EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

EHDEN
Virtual Roadshow
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Public report

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Executive Summary

The European Health Data and Evidence Network (EHDEN) is a pan-European public-private partnership of 22 organisations, led by Erasmus Medical Center and Janssen Pharmaceutica, whose mission is to make large-scale analysis of health data in Europe a reality. Under the aegis of the EU´s Innovative Medicines Initiative and scheduled to run until 2024, it is spearheading the development of a federated data network standardised to a common data model. This greatly facilitates the sharing of health data and research regardless of the organisation or country they originate from.

In October 2020, EHDEN held its first annual roadshow to highlight accomplishments to date, share perspectives on where the health research ecosystem is headed, and map in broad strokes its vision for the remaining four years of its mandate. Due to the ongoing COVID-19 pandemic, the event took place virtually, but that did not impede it from bringing together some of the most passionate defenders of future-forward ideas and approaches to real-world evidence collection, data governance, data ownership, health technology assessment, health data science, patient and stakeholder engagement, biopharma´s future, and public policy, both within and beyond the boundaries of the EHDEN project.

This report presents the main takeaways that emerged from those discussions, which can be heard in their entirety across three individual podcasts (podcast 1, podcast 2, and podcast 3) and three roundtable-style webcasts (webinar 1, webinar 2, and webinar 3). The conversations centred around the following themes:

- The value of real-world data for assessing treatment effectiveness
- The research potential of standardising health data across Europe and mapping them to a common data model that enables systematic analysis of disparate observational databases
- The role of open source software for building out a data strategy for secondary use of health data, while preserving data ownership through built-in privacy mechanisms
- EHDEN´s role as an accelerator of these processes by creating a “marketplace” for data partners and data translators to connect
- The role of early patient involvement and participation in outcomes research
- New ways to think about the value of health data, data access requirements, and marketing authorisation as a way to propel open science research forward

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Webinar One: RWE, OMOP, and COVID-19

The overarching theme of the EHDEN virtual roadshow was the importance of strengthening Europe´s ability to generate, collect, and collate high-quality observational health data in the context of an increasing willingness on the part of regulators to factor in real-world evidence (RWE) into decision-making on the effectiveness of new biopharmaceutical products. As a cornerstone of its RWE gathering approach, EHDEN relies on the Observational Health Data Sciences and Informatics (OHDSI) network of over 300 institutional collaborators with access to data on nearly 600 million patients worldwide.

At the opening of the roadshow, OHDSI was briefly described by **George Hripcsak**, Chair of Columbia University´s Department of Biomedical Informatics, which hosts OHDSI´s global Coordinating Center. OHDSI´s contribution to the world of health research is its proprietary software-as-a-service Observational Medical Outcomes Partnership (OMOP) Common Data Model, which is transforming the way health data gets accessed and utilised with minimal disruption to data owners.

In a podcast leading up to the event, **Matt Wiener**, Director of Informatics and Predictive Science at Bristol-Myers Squibb, who is involved in one of the EHDEN work packages, walked listeners through what OMOP is: a data infrastructure that enables EHDEN´s “data translators” – a cohort of small and medium enterprises specialised in data analytics – to access and convert data from disparate observational databases to a standardised format and vocabulary. It lets them query the data and perform research of interest locally, so that administrative, EHR, or patient-reported data never leave the organisation where they are collected.

Kees van Bochove, founder of the open source software company The Hyve, which supports EHDEN in FAIR-ifying the data it works with, added colour to EHDEN’s description:

“EHDEN is a sort of a personal health train, where we leave the health data where it is – no matter if it´s in a hospital, pharmacy, people´s homes where they record their own activity data – and we send a kind of ´train analysis´ around all these sources to compute locally the results and then bring those back together. So you get a result that is based on all the sources involved, but at no time do you actually share patient-level data outside the data custodian, which is the site where the responsible party is for handling that data.”

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This capacity for crunching and analysing data locally is crucial for gaining stakeholders' trust and buy-in, as EHDEN seeks to expand European healthcare organisations´ participation in the project. It currently has 65 participating data partners, 25 of which joined after submitting expressions of interest to a COVID-19-specific call EHDEN published last April (and were selected among a total of 75 applicants).

Against this background, **Xavier Kurz**, Head of Surveillance and Epidemiology Service at the European Medicines Agency (EMA), noted that EHDEN´s use of OMOP is important from a regulatory perspective of assessing the validity of data sources and the methodologies used to generate RWE in different circumstances and scenarios. He explained that while regulators are increasingly open to factoring in such evidence in addition to traditional RCTs, being able to evaluate the validity of the data source is a critical element of their work – a consideration EHDEN has embedded into its approval process for each new data partner, essentially guaranteeing the provenance of the data.

To illustrate the utility of the OMOP data model from a public health perspective, **Dani Alhambra-Prieto**, Professor of Pharmaco- and Device Epidemiology at the University of Oxford as well as EHDEN Research Coordinator and Lead for Work Package 1 on Evidence Workflow Development, said the routinely collected health data provided by EHDEN´s COVID-19 data partners has been used to track what happens to people who were infected or hospitalised with the virus. Based on that information, over time and with more data coming in, EHDEN aims to develop a prediction model that can anticipate what is likely to happen to patients with given clinical characteristics and social demographics, and eventually to perform causal inference on a population level.

"We´ve had a lot of bad COVID-related decision-making, both internationally and nationally, because we were not using observational evidence and everybody was waiting for some sort of massive RCT in relation to some of the decisions that had to be taken, and that at the policy level is not useful," said **Rafael Bengoa**, Director of SI-Health, a health consultancy firm in Bilbao, and former Health Minister of Spain´s Basque Region. Providing a country-level perspective, he added that beyond the challenges of obtaining RWE at a European level, lack of interoperability is also a significant problem for Spain, whose national health system decision-making is devolved to the 17 autonomous regions. Therefore, EHDEN´s data collection approach with its built-in privacy protections could be useful for accessing real-world data without threatening regional and institutional data ownership, Bengoa suggested.

"EHDEN could suggest to governments what kind of planning approach can be useful to accelerate interoperability instead of them waiting for something magical to happen – because it isn´t happening."

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Indeed, the "train analysis," privacy-by-design nature of EHDEN's approach to collecting health data could be key to overcoming some of the institutional resistance to data sharing that researchers often report encountering. In the words of Hripcsak, "OHDSI is a voluntary network, so we ask people to participate and they participate if they so wish. That´s made them comfortable and that´s how we´ve been able to aggregate such a large dataset. The laws for data sharing between Taiwan and South Korea are very different and we can accommodate all the different cultures of privacy by enabling [organisations] to control their own data."

This sentiment was shared by Prieto-Alhambra, who said that privacy-masking features such as those built into OMOP should help guide European health data policy going forward:

"There´s a fine balance between access to data and privacy and data regulation issues, and Europe has to find a way to make data actionable and to make sure that the right data is ready at the right time.

In EHDEN our approach is to work with people who know and have access to data rather than try and grab data ourselves. To date we are mapping data for over 120 million citizens in Europe and we hope that our colleagues in Europe will be willing to participate in studies when they are available…

Eventually, I would love to see the EU create something like the CDC in the U.S., an organism that could handle data from all the countries in Europe and make important decisions based on the data that´s collected."

Anchoring the discussion around RWE curation, **Raquel Yotti**, Director of Spain´s Instituto de Salud Carlos III, reminded everyone that in the desire to advance on the data front, technology companies and decision-makers should not overlook the most precious asset of all: human resources. "It´s very important to strengthen scientific and technical capabilities within public health departments at the regional and central level, including at our institution, because we need talent and public health is an area that has not been considered enough in the last decade," said Yotti.

Webinar Two: HTAs, PROs, and rare diseases

The utility of RWE for HTA procedures and the relevancy of EHDEN´s OMOP-translated RWE data in particular were another major point of interest that was keenly debated in the context of determining value for patients. With increasing pressure on national and regional HTA bodies to take into account patient-reported outcomes (PROs), such as those registered in digital patient

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diaries or through digital therapeutics interventions, the question now is how and at what stage in the HTA workflow such measures can be most useful.

Niklas Hedberg, Chair of the Executive Board of the European Network for Health Technology Assessment (EUnetHTA), confirmed this is a relevant issue for HTAs even at the EU level, as most countries agree on a common methodology for integrating PROs, but there is no consensus on the ideal use cases. **Anja Schiel**, Senior Advisor and Statistician for the Norwegian Medicines Agency, expanded on this by saying that there might be a good reason for that, as HTAs know they ought to use RWE only if and when it can answer relevant questions and not just for the sake of using it. Schiel added that because of this caution, there is a perception that European regulators and HTA authorities are more rigid than their U.S. counterparts when it comes to embracing the use of real-world data, but that it is only that – a perception. She said the real issue is rightness of fit:

"Any discussion around this topic has to be around the ability of the evidence generated by RWD to be used by the different stakeholders. Is it fit for purpose? Is it better than any other evidence we are using? And do such data reduce uncertainty for stakeholders or do they actually increase it? At all times we should aim for the best possible and most robust evidence, not for the most attractive way to generate any evidence."

Still, although the utility of RWE for multi-country studies is limited due to the fact that most HTAs operate at national or regional level, there is a case to be made for building up Europe´s capacity to harvest patient-reported data collected across borders: rare diseases. Since studying the effects of drugs and treatments for rare conditions necessarily rules out the availability of large patient cohorts at any one organisation or country, this is one clear scenario where HTAs could create a "common good" by processing RWE from widely disparate data sources.

"Combining data from different sources is one of the advantages of using a federated data network such as EHDEN. But it still depends a bit on what the intended use is for these data – whether you want to use them for characterising a population and looking at baseline risk [or for drug effectiveness], for example. Some uses are much less controversial than others and the main controversial use is will you be able to do comparative effectiveness research based on RWD and RWE," said **Jacoline Bouvy**, Senior Scientific Advisor at the National Institute for Health and Care Excellence (NICE), who leads EHDEN´s Work Package 2 on Outcomes-Driven Healthcare.
Bouvy commented that WP2 is precisely working to determine whether OMOP can be applied and useful for HTA settings, which would provide much needed clarity on the HTA-RWE conundrum, as well as on possibly expanding the inventory of OMOP standards and definitions:

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"A lot of the data sources that we are exploring in EHDEN tend to be EHRs. When developed in collaboration with patients, those record-taking systems really allow you to get useful insights into how conditions affect patients.

The International Consortium for Health Outcome Measurement (ICHOM) is one of the partners in EHDEN and works a lot on this and we are trying to see how we can incorporate the ICHOM outcomes sets into the EHDEN network and use them for different purposes."

A rarely heard perspective on RWE use was shared by **Slaveyko Djambazov**, a Bulgarian physician and Founder and Managing Director of HTA Ltd., an HTA consultancy focused on Central and Eastern Europe (CEE). Highlighting the limitations to using outcomes data in the region, he said there is no local framework for generating or collecting RWE, therefore the type of data that is most readily available for such purposes is administrative inpatient outcomes data, although some physicians and facilities provide outpatient data as well. Djambazov said he sees great potential for EHDEN to propel the use of RWE in the CEE region by mapping and translating the data to OMOP, since much of the scarce data that are currently available also require a lot of wrangling: patient-by-patient analysis, cross-linking, and integrating to get a decent analysis. "We use international methodologies, but sometimes we get into really tough academic conversations."

The "other side of the coin" of RWE´s usefulness for HTAs is how well RWE reflects patient preferences and stakeholder engagement in the first place, and how those elements are used to build optimal RWE question sets. To this point, **Gözde Susuzlu Briggs**, Coordinator of the *Data Saves Lives* project at the European Patients Forum (EPF), said it is fundamental for patients to be involved in developing patient-reported outcome sets from the beginning, because this is the only way to ensure that the data being collected reflect the metrics and expectations that are important to them.

"More robust data sets can be built with patient inputs and can be beneficial to decision-making as they increase the reliability of the outcomes. This is particularly true when it comes to making marketing authorisations for new treatments in the HTA. So it applies to defining the right framework for decision-making – collecting the right data is only one piece of the puzzle and patients should also have a say in how they are safely stored, analysed, and used to concretely improve their health."

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Webinar Three: Digital drug discovery, R&D, and post-authorisation

Science´s inexorable march towards increasingly targeted medicines, driven by advances in genomics, phenomics, and other ´omics´ on the one hand, and the maturation of the Quantified Self movement on the other, underscore the need for alternative approaches to R&D than the traditional drug discovery model. Over the next decade, this shift will be led by new levels of integration between data, human biology, new products and services, and technologies through which these products and services are delivered.

This prognosis framed discussions around the third main theme of the EHDEN roadshow, on the outlook for the biopharma industry in the coming decade. The predictions that were floated converged largely around the notion of research moving closer to patients´ real lives (as opposed to being conducted in a lab) and research being based on continuous measurements (as opposed to on periodic measurements and check-ins).

Kai Langel, Director of Clinical Innovation at Janssen, who leads Work Package TECH of EHDEN´s Trials@Home project, which is focused specifically on operationalising randomised decentralised clinical trials (RDCTs) in Europe, explained the idea behind enabling technologies that bring research closer to people thus:

"We need to be able to measure those things that are most meaningful to patients, which means that we have to move closer to real patients´ lives. So we need at-home measures, which often are digital. We need more opportunities to do continuous measures and to measure things that were not possible to be measured before.

The challenge is that it´s really hard to develop these new measurement tools, because there is a discrepancy in the rate at which technology evolves, which is very fast (measured on a yearly basis), whereas clinical development can easily take 10 years. We need better frameworks in place to be able to manage these complexities. And we need to develop alignment standards to be able to share data with each other to develop these research tools."

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As with RWE, the research-enabling technologies of the future also have a “push” and a “pull” side, whereby not only researchers, but also patients, carers, and citizens need to play an active role in shaping their development. However, whether users are actually empowered to participate cannot be taken for granted, as can be observed in much of today´s RWE research, where preference studies and PRO measures are often designed by people with no personal experience or connection with the disease. **Elizabeth Vroom**, Chair and Co-President of the World Duchenne Foundation and founder of the Duchenne Parent Project Netherlands, said this explains why RWE studies often end up being more of an academic exercise and do not reflect patients´ reality:

“The important thing going forward is not say that a tool is patient-centred, but really to start from the patient and understand what is relevant to them, so that it measures the right thing. I know this intention is always there, but sometimes researchers have already collected the data and they try to find a story that fits the outcome measure. We could do better.”

EHDEN´s focus on unlocking data insights from sources that were previously inaccessible to research due to administrative, software, or cultural barriers inspired further discussion on the future uses of data beyond drug discovery. In relation to the still barely tapped potential of predictive health data analytics, **Magda Chlebus**, Executive Director for Science Policy and Regulatory Affairs at the European Federation of Pharmaceutical Industries and Associations (EFPIA), commented that in the next decade data will deliver health far beyond “the pill” – from enabling clinicians to intercept diseases long before symptoms appear to detecting side effects of medications before they manifest. She said she expects standardised and connected data to also help deliver the best combinations of interventions to improve the patient journey and that those discoveries will come not only from data in the pharmaceutical industry, but also from diagnostics, delivery drugs, and devices.

This is how Chlebus summarised her optimism:

“This progress in Europe will be enabled by projects like the European Health Data Space. And these projects need to fully integrate and upscale enabling initiatives like EHDEN that creates those standards and make the European data space a reality.”

However, she also offered a note of realism: “Technology advances superfast, but its integration with decision-making is painfully slow.”

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Tying in all the discussion points that were brought up around health data, new research technologies, and the capacity of EHDEN to advance Europe´s competitive position on this front, **Nigel Hughes**, Scientific Director at Janssen and EHDEN Project Lead, said the time has come for the scientific and medical communities to expand their concept of health data. He explained that most of the health data the healthcare and research ecocystems are currently using is clinical and claims data, which gives them a snapshot of patients' illness, but they need to get a lot better at understanding temporal trajectories of individuals as well. This expanded view of personal health and disease is only possible by merging different types of data that give a 360 view of an individual´s existing comorbidities.

Hughes pointed out that with society´s changing expectations, which will invariably accompany this technological journey, healthcare leaders need to ensure that new ways of tracking and reporting patient outcomes do not increase the digital divide between those who can and cannot use such devices. "A much higher degree of health system maturity is needed to respond to this kind of evolution, but with the right vision, talent, and commitment to collaboration we will get there," he said.

In conclusion, the EHDEN Virtual Roadshow provided a robust platform for a broad range of experts to share thoughts on Europe's health research ecosystem. The collaboration that was in full force during the event is a critical aspect of a federated data network and is key to fostering a research community that more smartly manages and shares real-world data.

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