Opportunities and Barriers to Integrating Real-World Evidence in US Payer Decision Making

Pannu K[a], Foy C[a], Crowe L[a]
[a] Petauri Evidence, Bicester, United Kingdom

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Background

What is real-world evidence?
Real-world evidence (RWE) is the analysis of real-world data (RWD) from sources including, but not limited to (1-3):

- **Administrative claims**
- **Electronic health records (EHRs)**
- **Patient registries**
- **Pharmacy claims**
- **Medical claims**
- **Consumer surveys**

RWE provides insight into patient populations and real-world treatment patterns that are often absent from randomized controlled trials (RCTs) (1). Although RCTs remain the current gold standard for evidence (4,5), their strict eligibility criteria can often limit the diversity of patients included (1). As a result, RCT-driven evidence may not fully reflect insured populations or the outcomes seen in routine clinical practice (4).

The evolving role of RWE in US payer decision making
US payers increasingly recognize that RWE, when combined with data from RCTs, can be a powerful tool to guide formulary and coverage decisions (6). In limited instances, the Food and Drug Administration (FDA) has accepted RWE to support drug product approvals, primarily in the setting of oncology and rare diseases (2). RWE has gained traction in regulatory submissions following FDA guidance on its use for supporting initial drug approvals and new indications (7). However, no comparable guidance exists for payers on how to evaluate and incorporate RWE into coverage and reimbursement decisions (6). As a result, despite its potential to inform comparative effectiveness, safety, and economic outcomes, payer adoption of RWE remains limited (6).

Objectives

To identify the following factors influencing the integration of RWE into US payer decision making:

1. **Key barriers**
2. **Key priorities**
3. **Relevant frameworks**

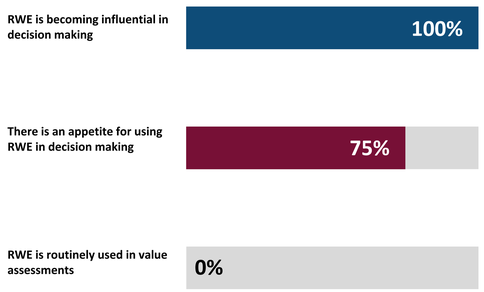
Methods

A targeted literature review was conducted to identify recent studies and policy initiatives addressing the role of RWE in US payer decision making.

Results

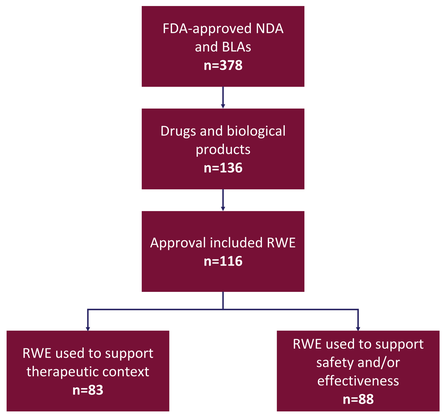
Published interviews indicated that payers recognize the value of RWE in supporting reimbursement decisions (6). However, despite this interest and its potential, RWE is still not used routinely in their assessments. Payers reported that RWE is becoming more influential in decision making, and that there is strong appetite for expanding its use (Figure 1); yet routine integration into value assessments remains limited (6).

Figure 1: Payer perspectives on the role of RWE in decision making (6)



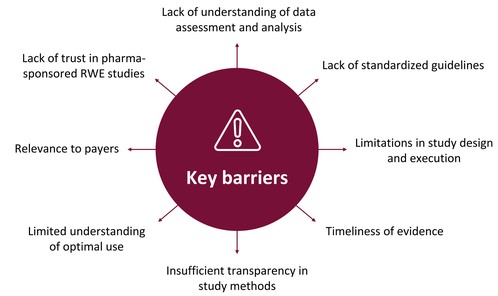
A review of FDA approvals (2019–2021) found that **65%** (88/136) of new drugs and biologics included RWE, intended to support safety and/or effectiveness. Of these, the FDA used **74%** of the submitted RWE studies in their benefit–risk assessments, with some contributing substantial/primary evidence and most providing supportive evidence that strengthened the overall evaluation of a product's performance (7) (Figure 2).

Figure 2: Use of RWE in FDA drug and biologic approvals (2019–2021) (7)



Across several sources, key barriers to RWE adoption include limited understanding of data assessment, analysis, and optimal use of RWE, lack of standardized guidelines, and insufficient transparency in study methods (1,3,6,8). Timeliness is also a major challenge, as RWE is often generated post-launch and arrives too late to inform early coverage decisions (1,3,7). Additional obstacles include limitations in study design and execution, such as variability in data quality, inconsistencies across RWD sources, challenges in combining multiple data types, and other methodological limitations (1,7,8) (Figure 3).

Figure 3: Key barriers in RWE adoption (1,3,6-8)



To overcome the barriers identified in Figure 3, industry stakeholders should adopt the recommendations outlined in Figure 4, which aim to strengthen the generation, communication, and utilization of RWE and unlock its full potential to inform payer decision making (3,4,6,9).

The development of guidelines and universal frameworks is a key recommendation to improve RWE adoption. In particular, the Academy of Managed Care Pharmacy (AMCP) framework was highlighted as a valuable approach for guiding RWE assessment, with payer-focused criteria that support industry in clearly articulating study relevance, data source selection, methodological rationale, and key limitations (Table 1) (4).

Figure 4: Recommendations for industry (3,4,6,9)

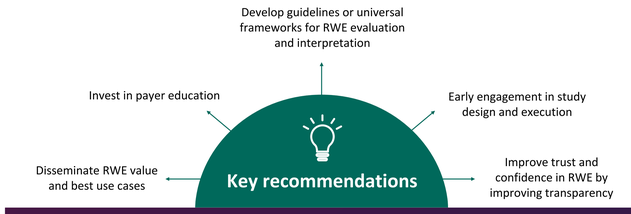


Table 1: AMCP RWE criteria framework (4)

Category	Criteria
General study questions	• Findings are generalizable and appropriate for the study objective • Clear settings and practice patterns • Population is relevant • Interventions are relevant
Data source	• Clearly defined data source • Appropriate to address the research question • Description of how exposures were identified and measured • Description of patient selection process • Discussion of any potential patient selection bias
Outcomes measured	• Clearly defined outcomes • Clear description of how the outcomes were measured • Clear description of background treatment and/or comparator • Validated outcomes, as appropriate • Subgroup analyses, as appropriate • Measured outcomes are relevant and clinically meaningful
Analytics	• Appropriate statistical methods for the research question • Clear statistical analysis plan • Appropriate methodological rigor • Descriptive statistics for cohorts • Study timeframes appropriate for the research question • Confounders are considered and addressed • For economic analyses – clearly stated perspective (e.g., payer) • For economic analyses – clearly stated cost estimation methods
Results	• Consistent with prior known information (as appropriate) or adequate explanation provided • Consistent across different studies • Clear and readily interpretable • Statistically significant • Clinically significant
Limitations	• Clear description of study limitations

Discussion

These findings illustrate a growing disconnect between regulatory and payer use of RWE. Whilst regulators such as the FDA increasingly accept and review RWE as part of approval pathways, evidenced by the frequent inclusion of RWE in regulatory submissions (7), payer respondents reported that RWE is not yet routinely integrated into value assessments for coverage and reimbursement decisions (6). This suggests that regulatory acceptance alone has not been translated into consistent downstream payer adoption, largely due to persistent gaps in standardization, transparency, and payer-specific evaluation frameworks.

To address the barriers identified, industry stakeholders must move beyond evidence generation and focus on enabling RWE use. Investment in payer education was consistently highlighted as critical to improving understanding of RWE strengths, limitations, and application in decision making (1,3,6-8). Clear and transparent methods and analytical criteria were also identified as essential to increasing confidence and adoption (1,3,6-8). The AMCP framework provides a practical set of payer-focused assessment criteria to support industry communication of study relevance, rigor, and limitations (4). In addition, AMCP has published a complementary lifecycle-based framework outlining when different types of RWE may be most appropriate across the drug lifecycle (4).

Conclusion

RWE, as a complement to traditional RCTs, has significant potential to enhance payer decision making by providing insights into real-world effectiveness, safety, and resource use. However, despite increasing regulatory acceptance of RWE, its routine and consistent use in payer value assessments remains limited.

These findings indicate that the gap is driven by persistent challenges, including a lack of standardized approaches for RWE assessment, limited transparency in study design and reporting, and uncertainty regarding relevance to payer populations and decision contexts.

Establishing common standards, improving transparency, and fostering early and ongoing collaboration between industry and payers can support more consistent, trusted, and decision-relevant use of RWE in US payer decision making.

Frameworks such as the AMCP RWE standards provide a practical foundation to align evidence generation with payer needs and maximize the full potential of RWE as part of the totality of evidence.

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Abbreviations

AMCP – Academy of Managed Care Pharmacy
BLA – Biologics license application
EHR – Electronic health record
FDA – Food and Drug Administration
NDA – New drug application
RCT – Randomized controlled trial
RWD – Real-world data
RWE – Real-world evidence

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