Real World Data and decision-making procedures

Facing the Challenges: Equity, Sustainability and Access
29th-30th November 2018, WHO/INFARMED Conference

Dr Chantal Bélorgey
Director of Medical, Economic and Public Health Assessment | National Authority for Health (HAS), France
Outlines

1. Challenges with Real World Data (RWD)
2. How to deal with?
   - HAS experience of RWD
   - EUnetHTA initiatives
1. RCTs, the gold standard

2. But,
   - RCTs do not answer all HTA questions
   - MA increasingly granted on limited data

3. Increasing uncertainty situations

4. Use of real world data to complement/enrich evidence?
RWD and RWE, what are we talking about?

1. **Real world data (RWD)**
   - Data regarding the effects of health interventions (e.g., safety, effectiveness, resource use, etc.) that are not collected in the context of controlled RCTs
   - Observational (non RCTs) or administrative data that provides information on the routine use delivery of health care and the health status of the target population.
   - Pragmatic studies

2. **Real world evidence (RWE)**
   - Evidence derived from the analysis of real world data.
Use of real world data

<table>
<thead>
<tr>
<th>Objectives of RWD</th>
<th>Impact</th>
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<tr>
<td><strong>Safety</strong> Monitoring</td>
<td>Regulatory and HTA assessment</td>
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<tr>
<td>Relative <strong>Effectiveness/Cost-Effectiveness</strong> in real life setting</td>
<td>Regulatory and HTA assessment</td>
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<td><strong>Conditions</strong> of use</td>
<td>HTA assessment</td>
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<tr>
<td>Monitoring <strong>Drug Financing Mechanism</strong></td>
<td>P&amp;R Decision</td>
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<td>- Financial condition of usage</td>
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<td>- Performance based payment</td>
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<tr>
<td>Sharing experiences/practices for <strong>optimization</strong> of patient management</td>
<td>Clinical practice recommendations/guidelines</td>
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Potential use of RWE

NEW:

– Absence of RCT: Indirect comparison
– Supplement specific populations
– Uncertainty management
– Reassessment
Challenges

1. Lower evidence:
   - safety and efficacy?
   - added clinical value?

2. Quality of data and confidence

3. Transferability

4. For which HTA questions RWE is acceptable?

5. When and how to use RWE?

6. How to assess?
What to do?

Policy

- Harmonised policy
- Governance

Methodology

- Which quality (data & methods)
- Good practices and reproducibility
Post Launch Evidence Generation, HAS experience so far

1. RCTs gold standard; RWD to complement
2. Requests for PLEG 10% of new drugs assessment
   - Conditions of use, effectiveness, long term safety, place in clinical strategy
   - Increasing role of academic cohorts/registries and data from social security database
   - Validation of protocols by HAS
3. Context of Uncertainty
The National Health Data System (2018) in France: SNDS

- Law in 1998 = creation of a unique information system of social health insurance funds (SNIIRAM)
- New legal context in 2016 = extension and creation of the National Health Data System (SNDS)

2019 French HEALTH DATA HUB

Electronic health records / professional records

Hospital Data warehouse

Genomic data

Social networks

Data collected / connected objects

Samples, cohorts,…

Data collected for administrative purposes (claims, …)

Registries, cohorts

Surveys

The National data warehouse
67 million people
The main objective of WP5 is to help to generate, all along the technology lifecycle, optimal and robust evidence for different stakeholders, bringing benefits for patient access and public health.

- **Strand A: Early Dialogues**
  
  Opportunity to seek advice for PLEG

- **Strand B: Tools and pilots for Post-Launch evidence generation (PLEG)**
  
  → Guidelines
  
  → Standards Tool supporting the quality of Registries (REQueST)
  
  → Product specific pilots arising from assessment
  
  → Registry qualification advice

Generation of good quality RWE is part of EUnetHTA Objectives
Available EUnetHTA tools for PLEG

Technology selection for AEG
Definition of the research question
Choice of data sources and methodology
Core protocol template
Pilot templates and documents
Quality of registries

EUnetHTA
Criteria to select and prioritize health technologies for additional evidence

www.euneththa.eu

EUnetHTA JA2 WP7 DELIVERABLE
Position paper on how to best formulate research recommendation for primary research arising from HTA reports

Core protocol Pilot for Additional Evidence Generation

JA3 deliverable
Objectives of REQueST

• Adapt existing quality standards for registries into a practical tool to assess registry quality
• Build upon the work of PARENT Joint action

Highlights thus far

• First draft of REQueST
  ISPOR POSTER; Gimenez E et al  nov 2018
• Vision paper on the sustainable availability of REQueST

Next steps

• Public consultation (mid 2019)
• Final version (September 2019)

*Registries = An organized system that collects, analyses, and disseminates the data and information on a group of people defined by a particular disease, condition, exposure or health-related service, and that serves a predetermined scientific, clinical or public health(policy) purpose.
### EUnetHTA PLEG pilots

#### Product specific pilots arising from HTA

- **Two ongoing pilots, one planned:**
  - Orphan drug,
    - Start: April 2018.
    - 7 countries.
  - Breast cancer,
    - Start: May 2018.
  - Expected end (both pilots) mid-2019.
  - Medical device, Upcoming.

#### Disease/registry specific collaborative pilots

- Registry qualification exercise
  - Participation to EMA registry initiative
- Two pilots carried out
Participation to EMA Registry initiatives

Qualification of novel methodologies for medicine development

The European Medicines Agency offers scientific advice to support the qualification of innovative development methods for a specific intended use in the context of research and development into pharmaceuticals.

The advice is given by the Committee for Medicinal Products for Human Use (CHMP) on the basis of recommendations by the Scientific Advice Working Party (SAWP). This qualification process leads to a CHMP qualification opinion or CHMP qualification advice.

- EUnetHTA Participation to two Disease Registry Qualifications
- Qualification advice covering both Quality aspects and registry data set
## EMA-EUnetHTA three-year work plan 2017-2020

<table>
<thead>
<tr>
<th>Activity</th>
<th>Expected outcomes</th>
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<tr>
<td><strong>Early Dialogue / Scientific Advice</strong></td>
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<tr>
<td>Design and implement a single, common,</td>
<td>A single process that reflects the evidence generation needs of both regulators</td>
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<td>European procedure for Parallel</td>
<td>and HTABs</td>
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<tr>
<td>Consultation (previously known as</td>
<td>Milestones for launch of single platform for parallel consultation and process</td>
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<tr>
<td>parallel scientific advice/early</td>
<td>reviews</td>
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<td>dialogue)</td>
<td>Communication with stakeholders at each critical design change</td>
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<tr>
<td>Facilitate learning and understanding</td>
<td>Mutual observerness in scientific advice / early dialogue</td>
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<tr>
<td>of evidence needs</td>
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<tr>
<td>**“Late dialogues” / peri-licensing</td>
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<tr>
<td>advice**</td>
<td>Provision of parallel consultation on requirements for post-authorisation data</td>
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<tr>
<td>Gaining experience with peri-licensing</td>
<td>collection plans (including registries)</td>
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<tr>
<td>advice on post-licensing data generation plans with a focus on</td>
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<td>specific products (e.g., ATMPs) or</td>
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<tr>
<td>regulatory processes or tools (e.g.,</td>
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<td>CMA, Adaptive Pathways, or PRIME)</td>
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<tr>
<td>Optimise utilisation of post-licensing</td>
<td>Collaboration in requirements for data collection and analysis of real world</td>
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<tr>
<td>evidence generation for decision</td>
<td>data including registries</td>
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<td>making</td>
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Multiple on going initiatives … collaboration to be developed!

Original Report

Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making

Marc L. Berger1,*, Harold Sox2, Richard J. Wilke3, Diana L. Brinser4, Hans-Georg Eichler5, Wim Goettsch6, David Malligan7, Amr Melehy2, Sebastian Schneeweiss8, Rosanna Terricone9, Shirley V. Wang9, John Watkins10 and C. Daniel Mulrow11

1New York City, NY, USA; 2Patient-Centered Outcomes Research Institute, Washington, DC, USA; 3International Society for Pharmacoeconomics and Outcomes Research, Launnenville, NJ, USA; 4University of Utah, Salt Lake City, UT, USA; 5European Medicines Agency, London, UK; 6Zorginstituut Nederland and University of Utrecht, Utrecht, The Netherlands; 7Columbia University, New York City, NY, USA; 8Bingham and Women’s Hospital, Harvard Medical School, Boston, MA, USA; 9Bocconi University, Milan, Italy; 10Prevea Blue Cross, Menominee Terrace, WA, USA; 11University of Maryland, Baltimore, MD, USA

ABSTRACT

Purpose: Real-world evidence (RWE) includes data from non-RCT prospective observational studies and observational registries and provides insights beyond those addressed by randomized controlled trials. RWE studies aim to improve health care decision making. Methods: The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the International Society for Pharmacoepidemiology (ISPE) created a task force to make recommendations regarding good procedural practices that would enhance decision makers’ confidence in evidence derived from RWE studies. Peer review by ISPOR/ISPE members and task force participants provided a consensus-building iterative process for the topics and framing of recommendations. Results: The ISPOR/ISPE Task Force recommendations cover seven topics such as study registration, replicability, and stakeholder involvement in RWE studies. These recommendations, in concert with earlier recommendations about study methodology, provide a trustworthy foundation for the expanded use of RWE in health care decision making. Conclusion: The focus of these recommendations is good procedural practices for studies that test a specific hypothesis in a specific population. We recognize that some of the recommendations in this report may not be widely adopted without appropriate incentives from decision makers, journal editors, and other key stakeholders.

Keywords: comparative effectiveness, decision making, guidelines, pharmacoepidemiology, real-world data, treatment effectiveness.

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Discussion paper:
Use of patient disease registries for regulatory purposes – methodological and operational considerations

The Cross-Committee Task Force on Patient Registries
A new paradigm for HTA bodies

1. Need for RWD and RWE is now a reality
2. HTA to stay as robust as today
3. Still challenges and concerns to be solved
4. Call for Organization and Collaboration
5. International level
THANKS for your attention!

http://www.has-sante.fr

@HAS-sante.fr