Questions to ask after the first RCT demonstrates efficacy of a new therapy?

- How much better are the outcomes?
- Were the right outcomes measured?
- What was the comparison group in the study?
- Were the patients in the study representative of the broader population of patients for which the new therapy is targeted?
- What kind of training would be required to provide the therapy described in the study?
- How much of an investment is required to “try out” the new therapy?

Questions to ask after the first RCT demonstrates efficacy of a new therapy?

- How much does the new therapy cost?
- Will payers cover the costs? What are the out-of-pocket costs?
- Will providers adhere to the study protocol in the clinical trial?
- Will patients adhere to the study protocol in the clinical trial?
- After more widespread use, is the safety of the new therapy confirmed?
- After more widespread use, is the effectiveness of the new therapy confirmed?
Health Services Research

- Multidisciplinary field of inquiry, both basic and applied, that examines the use, costs, quality, accessibility, delivery, organization, financing, and outcomes of health care services

Health Services Research

- Descriptive
  - Who receives care?
  - What care is provided for a condition?
  - Does health manpower match need?
  - Ex.: How do you measure the "natural history" of a disorder without accounting for treatment received?

- Quality of care
  - Is care patient-centered, timely, accessible, evidence-based and safe? (IOM Report: Crossing the Quality Chasm?)
  - Is there variation in medical care and how is that explained?
Efficacy and Effectiveness

- Efficacy: Does an intervention improve outcomes under ideal conditions?
- Effectiveness: Does the intervention improve outcomes in routine or usual clinical care?

Comparative Effectiveness Research (CER)

- Definition from the IOM Report on Priorities for CER
  - "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."

- Definition from the FCC-CER Report
  - CER is 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. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.
  - To provide this information, CER must assess a comprehensive array of health-related outcomes for diverse patient populations and subgroups.
  - Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
  - This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results."
Comparative Effectiveness Research

- Clinical trials in everyday care settings
  - Practice-based research networks
  - Compare two active treatments and not placebo
- Observational assessments
  - Clinical research registries
  - Administrative data (ex. CMS)
- Evidence-synthesis

Evidence Synthesis

- Why is the result of so many evidence synthesis exercises that there are many relevant studies but few address the most pressing question?
- Meta-analysis
- Decision Analysis
Why does efficacy not always translate to effectiveness?

- Patients in ideal trial are different than usual care
  - Less comorbidity (frequently younger)
  - More willing to accept side effects
  - Not paying for the treatment
  - More rigorous follow up to continue with treatment
- Providers are different
  - Better training
  - Willing to follow protocol

Evaluating Effectiveness

- Clinical trials not that common
- Using observational methods
  - Large datasets with less depth
  - Large sample needed to assess safety
  - Most vexing issue is how to control for case-mix? Patient differences in who gets one intervention/treatment as compared to another
    - Propensity scores
    - Instrumental variables

Propensity Scores

- Propensity score is the probability of taking treatment given a vector of observed variables.
- If we take individuals with the same propensity score, and divide them into two groups –those who were and weren’t treated-the groups will be approximately balanced on the variables predicting the propensity score.
Moving to Ultimate Implementation

• Efficacy to Effectiveness
• Comparative Effectiveness
  – Deciding on best approach in usual care settings
• Knowledge Implementation or Knowledge Transfer
  – More quickly moving evidence-based approaches to all practice settings

Diffusion Theory

• Everett Rogers
• Agricultural Cooperative Agents
• Diffusion depends on:
  – Relative advantage
  – Compatibility
  – Complexity
  – Trialability
  – Observability

Strategy for translating evidence into practice
Cost-Effectiveness

- Costs
  - Direct
  - Indirect
- Effectiveness
  - Quality adjusted life years
- Cost-effectiveness
  \[
  \frac{\text{Costs}(\text{new}) - \text{Costs}(\text{old})}{\text{Effectiveness}(\text{new}) - \text{Effectiveness}(\text{old})}
  \]

Good example for Observational Analysis

- Phillip S Wang et al
- Risk of Death in Elderly Users of Conventional versus Atypical Antipsychotic Medications
- NEJM 2005; 353:2335-41

Conclusions

- Goal of medical research does not stop when treatment/diagnostic test evaluated in academic centers
- Need to always consider ultimate customers of research
- Secondary translation is a science but with a different methodology toolbox