



Agency for Healthcare Research and Quality

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Integrating Biomarkers into Practice: The Need for Data on Clinical Outcomes

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Outline

- AHRQ mission
- Biomarkers and Genomics
- Evidence-based Decision-making: USPSTF model
- Current landscape of Genomics
- Future steps



AHRQ Mission

- Improve quality, safety, efficiency and effectiveness of health care
 - Supports evidence-based decision-making by clarifying the evidence of benefits and harms of clinical interventions (diagnostics & therapeutics)
 - Example: Effective Health Care Program
www.effectivehealthcare.ahrq.gov



Biomarkers and Genomics

- **Biomarker:** indicator of a biologic state
- **Genome:** totality of genetic information belonging to a cell or an organism
- Biomarkers often gene-based products:
Troponin, lipoproteins, CRP, PLA2,
ApoE, fibrinogen etc.

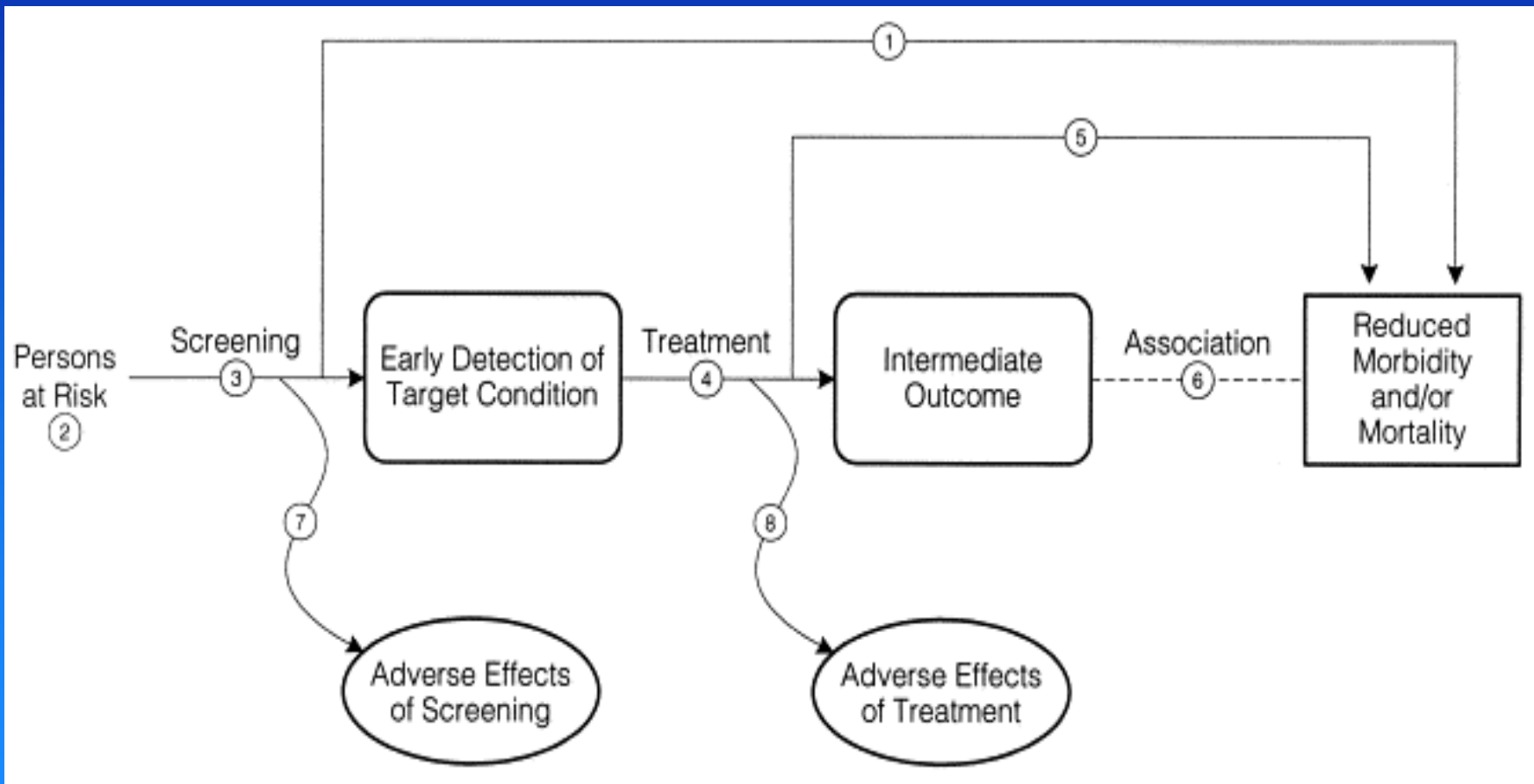


USPSTF

- AHRQ-supported independent expert panel that makes **evidence-based** recommendations on **preventive** services in a **primary care** setting
- Two step decision-making process:
 - a) Evidence evaluation and synthesis (EPC)
 - b) Assessment of strength of evidence and magnitude of net benefit (USPSTF)

www.preventiveservices.ahrq.gov

Analytic Framework: Screening for a Disease





USPSTF Letter Grades

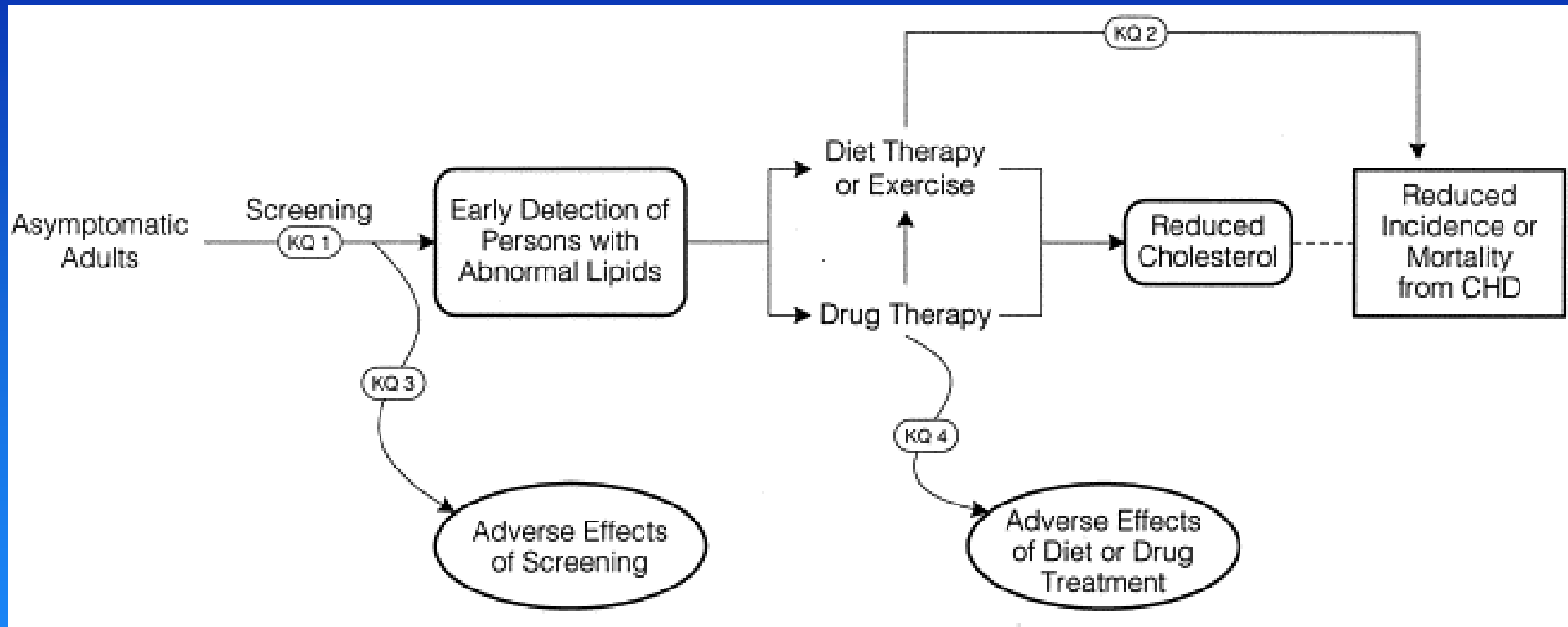
- **A:** good evidence; benefits substantially outweigh harms.
- **B:** fair evidence; benefits outweigh harms
- **C:** fair evidence; balance of benefits and harms is too close
- **D:** fair evidence; ineffective or that harms outweigh benefits.
- **I:** evidence is lacking, poor quality, or conflicting



USPSTF: Example 1

- Screening for Lipid Disorders

Screening Adults for Lipid Disorders (2001)





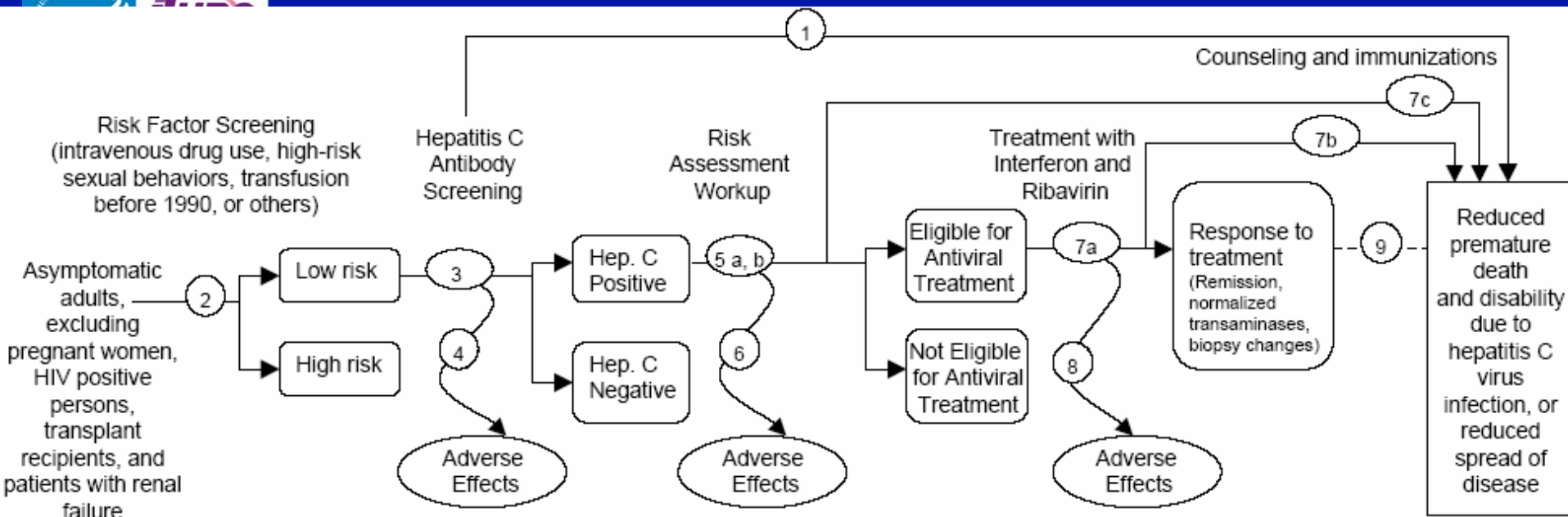
Recommendations

- A: Men ≥ 35 + risk; Women ≥ 45 + risk
- B: Men 20-35 + risk; Women 20-45 + risk
- C: Men 20-35 at average risk; Women 20-45 at average risk



USPSTF: Example 2

- Hepatitis C screening



Key Questions

- Arrow 1: Does screening for hepatitis C reduce the risk or rates of harm and premature death and disability?
- Arrow 2: Can clinical or demographic characteristics identify a subgroup of asymptomatic patients at higher risk for HCV infection?
- Arrow 3: What are the test characteristics of hepatitis C virus antibody testing?
- Arrow 4: What is the predictive value of a positive screening test and what are the harms associated with screening for hepatitis C virus?
- Arrow 5: a) What are the test characteristics of the work-up for active disease?
b) In patients found to be positive for hepatitis C virus antibody, what proportion of patients would qualify for treatment?
- Arrow 6: What are the harms associated with the work-up for active hepatitis C virus disease?
- Arrow 7: a) How well does antiviral treatment reduce the rate of viremia, improve transaminase levels, and improve histology?
b) How well does antiviral treatment improve health outcomes in asymptomatic patients with hepatitis C?
c) How well do counseling and immunizations in asymptomatic patients with hepatitis C improve clinical outcomes or prevent spread of disease?
- Arrow 8: What are the harms (including intolerance to treatment) associated with antiviral intervention?
- Arrow 9: Have improvements in intermediate outcomes (liver function tests, remission, histologic changes) been shown to reduce the risk or rate of harm from hepatitis C?

Findings

- Accurate screening tests
- High prevalence in high-risk
- 10%-20% progress to cirrhosis in 20-30 years
- 30%-40% referred are eligible for therapy
- Therapy reduces viremia
- Therapy has unknown long-term benefit (cirrhosis, mortality), high AEs (50-60%) and drop-out, expensive



Recommendations

- I: Insufficient evidence in high-risk
- D: Against screening in general population



Important Questions for Decision-Makers

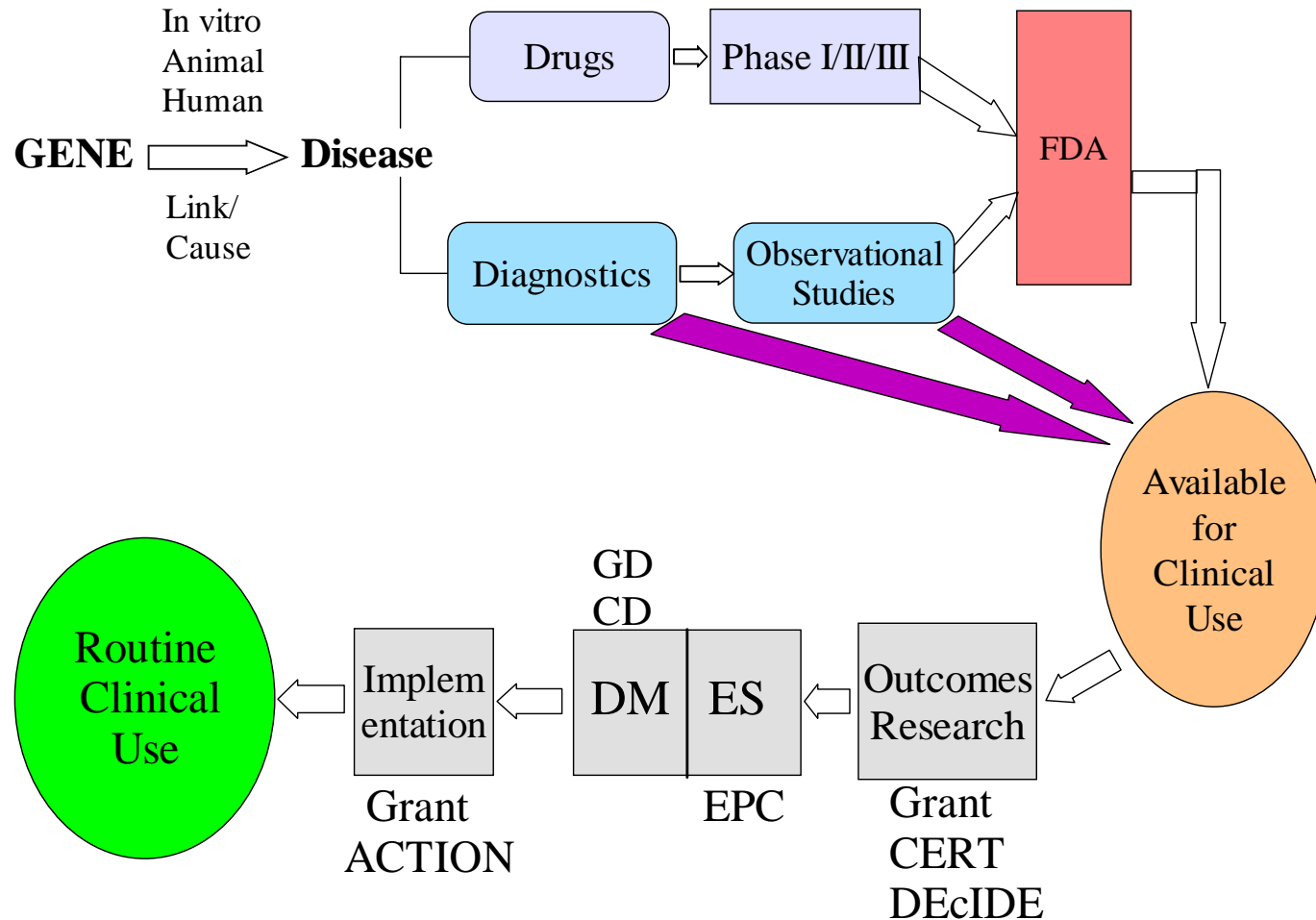
1. Are patient outcomes improved?
2. What are the harms?
3. Do benefits outweigh harms?
4. What is the incremental benefit?
5. Is the real-world **net** benefit the same as in clinical trials?
6. What are the costs?
7. Given the net benefit and costs, is the intervention worth it?



Current Landscape of Genomic Tests

- Gene-based tests are available with no or poor-quality data on outcomes
- Lab-developed tests are not currently regulated by FDA (BRCA, Oncotype DX)
- Gene-based applications are expensive
- Direct-to-consumer marketing prevalent
- Pathway of integrating genomic applications into practice is complex

Integrating Genomics into Practice





Future Steps

- National sample repositories with standardized information
- Standardized molecular data analysis methods
- Clinical databases with linked diagnostic, drugs, patient outcomes and hospital data
- Improve data collection and analysis to minimize bias in observational studies
- Strengthen and create public-private and private-private partnerships