Using Real-World Data for Outcomes Research and Comparative Effectiveness Studies

Kathy Lang, PhD
Christina Mack, MSPH, PhD
Your Presenters

Kathy Lang
Senior Director, EMR Data & Analytics, Quintiles

Dr. Lang is a health economist with more than 20 years of experience in the field of health economics and outcomes research, with exposure to both the consultant and pharmaceutical side of the business, and particular expertise in database research using a broad range of real-world data sources. She has designed and lead outcomes research studies across a wide array of therapeutic areas and study designs including model-based cost-effectiveness and budget impact analyses, trial-based economic evaluations, retrospective database studies, and software tools for field-based teams. She has published widely in peer-review journals and presented at scientific meetings.

Christina Mack
Associate Director, Epidemiology, Real-World & Late Phase Research, Quintiles

Dr. Mack is a pharmacoepidemiologist with global biopharmaceutical experience in applied epidemiologic research, methods development and observational study project management. She has experience with design and analysis of numerous large epidemiologic studies in various real-world data sources and is the lead scientist for the Quintiles COMPASS program, a large distributed data network. She holds a PhD and masters degree in Epidemiology from the University of North Carolina at Chapel Hill and a degree in Computer Science Engineering from the University of Notre Dame. Prior to her current role, Dr. Mack has held positions within large pharmaceutical companies and non-governmental organizations. Dr. Mack is an adjunct assistant professor of epidemiology at the University of North Carolina at Chapel Hill and is an active contributor, presenter and peer reviewer for leading journals and international conferences.
Agenda

• Background
• Continuum of sources
• Key considerations for selecting optimal source
• Study examples
• Q&A
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.
Using Real-World Data: Background
Background

• Advances have improved and expanded available real-world data sources for research use by the biopharmaceutical industry
  > Greater leverage of information technology for healthcare data administration
  > Strengthening of observational research methods

• Insights from real-world data have the potential to influence value-based purchasing and pricing and access to therapy

• Given the number of potential primary and secondary data sources available, selection of an appropriate source is challenging
Objectives

Pragmatic Approaches to Real-World Data Source Selection & Use

• Discuss evolving continuum of real world data sources
  > Real-world evidentiary needs across pharmaceutical product lifecycle

• Strengths & limitations of alternative types of real-world data

• Example applications using real-world data

• Key considerations in the selection of an appropriate source for outcomes research, safety and comparative effectiveness studies

With proliferation of Big Data & machine learning tools, the importance of forethought can get lost. But Big Data without intelligent analytics will fail to deliver meaningful insights, regardless of computer processing power.
# Evidentiary Needs

*Real-World Data Support Variety of Activities Across the Product Lifecycle*

<table>
<thead>
<tr>
<th>Preclinical</th>
<th>Phase I-II</th>
<th>Phase III</th>
<th>Peri-Launch</th>
<th>Phase IV</th>
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<tbody>
<tr>
<td>Market Sizing</td>
<td>Market Landscape</td>
<td>Competitor Reconnaissance</td>
<td>Registries</td>
<td>Safety Surveillance</td>
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<tr>
<td>Unmet Need</td>
<td>Economic Burden</td>
<td>Patient Burden</td>
<td>Global BOIs</td>
<td>Continuous Monitoring</td>
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<tr>
<td>Patient Profiling</td>
<td>Disease History</td>
<td>Treatment Patterns</td>
<td>Target Product Profile</td>
<td>Tailored Therapeutics</td>
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<tr>
<td>Early Modeling</td>
<td>Model Refinements</td>
<td>CE/BI Modeling</td>
<td>CEAs &amp; BIAs</td>
<td>Health Technology Assessments</td>
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<td>Endpoint Development</td>
<td>Labeled Claims</td>
<td>New Indications</td>
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<td>Endpoint Assessment</td>
<td>Global Value Dossiers</td>
<td>Comparative Effectiveness</td>
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<td>Instrument Validation</td>
<td>Piggyback Evaluations</td>
<td>Pricing &amp; Reimbursement</td>
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<td>Risk Sharing Arrangements</td>
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Polling Question

• In which phases of the product lifecycle have you done research involving use of real world data (check all that apply)?

• Phase I
• Phase II
• Phase III
• Phase IV
Using Real-World Data

- Monitor Safety and Evaluate Risk
- Demonstrate Efficacy and Effectiveness
- Gain Market Access

- Expand Labeling and Approved Indications
- Understand Natural History of Disease and Treatment

- COMPREHENSIVE EVIDENCE DEVELOPMENT
- INTERVENTIONAL
- PHASE IIIB/IV TRIALS
- PROSPECTIVE OBSERVATIONAL
- REGISTRIES
- RETROSPECTIVE DATA ASSETS AND ANALYTICS
Real-World Data Fundamentals

Sources as Defined by ISPOR

Sources of RW Data
Real-world data can also be categorized by type of data source. Our Task Force defined six such sources:
1) supplements to traditional registration RCTs; 2) large simple trials (also called practical clinical trials); 3) registries; 4) administrative data; 5) health surveys; and 6) electronic health records (EHRs) and medical chart reviews.

Results: We defined RW data as data used for decision-making that are not collected in conventional randomized controlled trials (RCTs). We considered several characteriza-
Real World Data Types

Primary Data

• **Supplements to traditional RCTs:**
  > Commonly known as trial-based or ‘piggyback’ evaluations
  > Useful for collecting health economic information alongside clinical trials (quality of life, PRO, healthcare utilization)

• **Large simple trials:**
  > Commonly known as pragmatic or naturalistic trials
  > Attempt to measure effectiveness of an intervention in a real-world setting (routine practice)

• **Registries:**
  > Include prospective cohort studies
  > Collect data on group of patients with a given condition

All involve a CRF or data collection instrument
Real World Data Types

Primary Data (Cont.)

- **Health surveys:**
  > Useful for basic epidemiologic data or macro-level views on utilization
  > Useful for obtaining PROs and patient and physician views

- **Medical chart reviews:**
  > Abstracting patient demographic and clinical data from patient charts

All involve a CRF or data collection instrument
Real World Data Types

**Secondary Data**

- **Administrative data:**
  - Also known as claims data
  - Collected for billing purposes
  - Organized by bill for service (inpatient, outpatient, physician, Rx)

- **Electronic health or medical records:**
  - Electronic health records also called electronic medical records (EMRs)
  - Aggregated from medical practices, giving point of entry to provider networks
  - Collected for patient care purposes
Real World Data Types
Secondary Data (Cont.)

- **Linked EMR-claims:**
  - Integrated delivery networks (IDNs)
  - A network providing patients with a continuum of care
  - Gives rise to innovative research possibilities
    - Hybrid designs
Classifying Real-World Data Sources

Two-by-Two Typology Facilitates Critical Review

<table>
<thead>
<tr>
<th>Primary Data Collection</th>
<th>Retrospective Designs</th>
<th>Prospective Designs</th>
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<tbody>
<tr>
<td></td>
<td>Medical Chart Review</td>
<td>RCT Piggybacks</td>
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<td>Pragmatic Trials</td>
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<td></td>
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<td>Registries</td>
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<td></td>
<td></td>
<td>Health Surveys</td>
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<tr>
<td>Secondary Data Collection</td>
<td>Administrative Claims EMR</td>
<td>Automated EMR Data Feeds</td>
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<tr>
<td></td>
<td>EMR</td>
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Classifying Real-World Data Sources

**Strengths & Limitations of Prospective Sources**

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<td>Health Surveys</td>
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</tr>
</tbody>
</table>

| Secondary Data Collection | Automated EMR Data Feeds |

**Key Strengths:**
- High degree of control over what data are collected—and how
- For stand-alone studies, fine-tuning of sample size is possible
- For stand-alone studies, upfront control of confounding & bias is possible, even for real-world care patterns

**Key Limitations:**
- Prospective data more costly than retrospective—sometimes by orders of magnitude
- For RCT piggybacks, no fine-tuning of sample size is possible—and statistical power is usually lacking for RW measures
- For RCT piggybacks, protocol-driven care undermines generalizability to real world
Classifying Real-World Data Sources

Strengths & Limitations of Retrospective Sources

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<tbody>
<tr>
<td>Medical Chart Review</td>
<td></td>
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</table>

| Secondary Data Collection | EMR                  |

- **Key Strengths:**
  - Data already exist in charts / computer systems ➔ Economy of data collection
  - Potential for enormous sample sizes almost instantaneously
  - Data reflect real-world patterns of care, not affected by study protocol
  - Data mining approaches can uncover key relationships not on clinical radar

- **Key Limitations:**
  - Data already exist in charts / computer systems ➔ What you see is what you get
  - Potential for enormous sample sizes, yes, but not for products in development
  - Numerous sources of confounding & bias, not all of which can be controlled
## RWD Practical Comparison

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Administrative Claims</th>
<th>Electronic Medical Records</th>
<th>Primary Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Details</strong></td>
<td>Basic demographics (age, sex) plus enrollment</td>
<td>Demographics plus vital signs, BMI, allergies, smoking status</td>
<td>Flexibility on what is collected (demographic and clinical characteristics and vitals and history)</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td>Drug code (name, form, strength), Rx fill date, amt supplied, dose &amp; freq for pharmacy-dispensed drugs; no OTC</td>
<td>Mostly same detail for Rx’s written (but no Rx fill date); current meds, including OTC products, available</td>
<td>Detail on medications prescribed including OTC</td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
<td>ICD-9 codes</td>
<td>ICD-9 codes, problem lists, severity, symptoms</td>
<td>Full detail from chart with flexibility on collection</td>
</tr>
<tr>
<td><strong>Procedures</strong></td>
<td>CPT® codes</td>
<td>CPT® codes</td>
<td>Full detail from chart with flexibility on collection</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td>CPT® codes, date; limited availability of lab results</td>
<td>CPT® codes, date, &amp; e-feed of lab results sometimes including pathology &amp; radiology</td>
<td>Detail on labs and pathology collected and results available</td>
</tr>
<tr>
<td><strong>Hospital</strong></td>
<td>Dates of admission &amp; discharge, diagnoses, major procedures; usually nothing on inpatient drugs</td>
<td>Hospital EMR: detail on all aspects of inpatient care, including day:time info; ambulatory EMR: not much</td>
<td>Full detail from chart with flexibility on collection</td>
</tr>
<tr>
<td><strong>Financial</strong></td>
<td>Charges, amounts reimbursed, co-pays</td>
<td>Usually not available</td>
<td>Usually not available</td>
</tr>
</tbody>
</table>
# RWD Practical Comparison

<table>
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<th>Characteristic</th>
<th>Administrative Claims</th>
<th>Electronic Medical Records</th>
<th>Primary Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insurance Coverage</td>
<td>Insured only (usually one type)</td>
<td>Treatment independent of insurance, includes uninsured</td>
<td>Treatment independent of insurance; includes uninsured</td>
</tr>
<tr>
<td>Geographic Settings</td>
<td>Mostly US only</td>
<td>EMRs proliferating in US &amp; ex-US settings</td>
<td>Generally smaller settings</td>
</tr>
<tr>
<td>Ease of Analysis</td>
<td>Relatively easy</td>
<td>Harder, particularly for unstructured data</td>
<td>Easy given control over how data are collected</td>
</tr>
<tr>
<td>Ease of Linkage</td>
<td>Do-able but not easy without compromising PHI</td>
<td>Do-able but not easy without compromising PHI</td>
<td>Can sometimes link to claims or other information</td>
</tr>
<tr>
<td>Data Completeness</td>
<td>High for elements essential to reimbursement</td>
<td>High for elements essential to patient management</td>
<td>Complete given control over CRF</td>
</tr>
<tr>
<td>Timeliness</td>
<td>Time lag usually measured in months or quarters</td>
<td>Time lag usually measured in days or weeks</td>
<td>Takes time to collect and enter</td>
</tr>
</tbody>
</table>
Classifying Real-World Data Sources

How Real-World Sources Array Across the Cost Spectrum

- Studies involving different kinds of RWD sources naturally array across the cost spectrum according to time & effort in data collection
- Retrospective sources congregate on the lower end, purely prospective sources on the higher end
- Emerging approaches involving retro-to-pros hybrid designs are in between
Polling Question

For your future research, what type of data do you see as being most important:

- Primary data collection
- Use of secondary data sources
- Combination (hybrid studies)
Study Examples
Comparing Patient-Centered Outcomes after Treatment for Uterine Fibroids

**Sponsor**
Patient-Centered Outcomes Research Institute (PCORI)

**Research challenge**
Guide informed decisions about which uterine fibroid treatment options are most likely to result in outcomes of greatest importance to each patient.

**Objective**
- Compare durability of symptom relief, measured by subsequent procedures, after uterus-conserving treatments
- Compare durability of symptom relief, measured by recurrent symptoms, after any procedural treatment (including hysterectomy)

Comparing Patient-Centered Outcomes after Treatment for Uterine Fibroids

Key drivers:
- Geographic differences in treatment
- Length of follow-up
- Hysterectomy makes randomization challenging

Durability of Symptom Relief, measured by:
- Subsequent procedures
- Recurrent symptoms

Uterine Fibroid Patients
1) Medications
2) Uterus-conserving procedures
3) Hysterectomy
Retrospective observational study: EMR and claims

• **Quintiles EMR and Truven MarketScan claims data**
  - Over 13,000 patients with UF diagnosis
  - Clinical and laboratory information from outpatient EMR records
  - Hospitalizations, emergency dept visits, other medical care and healthcare costs by service type from claims

• **Quintiles COMPASS* Research Network**
  - Over 12,000 patients with UF diagnosis
  - Federated network of integrated healthcare delivery systems (IDNs)
  - Patient information available across the continuum of care; EMR records include hospitals, clinics, physician offices

* COMparative effectiveness and PAtient Safety and Surveillance
Patterns of Diabetes Care

Industry

Research question

How do practice and referral patterns affect outcomes in management of patients with type 2 diabetes?

Objectives

• Describe usual care practice patterns at the sites providing initial diabetes care overall and by specific site/provider characteristics
• Describe usual care practice patterns and transition of diabetes care at referral sites
• Describe the effect of practice and referral patterns on selected outcomes, including:
  • Glycemic control
  • Titration and Dose
  • Persistence & Adherence
  • Discontinuation & Switching
  • Side effects
  • Complications
Hybrid study design

Key drivers:
• Reduce burden of data collection on sites

• Important endpoint: reasons for switching and discontinuation

• Incorporate active and automated (passive) data collection

• Observational follow-up with *de novo* data collection or the use of routine data

• May have interventional/experimental design (Pragmatic Trial)
Hybrid study: EMR and prospective surveys

Engaged two large research groups:
- FORWARD: Large diabetes-focused Provider-Based Research Network (PBRN)
- COMPASS: Collaborative group of Integrated Delivery Networks

Quarterly EMR Data

Harmonize data elements within an Quintiles Infosario EDC system

Provider Surveys

Site Surveys

Patient Surveys (MediGuard)

Analytic data file
Registry in Glaucoma Outcomes Research (RiGOR)

**Objective**

Compare response to treatment for (1) patients treated with laser surgery and (2) incisional/other surgeries with (3) patients receiving additional medication, at one year post-treatment for the following outcomes:

- \( \geq \) 15% reduction in Intraocular Pressure (IOP) - primary endpoint
- Improvement in Patient-Reported Outcomes and Quality of Life
- Glaucoma severity and visual acuity measures
- Subsequent surgeries, incidence of complications

**Research challenge**

Compare the effectiveness of treatment strategies for primary open-angle glaucoma, in response to the U.S. IOM “Initial National Priorities for CER”

**Sponsor**

U.S. Agency for Healthcare Research and Quality (AHRQ)

Registry in Glaucoma Outcomes Research (RiGOR)

Open-angle glaucoma patients who failed initial medication therapy

1) Laser surgery or Incisional/other surgery

2) Compared to

3) Additional medication therapy

Primary Outcome
• ≥ 15% reduction in Intraocular Pressure Reduction

Patient-Reported Outcomes
• Improvement in QOL -Glaucoma Symptom Score -NEI-VFQ-25

Clinician-Reported Outcomes
• Glaucoma Severity Scale
• Improved Visual Acuity (Snellen method)

Study-specific clinical
• Subsequent surgeries
• Incidence of complications

Key drivers:
• Consistency of clinical measures
• Direct to patient measures

Primary data collection: Prospective patient registry

**Patient registry:** Organized system that uses observational study methods to collect uniform data (clinical and other).

RiGOR was able to collect data on a large enough sample to perform subgroup analyses in key populations, and capture endpoints in a real-world setting.

Evidentiary Needs as a Guide to Selection of Real-World Data Sources
Data element identification

How to use evidentiary needs to guide optimal choice of real-world data sources

- Systematically determine evidentiary needs
- Define research question
- Design study:
  - Protocol synopsis
  - Identification of key data elements

Data element groupings:
- Baseline demographic and clinical characteristics
- Treatments and procedures
- Clinical outcomes
- Diagnoses of interest and comorbidities
- Hospital and provider information
- Financial and payor information
Pathway to determining data source

How to use evidentiary needs to guide optimal choice of real-world data sources

Data elements of interest to answer the research question?

Data elements recorded in clinical practice or healthcare administration?

- Available in electronic databases?
- Available in localized clinic records?
- Data elements not collected routinely

Real-World Database Assessment
Pathway to determining data source

How to use evidentiary needs to guide optimal choice of real-world data sources

Real-World Database Assessment

1. Identify databases
2. Ascertain interest
3. Survey database attributes
4. Score & weight
5. Analyse
Real-world Database Assessment

1. Identify databases
   Local contacts
   Internal knowledge
   Literature searches
   Database repositories:
   • Bridge to Data
   • ENCePP
   • ISPOR Intl Digest of DB

2. Ascertain interest
   Initial outreach for interest in commercially sponsored research

3. Survey database attributes
   Survey databases to gather information for decision-making

4. Score & weight

5. Analyse
Key questions for evaluating an external data source

• Are the key variables available to define an analytic cohort and identify relevant exposures, outcomes, endpoints and covariates?

• Are the key variables available for identifying important subpopulations for the study?

• Are the data sufficiently granular for the purpose of the study?

• Are there a sufficient number of exposed individuals in the dataset?

• How would this work? [Ownership, contracting, price, ability to directly contact sites]

## General database attribute checklist

### General information:
Description and type of database (in patient, out patient, claims data, other)

### Database content:
- Patient demographics (address, age, gender, race)
- Outcome data (clinical endpoints, mortality, lab reports, other)
- Treatment data (prescriptions, surgeries, other)
- Resource utilization (admissions, referrals, doctor visits, other)

### Technical details:
- Coding system (for diagnosis, prescriptions, and surgical procedures)
- Data linkage potential (unique identifiers, legal aspects)
- Access scheme (open for public, for fees, ethical approval obligation to publish)

Questions determined according to evidence gaps

Access to Real-World Databases in Europe – How to find the right one to answer your research question. ISPOR. 17th Annual Meeting, June 2-6, 2012 – Washington, DC, USA
Real-world Database Assessment

1. Identify databases
2. Ascertain interest
3. Survey database attributes
4. Score & weight
5. Analyse

Assign values based on importance and availability of information
Analyze attributes against research interest
Pragmatic Approaches to Real-World Data Source Selection & Use

- Real-World data are a valuable asset for research at all points of the drug development process
- The various types of real-world data are associated with specific strengths and weaknesses
- A systematic approach to database selection can help achieve your study goals
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?