

## Does observational research support the goals of comparative effectiveness research (CER) ?

Rachael Fleurence, PhD  
Oxford Outcomes  
November 6<sup>th</sup>, 2011

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## Introductions

The Role of RCTs and observational Research in meeting CER/PCOR goals: Rachael Fleurence, PhD

Analytical challenges in observational research: Alex Exuzides, PhD

Use of observational research at NICE: Hannah Patrick, MD

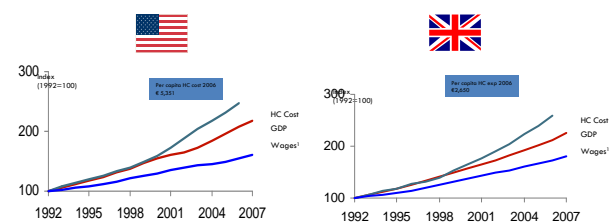
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## Outline

- The Rise of CER/PCOR
- Evidence for CER/PCOR
- The role of the RCTs
- The role of observational research
- Conclusions

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## Rising HC costs not matched by rise in quality



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## Many problems plague the US HC system



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## Current focus on PCOR



Affordable Care Act 2011



Creation of PCORI



Rising bar for market access



High uncertainty around evidence standards

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## What kind of evidence for CER?



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## Better evidence informed by the patient: Patient Centered Outcomes Research

**Comparative** Comparison of alternative treatments and interventions on relevant outcomes

**Real World** Real-world and timely evidence

**Patient Centered** Emphasis on subgroup populations  
Identifying, measuring outcomes relevant to the patient

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## The role of the RCT

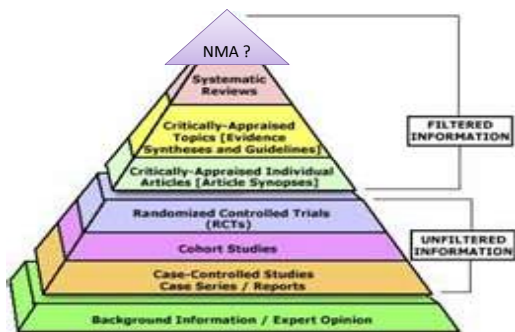
- Preserves randomization
- Comparative evidence
- Timely ?
- Real world ?
- Patient-centered ?

## Evidence-based medicine hierarchy

Table 2. Hierarchy of research design

I	Evidence obtained from at <u>least one properly randomized controlled trial</u> .
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

## Evidence Hierarchies with SR



## Evidence that is comparative

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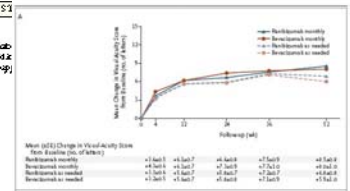
MAR 10, 2011 VOL 364 NO 10

#### Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration

The CATT Research Group

ASST

**BACKGROUND:** Clinical trials have established the efficacy of ranibizumab versus age-related macular degeneration (AMD). In addition to ranibizumab, bevacizumab is used off-label to treat AMD, despite the absence of comparative data.



## Real world, timely and patient centered evidence ?



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Perspective

Comparative Effectiveness Research and Patients with Multiple Chronic Conditions

Mary E. Tenetti, M.D., and Stephanie A. Studenski, M.D.  
N Engl J Med 2011; 364:2478-2481 | June 30, 2011

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## Improving RCT efficiency: Adaptive Trials

Trials in which key **design parameters change** during trial execution based upon ***a priori* predefined rules** and **accumulating data** from the trial to **achieve goals of validity, scientific efficiency, and safety**



ALLHAT : Bayesian adaptive trial design study funded by the NIH.

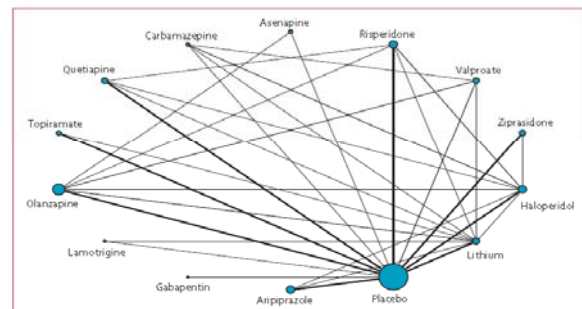
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## The role of observational research

- Limitations of observational research are well known
- Network meta-analyses
- Health information technology

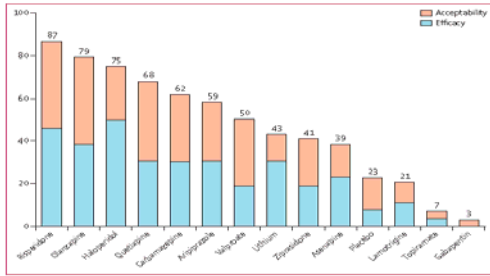
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## NMA: Network of Evidence



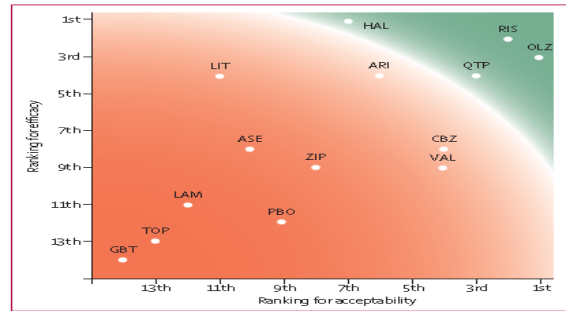
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## Improving timeliness and comparativeness: Drugs by probability of being the “best” treatment



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## NMA: Ranking of anti-manic drugs



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## Timely, real-word data: EHR and HIT



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## Example: DARTNet

ACADEMIA AND CLINIC

Annals of Internal Medicine

### An Electronic Practice-Based Network for Observational Comparative Effectiveness Research

Wilson D. Pace, MD; Maribel Chirbaes, RN, BSN; Robert J. Valicak, PhD; Elizabeth W. Sklar, MSc; Elise C. Brandt, BS; and David R. West, PhD

The Distributed Ambulatory Research in Therapeutics Network (DARTNet) is a federated network of electronic health data from 6 organizations representing more than 800 clinicians and more than 400,000 patients. DARTNet was designed to increase knowledge of the comparative effectiveness of prescription medications and medical devices. Traditional observational comparative effectiveness research is conducted using large datasets, such as claims databases. Such databases do not provide important clinical information that is critical to understanding comparative effectiveness, by linking elec-

tronic health records, laboratory and imaging data, and administrative data from diverse and geographically disparate patients. DARTNet provides important new insight into the comparative effectiveness of oral diabetes medications, and it is ready for expansion to further enable effectiveness research.

Ann Intern Med. 2009;151:338-340.

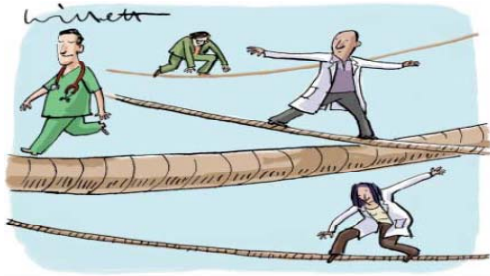
For author offprints, see end of text.

This article was published at www.annals.org on 28 July 2009.

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## Conclusions



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