A Framework to Assess the Quality of RWE

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Disclosure

• The expressed views in this presentation do not represent the views of the organizations I am affiliated with
Contents

• Intro RWE
• Quality of RWE design
• Quality of RWE data
• Quality of RWE methods
• Quality of RWE reporting
Randomized Controlled Trials (RCT) = Gold Standard

Yetley et al. (2016). Am J Clin Nutr:105(1)
But....RCTs are

• Labor intensive
• “Relatively” expensive
• “Limited” follow-up time
• Sometimes “impossible”
• “Limited” generalizability

Yetley et al. (2016). Am J Clin Nutr:105(1)
Real-world data (RWD) & Real-world evidence (RWE)

“Real world data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.”

“Real world evidence (RWE) is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.”

Why use RWE?

- Greater external validity -> generalizable
- Longer follow up times
- Relatively inexpensive

Yetley et al. (2016). Am J Clin Nutr:105(1)

1. Framework for FDA’s Real-World Evidence Program. Dec 2018
The use of RWE

When to use RWE?¹,²

- Determine the efficacy/safety of new drugs

“…potential for patient harm if therapies are adopted solely on the basis of analyses of RWD.”¹

- Determine effectiveness when prior RCTs have shown a lack of efficacy

Source: Gavura, S (2019, November). *Getting Real about RWE*. Presentation at Canadian Association for Population Therapeutics. Toronto, ON
Agenda

- Intro RWE
- **Quality of RWE design**
  - Quality of RWE data
  - Quality of RWE methods
  - Quality of RWE reporting
Design! Design! Design!

**What is the research question? Who is the user?**
Research Design: Defined a priori, Transparent

**Population**
- Population-based vs selected sample?
- Sample size?
- Disease of interest?
- Patient of interest?
- What is the accrual or observational window?

**Intervention**
- Exposure of interest?
- How is it defined?

**Comparison**
- Comparative vs single-arm?
- Historical vs contemporaneous?

**Outcome**
- Effectiveness?
- Safety?
- Cost-effectiveness?
- Resource utilization?
- Patient-reported outcomes?
Quality of Design

• Established a priori, agreed upon study design/protocol is critical to the success of generating RWE

• In 2019, Health Canada outlined overarching principles for generating RWE and highlighted the following guidelines for protocol development\(^1\)
  
  - European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Protocol Checklist\(^2\)
  
  - Guidelines for Good Pharmacoepidemiology Practices (GPP) from the International Society for Pharmacoepidemiology\(^3\)

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Agenda

• Intro RWE
• Quality of RWE design
• **Quality of RWE data**
• Quality of RWE methods
• Quality of RWE reporting
Data gaps? What data are we looking for?

**Population**
- Patient characteristics
  - Age
  - Sex
  - Income quintile
  - Rural/urban residence
- Disease characteristics
  - Clinical
  - Pathological/Lab
- Treatments:
  - Prior treatments
  - Subsequent treatments

**Intervention**
- Exposure
  - Date of treatment
  - Dosage
  - Treatment duration
  - Line setting (if applicable)

**Comparison**
- Controls
  - Date of treatment
  - Dosage
  - Treatment duration
  - Line setting (if applicable)

**Outcome**
- Effectiveness
  - Date of death
  - Censoring date
  - Patient-Reported Outcomes
- Safety
  - Hospitalization visits
  - Emergency department visits
- Cost-effectiveness
  - Cost of drug
  - Resource utilization
  - Incremental cost-effectiveness estimates
It’s Complicated
Life is complicated – finding a therapist shouldn’t be.

https://www.complicated.life/find-a-therapist
Examples:
Datasets (ON)

- ADP
- CIHI-DAD
- CIHI-OMHRS
- OCR
- ALR
- CIHI-SDS
- CIHI-NACRS
- OHIP
- ODB
- NDFP
- LTC
- CCC
- NRS
Data availability varies between provinces

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- **Data available**
- **Data available with caveat**
- **Data not available**

![CanREValue Logo](image-url)
Quality of Data

• In 2018, Canadian Institute of Health Information (CIHI) and Canadian Partnership Against Cancer (CPAC) developed a pan-Canadian Oncology Drug Data Minimum Data Set.

• CanREValue Collaboration’s Data Working Group is working on developing a data asset catalogue for conducting real-world evaluation of oncology drugs.

1Canadian Institute of Health Information. Pan-Canadian Oncology Drug Data Minimum Data Set; https://secure.cihi.ca/free_products/Oncology-drug-data-MDS-2017-2018_en.pdf Published 2018
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- **Quality of RWE methods**
- Quality of RWE reporting
Generating RWE from RWD

Two steps are required to generate robust RWE from RWD
1. Adjusting for differences between exposure and control groups
2. Statistical analysis to examine associations between exposure and outcome
Control group?

RWE -> no randomization; but what if exposure differ from controls?

- Example 1: Contemporaneous control
  - Confounding by indication
  - Selection bias
- Example 2: Historical Controls
  - Secular trends
  - Differences in clinical practice

Pre-Policy / Historical Period

Post-Policy / Contemporaneous Period

Bevacizumab Treated

Contemporaneous Control

Bevacizumab funding date
ON: July 2008

2000

2016
Potential statistical methods

- Propensity score related analysis
  - Propensity score matching
  - Inverse probability treatment weighting
- Stratification/multivariable-based regression
- Instrumental variable

NICE Decision Support Unit (DSU) has published a report and an algorithm of the selection of methods for comparative individual patient data

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Sensitivity analysis

Sometimes sensitivity analysis might be required depending on context:

- Missing data
  - Conduct multiple imputation

- Certain data is not available
  - When confidential price is not available, incremental cost-effectiveness ratio can be generated with different percentages off the listing price

- Time-varying subsequent treatments
  - When patients move onto another line of treatment
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- **Quality of RWE reporting**
What are reporting guidelines?

- Groups of clinicians, academics, systematic reviewers, and statisticians have come together to define the **minimum set of information** that each group needs to be able to use a particular kind of study¹

- “The resulting manuscripts can be understood, replicated, and used in decision-making.”¹

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¹ Equator Network. Enhancing the QUALity and Transparency Of health Research. https://www.equator-network.org
Developing RWE reporting standards

• Existing standards for reporting guidelines can be leveraged

• Some examples:
  
  • **STROBE** statement: **STrengthening the Reporting of OBservational studies in Epidemiology**¹
  
  • **RECORD-PE** statement: **REporting of studies Conducted using Observational Routinely collected health Data statement for PharmacoEpidemiology**²
  
  • **CHEERS** statement: **Consolidated Health Economic Evaluation Reporting Standards**³

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Summary

• A framework to assess the quality of RWE should consider:
  • **Quality of design:** A priori, well-established, agreed upon study design/protocol is critical to the success of generating RWE
  • **Quality of data:** Quality standards for collecting, maintaining, and reporting real-world data is needed
  • **Quality of methods:** Appropriate methods and sensitivity analyses are required when conducting the analysis
  • **Quality of reporting:** Standardized reporting is important to ensure RWE can be implemented by relevant stakeholders
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Questions?

Thank you!

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Link to register:
https://www.eventbrite.ca/e/canrevalue-stakeholder-engagement-webinar-registration-75742456727