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

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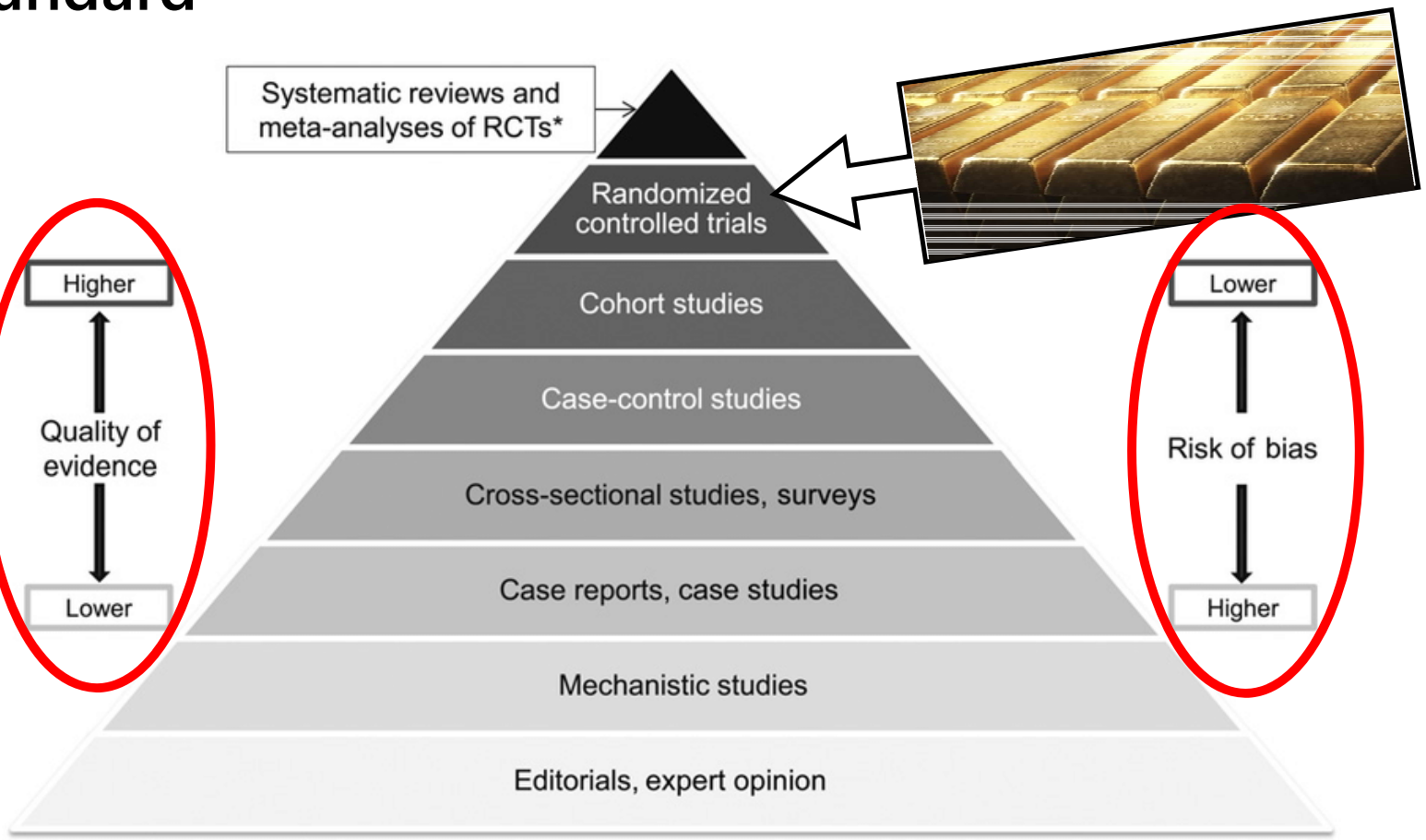
Contents

- **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

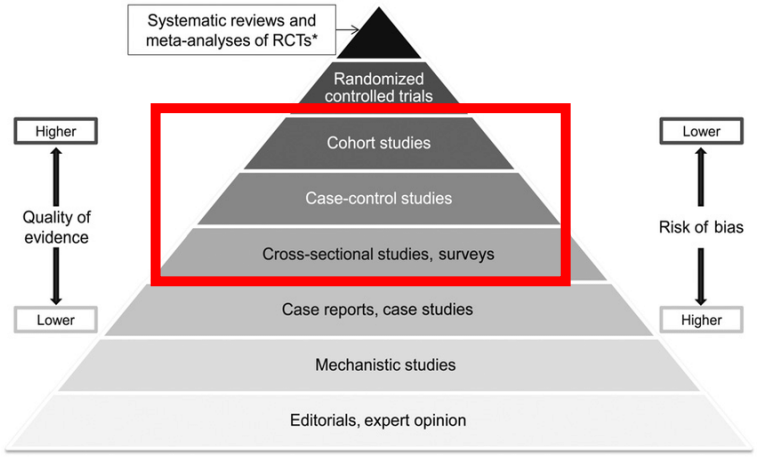
- Labor intensive
- “Relatively” expensive
- “Limited” follow-up time
- Sometimes “impossible”
- “Limited” generalizability

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."[1]

"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."[1]



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

Why use RWE?

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

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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]

[1]Karim S, Booth CM. J Clin Oncol. 2019 May 1;37(13):1047-1050.
[2]Booth CM, Tannock IF. Br J Cancer. 2014 Feb 4;110(3):551-5.

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When to use RWE?[1,2]

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

[1]Karim S, Booth CM. J Clin Oncol. 2019 May 1;37(13):1047-1050.
[2]Booth CM, Tannock IF. Br J Cancer. 2014 Feb 4;110(3):551-5.

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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**
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- 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	Intervention	Comparison	Outcome
Population-based vs selected sample?	Exposure of interest?	Comparative vs single-arm?	Effectiveness?
Sample size?	How is it defined?	Historical vs contemporaneous?	Safety?
Disease of interest?			Cost-effectiveness?
Patient of interest?			Resource utilization?
What is the accrual or observational window?			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]

[1]Health Canada. Elements of Real World Data/Evidence Quality throughout the Prescription Drug Product Life Cycle. https://www.canada.ca/en/services/health/publications/drugs-health-products/real-world-data-evidence-drug-lifecycle-report.html. Published 2019.
[2]The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Standards and Guidances. http://www.encepp.eu/standards_and_guidances/methodologicalGuide.shtml
[3]Epstein, M. (2005). Guidelines for good pharmacoepidemiology practices (GPP). *Pharmacoepidemiology and drug safety*, *14*(8), 589-595.

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Data gaps? What data are we looking for?

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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

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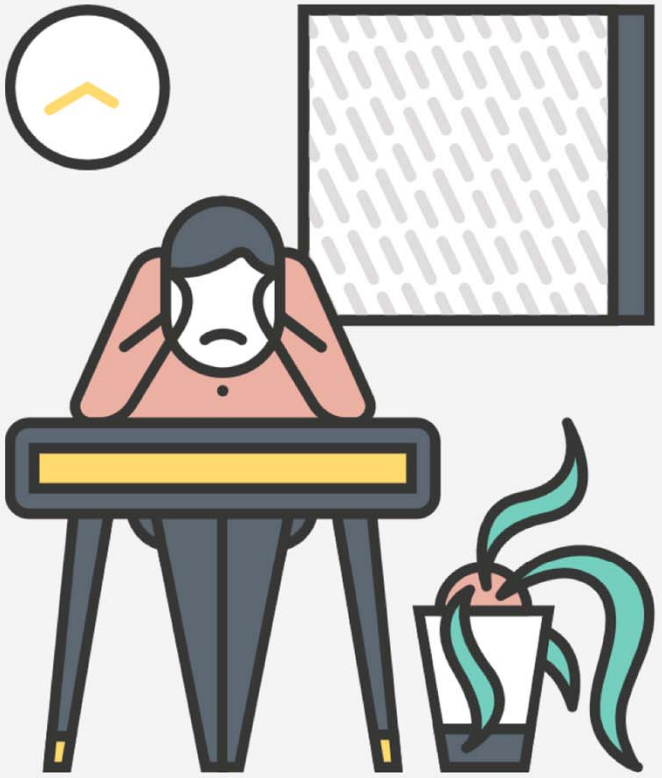
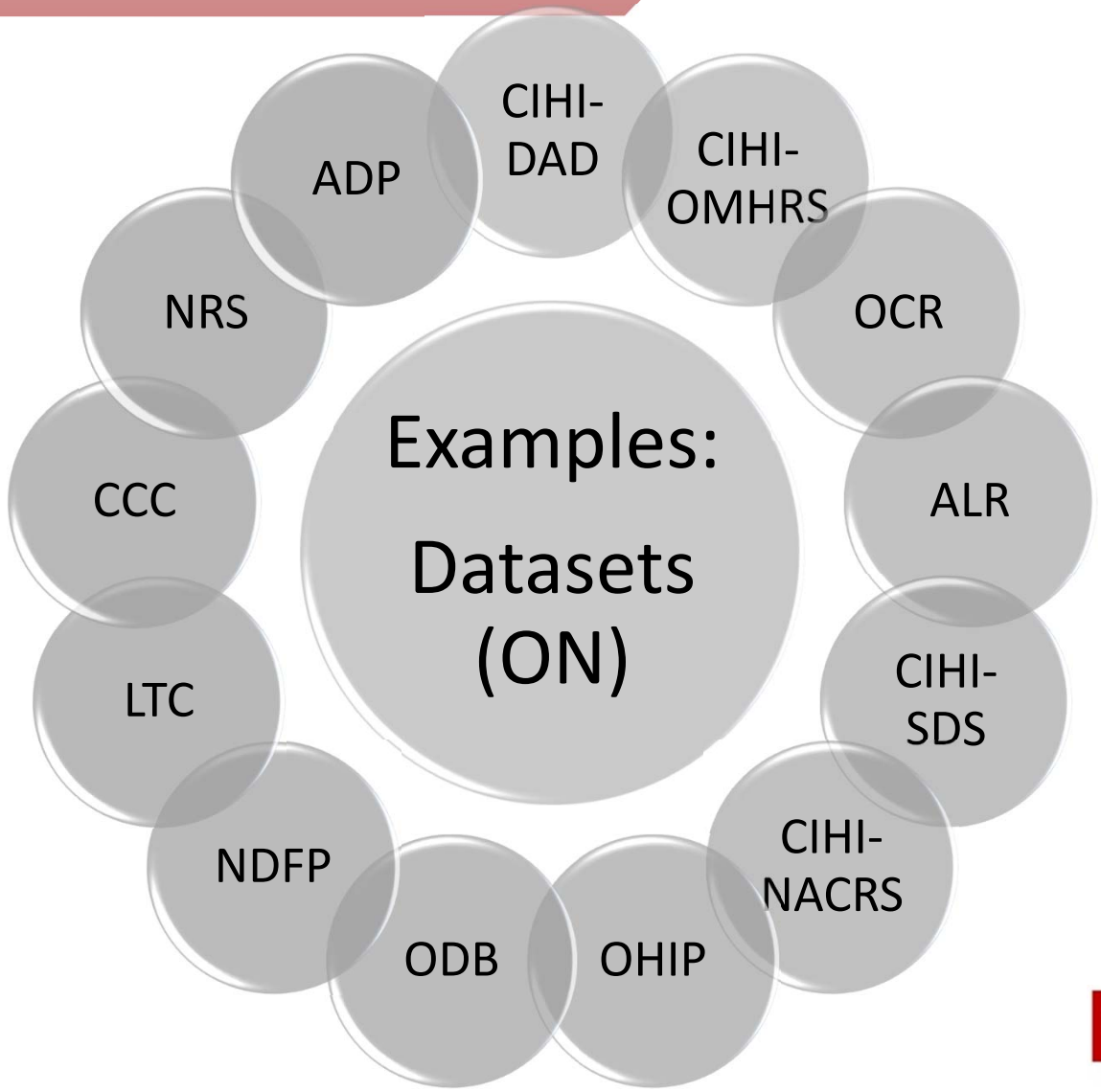
It's Complicated

Life is complicated – finding a therapist shouldn't be.



https://www.complicated.life/find-a-therapist



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Data availability varies between provinces

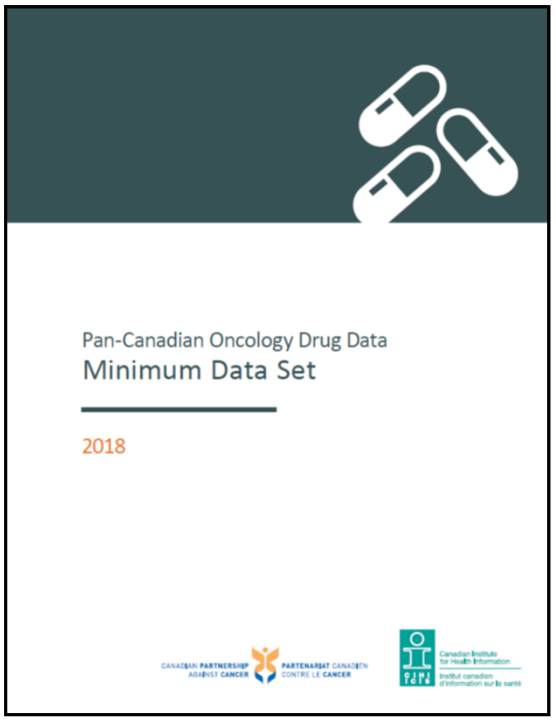
Intravenous Cancer Drug	BC	AB	SK	MB	ON	QB	NB	NS	NL	PEI
Effectiveness (survival)										
Safety & Toxicity										
Budget Impact (payer's perspective)										
Cost-Effectiveness Analysis										
PROs/QOL (e.g. ESAS)										

Oral Cancer Drug	BC	AB	SK	MB	ON	QB	NB	NS	NL	PEI
Effectiveness (survival)										
Safety & Toxicity										
Budget Impact (payer's perspective)										
Cost-Effectiveness Analysis										
PROs/QOL (e.g. ESAS score)										

Data available
Data available with caveat
Data not available

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



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[1]Canadian 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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Generating RWE from RWD

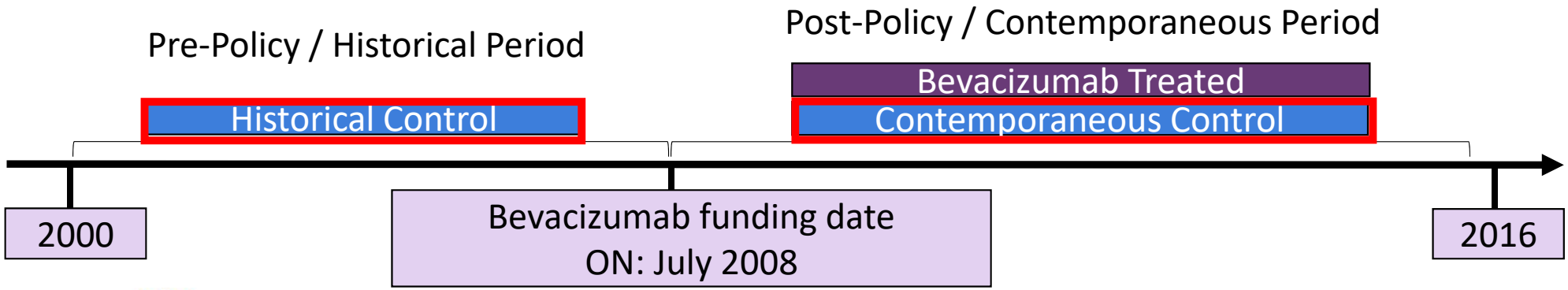
Two steps are required to generate robust RWE from RWD

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



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[1]

[1]Faria, R., Hernandez Alava, M., Manca, A., & Wailoo, A. (2015). NICE DSU technical support document 17: the use of observational data to inform estimates of treatment effectiveness for technology appraisal: methods for comparative individual patient data. *Sheffield: NICE Decision Support Unit*.

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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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 study[1]
- "The resulting manuscripts can be **understood**, **replicated**, and **used in decision-making**."[1]

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]

[1]Knottnerus, A., & Tugwell, P. (2008). STROBE--a checklist to Strengthen the Reporting of Observational Studies in Epidemiology. *Journal of clinical epidemiology*, *61*(4), 323.
[2]Langan, S. M., Schmidt, S. A., Wing, K., Ehrenstein, V., Nicholls, S. G., Filion, K. B., ... & Guttmann, A. (2018). The reporting of studies conducted using observational routinely collected health data statement for pharmacoepidemiology (RECORD-PE). *bmj*, *363*, k3532.
[3]Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., ... & Loder, E. (2013). Consolidated health economic evaluation reporting standards (CHEERS) statement. *Cost Effectiveness and Resource Allocation*, *11*(1), 6.

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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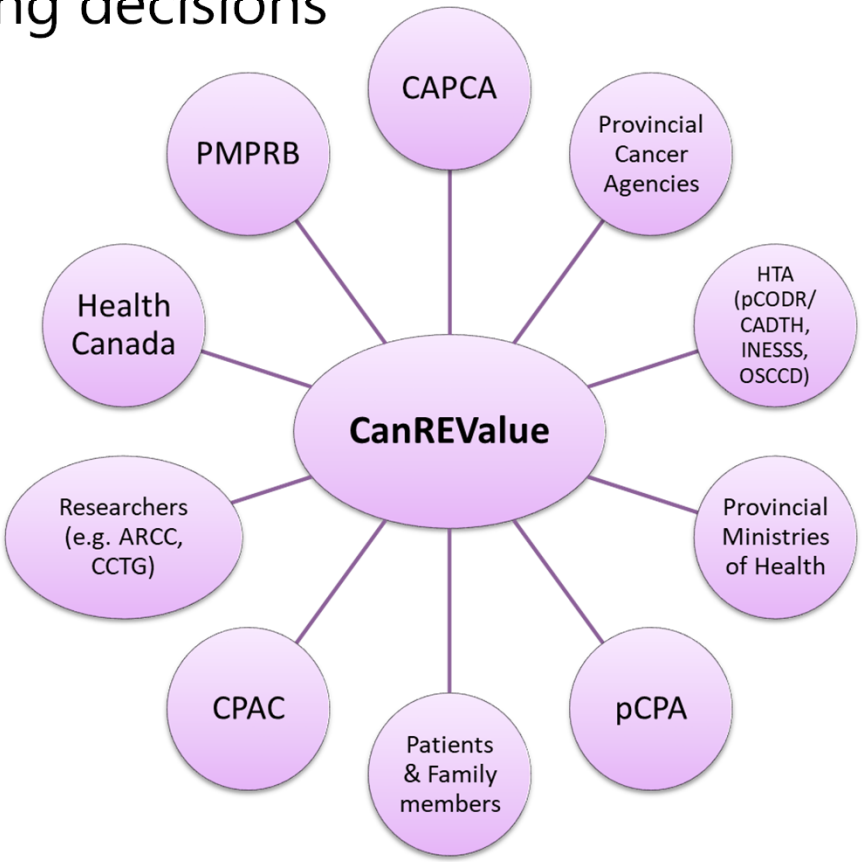
Acknowledgement: CanREValue Collaboration

To develop a framework for the generation and use of RWE to inform cancer drug funding decisions



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Questions?

Thank you!

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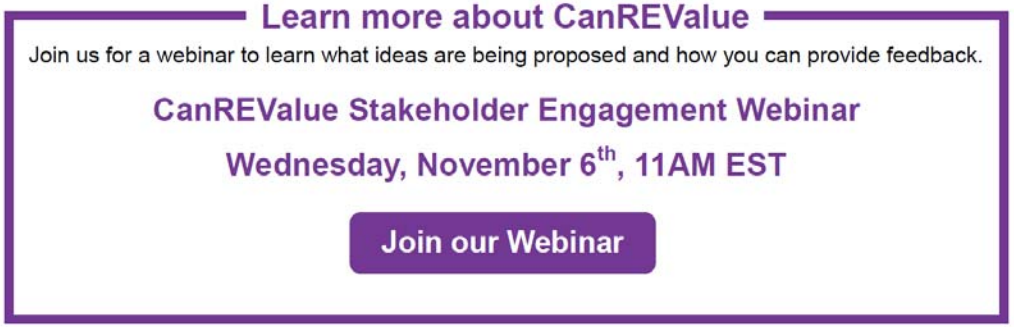

Link to register:
https://www.eventbrite.ca/e/canrevalue-stakeholder-engagement-webinar-registration-75742456727

Developing a framework for the incorporation of real-world evidence into cancer drug funding decisions

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