



Systematic Literature Reviews and Analytic Frameworks

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Issues to Consider

- How can we do a better job determining when and what large trials are worth pursuing?
- When is evidence sufficient for clinical decision-making?
- When evidence is not sufficient, what types of studies are needed?

Rationale for Systematic Reviews

- AIM: To reduce potential for bias and error
- Explosion of medical literature – 400,000 Medline/yr
- Complex links between interventions and outcomes
- Effects may be modest, develop over long time
- Need to balance benefits, harms and costs
- Variable design and quality of published studies
 - Internal validity
 - External validity (generalizability or applicability)

Attributes of Systematic Reviews

- Explicit methods
- Complete and unbiased review
- Transparent reasoning
- Consistent (reproducible) results

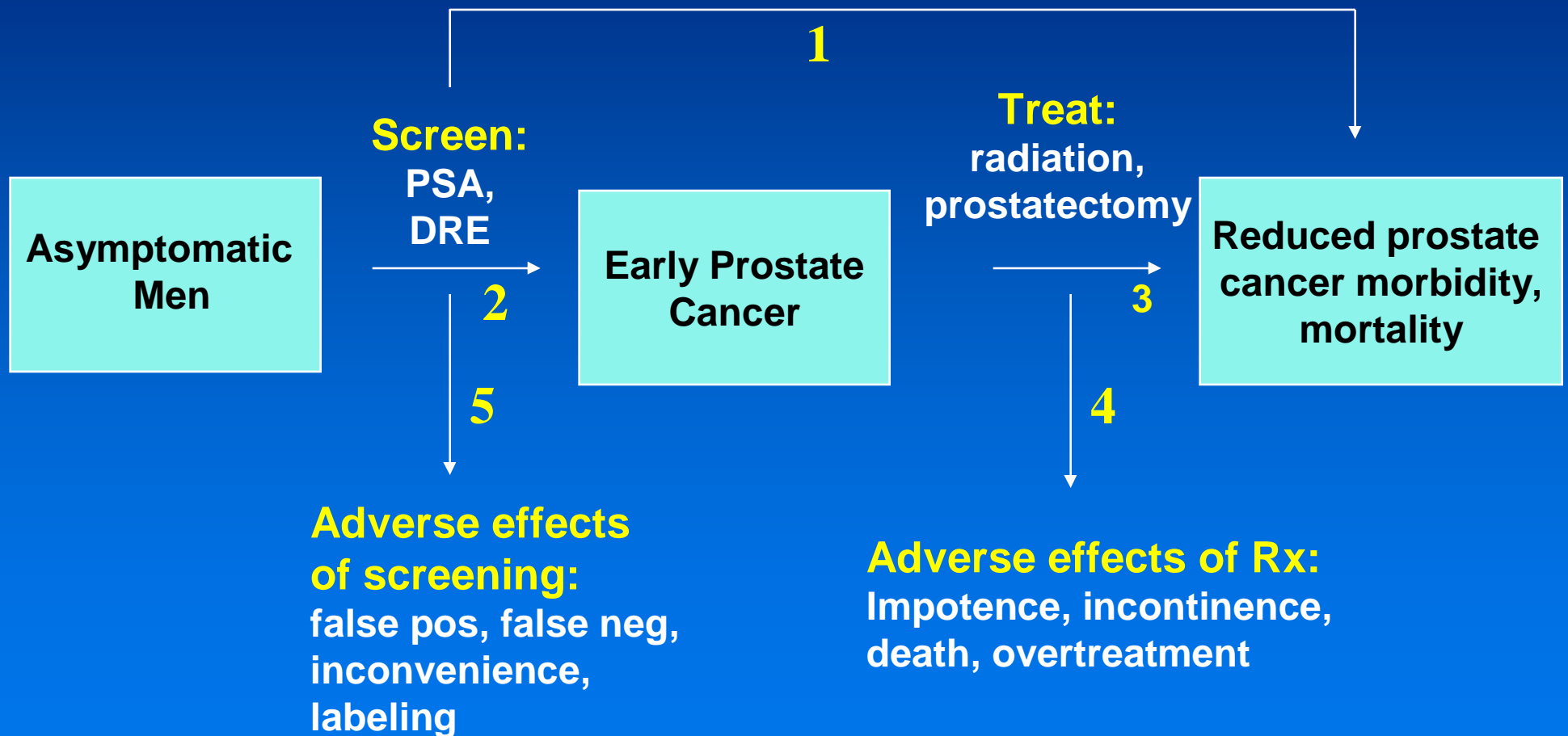
AIMS:

- Facilitate decision making
- Identify critical research gaps

Steps in Systematic Review Process

1. Clarify critical questions: Analytic framework
2. Complete and unbiased search for evidence
3. Assess quality of evidence
4. Link conclusions to:
 - quality of evidence
 - balance of benefits vs. harms

Analytic Framework - 1



2. Unbiased search for evidence

- What outcomes are relevant?
 - Intermediate measures vs. health outcomes
- What types of studies are included/excluded?
 - Animal vs. human?
 - Developing vs. developed countries?
- What study designs are adequate?
 - RCTs vs. observational studies

3. Assess quality of evidence

■ What do we mean by quality?

“Extent to which a study’s design, conduct, and analysis has minimized selection, measurement, and confounding biases.”

– Lohr, *J Qual Improvement*, 1999

“Extent to which one can be confident that an estimate of effect is correct”

– GRADE , *BMJ* 2004

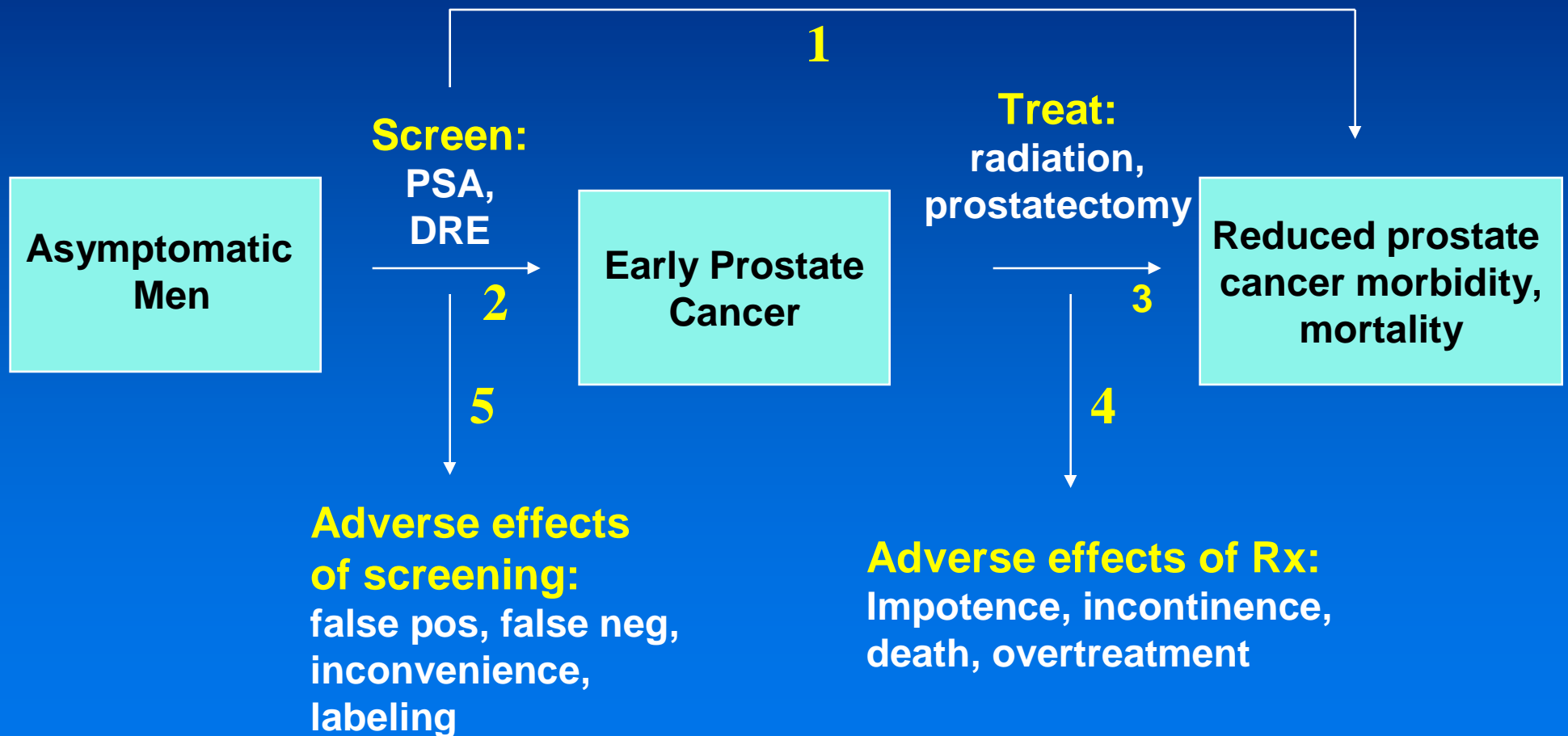
Quality of Individual Studies

- GOAL: Identify those studies with highest quality (internal validity)
- Depends on study design (e.g., RCT vs. cohort)
- Depends on study execution (e.g., blinding)
- Critical elements vary by study design and specific topic
 - Best established for RCTs
 - Evolving methods for observational studies

3 levels of quality

- Quality of individual studies
- Overall quality of studies addressing a specific question
- Quality of collected evidence to inform a clinical issue

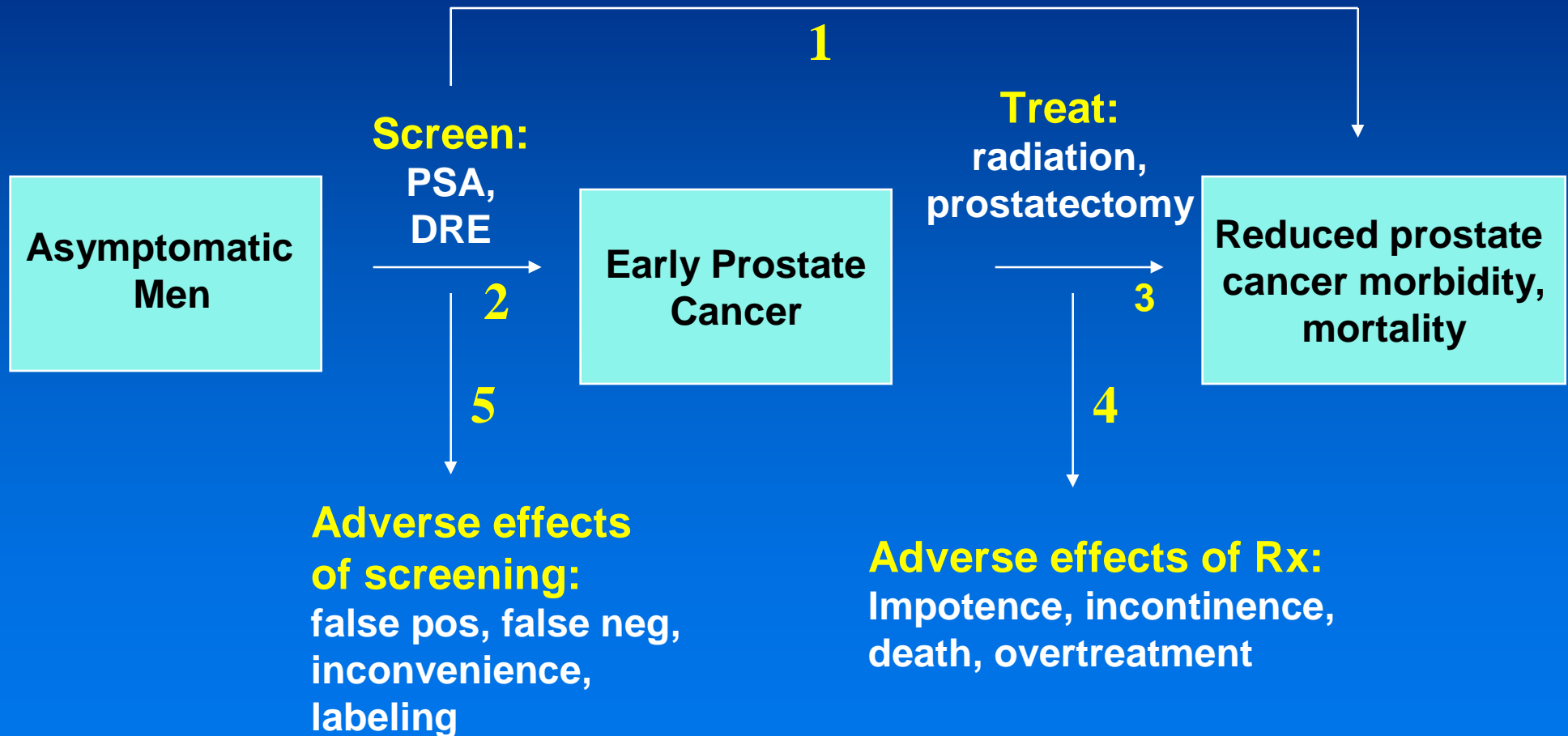
Analytic Framework - 1



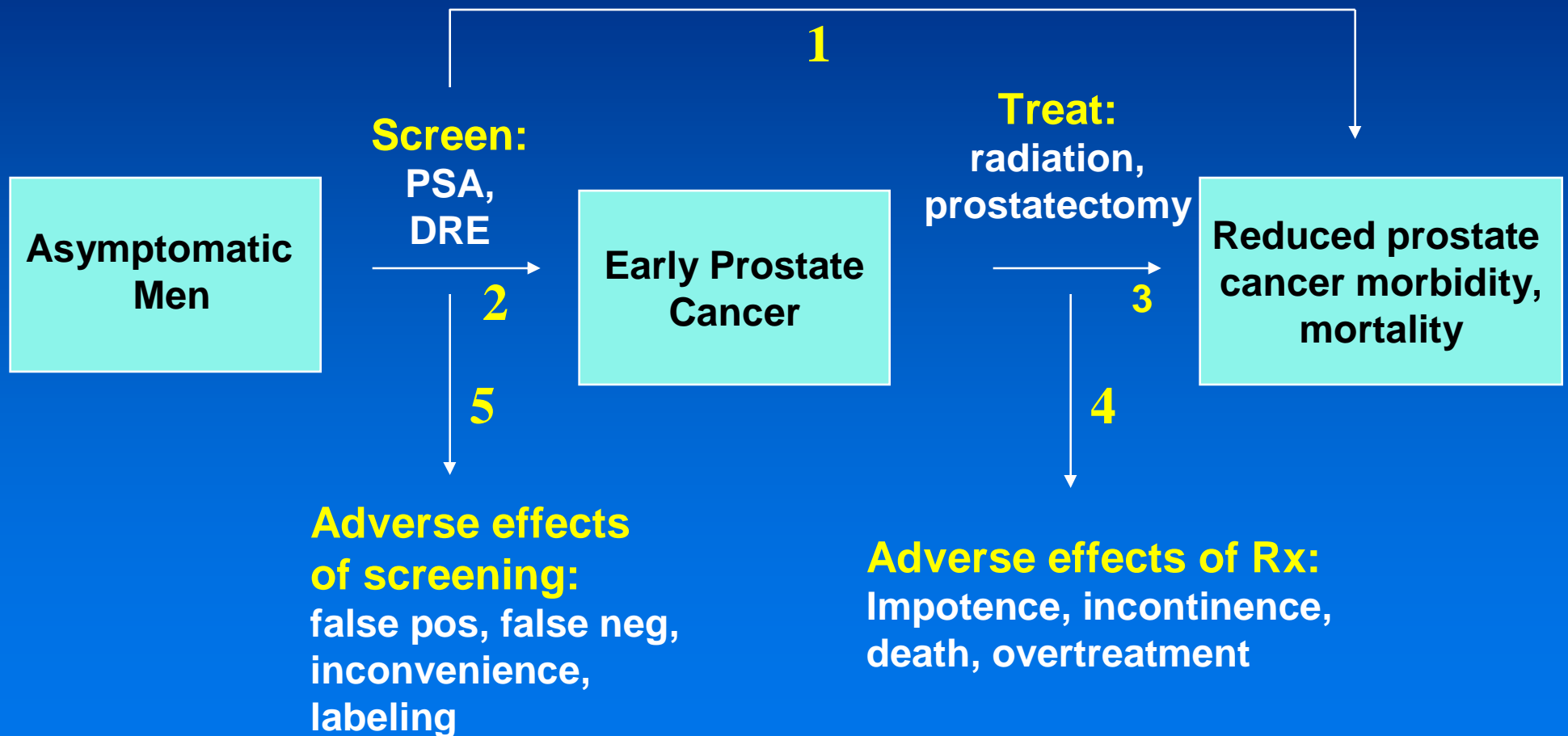
4. Synthesis and Reporting

- Summarize evidence for each key question
 - Strength of evidence depends on internal validity, external validity, and other factors
- Quantitative or qualitative synthesis as appropriate
- Conclusions linked to evidence in explicit and transparent way

Analytic Framework – Use for clinical decisions



Analytic Framework – Use research



Challenges in Systematic Reviews

- Labor intensive
 - Not necessarily more than any comprehensive review
- Requires more up-front work
 - Specify questions, outcomes, designs
- May find little high quality literature or be overwhelmed by volume of literature
 - Expand or restrict scope if needed

Other considerations

- Systematic reviews will not eliminate controversy over evidence or resolve contentious policy questions
- Conflicts over evidence or policy usually reflect conflicts over *values*
 - What constitutes “good enough” evidence?
 - What outcomes are most important?
 - When is a benefit “important”?

Conclusions

- Systematic reviews provide more consistent and transparent approach to summarizing existing evidence
- Useful for developing clinical recommendations
- Useful for identifying research gaps or important implications of policy decisions
- May separate questions of evidence from questions of values