The Right Approach for the Right Question™

Comprehensive Approaches to Evidence Development for Real-World and Late Phase Research

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Nancy Dreyer, MPH, PhD

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Your Presenters

Richard Gliklich, MD
Professor, Harvard Medical School, President, Quintiles Outcome

Dr. Gliklich is President of Quintiles Outcome, which is the leading provider of services and integrated technologies for real-world and late phase research. Dr. Gliklich is a frequently invited speaker on post-approval research and patient registries and has served on numerous advisory boards. He has published extensively in the areas of outcomes assessment and patient registries as well as in the clinical area of diseases of the head and neck. He is a senior editor and author of the Agency for Healthcare Research and Quality (AHRQ) handbook, “Registries for Evaluating Patient Outcomes: A User’s Guide.” He is editor of a textbook on outcomes and performance measurement in clinical practice, “Profiting from Quality: Outcome Strategies for Medical Practice” (Jossey-Bass, Inc., 1999).

Nancy Dreyer, MPH, PhD
Global Chief of Scientific Affairs, Senior Vice President, Quintiles Outcome

Dr. Nancy Dreyer is Global Chief of Scientific Affairs and Senior Vice President at Quintiles Outcome, a leading provider of strategies and information-based solutions for marketed drugs and medical devices. She leads a team of researchers who design, conduct, and interpret observational research on comparative effectiveness and safety, and quality improvement programs. Her recent accomplishments include serving as a senior editor and co author of the handbook, “Registries for Evaluating Patient Outcomes: A User’s Guide,” commissioned by the US Agency for Healthcare Research and Quality and her leadership role in developing guidance on Good Research Practices for Observational Studies of Comparative Effectiveness.
Agenda

- Evolution of Evidentiary Needs
- What is Comprehensive Evidence Development
- Determining the Right Question
- Delivering the Right Approach
- The Way Ahead
Today’s Webinar Audience

- Academia
- Biostatistician
- Clinical Operations
- Epidemiology
- Health Economics/Health Outcomes
- Medical Affairs
- Market Access
- Regulatory Affairs
- Risk Management
- Other
Polling Questions

• A small number of polling questions have been added to today’s webinar to make the session more interactive
Polling Question

• Which research approach do you use most often?

> Interventional (randomized) Studies
> Prospective Observational Studies
> Retrospective Database Studies
Polling Question

• Why do you use that approach most often?
  > It provides the most valid results
  > It’s what the decision-makers (regulators, payers, etc.) ask for
  > It answers the question most efficiently
Evolution of Evidentiary Needs

Research Approach

- Genomics
- Patient Reported Outcomes
- Observational Research
- Pragmatic Trials
- Randomized Controlled Trials
- Case Reports

Stakeholder Expansion

1900 - 2020

Physician - Regulator - Payer - Patient

Evidentiary Needs

- Personalized Medicine
- Convenience, Quality of Life
- Safety, Effectiveness & Value
- Quality, Safety, Efficacy
- Expert Opinion

Research Approach
Incorporating stakeholder perspectives in developing a translation table framework for comparative effectiveness research

This project used a stakeholder-driven process to understand the factors that drive the selection of study designs for comparative effectiveness research (CER). The project assembled a diverse stakeholder committee to explore the basis of a translation framework and gathered input through surveys, interviews and an in-person meeting. Stakeholders recommended different study designs for the CER topic areas and identified different outcomes as the most important outcomes to study in each area. During the discussions, stakeholders described a variety of factors that influenced their study design recommendations. The stakeholder activities resulted in the identification of several key themes, including the need to have a highly specific detailed research question before discussing appropriate designs and the need to use multiple clinical potentially of different designs to address the CER topic.

Journal of Comparative Effectiveness Research

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Research Question Varies with Perspective

<table>
<thead>
<tr>
<th>Decisions Relevant to Medical Therapies</th>
<th>Example: Therapy for Osteoporosis</th>
<th>Research Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Approval</td>
<td>Is slow release sodium fluoride safe and effective for preventing fractures?</td>
<td>Safety, Quality Efficacy</td>
</tr>
<tr>
<td>Drug Coverage</td>
<td>Which bisphosphonate drugs should be included on a drug formulary?</td>
<td>Effectiveness</td>
</tr>
<tr>
<td>Clinical Practice Guidelines</td>
<td>When should therapy for low bone density be initiated?</td>
<td>Effectiveness, Quality of Life</td>
</tr>
<tr>
<td>Patient Decisions</td>
<td>Should I take raloxifene, alendronate, or calcium and vitamin D to prevent osteoporosis?</td>
<td>Quality of Life, Convenience</td>
</tr>
<tr>
<td>Health Plans and Insurers</td>
<td>Should we pay for follow-up assessment of bone density in women on treatment, and how often?</td>
<td>Effectiveness</td>
</tr>
<tr>
<td>Health System Policies</td>
<td>Should we institute primary care-based ultrasound screening for osteoporosis?</td>
<td>Effectiveness</td>
</tr>
<tr>
<td>Quality Measurement</td>
<td>What is an appropriate measure of high quality care in the treatment of osteoporosis?</td>
<td>Effectiveness, Value</td>
</tr>
</tbody>
</table>

Atkins, D. Creating and Synthesising Evidence with Decision Makers in Mind. Medical Care 2007;45: S16-S22
The Right Approach for the Right Question

- INTERVENTIONAL
- PROSPECTIVE OBSERVATIONAL
- REGISTRIES
- EMR DATA ASSETS AND ANALYTICS
Let’s take a closer look
Study Designs

Interventional Designs

• Explanatory Randomized Controlled Trials
• Pragmatic Randomized Trials

Studies designed to test a hypothesis by modifying an exposure within the study population

Observational Designs

• Prospective Observational Cohort Studies and Patient Registries
• Retrospective analysis of existing clinical or administrative health insurance data

Studies that examine treatments, risk factors and outcomes without doing anything to change factors that influence them
Prospective Studies

If the outcome occurs after the research begins, it is prospective...
Hybrid Designs

May capitalize on speed, cost efficiency & strength of different methods

Utilize retrospective and prospective data to shorten time and cost

Conduct sub-studies along-side larger prospective studies for added value

- Large Pragmatic Trial
- Or
- Disease Registry
- Health Economic Study
- PRO Study
- Etc.
Electronic Health Records

Sufficient in themselves or a springboard?

Rich clinical data are becoming increasingly available for large populations, but may not have enough information on key items of interest due to:

- Care provided outside of the EHR network coverage
- Items may not be recorded or are difficult to retrieve, e.g., unstructured notes
- Follow-up may be limited or haphazard
Background

Objective: To describe the usual care practice patterns at sites providing initial care for a chronic disease; patterns of condition-specific care will be described overall and by site/provider characteristics

Approach

Retrospective data collection
  • Quarterly EMR data pull

Prospective data collection
  • Annual physician survey
  • Physician survey after each treatment change or referral
  • Patient survey after each treatment change or referral

Study Cohort: ~7 Integrated Delivery Networks (enrollment ongoing)

Value added

• Real-world evaluation of treatment patterns including the effect of first injectable therapies over time
• Novel hybrid approach add information about why physicians changed treatment practice and how patients perceive their health
Hybrid: “Randomized Registry Trial”

NEJM 2013;369:1587-97. TASTE Trial

- Patients enrolled from a registry and randomized
  - 7012 patients randomized from 11,709 eligible
  - Also followed cohort that did not undergo randomization
  - Primary end-point: all cause mortality at 30 days
  - Followed entirely through existing record systems in Sweden

Research Question:
Does thrombus aspiration before PCI improve 30-day mortality?

Answer:
NO
Rapid Randomization in the TASTE Trial, with Enrollment of Most Patients Receiving Primary Percutaneous Coronary Intervention (PCI). Adapted from the Institute of Medicine (www.iom.edu/~/media/Files/Activity%20Files/Quality/VSRT/LST%20Workshop/Presentations/Granger.pdf). The incremental cost of the Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) trial was $300,000, or $50 for each participant who underwent randomization.

Lauer MS, D’Agostino RB. NEJM 2013; 369:1579-1581
Access to patient communities offers a new channel for observational research.

**Observational Research**

- **Retrospective**: (EMR, Claims)
  - Unstructured (e.g., scanning blogs for adverse events)
  - Structured (e.g., TSQM data)

- **Prospective**: (Site-based enrollment)
  - Cross-sectional (e.g., burden of illness, disease prevalence)
  - Longitudinal (e.g., registries)

**Direct-to-Patient Research**
The research leading to these results was conducted as part of the PROTECT Consortium (Pharmacoepidemiologic Research on Outcomes of Therapeutics by a European ConsorTium, www.imi-protect.eu) which is a public private partnership coordinated by the European Medicines agency. The Project has received support from the Innovative Medicines Initiative Joint Undertaking (www.imi.europa.eu) under Grant Agreement no 115004, resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies’ in kind contribution.

The views expressed here are those of the author only.
PROTECT: New tools for data collection from consumers

**Background** - Pregnancy PhV studies have their limitations:

- **Health Care Professional (HCP) reporting**
  - Labour intensive research – Expensive
  - Limited HCP-participant interactions – loss of data
  - Reporting >HCP booking – loss of early pregnancy data

- **Electronic Health Record (EHR) integration**
  - Missing data – OTC medication, herbal/traditional remedies, homeopathic preparations, tobacco/alcohol/recreational drug use, cosmetic procedures
  - Prescribed/dispensed – maternal validation & accuracy

**Aims** - Assess the extent to which data collected directly from pregnant women via the internet and IVRS provides information on medication use and other potential risk factors throughout pregnancy and is suitable for research purposes
Recruitment Strategies

**Leaflets & posters**
Leaflets & posters in pharmacies are cumbersome to distribute and yielded ~0

**Social Media**
Social Media was slightly better, but time intensive & difficult to build a “following”

**Website Ads**
Website Advertisements yielded more, but require budget; expect wide range of costs

**Emails**
Emails from online pregnancy clubs performed best; also require budget
Expected key contributions

Can we get data earlier in pregnancy than traditional routes?

Is information of sufficient quality to be used for pharmacovigilance?

How important are data not captured by EHR or pharmacy databases?
Using Existing Digital Communities

• PATIENTS LIKE ME
• >220,000 members, 2,000+ conditions, >1 million treatment & symptom reports
Considerations when Using Data Collected Directly from Patients

In what situations will these types of data be useful for pharmacovigilance and safety?

How much follow-up is needed and what is the site’s track record?

How representative are these patients? How representative do they need to be?

What types of information can patients report accurately and when/what do you need to verify?
From the Post-Approval Summit at Harvard, 2013

“Eternal vigilance is the price of liberty”
- attributed to Thomas Jefferson

“Eternal vigilance is the price of reliable data”

With permission of Dr. Richard Platt

Mini-Sentinel
Polling Question

- Do you see your company as innovative in research approaches?
  - Still catching up to most companies like us
  - About the same as most companies like us
  - More innovative than companies like us
Conclusion

Paradigm Shift in Real-World Methodologies

- Stakeholder Need
- Research Question
- Insight
- Research Approach
Upcoming Events

Quintiles experts run regular webinars on Real-World & Late Phase services.

Topics include:

- DIABETES VALUE DEMONSTRATION
- ONCOLOGY VALUE DEMONSTRATION
- RARE DISEASE REGISTRIES
- EUROPEAN PHARMACOVIGILANCE LEGISLATION
- REGISTRIES 101
- MARKET ACCESS
- MAXIMIZING VALUE AND QUALITY IN PHASE IV

To register or view previous webinars please go to
www.quintiles.com/real-world-late-phase-webinars
Thank you

Questions?