Systematic Literature Reviews at the Heart of Health Technology Assessment: a Comparison Across Markets

Catherine E Rycroft,[1] Maria Fernandez,[2] Catherine Copley-Merriman[3]

[1]RTI Health Solutions, Manchester, United Kingdom; [2]RTI Health Solutions, Research Triangle Park, NC, United States; [3]RTI Health Solutions, Ann Arbor, MI, United States

BACKGROUND AND OBJECTIVES

- The requirements for systematic literature reviews (SLRs) within a health technology assessment (HTA) submission vary across the world.
- The objective of this study was to compare clinical and economic SLR requirements issued by nine HTA agencies in Australia, Canada, and Europe (England, France, Germany, Ireland, Scotland, Sweden and Wales).

METHODS

- Requirements for SLRs as issued within guidance for HTA submissions in Australia (Pharmaceutical Benefits Advisory Committee [PBAC]), Canada (Canadian Agency for Drugs and Technologies in Health [CADTH]), England and Wales (National Institute for Health and Care Excellence [NICE] Single Technology Appraisal [STA] guidance), France (Haute Autorité de Santé [HAS]), Germany (Gemeinsamer Bundesausschuss [G-BA; Federal Joint Committee]), Ireland (National Centre for Pharmacoeconomics [NCPE]), Scotland (Scottish Medicines Consortium [SMC]), Sweden (The Dental and Pharmaceutical Benefits Agency [TLV]), and Wales (All Wales Medicines Strategy Group [AWMSG]) were examined from the relevant, respective websites in September 2013.
- Requirements were compared, and a summary checklist of requirements and a more detailed summary of guidance were compiled.

RESULTS

- Table 1 presents a summary checklist comparing the submission requirements for each of the nine HTA bodies investigated.
- Tables 2 and 3 provide more detail on the requirements for clinical systematic reviews for each HTA body. Table 4 provides detail on the requirements for economic reviews (including economic models, utilities, and cost and resource use) for those HTA bodies that provide guidance on these reviews (i.e., CADTH, NICE, HAS, NCPE, and SMC).
- NICE and G-BA requirements are the most prescriptive, whereas AWMSG and TLV have few stated SLR requirements.
- All agencies require a clinical SLR; AWMSG does not specify this outright but a clinical SLR is required to determine economic model inputs.
- Five agencies require both a clinical SLR and a critical appraisal of the included studies (PBAC, NICE, HAS, G-BA, and NCPE), although recommended appraisal tools vary.
- CADTH, NICE, and HAS require both an SLR and a critical appraisal of existing economic evaluations for the intervention of interest; PBAC requires an SLR of only economic evaluations and no critical appraisal.
- NICE, NCPE, SMC, and AWMSG require an SLR of utility data, but only NICE and SMC specify the need for an SLR of cost and resource use data.

CONCLUSIONS

- Although SLR requirements vary between HTA agencies, a clinical SLR is a key requirement for eight of the nine agencies investigated.
- Efficiencies can be gained by conducting SLRs designed to satisfy requirements of several HTA bodies.
- Clinical SLRs intended for use across several markets should be conducted in line with the most prescriptive guidance (i.e., G-BA and NICE). However, quality assessment guidance for clinical data varies between HTA bodies, with G-BA requiring the most detailed assessment.
- SLRs of economic models, utility data, and cost and resource use intended for use across several markets should be conducted to satisfy the prescriptive CADTH and NICE criteria. However, guidance for critical appraisal of economic models varies between HTA bodies requiring these (NICE, CADTH, and HAS).
- The checklist and summary tables should be updated as newer HTA guidance is issued.

REFERENCES

Please see handout for complete reference list.

CONTACT INFORMATION

Catherine Rycroft, PhD
RTI Health Solutions

Phone: +44.161.447.6022
E-mail: crycroft@rti.org

Presented at: ISPOR 16th Annual European Congress
November 2-6, 2013
Dublin, Ireland

Table 1. Checklist for Submission to Nine HTA Bodies

Submission Requirement	Australia	Canada	England and Wales	France	Germany	Ireland	Scotland	Sweden	Wales
	PBAC	CADTH	NICE STA	HAS	G-BA	NCPE	SMC	TLV	AWMSG
SLR of clinical data for the technology and its comparators	✓	✓	✓	✓	✓	✓	✓	✓, if no head-to-head trials available	✗
Critical appraisal of RCTs and non-RCTs	✓	✗	✓	✓	✓	✓	✗	✗	✗
SLR of economic models for technology	✓	✓	✓	✓	✗	✗	✗	✗	✗
Critical appraisal of economic models	✗	✓	✓	✓	✗	✗	✗	✗	✗
SLR of utility data	✗	✗	✓	✗	✗	✓	✓	✗	✓
SLR of resource use and cost data	✗	✗	✓	✗	✗	✗	✓	✗	✗

✓ = required; ✗ = not required or no guidance provided. RCT = randomised controlled trial; SLR = systematic literature review; STA = single technology appraisal.

Table 2. Comparing Clinical SLR Requirements of HTA Bodies

Type of Methodology	PBAC	CADTH	NICE	HAS
Search strategy and literature search	Include search strategies, date of search, date span of search Databases: Medline, Embase, and Cochrane, at least	No language restrictions; list other restrictions Predefined protocol required; discuss deviations Include: Cochrane Library, PubMed, NHS CRD Optional: Embase, BIOSIS Previews, CINAHL, PsycINFO	Specify databases and service providers; include Medline, Embase, Medline (R) In-Process, and Cochrane Library Include complete search strategies, date of search, date span of search	Clear, reproducible search strategy, using explicit selection criteria Date span of search must be appropriate (see Institute of Medicine [2011] guidance)
Desktop research	Registers of RCTs (e.g., Australian Clinical Trials Registry, ClinicalTrials.gov), company databases, and dossiers seeking marketing approval submitted to the Therapeutic Goods Administration; further unpublished trials, bibliographies of retrieved papers	Trial registries, websites of INAHTA agencies, manufacturers' websites, internet search tools (e.g., Google), and consultation with experts and agencies	Include details of additional searches, e.g., company databases (include description of each database)	Relevant websites (government agencies, learned societies, conferences), other legislative and regulatory texts
Selection of studies	Include all relevant direct randomised trials The Pharmaceutical Evaluation Section will run an independent literature search to retrieve all relevant direct randomised trials	Use PICOS selection criteria List reviewers involved (using initials) and describe resolution of disagreements Describe data extraction process	Include inclusion/exclusion criteria, data abstraction strategy, PRISMA flow diagram Follow CRD (2008) guidance Papers should be assessed by ≥ 1 researcher	Follow Institute of Medicine (2011) guidance: 2 reviewers, use of predefined form, double data extraction
Quality assessments of comparator RCTs	Assess RCT quality in terms of concealment of randomisation, blinding, and basis of analysis Assess quality of nonrandomised studies	Describe methods used (e.g., type of quality assessment scale/checklist)	NICE-specific template of 7 questions	Review articles according to principles of critical appraisal using checklists

CINAHL = Cumulative Index to Nursing and Allied Health Literature; CRD = Centre for Reviews and Dissemination; INAHTA = International Network of Agencies for Health Technology Assessment; NHS = National Health Service; PICOS = participants, interventions, comparators, outcomes, study design; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; US = United States.

Sources: Australian Government Department of Health and Ageing, 2008; CADTH, 2003; 2006; 2009; HAS, 2009; 2011; 2012; CRD, 2008; Institute of Medicine, 2011; NICE, 2012 .

Table 3. Comparing Clinical SLR Requirements of HTA Bodies (Continued)

Type of Methodology	G-BA	NCPE	SMC	TLV	AWMSG
Search strategy and literature search	Databases: Medline, Embase, Cochrane (Optional: CINAHL, PsycINFO) Include search strategies, adapted for each database; use current validated filters if the strategies are restricted to certain study types (e.g., RCTs)	Define protocol, including search strategy, inclusion/exclusion criteria, restrictions (e.g., language, population, year) No guidance on specific databases See Cochrane Handbook (Higgins and Green, 2011)	Conduct if no direct clinical data for the drug under review relative to comparators are available No specific databases recommended Include list of sources, databases, and search platforms; full search strategies including filters and their sources	Conduct if no direct evidence available No further guidance	No guidance
Desktop research	Required: Registries such as clinicalstudyresults.org and the International Clinical Trials Registry Platform Search Portal Optional: Specific study registers or registers of pharmaceutical companies	Unpublished and partially published studies; commercial or academic in-confidence data No guidance on specific sources to search	No specific guidance, but include details of all sources; also cite relevant personal communications	No further guidance	No guidance
Selection of studies	Systematic review: 2 reviewers for level 1 and level 2 screening Justification if 2 reviewers were not used	≥2 reviewers for selection process; outline methods used to resolve disagreement Maintain log of the ineligible studies and reasons for exclusion	Include inclusion/exclusion criteria (according to PICOS methodology), PRISMA diagram, and list of included/excluded articles Follow PRISMA checklist	No guidance	No guidance
Quality assessments of comparator RCTs	Assess bias at: Study level: Randomisation, allocation concealment, time parallelism (nonrandomised), comparability of the groups (nonrandomised), blinding, result-controlled reporting, etc. Endpoint level: Blinding, implementation of ITT principle, result-controlled reporting, etc.	Required but no particular system recommended; however, GRADE and the NHMRC Designation of Levels of Evidence methods were listed	Assess quality of data used in indirect comparison/mixed-treatment comparison; specific tool not provided	No guidance	Not required

GRADE = Grading of Recommendations Assessment, Development and Evaluation; ITT = intent to treat; NHMRC = National Health and Medical Research Council.

Sources: AWMSG, 2012; G-BA, 2011; Higgins and Green, 2011; HIQA, 2010; 2011; IQWiG, 2011; NCPE, 2013; SMC, 2013; The Dental and Pharmaceutical Benefits Agency, 2013.

Table 4. Comparing Economic SLR Requirements of HTA Bodies

Type of Methodology	CADTH	NICE	HAS	NCPE	SMC
Literature search of economic models for technology under assessment	Requires predefined protocol No language restrictions; indicate other restrictions Databases: NHS EED and HEED	Specify databases and service providers; include Medline, Embase, Medline (R) In-Process, NHS EED, EconLit Include search strategies, search date, and date span	Clear, reproducible search strategy, using explicit selection criteria Appropriate date span of search (see Institute of Medicine [2011] guidance)	No guidance	Not required
Critical appraisal of cost-effectiveness evaluations	Describe quality assessment—2 possible checklists: BMJ guidelines for economic submissions and the CHEC 2 reviewers should apply the criteria list	Specific template of 36 questions, adapted from Drummond checklist (Drummond and Jefferson, 1996)	Use Drummond and Jefferson (1996) checklist for economic evaluation; use Weinstein et al. (2003) checklist for assessing quality of models	No guidance	Not required
Literature search of cost and resource use data	Same methodology as for economic models	Specify databases and service providers; include Medline, Embase, Medline (R) In-Process, NHS EED, EconLit Include search strategies, date of search, date span of search	No guidance	Not required	For NHS and social work costs, present evidence that data were identified systematically No databases recommended Define methods for identifying sources; if alternative sources available, justify chosen costs Use sensitivity analysis to assess implications of alternative sources
Literature search of utility data	Same methodology as for economic models	Specify databases and service providers; include Medline, Embase, Medline (R) In-Process, NHS EED, EconLit Include search strategies, search date, and date span	No guidance	Transparent, systematic search to obtain published utility values Justify data choice, describe methods; if several options available, explore uncertainty by sensitivity analysis	If utility data from generic validated instruments are unavailable, SMC accepts utilities from 3 other sources (e.g., SLR) Present selection process and all published utility values No guidance on databases or details to include in submission
Selection of studies	Use PICOS methodology 2 reviewers for study selection; use predefined method for disagreements 2 reviewers for data extraction using a predetermined form	Present inclusion/exclusion criteria, data abstraction strategy, PRISMA flow chart See CRD (2008) guidance Papers should be assessed by ≥ 1 researcher	See Institute of Medicine (2011) guidance: 2 reviewers should perform double data extraction using predefined form	≥ 2 reviewers for selection process Describe methods for resolving disagreements Maintain log of ineligible studies and reasons for exclusion	No guidance

BMJ = British Medical Journal; CHEC = Consensus on Health Economic Criteria; HEED = Health Economic Evaluations Database; NHS EED = National Health Service Economic Evaluation Database.

Sources: CADTH, 2003; 2006; 2009; CRD, 2008; Drummond and Jefferson, 1996; HAS, 2009; 2011; 2012; HIQA, 2010; 2011; Institute of Medicine, 2011; NCPE, 2013; NICE, 2012; SMC, 2013; Weinstein et al., 2003.

PBAC, G-BA, TLV, and AWMSG guidance are not presented in this table. AWMSG provide guidance only for a review of utilities: if utility estimates are used from the published literature, they should be identified and selected systematically. PBAC, G-BA, and TLV do not provide guidance on economic, utility, or cost and resource use systematic reviews.