A lifecycle approach to the use of RWE in HTA submissions and re-submissions, a decade's experience

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INTRODUCTION

- Health Technology Assessment (HTA) bodies worldwide recognize the importance of real-world evidence (RWE) in addressing uncertainties around the effectiveness of new drugs at time of launch and in reassessments. In recent years, we have witnessed the emergence of frameworks in support of the use of RWE
- We assessed the use and acceptability of RWE by analyzing HTA reports

METHODOLOGY

- Using IQVIA's HTA Accelerator, we analyzed 16,516 HTA reports for single drug assessments including original submissions, resubmissions, extensions of original indications and assessments of new formulations or strengths, published from January 2011 to December 2021* from 83 HTA agencies across 33 countries
- We performed a quantitative analysis of HTA reports with and without RWE per year and per therapeutic area, looking at the areas supported by RWE, the type of real-world data (RWD) sources used and acceptance of the RWE by the HTA body. RWD source types classified as RWE are outlined in Box 1. A qualitative analysis was conducted to better understand acceptability of RWE, approaches to RWD use and the key critiques raised by HTA bodies
- Acceptability was inferred based on syntax. Vocabulary such as "appropriate, suitable, low risk of bias, etc." or absence of specific negative critique was categorized as accepted. Negative vocabulary such as "not accepted, not appropriate, not suitable, etc." was considered as not accepted. Partially accepted reflects mixed language such as "despite risk of bias, RWE was considered appropriate only for one patient subgroup, etc." Reports were searched in original language

RESULTS

USE OF RWE BY THERAPEUTIC AREA AND AREAS SUPPORTED

- Of all 16,516 HTA reports, 3,282 (20%) reports mentioned RWE. Between 2011-2021, there has been more than six-fold increase in the use of RWE, from 6% in 2011 to 39% in 2021. For resubmissions, the use of RWE increased from 14% in 2011 to 44% in 2021 (Graph 1)
- RWE has been commonly included in oncology (n=942), followed by endocrine and metabolic diseases (n=480), infectious and parasitic diseases (n=342), musculoskeletal diseases (n=214) and cardiovascular diseases (n=200)
- Details on RWD sources was available in 1,508 reports. For these, main areas supported were epidemiology (39%), safety (39%), effectiveness (33%), utilities / dis-utilities (14%) and treatment costs (10%) (Graph 2). RWE has also been considered to supplement evidence on external comparator, treatment patterns, extrapolation of clinical endpoints, health resource utilization etc. (Graph 2)

TYPE OF RWD SOURCES

- In the 1,508 reports analyzed and irrespective of area supported, patient disease registries (40%), observational studies (34%) and retrospective cohort studies (23%) were mostly used. Other RWE data sources were administrative data, prospective cohort studies and pharmacovigilance data. More specifically, epidemiology data were collected from patient disease registries (67%) and administrative data (23%). Observational studies (37%), retrospective cohort studies (34%) and patient disease registries (21%) were used to derive clinical effectiveness (Graph 3)

USE AND ACCEPTABILITY OF RWE BY HTA BODIES

- NICE (55%), HAS (41%), AOTMiT (39%), IQWiG (35%) and FIMEA (32%) are the 5 HTA bodies who referenced the most RWE in their HTAs.
- HAS and IQWiG leveraged RWE mostly for safety (95%) and epidemiology (98%), respectively. The high number of RWE sources used by HAS may be due to French process whereby products are reassessed frequently, and inclusion of Periodic Safety Update Reports is mandatory. In Germany, RWE sources are submitted to support sizing of the population. NICE and PBAC have cited RWE in support of clinical effectiveness (40% and 61%, respectively) followed by safety (19% and 44%, respectively) and epidemiology (10% for both)
- RWE has been most accepted (including partially accepted) when it was supporting epidemiology (81%), safety (78%), QoL (77%) and dis-utilities (77%) considerations. The use of RWE to support external comparison is the application the most critiqued (33% of RWE rejected) (Graph 4)
- In general, HTA bodies critique the lack of transferability to local practice, small sample sizes, study design, high risk of bias resulting from retrospective design or incomplete data collection and misalignment between RWE population and that of the clinical trial

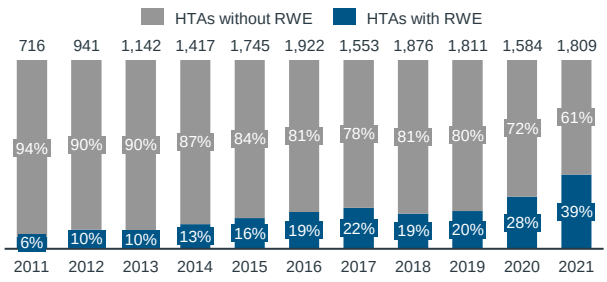
CONCLUSIONS

The inclusion and acceptability of RWE in HTA recommendations varies between HTA bodies according to their data requirements and assessment methods. While it is not always specified how RWE was considered, there is a clear tendency of accepting RWE albeit not on all areas. Greater use and transparency around RWE are likely to continue as multiple RWE initiatives are burgeoning globally.

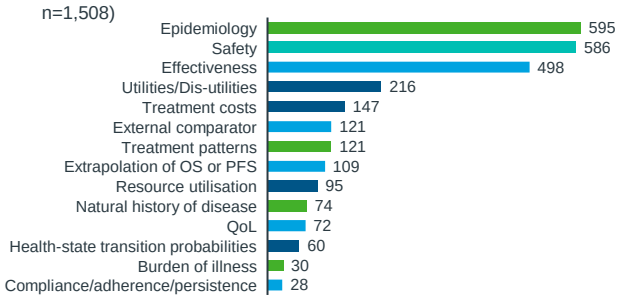
Box 1: RWD source types classified as RWE

RWE data sources	
Administrative data	Post-marketing study
Case control study	Practical/ Pragmatic trial
Case-series study	Prescription
Cross-sectional study	Prospective cohort study
Electronic patient record	Retrospective chart review
Hospitalization	Retrospective cohort study
Insurance claim	Supplement to registration RCT
Non-randomized controlled trial	Systematic patient survey/interview
Observational study	Systematic physician survey/interview
Patient disease registry	Uncontrolled study
Pharmacovigilance data	Vignette study
Population health survey	

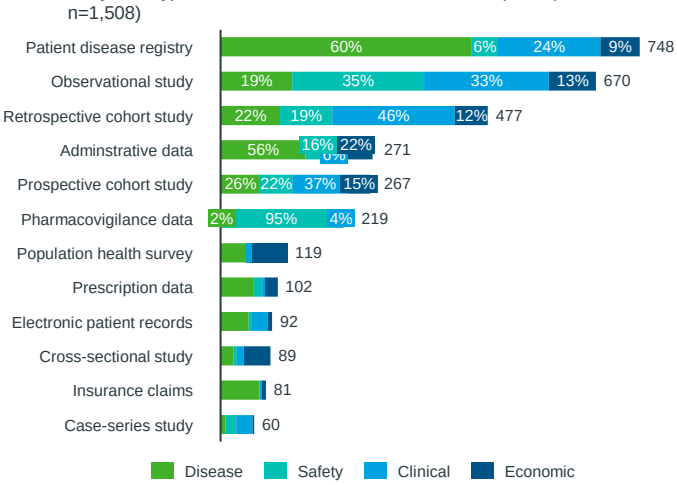
Graph 1: Number of HTA records per year with RWE used (n=16,516)



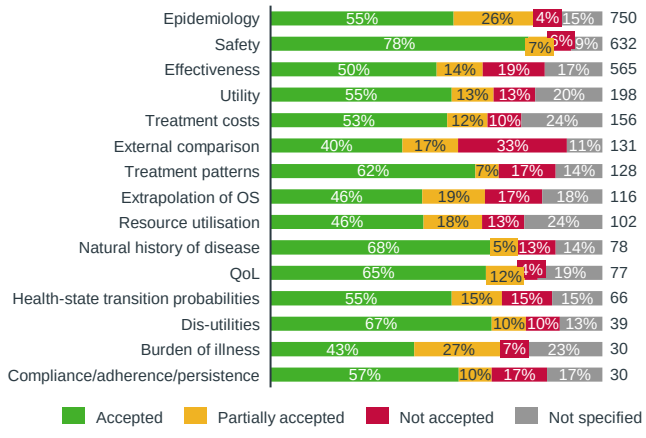
Graph 2: Number of RWE used across areas supported (2011-2021; n=1,508)



Graph 3: Type of RWE data sources used in HTA reports (2011-2021; n=1,508)



Graph 5: HTA acceptance of RWE (2011-2021; n=1,508)



Legend: On all graphs, the number represents the number of HTA reports

LIMITATIONS: 1) The analysis leverages published HTA reports, as such data may be missing for some countries and use of RWE may be underestimated. 2) While many HTA reports cite evidence from RWD sources, acceptability, and its impact on the HTA recommendation is not always specified. 3) Each mention of a RWD source was accounted for and as such one RWD source may have been used to support different areas of the assessment and so double counting could be possible. | **REFERENCES:** IQVIA HTA Accelerator | **ACKNOWLEDGEMENT:** Ajinkya Bendre, Khavya Ramachandran, Qian Shen and Robert Krüger have contributed to the development of this analysis. | **ABBREVIATIONS:** AOTMiT = Agencja Oceny Technologii Medycznych i Taryfikacji; FIMEA = Lääkealan turvallisuus- ja kehittämiskeskus Fimea; G-BA = Gemeinsamer Bundesausschuss; HAS = Haute Autorité de Santé; HTA = Health Technology Assessment; IQWiG = Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; NICE = The National Institute for Health and Care Excellence; QoL = Quality of Life; RCT = Randomised Controlled Trial; RWE = Real-World Evidence

*We included HTA reports from November and December 2021 that were published after the abstract was posted.

HTAi 2022 Annual Meeting Utrecht, Netherlands