RWE4Decisions REAL WORLD EVIDENCE

2024 ANNUAL SYMPOSIUM

Developing Real-World Evidence to Deliver Innovation in HTA

RWE4Decisions Annual Symposium | Brussels, 14 November 2024

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EXECUTIVE SUMMARY

Held in Brussels on 14 November 2024, the RWE4Decisions Annual Symposium convened more than 100 stakeholders both online and in person, representing some 15 nationalities across Europe and Canda. Participants included regulators, HTA bodies, payers, clinicians, patients, academics and industry.

The theme of this year's event - "*Developing Real-World Evidence to Deliver Innovation in HTA*"- reflected the urgency and opportunity created by two major European policy initiatives: the EU Health Technology Assessment (HTA) Regulation and the European Health Data Space (EHDS).

Key themes of the Symposium included:

- The continuous dialogue and interactions between regulatory and HTA stakeholders on the potential of Real-World Evidence (RWE) to contribute to the assessment of health technologies, especially in rare diseases and complex treatment landscapes.
- The critical role of infrastructure, interoperability, and data quality in enabling secondary use of health data under the EHDS.
- The need for early and continuous engagement between stakeholders, supported by shared methodological guidance and collaborative platforms such as DARWIN EU.
- The updated 2024 **Stakeholder Actions to Generate Better RWE**, revised and launched at the Symposium to reflect the evolving scientific, regulatory, and data policy landscape in Europe.

The Symposium highlighted both progress and persistent gaps in how RWE is understood, accepted, and applied in HTA and reimbursement processes. While the tools and frameworks are emerging, sustained investment, trust-building, and coordination are essential to deliver on their promise.

OPENING SESSION

Ms Laura Batchelor, from the RWE4Decisions Secretariat and Chair of the 2024 Symposium, welcomed participants by reaffirming RWE4Decisions' mission: to serve as a learning network that helps stakeholders navigate the complexities of developing and applying RWE in HTA and pricing and reimbursement (P&R) decision-making. She noted that 2024 was a pivotal year for RWE, as the EHDS and HTA Regulation both moved from legislative negotiation into implementation planning. She invited attendees to use the day to explore what it means to generate "fit-for-purpose" RWE under these frameworks - and how stakeholders can prepare for a future where RWE is routinely expected.

PLENARY SESSION I: The Policy Context for Real-Worl Evidence

Chaired by François Meyer, RWE4Decisions

Dr Enrique Terol García, Coordinating Advisor on Health at the Permanent Representation of Spain to the EU, offered a Council perspective on the implementation challenges and opportunities of the EHDS. He described the EHDS as "one of the most innovative legislative frameworks in EU health policy," but warned that it would only succeed if Member States build the technical and institutional capacity to support high-quality data production and sharing, for primary and secondary use.

Dr Terol highlighted the fragmentation in digital maturity across Europe. While countries like Estonia and Finland are highly digitalised, many others are still grappling with basic EHR rollout, inconsistent data governance, or the absence of national data strategies. "Most Member States are still far from being fully digitalised," he noted, adding that without investment in infrastructure and training, even the best-designed regulation would fall short.

He also stressed the importance of a cultural shift. For EHDS to function, data holders - including clinicians, registry owners, and public authorities - must embrace the value of sharing their data with external users. "There are hundreds of registries in Europe that were built over decades," he observed. "Now, they are being asked to make their data available to others. This requires not just regulation, but a new mentality."

In parallel, **MEP Tomislav Sokol**, who served as the European Parliament's rapporteur for the EHDS, described the compromise that emerged during legislative negotiations. The Regulation establishes a dual system:

- **Primary use of data**, focused on clinical care, where patients can access and share their health records across borders.
- **Secondary use**, where anonymised data may be used for public-interest research, policymaking, and innovation - subject to an opt-out mechanism.

MEP Sokol acknowledged that legal complexities - especially around General Data Protection Regulation (GDPR) GDPR interpretation - made secondary use a contentious topic. But the opt-out option, that allows people who do not wish to take part in secondary use to opt out in a simple and reversible manner. struck a balance between preserving patient rights and ensuring representative datasets. The EHDS, he explained, introduces clear access procedures and research purposes to ensure legal certainty.

Looking ahead, he cautioned that EHDS implementation would require five to ten years, with different countries advancing at different speeds. Member States must build technical infrastructure, conduct

professional training, and develop new data-sharing protocols - all while responding to rapid innovation in AI, digital health, and real-time analytics.

The session continued with a presentation by **Dr Patrice Verpillat**, Head of Real-World Evidence at the European Medicines Agency (EMA), presenting the latest developments from the EMA's Data Analysis and Real-World Interrogation Network (DARWIN EU).

Dr Verpillat described DARWIN as the cornerstone of EMA's strategy to integrate real-world data (RWD) into regulatory science. Since its launch in 2022, DARWIN EU has expanded to 20 active data partners, with ten additional partners in the onboarding pipeline. It now supports more than 60 study requests annually and has significantly increased its operational maturity and study throughput.

In 2024, DARWIN studies focused on three core areas: drug utilisation, safety monitoring, and treatment effectiveness. While regulatory use cases are expanding, Verpillat acknowledged that the integration of DARWIN into HTA processes is still developing. He stressed that comparative effectiveness analysis remains a methodological challenge, particularly due to difficulties in identifying appropriate comparators, confounding variables, and consistent outcome measures across data sources. To address these challenges, EMA hosted targeted technical workshops in 2024 that brought together HTA agencies, registry holders, industry experts, and academics. These workshops sought to align expectations and design criteria, improve data quality, and promote broader stakeholder buy-in.

He also introduced the **EMA Network Strategy 2025–2028**, which includes a strategic focus on **accessibility** - ensuring that evidence generated by regulators is also understandable and actionable for HTA and payer stakeholders. One of its key aims is to promote more lifecycle-aligned evidence generation, so that data collected for regulatory purposes is relevant and acceptable for downstream reimbursement decisions.

DARWIN, he emphasised, was never intended to be an exclusive tool for regulators. Its long-term potential lies in supporting the entire healthcare ecosystem - from early advice and clinical development through to HTA and post-market surveillance. EMA remains open to co-developing methodologies with HTA bodies, but further work is needed to build trust, clarify expectations, and define use cases.

PANEL DISCUSSION

The panel discussion brought together voices from the patient community, payers, and the pharmaceutical industry to explore practical implications of the HTA Regulation and the EHDS.

Dr Enrique Terol García, returning to the panel, offered a national perspective on Spain's readiness for Joint Clinical Assessments (JCAs). He described Spain's HTA system as decentralised, with competencies split between a central agency and eight regional bodies. While this has posed coordination challenges, recent efforts under the national HTA network have improved consistency and capacity. He affirmed that Spain is **well positioned** to contribute to JCAs and highlighted early engagement with DARWIN EU as a promising development.
Dr Patrice Verpillat elaborated that DARWIN currently includes several Spanish data partners and that even in decentralised systems, **RWE generation is feasible**. However, industry cannot directly commission DARWIN studies for HTA purposes. A broader stakeholder engagement process may be developed once the platform reaches full maturity.

Mr Christoph Rupprecht, Head of Health Policy and Economics at AOK Rheinland/Hamburg, offered a payer perspective. He supported the HTA Regulation's potential to harmonise decision-making across Europe, reduce duplication, and speed access to innovation. However, he cautioned that the evidence provided must be relevant to national contexts. Drawing on Germany's **AMNOG procedure** (Pharmaceuticals Market Reorganisation Act) and the routine practice collection of real-world data to demonstrate real-life relative effectiveness **- the AbD model** - he illustrated how Germany has successfully integrated routine data to complement RCT evidence in reimbursement decisions.
He cited AdD's role in enabling indirect comparisons when head-to-head trials are unavailable, stressing that such methodologies provide a pragmatic "middle ground" between gold-standard RCTs and less robust single-arm trials.

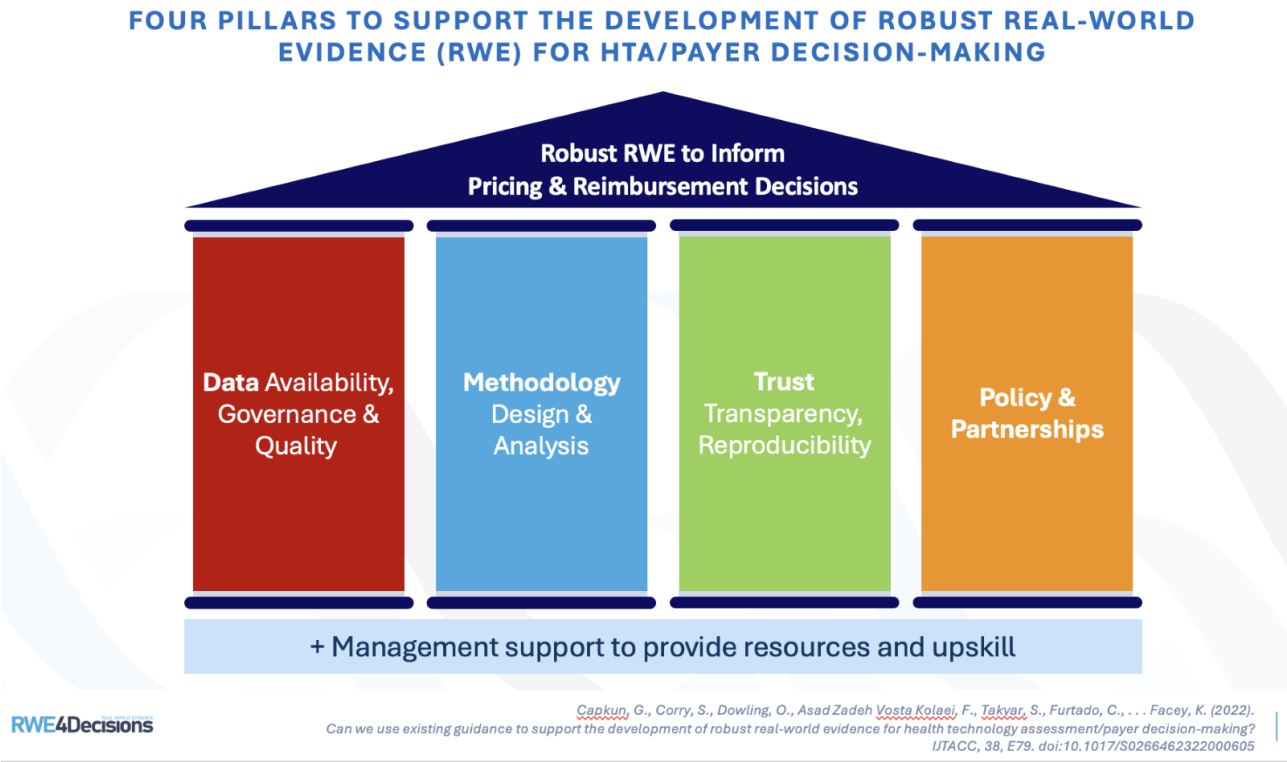
Ms Anne-Pierre Pickaert, representing the Acute Leukemia Advocates Network, welcomed the HTA Regulation's emphasis on comparative effectiveness. From a patient perspective, she highlighted that many traditional RCTs fail to reflect real-world care, particularly when comparators are outdated or even unethical. Conversely, single-arm trials often provide insufficient context. She advocated for **flexible designs**, such as pragmatic trials and the use of registry data, that can deliver meaningful evidence without sacrificing scientific rigour or patient acceptability.

Dr Alexander Natz, Secretary-General of the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), agreed that RCTs remain central but are often not feasible for rare diseases or highly targeted therapies. He urged HTA bodies to **accept real-world data** not just as supplementary, but as essential when RCTs are impractical. He also underscored the importance of designing evidence strategies from the outset - aligned with both regulatory and HTA requirements - and cited examples from Germany where RWE has closed data gaps identified by payers.

PLENARY SESSION II: Launching the new RWE4Decisions Stakeholder Actions to Generate Better Real-World Evidence for HTA/Payers Decisions

Chaired by Ashley Jaksa, Aetion

Dr Karen Facey opened the session by reflecting on the work of RWE4Decisions over 2024 in alignment with the four pillars to build robust RWE for HTA/Payers that guide the work of the learning network. She outlined how the initiative remains a catalyst for multi-stakeholder dialogue to improve the generation and use of RWE across the life cycle of highly innovative medicines.



Webinars explored the potential use of digital endpoints in HTA (Data Availability and Governance pillar) and the new joint Nordic HTA initiative and implications for RWD (Policy and Partnerships pillar).

Dr Facey presented findings from multi-stakeholder discussions about **post-launch evidence generation (PLEG)** - a topic not explicitly covered in the EU HTA Regulation but deemed vital by many national agencies. Drawing on use cases from five countries, she called for international coordination in defining PLEG frameworks and data protocols. These efforts, she argued, should reduce burden on clinicians, align outcome priorities with patient needs, and avoid duplicative data collection.

She concluded by urging stakeholders to continue exploring how digital endpoints, early scientific advice, and clear reporting of RWE studies and assessments of submitted RWE can inform more consistent, high-quality real-world evidence generation. Solid actions that can be taken by all stakeholders to further these goals were developed by the RWE4Decisions learning network in extensive research over 2024 and were discussed in the next section.

Ms Ashley Jaksa, Vice President of Scientific Strategy and Partnerships at Aetion, took the floor and introduced the new set of **Stakeholder Actions to Generate Better Real-World Evidence,** marking the culmination of a 12-month, highly participatory development process with the wider RWE4Decisions Learning Network.

She walked the audience through the development process of the new Stakeholder Actions, highlight the main steps in concluding this important piece of work of RWE4Decisions:

1. **Focus group meetings** with each stakeholder group, which began in January 2024
2. **A multi-stakeholder roundtable** followed, enabling cross-cutting discussion on where and how to improve alignment
3. A **public webinar** aimed at gathering wider input, followed by a **public consultation** phase gathering structured feedback from the wider community
4. The Actions were finalised mid-year and have been submitted for peer-reviewed publication

Ms Jaksa described the updated Actions as a "whole-of-ecosystem framework" designed to reflect current capabilities and policy realities. Each action is mapped to one of the four pillars and includes **indicators of progress** for different stakeholder groups:

Importantly, she emphasised that while scientific methods have matured and data access has expanded, RWE remains underused in HTA decision-making. The updated Actions aim to change that by providing practical, role-specific pathways for collaboration, trust-building, and operational readiness.

PANEL REFLECTIONS ON THE UPDATED STAKEHOLDER ACTIONS

The updated Actions were then discussed in a panel featuring representatives from across the health ecosystem. Each speaker was invited to present three priority actions from their stakeholder group.

Ms Pia Rannanheimo, Chief Specialist at the Finnish Medicines Agency (FIMEA), spoke from the perspective of national HTA bodies and payers.
She emphasised the need to overcome fragmentation among HTA agencies by investing in shared infrastructure and building analytical capacity. She highlighted the importance of influencing national data policy to align HTA data needs with EHDS implementation and called for more transparent use of RWE through published use cases. Rannanheimo also recommended that HTA agencies produce

annual RWE impact reports - modelled on the EMA's DARWIN EU updates - to drive shared learning and improve consistency across countries.

Mr Shaun Rowark, Associate Director for Data Access and Analysis at NICE, addressed actions relevant to collaborative HTA efforts.
He stressed the importance of engaging early with data controllers to articulate data gaps, particularly as more advanced therapies enter the system. He outlined the development of secure data environments as a way to safely analyse sensitive patient data and noted that, despite Brexit, NICE remains involved in European initiatives such as DARWIN EU. Rowark also proposed the creation of a shared PLEG repository to consolidate ongoing evidence generation efforts and facilitate reuse of real-world study outputs across Member States.

Mr Stefan Joris, Chair of RaDiOrg (Rare Disease Belgium), represented the patient community, focusing on building capacity for structured and informed patient involvement in HTA.
He called for greater investment in advocacy training and for involving patient groups earlier - ideally before early scientific advice - to help shape trial designs and prioritise meaningful outcomes. Joris stressed that transparency around how patient data is used is essential to build trust and promote engagement. He pointed to cystic fibrosis registries as a successful example of long-term patient data collection that reflects real-world quality-of-life outcomes, which often matter more than clinical measures alone

Dr Andre Vidal Pinheiro, Vice-President and Head of Patient Value & Access – Europe & Canada, at Takeda, presented the priority actions identified for medicine developers, with a focus on operationalising RWE in the evolving EU HTA context.
He stressed that early understanding of JCAs and PICO (Population, Intervention, Comparator, Outcome) definitions is essential to inform RWE study designs. He highlighted France's early access programme as a model for embedding RWE into managed entry processes and called for scaling up early advice opportunities, noting that Germany's G-BA held over 100 early scientific consultations in 2023, compared to the 10 planned Joint Scientific Consultations under the EU Regulation. He concluded by reinforcing the importance of flexibility in RWE methodologies, especially for rare diseases and small populations, and expressed strong support for tools such as the updated Stakeholder Actions to help developers identify practical steps for improvement.

CLOSING SESSION

The final session of the Symposium turned toward the future of HTA implementation in Europe, as well as the role RWE4Decisions should continue to play in supporting stakeholder alignment and system readiness.

Next steps for the implementation of EU HTA Regulation

Dr Carlos Martín Saborido, former Advisory Member at the Directorate General for the Common Portfolio of SNS and Pharmacy Services in the Spanish Ministry of Health

Dr Saborido delivered the closing keynote on **next steps for the implementation of the EU HTA Regulation**. Reflecting both policy insight and operational urgency, Saborido's remarks offered a clear and strategic roadmap for ensuring that RWE contributes meaningfully to HTA processes under the new Regulation.

He emphasised two key ideas. First, RWE must not be viewed as a post-launch afterthought - it must be **proactively integrated into HTA processes alongside JCAs**. Second, Member States must **prepare in parallel** with the development of JCAs. He warned against a reactive approach, cautioning that delayed national readiness could create bottlenecks and implementation gaps.

Dr Saborido then laid out **three concrete actions** for improving the HTA landscape:

1. **Specific and proactive data collection**: Member States must begin collecting real-world data **before** the JCA stage, particularly in rare diseases. Assessments must go beyond clinical efficacy and safety to include **resource use, caregiver burden, and quality of life**. These data should be framed with a view toward **transferability** across Member States.
2. **Early dialogue to address uncertainty**: National authorities should engage early with developers to **plan how to address clinical and financial uncertainty** - including through RWE. He stressed the need for better alignment between EMA and HTA agencies on how to handle **effect modifiers in single-arm trials**, so that indirect comparisons are more robust and relevant.
3. **Horizon scanning for early evidence planning**: Rare diseases, in particular, require proactive evidence strategies. By identifying pipeline products early and launching targeted RWD collection in parallel, HTA and payer systems can be better prepared for budget impact assessments and managed entry agreements. This would also allow developers to generate more accurate prevalence and burden-of-disease estimates.

Dr Saborido concluded with a call to action for the RWE4Decisions Learning Network to continue advocating for **cross-border data collaboration**, **early advice structures**, and **RWE integration into national reimbursement pathways**.

Conclusions and Payer reflections

Dr Johan De Cock, Senior Adviser and former CEO of Belgium's National Institute for Health and Disability Insurance (INAMI-RIZIV)

Closing the day, **Jo de Cock**, delivered his reflections on the evolution of real-world evidence and its trajectory in European healthcare decision-making.
He began by acknowledging the tremendous progress made in the last decade. A decade ago, he noted, the primary debate was **whether** RWE should be considered. That has now shifted to **under what conditions** and **how best** to generate, interpret, and apply RWE. Regulatory frameworks have evolved, and methodologies are maturing. The operational reality of RWE in the lifecycle of medicines is no longer theoretical - it is **real and irreversible**.

Dr De Cock praised the emergence of **guidance documents and international repositories**, citing work by the EMA, FDA, and the EHDEN and EDERA initiatives as examples of progress in consolidating best practices. However, he noted that HTA is lagging behind regulation in terms of clear guidance and called for the creation of a **centralised repository** of HTA-specific methodologies and tools for RWE assessment.

He reminded participants that RWE cannot be developed in silos. It must be part of a **full lifecycle evidence strategy**, with early dialogues, structured post-launch follow-up, and transparency around evidence standards. Real-world studies should not be left to chance or vary significantly across jurisdictions.

Turning to the payer perspective, de Cock outlined several persistent challenges:

- Lack of clarity on the value of RWE for payers
- Difficulty in defining and measuring real-world outcomes
- Lack of consistent **guidelines on interpretation**
- Resource constraints and concerns around **study costs and transparency**

Despite these challenges, he made a compelling case that RWE is indispensable to assess performance, evaluate diverse patient populations, support cost-effectiveness modelling, and design outcome-based managed entry agreements. He reiterated the importance of collaboration, noting that "only together with all stakeholders will we be able to overcome these challenges."

He closed with a forward-looking message. The EHDS and HTA Regulation are major milestones, but they must be followed by **actionable implementation plans**, including national strategies for clinician involvement, patient engagement, and analytical harmonisation. RWE4Decisions, he concluded, is "a unique forum and learning platform" that must continue to foster shared learning, co-creation, and practical tools for evidence-based decision-making.

"Real-world evidence cannot be seen in isolation. It must be generated across the full life cycle of a product - from early dialogue to post-launch - and that requires trust, transparency, and cooperation. RWE4Decisions is a unique forum where all stakeholders come together to exchange knowledge and develop robust approaches to evidence that truly inform healthcare decisions."

RWE4Decisions REAL WORLD EVIDENCE

RWE4Decisions is a payer-led multi-stakeholder learning network, which has developed **stakeholder actions** that will better enable the use of real-world evidence in HTA/payer decisions about highly innovative technologies.

The work has been commissioned by the Belgian National Institute of Health and Disability Insurance (NIHDI) and is led by a multistakeholder **Steering Group** with a wider community of contributors including HTA bodies and payers, regulatory agencies, patient groups, clinicians, industry, analytics experts and academic experts/researchers.

The RWE4Decisions Secretariat is provided by FIPRA, with sponsorship in 2025 by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), Astellas, AstraZeneca, Gilead, MSD, Roche and Takeda.

For further information and to watch the recording of the symposium, visit our website at: https://rwe4decisions.com/event/rwe4decisions-symposium-developing-real-world-evidence-to-deliver-innovation-in-hta/

What are you are doing to progress learnings on the use of RWE?

Contact us at **secretariat@rwe4decisions.com** to join the RWE4Decisions Learning Network.

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