RWE4Decisions REAL WORLD EVIDENCE

Webinar Report

HTA/Payer Collaboration in the Nordics: The Role of Real-World Evidence

Wednesday, 23 October 2024, 15:00-16:30 CEST

Speakers

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The **23 October RWE4Decisions Webinar "HTA/Payer Collaboration in the Nordics: the Role of Real-World Evidence"** explored the Joint Nordic HTA Bodies (JNHB) model of collaboration, and the role of Real-World Evidence (RWE) in their decision-making processes. The speakers discussed the genesis and role of the Nordic collaboration, its relation to national HTA processes, the impact of the upcoming EU HTA Regulation, and the role of RWE in HTA collaborative initiatives with a regional focus.

Dr. Ehm Andersson Galijatovic presented an overview of the JNHB. Its predecessor, FINOSE, was founded in 2017 as a bottom-up initiative of the Finnish, Norwegian, and Swedish authorities. The collaboration was renamed 'Joint Nordic HTA Bodies' in 2024, following its expansion to include Denmark and Iceland.

The collaboration focuses solely on creating a joint Health Technology Assessment (HTA) to inform national decision-making process for new medicines. This has been feasible given the similar processes and methodologies across the Nordics. Although outside the scope of the JHNB, price negotiations may occur at the joint Nordic level if agreed by the company and negotiators.

The JNHB represents a **gathering of best practices from the Nordic HTA bodies,** aimed at improving data quality, convergence of HTA methodologies and evidence requirements. This facilitates more equal access for patients across the Nordic countries, and, eventually, resource-sharing. The collaboration is supported by a series of common background documents:

- The Memorandum of Understanding, which acts as the basis of the collaboration, defines its scope and legal basis.
- The Waiver of Confidentiality, to be signed by the company when engaging with JHNB, allows the HTA bodies to share confidential information during an assessment. It encompasses, for example, unpublished data or study reports, and does not extend to confidential price information.
- A Process Guideline, defining the process, steps, timelines, roles and responsibilities,
- A Submission Dossier Template, offering guidance to health technology developers (HTD) on the information needed for the joint Nordic HTA, such as how to include national elements in the health economic model, which should be flexible and adjustable for all countries.

As far as the roles are concerned, for each assessment, an assessor and a co-assessor HTA body are appointed. The assessor is responsible for coordinating the process itself, contact with the HTD, and keeping to timelines. The assessor will critically assess the clinical part of the submission or the health economic part, and the co-assessor will assess the other part. Together, the assessors create a draft report. The HTA bodies from the other JNHB members will act as reviewers or, if the assessment of a specific product is outside their remit, as observers.

The process begins following one of three pathways: (1) JNHB contacts the HTD regarding potentially suitable products identified through horizon scanning, (2) national HTA bodies suggest products for joint assessment, or (3) the HTD sends the JNHB a **request for assessment**, including the waiver of confidentiality and an overview of the Nordic treatment landscape, which should be similar enough to warrant collaboration. A request by the HTD is the option that is used the most.

If the product is suitable for a joint assessment, this request and other specific questions are then discussed in a **scoping meeting** between the JNHB and the developer, followed by the **submission** of the dossier including the health economic model. The **assessment** then commences, which the JNHB aims to finalise within 90 days. **National steps** are taken simultaneously: any information particular to one country, the currency conversion, and a summary in the national language are included in a country-specific appendix. Finally, the report is used for decision and negotiation in the various countries.

Dr Maria Eriksson continued with insights on how the work of the JNHB is used in national processes and the interactions with the upcoming EU HTA Regulation, drawing on her experience at TLV, the Dental and Pharmaceutical Benefits Agency under the Swedish Ministry of Health & Social Affairs.

TLV undertakes two types of processes. Firstly, pricing and reimbursement (P&R) decisions for **out-patient products**, where the company applies through TLV, who perform the HTA. P&R is then decided by TLV's Pharmaceutical Benefits Board. Secondly, TLV conducts HTA for **in-patient products**, based on requests from the regions and the NT-Council for a specific product. After the report is delivered, the P&R process occurs between the regions and the company. Based on this, the NT-Council issues recommendations to the regions on how to use the product.

When companies apply through **JNHB**, the HTA step is conducted at Nordic level instead of national level. The remaining steps stay the same, unless agreed by the company and countries to also undergo the voluntary Nordic price negotiation.

From the Swedish perspective, the above-mentioned JNHB national appendix would include a summary of the main findings and conclusions of the joint report in Swedish, a currency conversion into Swedish Kroner, Sweden-specific factors when relevant and, for out-patient products, an assessment of the disease severity, the results of the price negotiation (if done on national level), and, the decision document written in Swedish.

The evolution **from FINOSE to JNHB** expanded the collaboration's resources and enhanced available knowledge, while also leading to the development of supporting documents clarifying roles and responsibilities, and a joint webpage and email address for increased transparency. Documents currently published on their website have received feedback from Nordic pharmaceutical industry organisations, to be considered for document updates.

The **HTA Regulation (HTAR)** will be implemented stepwise between 2025 and 2030, starting with oncology and advanced therapy medicinal products (ATMPs). Oversight will be provided by the Committee on HTA which includes DG SANTE and Member States

representatives, and the HTA Coordination Group of national HTA bodies' representatives. The latter is further split into four subgroups: (1) Development of methodologies and procedural guidance, (2) Joint Clinical Assessments (JCA), (3) Joint Scientific Consultations (JSC), and (4) Identification of Emerging Health Technologies. The JNHB is represented in all of these groups though Nordic country representatives.

The upcoming Regulation has had significant impact on preparatory work at national level, with several JNHB members having been involved previously in EUnetHTA. In line with the HTAR, **JCA reports will be considered valid document in the Nordics' national and JNHB assessments**: if the relative effectiveness of a product has already been assessed in a JCA report, it will be used as basis for the Nordic health economic evaluation.

Following the HTAR implementation, the JCA process will start when the company submits an application for market authorisation to the European Medicines Agency (EMA). The JCA assessor and co-assessor then send the Population, Intervention, Comparator, Outcomes (PICO) assessments to the Member State, who submits a reply. The PICO is consolidated and represents the basis of the dossier, to be submitted by the HTD. The assessment is then performed, and the report should be finalised maximum 30 days after the marketing authorisation. This will facilitate the JNHB process: as the PICO and comparator are determined at an earlier stage, which will help determine whether a product qualifies joint Nordic assessment.

Moving forward, the JNHB will continue knowledge-sharing and producing high-quality assessments across the Nordics, increase the number of regional assessments, decrease divergences in methodology and evidence requirements, increase the transparency of the joint work, and adapt to the HTAR.

Prof Kimmo Porkka discussed the role of RWE in HTA/Payer national collaborative initiatives, with a focus on integrating **clinical data from hospital sites** in HTA and regulatory processes. This type of real-world data (RWD) is collected from the electronic health records and generic databases, and can be used, for example, for clinical purposes, medical research and development, digital phenotyping, and HTA.

As many of the diseases for which data is collected are **rare diseases**, there is a need to network to upscale RWD generation. For this purpose, the key is ensuring **data interoperability and standardization**, especially regarding new predictive modeling techniques such as neural networks or machine learning. Once this is ensured, it becomes possible to query these datasets and networks in an almost real-time manner, obtaining results in a matter of days. The system can then easily be automated, paving the way to providing reliable, transparent, and reproducible evidence, and then upscale this to cover very large groups of patients. To ensure EU General Data Protection Regulation (GDPR) and European Health Data Space (EHDS) compliance, only anonymous aggregate data is shared in a federated manner.

An example of such system is the **Fin-OMOP project for data interoperability** in Finland. Started in 2019, it harmonises all available secondary care sites, university hospitals, and national registries to the OMOP data model. It aims to have a population-based network

of harmonised data by 2025, and most major governmental registries and three of the biggest hospitals in Finland have already been advanced.

Similar initiatives exist at EU-level, with the most important being the EMA-sponsored **DARWIN-EU.** It is creating a substantial federated data network and piloting a range of RWE studies to answer regulatory and HTA questions for specific products/indications. A similar approach has been piloted in Finland, funded by Sitra, to generate RWE to answer questions posed by the Finnish Medicines Agency (national HTA body Fimea). They used the FinOMOP network to provide RWE to address the following three case studies:

1. Daratumumab for multiple myeloma: use and outcomes
2. CAR-T: treatment use and outcomes
3. Spinal muscular atrophy: demographics and medicine's use

A federated approach was used, with analytical scripting done by local data teams. The goal was to test the usefulness of this data model harmonisation in the present setting, and whether its combination with data federation could provide fit-for-purpose data as additional evidence for HTA/Payer purposes.

To conclude, Prof Porkka shared a number of learnings from this pilot: firstly, the information requested by Fimea for their analyses was mostly available from the available sources, in the format of federated data. As far as the usability of data is concerned, the quality and validation of data mapping to the common data model may still pose a challenge in assessing the impact and value of treatment, and resource use. At the hospital level, very granular data needs to be mapped in the data model, reflecting indications of use for the medical product in question. Finally, to enhance speed and efficiency of data analysis, local legislation and its interpretation must be streamlined.

Dr Christian Dehlendorff shed light on the use of RWD in HTA in Denmark: under the current processes, HTDs provide evidence packages, which may include RWD and RWE for patient characteristics, external control arms, or natural history. To ascertain relative effectiveness, **using an external control arm** (e.g. US data) may be challenging, but represents the only solution in cases such as single arm studies on very small patient groups. However, Nordic data is preferable, as this is closer to the target patient population and can aid data transportability.

Lars Møller highlighted the increasing demand to obtain access to innovative medicines, especially in the areas of **oncology and rare diseases**. Access to oncology and orphan medicines is becoming more and more demanding in all Nordic countries, but availability is insufficient. An unsuccessful outcome in HTA decisions is correlated with the absence of a standard of care and decreasing number of patients, underlining the need to incorporate data from alternative sources, such as RWE.

In the Nordic markets, HTA bodies have taken a more prominent role in decision-making over the years; however, a balance must be struck between a rational, evidence-based approached in a value-based healthcare budget and the introduction of new innovative medicines. A key factor contributing to this challenge is the increasing fragmentation of

diseases and medicines, particularly for **personalised medicines and ATMPs**. With fewer eligible patients, it becomes difficult for HTDs and HTA bodies alike to apply existing methodologies to ensure the right clinical outcomes.

Many of the products currently under development or being brought to market are highly efficacious due to the emerging stratified and personalised approach to treatment. However, they also require longer timeframes to measure outcome measurements normally associated with clinical effects, such as progression-free survival or overall survival. Consequently, this creates a strong case for the use of RWD to validate clinical effects and outcomes. Thanks to their rich registries and previous use of RWD, the Nordic countries are in a favourable position for this task. In Pfizer, RWE has been delivered alongside traditional data on multiple occasions, and has occasionally represented a decisive factor for a favorable outcome.

Implementing innovative funding models is a critical step towards linking cost and effectiveness. For this, RWE has a significant role, including its ability to capture the dynamic effects of medication in the evaluation process, by tracking patients' long-term outcomes and progression. Finally, it is of importance to ensure that data is developed and evaluated in a standardized and transparent manner.

A panel discussion followed, where the speakers responded to the following questions:

1. How do we make sure to integrate RWE more in the trials?
2. Is there collaboration with other similar initiatives, such as the BeNeLuxA?
3. Do JNHB-level dialogue meetings include a discussion on how to use RWE in the joint assessment?
4. The EU-HTA focuses solely on clinical effectiveness, but your process also includes cost effectiveness, if relevant. What is the demarcation?
5. When discussing RWE in the JNHB, how important would you consider that the pharmaceutical companies discuss the RWE study design and whether it's fit for purpose for your organization in the early stage in a consultation meeting?
6. In your pilot projects, what processes did you use to determine your outcomes to measure? Are there any publicly-available results and reports?
7. What do you think is the value of DARWIN EU to help increase utilization of RWE?

A number of important learnings followed from this conversation. Firstly, there are currently **no Nordic national or joint guidelines for the use of RWE**: high quality guidelines from different sources are used instead, such as the ones developed by the English National Institute for Health and Care Excellence (NICE), the Canadian Drug Agency, and EMA. The HTA Regulation will also complement standards currently in use. Secondly, **methodological and legal challenges to the effective use of RWE** remain: among others, the panelists underlined data access timelines, resources, small patient populations, and difficulties in analysing data across countries. Nevertheless, the similar treatment landscapes that exist in the Nordics facilitate **RWD transportability** and acceptability between these States, as long as the data is of high quality and comparable to what is needed. **Data standardisation** and **developing new methods of analysis** were encouraged.

Thirdly, **collaboration between HTA bodies and HTDs, and submission of fit-for-purpose data** were identified as critical steps to improve the use of RWE in HTA in the Nordics. Early dialogue between HTA bodies and HTDs regarding study design was also underlined, but in the Danish and Swedish national systems, there is no opportunity for early scientific advice, particularly regarding RWE. The only remaining option is the JSC system created by the HTA Regulation, but are limited slots for this advice. Also regarding the relation between the HTA Regulation and the JNHB, the speakers emphasised that, although the JCA reports replace the clinical and relative effectiveness assessments, analyses regarding health economics modelling and cost utility remain up to the Member States and so there is a role for the JNHB here.

Final conclusions focused on what the speakers believed could **support the use of RWE in joint HTA in the Nordics**, with the following themes emerging:

- Need for **clear methodology and guidance** to allow for interoperability of RWE
- **Collaboration, transparency,** and **high-quality RWD** to ensure that medicines get approved and are accessible to patients, with the VALDATA initiative as an example
- Easier combination of data sources across the Nordics
- Submission of fit-for-purpose RWE by HTDs.

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 multi-stakeholder 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 2024 by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), AstraZeneca, Boehringer Ingelheim, Gilead, MSD, Novartis, Pfizer, Roche and Takeda.

For further information and to watch the recording of the webinar, visit our website at:

https://rwe4decisions.com/event/public-webinar-can-endpoints-from-digital-technology-provide-meaningful-outcomes-for-hta/

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

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