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# How has real-world evidence been leveraged in non-oncology HTA submissions in the UK, France, and Germany?

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## Introduction

Real-world evidence (RWE) obtained from an analysis of real-world data can bridge gaps in evidence not addressed by research based on interventional clinical trials, and is thus valuable to inform payer decision-making. The use of RWE to support pivotal trial data is rapidly increasing in oncology but remains relatively unexplored in other indications. The use of RWE in non-oncology payer submissions has the potential to bridge evidence gaps such as demonstrating long-term comparative effectiveness in chronic conditions, identifying treatment outcomes in more diverse patient populations in a plethora of therapeutic areas, and assessing long-term safety for first-in-class treatments. However, there are limitations that need to be mitigated to ensure successful implementation of RWE, including understanding and minimizing biases and confounding factors.

## Objectives

- To assess the historic use of RWE in non-oncology HTA EU submissions.
- To evaluate the acceptability of RWE for each HTA agency, in order to understand the future value of such evidence for payer submissions.
- To outline potential ways manufacturers could leverage RWE to optimize the reimbursement process in new product launches.

## Methods

HTA reports published by the UK National Institute for Health and Care Excellence (NICE), French National Authority for Health (Haute Autorité de Santé, HAS), and German Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) between January and December 2023 were reviewed to identify non-oncology submissions that used RWE, and trends in the use and acceptability of such evidence were analyzed. RWE was defined as research in a non-trial setting on data relating to clinical effectiveness, tolerability, health-related quality of life (HRQL), and/or economic evidence, such as resource use.

## Results

In total, 39 non-oncology appraisals were found for NICE, 14 for HAS, and 60 for the G-BA. NICE appeared to accept RWE and to use it in decision-making: the majority of submissions included some form of RWE and one-third included multiple forms of RWE (eg, from literature and registries). HAS recommendations did not appear to be influenced much by RWE; the agency focused more on the credibility and quality of the submitted RWE. The G-BA appeared hesitant in adopting RWE as a main driver of decisions; HTA submissions to the G-BA included the least use of RWE across the three markets.[1]

**Figure 1:** Use of RWE in HTA submissions to NICE, HAS, and the G-BA

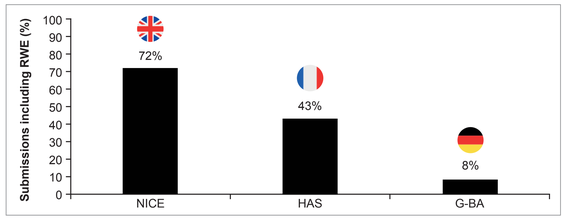
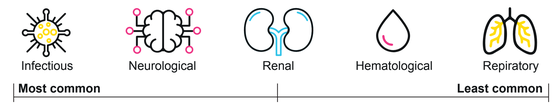
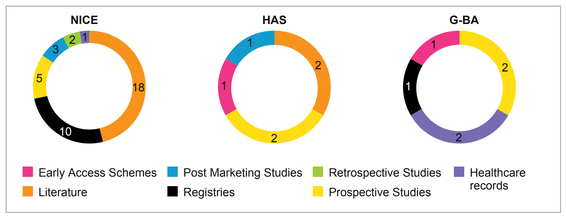



**Figure 2:** Most common therapeutic areas for non-oncology submissions that included RWE



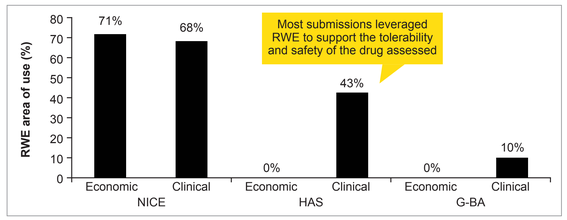

The most common source of RWE used in HTA submissions was published literature. For NICE and HAS, published literature on clinical effectiveness and safety was used to inform network meta-analyses. Literature sources of costs and utilities were consistently used across NICE submissions to support economic models. Prospective studies and registries focusing on real-world effectiveness were also widely used in submissions to all three agencies (Figure 3).

**Figure 3:** Sources of real-world data used in payer submissions




Submissions to all three agencies included RWE to support the clinical value of the asset (Figure 4). The most common types of RWE used for this purpose were clinical results, most focusing on effectiveness and safety outcomes, several on treatment patterns, and a few on HRQL. As cost-effectiveness is a formal requirement for NICE, submissions that included RWE to support economic value (eg, real-world resource use, reference costs, generation of utilities) were more common than those with RWE supporting only clinical value (71% vs 68%). In the context of economic modeling, RWE was most commonly used to inform utilities and provide reference costs for estimating resource use. HAS only requires an economic evaluation if the improvement in medical benefit (amélioration du service médical rendu, ASMR) is rated 3 or better; as this was not the case for any of the submissions reviewed, no economic RWE was included. As the G-BA do not assess economic evidence, there were no reports to analyze for RWE usage.

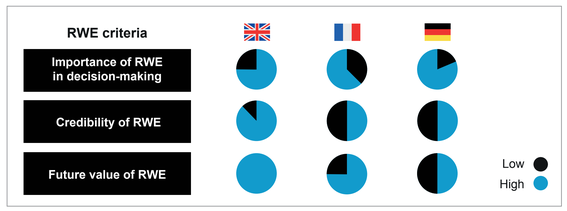
**Figure 4:** Area of RWE utilization in payer submissions




## Discussion

RWE is an established and effective method of collecting valuable data that can bridge evidentiary gaps for payers. The use of RWE varies among HTA agencies, with NICE having the lead in both the number of submissions that include RWE and the different types of RWE used in these submissions. About 43% of HAS submissions included RWE, but the total number of non-oncology submissions to HAS in 2023 was notably lower than to NICE or the G-BA. Despite the G-BA having the most non-oncology submissions in 2023, only a handful of these included RWE.

**Figure 5:** Perceptions of RWE use across markets




The acceptability of RWE also varied across markets. RWE was mostly accepted by NICE and HAS, but the G-BA accepted it only in one instance, from an early access program for an orphan drug. When RWE was not accepted by the HTA agencies, the main barriers to acceptance were:

| Design quality | Data validity and quality | Data quantity |
|---|---|---|
| (eg, lack of randomization for prospective studies and registries) | (eg, scalability and generalizability concerns) | (eg, completeness of data by the time of submission) |

### The advent of artificial intelligence

With payers such as NICE publishing their vision to use RWE to resolve gaps in knowledge and drive forward access to innovations for patients by 2026, artificial intelligence (AI) tools have enormous potential in automating processes such as data collection and quality control.[2]

AI-driven processes can mitigate the bias and confounding factors of RWE to promote data quality and ensure both internal and external validity of evidence before payer submissions.[3]

However, it is important for manufacturers to use well-designed AI processes that avoid technical issues such as hallucination bias, and ensure a human-in-the-loop approach with all use of AI.

**Figure 6:** Examples of how AI tools can be leveraged in the context of RWE

| Data collection | Data quality control |
|---|---|
| Processing and harmonization of large volume of heterogeneous data, enabling comprehensive and longitudinal assessments of treatment outcomes and healthcare utilization patterns | Machine learning techniques such as anomaly detection and data validation algorithms to identify data inconsistencies, errors, and missing values, ensuring the reliability and integrity of datasets |

### Key considerations for manufacturers

**Be informed**
- Monitor guidance published by HTA agencies on their RWE frameworks
- Develop in-house understanding and expertise in RWE

**Be proactive**
- Work with technical experts and clinical key opinion leaders to produce updated guidelines for RWE that consider new technologies (eg, machine learning)
- Introduce incentives for clinicians to record data[4]

**Be innovative**
- Actively explore the use of AI tools to support RWE collection and quality control, and streamline patient access to innovative therapies

## Conclusions

The use of RWE in non-oncology HTA submissions varies across the markets in scope, with the UK being the most accepting market, and Germany the least. RWE was used in multiple ways, including supporting clinical effectiveness, tolerability, and cost-effectiveness. Where RWE was not accepted, the main criticisms concerned the quality and completeness of the data. In addition to designing high-quality real-world studies, manufacturers should take into consideration the acceptance of RWE by each HTA agency before submission. With the advent of AI tools that facilitate data collection and quality control, these critiques may be more easily addressed by manufacturers in the future.

### References

1. LSE. https://www.lse.ac.uk/business/consulting/assets/documents/the-use-of-real-world-evidence-in-the-european-context.pdf [Accessed March 25, 2024].
2. NICE. https://www.nice.org.uk/corporate/ecd9/resources/nice-realworld-evidence-framework-pdf-1124020816837 [Accessed March 25, 2024].
3. Forbes. https://www.forbes.com/sites/garydrenik/2023/08/15/data-quality-for-good-ai-outcomes/?sh=290d08281184 [Accessed March 25, 2024].
4. LSE. https://www.lse.ac.uk/business/consulting/assets/documents/real-world-evidence-in-europe-the-results-of-an-expert-survey.pdf [Accessed March 25, 2024].

Poster presented at ISPOR US, May 5–8, 2024, Atlanta, GA, USA