

# **The Need for Improvements in Methodology to Support Evidence Development**

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Vice President

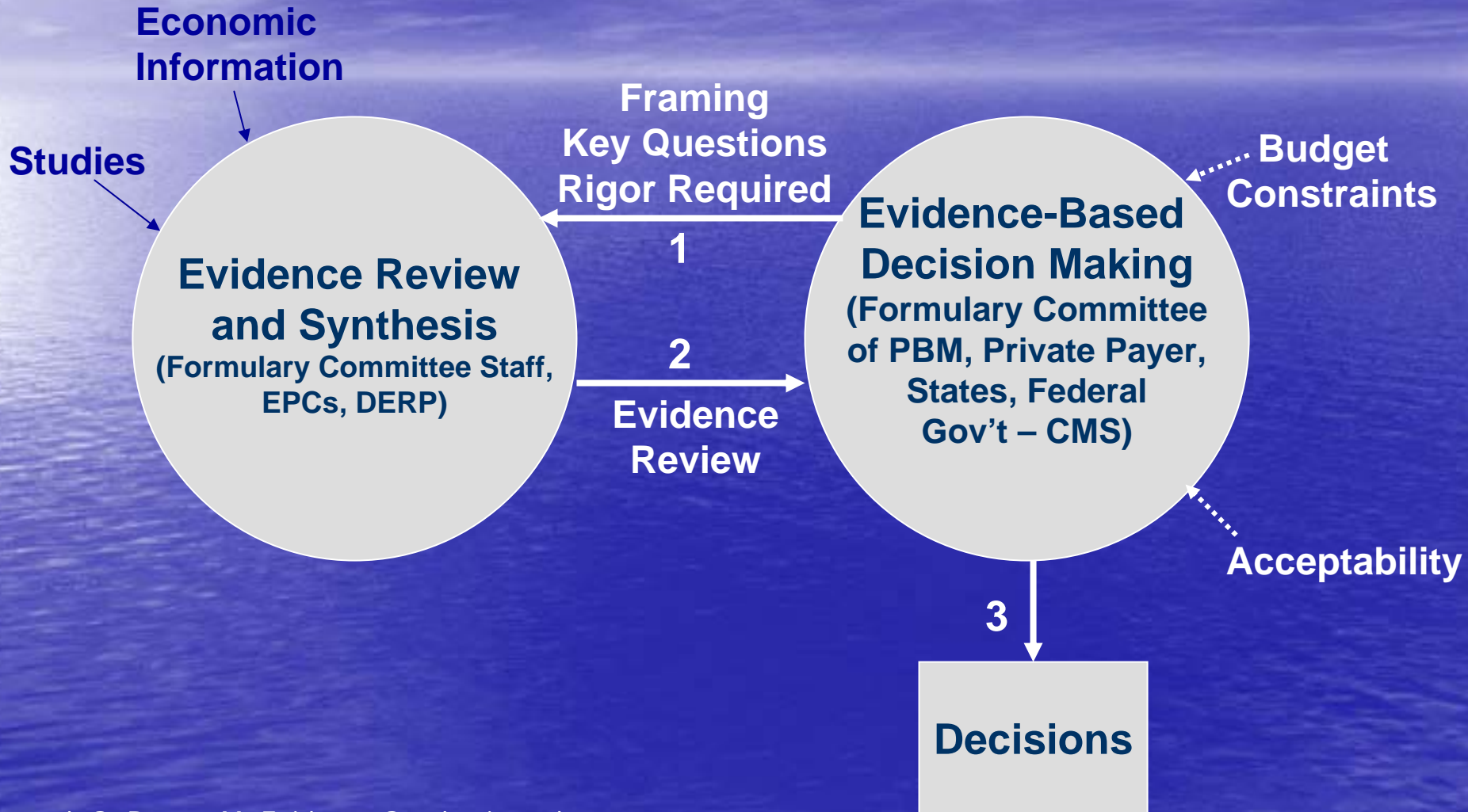
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# Methodology Meets Policy

- What makes information useful to decision makers?
  - What do we know?
    - How confident are we about what we know scientifically?
  - What would we like to know?
    - Are there critical gaps in our scientific knowledge?
      - Use of colloquial evidence as a complement or substitute for missing scientific evidence
- Options for decision makers
  - Make decisions based upon imperfect information
    - Combine scientific evidence with contextual considerations
      - Resources, Values, Habits, Traditions, Political Judgments
    - Revisit decisions if and when more information become available
  - Defer decision and ask for additional information
  - “Coverage with Evidence Development”

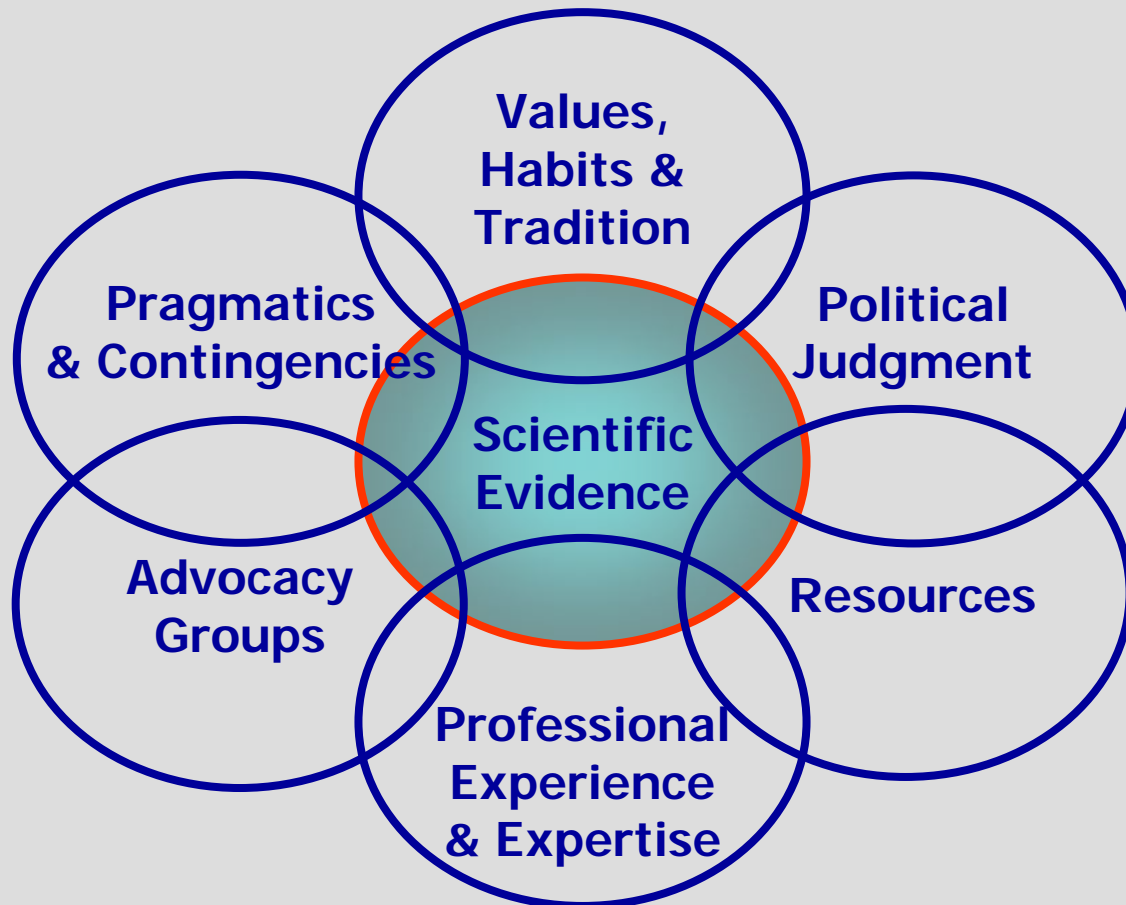
# Dynamic Relationship Between Evidence Review & Synthesis and Evidence-based Decision Making



# Conceptualizing and Combining Evidence for Health System Guidance

J. Lomas, T. Culyer, C. McCutcheon, L. McAuley, S. Law  
Canadian Health Services Research Foundation, May 2005

**"Evidence is inherently uncertain, complex, contestable, and rarely complete."**



# Transparency Requires that the Use of Different Kinds of Evidence is Clearly Identified

## Scientific Evidence

(ex Rigorous Evidence Reviews)

- Context-free
- Explicit (codified & propositional)
- Systematic (transparent & explicit methods)
- Replicable

## Social Science Evidence

(ex CEA)

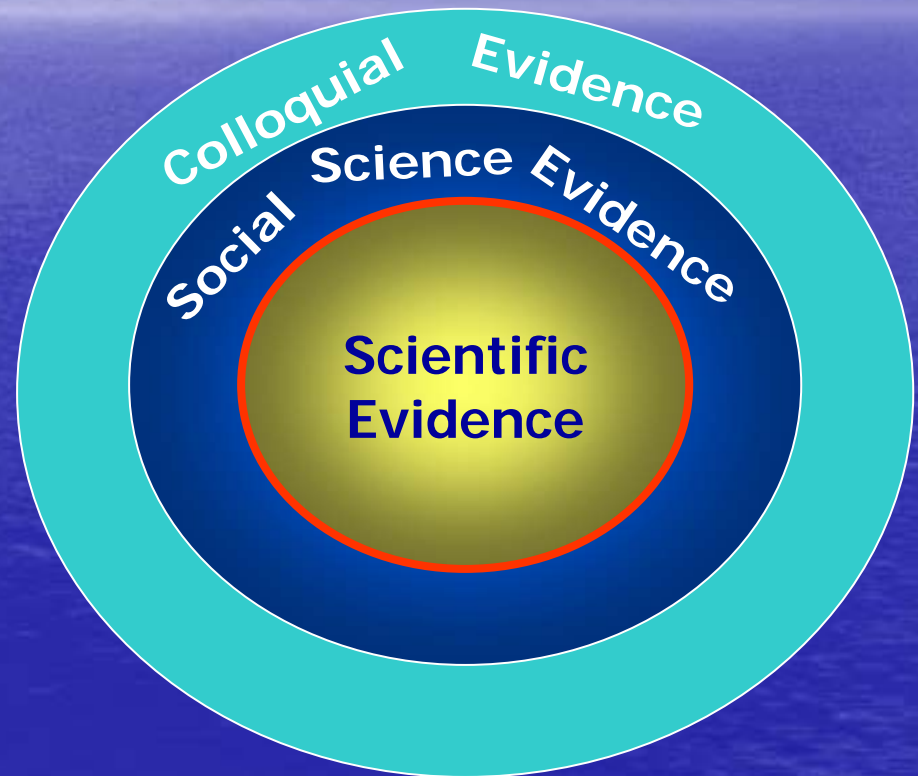
- Context-sensitive
- Explicit
- Systematic
- Goes beyond Scientific Evidence

## Colloquial Evidence

(ex Values, Habits, Tradition, Political Judgment, Pragmatics & Contingencies, Resources, Professional Experience & Expertise, Advocacy Groups)

“Anything that establishes a fact or gives reason for believing something”

- Context-sensitive
- Practical
- Defined by relevance



# PERSPECTIVE

## **Comparative Effectiveness: Asking The Right Questions, Choosing The Right Method**

Methodological choice should be driven by policy goals.

**by Steven M. Teutsch, Marc L. Berger, and Milton C. Weinstein**

**ABSTRACT:** The Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 has placed renewed focus on assessing the comparative effectiveness of various therapeutic options. Unfortunately, all of the evidence needed to fully assess these options is rarely available to drug formulary decisionmakers. Comparative randomized trials frequently fail to find differences when there indeed are some, while decision-modeling approaches are more likely to identify differences where there are none. We consider the consequences of these strategies. This paper proposes a framework for using different methods to assess available evidence. We contend that choosing the appropriate method can occur only when there are clear policy goals.

# Policy Goals and Certainty of Comparative Evidence

What is the tolerance for error?

- **Type I – Error of Commission (False Positive)**
  - Thinking there is a difference when there is none
- **Type II – Error of Omission (False Negative)**
  - Thinking there is no difference when there is one

# Level of Certainty Required Depends on the Clinical Situation

- **Serious Life-threatening Health Condition**
  - Greater willingness to accept less than perfect information as decisions must be made by doctors and patients
- **Asymptomatic Population at Risk for Developing an Illness**
  - Greater desire for certainty before widespread use



# Acting on Imperfect Evidence: How Much Regret Are We Ready to Accept?

B. Djulbegovic et al J Clin Oncol 23: 6822-6825, 2005

Goals of Treatment	Uncertainty About Benefits/Harms of Alternative Tx Options	Benefit-Harm Ratio	Regret Associated with Wrong Recommendations	Acceptable Evidentiary Standards	Examples
Prevention of the dz in asx individuals	High	There are important trade-offs between benefits and harms	High	Highest standard of experimental evidence	Tamoxifen in prevention of breast cancer
Cure	Low	The vast majority of practitioners believe that the intervention does more harm than good.	Low	May accept lower level of evidence	Antibiotics in H Pylori positive MALT gastric lymphoma
Prolongation of survival in years	Low	The vast majority of practitioners believe that the intervention does more harm than good.	Low	May accept lower level of evidence	Imatinib in chronic myeloid leukemia
Prolongation of survival in months	High	There are important trade-offs between benefits and harms	High	Highest standard of experimental evidence	Chemotherapy in metastatic lung cancer
Palliation (improvement in QoL)	Low/Moderate	The vast majority of practitioners believe that the intervention does more harm than good.	Low	May accept lower level of evidence	Morphine in pain control
Palliation (improvement in QoL)	High	It is not clear whether the intervention does more good than harm	Moderate	High quality evidence particularly if costs are high	Bisphosphonates in prevention of skeletal-related morbidities

# Health Technology Assessment and Evidence-based Medicine

- Assessment of benefits, harms, and costs of alternative treatments based upon best available evidence
- Types of Evidence
  - RCTs
    - Practical Clinical Trials
  - Observational Studies
    - Longitudinal Registries
    - Case – Control, Cohort Studies, etc.
      - Retrospective Claims Analyses
      - Retrospective Analyses based on EMR or Chart Review
      - Prospective Observational Studies
  - Systematic Reviews
    - Meta-analyses

# Outstanding Methodologic Issues

<b>Type of Study</b>	<b>Issues</b>
<b>RCTs</b>	Generalizability Head-to-Head Outcomes Studies are complex, require large sample sizes over long time periods
<b>Treatment Registries</b>	Effectiveness: Channeling and other potential biases Use of surrogate vs outcomes endpoints Safety: Sample Size and NNH May lack comparison group Need for GCPs (AHRQ Handbook Project)
<b>Retrospective Analyses</b>	Effectiveness: Bias (including incomplete and inaccurate information) Correlation vs Causation Safety: Signal Identification vs Validation
<b>Systematic Reviews</b>	Questions addressed Appropriate standards of evidence Analysis, Interpretation and Communication of Results ( Eisenberg Center)

**Good Decisions Require Good  
Methods**