Real-World Evidence (RWE) to Support Regulatory Submissions: Landscape Assessment & Review

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Introduction

- Real-world evidence (RWE) and real-world data (RWD) are increasingly important in evaluating the safety and effectiveness of medical products.
- Randomized clinical trials (RCTs) are considered the gold standard for producing evidence, but they are not always feasible and do not fill all evidentiary gaps.
- Regulatory agencies, including the FDA and EMA, are increasingly considering the use of RWE to support regulatory decision-making in the pre-approval setting.
- There is a need for a comprehensive review and synthesis of published materials on RWE use cases that supported regulatory decisions in the pre-approval setting.

Objective:

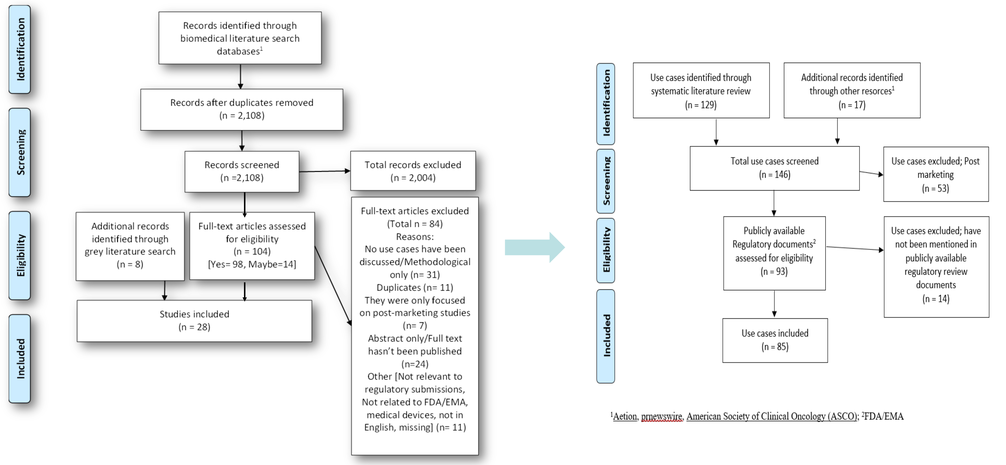
- **To characterize regulatory applications with RWE in the pre-approval setting by design, approach, and other parameters in the U.S. and Europe**

Methods

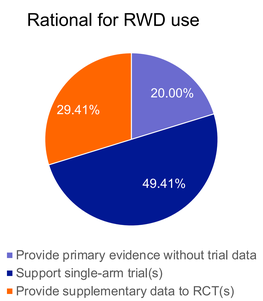
- RWE regulatory use cases were identified through systemic review and screening of publications (January 2016-June 2022) from PubMed, Embase, Web of Science, and FDA/EMA regulatory review documents.
- Data were extracted and synthesized from eligible publications, and unique features such as RWD sources, study design, and endpoints used to support regulatory decision-making were characterized. Further, we conducted a detailed review and data extraction from FDA/EMA approval packages to provide additional information.

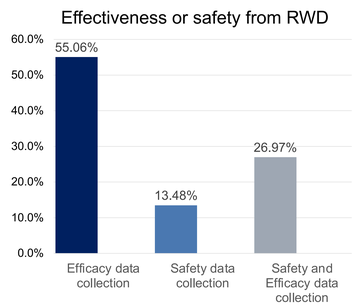
Results

After the screening, the systematic review identified 85 regulatory applications with RWE:



- Of these cases, 31 were in the oncology and 54 were in the non-oncology therapeutic area
- Most were for indications in adults only (N=41, 48.2%), while 13 were in pediatrics only (15.3%) and 30 were in both (35.3%)
- In terms of regulatory use, 59 cases (69.4%) were approved through an original marketing application, 24 (28.2%) were for label expansion, and 2 (2.4%) for label modification.
- Most also received special regulatory designations (e.g., orphan indication, accelerated approval, breakthrough therapy, fast track, and conditional).





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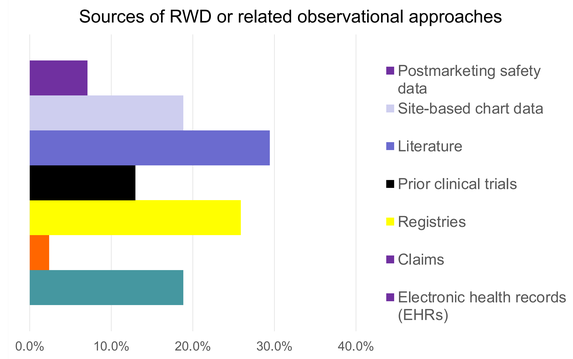

- The common endpoints in oncology use cases were overall survival, progression-free survival, and objective response, while a wide range of endpoints was used in non-oncology use cases.
- In 13 use cases, RWE was not considered supportive/definitive in the regulatory decision-making due to design issues such as small sample size, selection bias, and missing data.

Conclusion

- **This review suggests that RWE is utilized in regulatory approval processes for new indications/label expansion across various therapeutic areas with a wide range of approaches and data sources.**
- **This evolving landscape of RWE utilization underscores its potential to revolutionize healthcare by bridging the gap between clinical trial data and real-world clinical practice, ultimately improving the overall quality and efficiency of healthcare delivery.**