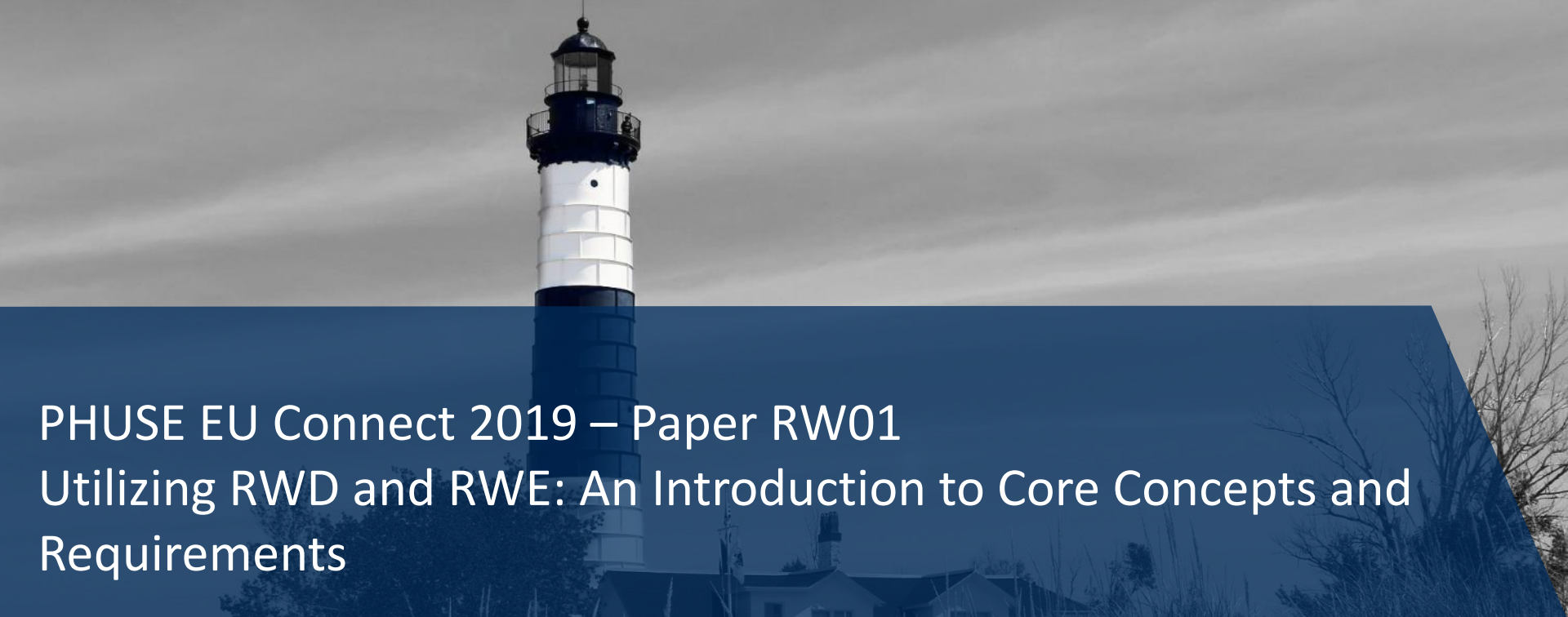




PHUSE EU Connect 2019 – Paper RW01

Utilizing RWD and RWE: An Introduction to Core Concepts and Requirements



The difference is in the data.™

Authors

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- **Introduction**
 - Vision and regulatory scope
 - FDA Framework for Real-World Evidence Program
 - Emerging use cases and an example
- **RWD/RWE Definitions and Framework**
 - What is RWD/RWE and an example of scale
 - Provenance of the data
 - Common sources
 - Live example using Twitter data
 - Data models
- **RWE in practice – how programmer's may take advantage of new opportunities with RWE**
 - Opportunity for programmers within a data science methodology
 - Opportunity across functions to utilize RWE
 - Demonstration projects at PHUSE/FDA Data Science Innovation Challenge

- **The 21st Century Cures Act (US - 2016)**

- Accelerate the discovery, development and delivery of 21st century cures
- Support approvals for new indications and support or satisfy post approval study requirements
- Laid the Framework for FDA's Real-World Evidence Program

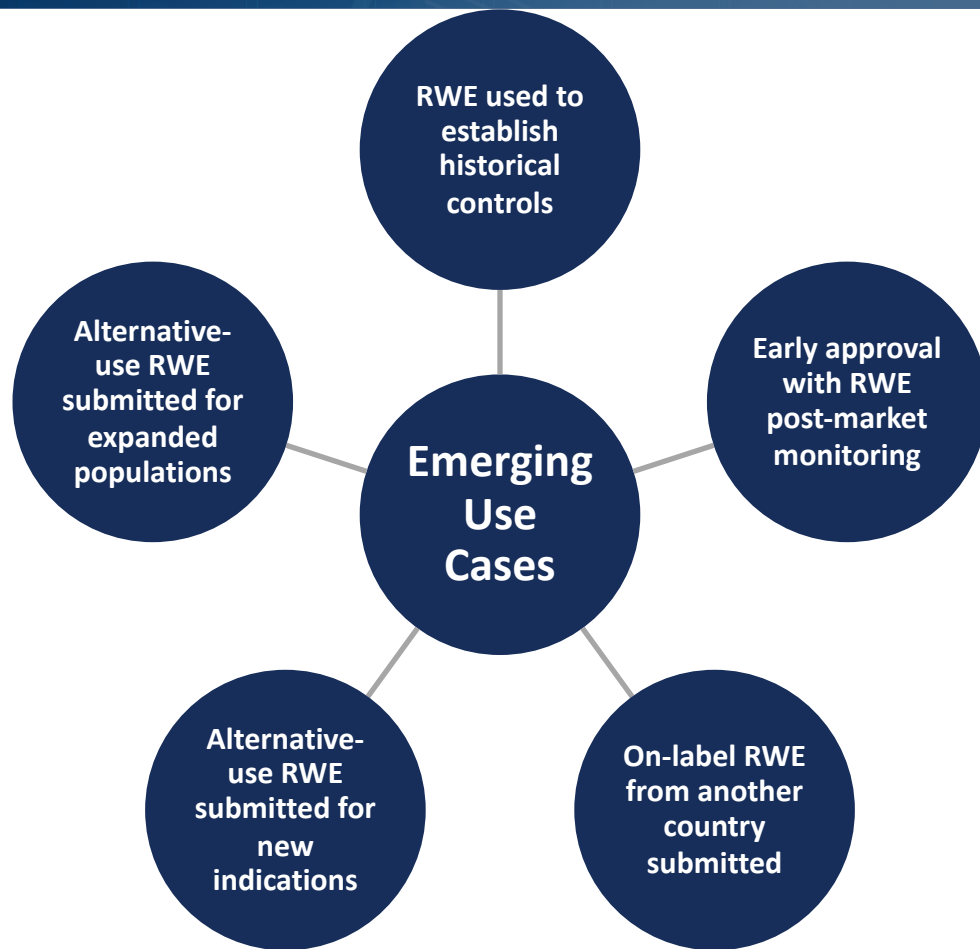
Canada	Canadian Agency for Drugs and Technologies in Health (CADTH)
Europe	Innovative Medicines Initiative (IMI) IMI GetReal project European Medical Information Framework (EMIF) European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP)
USA	FDA's RWE Framework Duke-Margolis RWE Collaborative Bipartisan Policy Center

FDA Framework - Generate RWE of product effectiveness to help support approval of new indications or support or satisfy post-approval study requirements

Some key ways RWE can improve the efficiency of trials:

- Generating hypotheses for testing in randomized controlled trials
- Identifying drug development tools (including biomarker identification)
- Assessing trial feasibility by examining the impact of planned inclusion / exclusion criteria in the relevant population, both within a geographical area or at a particular trial site
- Informing prior probability distributions in Bayesian statistical models
- Identifying prognostic indicators or patient baseline characteristics for enrichment or stratification
- Assembling geographically distributed research cohorts (e.g., in drug development for rare diseases or targeted therapeutics)





CHALLENGE

- Support for an orphan drug response required identification of prevalence for a disease subset population not obtainable through scientific literature.
- Orphan drug application had been held in abeyance on two previous occasions due to concerns from the Office of Orphan Products Development (OOPD) regarding prevalence.

SOLUTION

- Out of the box thinking and some creativity led us to identify real world data (RWD) routinely collected from the delivery of health care
- Using **actual sales data** from the US and **shipment data** from Europe for a marketed competitor would best support a prevalence estimate in the subset disease population.

OUTCOME

- The analyzed data effectively demonstrated that the population subset was less than the threshold of 200,000 patients required for orphan products.
- While the use of non-traditional data and real-world evidence is usually less often considered, we believe that there is **limitless potential** for its continued use in drug development and global regulatory submissions.

RWD – Real World data are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWD can come from several sources, for example:

- Electronic Health Records (EHRs)
- Claims and billing activities
- Product and disease registries
- Data gathered from other sources that can inform on health status, such as mobile devices

RWD



RWE

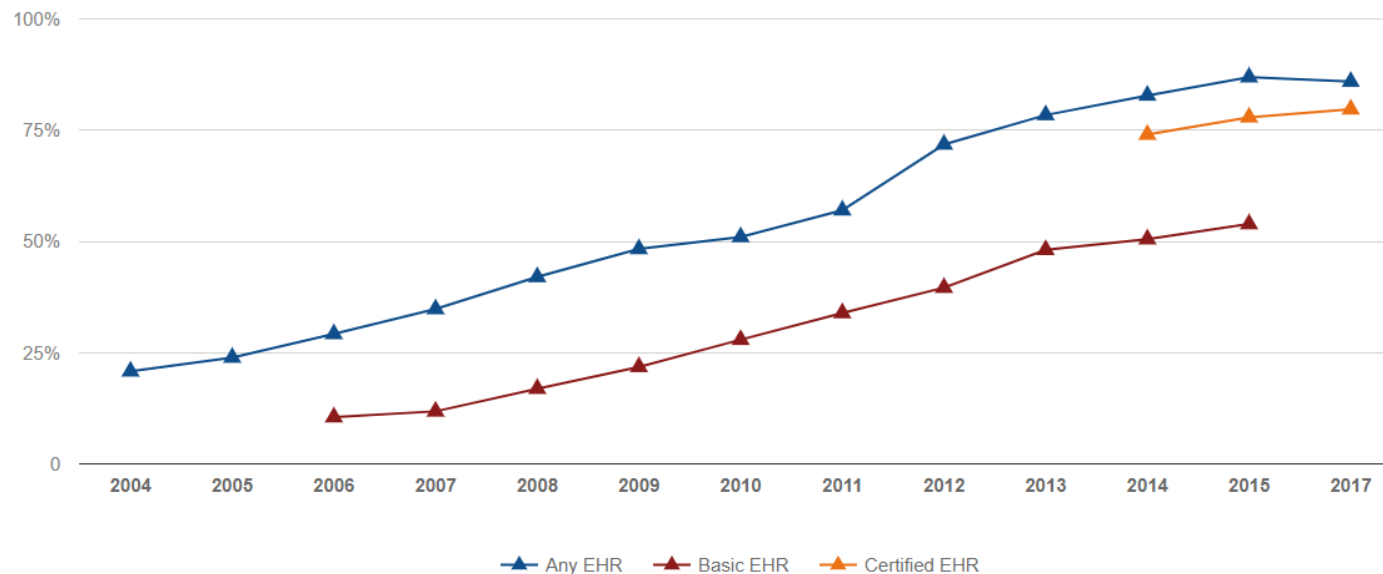
RWE - Real World Evidence is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD. RWE can be generated by different study designs or analyses, including but not limited to:

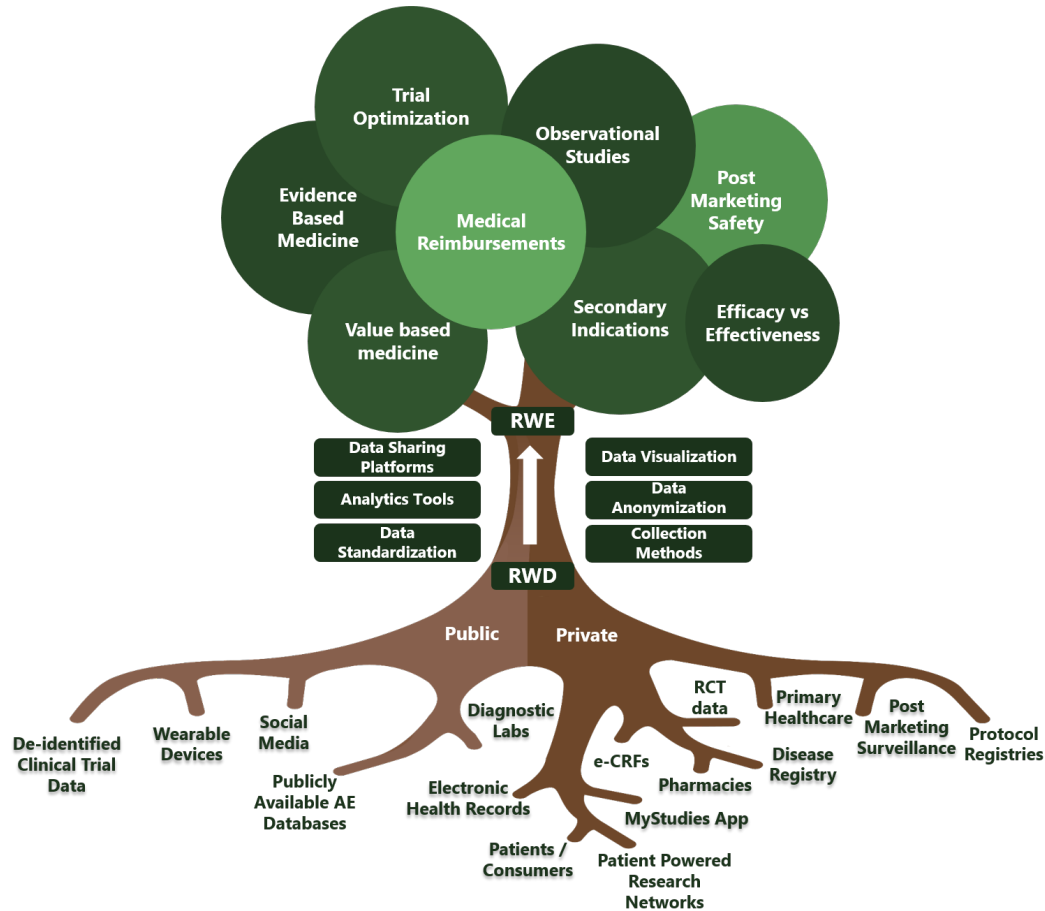
- Randomized trials including large simple trials
- Pragmatic trials
- Observational studies (prospective and/or retrospective)

Office-based Physician Electronic Health Record Adoption

EHR adoption has more than doubled since 2008

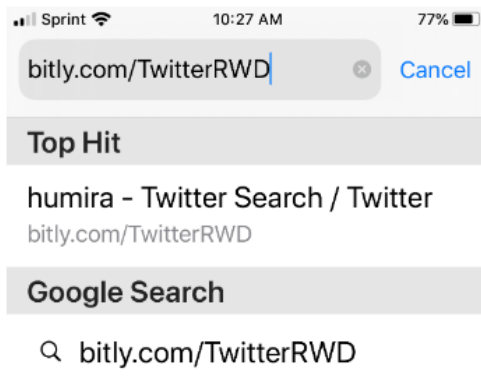
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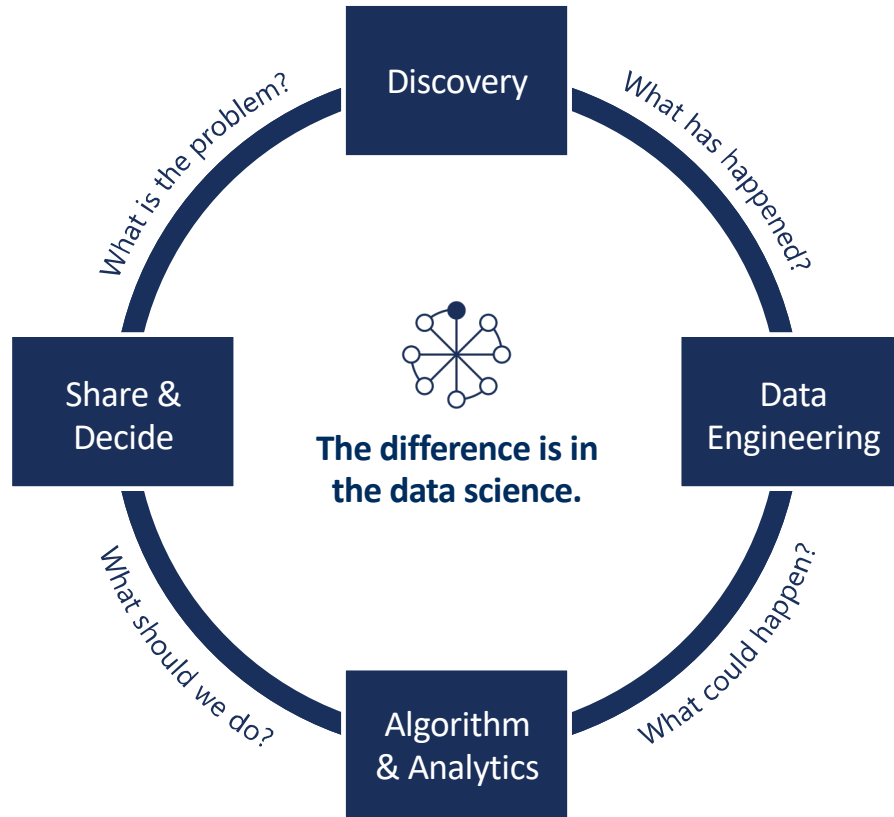


S.No	RWD Sources	RWD Access Examples
1	Patient registries	The European Cystic Fibrosis Society registry - www.ecfs.eu/ecfspr
2	Healthcare Databases including EHR	TRANSFoRm project bitly.com/TheTransformProject
3	Patient Powered Research Networks	Patients Like me patientslikeme.com
4	Social media	Twitter, Facebook, etc.
5	Regulatory agency maintained databases	FAERS
6	Data networks	ORIEN
7	Pharmacy and Health Insurance databases	FDA's Sentinel Initiative sentinelinitiative.org

- Twitter example:
 - Try Searching for "Humira"
 - What tweets do you think are Adverse Events
 - Sentiment Analysis
 - bitly.com/TwitterRWD
- Additional Data Sources:
 - Wearables like Apple Watches, Fitbits etc. --> bitly.com/JJWatchAFib
 - FDA's MyStudies App - bitly.com/FDAMyStudiesApp
 - Location data, voice assistants like Alexa, Google, etc.
 - National Healthcare Databases and Accessibility --> bitly.com/RWDSources



- Sentinel, PCORnet, OHDSI, OMAP, I2B2 etc.
- Multiple data sources in different standards, purposes, devices and platforms
- Needed - a common platform enabling developers to integrate data faster than previously possible
- Industry, standards and service working groups working towards solutions
 - PHUSE has dedicated a working group toward Investigating the use of Fast Health Interoperability Resources (FHIR) in Clinical Research
 - CDISC 360 Project is a good example of facilitating automation with linked data.
 - MedDRA MSSO experience from the collaboration with the FDA may increase the ability to reach out and build semantic relations with other data models and sources of RWD.



Discovery: Identify where we can leverage data for making better business decisions, define goals and objectives of the analytic approach.

Data Engineering: Gather data requirements, collect and build understanding of the data, clean and prepare data for analysis.

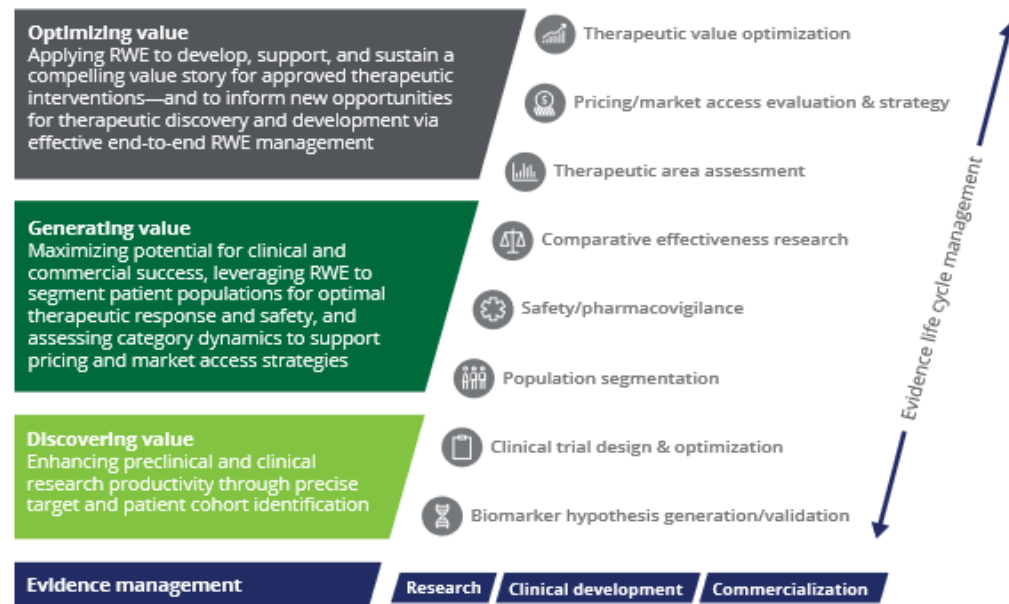
Algorithms & Analytics: Analyze/refine the cleaned data to develop the model and analytics that pertain to the business problems.

Share & Decide: Share valuable results and develop actionable insights with stakeholders, get feedback and repeat methodology as necessary.

- Consider an end-to-end holistic approach
 - Increase therapeutic effectiveness
 - Special populations
 - Fulfill post-marketing requirements
 - Enhance the label
 - Market strategy

Figure 3. End-to-end evidence management approach

Pharma companies can maximize the value of their data by using it for decision-making at an enterprise level (vs. traditional siloed approaches)



Source: Deloitte analysis.

Deloitte Insights | deloitte.com/insights

PHUSE/FDA Data Science Innovation Challenge

- Opioid Substance Use Disorder
 - Facilitate effective intervention for prevention and treatment of opioid/substance use disorder by harnessing social media data.
- Drug Safety Surveillance
 - Define an ideal process for surveillance of multiple data sources that would be useful in the development of a pharmacovigilance tool.
- Approach for Predicting Drug Interactions
 - Overcome the limitations of traditional methods for mining post-market data sources or observational healthcare data to better predict drug interactions.
- <https://innovation.phuse.eu/>



THANK YOU!

Email churley@mmsholdings.com with any additional questions



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