HTA368

# Do we need to adapt our health technology assessment (HTA) systematic literature review (SLR) methods to comply with the new Joint Clinical Assessment (JCA) SLR

*Oikonomidi T,[1] Chaudhary T,[2] Kamra S,[2] Pulleddula K,[4] Geddamuri BG,[4] Agrawal P,[2] Gaultney J,[3] Rtveladze K[3]*

*1 IQVIA Ltd, Athens, Greece, 2 IQVIA Ltd, Gurgaon, India, 3 IQVIA Ltd, London, UK, 4 IQVIA Ltd, Hyderabad, India*

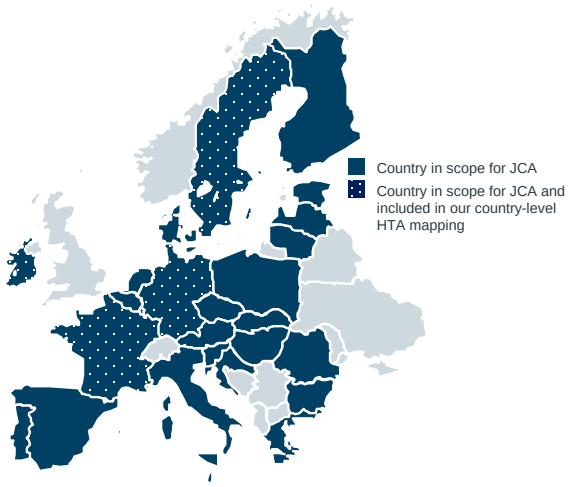
## Background and objectives

- Member-state HTA bodies across the European Union (EU) have different SLR methodology requirements. The pan-EU HTA and JCA further establish a new set of evidence requirements.[1]
- In 2022 we conducted a landscape mapping[2] to compare the methodological requirements for clinical SLRs between the JCA and country-level HTA bodies. In 2024, we updated our mapping with newly-disseminated guidance.

## Methods

- In June 2024, we sought to identify the most up-to-date guidance from:
  - EUnetHTA [3-5] and JCA [6-7]
  - France (HAS)[8]
  - Ireland (NCPE) [9]
  - Sweden (TLV) [10]
  - Germany (G-BA) [11] (Figure 1)
- From each guidance document, we extracted requirements for the following SLR steps:
  - ✓ Search strategies
  - ✓ Literature databases
  - ✓ Time and language limits
  - ✓ Eligible study designs
  - ✓ Study selection and data extraction
  - ✓ Critical appraisal
  - ✓ AI use

**Figure 1. Countries in scope for the JCA (blue) and countries included in our mapping of national HTA body requirements (dotted pattern)**




Abbreviations: HTA, Health technology assessment; JCA: Joint Clinical Assessment

## Results

- Table 1 presents information drawn from submission guidance. For JCA, these include the submission template files as well as prior EUnetHTA documents (in italics)
- Most HTA bodies provide guidance on all aspects of SLR conduct except for the use of artificial intelligence tools, which is not covered in the examined documents

### Search strategies

- JCA searches should be systematic, transparently reported, with justified limits
- This is in line with country-level guidance; G-BA additionally requires validated filters
- EUnetHTA advises review of searches with the PRESS checklist

### Databases

- JCA-compliant SLRs should search MEDLINE® and CENTRAL at minimum; prior EUnetHTA guidance advises to search Embase® also
- This is in line with G-BA requirements. HAS also requires PASCAL and HealthSTAR

### Time and language limits

- JCA-compliant searches should be undertaken within 3 months prior to HTA
- This is in line with G-BA, but shorter than HAS and NCPE guidance (6 months)
- Any language limits should be justified

### Study designs

- Randomised and non-randomised controlled trials are eligible for JCA and most national bodies (in exceptional cases for the G-BA)
- JCA does not directly advise on the inclusion of real-world and uncontrolled studies but proposes they may be of limited value

### Study selection and data extraction

- JCA requires key information (e.g., list of included studies, eligibility criteria) to be listed for each scoped PICOS
- In line with national HTA bodies, JCA requires use of the PRISMA flow chart

### Critical appraisal

- JCA requires critical appraisal of included studies with the RoB-2 or ROBINS-I tools
- The JCA goes beyond national HTA body requirements by mandating that bias must be assessed for each outcome in scope (i.e., at endpoint level)

**Table 1. Clinical SLR requirements of country-level HTA agencies and of the EUnetHTA and JCA**

| | NCPE | HAS | TLV | G-BA | JCA and EUnetHTA |
|---|---|---|---|---|---|
| **Search strategies** | Follow PRISMA checklist | Clear, reproducible searches with explicit selection criteria | Follow PRISMA checklist | Use validated filter for randomised trials<br>Report search strategies, databases and trial registries<br>Use the PRESS checklist | Conduct systematic searches for all sources (databases, study registries, HTA websites)<br>Report the date of search and the search strategy for each database<br>Any restrictions should be justified.<br>*Use the PRESS checklist* |
| **Databases** | - | MEDLINE®, Embase®, Cochrane, HealthSTAR, PASCAL | - | MEDLINE®, Embase®, Cochrane | MEDLINE®, CENTRAL<br>*Embase®* |
| **Time and language limits** | Inception-6 months<br>No language limits | Inception-6 months<br>- | - | Inception-3 months<br>English, German | Inception-3 months<br>*Any language limits applied should be justified* |
| **Study designs** | Randomised, non-randomised and single arm trials, observational studies | Randomised and non-randomised trials, observational studies | - | Randomised trials and in justified exceptional cases non-randomised trials and observational studies | Randomised and non-randomised trials<br>Case control, cohort studies, RWE and registries suffer limitations compared to trials. Cross-sectional studies, case series/reports are of very limited value; uncontrolled trials are of very limited value but can be used with external comparator data |
| **Study selection Data extraction** | Specify eligibility criteria, double review, present PRISMA chart, list excluded studies | Double review using predefined form, double data extraction | Follow PRISMA checklist | Clearly specify eligibility criteria (according to German label), double review | List all included studies in one overall list and in separate lists per PICO, specify eligibility criteria per PICO, use PRISMA chart<br>*Double review* |
| **Critical appraisal** | Use GRADE | Conduct critical appraisal | Conduct critical appraisal | Use RoB2 for randomised trials, ROBINS-I for non-randomized trialss | Assess bias for each outcome in scope; for randomised trials, use RoB-2, for non-randomised trials, case-control and cohort studies use ROBINS-I. Appraisal is not needed for other study designs<br>*Assess bias at study and endpoint level* |

Abbreviations: CENTRAL: Cochrane Central Register of Controlled Trials; CINAHL: Cumulated Index to Nursing and Allied Health Literature; EU: European Union; EUnetHTA: European network for Health Technology Assessment; G-BA: The Federal Joint Committee (Gemeinsamer Bundesausschuss); GRADE: Grading of recommendation, assessment, development and evaluation; HAS: Haute Autorité de Santé; HTA, Health technology assessment; JCA: Joint Clinical Assessment; NCPE: National Centre for Pharmacoeconomics; PRESS, Peer Review of Electronic Search Strategies; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RoB, Risk of Bias; ROBINS I, Risk of Bias In Non-Randomised Studies - of Interventions; TLV: The Swedish Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket)

## Conclusions

- **We have summarised key requirements for JCA-compliant SLRs**
- **Though JCA requirements largely align with pre-existing SLR best-practice, sponsor timelines must additionally account for the broad scope to ensure timely JCA submissions**

Source: 1. Rtveladze et al. Value in Health. 2022 Dec 1;25(12):S310. 2. European Commission. Implementation of the Regulation on health technology assessment. https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment_en, 3. EUnetHTA, Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness December 2017. 4. D4.6 – EUnetHTA. D5.1 Submission Dossier Template. EUnetHTA-21-D5.1_Submission-Dossier-Template_MD_Supplement-1.pdf. 5. EUnetHTA. D5.1 Submission Dossier Guidance. EUnetHTA-21-D5.1-Submission-Dossier-Guidance-v1.0.pdf. 6. Template for the dossier of the Joint Clinical Assessment of a medicinal product. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=OJ:L_202401381#d1e37-16-1 7. HTA CG. Guidance on Validity of Clinical Studies. https://health.ec.europa.eu/document/download/9f9dbfe4-078b-4959-9a07-df9167258772_en?filename=hta_clinical-studies-validity_guidance_en.pdf. 8. HAS. Real-world studies for the assessment of medicinal products and medical devices, June 2021. 9. https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fncpe.ie%2Fwp-content%2Fuploads%2F2018%2F07%2FNCPE-requirements-for-conducting-and-reporting-clinical-evidence-synthesis-v1.1.docx&wdOrigin=BROWSELINK. 10. https://www.tlv.se/in-english/medicines/pricing-and-reimbursement-of-medicines.html. 11. https://www.g-ba.de/english/benefitassessment/; https://www.g-ba.de/themen/arzneimittel/arzneimittel-richtlinie-anlagen/nutzenbewertung-35a/informationen-fuer-unternehmen/formulare-und-vorgaben/#anlage-ii-format-und-gliederung-des-dossiers-einzureichende-unterlagen-vorgaben-fur-technische-standards

**ISPOR 2024. 17-20 November 2024, Barcelona, Spain.**