Real World Evidence – Why and Why Not?

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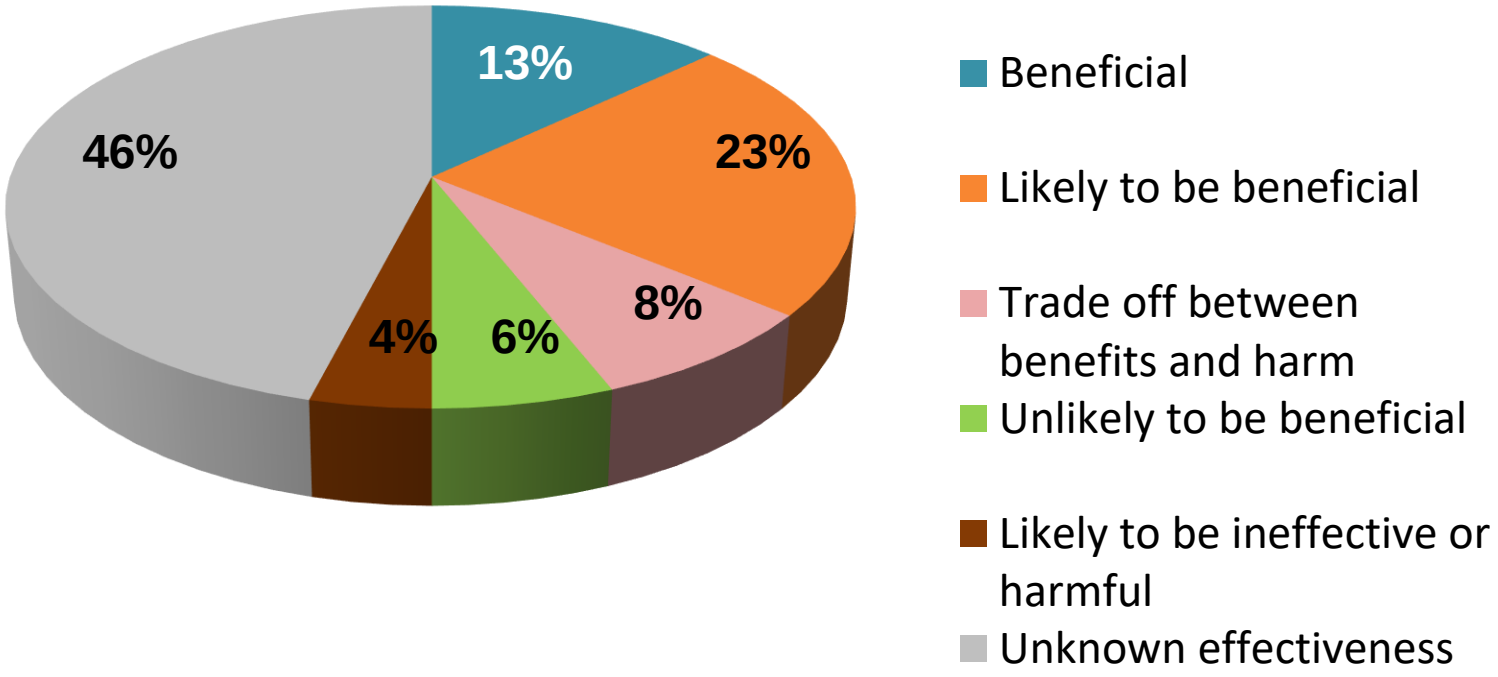
Disclosures

Company name	Honoraria/ expenses	Consulting/ advisory board	Funded research	Royalties/ patent	Stock options	Ownership/ Equity position	Employee	Other (please specify)
BMS	X	X	X					
Pfizer	X	X	X					
Bayer	X	X						
St. Jude Medical	X							
Boehringer-Ingelheim	X							

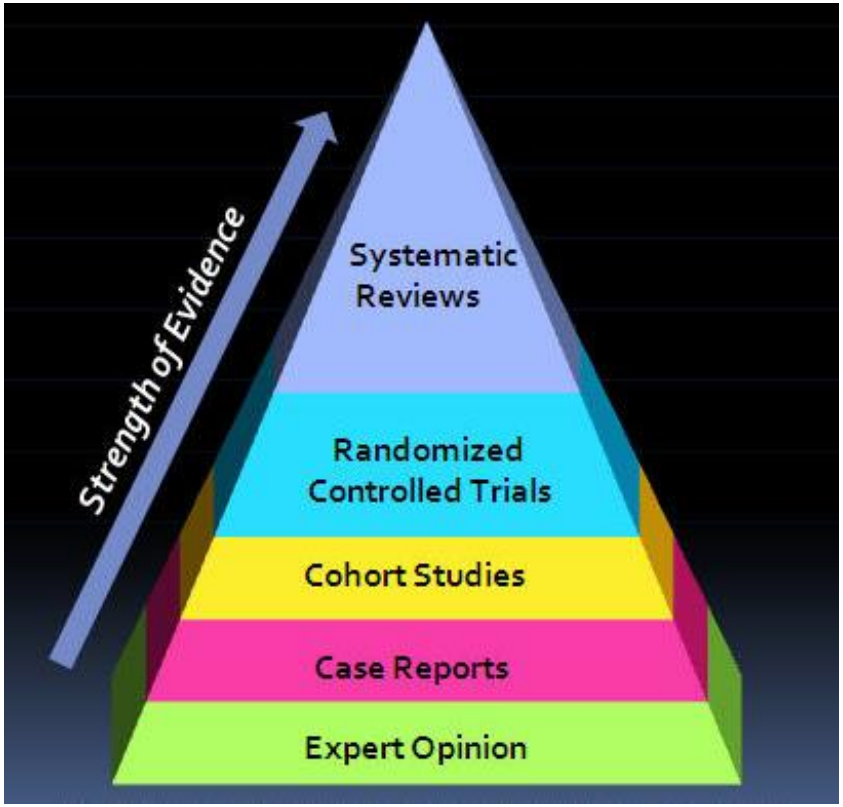
Evidence base of modern health care

Proportion of commonly used treatments supported by good evidence



Redrawn from: Clinical Evidence. http://clinicalevidence.com/ceweb/about/knowledge/jsp.

Hierarchy of evidence

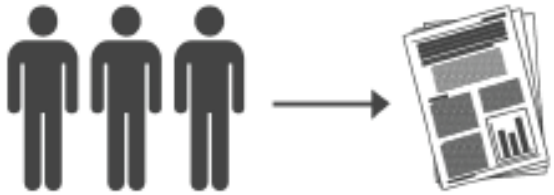


Adapted from: Sacket DL, et al. *Evidence-based medicine: how to practice and teach EBM*. 2nd Edition. Edinburgh: Churchill Livingstone, 2000.

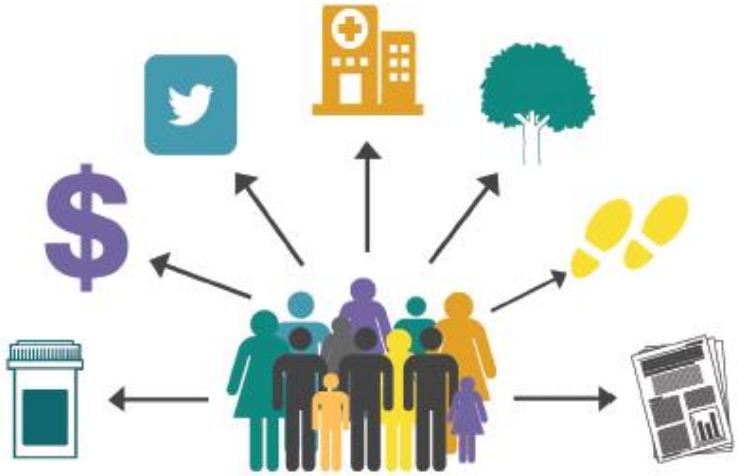
The randomized controlled trial approach

The real-world evidence approach

Traditional versus real-world evidence



RCTs traditionally recruit highly homogenous patients and data collected for the specific study. The data collection is standardized and data closely controlled and monitored.



RWE is characterized by the combination of multiple types of data from heterogenous patient populations, including:

- Claims Data (from insurance reimbursements).
- Clinical Setting Data (e.g., from medical records)
- Pharmacy Data (from filled prescriptions).
- Patient-reported Data (directly from the patient).

The potential of real-world evidence

RWE can inform on:

- Therapeutic development
- Outcomes research
- Patient care
- Research on health care systems
- Quality improvement
- Safety surveillance
- Well-controlled effectiveness studies

Use of RWE has the potential to:

- Enable efficient research, saving time and money
- Provide answers relevant to broader populations of patients than would be possible in a specialized research environment

Background

- Real life studies are often a rich resource for meaningful information about:
  - Treatment effectiveness
  - Adherence
  - Tolerance
  - Use of concomitant therapies,
  - Decision-making processes and consequences of selecting or switching treatments.
- Real-world studies sometimes provide the only information about sensitive populations, sustained therapeutic effectiveness, and health services–related issues such as how the type of practitioner affects the choice of treatment.

Efficacy, Effectiveness of Efficiency?

Challenges with RWE

- Uncertain quality and provenance of data
- Insufficient transparency in design and conduct of studies
- Facile analytic tools that can be used by non-experts to do very complex analyses
- Shortage of researchers with adequate methodologic training

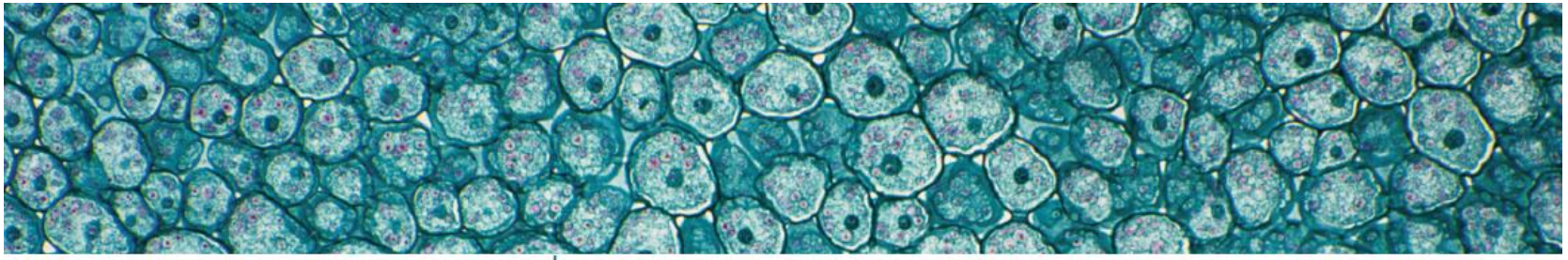
Challenges with data quality: Misclassification

Observed prevalence (p*) (%) of an attribute in a population for different levels of the true prevalence (p), and different values of sensitivity and specificity of the measurement procedure.

True prevalence (%)	Specificity (%)	Sensitivity (%)		
		99	90	80
0.1	99	1.1	1.1	1.1
	90	10.1	10.1	10.1
	80	20.1	20.1	20.1
0.5	99	1.5	1.4	1.4
	90	10.4	10.4	10.4
	80	20.4	20.4	20.3
2.5	99	3.5	3.2	3.0
	90	12.2	12.0	11.8
	80	22.0	21.8	21.5
12.5	99	13.3	12.1	10.9
	90	21.1	20.0	18.8
	80	29.9	28.8	27.5
50.0	99	50.0	45.5	40.5
	90	54.5	50.0	45.0
	80	59.5	55.0	50.0
62.5	99	62.3	56.6	50.4
	90	65.6	60.0	53.8
	80	69.4	63.8	57.5

dos Santos Silva, I. Cancer epidemiology: principles and methods. IARC, WHO. 1999

GRACE Checklist



grace
PRINCIPLES

A Validated Checklist
for Evaluating the Quality of Observational Cohort Studies for Decision-Making Support

Find more information on:

http://www.graceprinciples.org/

Three core questions addressed by GRACE

1. Were the study plans (including research questions, main comparisons, outcomes, etc.) specified before conducting the study?
2. Was the study conducted and analyzed in a manner consistent with good practice and reported in sufficient detail for evaluation and replication?
3. How valid is the interpretation of the findings for the population of interest, assuming sound methods and appropriate follow-up?

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

Pragmatic RCTs

Dimension	Assessment of Pragmatism
Recruitment of investigators and participants	
Eligibility	To what extent are the participants in the trial similar to patients who would receive this intervention if it was part of usual care?
Recruitment	How much extra effort is made to recruit participants over and above what would be used in the usual care setting to engage with patients?
Setting	How different are the settings of the trial from the usual care setting?
The intervention and its delivery within the trial	
Organization	How different are the resources, provider expertise, and organization of care delivery in the intervention group of the trial from those available in usual care?
Flexibility in delivery	How different is the flexibility in how the intervention is delivered from the flexibility anticipated in usual care?
Flexibility in adherence	How different is the flexibility in how participants are monitored and encouraged to adhere to the intervention from the flexibility anticipated in usual care?
The nature of follow-up	
Follow-up	How different is the intensity of measurement and the follow-up of participants in the trial from the typical follow-up in usual care?
The nature, determination, and analysis of outcomes	
Primary outcome	To what extent is the primary outcome of the trial directly relevant to participants?
Primary analysis	To what extent are all data included in the analysis of the primary outcome?

Ref: N Engl J Med. 2016:375:454-63

Conclusion

- Knowledge of RWE data are essential for any modern health care systems.
- A high level of rigour and methodological attention is are clearly warranted when designing, conducting, reporting and interpreting RWE research