Systematic Literature Review Requirements For Health Technology Assessment In European Markets

Ciara Wright, Amy Swanston, Lindsay Nicholson, Zoe Marjenberg, Nick Pooley

Maverex Limited, Newcastle, UK

Poster no: HTA44

BACKGROUND

- An integral part of a health technology assessment (HTA) is a systematic literature review (SLR), an unbiased, high-quality synthesis of available evidence.
- For many HTA agencies, guidance on data sources, methodology, required outcomes, and reporting of the SLR varies considerably

OBJECTIVE

- The objective of this study was to conduct a comparative assessment of the clinical and economic SLR methodological requirements of HTA agencies in different countries across European markets.

METHODS

- We searched seven HTA agency websites (www.nice.org.uk [England], www.has-sante.fr [France], www.g-ba.de [Germany], www.zorginstituutnederland.nl [Netherlands], www.aifa.gov.it [Italy], www.aemps.gob.es [Spain], www.tlv.se [Sweden]) and the proposed JCA dossier information [www.eunethta.eu/jca]) to identify guidance on the use of SLRs in HTA.
- Relevant information was extracted and compared.

DISCUSSION AND CONCLUSION

- While all seven countries require an SLR as part of the HTA submission, a limited consensus was found in terms of SLR requirements.
- The specific requirements for conducting SLRs in HTAs vary globally due to differences in regulatory frameworks, healthcare systems, and decision-making processes.
- The JCA is not a full HTA and will streamline the clinical evidence submission only, and local agencies can continue to reach their own decisions on relative safety and efficacy
- The most stringent requirements were found in England and France.
- Differences between HTA agency guidance should be a consideration when carrying out an SLR for use in HTA submissions in any of the 27 European markets.
- Efficiencies in conducting SLRs that can fulfil the requirements for multiple HTA bodies can be made with strategic planning.

RESULTS

- All seven countries and the JCA require an SLR of clinical data for the technology and its comparators.
- Only two countries (England and France) requested an SLR of economic models for the technology, and a critical appraisal of the models is also requested (Figure 1).
- SLRs of utility, resource use, and cost data were less frequently mandated, with only NICE in England suggesting the inclusion of an SLR of utility data (Table 1).
- Two countries state a clear preference for randomised controlled trials (RCTs) in the search strategy for SLRs. Most countries recommend searching specific literature databases, most commonly Medline and Embase (Table 2).
- A requirement for transparency in relation to study selection is evident, with six countries mandating the reporting of details of included and excluded literature (Table 2).

Table 1. SLR requirements for HTA submission

	Country	England NICE[1]	France HAS[2]	Germany IQWIG/G-BA[3]	Netherlands ZiN[4]	Italy AIFA[5]	Spain† AEMPS[6]	Sweden TLV[7]	JCA EUnetHTA[8]
Focus of SLR	Clinical data for technology and its comparators	✓	✓	✓	✓	✓	-	✓	✓
	Economic models for technology	✓	✓	✗	✗	✗	-	✗	✗
	Resource use and cost data	✓	✗	✗	✗	✗	-	✗	✗
	Utility data	✓	✓*	✗	✗	✓**	-	✗	✗
Quality assessment and critical appraisal	Quality assessment	✓	✓	✓	✓	✗	-	✓	✓
	Critical appraisal of RCTs and non-RCTs	✓	✓	✓	✓	✓	-	✓	✓
	Critical appraisal of economic models	✓	✓	✗	✗	✗	-	✗	✗

*if not derived from an ad-hoc study specifically designed for the collection of the required quality of life data, ** if available

† The situation in Spain is unclear. "REvalMed " was established in 2020. The goal was to evaluate the incremental clinical benefit and formally include pharmaco-economic evaluation. However, the evaluation criteria were uncertain. Definitions and a framework for the evaluation of incremental benefit were absent. In 2023, REvalMed was revoked. Since then, AEMPS has published 21 therapeutic positioning reports, omitting the logo of REvalMed, any mention of those responsible for the information contained in the dossiers and any information on economic evaluation.

Figure 1. Economic SLR requirements

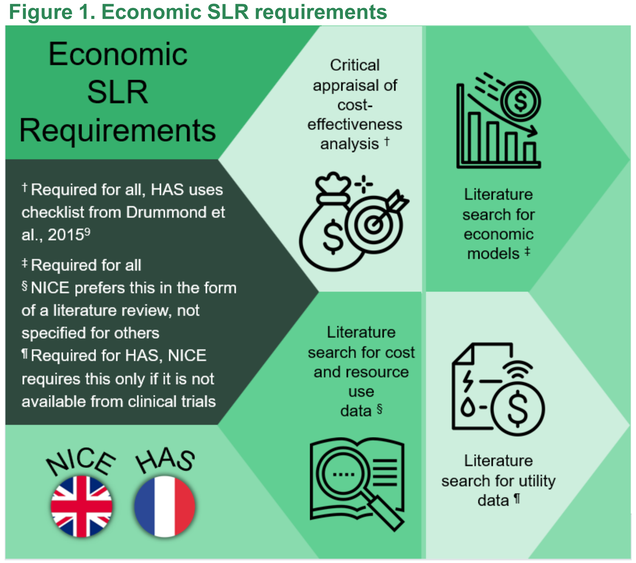

Table 2. Clinical SLR requirements

	Country	England NICE[1]	France HAS[2]	Germany IQWIG/G-BA[3]	Netherlands ZiN[4]	Italy AIFA[5]	Spain† AEMPS[6]	Sweden TLV[7]	JCA EUnetHTA[8]
Search strategy	Permitted trial types	RCTs preferred, non-randomised may complement where there is a gap in evidence	RCTs preferred, non-randomised if appropriate. Prefer French studies	All relevant studies. English or German language	All relevant publications. RCTs strongly recommended	All relevant publications	-	All relevant data	All relevant data
Sources	Databases specified	Medline, Embase, Medline (R) In-Process,and Cochrane Library	None specified	Medline, Embase	None specified	None specified	-	None specified	MEDLINE Cochrane Central Registry of Controlled Trials (e.g. Embase, CINAHL, PsycINFO, etc.).
	Other specified sources	Unpublished data, reference searching, citation searching, inclusion list of systematic reviews, websites	Relevant websites (government agencies, learned societies, conferences), legislative and regulatory texts	Trial registries, manufacturer data, Cochrane library, HTA agency websites, PROSPERO, Dynamed, UpToDate, Pubmed	None	None	-	None	Study registries and study results registries: ClinicalTrials.gov[10], Clinical Trials Information System[11], EU Clinical Trials Registry[12], International Clinical Trials Registry Platform Search Portal[13]. In addition, a search can be conducted in subject-specific study registries (e.g. disease-specific study registries) or study registries of individual pharmaceutical companies.
Selection of studies	PICOS	✓	✗	✓	✓	✗	-	✓	✓
	PRISMA flow diagram	✗	✓	✓	✗	✓	-	✓	✓
	Report reasons for inclusion and exclusion	✓	✓	✓	✓	✓	-	✗	✓
	Details of included studies	✓	✓	✗	✓	✓	-	✓	✓

CSR, clinical study report; RCT, randomised controlled trial

References

1. NICE. NICE health technology evaluations: the manual. 2022.
2. Haute Autorité de Santé. Choices in Methods for Economic Evaluation. 2020.
3. IQWIG. General Methods. 2022.
4. Zorginstituut Nederland. Guideline for economic evaluations in healthcare. 2024.
5. AIFA. Italian Medicines Agency. 2023.
6. AEMPS. Agencia Española de Medicamentos y Productos Sanitarios. 2022.
7. Tandvårds- och läkemedelsförmånsverket (TLV). Handbook for companies when applying for subsidies and prices for pharmaceuticals. 2023.
8. EUnetHTA. Joint Clinical Assessment (JCA). 2021.
9. Drummond MF, Sculpher M, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Fourth edition. 2015. Oxford University Press
10. ClinicalTrials.gov. Available at www.clinicaltrials.gov
11. Clinical Trials Information System. Available at https://euclinicaltrials.eu/
12. EU Clinical Trials Registry (EU-CTR). Available at www.clinicaltrialsregister.eu
13. International Clinical Trials Registry Platform Search Portal (ICTRP Search Portal, the search portal of the WHO). Available at https://www.who.int/clinical-trials-registry-platform/the-ictrp-search-portal

maverex