Assessing Real-Word Data Quality From Electronic Health Records for Health Technology Assessment

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Presented by the ISPOR Using EHRs in HTA Task Force
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Rachael Fleurence, PhD, Senior Advisor, National Institutes of Health, Bethesda, MD, USA

Speakers:
• Scott Ramsey, PhD, MD, Full Member & Co-Director, Fred Hutchinson Cancer Research Center, Lake Forest Park, WA, USA
• Seamus Kent, PhD, Senior Adviser, HTA and Market Access, Flatiron Health, Amsterdam, the Netherlands
• Blythe Adamson, PhD, MPH, Principal Scientist, Flatiron Health, New York, NY, USA
Agenda

1. Task Force overview and rationale (Dr Scott Ramsay)
2. The complexities of EHR data (Dr Blythe Adamson)
3. Understanding the suitability of real-world data to answer questions in HTA (Dr Seamus Kent)
4. Elements and format under consideration for the recommendations (Dr Blythe Adamson)
5. Q&A moderated by Dr Rachael Fleurence
Members of the task force - 1

- **Rachael Fleurence, PhD**, (Co-Chair), Senior Advisor, National Institutes of Health, USA
- **Scott Ramsey, PhD, MD**, (Co-Chair), Full Member & Co-Director, Fred Hutchinson Cancer Research Center, USA
- **Blythe Adamson, PhD, MPH**, Principal Scientist, Flatiron Health, USA
- **Ran Balicer, PhD, MD**, Chief Innovation Officer, Clalit Health Services, Tel Aviv, Israel
- **Elsa Bouee Benhamiche, PharmD, RPh**, Project manager, Institut National du Cancer, France
- **Jon Campbell, PhD**, Senior Vice President, Health Economics, Institute for Clinical and Economic Review (Seamus Kent, PhD, Senior Adviser, HTA and Market Access, Flatiron Health, the Netherlands
Members of the task force - 2

- Sebastian Garcia Marti, MSc, MD, HTA and Health Economics Coordinator, IECS - Institute for Clinical Effectiveness, Argentina
- Kevin Haynes, MS, PharmD, Associate Director of Epidemiology, Janssen Research and Development, LLC, USA
- Seamus Kent, PhD, MSc, Senior Adviser, HTA and Market Access, Flatiron Health, Amsterdam, the Netherlands
- Patrick Muller, MSc, PhD, National Institute for Health and Care Excellence (NICE), UK
- Joseph Ross, MD, PhD, Professor of Medicine and Public Health, Yale University, USA
- James Tcheng, MD, Professor of Medicine & Professor of Family Medicine and Community Health (Informatics), Duke University School of Medicine, USA
Motivation of ISPOR Task Force on EHR Data for HTA
Background and Objectives

• Background
  – Rapid growth in availability of EHR-derived RWD and organizations devoted to providing and analyzing EHR’s for industry and regulators
  – Lack of frameworks for use of EHR derived RWD for Health Technology Assessment (HTA)
  – Need for users to understand the similarities and unique aspects of EHR relative to other types of RWD

• Overall Objective
  – Establish consensus on and provide emerging good practices for conducting, reporting and evaluating data quality of EHRs for health technology assessments

• Key elements:
  – Targeted literature review of standards for regulatory decision making
  – Recommendations and Data Quality Checklist
  – Limitations of EHR’s and future directions
Feasibility assessment: What data is best fit for this question?

<table>
<thead>
<tr>
<th>Patient Population(s) Included</th>
<th>Claims</th>
<th>Registries</th>
<th>Prior Clinical Trials Data</th>
<th>EHR-derived Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Population(s) Included</strong></td>
<td>+</td>
<td>+/-</td>
<td>+ / -</td>
<td>May be broad and/or disease-specific cohorts</td>
</tr>
<tr>
<td>Typically, very large broad patient populations</td>
<td>Population defined by particular disease, condition, or exposure</td>
<td>Disease and drug specific cohorts, unlikely representative</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical Depth</strong></td>
<td>-</td>
<td>+ / -</td>
<td>+ / -</td>
<td>Usually able to leverage all structured and unstructured data from patients’ charts</td>
</tr>
<tr>
<td>Limited granularity (e.g., biomarker test performed, but not result)</td>
<td>Collects uniform data on patients; range of clinical depth possible</td>
<td>Collects uniform data on patients; range of clinical depth possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Completeness/Data Quality</strong></td>
<td>+</td>
<td>+/-</td>
<td>+ / -</td>
<td>Visibility may be limited to specific sites of care and information transferred from other sites</td>
</tr>
<tr>
<td>Full visibility into events across full healthcare ecosystem (not limited to site of care). Need to consider open/closed claim tradeoffs</td>
<td>Serves more predetermined scientific, clinical or policy purpose → informs data collection &amp; completeness</td>
<td>Serves more predetermined scientific, clinical or policy purpose → informs data collection &amp; completeness</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There are multiple consortia with organizations in the private and public sectors focused on evaluating EHR data...

REAL-WORLD EVIDENCE ALLIANCE

We are a coalition of real-world data and analytics organizations with a common interest in harnessing the power of real-world evidence to inform regulatory decision making to improve patients’ lives.
SECTION 2

The Complexities of EHR Data
Electronic Health Record (EHR) source data requires curation of structured data and unstructured documents
Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

POINT OF CARE

“Truth”
Health status of the patient

Concept
Clinicians or patients conception

Records
Clinicians or patients choice of coding

Model
Computable representation of patients data

Data
Research data repository or Registry

Evidence
Insights in Reports and Publications

Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

Process of Health Status to Clinical Data Documentation, Extraction, and Transformation for Research

Understanding the suitability of real-world data to answer questions in HTA

Seamus Kent, PhD, Senior Adviser, HTA and Market Access, Flatiron Health, the Netherlands
We are building on existing work

Foundational data quality

Automating Electronic Health Record Data Quality Assessment

Obinna Ozonze, Philip J. Scott & Adrian A. Hopgood

Journal of Medical Systems 47, Article number: 23 (2023) | Cite this article

Fitness for purpose / Policy

A Harmonized Data Quality Assessment Terminology and Framework for the Secondary Use of Electronic Health Record Data

Michael G. Kahlo, MD, PhD,1 Tiffany J. Callahan, MPH,1 Juliana Barnard, MA,1 Alan E. Bauck,2 Jeff Brown, PhD,3 Bruce N. Davidson, PhD,4 Hossein Esfandi, PhD,4 Carsten Goergen, PhD,1 Erin Holve, PhD, MPH, MPP,1

Steven G. Johnson, MS,5 Siaw-Teng Law, MBBS, PhD, FRACGP, FACHI,6,7 Marianne Hamilton-Loosee, PhD, MPA,4,8 Daniela Meeker, PhD,9 Toan C. Ong, PhD,7,10 Patrick Ryan, PhD,7 Ning Shang, PhD,7,11 Nicole G. Weiskoff, PhD,4,5

Chunhua Weng, PhD, FACMI,12 Meredith N. Zozus, PhD,12 and Lisa Schilling, MD12

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PMCID: PMC5051581
PMID: 27713906

Use of Real-World Data and Real-World Evidence to Support Drug Reimbursement Decision-Making in Asia.
We are building on existing work

Foundational data quality

• Tools are focused on understanding inherent quality of the data and data processing/curation
• Agnostic to research question
• Large number of distinct frameworks with substantial variation in definitions and nomenclature
• Frameworks often specific to CDMs
• Key concepts: completeness, conformance, plausibility, consistency, accuracy, timeliness
• Can be assessed internally or using external data

Summary
We are building on existing work

**Policy frameworks**

- NICE
- HAS
- IQWiG
- cadth
- Duke
- MARGOLIS CENTER for Health Policy
- FDA
- EMA

**Summary**

- Differentiate between data provenance and data fitness for purpose
- Focus on fitness for purpose in relation to a specific research question
- Distinguish between data reliability and data relevance when assessing fitness for purpose
- Some frameworks agnostic to data source (e.g., NICE); others focused on specific sources of data (e.g., FDA, IQWiG)
How are we building on this work?

- Identify common strands from existing frameworks – strive for international alignment
- Ensure relevance to HTA needs and HTA evaluation processes
- Focus on user & application – developers of evidence to meet HTA needs
- Be specific to challenges and opportunities of using EHR data
- Develop useable and introductory guide for those less familiar with EHR data
Proposed framework

Data must be trustworthy, enable internally valid estimates, and be relevant to the decision context.

Proportionate risk-based approach depending on use case and decision context.

Data Provenance
- Collection
- Quality management
- Documentation

Data Fitness for Purpose
- Data Reliability
  - Completeness
- Accuracy

Data Relevance
- Data content
- Settings & time
- Size & follow-up
Data provenance

Is it reasonable to use the data to inform HTA decisions?

<table>
<thead>
<tr>
<th>Challenges to using EHR data</th>
<th>Questions to understand data provenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Data processing is a complex process, potentially involving multiple parties</td>
<td>• What was the initial purpose of data collection?</td>
</tr>
<tr>
<td>• Learning from unstructured data contained within EHR records</td>
<td>• How has data been processed (incl. linkage, transformations, etc.)?</td>
</tr>
<tr>
<td>• Ensuring appropriate permissions for secondary use of data, which varies across countries</td>
<td>• Is documentation sufficient for reviewers to fully understand the data and its processing? Are steps in place to share proprietary software where necessary?</td>
</tr>
<tr>
<td>• Data networks may need to integrate data from different systems</td>
<td>• What quality management processes are in place to ensure the integrity of the data? How is quality assessed over the data lifecycle?</td>
</tr>
<tr>
<td></td>
<td>• What is the legal basis for the secondary use of the EHR data?</td>
</tr>
<tr>
<td></td>
<td>• What data governance processes are in place?</td>
</tr>
</tbody>
</table>
Proposed framework

Data must be trustworthy, enable internally valid estimates, and be relevant to the decision context.

Proportionate risk-based approach depending on use case and decision context.

<table>
<thead>
<tr>
<th>Data Provenance</th>
<th>Data Fitness for Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collection</td>
<td>Data Reliability</td>
</tr>
<tr>
<td>Quality management</td>
<td>Completeness</td>
</tr>
<tr>
<td>Documentation</td>
<td>Accuracy</td>
</tr>
<tr>
<td>Processing</td>
<td>Data Relevance</td>
</tr>
<tr>
<td>Governance</td>
<td>Data content</td>
</tr>
<tr>
<td>Funding</td>
<td>Settings &amp; time</td>
</tr>
<tr>
<td></td>
<td>Size &amp; follow-up</td>
</tr>
</tbody>
</table>
Data reliability

Is the data reliable enough to produce internally valid estimates for a given research question?

Challenges to using EHR data

- Substantial missing data from:
  - Partial reporting of full health journey
  - Missing clinical/other events and results
- Data may not be recorded accurately
- Delays in integrating data into EHR systems
- Complex data processing

How can we understand data quality?

- Understand amount, patterns, and reasons for missing data
- Present quantitative data on data accuracy for all key study variables
- Metric depends on variable – e.g., categorical or continuous
- For accuracy of endpoints validation should ideally compare data against a known gold standard
- Where not feasible, alternative approaches include assessing plausibility, consistency, and conformance
- Address data limitations using appropriate study design and statistical methods
- Use sensitivity/bias analysis to assess the potential impact on results or adjust

Challenges to using EHR data

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Data Provenance
- Collection
- Quality management
- Documentation
- Processing
- Governance
- Funding

Data Fitness for Purpose
- Data Reliability
  - Completeness
  - Accuracy
- Data Relevance
  - Data content
  - Settings & time
  - Size & follow-up
Data relevance

Does the data allow the research question to be answered?

Challenges to using EHR data
- Data items reported reflect what is needed for clinical and administrative purpose rather than for research
- Data may come from particular care providers, regions, or countries and may not be relevant to target population
- Delays in access may limit relevance of the data to current treatment and limit follow-up of data.

How can we understand data relevance?
- Are all required data elements collected and at the right level of granularity?
- Is data collected at relevant time points?
- Is the population similar to the intended target population?
- Are care settings and treatment patterns relevant to the target country?
- Does the study period reflect current clinical practice and outcomes?
- Are sample size and length of follow-up sufficient to answer the research question?
Elements and format under consideration for the recommendations

Blythe Adamson, PhD, MPH,
Senior Principal Scientist
Flatiron Health, USA
# What format and style of checklist would be most useful?

<table>
<thead>
<tr>
<th>CHEERS</th>
<th>Cost-Effectiveness Impact Inventory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title and abstract</td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>Y Y Y Y Y Y N Y Y</td>
</tr>
<tr>
<td>Abstract</td>
<td>Y Y Y Y Y Y P P P</td>
</tr>
<tr>
<td>Introduction</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Background and objectives</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Methods</td>
<td></td>
</tr>
<tr>
<td>Target population and subgroups</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Setting and location</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Study perspective</td>
<td>N N N N Y Y Y Y Y</td>
</tr>
<tr>
<td>Comparisons</td>
<td>Y Y Y Y Y Y P N Y</td>
</tr>
<tr>
<td>Time horizon</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Discount rate</td>
<td>N N N N Y Y Y Y N</td>
</tr>
<tr>
<td>Choice of health outcomes</td>
<td>Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Measurement of effectiveness (cost-utility approach)</td>
<td>11a NA NA NA NA NA NA NA N P</td>
</tr>
<tr>
<td>Measurement of effectiveness (synthetic-based estimation)</td>
<td>11b P P P P P Y Y Y P P</td>
</tr>
<tr>
<td>Measurement and valuation of preference-based outcomes</td>
<td>12 Y Y Y Y Y Y N N N</td>
</tr>
<tr>
<td>Estimating resources and costs (cost-effectiveness analysis)</td>
<td>13a NA NA NA NA NA NA NA N P</td>
</tr>
<tr>
<td>Estimating resources and costs (cost-benefit analysis)</td>
<td>13b P P P P P P P P P</td>
</tr>
<tr>
<td>Currency, price index, and time horizon</td>
<td>14 Y Y Y Y Y Y Y Y Y N Y</td>
</tr>
<tr>
<td>Choice of model</td>
<td>15 Y Y Y Y Y Y P N N</td>
</tr>
<tr>
<td>Assumptions</td>
<td>16 Y Y Y Y Y Y Y Y N</td>
</tr>
<tr>
<td>Analytical methods</td>
<td>17 P P P P P P P P P</td>
</tr>
<tr>
<td>Sensitivity analysis and what-if analyses</td>
<td>18 Y Y Y Y Y Y Y Y Y</td>
</tr>
<tr>
<td>Incremental costs and outcomes</td>
<td>19 Y Y Y Y Y Y Y Y Y</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sector</th>
<th>Type of Impact</th>
<th>Included in Analysis from the following perspective?</th>
<th>Notes on Sources of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEALTH</td>
<td>Cost-Effectiveness (Effects)</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Mortality, years</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Incidence, years</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Health-related quality of life (HRQoL), QALYs</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Compliance</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Safety and tolerability</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Cost (USD, QALYs, % change)</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>INFORMAL HEALTHCARE SECTOR</td>
<td>Patient time costs, earnings</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Unpaid caregiver time costs</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Transportation costs</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>NON-HEALTHCARE SECTOR</td>
<td>Productivity</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Educational productivity</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Income</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Consumption</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Social services</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>LEGAL / CRIMINAL JUSTICE</td>
<td>Police</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td></td>
<td>Legal costs associated with health</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>EDUCATION</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td></td>
</tr>
<tr>
<td>ENVIRONMENT</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td></td>
</tr>
</tbody>
</table>

*CHEERS as a checklist for evaluating healthcare value, Cost-Effectiveness Impact Inventory for evaluating healthcare costs and effects.*
Proposed Elements for Consideration: **Data Relevancy**

The availability of critical variables and sufficient number of representative patients within the appropriate time period to address a given use case.

- Availability of key study elements
- Representativeness of population
- Timeliness and study time period
- Care setting and treatment pathways
- Timing and frequency of measurements
- Sufficiency of sample size and follow-up time
Proposed Elements for Consideration: Data Reliability

The degree to which data represent the clinical concept intended

- Accuracy
  - Validation
  - Verification
- Completeness
- Target concept and operational definition
- Provenance
Approaches for validation and verification of EHR data under consideration as good practices

Points of validation:
- Field Level
- Patient Level
- Site Level
- Sub-Cohort of Cohort Level

Types of validation output:
- Sensitivity, Specificity
- Positive and Negative Predictive Values
- Descriptive Statistics
- Agreement Metrics
- Completeness Rates
- Error Rates

Robustness

Indirect Benchmarking

Internal Reference

External Reference

Verification Checks

Feasibility
Additional recommendations under consideration

- Meaningful EHR use-cases for HTA include natural history, modeling inputs, extrapolation, real world comparative-effectiveness analysis, and more. Access to recent relevant data may enable “living HTA” with more dynamic value assessment over the lifetime of a product.

- Curation of variables for known confounders of the research question (eg, genomic testing results, functional status, vitals, endpoints) using unstructured documents is a key advantage over other types of RWD sources.

- Documentation of protocols and statistical analysis plans may require more detail and amendments (compared to analyses using other RWD data types) as often more decisions need to be made in the analysis of more complex health data.
Seeking Your Feedback

These are elements the ISPOR Task Force on EHR for HTA believes are important to assess EHR data quality for HTA and are considering including in our recommendations.

Is this appropriate and useful? What are we missing?
Thank you
Q&A

To contact the presenters:
taskforce@ispor.org
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Use of Electronic Health Records for HTA

**You must be an ISPOR member to join a Task Force Review Group.**

Likely timeline: Fall 2023
Open questions for discussion

- To what extent should we focus on innate data quality versus data suitability or relevance?
- Do we identify the key challenges of EHR data?
- Is our proposed framework structure appropriate? What items should be removed or added?
- Do we identify relevant challenges across countries?
- Can the framework support users of EHR data when generating evidence for HTA evaluations?
- What are useful formats for this Task Force?