Interpreting and Conducting Practice-Based Research: An Overview of Real-World Evidence

June 29, 2021

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Webinar Agenda and Faculty

- Overview of Real-World Evidence (RWE)
- Conducting Real-World Studies
- Payer Use of RWE
- RWE and the Managed Care Pharmacy Research Agenda
- Q&A

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COLLEGE OF PHARMACY UNIVERSITY OF UTAH

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Overview of Real-World Evidence (RWE)

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Real-World Data (RWD)

- Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources
- Example sources:
  - claims and billing data
  - electronic health record (EHR)
  - clinical registries
  - digital health data

Real-World Evidence (RWE)

- The clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD
- Example study designs:
  - case control
  - retrospective cohort
  - prospective cohort
  - pragmatic trials

Sherman RE, et al. Real-world evidence – what is it and what can it tell us? NEJM. 2016;375:2293-97. (All authors employed by the FDA)
Real World Evidence (RWE) Navigator EU. https://rwe-navigator.eu/

Spectrum of RWD in Clinical Studies

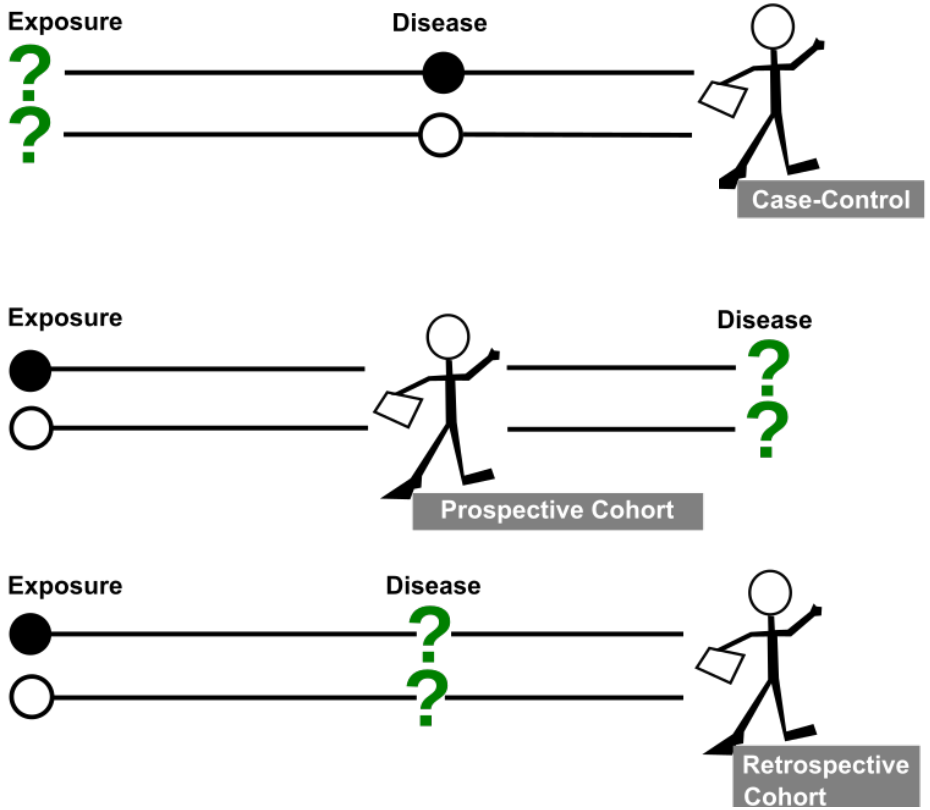
	Interventional, Randomized	Interventional, Non-randomized	Non-interventional, Non-randomized
Study design	Randomized controlled trials	Single-arm trial with historical control	Retrospective or prospective observational studies
Use of RWD	• Assess trial feasibility • Identify trial sites • Support secondary endpoints	• Identify historical control group • Data used to support clinical evaluation	• RWD used to generate RWE in cohort, case control and pragmatic studies

BLINCYTO (blinatumomab) LUTATHERA Brineura (cerliponase alfa)

Increasing reliance on RWD

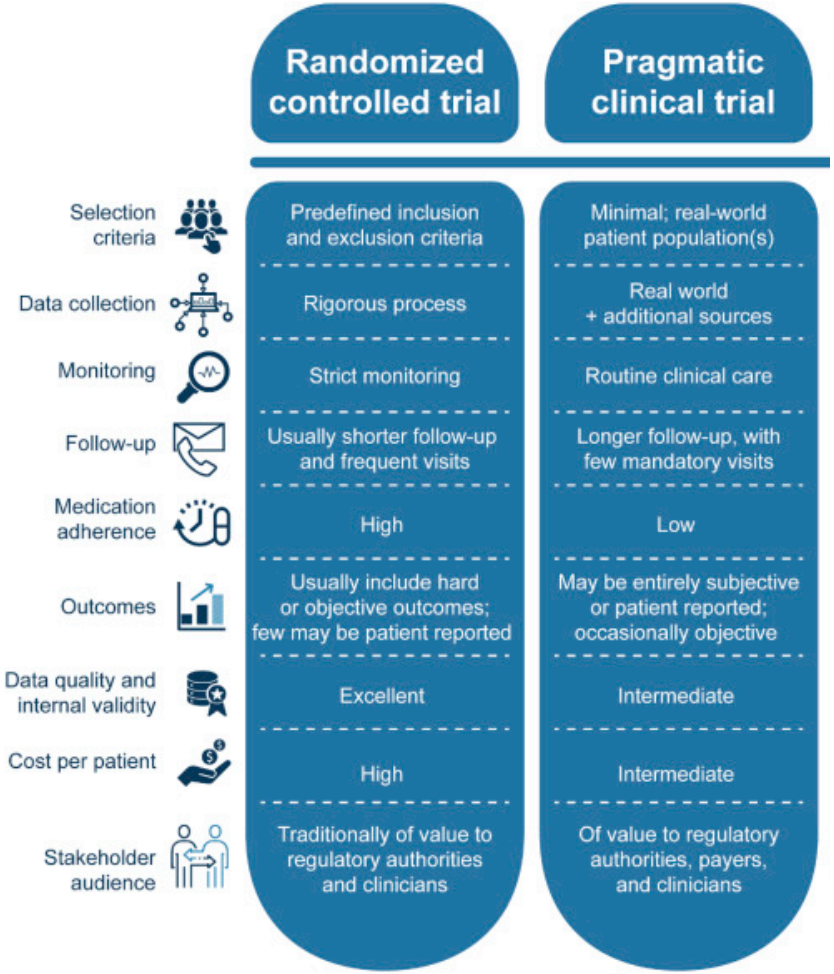
Slide adopted from FDA

Observational Study Designs



Wikipedia

Pragmatic Trial Designs



https://www.sciencedirect.com/science/article/pii/S2590143520300038

Conducting Real-World Studies

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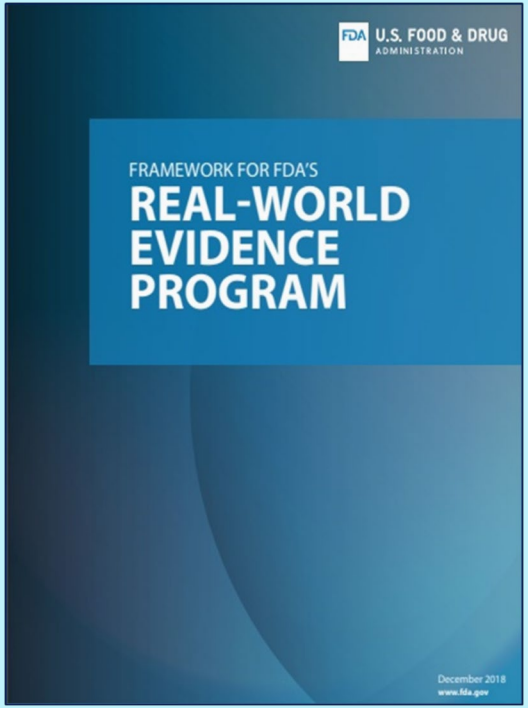
RWE Gaining Prominence Among Regulatory, Policy, Provider and Payer Decision Makers



21ST CENTURY CURES ACT:

An Act to accelerate the discovery, development, and delivery of 21st century cures, ...

Signed into law on December 13, 2016

Provisions for sNDA allowing companies to provide ... "real world evidence" such as observational studies, insurance claims data, patient input, and anecdotal data ... ,

https://www.pri.org/stories/2016-12-15/americas-new-21st-century-cures-act-will-speed-drug-approvals-good-thing

International Journal of Technology Assessment in Health Care, 31:1/2 (2015), 90–98.

doi:10.1017/S0266462315000203

PAYER PERSPECTIVES ON FUTURE ACCEPTABILITY OF COMPARATIVE EFFECTIVENESS AND RELATIVE EFFECTIVENESS RESEARCH

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Penny Mohr
Patient-Centered Outcomes Research Institute

Emma Howe, Koonal Shah, Martina Garau, Adrian Towse
Office of Health Economics

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Real-World Evidence — What Is It and What Can It Tell Us?

Rachel E. Sherman, M.D., M.P.H., Steven A. Anderson, Ph.D., M.P.P., Gerald J. Dal Pan, M.D., M.H.S., Gerry W. Gray, Ph.D., Thomas Gross, M.D., M.P.H.,

RWE and Efficacy/Effectiveness Measures

Example: Multiple Sclerosis (MS)

Efficacy Measures

- ✓Expanded Disability Status Scale (EDSS)
- ✓MRI activity
- ✓Number of relapses

Effectiveness Measures

- ✓Reduction in mortality
- ✓Number of symptom-free days
- ✓Patient quality of life (QoL)
- ✓Absenteeism and productivity

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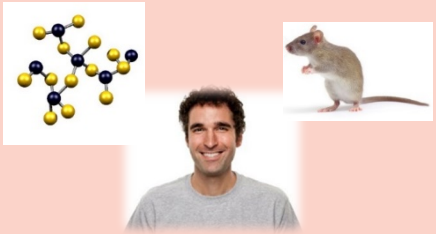
Experimental vs. Observational

Experimental



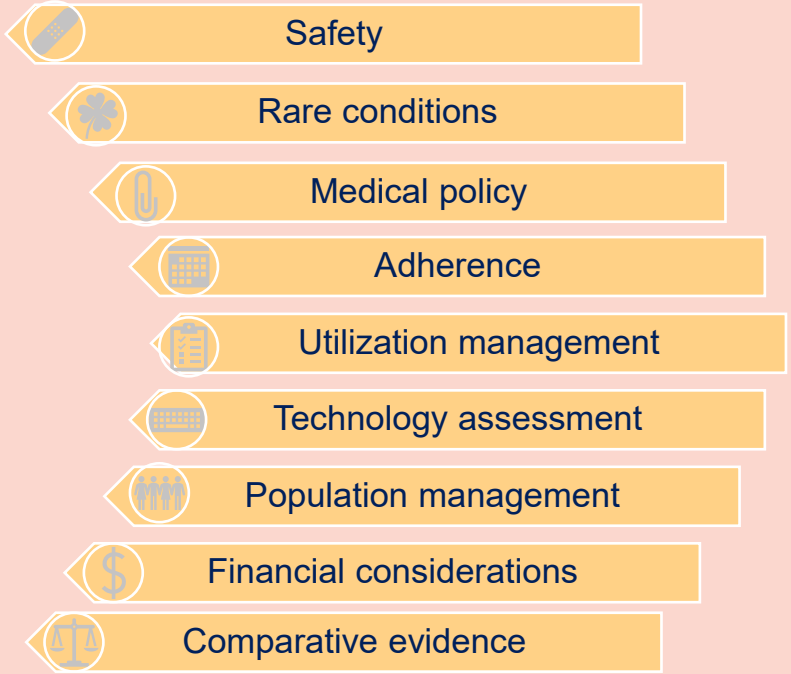
- Efficacy: “Can it work?”
- Causation
- Randomization
- Low generalizability

Observational

- Effectiveness: “Does it work?”
- Correlation
- Non-randomized (self-selected)
- High generalizability

RWE Applications

RWE can be useful for many activities:



Malone, et al. *Value in Health*; 2018; 21(4):389-399

Limitations of RWE

- RWE is subject to numerous biases:
  - Bias is prejudice in favor of or against one thing, person, or group compared with another, usually in a way considered to be unfair.
    - Selection bias (where patient groups are not comparable)
    - Performance bias (where patients are exposed to different interventions)
    - Exclusion bias (when patients are lost to follow-up because of sickness)
    - Detection bias (where patients are assessed at different points in time)
- Confounding
  - Confounding is when the measured association between an exposure and disease occurrence is distorted by an imbalance between exposed and non-exposed persons with regard to one or more risk factors for the disease
- Observational studies potentially have high external validity and low internal validity
  - Reduction of bias can enhance internal validity

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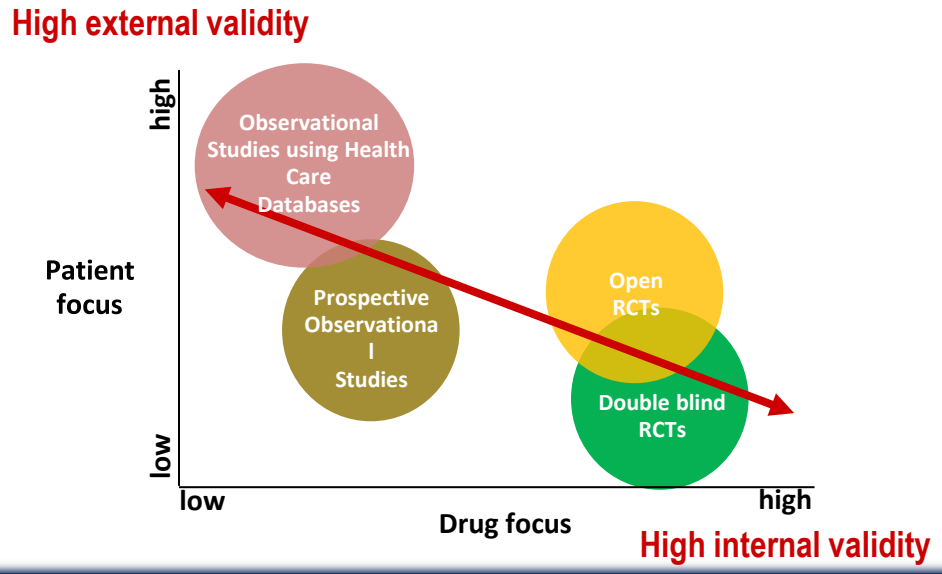
Am J Manag Care. 2010;16(6):467-471

Trade-Off Between Internal and External Validity



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Sources of Real-World Evidence

Healthcare Databases

Systems into which healthcare providers enter routine clinical and laboratory data during usual clinical practice

- Typically electronic health records (EHRs)
- Document the care that was provided to a patient

Administrative Claims Databases

Medical and pharmacy claims systems

- Document the care that was paid for by a payer

The ideal source would be an EHR that is linked to a claims database, with PRO data, biomarker test results and data on mortality and health care disparities!

https://rwe-navigator.eu/use-real-world-evidence/sources-of-real-world-data/patient-powered-research-networks/

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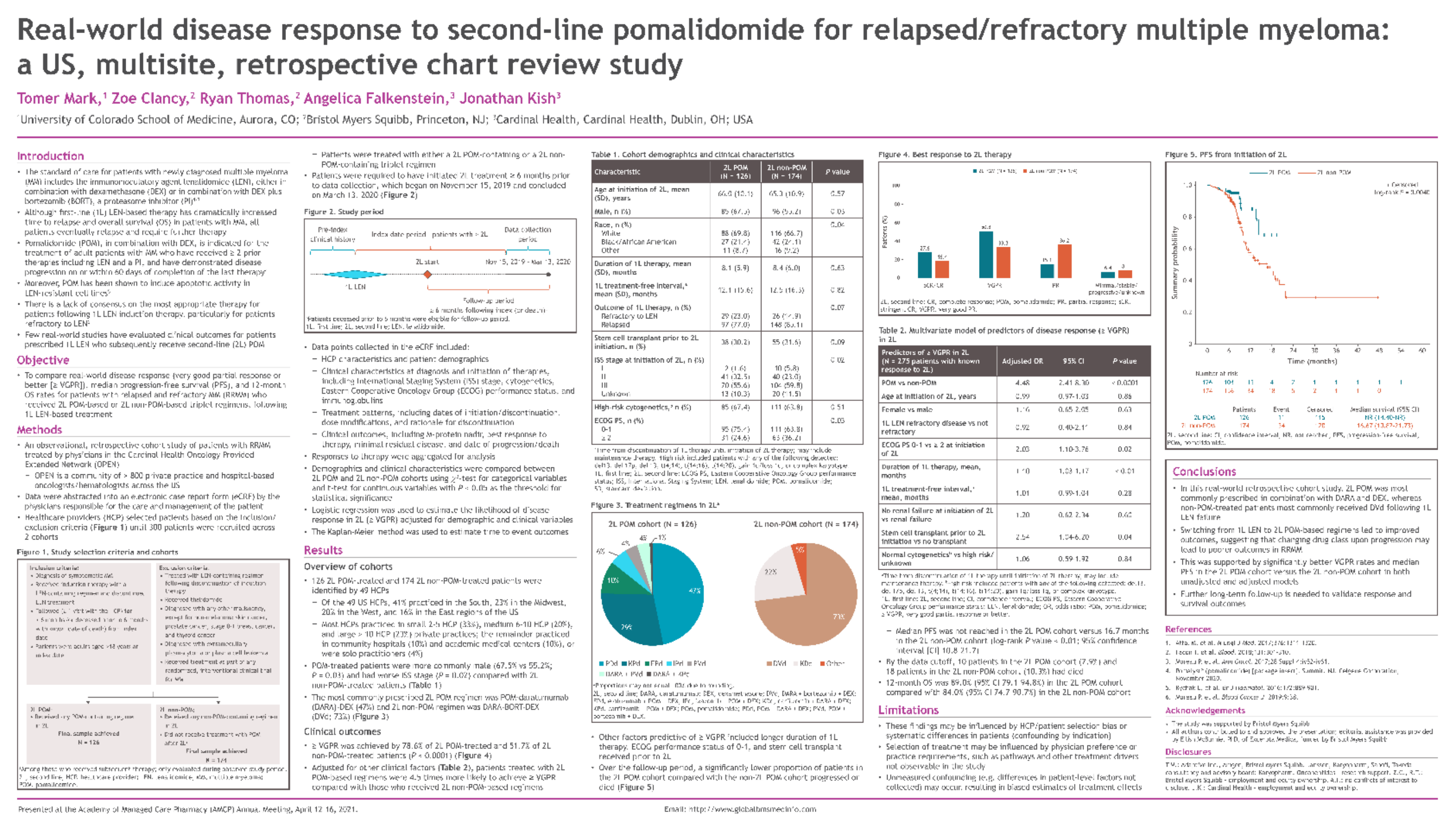
Sample Study

Retrospective Analysis of Clinical Outcomes

Real-world disease response to second-line pomalidomide for relapsed/refractory multiple myeloma: A US, multisite, retrospective chart review study

Tomer Mark, Zoe Clancy, Ryan Thomas, Angelica Falkenstein, Jonathan Kish



Poster presented at AMCP 2021: April 12-16, 2021; Virtual.

Sources of Real-World Evidence (cont.)

Patient Registries

Organized systems to prospectively collect, analyze and disseminate observational data on a group of patients with specific characteristics

- Cystic Fibrosis Foundation Patient Registry (https://www.cff.org/Research/Researcher-Resources/Patient-Registry/)
- Upper Limb International Spasticity (ULIS-III) prospective longitudinal cohort study (https://bmjopen.bmj.com/content/3/3/e002230)

Patient-Powered Research Networks (PPRNs)

Online platforms by patients, advocacy groups or others (caregivers, clinicians or researchers)

Goal is to conduct outcomes research that matters to patient to impact development of new therapeutic interventions

- PCORnet (https://pcornet.org)

Social Media

Internet platform for patients to share information

- Find info about their condition, discuss their experience (with disease or treatments) and find social support
- Adverse effects, treatment adherence and discontinuation and QoL

https://rwe-navigator.eu/use-real-world-evidence/sources-of-real-world-data/patient-powered-research-networks/

Real-World Study Designs and Data Sources Summary

- There are many sources of data for observational research – the key is to match the right data to the right question.

- The limitations of real-world data require adjustments to methodology.
  - Choosing the appropriate study design
  - Considering confounding and the appropriate methods to address it
  - Considering the influences of various types of biases and how to control for them.

Am J Manag Care. 2010;16(6):467-471

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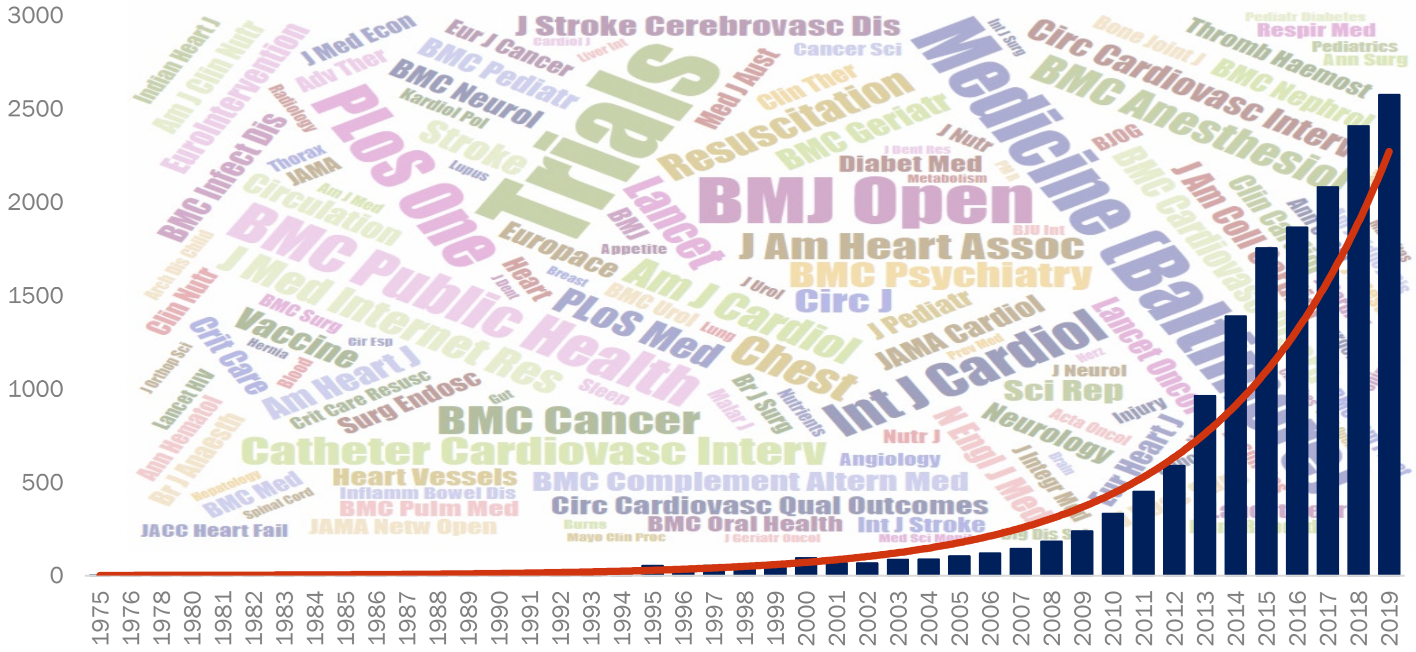
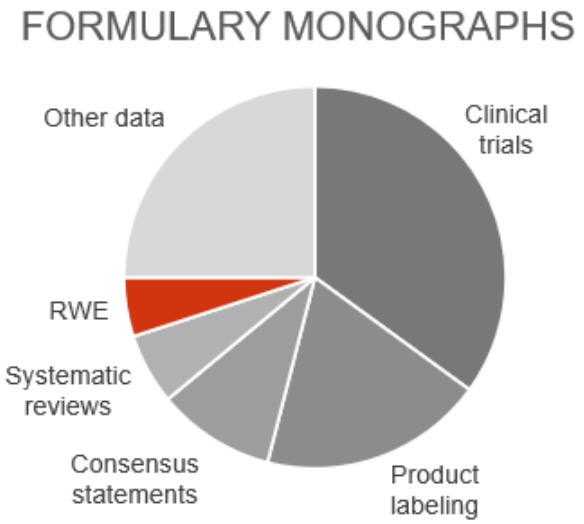
Payer Use of RWE

Growth in RWE Publications



Search query: ((((("Health claims"[Title/Abstract]) or ("real-world evidence"[Title/Abstract])) OR ("registry"[Title/Abstract])) OR ("electronic medical records"[Title/Abstract])) OR ("cost-effectiveness analysis"[Title/Abstract])) AND ("clinical study"[Publication Type] OR "observational study"[Publication Type])

RWE Use by Payers



Beyond formulary decisions…
Safety programs
Value Assessment

Quality measurement
Clinical programs
Utilization management
Outcomes-based contracts

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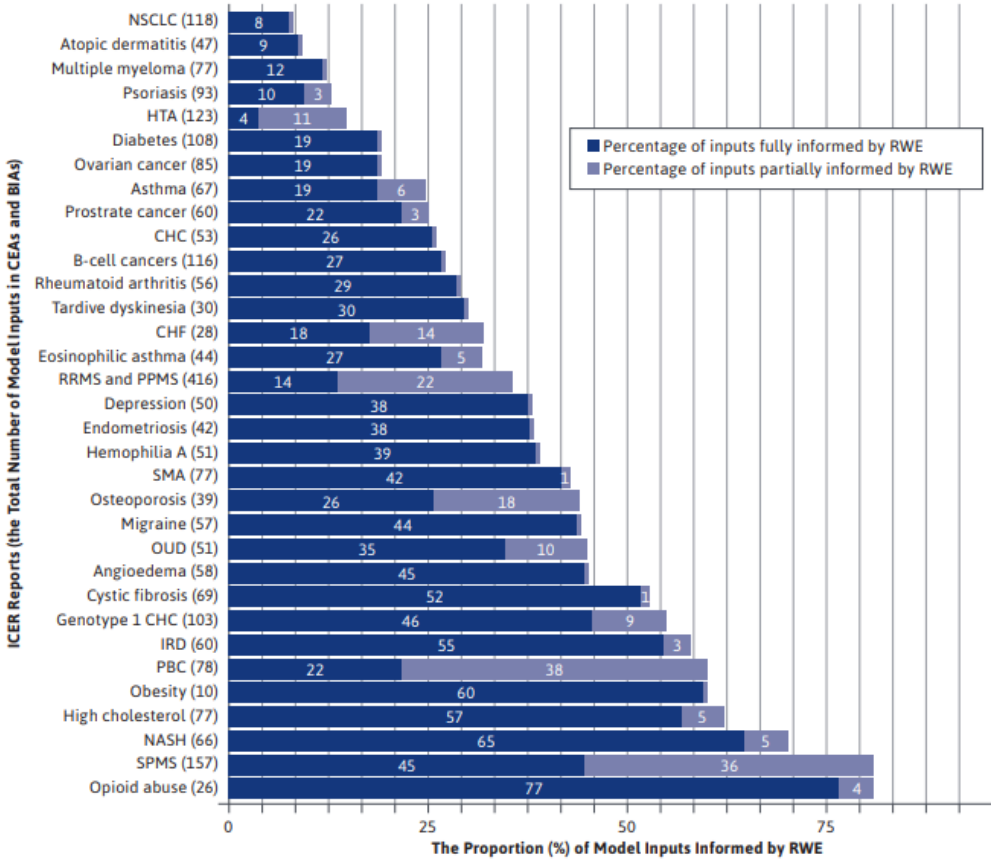
FIGURE 2 The Number of Model Inputs and Proportion Informed by RWE



https://www.jmcp.org/doi/pdf/10.18553/jmcp.2017.16368
Lee W, Dayer V, Jiao B, Carlson JJ, Devine B, Veenstra DL. Use of real-world evidence in economic assessments of pharmaceuticals in the United States. *J Manag Care Spec Pharm*. 2021;27(1):5-4.

Sample Study

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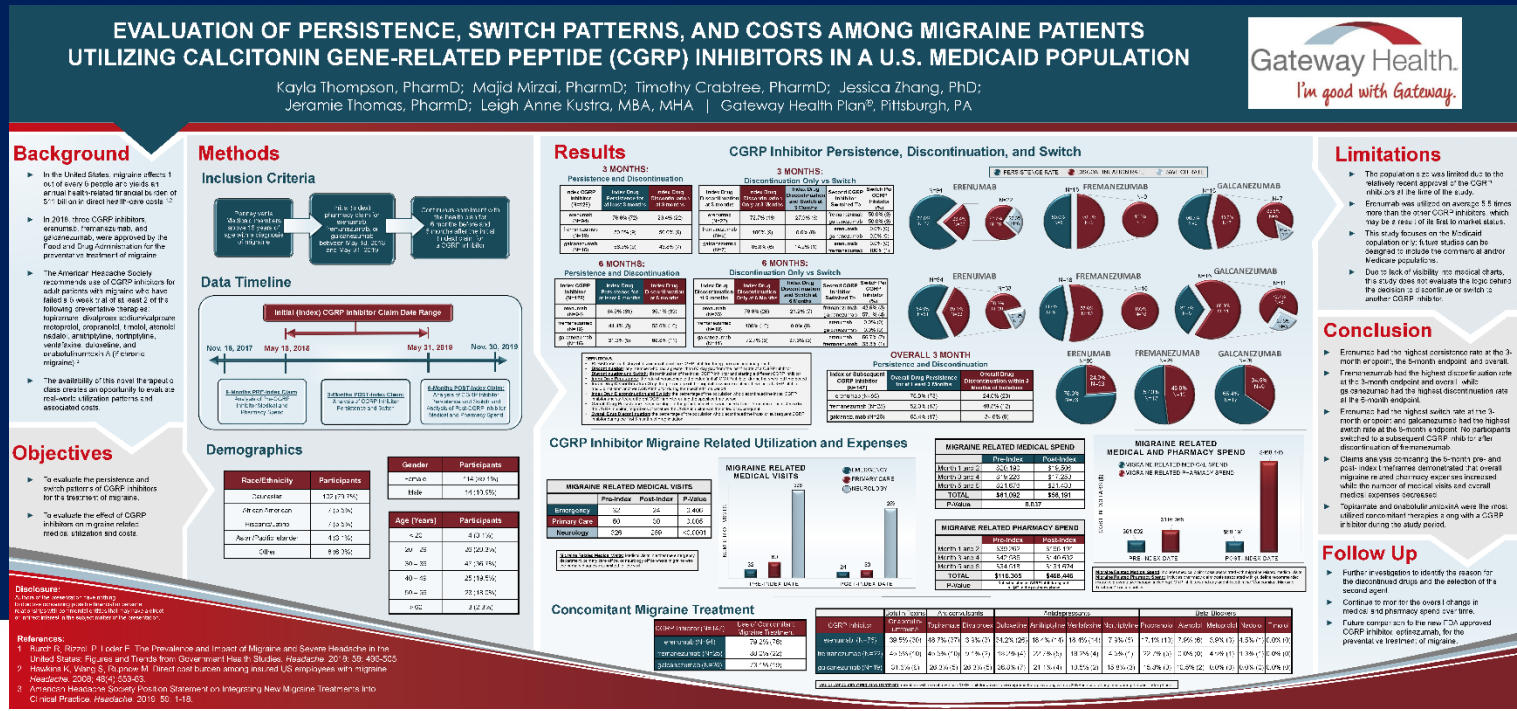
Retrospective Analysis of Claims Data
Conducted by PGY1 Resident

Evaluation of persistence, switch patterns, and costs among migraine patients utilizing calcitonin gene-related peptide (CGRP) inhibitors in a U.S. Medicaid population

Kayla Thompson, PharmD; Majid Mirzai, PharmD; Timothy Crabtree, PharmD; Jessica Zhang, PhD; Jeramie Thomas, PharmD; Leigh Anne Kustra, MBA, MHA



Poster presented at AMCP eLearning Days; April 20-24, 2020; Virtual.

RWE and the Managed Care Pharmacy Research Agenda

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The Future of Real-World Evidence

- RWE is becoming more widely accepted by providers and payers in patient care and decision making.

- Regulatory agencies are increasingly considering the use of RWE in approval and in validation of efficacy, effectiveness, and safety of NMEs.

- Follow-up studies are increasingly being used to:
  - Confirm RCT data from approval
  - Confirm reimbursement decisions
  - Validate patient outcomes

- Real-world evidence is a **STRATEGIC INITIATIVE** in drug development and life-cycle management.

Managed Care Pharmacy Agenda

PILLARS →

PRIORITIES ↓

Real-world evidence to inform managed care pharmacy decision-making	Value-based models in managed care pharmacy to address total cost of care	Impact of benefit design or utilization management strategies on patient outcomes	Impact of direct patient care services provided by managed care pharmacy on patient outcomes
Drugs approved in expedited manner by FDA as they typically have very limited clinical or economic evidence at time of launch	Opportunities for outcomes-based contracting	Drugs or clinical care services whose price and/or expected use would have a significant impact on managed care pharmacy budget	Managed care pharmacy programs focused on patient care in response to COVID-19
Disparities in designing and delivering health care through managed care pharmacy while considering DEI as well as SDoH	Impact of legislative activities and policies	Impact of legislative activities and policies	MTM and impact on clinical outcomes across various patient demographics
Disease states where there are limited or outdated clinical guidelines			Impact of legislative activities and policies
Impact of legislative activities and policies			

Yellow = New Priority Established 2020-21

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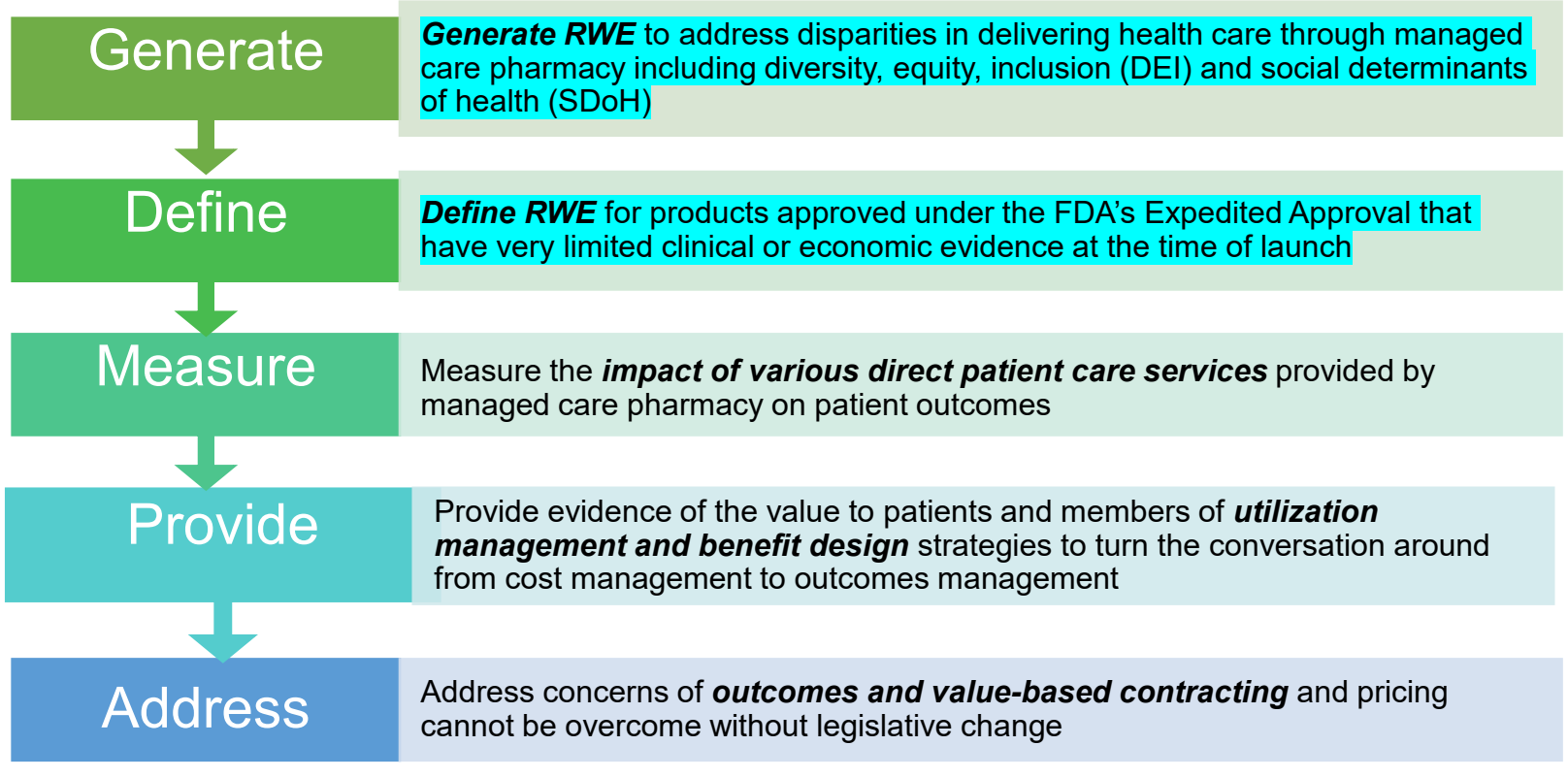
RWE in Research Agenda



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Future Directions for Our Research Agenda

Images:
KOTESOL
The Intrepid Catalyst

JMCP AMCP
BBCIC Biologics & Biosimilars Collective Intelligence Consortium
AMCP Foundation

Speaker Q&A

Diana Brixner

Laura Happe

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Additional References

References Noted on Slides

Additional Background

- "A Primer for Managed Care Residents: How to Conduct Research Using Live Medical and Pharmacy Claims Data." J Manag Care Spec Pharm, 2019 May;25(5):538-543.
- "Concept Series: What Is Outcomes Research?" AMCP, 2019 Jul.
- "Top Evidentiary Gaps in Managed Care Pharmacy: A Research Agenda." J Manag Care Spec Pharm, 2020 Apr;26(4):375-381.
- "Advancing the Managed Care Pharmacy Research Agenda via Mapping of Research Pillars and Priorities." Poster presented at: AMCP 2021; April 12-16, 2021; Virtual.

Sample Studies

- "Real-world disease response to second-line pomalidomide for relapsed/refractory multiple myeloma: A US, multisite, retrospective chart review study." Poster presented at AMCP 2021; April 12-16, 2021; Virtual.
- "Evaluation of persistence, switch patterns, and costs among migraine patients utilizing calcitonin gene-related peptide (CGRP) inhibitors in a U.S. Medicaid population." Poster presented at AMCP eLearning Days; April 20-24, 2020; Virtual.

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Acknowledgments

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