RWE in HTA: Overcoming Barriers and Challenges

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Disclosures

I am an employee of and have options in Aetion, Inc.

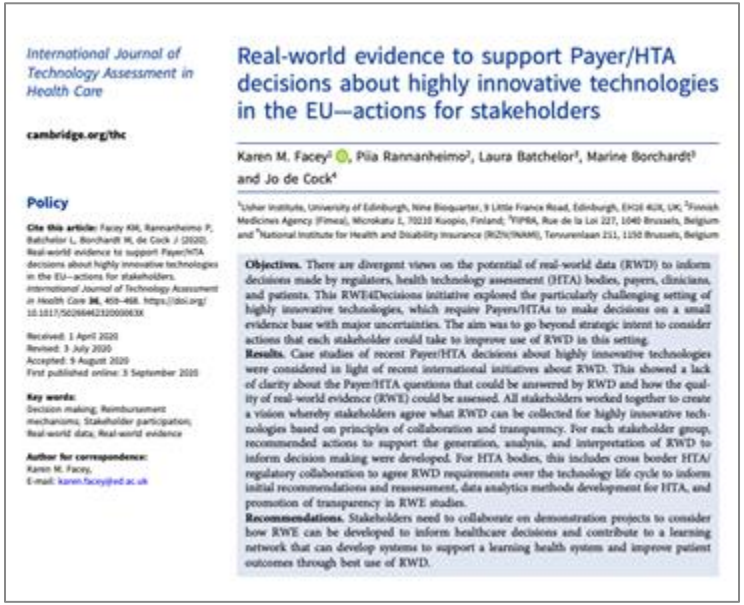
Agenda

Successes, Challenges, and the Path Forward

1. Data Quality
2. Methods - Transportability
3. Lifecycle management

Path Forward - RWE4Decisions Stakeholder Actions

- RWE4Decisions is a multi-stakeholder initiative commissioned by the Belgian National Institute for Health and Disability Insurance (INAMI-RIZIV)
- In 2020, published stakeholder actions for use of RWE in HTA decision-making for highly innovative medicines
- Since 2020, numerous changes in decision-making environment and advancement in RWD/RWE methods warrant an update to the stakeholder actions
- 2024 stakeholder actions developed through focus groups, roundtable discussions, public webinar, and a public consultation period
- Stakeholders include: HTA bodies/payers, pharmaceutical industry, clinical teams, patients, registry holders, and analytic and academic groups



International Journal of Technology Assessment in Health Care

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Policy

Real-world evidence to support Payer/HTA decisions about highly innovative technologies in the EU—actions for stakeholders

Karen M. Facey, Piia Rannanheimo, Laura Batchelor, Marine Borchardt and Jo de Cock

Objectives. There are divergent views on the potential of real-world data (RWD) to inform decisions made by regulators, health technology assessment (HTA) bodies, payers, clinicians, and patients. This RWE4Decisions initiative explored the particularly challenging setting of highly innovative technologies, which require Payers/HTAs to make decisions on a small evidence base with major uncertainties. The aim was to go beyond strategic intent to consider actions that each stakeholder could take to improve use of RWD in this setting.

Results. Case studies of recent Payer/HTA decisions about highly innovative technologies were considered in light of recent international initiatives about RWD. This showed a lack of clarity about the Payer/HTA questions that could be answered by RWD and how the quality of real-world evidence (RWE) could be assessed. All stakeholders worked together to create a vision whereby stakeholders agree what RWD can be collected for highly innovative technologies based on principles of collaboration and transparency. For each stakeholder group, recommended actions to support the generation, analysis, and interpretation of RWD to inform decision making were developed. For HTA bodies, this includes cross border HTA/regulatory collaboration to agree RWD requirements over the technology life cycle to inform initial recommendations and reassessment, data analytics methods development for HTA, and promotion of transparency in RWE studies.

Recommendations. Stakeholders need to collaborate on demonstration projects to consider how RWE can be developed to inform healthcare decisions and contribute to a learning network that can develop systems to support a learning health system and improve patient outcomes through best use of RWD.

Data Quality

Data quality: variability in how data quality is defined

Successes: Decision-makers agree, data quality is essential and have published recommendations/guidance on the topic

Problem that data quality can solve:

- Data quality can overcome some of these limitations that stem from RWD not being collected for research purposes

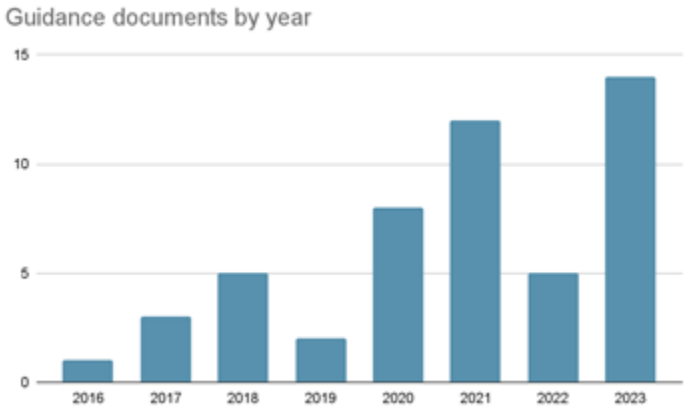
Figure 2. Data relevancy and quality are equal components of a fit-for-purpose real-world dataset

Source: Duke Margolis Characterizing RWD Quality and Relevancy for Regulatory Purposes. 2018

Data quality: variability in how data quality is defined

Key Findings related to "Data Quality" assessment of published guidance documents:

- Agreement that data quality is fundamental for RWE studies
- Variability in the level of detail on how to evaluate quality and the important components of quality
    - Though "accuracy," "timeliness," and "representativeness" were common
- There is no clear consensus on how researchers need to demonstrate/justify data quality



Source: IDERHA, Report on Global Regulatory Best Practices Analysis: A scoping review of HTA and Regulatory RWD/E policy documents https://www.iderha.org/sites/iderha/files/2024-05/D6.2%20Report%20on%20Global%20Regulatory%20Best%20Practices%20Analysis_v2.0.pdf

Data quality: variability in how data quality is defined

Path forward

- Harmonization of data quality standards
- Improved transparency from data and registry providers - data quality and transparency is often out of the researcher's control
- Improve data collection efficiency and quality

Data quality: variability in how data quality is defined

2024 stakeholder actions

Pharma Industry

[3.1] At an early stage of product development, engage with clinical networks to create or further develop registries and databases following unified data standards, to collect high quality and interoperable data.

Payers and HTA Bodies

[2.8] Collaborate with regulators on common frameworks for data quality assessment, data standardisation efforts and methodologies for feasibility assessment. Advise health data holders of the common requirements so that they can develop their datasets accordingly.

Clinical teams

[4.4] Clinical networks and study groups should advise on the most suitable and efficient way for health systems to collect real-world data (RWD) to avoid multiplicity of data entry and clarify the support clinical teams require to collect good quality RWD.

Registry holders & Analytics Groups

[6.6] Align to RWD standards to ensure data meets quality standards required by HTA bodies.

[7.9] Work with data providers to explain the requirements of decision-makers to clearly demonstrate data quality and encourage standardised documentation they can use for all RWE studies.

2024 stakeholder actions manuscript has been submitted to the International Journal of Technology Assessment in Health Care in Oct 2024. Actions have been summarized here for brevity.

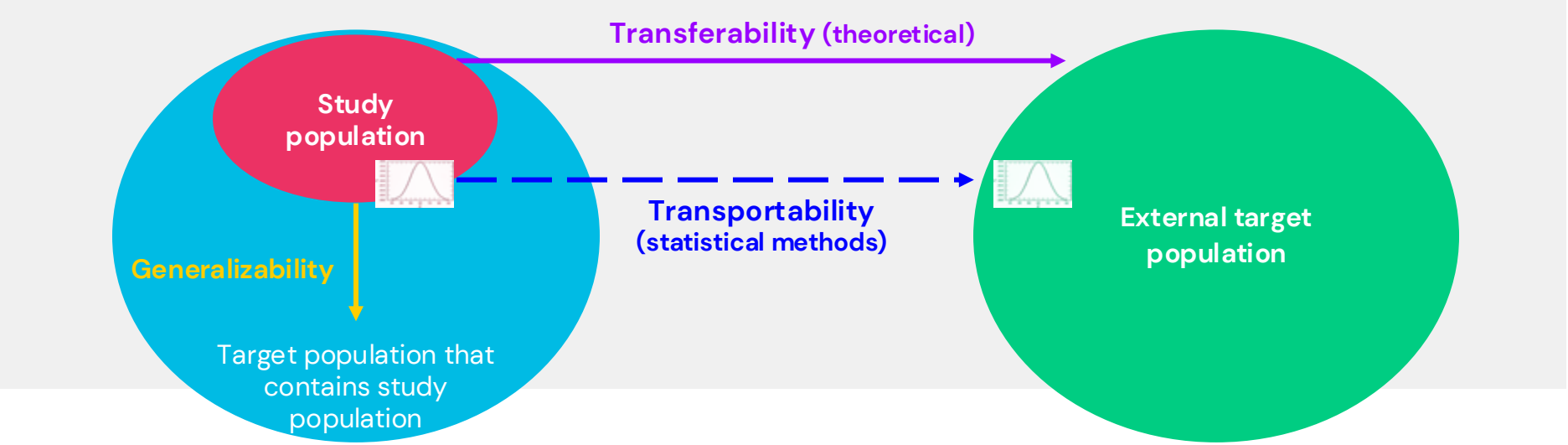
Transportability

Transportability: How do results apply to my patient population?

Successes: Decision-makers are becoming more comfortable with RWE to address causal questions

Problem that transportability is trying to solve:

- Fit-for-purpose RWD is not available, has poor quality, or is easily accessible in all jurisdictions
- Industry has limited resources and cannot run RWE studies in every jurisdiction where they are seeking access



Transportability: How do results apply to my patient population?

Current challenge

- Methods exist (e.g., applying RCT results to target population), but can they be extended to RWE?
- Limited use cases of transporting RWE results to other RWE populations

Table 1. Overview of key study characteristics from the six identified case studies.

First author	Study year	Therapeutic area	Primary reason for transporting	Data type		Transported estimate	Transportability method	Ref.
				Original	Target			
Basu	2023	Mental health	Limited RWD available	US RCT data	US RWD (claims)	Mean difference	Weighting	[48]
Cook	2023	Substance use	Unrepresentative RCTs	US RCT data	US RWD (multiple)†	Hazard ratio	Weighting	[47]
Inoue	2021	Oncology	Demonstrate utility/feasibility of transportability	US RCT data	US RCT data‡	Hazard ratio	Weighting	[30]
Mollan	2021	Infectious disease	Discrepancies between RCTs & observational data	US RCT data	US RWD (EMR)	Hazard ratio & incidence rate difference	Weighting	[49]
Montez-Rath	2022	Rheumatology/ inflammation	Limited RWD available	US RWD (claims)	US RWD (claims)	Incidence rate	Weighting	[46]
Ramagopalan	2022	Oncology	Demonstrate utility/feasibility of transportability	US RWD (EMR)	Canada RWD (EMR, registry)	Overall survival	Outcome regression	[50]

Source: Levy et al. Use of transportability methods for real-world evidence generation: a review of current applications. JCER 2024

Transportability: How do results apply to my patient population?

Path forward

- More demonstration projects that transport RWE effect estimates to external RWE populations
- Guidance on methods and reporting

Transportability: How do results apply to my patient population?

2024 stakeholder actions

RWE4Decisions REAL WORLD EVIDENCE

Pharma Industry

[3.5] Lead discussions about transportability of RWD across borders and support efforts to align data collection requirements across jurisdictions.

[3.10] Share, publish and enable discussion of case studies to show how RWE has been assessed and used in HTA/Payer decision-making, focussing on specific issues (e.g. external control arms, transportability), and challenging cases scenarios

Payers and HTA Bodies

[1.4] Initiate and engage in multi-stakeholder discussions with companies about RWE generation plans. Determine which data are transferable and identify additional local RWD that may be needed to inform decision-making, aligning with other jurisdictions when possible.

RWD/Analytics Groups

[7.2] Continue to engage in demonstration projects

[7.4] Work with HTA bodies to share and operationalize the implications from available demonstration projects to build mutual understanding and trust in RWE.

[7.6] Support HTA bodies in developing detailed published guidance, where appropriate.

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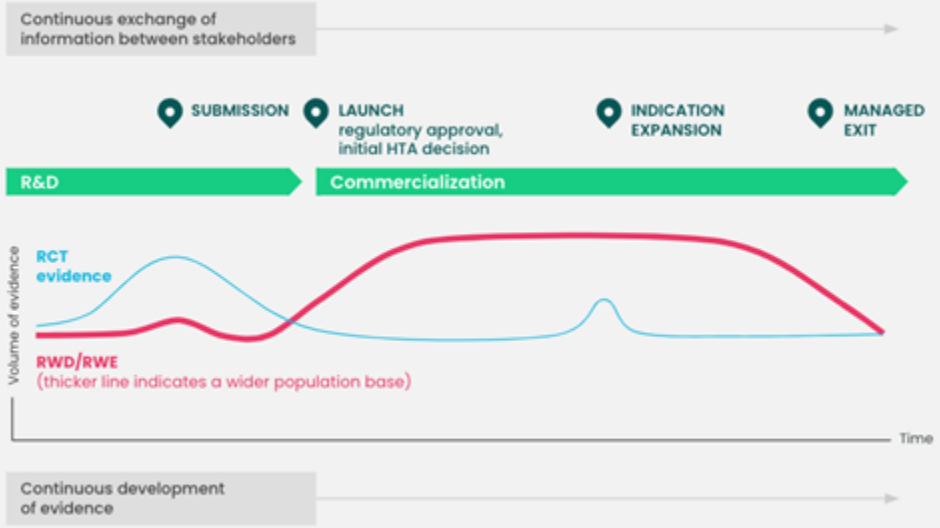
Lifecycle management

Lifecycle management: Realizing the potential of RWE

Successes: Agencies recognize the need to evaluate drugs at multiple timepoints and are updating processes to reassess products after launch (e.g., NICE's Cancer Drugs Fund and Innovative Medicines Fund, CDA's post-market drug eval program and time-limited decisions) and are incorporating RWD/E into these reassessments

Problem that lifecycle management is trying to solve:

- Uncertainties at launch, especially in therapies with accelerated approvals
- Uncertainties in how RCT evidence translates to current clinical practice and a real-world population



For illustration purposes only

Lifecycle management: Realizing the potential of RWE

Opportunity and expectations for RWE to address clinical uncertainties

- Payers across 5 countries agree that RWE should be used to confirm efficacy results from RCTs post-launch

Currently, RWE plays only small roll

Evaluation of first 24 drugs exiting NICE's Cancer Drugs Fund

- Limited use of RWE to address the main clinical uncertainties, instead clinical trial data was used
- RWE used more to justify assumptions in CE models

In recent HTA reassessments across 6 agencies

- RWE was used to address clinical uncertainties, but most often in addition to RCT evidence
- No *de novo* comparative effectiveness RWE studies were used

Sources:
Bharmal et al (2024) DOI: 10.2217/fon-2023-1004
Kang & Cairns (2022) DOI: 10.1017/S0266462324000291
Jaksa et al (2024). Use of RWE in HTARs across 6 HTA agencies. Poster at ISPOR EU 2024.

Lifecycle management: Realizing the potential of RWE

Path forward

- Where RWE is relevant to addressing uncertainties, we need a more concerted effort to develop RWE generation plans. For example,
  - prioritized list of research questions
  - identification of fit-for-purpose data
  - timeline to ensure data is mature and identify when study results will be available

Lifecycle management: Realizing the potential of RWE

2024 stakeholder actions

RWE4Decisions REAL WORLD EVIDENCE

Pharma Industry

[3.1] Discuss plans for RWE generation at scientific advice meetings at several points during the lifecycle of the medicine.

[3.5] Continue to drive discussions about use of, and alignment of, Outcomes-Based Managed Entry Agreements (OBMEA)/Post-Launch Evidence Generation (PLEG).

Payers and HTA Bodies

[1.3] Collaborate with other HTA bodies and Payers and regulators to align post-launch evidence generation (PLEG) requirements needing national data collection.

[2.6] Encourage and support industry to consider possibilities to expand post-authorisation studies and data collection plans intended to support regulatory decision making to also address HTA/Payer evidence needs.

[2.5] Collaborate to expand Early Dialogue/scientific advice/Joint Scientific Consultation to cover RWE generation throughout the product life cycle to address uncertainties in clinical and cost effectiveness.

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Summary

Summary

Successes	Challenges and Gaps	Path Forward	Key Stakeholders
Agreement on importance of data quality Increase in data availability	Variability in definitions of data quality	Harmonization Data provider transparency Data entry efficiencies and improvements in quality	-Pharma -HTA bodies -Clinical teams -Data holders -Analytics groups
Acceptance of RWE for causal research questions	Lack of transportability methodology recommendations	Demonstration projects	-Pharma -HTA bodies -Analytics groups
Agencies implementing lifecycle management processes	Historically limited use of RWE. RWE is likely not optimized.	Concerted effort to prioritize RWE, where appropriate, to fill evidence gaps	-Pharma -HTA bodies

Thank you

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