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How does real-world evidence support regulatory and HTA agency assessments and beyond?

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RWD183

Introduction

There is growing recognition of the value that real-world evidence (RWE) and real-world data (RWD) can bring to regulators and payers who seek to understand the value of new treatments. Clinical trial evidence may lack generalizability to real-world settings, with challenges such as a lack of broader representation of complex patient populations, difficulties recruiting sufficient participants with rare diseases, lack of established treatment comparators, and limited data on long-term effectiveness, safety, and patient-reported outcomes. RWE evidence can potentially bridge the evidence gap by providing additional insights into the disease and its treatment.

As RWE becomes increasingly embedded within new drug assessments, consistency across regulatory and health technology assessment (HTA) agencies regarding the role of RWE will be critical to ensuring effective and efficient decision-making.

Objectives

To explore alignment among regulatory and HTA agencies across Europe and the United States (US) regarding the use of RWE in the decision-making process for drug assessments, as well as how RWE might be leveraged to support accelerated patient access strategies.

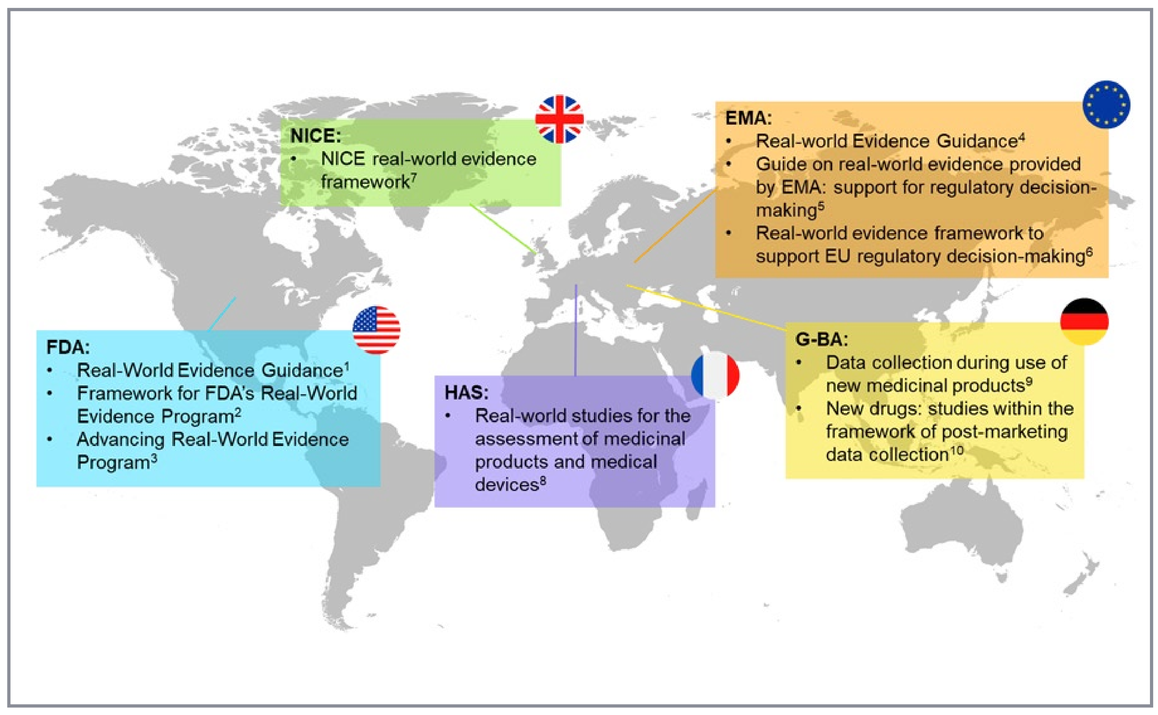
Methods

Published guidance (such as frameworks, programs, and other types of initiatives) related to the use of RWE to support regulatory and HTA decision-making were identified from the following agencies' websites:

- US Food and Drug Administration (FDA)
- European Medicines Agency (EMA)
- National Institute for Health and Care Excellence (NICE)
- Haute Autorité de Santé (HAS)
- The Federal Joint Committee or Gemeinsamer Bundesausschuss (G-BA)

In total, 10 online sources, including guidance documents and webpages (Figure 1), were reviewed to capture regulator and payer perspectives on the definition and role of RWE in decision-making. Potential opportunities and future approaches to using RWE to accelerate patient access across global markets were also explored.

Figure 1: RWE guidance published by regulatory and HTA agencies



EMA, European Medicines Agency; EU, European Union; FDA, US Food and Drug Administration; G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; NICE, National Institute for Health and Care Excellence.

Results

RWE is broadly defined by regulatory and HTA agencies as clinical evidence derived from analysis of RWD related to patient health outcomes or experience, and/or treatment utilization/delivery in routine practice (Table 1).[1-10] Agencies consider electronic health records, product or disease registries, and medical insurance claims as key sources of RWD.[1-10] Based on the EMA's description of RWE, evidence for new treatments can only be collected post launch, whereas RWE on treatment alternatives could have an impact; the same is true for HAS, the G-BA, and NICE.[4-10] Notably, HAS recognizes the role of RWE on a new treatment which is collected pre-launch,[8] and NICE gives the broadest descriptions of how RWE can be generated and used, eg, to design clinical trials and estimate effects of inteventions.[7]

Table 1: Overview of definitions of RWE/RWD by regulatory and HTA agencies

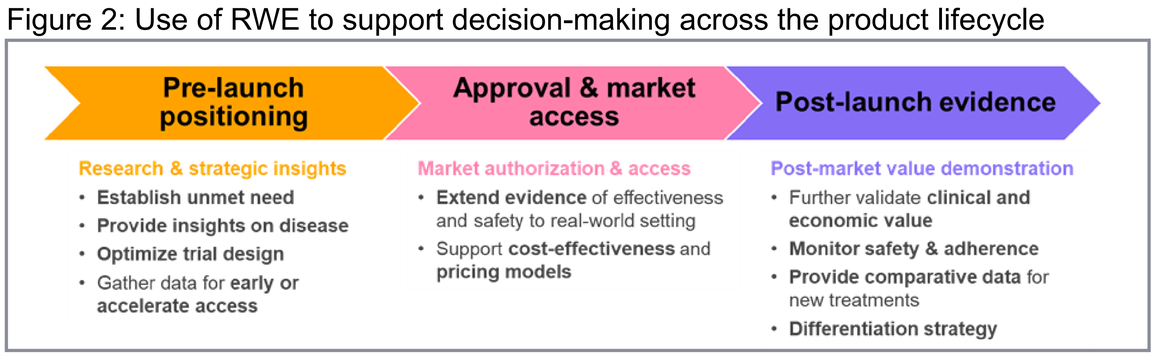
Agency	How is RWE defined?
FDA [1,2,3]	• Clinical evidence of the usage and potential benefits/risks of a product • RWD on patient health status and healthcare delivery in routine clinical practice
EMA [4,5,6]	• Routinely collected data on a patient's health status or the delivery of healthcare • RWD on patient characteristics and treatment outcomes/utilization in routine clinical practice
NICE[7]	• RWD gathered from routine and/or bespoke data collection • Generated from various study designs and methodologies (quantitative and qualitative); includes single-arm trials using RWD sources to establish external control • RWD on disease epidemiology, health service research, and causal estimation
HAS[8]	• Data generated post-marketing in France • Data collected for early access programs or temporary funding • Product use, efficacy, or safety data from sources outside conventional clinical trials • Includes RWD on epidemiology, burden of disease, outcomes of indirect comparisons
G-BA [9,10]	• Data collected in daily clinical practice, providing information beyond clinical trial data • G-BA/IQWiG instructs manufacturers on the type, duration, and scope of data collection

EMA, European Medicines Agency; FDA, US Food and Drug Administration; G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; HTA, health technology assessment; IQWiG, Institute for Quality and Efficiency in Health Care; NICE, National Institute for Health and Care Excellence; RWD, real-world data; RWE, real-world evidence.

Historically, the FDA has used RWE to conduct post-market safety surveillance and, in limited instances, to support clinical effectiveness.[1,2] Meanwhile, the EMA has used RWE to fill knowledge gaps by validating existing evidence or providing additional independent insights.[4-6] The need to accelerate patient access to new innovative treatments have prompted both regulatory bodies to establish frameworks, programs, and RWD generation pathways to better understand how RWE can be integrated alongside randomized controlled trial data into regulatory decisions.[1-6]

RWE can also play an important role for HTA agencies, providing context for the impact of the disease and, sometimes, providing comparative data for the new treatment under review (Figure 2).[7-10] The published guidance suggests that RWE can fill additional evidence gaps, eg, disease epidemiology and burden, treatment patterns, and to help validate assumptions around long-term clinical and economic value, especially for NICE and HAS who look to understand cost-effectiveness.[7,8] However, acceptance of RWE differs between HTA agencies, with more limited acceptance where the assessment paradigm is grounded in comparative trial evidence, eg, the G-BA focuses on the types of RWE to collect post-assessment rather than how to include RWE within their assessment.[9,10] Conversely, NICE suggests the use of RWE could be more commonplace and a preferred data source, provided these data are representative and of sufficient quality,[7] while HAS acknowledges the growing role of RWE internationally and remains attentive to regulatory initiatives concerning RWD.[8] Agencies such as NICE also note that capturing treatment outcomes post-approval from routine clinical practice is an important element of demonstrating the value of an asset and can be useful in HTA reassessments.[7]

Figure 2: Use of RWE to support decision-making across the product lifecycle



Conclusions

Overall, RWE serves as an essential resource and has historically been used to support and provide context to clinical effectiveness evidence. Advances in the availability of RWD have increased the potential for RWE to play a critical role in supporting regulatory and HTA decision-making. As more innovative treatments launch and the use of artificial intelligence to enhance RWD collection increases, perspectives on the use of RWE in evidence submissions will likely evolve rapidly. The upcoming implementation of the EU Joint Clinical Assessment (JCA) could enable manufacturers to further leverage RWE in national evidence submissions. However, given the varying levels of acceptance of RWE across HTA agencies, challenges may arise where the central advice on the use of RWE to support JCA assessments may not reflect the requirements of individual markets.

Scan here for poster references

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