Utilisation of real-world evidence in European HTA appraisals

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Acceptance code 129589

Background and objective

- RCTs are the gold standard of evidence for reimbursement decisions by HTA bodies (1,2)
- Drug development is increasingly focused on highly targeted populations, presenting challenges for the utilisation of RCTs
- RWE may provide complementary evidence for HTA, or it may offer alternatives when RCTs are not possible
- RWE is derived from real-world data sources such as observational cohort studies, patient registries, and electronic health records
- This study investigated how RWE was utilised in HTA submissions over a 3-month period in England, Scotland, France, and Germany

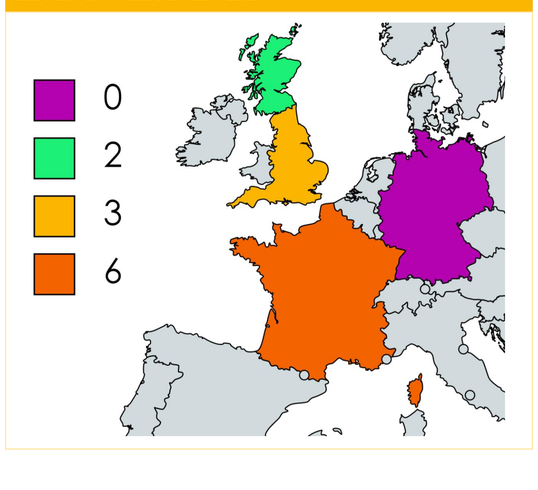
Methods

- HTA reports published between 8 March and 8 June 2023 were retrieved from the websites of 5 HTA bodies: NICE (England), SMC (Scotland), HAS (France), and IQWiG and G-BA (Germany)
- Data on RWE sources and reasons for inclusion were extracted, as were appraisal decisions
- The frequency of RWE use among HTA bodies was examined by review of each submission

Results

- Ninety HTA submissions were identified, among which 4 were terminated. Of the remaining 86 submissions, 11 (12.8%) made use of RWE, with the highest number of RWE-containing appraisals submitted in France (6/11, 54.5%), and none reported in Germany (Figure 1)
- RWE was utilised to support clinical effectiveness assessments in England, Scotland, and France. RWE was also used to support safety outcomes in France, as well as cost-effectiveness outcomes in England and Scotland (Figure 2)
- Among all 11 submissions utilising RWE, 6 (54.5%) were in cancer indications, 2 (18.1%) were in atypical haemolytic and uraemic syndrome, and 1 (9.1%) each was in coronavirus 2019, cardiac, and respiratory indications

Figure 1. Number of submissions utilising RWE between 8 March and 8 June 2023



RWE data sources

- The most common data sources for RWE were observational studies (n=9), followed by databases (n=3)
- In the 3 RWE-containing submissions to NICE, 1 utilised a database, 1 used an observational study, and 1 used both. Of the 2 RWE submissions to SMC, 1 was a prospective observational study and the other was a database. All 6 submissions to HAS contained RWE from observational studies

Germany

- RWE was not submitted in support of any IQWiG or G-BA submissions
- Evidence submitted to IQWiG consisted of 21 appraisals reporting RCT data and 2 appraisals reporting single-arm trial data. A further submission included both single-arm and RCT data, and 2 submissions presented no data that IQWiG deemed suitable for benefit assessment
- Benefit of treatment was not proven in 19 submissions. G-BA issues a final decision on benefit assessment within 3 months of IQWiG recommendations; no G-BA decisions on the 21 IQWiG appraisals included in the present study had been published at the time of this work

England

- RWE was utilised in 3 of 20 (15%) submissions to NICE
- In those 20 submissions, supporting evidence primarily consisted of RCTs (n=15). Four submissions utilised single arm-studies, and 1 submitted both single-arm and RCT data
- Of the submissions utilising single arm-studies, 1 was recommended for use within the Cancer Drugs Fund, while the remaining 3 did not receive approval (2 because of lack of additional impact versus current treatment, and 1 because of insufficient clinical and economic analysis). The submission utilising both single-arm and RCT evidence was recommended. Fourteen (93.3%) RCT submissions were recommended
- RWE was acknowledged as strengthening the evidence body, and all 3 submissions were recommended. In the application for daratumumab with bortezomib and dexamethasone in previously treated multiple myeloma, the committee said the RWE “allowed more accurate baseline data”

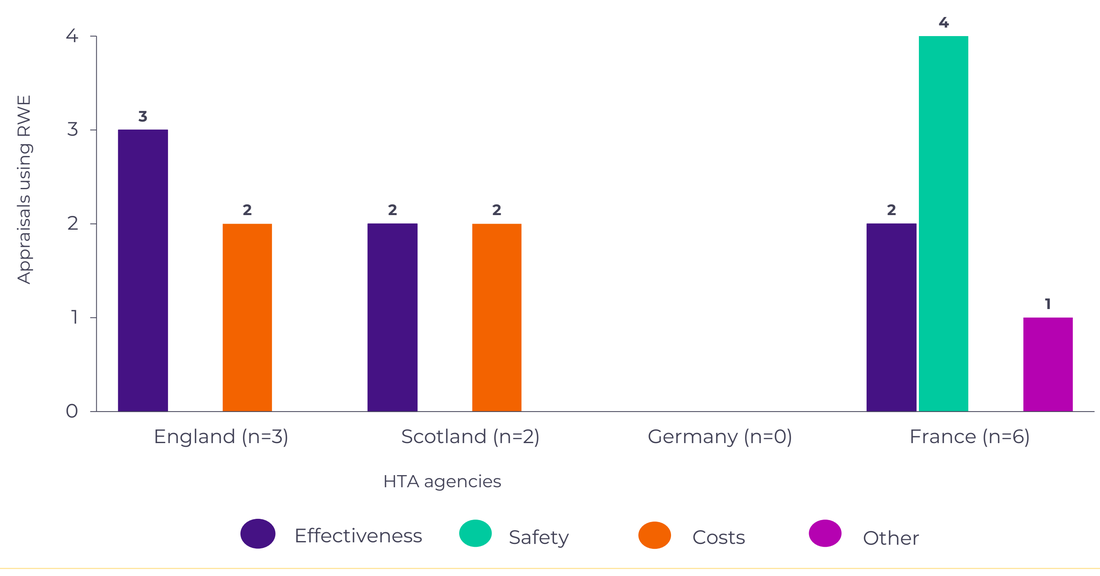
Scotland

- RWE was reported in 2 of 15 (13.3%) SMC submissions in support of the primary single-arm trial. One submission presented RWE in the base case for the comparator, and the other utilised RWE for cost-utility analysis. One submission presenting RWE was recommended on an interim basis, subject to ongoing evaluation and future reassessment
- SMC were uncertain about the inclusion of RWE because it may limit generalisability. Furthermore, comparisons between RWE and trial data are subject to bias
- Ten appraisals that did not utilise RWE but presented RCT data [n=10 (1 also utilised single-arm trial data)] were recommended

France

- RWE was utilised in 6 of 25 (24%) submissions to supplement clinical effectiveness outcome data from single-arm (n=3) studies and RCTs (n=3). Four submissions were recommended (2 supported by single-arm studies and 2 by RCTs)
- Twelve of the total submissions made to HAS were supported by RCTs (10 of which were recommended) and 8 by single-arm studies (7 recommended). A further 2 studies utilised both RCT and single-arm evidence, both were recommended
- One French appraisal incorporated RWE to estimate the proportion of patients receiving treatment in accordance with its marketing authorisation (Figure 2)

Figure 2. Inclusion of RWE in HTA submissions to each agency and reasons for inclusion



Conclusions

- It is becoming increasingly important to demonstrate products’ effectiveness and safety in the real world. There is opportunity for RWE to play a growing role in HTA and reimbursement decisions by complementing and supplementing clinical trial evidence, as well as reducing uncertainties that can delay reimbursement decisions
- This study demonstrates that acceptance and utilisation of RWE in HTA evaluations remains limited and is variable among European HTA agencies
- In the 3-month period studied, the inclusion of RWE differed among European HTA agencies, with no submissions utilising RWE to German HTAs
- In cases where RWE was utilised, data supported clinical and economic evidence, in addition to primary evidence from RCT and single-arm trial data

References

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2. Moloney R, Mohr P, Hawe E, Shah K, Garau M, Towse A. Payer perspectives on future acceptability of comparative effectiveness and relative effectiveness research. Int J Technol Assess Health Care. 2015;31(1-2):90-8.

Abbreviations: G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; HTA, health technology assessment; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; NICE, National Institute for Health and Care Excellence; RCT, randomised controlled trial; RWE, real-world evidence; SMC, Scottish Medicines Consortium

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