]**
(HR OR HER2 terms) OR HR/HER2 controlled vocabulary terms [EMTREE or MeSH terms]	Embase	9,381	493	5 [6, 9-12]
	CENTRAL	5,146	303	9 [6-14]
HR OR HER2 terms only	Embase	7,233	425	7 [6,9-14]
	CENTRAL	5,069	298	9 [6-14]
HR/HER2 controlled vocabulary terms only (EMTREE or MeSH terms)	Embase	7,697	550	10 [6,8-12,15-18]
	CENTRAL	1,009	168	20 [6-25]
HR OR HER2 terms- simplified	Embase	7,050	542	11 [9-19]
	CENTRAL	4,758	366	13 [6-18]
HR AND HER2 terms	Embase	2,124	236	15 [6,9-19,24,26,27]
	CENTRAL	1,850	206	17 [6-19,24,26,27]

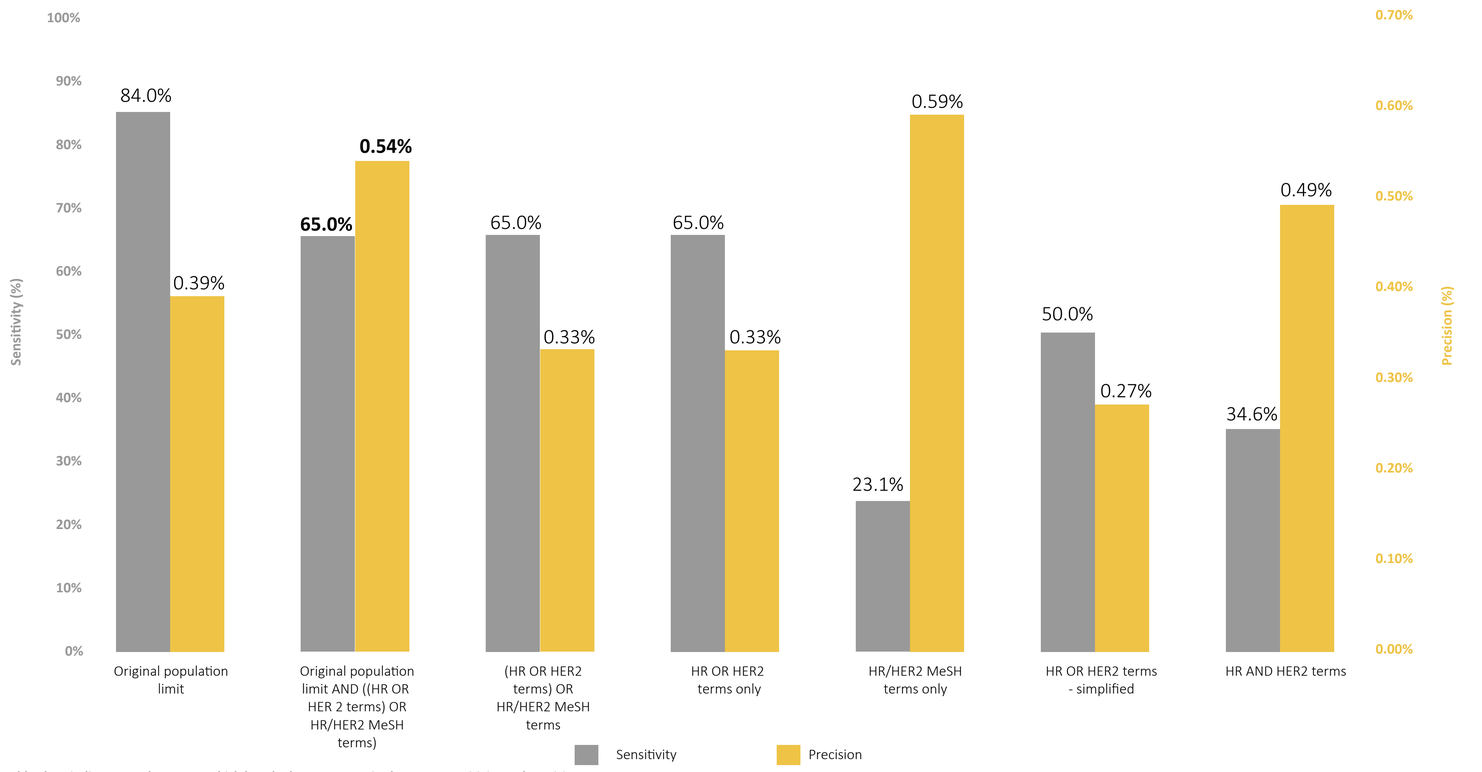
Bold indicates search strategy which has the best compromise between sensitivity, precision, and NNR.
Abbreviations: CENTRAL, Cochrane Central Register of Controlled Trials; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MeSH, medical subject headings; NNR, number needed to read.

Figure 1: Performance of search terms in Embase



Abbreviations: HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

Figure 2: Performance of search terms in CENTRAL



Bold values indicate search strategy which has the best compromise between sensitivity and precision.
Abbreviations: CENTRAL, Cochrane Central Register of Controlled Trials; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MeSH, medical subject headings.

References: 1. Davies BM., et al. BMC Med Res Methodol 2018;18:73, 2. Prady SL., et al. BMC Med Res Methodol 2018;18:106, 3. Waffenschmidt S., et al. Res Synth Methods 2020;11:617-26, 4. Tompson L. Journal of Experimental Criminology 2019;15:453-67, 5. Golder S, Loke YK. Health Info Libr J 2012;29:28-38, 6. Cortes J., et al. Annals of Oncology 2018;29:881-7, 7. von Minckwitz G., et al. The Lancet Oncology 2014;15:1269-78, 8. Vrdoljak E., et al. Annals of Oncology 2016;27:2046-52, 9. Corey-Lisle PK., et al. Cancer 2012;118(2):461-468, 10. Thomas ES., et al. Journal of Clinical Oncology 2007;25:5210-7, 11. Vahdat LT., et al. Breast Cancer Research and Treatment 2013;140:341-51, 12. Vahdat LT., et al. Journal of Geriatric Oncology 2013;4:346-52, 13. Martin M., et al. Lancet Oncology 2007;8:219-25, 14. Yardley DA., et al. Journal of Clinical Oncology 2015;33:1609-19, 15. Donoghue M., et al. Clinical Cancer Research 2012;18:1496-505, 16. Hortobagyi GN., et al. Breast Cancer Research and Treatment 2010;122:409-18, 17. Sparano JA., et al. Journal of Clinical Oncology 2010;28:3256-63, 18. Yuan P., et al. European Journal of Cancer 2019;112:57-65, 19. Cortes J., et al. The Lancet 2011;377:914-23, 20. Kaufman PA., et al. Journal of Clinical Oncology 2015;33:594-601, 21. Park IH., et al. Cancer Research and Treatment 2019;51:43-52, 22. Rugo HS., et al. Annals of Oncology 2022;33:S1258, 23. Schmid P., et al. Annals of Oncology 2022;33:S635-56, 24. Twelves C., et al., Breast Cancer: Basic and Clinical Research 2016;10:77-84, 25. Ueno NT., et al. Annals of Oncology 2022;33:S632-53, 26. Brufsky AM., et al. Journal of Clinical Oncology 2011;29:4286-93, 27. Pivot X., et al. Annals of Oncology 2016;27:1525-31.

ISPOR Europe 2024, 17–20th November 2024; Barcelona, Spain