Real-World Evidence from observational studies to pragmatic trials

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Food & Drug Administration (FDA)

- **Real World Evidence (RWE)** [FDA][1,2]: RWE is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of Real-World Data (RWD).

- **Real World Data (RWD)** [FDA][1,2]: RWD is data relating to patient health status and/or the delivery of health care **routinely** collected from a variety of sources.

- **Guidance**: Center for Biologics Evaluation and Research & Center for Drug Evaluation and Research Real-World Evidence | FDA

1. Food and Drug Administration. Framework for FDA's real-world evidence program. December 2018 (https://www.fda.gov/ media/120060/download).
2. Food and Drug Administration. August 2023. Considerations for the use of RWD and RWE to support regulatory decision-making for Drugs and Biological Products, Guidance for Industry

European Medicines Agency

- **Real World Evidence (RWE)** [FDA][1]: RWE is the evidence derived from the analysis of Real-World Data (RWD).

- **Real World Data (RWD)** [FDA][1]: RWD are **routinely** collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials (e.g. claims databases, hospital data, electronic health records, registries).

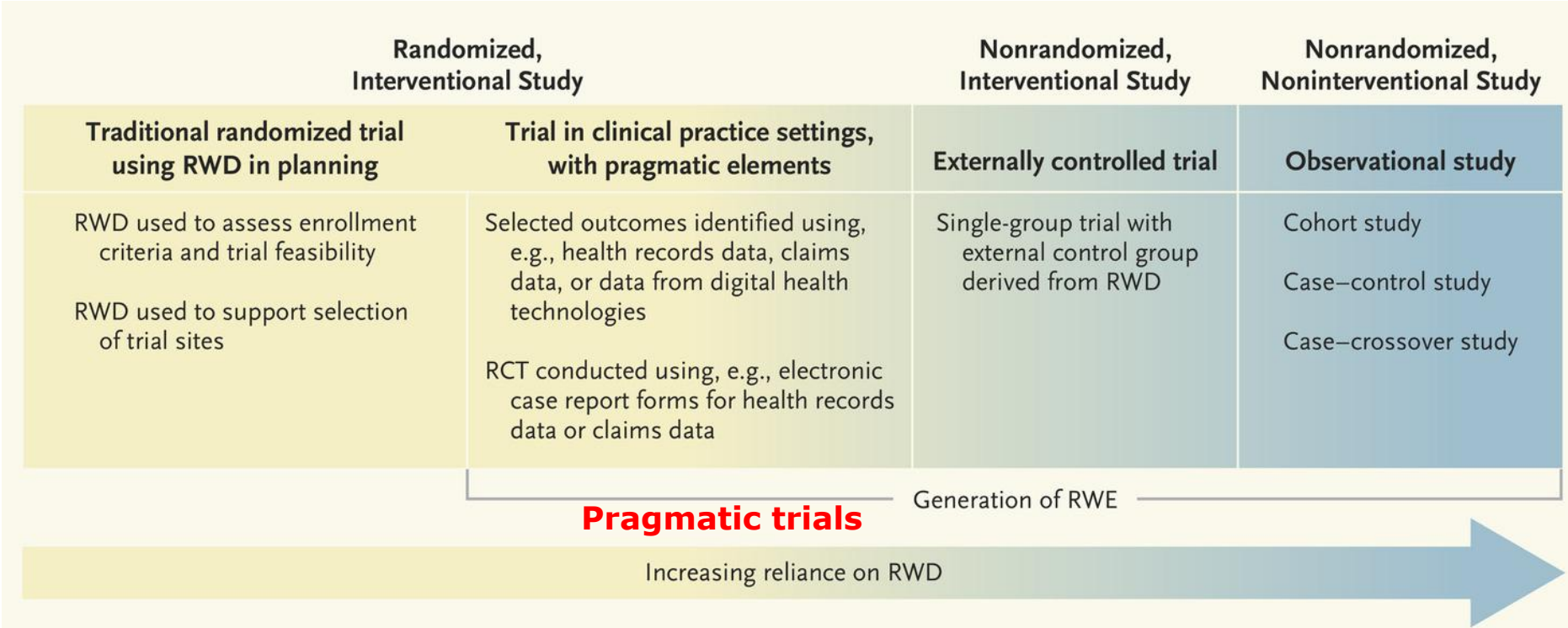
- **Guidance:** Real-world evidence | European Medicines Agency (EMA)

1. Arlett, P., Kjær, J., Broich, K. and Cooke, E. (2022), Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value. Clin. Pharmacol. Ther., 111: 21-23. https://doi.org/10.1002/cpt.2479

Real World Evidence (RWE)

- Long history of using RWE for post-marketing (vaccine) safety evaluation
- More recent use of RWE to inform vaccine effectiveness both to support product initial licensure and label changes
- Common misconception:
  - RWE == non-interventional (aka observational) studies: patients received drug of interest during routine medical practice
  - Interventional studies: patients are assigned to the intervention according to the study protocol

RWE from RCT to observational studies



Concato J, Stein P, Dal Pan GJ, Ball R, Corrigan-Curay J. Randomized, observational, interventional, and real-world-What's in a name? Pharmacoepidemiol Drug Saf. 2020 Nov;29(11):1514-1517. doi: 10.1002/pds.5123. Epub 2020 Sep 17. PMID: 32940401

Randomized Pragmatic Trials

- Pragmatic trials evaluate the effectiveness of interventions under conditions of routine practice

  - **Randomization**: participants still randomly assigned to intervention groups
  - **Real-world context**: care delivered as per routine medical practice
  - **Broad eligibility criteria**: diverse and representative patient population
  - **Real-world outcomes**: outcomes that matter for medical care, such as hospitalization and healthcare utilization
  - **Real-world data sources**: