Fit for Purpose Real World Data

Applying Decision Aids

The National Academies of Science, Engineering, and Medicine
Examing the Impact of Real-World Evidence on Medical Product Development:
A Three-Part Workshop Series
Workshop Three: Application
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Duke-Margolis RWE Framework

• Released in September 2017
• Proposes a framework of considerations to guide sponsors and FDA in RWE discussions, and puts forward near-term steps on priority issues
• Intends to help clearly establish the current RWD/RWE landscape and the potential process that stakeholders should go through when assessing RWE approaches for regulatory use
Duke Margolis Real-World Evidence Collaborative

- White papers
  - Real-World Data Quality and Relevance: Characterizing Data for Regulatory Use (working title)
  - Improving the Credibility of Observational Studies for Regulatory Use (working title)

- Will be released in conjunction with Oct. 1, 2018 Public Meeting
Understanding the origin and anatomy of real world data

*Perspective from a Pharmaceutical Company*

Brande Yaist
Sr. Director- Global Patient Outcomes and Real World Evidence
Eli Lilly and Company
Real world evidence is defined by use of real world data

Real world evidence is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

Real World Evidence (RWE) is one form of evidence (along with RCT, health economics studies, etc.) derived from primary or secondary real world data sources, with appropriate design/analyses, for the purpose of providing insights, on diseases, medicines, patient populations and healthcare practices, that will inform customer and internal decision making.

Source: Eli Lilly and Company
There is no commonly accepted definition of real world data

However, there are common themes…

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources

Data used for clinical, coverage, and payment decision-making that are not collected in conventional randomized controlled trials

An umbrella term for data regarding the effects of health interventions (e.g., benefit, risk, and resource use) that are not collected in the context of conventional RCTs. Instead, RWD are collected both prospectively and retrospectively from observations of routine clinical practice. Data collected include, but are not limited to, clinical and economic outcomes, patient-reported outcomes, and health-related quality of life. RWD can be obtained from many sources including patient registries, electronic medical records, and observational studies.
There is a wide variety of possible RWD sources

Administrative claims records
Linked data (secondary use)
Social media
Hybrid data (secondary use & primary data collection)
Patient generated health data
Pragmatic trials
Linked data
Public health surveys
Primary data collection observational study
Patient/disease state registries
Patient & provider surveys
Electronic medical/health records
Patient & provider surveys

Source: Eli Lilly and Company
Start with the question and context of the decision

1. State the RESEARCH QUESTION
2. LIST the DATA ELEMENTS of interest to answer the research question

Is the drug safe and effective …
• in an expanded population?
• using different dose schedules or dosing?
• in a sub-population?
• in very small population unlikely to have RCT?
• in a new disease state?

Are there additional benefits/claims (e.g. functional measures, symptom improvement) in already approved indication?

Source: Eli Lilly and Company
Identify possible data sources

1. Do accepted standards exist? (e.g. MACE endpoints are well established for claims)
2. Key data elements (exposure, outcome, & covariate variables)

Could all data elements be found in EXISTING data sources?

- No
- Yes

Could some of the data elements be found in EXISTING data sources?

- No
- Yes

Clinical Care or “Real Life”
- Provider
- Patient

Primary Care or “Real Life”

- Provider
- Patient

Primary (new) data collection

Hybrid

- Patient generated health data
- “Traditional” RWD

“Real Life”
- Passive
- Active

Recorded from a formal CLINICAL CARE setting?

- No
- Yes

EHR: primary care, hospital, specialty (facilitate care)
Claims: inpatient, outpatient, pharmacy, and enrollment (billing)
Registries: specialty (research)
Public Sources: population surveys, ER utilization, etc. (public health)

Source: Eli Lilly and Company
What is the comparative effectiveness of Carotid Artery Stenting versus Carotid Endarterectomy?

Could all data elements be found in **EXISTING** data sources?
- No
- Yes
  - Recorded from a formal **CLINICAL CARE** setting?
    - No
    - Yes
      - **PRIMARY** (new) data collection
      - **HYBRID**
      - **PATIENT GENERATED HEALTH DATA**
      - “**TRADITIONAL**” RWD

**Identifiers**

Medicare + Registries + AHAA Survey + AMA

## Stenting vs. Endarterectomy

### Considerations for data relevance

| Availability of key data elements (exposure, outcome, & covariate variables) | • Exposure (CAS vs. CEA)  
| | • Outcomes (death, stroke/TIA, MI)  
| | • Covariates: patient demographics, comorbidities, degree of carotid stenosis, elective vs. emergent procedure status, surgeon characteristics |
| Representativeness | • All Medicare patients receiving CAS or CEA during study period |
| Sufficient subjects | • 1999 CAS and 3255 CEA patients treated by 337 physicians across 69 centers in the SVS-VR |
| Complete exposure window | • Yes, survival model |
| Longitudinality | • Medicare vital status file has date of death and Medicare claims capture stroke/TIA and MI. |
| Availability of elements for patient linking | • Medicare ↔ Surgical Vascular Registry ↔ Cardiovascular Data Registry  
| | • Medicare ↔ American Hospital Association's Annual Survey Database  
| | • AMA Physician Masterfile ↔ Medicare |

What are factors influencing treatment choice among patients with Chronic Idiopathic Constipation and Irritable Bowel Syndrome with constipation (CONTOR)

Could all data elements be found in EXISTING data sources?

- No
- Yes

Could some of the data elements be found in EXISTING data sources?

- No
- Yes

Recorded from a formal CLINICAL CARE setting?

- No
- Yes

<table>
<thead>
<tr>
<th>PRIMARY (new) data collection</th>
<th>HYBRID</th>
<th>PATIENT GENERATED HEALTH DATA</th>
<th>“TRADITIONAL” RWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical &amp; Pharmacy Claims + Patient Survey &amp; Diary</td>
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# CONTOR: Considerations for data relevance

| Availability of key data elements (exposure, outcome, & covariate variables) | Claims: Diagnosis, drug exposure  
|                                                                             | Survey (168 questions)  
|                                                                             | Diary (77 questions) |
| Representativeness                                                        | Medical and pharmacy claims and enrollment information  
|                                                                             | approximately 12 million patients annually from a  
|                                                                             | U.S. health plan with national coverage  
|                                                                             | Geographically diverse and broadly representative of the U.S. insured population. |
| Sufficient subjects                                                       | 18,590 mailed, 2693 returned, 2052 complete/eligible |
| Complete exposure window                                                  | Yes |
| Longitudinality                                                           | December 2012 to June 2015 |
| Availability of elements for patient linking                              | IRB approval + patient consent |

Additional Case Examples
What is the relationship between muscle mass and walking speed and quadriceps strength test?

Could all data elements be found in EXISTING data sources?

- No
- Yes

Could some of the data elements be found in EXISTING data sources?

- No
- Yes

Recorded from a formal CLINICAL CARE setting?

- No
- Yes

PRIMARY (new) data collection

HYBRID

PATIENT GENERATED HEALTH DATA

“TRADITIONAL” RWD

Muscle Mass: Considerations for data relevance

| Availability of key data elements (exposure, outcome, & covariate variables) | • Quadriceps strength is not commonly done in patient care, BUT is done for NHANES |
| Representativeness | • Survey is weighted for representativeness of US Population |
| Sufficient subjects | • All survey subjects performed test |
| Complete exposure window | • Not applicable |
| Longitudinality | • Cross-sectional, assessing relationship at a point in time |
| Availability of elements for patient linking | • Not applicable |

What are the patient-perceived treatment effectiveness, medication use, and healthcare resource utilization in psoriasis patients?

Could all data elements be found in EXISTING data sources?

No

Could some of the data elements be found in EXISTING data sources?

No

PRIMARY (new) data collection

Yes

HYBRID

Recorded from a formal CLINICAL CARE setting?

No

PATIENT GENERATED HEALTH DATA

Yes

“TRADITIONAL” RWD

### Psoriasis: Considerations for data relevance

| Availability of key data elements (exposure, outcome, & covariate variables) | • Physician’s Global Assessment (PGA) and Body Surface Area (BSA) to determine disease severity (no proxy measurement required)  
• Patient assessment of treatment effectiveness  
• Treatment history, number of visits, and complexity of visits were available in coded fields. |
<table>
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<tbody>
<tr>
<td>Representativeness</td>
<td>• Dermatology-specific EHR platform used by over 4500 dermatology providers (30% of the market share across the US). This includes patients from 49 US states and 2 territories.</td>
</tr>
<tr>
<td>Sufficient subjects</td>
<td>• Over 500,000 psoriasis patients resulting in sufficient cohort after attrition</td>
</tr>
<tr>
<td>Complete exposure window</td>
<td>Yes</td>
</tr>
<tr>
<td>Longitudinality</td>
<td>September 2014- September 2015</td>
</tr>
<tr>
<td>Availability of elements for patient linking</td>
<td>NA</td>
</tr>
</tbody>
</table>

Comparative effectiveness from a single-arm trial and real-world data: alectinib versus ceritinib

Could all data elements be found in **EXISTING** data sources?

- Yes
- No

Could some of the data elements be found in **EXISTING** data sources?

- Yes
- No

Recorded from a formal **CLINICAL CARE** setting?

- Yes
- No

- PRIMARY (new) data collection
- HYBRID
- PATIENT GENERATED HEALTH DATA
- “TRADITIONAL” RWD

## NSCLC Control Arm
### Considerations for data relevance

| Availability of key data elements (exposure, outcome, & covariate variables) | • Exposure (certinib)  
| • Outcomes (death)  
| • Covariates: patient demographics, staging, prior treatments) |
| Representativeness | • ~15% of US cancer patients, geographically and demographically diverse |
| Sufficient subjects | • 67 patients from the Flatiron database (183 patients from 2 Phase 2 CTs) |
| Complete exposure window | • Yes, survival model |
| Longitudinality | • Jan 2011- Feb 2016 |
| Availability of elements for patient linking | • NA |