HTAi Workshop

A Primer on RICC: How to Generate Real World Evidence? A Modern Approach

Saturday 15 June 2019, 13:00-16:30
Maritim Hotel Cologne

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Chair, Regulatory Interactions and Conditional Coverage IG, HTAi
A paradigm change is under way!

Disease oriented care
EBM
Clinical trials

→

Patient oriented care
- RWE
- Observational studies
Increasing focus on RWE is associated with the greater supply of electronic patient-level data.

Cumulative publications; some of the research output is not related to medicines
Source: PubMed
The volume of « unused » data is massively growing.
RWD supply push causes a seismic shift in our approach.

**THE PAST**

- **RCT**
  - Controlled trials, manufacturer led

- **Few**
  - Few evaluators at launch, mostly regulators and large payers

- **Efficacy and Safety**
  - Initial view of benefit-risk

**THE PRESENT**

- **RCT and RWE**
  - Shift to secondary patient-level data across sources
  - **Many**
    - Many groups over time including clinical and small payers

- **Almost everything**
  - Insights on environment, outcomes, costs, comparative effectiveness
Generating evidence from real world data (RWD)

Data sources

Primary data collection (excluding RCTs)

Consumer data

Social media

Claims databases

Test results, lab values, pathology results

Hospital visits, service details

Electronic medical and health records

Pharmacy data

Mortality, other registries

Meaningful questions

Fit for purpose data

Appropriate Analyses

REAL-WORLD EVIDENCE (RWE)
### Step 1: Asking the right questions

<table>
<thead>
<tr>
<th>Regulatory</th>
<th>HTA</th>
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<tbody>
<tr>
<td>Exposure</td>
<td>Burden of target disease (mortality, morbidity prevalence, incidence, DALYs, QALYs)</td>
</tr>
<tr>
<td>Epidemiology of the indication(s)</td>
<td>Conditions of use</td>
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<tr>
<td>Prescribing conditions</td>
<td>Expected benefit of the technology</td>
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<tr>
<td>Characteristics of patients who actually receive the drug</td>
<td>- On burden of disease</td>
</tr>
<tr>
<td>New safety concerns, known ones, risk factors</td>
<td>- On management of disease</td>
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<tr>
<td><strong>Efficacy</strong> in real life / in specific populations</td>
<td>- Economical</td>
</tr>
<tr>
<td><strong>Effectiveness</strong> of risk minimization measures</td>
<td>- Organisational</td>
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<tr>
<td>Signal detection</td>
<td>Confirmation of the expected benefit versus risk</td>
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<td>Potential to cover unmet medical needs or to improve covered needs</td>
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Step 2: Finding fit-for-purpose data

Fit-for-purpose

- Relevance (appropriate data)
- Accuracy (less errors)
- Timeliness (data still useful)
- Linkability (identifying fields)
- Completeness (less missing records / variables)
- Accessibility (available easily)
- Representativeness
Cost effective approach to data collection

Begin with the research question.

- The data shall be collected entirely (primary)
- The data shall be collected partially (enriched, mosaic)
- The data resides in a database (secondary)
- We don't know if the data is available in a database (landscaping)

Design freedom

Time

Cost
Claims data

Initial purpose

- Economic management
- Reimbursement

Content

- Demographics
- Diagnoses
- Diagnostic related groups
- Procedures
- Reimbursed drugs/devices

Settings

- Mainly Hospitals
- Increasingly linked to outpatient claims

Good for

- Economic and resource utilization
- Epidemiology
- Healthcare system
EMR data

Initial purpose

• Clinical management
• Patient follow up

Content

• Demographics
• Diagnoses
• Signs and symptoms, allergies, smoking
• Lab values
• Drugs and to a less extent procedures

Settings

• Mainly primary care
• Increasingly secondary care and hospitals

Good for

• Exposure evaluation
• Drug utilization
• Disease epidemiology
• Benefit-risk assessment
• Unmet needs, burden, adherence

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Pharmacy records / sales data

Initial purpose

• Sales management
• Benchmarking

Content

• Demographics
• Drugs (packages sold)

Settings

• Retail pharmacies
• Wholesales
• Company outputs

Good for

• Exposure
• Treatment dynamics (switch, discontinuation…)
• Population movements
• Linkage
Registries

Initial purpose

- Research

Content

- Demographics
- Clinical details
- Procedures
- Drugs
- Lab values
- Relevant markers, genetic data, tests, etc

Settings

- Disease or drug oriented
- Mostly secondary care
- Mostly research intensive areas (oncology, ...)

Good for

- Disease epidemiology
- Benefit-risk assessment
- Treatment pathways
Social media, wearables, connected devices, etc

Initial purpose
- Networking
- Follow up
- Experimental

Content
- Demographics
- Narrow and specific data

Settings
- Everyday life
- Smoothly entering the healthcare system
- Telemedicine programs

Good for
- Hypothesis generation
- Signal detection / monitoring
- Population behavior
- Public health intervention evaluation
Syndicated surveys

Initial purpose
• Market Research

Content
• Demographics
• Clinical data
• Procedures
• Labs & specialized tests
• Drugs
• Outcome measures

Settings
• Inpatient & outpatient
• Focused on pathologies with high demand for data

Good for
• Disease epidemiology
• Treatment dynamics (split per indication, off label use,…)
• Clinician behavior and understanding
Linking different types of secondary data may be needed.

- National claims, dispensing data
- Electronic Medical Records
- Labs, registries, biobanks

T-Shaped model for better efficiency in database studies.
Step 3: Conducting the appropriate analyses

**Better Traditional Studies**

Improved execution of traditional studies, more precise selection of sites, reduced timelines and errors

**Innovative Study Design**

Collect data from clinicians and/or directly from patients; combine with existing data for broader stakeholder value

**Smarter Evidence Generation**

Reusable, scalable approaches to evidence generation
Data and technology make innovative designs possible

- Primary data collection
- Secondary data collection

**Traditional**
- Pragmatic clinical trials
- Prospective research (registries, RCTs)
- Extension studies with direct to patient follow-up
- Mosaic studies & Enriched studies
- Site less studies
- Augmentation studies
- Database studies
- Evidence platforms

**New**
Mosaic studies identify the best-fit data in each country

What are Mosaic studies?

- Due to the differences in secondary data availability across countries, one method for data collection cannot be always used in all countries
- Mosaic studies use multiple data collection approaches within a single study - countries are grouped according to the method for data collection – to provide an optimised study design to the client.

Case Study: A Global PASS

Challenge:

- Client wanted a cost effective and innovative solution for a PASS in US and EU (~5000 patients globally over 10 year time-frame)

Enriched opportunity:

- Bring together a segmented solution for the best-fit design for the US and each EU market, identified by the use of secondary data for feasibility and planning
- Use data from claims + primary site network to identify optimal US sites for recruitment & data collection
- Utilize network of registries to collect, analyse and pool relevant safety information

Enriched value points:

- Huge cost efficiencies (~$25M) through avoidance of unnecessary data collection in certain markets
- Early indication of improved site and patient recruitment timelines using IQVIA data-driven approach
Enriched studies combine primary and secondary data

STUDY PLANNING | RECRUITMENT | STUDY EXECUTION

EMR “backbone”
- Aids patient recruitment
- Provides core patient information

EMR data
Other datasets (e.g. claims)

STUDY DATABASE

- Linkage and de-ID patient information
- Final study database linking all data sources

E-CRF and PRO provide supplementary data on variables not in EMR, including QoL

Data collected directly from MD (e-CRF)
Patient reported outcomes (PRO)
Evidence platforms: the future of evidence generation

- **Evidence platforms** are built on a foundation of real world data that supports clinical and commercial needs.
- It embeds a layer of technology to extract and analyze the data in a consistent way across the organization, with appropriate governance and privacy protections.
- Applications designed to help teams use those insights appropriately for their needs.
Trends in real-world data, evidence, and insights

- Expanding application of RWD in clinical development
- Increasing use and acceptance of innovative study designs to generate RWE
- Scalable approaches to generate real world insights (RWI)
Thank you!

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