

Real-world evidence is in demand: a summary of ‘live’ requests for RWE studies published by a European health technology assessment (HTA) agency

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Background

The European Health Data Network (EHDEN) provides a rich source of real-world evidence (RWE) mapped to the Observational Medical Outcomes Partnership (OMOP) common data model (CDM). The potential benefits of the network and CDM for healthcare policy have been underlined by the European Medicines Agency (EMA) establishing the Data Analysis and Real-World Interrogation Network (DARWIN EU), an unequivocal signal that RWE is set to play a major role in pharmaceutical regulation in Europe. At present, there is no unified approach for the use of RWE to inform health technology assessment (HTA). HTA is a systematic approach to the assessment of clinical and economic benefits of licensed healthcare technologies. It informs decision makers who seek to ensure access to health technologies that are both effective and efficient at generating population health (for example, through reimbursement and pricing).^{1,2} When it comes to using RWE to inform decisions, individual HTA agencies are currently following their own preferred approaches, though some do engage in international collaborations to advance and promote consistency in RWE methods.^{3,4,5}

The HTA agency in England is the National Institute for Health and Care Excellence (NICE). As NICE’s decision-making committees develop recommendations about healthcare technologies, they identify gaps and uncertainties in the evidence base that could benefit from further research. The most important unanswered questions are formulated into research recommendations. Each research recommendation is supported by a PICO statement outlining the population, intervention, comparator and outcomes of interest. This often includes a recommended study type such as a randomised control trial or observational study—an EUnetHTA position paper provides guidance on how to formulate such information⁶. Developing research recommendations provides the basis for NICE to communicate their research priorities with funders, primarily the National Institute for Health and Care Research (NIHR), and to continue to ensure a robust evidence base to inform future guidance. To demonstrate the ‘live’ demand for RWE studies at NICE – and, therefore, opportunities for EHDEN and the OMOP-CDM – we sought to review NICE’s research recommendations that specifically ask for new RWE studies.

Methods

We searched the NICE website to identify research recommendations containing the following terms in their title or description: “case-control”, “cohort”, “observational”, “real[-]world” and “retrospective”. Each research recommendation is linked to the guidance from which it was developed. We reviewed the source guidance to confirm that each research recommendation met the following criteria: (1) it was made or last reviewed from 1 January 2017 to 7 April 2022; (2) it remains ‘live’, in that it has not been made redundant by a study addressing the research question; and (3) it specifically requests or suggests RWE to answer the research question. Here, we summarise the identified recommendations for research and highlight some for which EHDEN may be particularly well suited to providing the requested RWE.

Results

A total of 22 'live' research recommendations seeking RWE have been published or last reviewed by NICE decision-making committees since 2017. All of these seek to fill gaps in the evidence identified by the relevant decision-making committees in their reviews of available evidence. Most requests for RWE (n=15, 68%) have been made to inform NICE's clinical guidelines. Five (23%) have been requested to inform NICE's guidance on interventional procedures. Diagnostics assessment guidance and medical technologies guidance each contribute one (5%) request for RWE.

One such RWE recommendation is from the 'Delirium: prevention, diagnosis and management' clinical guideline⁷. There is scant evidence for adverse events consequent to delirium in long-term care settings; therefore, NICE would like to see observational studies that characterise the prevalence of delirium in this setting and predict whether delirium is predictive of adverse outcomes, including death. Another example was developed as part of the 'Age-related macular degeneration' clinical guideline⁸. Routine (anti-vascular endothelial growth factor) treatment may be effective, but it can be inconvenient for patients, costly for healthcare systems, and pose a risk of adverse effects. There is little evidence to inform when effective treatment should be stopped, either as the condition becomes dormant or when treatment is ineffective. Defining stopping rules could have a major impact on clinical practice. NICE would like to see observational hypothesis-generating research to examine the point at which benefits from continued treatment become unclear. The findings could be used to inform a research protocol for a randomised trial.

RWE requests from NICE's other guidance producing programmes include the following calls:

- Medical device, 'Endo-SPONGE for treating low rectal anastomotic leak'⁹: Real-world data to characterise patient selection, effectiveness, patient-reported outcomes and costs.
- Interventional procedure, 'Artificial iris insertion for acquired aniridia'¹⁰: Observational cohort or case-series studies to characterise patient selection, type of implant and patient-reported outcomes.
- Diagnostic technology, 'EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules'¹¹: A large retrospective analysis to predict the determinants of lung cancer prevalence and progression, characterise current practice for people with intermediate-risk nodules, examine the clinical consequences of computerised tomography surveillance, and predict the likelihood of unnecessary surgical procedures.

Conclusions

This study demonstrates that clear, active demand for RWE studies has emanated from the guidance development activities a major European HTA agency. Federated data networks provide a valuable resource to respond to such requests for RWE, with a view to informing evidence gaps, reducing decision uncertainty, and culminating in more effective guidance to healthcare systems. NICE has placed the use of RWE in its activities as a crucial pillar of its 5-year strategic plan¹² and has recently cemented this commitment by publishing a framework to guide the development and interpretation of RWE for HTA purposes¹³. As a result, NICE's appetite for RWE to inform its work is likely to continue to grow. Adopters of the OMOP-CDM and the EH DEN network should seek opportunities to provide value to healthcare systems by responding to NICE and other European HTA agencies' research recommendations. HTA agencies should capitalise on the existence of these resources by recommending observational research is undertaken, where appropriate, as suggested by EUnetHTA⁶.

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