(Patient-Centered )
Comparative Effectiveness Research

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Doctor, should I be taking aspirin to prevent a heart attack? I know that I have some worrisome risk factors…
Should I?
We all want to get the right treatment to the right patient at the right time.

Comparative effectiveness research generates the evidence to inform the decisions that we make as clinicians, and as payers, and as patients.
A Definition of Comparative Effectiveness Research

“... the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers and policy makers to make informed decisions that will improve health care at both the individual and population levels.”

Institute of Medicine, 2009
Questions, questions, questions

What do patients want to know …
What do patients want to know …

- Should I take aspirin?
- Should I start mammography now at age 40?
- Should I have my cancerous prostate removed or will I be safe just waiting for a bit?
- Should I take warfarin or one of the newer medicines to treat my blood clot?
What do doctors want to know …
What do doctors want to know …

• Should I use the robot in this hysterectomy or the usual open method?
• Should I recommend colonoscopy or are the new DNA-based stool cards adequate?
• Are the new medicines for diabetes better than metformin, which I always prescribe?
Questions, questions, questions

What does Medicare want to know…
What does Medicare want to know…

- Should we cover implantable defibrillators?
- Should we cover home care services after hip replacements?
- How often should we cover geriatrician visits for residents in nursing homes?
**Comparative effectiveness research**

**Translational research** studies how best to move evidence across the research continuum, from the lab bench to the patient’s bedside, and from there to the “curbside” – communities where patients and their families live, learn, work, and play. The faster the uptake of credible evidence, the quicker health care and health may improve, and the greater the returns on the nation’s research investment.
Why is this Research Important?

- Many important health care decisions have little scientific evidence
- Quality and value is uncertain
- Economic implications of increasing health care spending
- Slow translation into practice of evidence-based practices
What should be studied?

- The Institute of Medicine (IOM) was tasked with considering priorities for CER research funding (2009)
- IOM panel prioritized 100 research questions into 4 quartiles
Establish a prospective registry to compare the effectiveness of treatment strategies for low back pain without neural involvement.

Establish a registry to compare the effectiveness of treatment strategies for ductal carcinoma in situ (DCIS).

Establish a registry to compare the effectiveness of treatment strategies (e.g., pharmacologic and social/family support) for behavioral disorders in home and institutional settings.

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Health care delivery systems
### Who funds this research?

<table>
<thead>
<tr>
<th>Agency for Healthcare Research and Quality - AHRQ (1999)</th>
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<tr>
<td>AHRQ (in HHS) is the only federal research agency with the sole purpose of producing evidence to make health care safer; higher quality; more accessible, equitable, and affordable; and to ensure that the evidence is understood and used.</td>
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<tr>
<td>Committed to training the next generation of comparative effectiveness researchers.</td>
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<tr>
<th>Patient Centered Outcomes Research Institute (2010)</th>
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<td>PCORI funds research that will help patients choose healthcare options that best meet their needs.</td>
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<tr>
<td>Funds research that advances the quality and relevance of the evidence concerning how disease can effectively be diagnosed, treated, monitored and managed.</td>
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Highlighting some comparative effectiveness research and its impact
AHRQ invested in Dr. Peter Pronovost’s Comprehensive Unit-based Safety Initiative (CUSP) in 2003

He asked … is there a better way to prevent central line infections than what we are doing?

Collectively, more than 1,100 hospitals and 1,800 CUSP teams nationwide participated in a national initiative based on Dr. Pronovost’s research to eliminate catheter line infections.
Evidence-based Practice Centers

• Since 1998, EPCs have produced >500 comprehensive systematic literature reviews
• Used as the evidence
  – To support the U.S. Preventative Services Task Force recommendations
  – To support professional society guidelines
  – To inform NIH consensus conferences
  – To inform CMS coverage decisions
Treatment of Nonmetastatic Muscle-Invasive Bladder Cancer
Management of Acute and Recurrent Gout: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Russell P. Harris, MD, MPH; and Mary Ann Forciea, MD; for the Clinical Guidelines Committee of the American College of Physicians

Description: The American College of Physicians (ACP) developed this guideline to present the evidence and provide clinical recommendations on the management of gout.

Methods: Using the ACP grading system, the committee based these recommendations on a systematic review of randomized, controlled trials; systematic reviews; and large observational studies published between January 2010 and March 2016. Clinical outcomes evaluated included pain, joint swelling and tenderness, activities of daily living, patient global assessment, recurrence, intermediate outcomes of serum urate levels, and harms.

Target Audience and Patient Population: The target audience for this guideline includes all clinicians, and the target patient population includes adults with acute or recurrent gout.

Recommendation 1: ACP recommends that clinicians choose corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine to treat patients with acute gout. (Grade: strong recommendation, high-quality evidence)

Recommendation 2: ACP recommends that clinicians use low-dose colchicine when using colchicine to treat acute gout. (Grade: strong recommendation, moderate-quality evidence)

Recommendation 3: ACP recommends against initiating long-term urate-lowering therapy in most patients after a first gout attack or in patients with infrequent attacks. (Grade: strong recommendation, moderate-quality evidence)

Recommendation 4: ACP recommends that clinicians discuss benefits, harms, costs, and individual preferences with patients before initiating urate-lowering therapy, including concomitant prophylaxis, in patients with recurrent gout attacks. (Grade: strong recommendation, moderate-quality evidence)

Gout, one of the most common forms of inflammatory arthritis, is caused by accumulation of excess urate crystals (monosodium urate) in joint fluid, cartilage, bones, tendons, bursas, and other sites. Patients experience joint swelling and pain during gout attacks, known as acute gouty arthritis. In some patients, the frequency and duration of acute attacks increase over time and lead to chronic gout, which may be associated with deposits of uric acid crystals known as tophi. Risk factors for gout include overweight or obesity; hypertension; alcohol intake; diuretic use; a diet rich in meat; and had gout (5). This percentage increased by about 1% in the 10 years before 2007, probably because of a parallel increase in conditions associated with hyperuricemia. An estimated $1 billion is spent annually on ambulatory care for gout, largely on treatments and prescription medications (6).

Management of gout includes both pharmacologic and nonpharmacologic approaches. Pharmacologic therapies focus on urate-lowering strategies and anti-inflammatory drugs (Table 1). Nonpharmacologic man-
Generates Important Results for Medical Practice

- From VA's Surgical Quality Improvement Program (VASQIP)
- Is bariatric surgery more effective at preventing deaths than usual care (no surgery) in morbidly obese veterans?
Investigators identified 2,500 Veterans (74% male) who underwent bariatric surgery in VA bariatric centers.
Generates Important Results for Medical Practice

Original Investigation

Comparative Effectiveness of Intravenous vs Oral Antibiotics for Postdischarge Treatment of Acute Osteomyelitis in Children

Published online December 15, 2014.
Are oral antibiotics as good as intravenous antibiotics after hospital discharge?

Children treated with antibiotics by mouth did NOT have more treatment failures than those treated with antibiotics intravenously.

Far fewer adverse events requiring trips to the emergency room.
Pragmatic Trial Infrastructure

PCORNet

- Clinical Data Research Networks (CDRNs) are system-based networks that originate in healthcare systems.
- Patient-Powered Research Networks (PPRNs) are networks operated and governed by groups of patients and their partners.
Example:

PaTH is a Clinical Data Research Network comprised of:
- Geisinger Health System
- Johns Hopkins
- Penn State College of Medicine
- Temple University’s Lewis Katz School of Medicine
- University of Pittsburgh
- University of Utah
ADAPTABLE, the Aspirin Study

ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-Term Effectiveness): 3 year pragmatic trial to compare the effectiveness of different doses of aspirin to prevent heart attacks and strokes in individuals living with heart disease.

- Embeds the trial into the usual healthcare setting, and leverages data from health systems to produce results that can be readily used to improve patient care.
What Outcomes are Important

• Clinical trials do not always measure outcomes that patients consider important or relevant.
• Makes it hard to know the value of an intervention to patients
• Patient-Centered Outcome Measures (PCOM) are measures that assess the impact of the disease and treatment on patients
Examples

PAIN

0  NO HURT
2  HURTS LITTLE BIT
4  HURTS LITTLE MORE
6  HURTS EVEN MORE
8  HURTS WHOLE LOT
10 HURTS WORST

No pain  Moderate pain  Worst pain
0  1  2  3  4  5  6  7  8  9  10
THE HAMILTON RATING SCALE FOR DEPRESSION

(to be administered by a health care professional)

Patient’s Name

Date of Assessment

To rate the severity of depression in patients who are already diagnosed as depressed, administer this questionnaire. The higher the score, the more severe the depression.

For each item, write the correct number on the line next to the item. (Only one response per item)

1. **DEPRESSED MOOD** (Sadness, hopeless, helpless, worthless)
   - 0 = Absent
   - 1 = These feeling states indicated only on questioning
   - 2 = These feeling states spontaneously reported verbally
   - 3 = Communicates feeling states non-verbally—i.e., through facial expression, posture, voice, and tendency to weep
   - 4 = Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. **FEELINGS OF GUILT**
   - 0 = Absent
   - 1 = Self reproach, feels he has let people down
   - 2 = Ideas of guilt or rumination over past errors or sinful deeds
   - 3 = Present illness is a punishment. Delusions of guilt
   - 4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. **SUICIDE**
   - 0 = Absent
   - 1 = Feels life is not worth living
   - 2 = Wishes he were dead or any thoughts of possible death to self
Others

• Survival
• Out of pocket costs
• Time to return to work
Aspirin?
Let me find the evidence...
Evidence Synthesis
Number 131

Aspirin for the Primary Prevention of Cardiovascular Events: A Systematic Evidence Review for the U.S. Preventive Services Task Force

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
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Contract No. HHSA-290-2012-00015-4, Task Order No. 2

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AHRQ Publication No. 13-05195-EF-1
September 2015
# Final Recommendation Statement: Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer: Preventive Medication

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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## Recommendation Summary

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<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
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<tbody>
<tr>
<td>Adults aged 50 to 59 years with a ≥10% 10-year CVD risk</td>
<td>The USPSTF recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.</td>
<td>B</td>
</tr>
<tr>
<td>Adults aged 60 to 69 years with a ≥10% 10-year CVD risk</td>
<td>The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a high value on the potential benefits than the potential harms.</td>
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Summary

- CER described in the literature since the 1950s
- Pragmatic trials described in the late 1960s (in France)
- Focus on health services research by the VA in the 1970s
- Growing attention to CER in the 1980s with appreciation for “evidence” and rising healthcare costs
- Establishment of AHRQ and later PCORI
- CER recognized as the essential late part of the translational pathway to improved patient outcomes, in a sustainable healthcare system
PCORI is funded through the PCOR Trust Fund, which was established by Congress. The PCOR Trust Fund receives income from three funding streams:

- appropriations from the general fund of the Treasury ($120M in FY15)
- transfers from the Centers for Medicare and Medicaid trust funds ($90M in FY15), and
- a $2.26 per covered person per year fee assessed on private insurance and self-insured health plans ($210 M in FY15)