HTA83

Comparing Risk of Bias Assessment Requirements Between the EU JCA and European HTA Agencies

Alys Ridsdale,[1] Isobel Munro,[1] Neil Webb[1]
1. Source Health Economics, Floor 2, 226 Banbury Road, Summertown, Oxford, OX2 7BY, UK

Background and objectives

- Systematic literature reviews (SLR) for health technology assessment (HTA) submissions should comprehensively summarise existing evidence for an intervention and its comparator(s).
- HTA bodies typically require an assessment of the internal validity of each included study – that is, the risk of bias (RoB) – to inform the overall certainty of the effectiveness results.
- In an effort to reduce duplication of HTA activities across European Union (EU) member states (MS), the first new oncology and advanced therapy medicinal products became subject to the EU Joint Clinical Assessment (JCA) as of January 2025.[1]
- Following the publication of recent guidance[2] and implementing acts,[3] we aimed to compare RoB assessment requirements between individual national HTA agencies and the EU JCA.

Methods

- A structured search and review was conducted of publicly available online HTA submission guidance for all EU MS, UK HTA bodies and the HTA Coordination group (HTACG) – which is responsible for coordinating and implementing JCA guidance under Regulation (EU) 2021/2282 on HTA (HTAR).
- The review focused on requirements for RoB assessment in both randomised controlled trials (RCT) and real-world evidence (RWE).
- In cases where published guidance on RoB was unavailable or unclear, HTA agencies or their national representatives were contacted directly for clarification.

Results

- In total, 31 HTA or regulatory bodies (comprising 27 EU MS, 3 UK bodies, and the European HTA Coordination Group [HTACG]) were reviewed (Figure 1):
  - 12 HTA bodies recommended the use of appropriate, though unspecified, RoB tools
  - 7 bodies explicitly required specific tools for assessing bias in both RCTs and RWE
  - No published guidance or response regarding RoB evaluation criteria could be identified for 12 EU MS.
- Further details on the specific guidance provided by the 7 HTA or regulatory bodies (6 EU MS, and the EU HTACG) are presented in Table 1.
- Among the cases where specific tools were required (6 EU MS, and the EU HTACG), the most frequently referenced were:
  - Cochrane RoB 2 for RCTs (n=5)
  - ROBINS-I for RWE studies (n=5).

Discussion & conclusions

- RoB assessment requirements for reimbursement submissions vary across Europe.
- Whilst many countries do not mandate the use of specific RoB tool use, six countries have requirements that conflict with those of the recently introduced JCA process under HTAR.[4]
- This discrepancy arises primarily because the EU JCA requires the use of Cochrane RoB 1, whereas the previous EUnetHTA guidance recommended Cochrane RoB 2.[5]
- Consequently, despite the implementation of the JCA, this misalignment in RoB guidance may lead to additional or repeated bias assessments at the national level for certain countries.

Figure 1: Summary of RoB assessment requirements in Europe

†Countries did not have any published guidance or respond to email enquiries made during the research period 22nd May 2025 to 22nd August 2025.
Abbreviations: EU, European Union; JCA, Joint Clinical Assessment; RoB, Risk of Bias.

Table 1: HTA and regulatory bodies with specific RoB requirements

Country/ countries	HTA/regulatory body	RoB tool required	
		RCT	RWE
EU MS (JCA process)[4]	European Commission	Cochrane RoB 1	ROBINS-I
Austria[6]	AIHTA	Cochrane RoB 2	Deeks et al, 2003[7]
Denmark[8]	DHTC	Cochrane RoB 2	ROBINS-I
Germany[9]	IQWiG	Cochrane RoB 2	ROBINS-I
Poland[10]	AOTMiT	'Cochrane Collaboration Tool for randomised studies'	NOS
Spain[11]	AETS	Cochrane RoB 2	ROBINS
Sweden[12]	SBU	Cochrane RoB 2 + COI assessment	ROBINS-I + COI assessment

Abbreviations: AETS, Agencia de Evaluación de Tecnologias Sanitarias; AIHTA, Austrian Institute for Health Technology Assessment; AOTMiT, Agency for Health Technology Assessment and Tariff System; COI, conflict of interest; DHTC, Danish Health Technology Council; EU, European Union; HTA, health technology assessment; IQWiG, Institute for Quality and Efficiency in Health Care; JCA, Joint Clinical Assessment; MS, member states; NOS, Newcastle-Ottawa Scale; RCT, randomised controlled trial; RoB, risk of bias; ROBINS(-I), Risk of bias in non-randomised studies (of interventions); RWE, real-world evidence; SBU, Swedish Agency for Health Technology Assessment and Assessment of Social Services.

References:
1. EC. Joint Clinical Assessments. https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment/joint-clinical-assessments_en. 2025.
2. EC. Health technology assessment - Key documents (legislation). https://health.ec.europa.eu/health-technology-assessment/key-documents_en?f%5B0%5D=topic_topic%3A226. 2025.
3. EC. Health technology assessment - Key documents (JCA guidance). https://health.ec.europa.eu/health-technology-assessment/key-documents_en?f%5B0%5D=topic_topic%3A227. 2024.
4. HTA Co-ordination Group. 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. 2024.
5. EC. Internal validity of randomised controlled trials. https://tools.eunethta.be/files/Internal%20validity%20of%20RCT.pdf. 2015.
6. AIHTA. Methodenhandbuch für Health Technology Assessment, Version 1. https://aihta.at/uploads/tableTool/UllCmsPage/gallery/methodenhandbuch-aihta1.pdf. 2012.
7. Deeks et al. Health Technol Assess. 2003;7(27):iii-x,1-173.
8. Danish Health Technology Council. The Danish Health Technology Council's methods guide for the evaluation of health technology 2023, Version 2.0. https://behandlingsraadet.dk/media/otjfhhzw/the-danish-health-technology-council-s-methods-guide-for-the-evaluation-of-health-technology.pdf. 2023.
9. IQWiG. Allgemeine Methoden, Version 8.0. https://www.iqwig.de/methoden/allgemeine-methoden_entwurf-fuer-version-8-0.pdf. 2025.
10. AOTMiT. Wytyczne oceny technologii medycznych (HTA, ang. health technology assessment). https://www.aotm.gov.pl/wp-content/uploads/2020/07/20160913_Wytyczne_AOTMiT-1.pdf. 2016.
11. AETS. Correspondence via aets-info@isciii.es. Responded 7 Aug 2025. 2025.
12. SBU. Utvärdering av insatser i hälso- och sjukvården och socialtjänsten. https://www.sbu.se/metodbok?pub=101442&lang=sv. 2024.

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