Integrating Health Outcomes into the Publication Plan

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Lecture Objectives

- Provide basic overview of health outcomes, with an emphasis on “Real World” research
- Explore key differences between RCT and health outcomes reporting
- Highlight some helpful resources for health outcomes publishing

Glossary of Abbreviations

- ARRA: American Recovery and Reinvestment Act
- CER: Comparative Effectiveness Research
- HIPAA: Health Information Portability and Accountability Act
- IOM: Institutes of Medicine
- OR: Outcomes Research
- PE: Pharmacoeconomics
- QOL: Quality of Life
- QUOROM: Quality of Reporting of Meta-analysis
- RCT: Randomized Clinical Trial
- RW: Real World
- STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

Health Outcomes Research Overview

ISPOR

- International Society of Pharmacoeconomics and Outcomes Research
- Global organization focusing on PE and OR
- Excellent resources on all aspects of PE and OR
- Numerous policy statements on designing, interpreting, and publishing outcomes research
- *Value in Health*, official, indexed, peer-reviewed journal of ISPOR
- www.ispor.org

ISPOR Definition of Outcomes Research

The science of pharmacoeconomics (health economics) and outcomes research (the scientific discipline that evaluates the effect of healthcare interventions on patient well-being, including clinical, economic, and patient-reported outcomes) that facilitates the translation of this research into useful information for healthcare decision-makers to ensure that society allocates scarce healthcare resources wisely, fairly, and efficiently.

From the ISPOR Mission Statement; www.ispor.org

Growing Importance of Health Outcomes Research

- Patients are living longer with chronic illnesses
- Few large-scale, head-to-head studies of therapeutic interventions
- Scant evidence for off-label treatments
- Wide variability in treatment patterns
- We spend the most (15% of GDP) but don't live the longest (78 yrs)

Randomized Clinical Trials

- Randomized clinical trials are important for determining efficacy and safety, and registration
- But they are
  - Expensive
  - Limited, controlled experiments
  - Often vs. placebo or a previous formulation of the same molecule
  - Not always generalizable to larger populations
- There is a need to follow RCTs with studies of how the product is used in the real world

Who Benefits from Outcomes Research

- Health care researchers
- Health technology assessors
- Government health regulators
- Payers of health care
- Health care providers
- Patients
- Producers of therapeutic interventions

Efficacy vs. Effectiveness

- Efficacy
  - What an intervention can or can't do
  - Good for patient
- Effectiveness
  - Evaluates interventions in real world
  - Good for population

Comparative Effectiveness Research

- Comparison of 2 or more agents that are considered true alternatives
- Evaluates outcomes of interventions derived from actual practice
- American Recovery and Reinvestment Act (ARRA) is investing $1.1B to support CER
- Approximately 100 high-priority research projects
- Goal is to spark innovation and provide information to assist clinicians in making sound evidence-based decisions

Lee EH, Nash DB, ISMPP 2009

Pharmacoeconomic Modeling

- Synthesizes evidence on health consequences and costs from many different sources including
  - Clinical trials
  - Observational studies
  - Insurance claims databases
  - Case registries
  - Public health statistics
  - Preference surveys

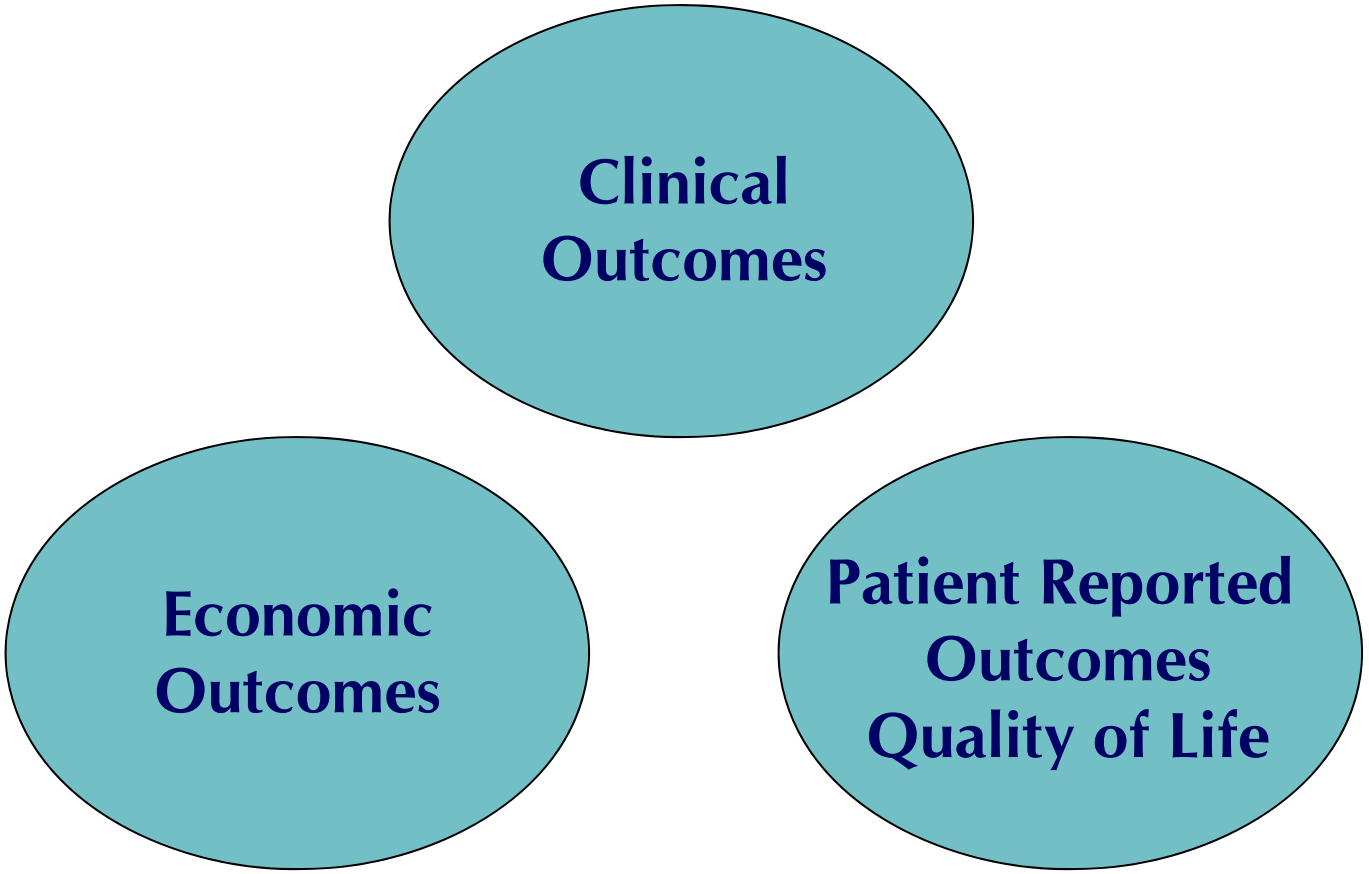
Weinstein MC, Value Health 2003

Pharmacoeconomic Evaluations

- Types of evaluations
  - Cost consequence
  - Cost utility
  - Cost benefit

Weinstein MC, Value Health 2003

Real World Outcomes



Real World Data Benefits

A different perspective on interventions, eg,

- Estimates of effectiveness vs. efficacy in a variety of settings
- Comparison of multiple interventions for optimal choices
- Evolving risk-benefit profiles of new interventions
- Clinical outcomes in a diversity of study populations
- Results on a broader range of outcomes than those for RCT
- Data on resource use for cost evaluations

Garrison Jr. LP, Value Health 2007

Real World Data Benefits, contd.

- Data on dosing and compliance in clinical practice
- Useful in situations where RCT is impossible
- Substantiation of RCT data
- Provide data to support reimbursement in urgent situations
- Source of interim evidence for preliminary decisions
- Net clinical and economic impact of payment policies

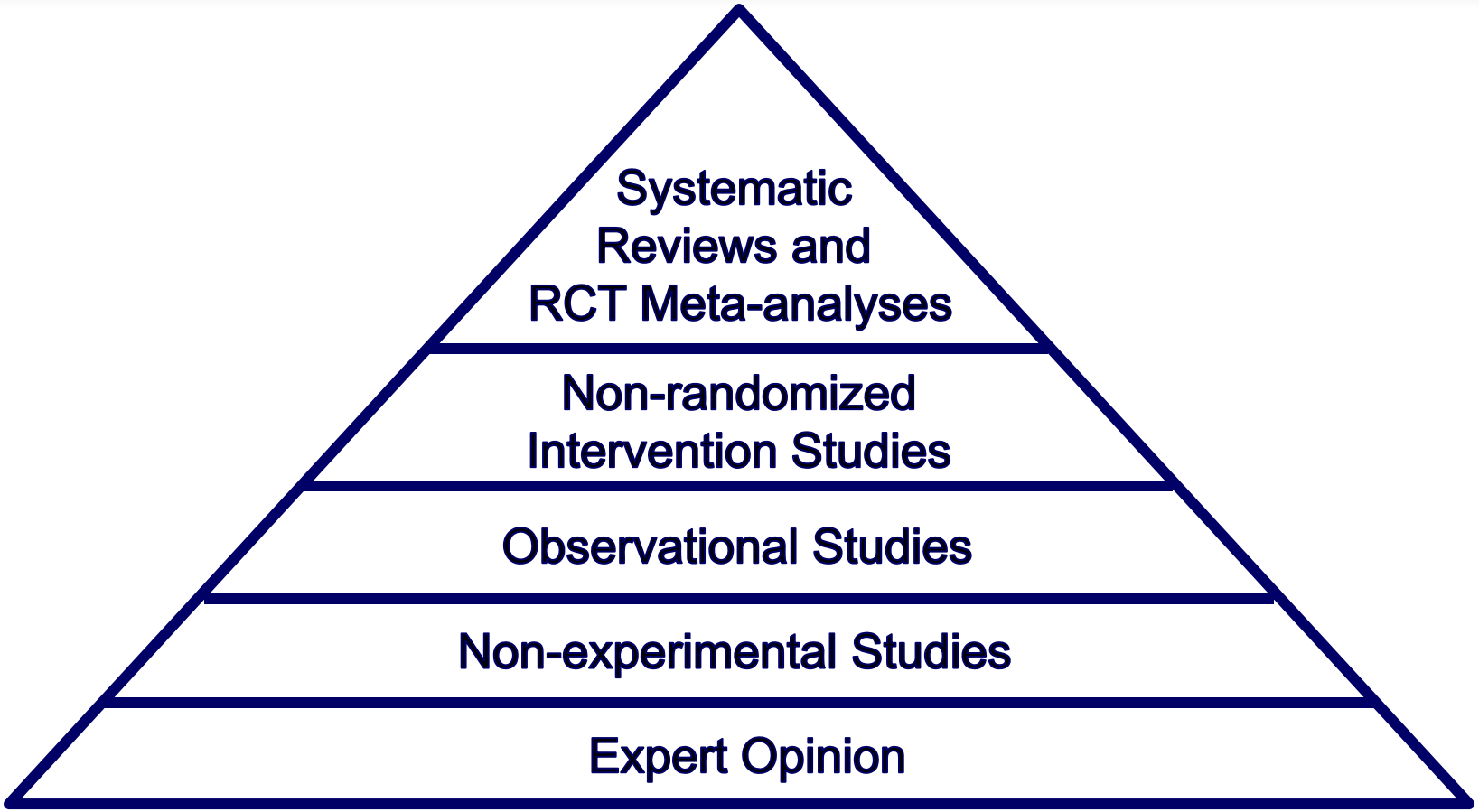
Garrison Jr. LP, Value Health 2007

Real World Data Categories

- Supplements to traditional registration RCTs
- Large simple trials (practical clinical trials)
- Registries
- Administrative data
- Health surveys
- Electronic medical records and chart reviews

Garrison Jr. LP, Value Health 2007

Evidence Hierarchy



Magnitude of Net Benefit

- What is the net benefit in support of a particular technology?
- Magnitude of net benefit must be taken into account when assessing real world evidence

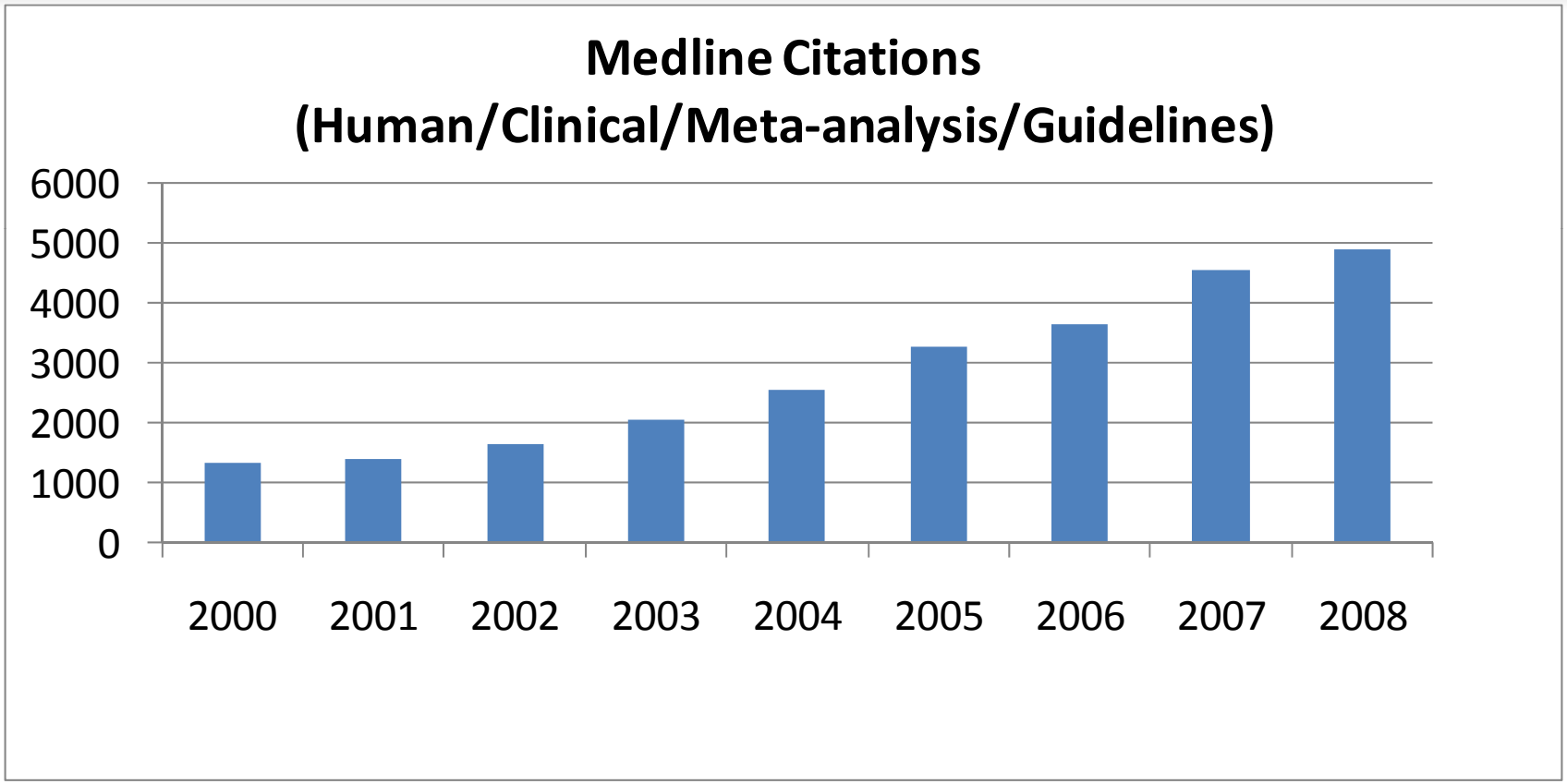
Limits of Real World Data

- Non-randomized
- Potential for bias and confounding
- Not likely to meet methodological rigor of an RCT
- Good research practices are needed and should be followed from study design through publication

Garrison Jr. LP, Value Health 2007

Health Outcomes and Publication Planning

Growth of Outcomes Publishing



Indexed Publications Focusing on Health Outcomes

Journal	Circulation	Impact
Health and Quality of Life Outcomes	37,041	3.2
Pharmacoeconomics	9,980	2.808
Value in Health	4,000	3.009

- Other journals have OR sections

CONSORT, QUOROM, STROBE, and STARD

- CONSORT (1996, 2001)
  - CONsolidated Standards Of Reporting Trials
  - Improve the reporting of a randomized clinical trial
- QUOROM (1999)
  - QUality Of Reporting Of Meta-analyses
  - Improve the quality of reporting meta-analyses of randomized, controlled clinical trials
- STROBE (2007)
  - Strengthening The Reporting of OBservational Studies in Epidemiology
  - Improve the quality of reporting of observational studies
- STARD (2003)
  - STAndards for the Reporting of Diagnostic accuracy studies
  - Improve reporting of studies of diagnostic accuracy

CONSORT, QUOROM, and STROBE

Checklist	CONSORT	QUOROM	STROBE
# of Items	22	21	22
Title, Abstract, Introduction	Similar	Similar	Similar
Methods	Randomization Blinding	Searching Selection Validity assessment Data abstraction Quantitative data synthesis	Study type •Cohort •Case-control •Cross-sectional Potential for bias
Results	Recruitment Adverse events	Quantitative data synthesis	Descriptive analysis
Discussion	Interpretation	Describe biases in review process	"Cautious" interpretation Limitations

Structural Considerations

- Safety, efficacy AND effectiveness
- Incorporate health outcomes research earlier in the drug development process
  - Protocol design
  - Analysis
  - Extension studies
- Add a health outcomes expert(s) to your publication planning team

Planning Considerations

- **Health outcomes should be a core element of a publication plan**
  - **Most congresses/journals now have sections for outcomes research**
- **A discussion of OR should be on the agenda of every pub planning meeting**
- **OR should be part of every gap analysis**
- **Timing is key**

Reporting Considerations

- OR often relies on non-randomized data
  - Not likely to meet methodological rigor of an RCT
- Detailed reporting is required for
  - Study design
  - Methods
  - Treatment effects
  - Bias and confounding
  - Generalizability
- Additional details may be included in appendix

HIPAA, IRBs, and Other Thorny Issues

- Non-interventional, observational, or retrospective studies are not exempt from HIPAA rules
- Was the study reviewed, or exempted from review, by an IRB?
- FDAAA currently applies to RCT. Will it apply to OR in the future?

Summary

- OR is research
  - Requires sound methodologies, privacy protection, unbiased data sources, and thorough analysis
- OR fills gaps
  - Helps to address questions and concerns that go beyond the scope of registration studies
- OR identifies gaps
  - Helps to identify newer, more effective approaches and interventions
- OR is publishable
  - Growing number of guidelines and journals/venues dedicated to OR
- OR is the future
  - CER will require continuing follow-up to remain relevant

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Thank You