Real-World Evidence to Inform Regulatory Decision Making: A Scoping Review

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Background

Real-world evidence (RWE) is increasingly considered in regulatory decision-making. However, when and to which extent RWE is considered relevant and necessary by regulators remains unclear. This review aimed to identify factors reported in literature that make RWE necessary or desirable in regulatory decision-making.

Methods

A **scoping review** was conducted using literature databases (PubMed, Embase, Emcare, Web of Science and Cochrane Library) and websites of regulatory agencies, HTA agencies, research institutes and professional organizations involved with RWE. Articles were included if: (1) they discussed factors or contexts that impact whether RWE could be necessary or desirable in regulatory decision-making; (2) focused on pharmacological or biological interventions in humans; and (3) considered decision-making in Europe or North-America, or without a focus on a specific region.

Results

We included **118 articles** in the scoping review. Two major themes and 6 subthemes were identified. Collectively, these themes encompassed **43 factors** influencing the need for RWE in regulatory decisions.

THEME 1
Questions addressable with RWE that facilitate regulatory decision-making

Subtheme 1.1: Epidemiology

Disease epidemiology
- Incidence, prevalence, event rates
- Natural history of a disease
- Population characteristics
- Landscape of standard of care

Regulatory purposes of epidemiology data
- Contextualisation
- Orphan designations
- Substantiation of trial design

Subtheme 1.2: Benefit-risk assessment

Pre-approval benefit-risk
- Expedited or alternative approval pathways

Post-approval benefit-risk
- Continued monitoring of benefit-risk
- Conditional approvals
- Evidence gaps related to benefit-risk
- Label modifications
- Evaluation of risk minimization measures

THEME 2
Contextual factors that increase the need or desire for RWE in regulatory decision-making

Subtheme 2.1: Feasibility
- Rare populations, recruitment difficulties
- Time and resource constraints
- Long-term outcomes
- Rare outcomes

Subtheme 2.2: Ethical considerations
- High unmet need
- No equipoise
- Vulnerable populations

Subtheme 2.3: Limitations of available evidence
- Generalizability
- Less robust trial evidence
- Limited existing knowledge

Subtheme 2.4: Disease & treatment-specific aspects
- Complex treatment settings
- Vaccine research
- Changing effectiveness over time

Summarized overview of the themes, subthemes, and factors.
A list of all factors can be viewed in the published article.

Interested to read more? Scan the QR-code for the published article. **Supplementary Material S2** contains a list of all factors, including comprehensive descriptions, illustrative quotes and their references.

Conclusion and takeaways

This overview provides valuable information that can contribute to ongoing discussions about the necessity or desirability of RWE to inform regulatory decision-making.

- The need for RWE to inform regulatory decisions is not a dichotomy but a continuum
- Some factors are more influential than others (e.g., high unmet need vs generalizability limitations)
- A single factor on its own may not make RWE fully necessary, but jointly multiple factors could make RWE to be essential in regulatory decision-making.

How can the results help stakeholders?

The current framework may help:

- Sponsors identify when RWE could be valuable to include in submission dossiers;
- Regulators in their assessment of whether RWE could be pivotal, and the weight it should receive in decision-making (along with other aspects, such as methodological quality of RWE, and the consequences of the decision to be made).

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