Comparative Effectiveness Research

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Overview

- **Expanding the Evidence Base**
- **Stimulus Funding—Framework and Priorities**
- **CER Methodologies**
  - Meta-analysis of existing studies
  - Inferring causality from non-randomized studies
  - Combination with QI methods
- **Consideration of Cost-Effectiveness**

Expanding the Evidence Base

- **Randomized controlled trials are regarded as the "gold standard"**

- **But…**
  - Safety and efficacy (*can* it work?), rather than effectiveness (*does* it work in routine care?)
  - Questions are narrow by design
    - "Pure" patient populations (non-elderly, single diagnoses)
    - Compare new drug to placebo or current therapy, not head-to-head against alternatives
  - Drug trial may take 10+ years and cost $10–300 million
    - Newer trial designs enhance efficiency

- **Pace of introduction of new products and technologies**

- **Lack of evidence to guide important decisions in routine practice**
  - Use of expensive diagnostic procedures
  - Screening strategies
  - New drug vs. established therapy
  - Medical therapy vs. surgical intervention
  - Complex patients—elderly, multiple chronic conditions
  - "Minority" populations

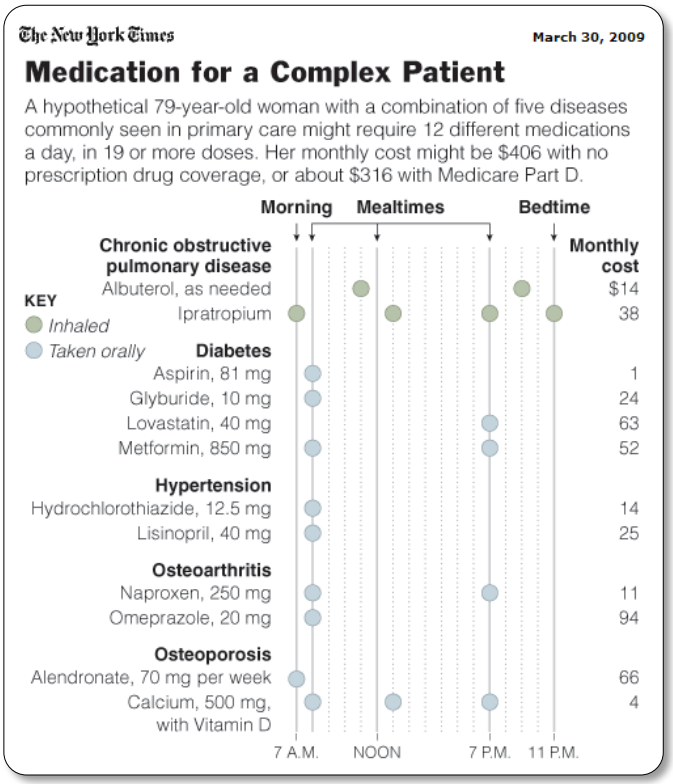
Hypothetical 79-year-old woman with

- chronic obstructive pulmonary disease,
- type 2 diabetes mellitus,
- hypertension,
- osteoarthritis, and
- osteoporosis,

all of moderate severity.

12 separate medications
19 doses per day
5 separate dosing times/day

$4,877 medication cost/year (generics)



Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Comorbid Diseases

Implications for Pay for Performance

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Context Clinical practice guidelines (CPGs) have been developed to improve the quality of health care for many chronic conditions. Pay-for-performance initiatives assess physician adherence to interventions that may reflect CPG recommendations.

Objective To evaluate the applicability of CPGs to the care of older individuals with several comorbid diseases.

Data Sources The National Health Interview Survey and a nationally representative sample of Medicare beneficiaries (to identify the most prevalent chronic diseases in this population); the National Guideline Clearinghouse (for locating evidence-based CPGs for each chronic disease).

Study Selection Of the 15 most common chronic diseases, we selected hypertension, chronic heart failure, stable angina, atrial fibrillation, hypercholesterolemia, diabetes mellitus, osteoarthritis, chronic obstructive pulmonary disease, and osteoporosis, which are usually managed in primary care, choosing CPGs promulgated by national and international medical organizations for each.

Data Extraction Two investigators independently assessed whether each CPG addressed older patients with multiple comorbid diseases, goals of treatment, interactions between recommendations, burden to patients and caregivers, patient preferences, life expectancy, and quality of life. Differences were resolved by consensus. For a hypothetical 79-year-old woman with chronic obstructive pulmonary disease, type 2 diabetes, osteoporosis, hypertension, and osteoarthritis, we aggregated the recommendations from the relevant CPGs.

Data Synthesis Most CPGs did not modify or discuss the applicability of their recommendations for older patients with multiple comorbidities. Most also did not comment on burden, short- and long-term goals, and the quality of the underlying scientific evidence, nor give guidance for incorporating patient preferences into treatment plans. If the relevant CPGs were followed, the hypothetical patient would be prescribed 12 medications (costing her $406 per month) and a complicated nonpharmacological regimen. Adverse interactions between drugs and diseases could result.

Conclusions This review suggests that adhering to current CPGs in caring for an older person with several comorbidities may have undesirable effects. Basing standards for quality of care and pay for performance on existing CPGs could lead to inappropriate judgment of the care provided to older individuals with complex comorbidities and could create perverse incentives that emphasize the wrong aspects of care for this population and diminish the quality of their care. Developing measures of the quality of the care needed by older patients with complex comorbidities is critical to improving their care.

JAMA. 2005;294:716-724 www.jama.com

THE AGING OF THE POPULATION and the increasing prevalence of chronic diseases pose challenges to the development and application of clinical practice guidelines (CPGs). In 1999, 48% of Medicare beneficiaries aged 65 years or older had at least 3 chronic medical conditions and 21% had 5 or more.[1] Health care costs for individuals with at least 3 chronic conditions accounted for 89% of Medicare's annual budget.[1] Comorbidity is associated with poor quality of life, physical disability, high health care use, multiple medications, and increased risk for adverse drug events and mortality.[2-4] Optimizing care for this population is a high priority.[5]

Clinical practice guidelines are based on clinical evidence and expert consensus to help decision making about treating specific diseases.[6] Clinical practice guidelines help to define standards of care and focus efforts to improve quality.[7,8] Most CPGs address single diseases in accordance with modern medicine's focus on disease and pathophysiology.[9] However, physi-

For editorial comment see p 741.

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"Inferential Gap"

- **Absence of evidence germane to common clinical situations**
- **Non-application of relevant existing evidence**

Comparative Effectiveness Research

- **Serious limitations of traditional databases**
  - Data standards driven by administrative processes—insurance claims
    - Depth and quality of data affected by economic interests
    - Critical clinical information has been recorded primarily on paper
  - Aggregate databases have focused primarily on hospital care
    - Medicare claims: hospitals, professional fees, pharmacy benefit (only recently integrated)
    - All-payer hospital discharge abstract databases—various states
  - Limited information about process-of-care and outcomes
- **Converging trends support CER**
  - Growth of analytics and "business intelligence" in other industries
  - EHR adoption
    - Clinical decision support—alerts and reminders, based on guidelines
    - Creates richer database as a by-product of routine care
  - Need for guidance to improve outcomes and control costs
  - Improved statistical methods for causal inferences from observational data

AHRQ Effective Health Care Program

- **Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA)**
- **Effective Health Care Program (effectivehealthcare.ahrq.gov)**
  - **Synthesize** Evidence-based Practice Centers (EPC)—reviews of existing evidence
  - **Generate** DEcIDE Centers/CERTs—new scientific evidence and analytic methods
    - Developing Evidence to Inform Decisions about Effectiveness (DEcIDE)
    - Centers for Education & Research on Therapeutics (CERTs)
  - **Translate** John M. Eisenberg Clinical Decisions and Communications Science Center
- **Structured process to choose specific topics, with stakeholder input**
  - 14 priority diseases/conditions

15 Sep 2008	Modified Insulin Most Effective for Controlling Post-Meal Blood Sugar Levels
18 Jun 2008	New Spanish-language Consumer Guide Compares Oral Diabetes Medications
4 Feb 2008	Outcomes Vary for Prostate Cancer Patients Choosing Surgery; Overall, No Treatment Proven Superior
17 Dec 2007	Many Osteoporosis Medications Prevent Fractures, but None Is Proven Best
19 Nov 2007	Combining Medications Often Best Strategy To Battle Rheumatoid Arthritis
1 Nov 2007	Common Medications Provide Equal Blood Pressure Control
15 Oct 2007	Surgery More Likely than Angioplasty To Relieve Pain for Patients with Coronary Artery Disease
17 Sep 2007	AHRQ and FDA To Collaborate in Largest Study Ever of Possible Heart Risks with ADHD Medications

ARRA Stimulus Funding

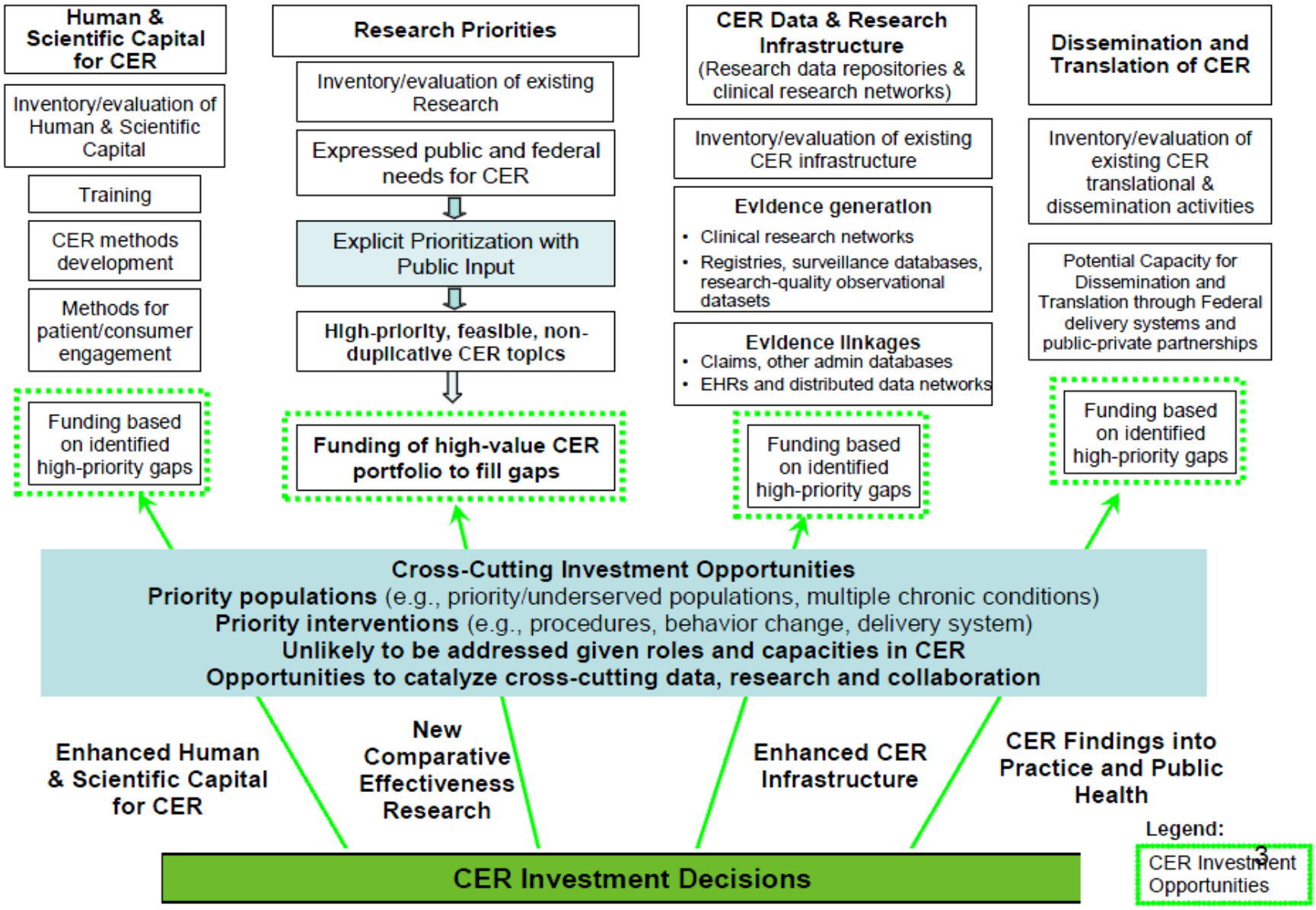
Stimulus funds for CER must be obligated by September 30, 2010, but may be spent by contractors and grantees over a longer timeframe, as appropriate for each project.

- **$1.1 Billion for Comparative Effectiveness Research**
  - $400 Million – Office of the Secretary
  - $400 Million – NIH
  - $300 Million – AHRQ (plus $50 Million in FY 2009 AHRQ appropriation)

- **Federal Coordinating Council for Comparative Effectiveness Research**
  - **Definition:** The conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings.
  - **Purpose:** To improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers…about which interventions are most effective for which patients under specific circumstances.
    - Assess an comprehensive array of health-related outcomes for diverse patient populations and subgroups.
    - Interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
    - Necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and to actively disseminate the results.

http://www.hhs.gov/recovery/programs/cer/cerannualrpt.pdf

Strategic Framework for CER



FCC CER Recommendations

- **Minimum threshold criteria**
  - Included within statutory limits of Recovery Act and the Council's definition of CER
  - Potential to inform decision-making by patients, clinicians, or other stakeholders
  - Responsiveness to expressed needs of patients, clinicians, or other stakeholders
  - Feasibility of research topic (including time necessary for research)

- **Prioritization criteria for scientifically meritorious research and investments**
  - Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)
  - Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and to engage communities in research
  - Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
  - Addresses need or gap unlikely to be addressed through other organizations
  - Potential for multiplicative effect—foundation for future CER (data infrastructure, methods development and training) or generates additional investment outside government

Guidance for Funding Decisions

- **FCC CER Recommendations** http://www.hhs.gov/recovery/programs/cer/cerannualrpt.pdf

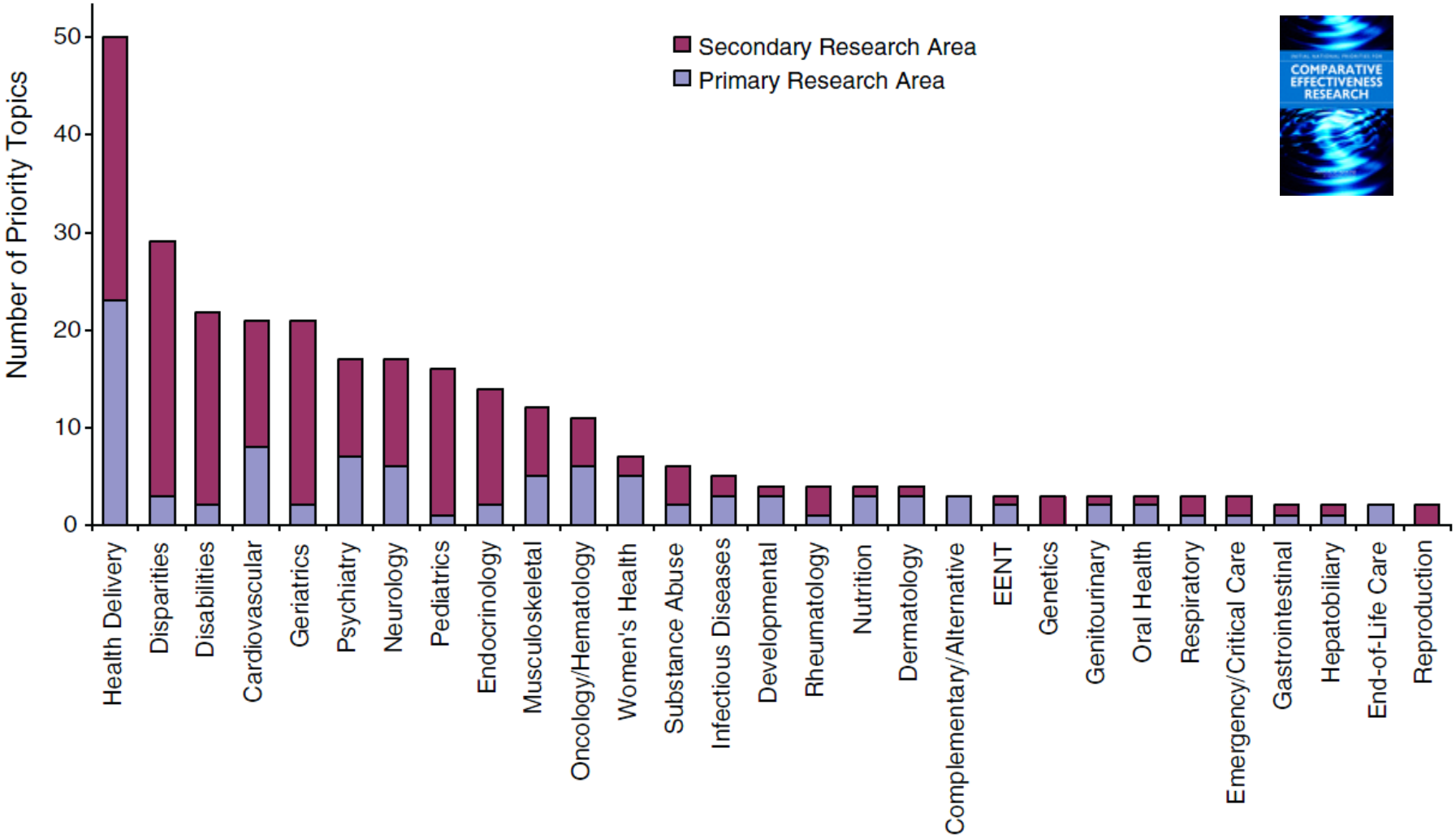
- **Priority Conditions in MMA 2003** http://effectivehealthcare.ahrq.gov/aboutUs.cfm?abouttype=program
  - Arthritis and non-traumatic joint disorders, plus osteoporosis
  - Cancer
  - Cardiovascular disease, including stroke and hypertension
  - Dementia, including Alzheimer's Disease
  - Depression and other mental health disorders
  - Developmental delays, attention-deficit hyperactivity disorder, and autism
  - Diabetes mellitus
  - Functional limitations and disability
  - Infectious diseases, including HIV/AIDS
  - Obesity
  - Peptic ulcer disease and dyspepsia
  - Pregnancy including preterm birth
  - Pulmonary disease/asthma
  - Substance abuse

- **IOM Priority Topics** (June 2009; see next slide for classification by research area)

  http://content.nejm.org/cgi/reprint/361/4/325.pdf

  http://www.nap.edu/catalog.php?record_id=12648

IOM's 100 Priority Topics for CER by Research Area



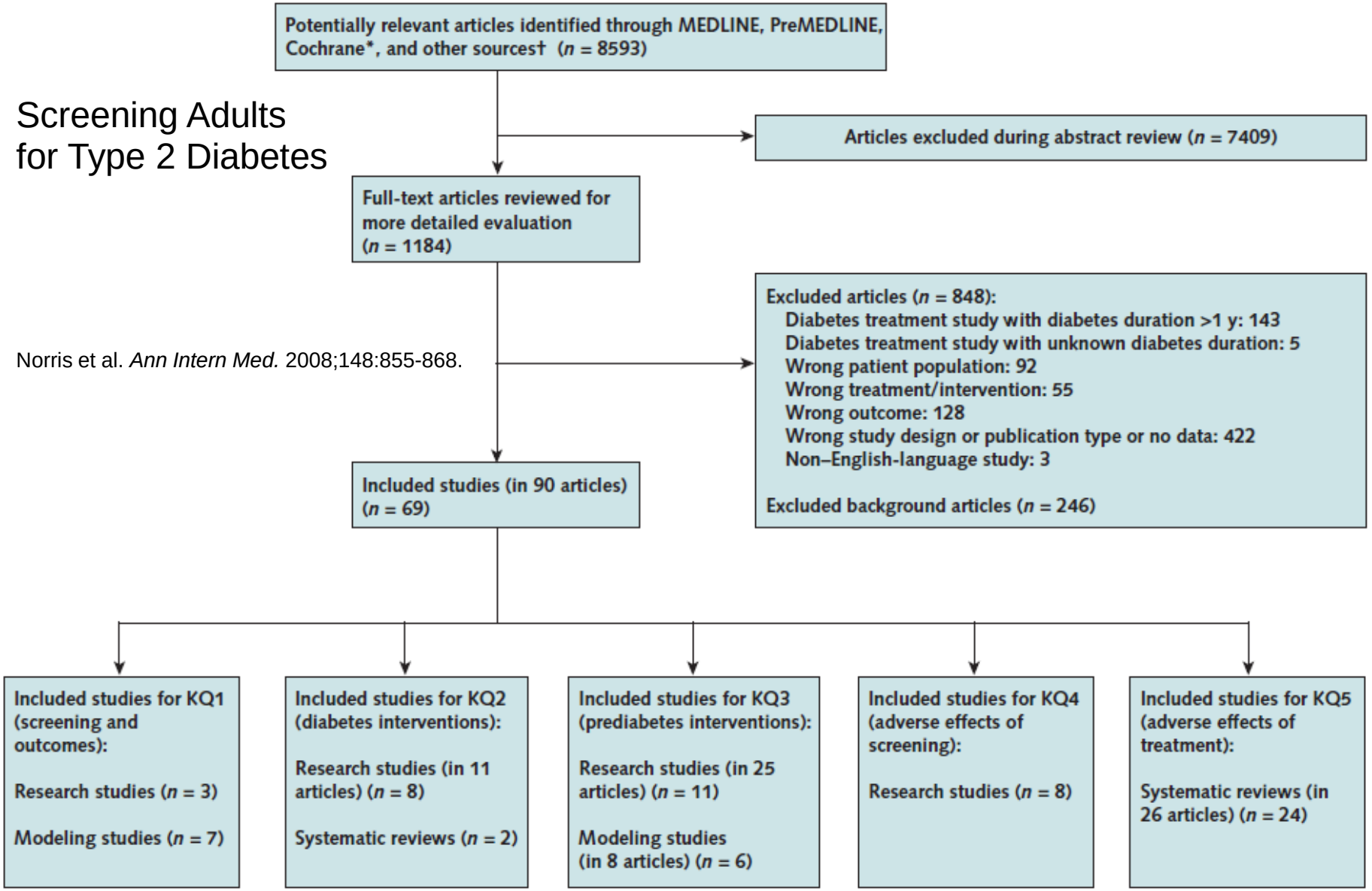
http://www.nap.edu/catalog.php?record_id=12648 (Section 5, page 5-3)

CER Methods

- **Meta analysis of existing studies**
  - Start with key clinical questions
  - Consider quality and relevance of evidence
- **Inferring causality from non-randomized studies**
  - A is associated with B
  - A causes B
- **Combination with QI methods**
  - Large database → inference
  - Data-driven QI—improvement cycles

USPSTF Evidence Review

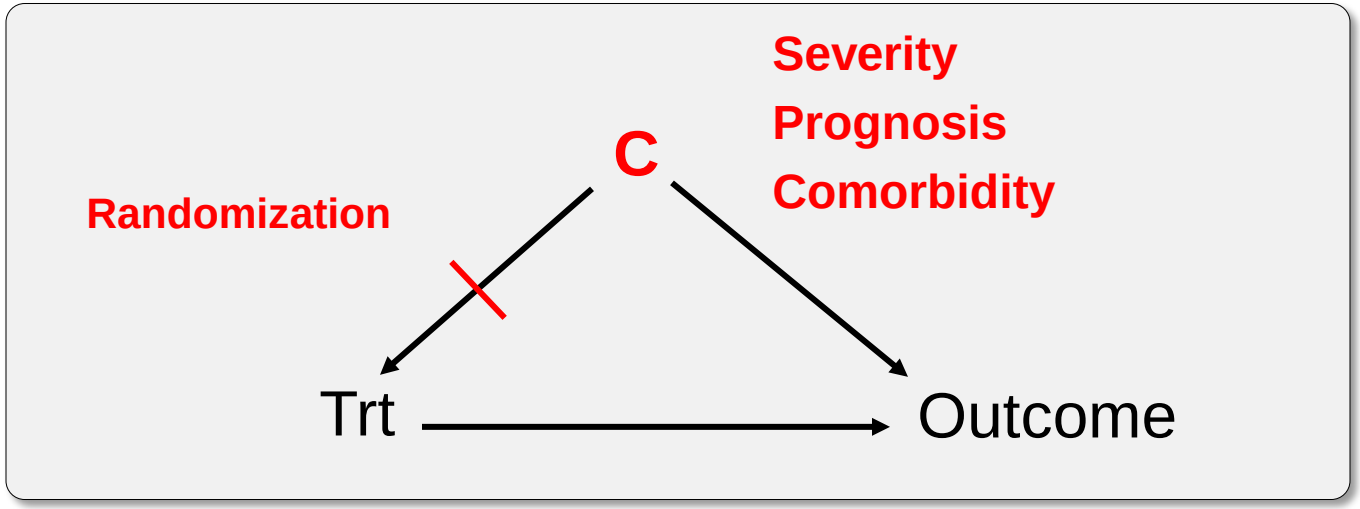
Screening Adults for Type 2 Diabetes



Norris et al. *Ann Intern Med.* 2008;148:855-868.

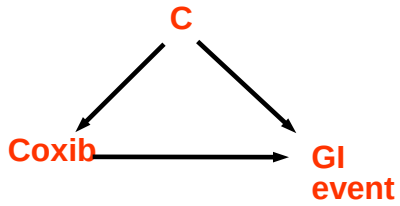
Inference from Non-Randomized Studies

- **Potential for bias due to patient selection into treatment groups**
- **Patient factors are confounders (C) if they are associated with treatment choice and are also independent predictors of outcome**

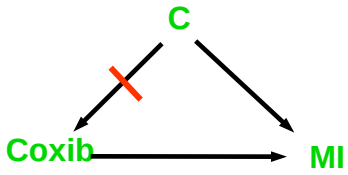


"Confounding by indication"

- **Depends on "intentionality of treatment effect" by provider**



Effectiveness research



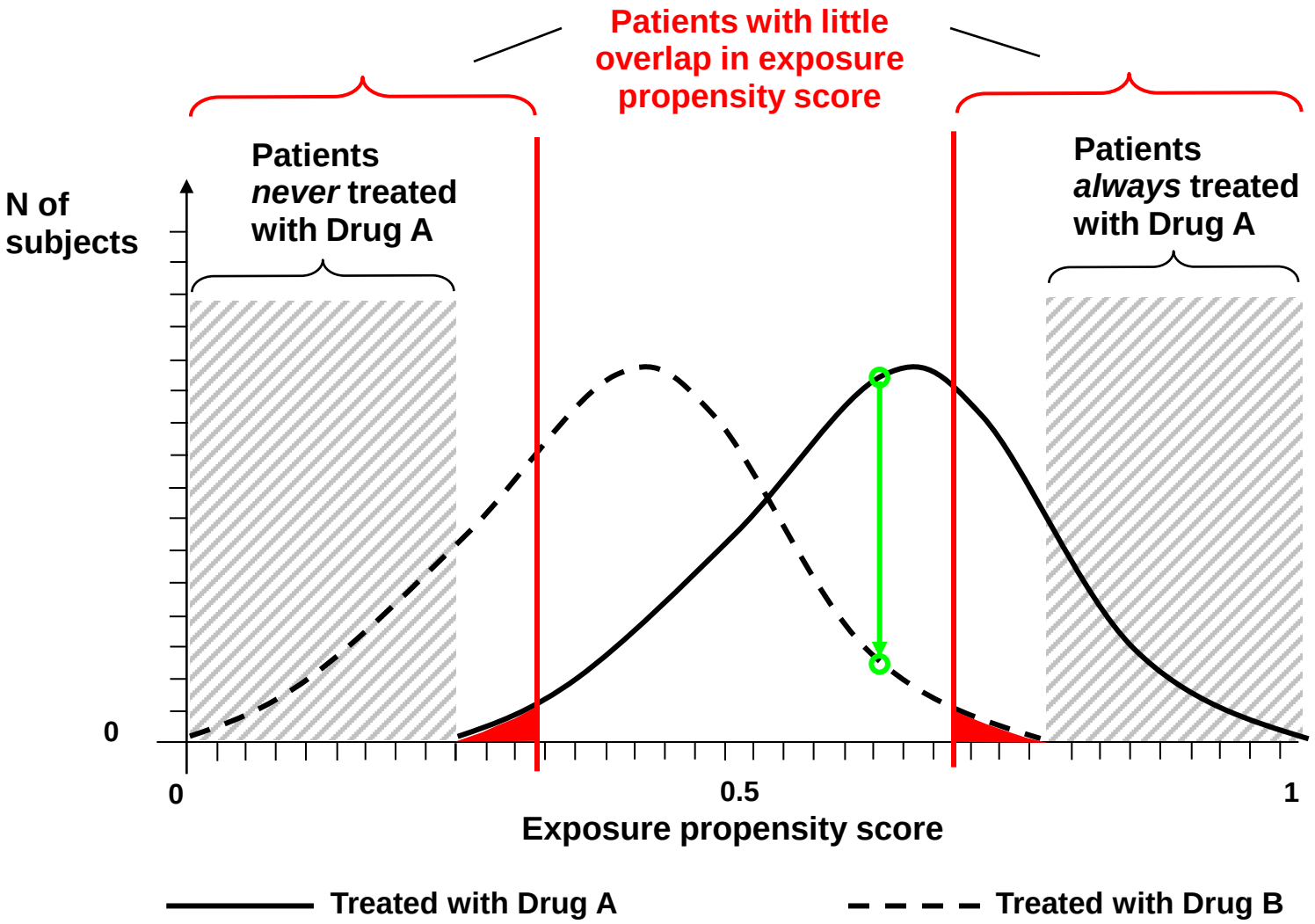
Safety research

Sebastian Schneeweiss, MD, ScD
Controlling for Bias in Non-randomized Studies
Methods of Comparative Effectiveness Research
AcademyHealth Annual Research Meeting 2009

Schneeweiss S. Developments in post-marketing comparative effectiveness research. Clin Pharm & Therap. August 2007; 82(2):143–156.

Propensity Score Matching

- Identify patients with equal *likelihood* of receiving treatment—but some will actually receive treatment, and others will not



Schneeweiss, *ibid.*

Organized Systems of Care

Structure

- Horizontal integration, efficient decision-making
- Safety as an intrinsic system priority
- Primary care centered, team-based care model
- Emphasis on prevention and wellness, rather than illness care
- Value orientation—shared benefits, incentives
- Accountability and performance transparency—individually, team-level
- Clinical IT—well-designed, consistently used
- Performance transparency

Randomized Controlled Trials

Expert Consensus

Real-World Data

Facilitated Collaboration

Care Protocols for Complex Patients

- Medication optimization
- Patient education and support for self-care
- Outreach, pro-active care
- Risk-stratified interventions
- Lifestyle support
- End-of-life care

Process

- Coordination of care
  - Interactions among members of the care team
  - Support for planned visits, pro-active care
  - Continuity across transitions of care
  - Feedback of performance data
  - Serious attention to continuous improvement

Outcomes

- Clinical parameters
- Perceived health status
- Overall cost of care
- Reimbursement impact

Anceta AMGA's Collaborative Data Warehouse

Recommendations for Comparative Effectiveness Research

1. Make the following two deliverables a priority for funding:
   - Set of optimized protocols for complex patients
   - Learnings about replicating data-driven improvement
2. Study delivery system design: Which aspects of structure and process are the strongest drivers of high-quality care at low relative cost, and which of those can be replicated?

AMGA
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"Typical" Cost

- Medicare claims data for comparable patients treated in other settings
- Limited outcome data

Δ

Cost in Organized Systems

- Medicare claims data for patients of organized systems of care
- Limited outcome data

Optimize Care Protocols and Understand Key Drivers of Outcomes and Cost for Complex Patients

Calibrate Cost vs. Other Organizational Models

Consideration of Cost-Effectiveness

- **Concerns of stakeholders**
  - Providers/vendors
  - Patients
- **Social imperative**
  - Control growth in healthcare costs

- The ARRA Conference Report recognizes that a “one-size-fits-all” approach to patient treatment is not medically appropriate.
- “ARRA statutory language signifies the preeminence of clinical outcome-based research and analysis (as opposed to research driven by cost analysis and cost containment).”