Are AI-based digital twins entering HTA? A review and insight into an emerging and evolving evidence-generation approach

HTA309

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INTRODUCTION

- Digital twins are dynamic digital representations that combine patient-specific multidimensional data with simulation and, increasingly, AI-based prediction[1,2]
- In healthcare, they are being explored for disease modelling, treatment optimisation and synthetic or in silico comparator generation, particularly where conventional comparative evidence is difficult to obtain[2,3,7]
- Despite rapid development, their role and acceptance within health technology assessment (HTA) remain unclear[4,8]

OBJECTIVES

1. To assess whether AI-enabled digital-twin comparator evidence has been used in formal HTA appraisal and identify the agency response
2. To describe emerging HTA positions and explore stakeholder views on acceptability, methodological requirements and barriers

CONCLUSIONS

Digital twins are beginning to intersect with HTA through methodological guidance, early HTA and post-launch economic evaluation,[9–11] but formal appraisal use was not identified

This suggests a gap between growing clinical and methodological interest in digital twins and demonstrated acceptance of digital-twin-generated comparative evidence in formal HTA. Existing experience with external and synthetic control arms provides relevant methodological precedent but should not be interpreted as direct precedent for AI-generated patients.[1–8]

Survey findings indicate that acceptance of AI-generated comparative evidence may be conditional on robust validation, transparency, reproducibility and appropriate characterisation of uncertainty. Respondents generally envisaged a limited or supportive role rather than use as primary evidence, although findings should be interpreted cautiously given the small sample (n=5)[8]

Further research and HTA experience are needed to establish when AI-enabled digital-twin comparators can credibly reduce uncertainty in comparative effectiveness and what evidentiary standards agencies will require

METHODS

TARGETED LITERATURE AND HTA REVIEW

A targeted review was conducted across PubMed, Google Scholar and Value in Health for digital twins, virtual patients, in silico trials and HTA. Grey-literature searches included European HTA bodies and regulators, with direct searches of publicly available appraisal and reimbursement documents from major agencies in France, Germany, Italy, Spain, Sweden and the UK

Searches were updated after abstract submission (June 2026) to a publication cut-off of 25 September 2026. For synthesis, evidence was grouped across four stages: clinical research, HTA position / guidance, early or post-launch HTA applications and formal HTA appraisal. AI-enabled digital-twin comparator evidence was distinguished from conventional external or synthetic control arms derived from observed patient data

STRUCTURED ONLINE SURVEY

Online survey (Microsoft Forms) of five former payer/HTA stakeholders, one from each of France, Germany, Italy, Spain and the UK. Responses were anonymised. Topics: appropriate use cases, credibility requirements, barriers and the anticipated role of AI-generated comparative evidence in HTA.[8] Descriptive analysis; results reported as counts (e.g. 3/5)

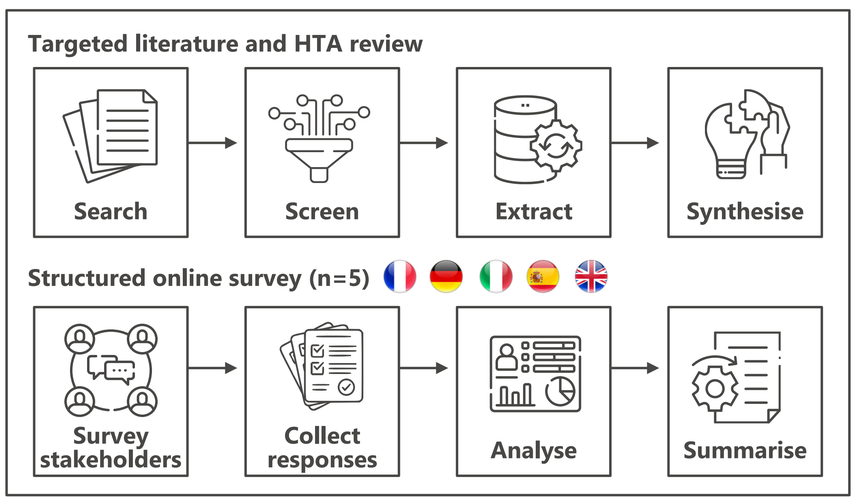


Figure 1. Overview of the research methodology

RESULTS

HTA APPRAISAL LANDSCAPE

No public European HTA appraisal using AI-enabled digital-twin comparator evidence was identified

A targeted review of publicly available appraisal and reimbursement documents from major European HTA agencies identified no case in which an AI-generated or digital-twin comparator formed the evidentiary basis for a formal HTA decision[8]

Although agencies have assessed external and synthetic control arms, these were predominantly based on observed historical or real-world patient data rather than AI-generated patients. [8] However, digital twins are beginning to intersect with HTA outside formal appraisal, including academic early HTA and post-launch economic evaluation[10,11]

CURRENT USE AND HTA APPLICATIONS

AI digital twins in clinical research: AI-enabled digital-twin comparator, counterfactual and simulated-comparator approaches have been reported in clinical research[2,3,7,8]

HTA position / guidance: Explicit consideration of AI-generated evidence is emerging. NICE states that AI may be used to generate synthetic data and external control arms and is exploring digital twins and in silico trials within its HTA methods research. No corresponding public appraisal precedent was identified[8,9]

Early / post-launch HTA applications: HTA methods are beginning to be applied to digital twin technologies outside formal appraisal. An academic early HTA evaluated a patient-specific digital twin approach for osteoporosis screening, while TLV and Region Stockholm used an artificial-cohort / digital-twin approach for post-launch economic follow-up of daratumumab[10,11]

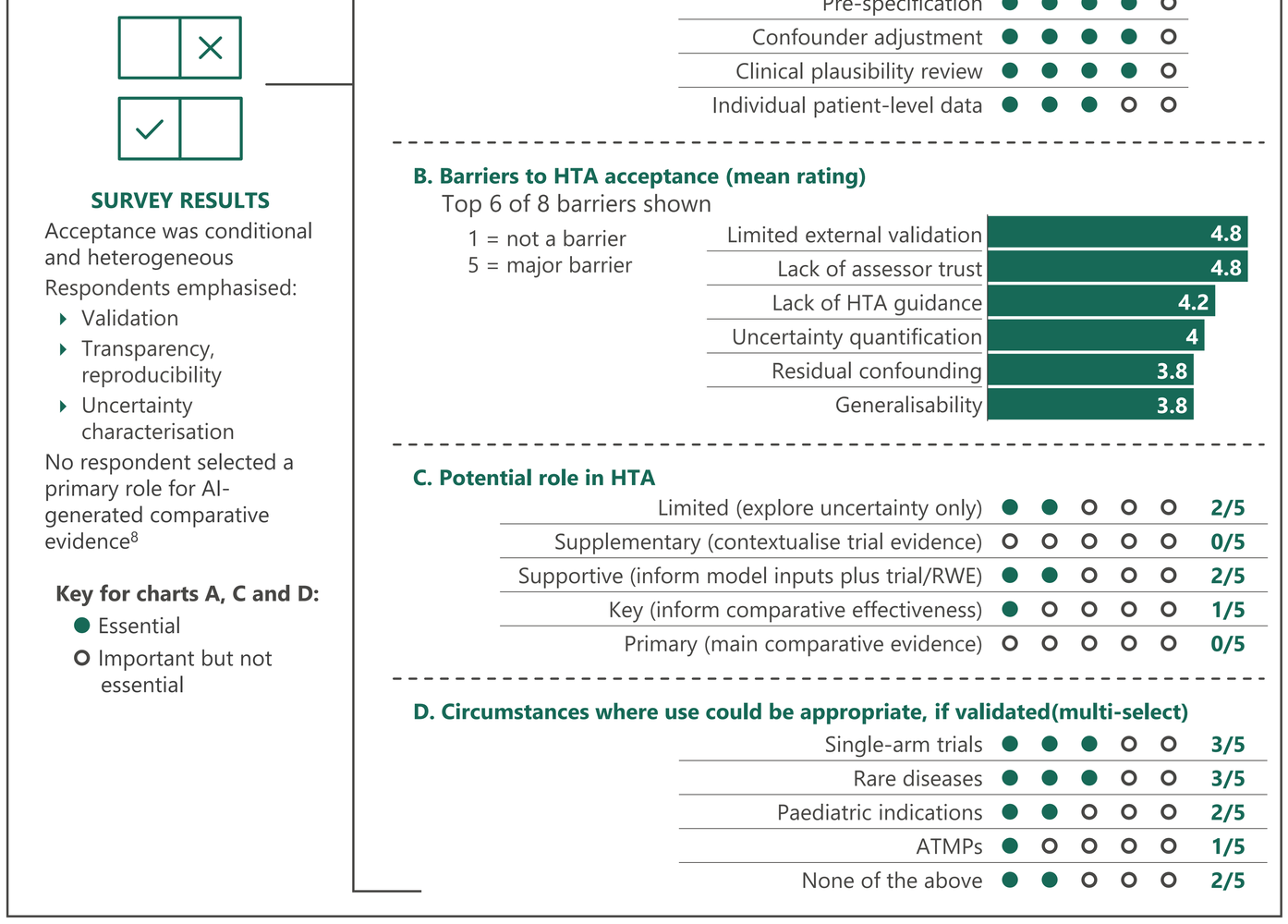


Figure 2. Former payer/HTA stakeholder views on the potential HTA use of AI-generated comparative evidence (n=5)[8]

References: 1. Gilbert S, Drummond D, Cotte F, Ziemssen T. Editorial: Digital twins in medicine-transition from theoretical concept to tool used in everyday care. Front Digit Health. 2025;7:1573727. doi:10.3389/fdgth.2025.1573727; 2. Ren Y, Pieper AA, Cheng F. Utilization of precision medicine digital twins for drug discovery in Alzheimer's disease. Neurotherapeutics. 2025;22(3):e00553. doi:10.1016/j.neurot.2025.e00553; 3. Arsène S, Parès Y, Tixier E, et al. In Silico Clinical Trials: Is It Possible? Methods Mol Biol. 2024;2716:51–99. doi:10.1007/978-1-0716-3449-3_4; 4. Leo CG, Tumolo MR, Sabina S, et al. Health Technology Assessment for In Silico Medicine: Social, Ethical and Legal Aspects. Int J Environ Res Public Health. 2022;19(3):1510. doi:10.3390/ijerph19031510; 5. Olawade DB, Akinro O, Oisakede EO, et al. Digital twin applications in radiology and radiotherapy: applications, challenges, and future perspectives. Eur J Radiol. 2026;200:112865. doi:10.1016/j.ejrad.2026.112865; 6. Strigari L, Schwarz J, Bradshaw T, et al. Computational Nuclear Oncology Toward Precision Radiopharmaceutical Therapies: Ethical, Regulatory, and Socioeconomic Dimensions of Theranostic Digital Twins. J Nucl Med. 2025;66(5):748–756. doi:10.2967/jnumed.124.268186; 7. Li G, Chen YB, Peachey J. Construction of a digital twin of chronic graft vs. host disease patients with standard of care. Bone Marrow Transplant. 2024;59(9):1280–1285. doi:10.1038/s41409-024-02324-0; 8. Remap Consulting. Data on file: targeted literature review, direct review of European HTA appraisal and reimbursement documents and structured online survey (n=5), 2026; 9. NICE. Use of AI in evidence generation: NICE position statement (ECD11). 2024; 10. Li J, Viceconti M, Li X, Bhattacharya P, Naimark DMJ, Osseyran A. Cost-effectiveness analysis of CT-based finite element modeling for osteoporosis screening in secondary fracture prevention: an early health technology assessment in the Netherlands. MDM Policy Pract. 2023;8(2):23814683231202993. doi:10.1177/23814683231202993; 11. TLV, Region Stockholm. Alternativa metoder för hälsoekonomisk uppföljning av daratumumab med hälsodata från Region Stockholm. Stockholm: TLV; 2022

Abbreviations: AI: artificial intelligence; ATMP: advanced therapy medicinal product; HTA: health technology assessment; NICE: National Institute for Health and Care Excellence; RWE: Real-World Evidence; TLV: Dental and Pharmaceutical Benefits Agency

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ISPOR Europe
8-11 November 2026
Vienna, Austria

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