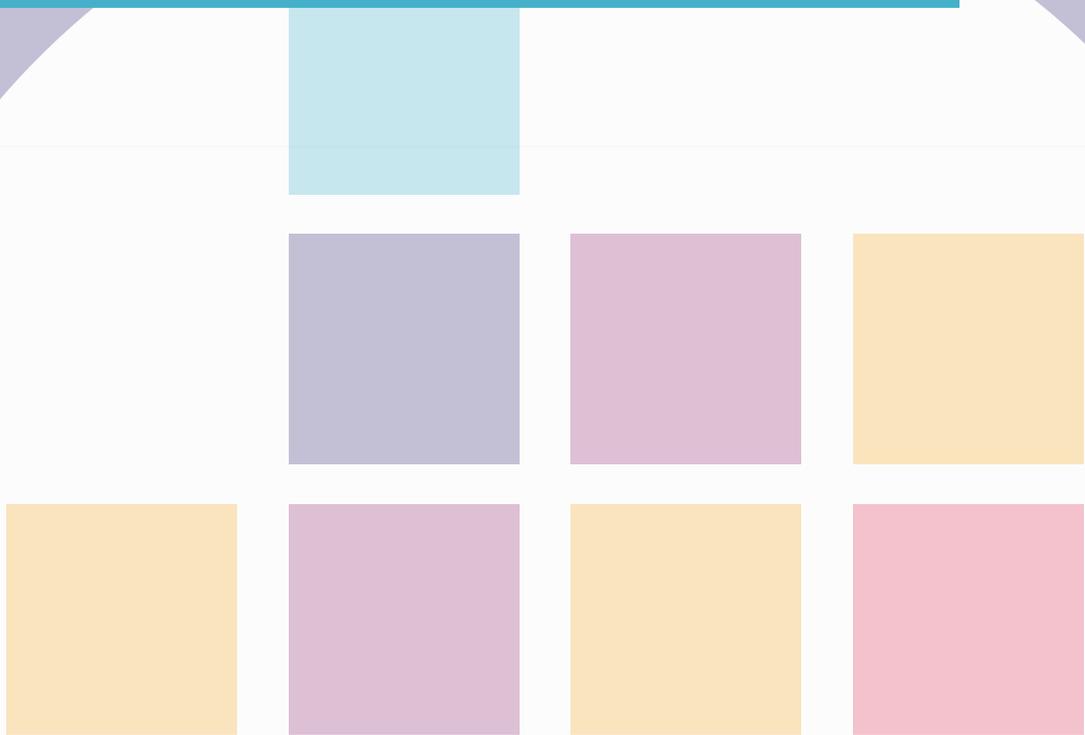




EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Building on success: EHDEN enters its fourth year



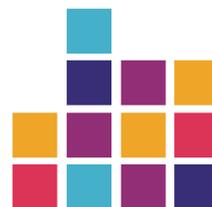
Building on success: EHDEN enters its fourth year

Research and use cases are making a meaningful difference

When the EU's Innovative Medicines Initiative launched the five-year EHDEN project in November 2018, it did so with an overarching goal in mind: **to significantly improve patient treatment and care by unlocking the under-utilised and transformational potential of real world data**. To this end, EHDEN began its journey to provide a new paradigm for the discovery and analysis of health data in Europe, by building a large-scale, federated network of data sources standardised to a common data model. More specifically, it set out to:

- Harmonise in excess of 100 million anonymised health records to the OMOP Common Data Model (CDM), supported by an ecosystem of certified SMEs (Small and Medium Sized Enterprises).
- Impact our understanding and improvement of clinical outcomes for patients in the many diverse healthcare systems within the EU.
- Establish a self-sustaining open science collaboration in Europe to support academia, industry regulators, payers, government, NGOs and others.
- Expand education by offering free, online courses via the EHDEN Academy.

Three years on, EHDEN has made significant headway, and has already eclipsed many of its targets, and this in the face of the COVID-19 pandemic, whereby travel restrictions limited face-to-face collaborations and working.



Research and use cases are making a meaningful difference

All the healthcare data in the world has little value unless it can be standardised, shared and analysed to generate real world evidence.

As part of EHDEN's commitment to impact its understanding and improvement of clinical outcomes for patients, it put in place the following goals:

- Build a geographically diverse Data Partner and SME network
- Work with Data Partners to map their health data to the OMOP CDM
- Drive the development of new tools & pipelines
- Create evidence (in no specific therapeutic areas)
- Strengthen the open science community

This was undertaken with three research principles in mind, be:

Transparent & Reproducible = trustworthy
Community-engaging
and **Disruptive – speedy and robust**

23 Consortium partners
11 public / 12 private

143
participating Data Partners
from **27** countries

>510M
anonymised health records
in the network

42
data sources mapped to the
OMOP CDM

47
participating & certified SMEs
from **19** countries

What have we learned?

Due to the power of a common data model at the heart of EHDEN, we can conduct several years of research in weeks or months!

Several key learnings

- **It's not only about the data**, but also about **collaboration**.
- The common data model is a powerful mechanism to support **interoperability** at-scale at the core of a growing **open science network**.
- **Data provenance** – for proper interpretation of study results, it's important to gain full transparency on the quality of the data and its provenance, e.g., how it's been gathered, mapped, harmonised, etc.
- **The importance of open science and developing standards for European open research:** be transparent; share ETL documents, data quality dashboards and protocols; use standardised analytics packages and study diagnostics; share results.

40

research studies /
study-a-thons

1,400

EHDEN Academy enrollees
1,800 completed courses

14

Free, online EHDEN
Academy courses

Use cases

Proof of concept - Oxford Study-a-thon

Objective: Forty experts came together for one week in December 2018 to validate EHDEN's study-a-thon approach. To this end, they generated evidence to compare the risk of post-operative complications and mortality between partial and total knee replacements. Twenty years of safety, implant survival, and effectiveness (pain and function improvement) research were replicated in one week.

Conclusions: Older patients showed better results with the partial knee replacement surgery and total knee replacement was better for younger patients. Results were published in [The Lancet Rheumatology](#).

Study-a-thon: The use of DMARDS for Rheumatoid Arthritis globally

Objectives: In January 2020, 50 experts met in Barcelona for one week. They examined a large, multinational drug usage study; a csDMARD safety study; and the prediction of cardiovascular disease, infections and leukopaenia.

Conclusions: Compared to MTX users, patients treated with LEF had a lower risk of overall cancer. Risk of four specific cancers did not differ by first line

csDMARD exposure.

Results were published in an [EULAR abstract](#).

Study: The use of Respiratory Medicines for Asthma/COPD

Objective: to study the use of medicines for Chronic Obstructive Pulmonary Disease (COPD), asthma and asthma/COPD overlap.

Conclusions: 1 in 3 of treated asthma patients start with SABA monotherapy as historically recommended followed by ICS (Europe) and systemic steroid bursts (US). In Europe, COPD patients start more often with LAMA than asthma patients (less so in the US). Systemic steroid bursts are frequently prescribed as first treatment in the US in asthma as well as in COPD patients. ACO (asthma COPD overlap) patients are more often treated and the differences are smaller between the US and Europe.

Complete results can be found [here](#).

PIONEER collaborates with EHDEN & OHDSI on a prostate cancer Study-A-Thon

Objective: More the 240 researchers came together virtually in March 2021

for five days representing seventeen prostate cancer patient databases from six countries. Two protocols were developed and submitted and are currently in execution: the first, assessing the impact of comorbidities and life expectancy on the long-term outcomes of patients managed with watchful waiting or active surveillance, and the second on the development of prediction models for the time to symptomatic progression, palliative treatment initiation or death within a specific timeframe for watchful waiting patients.

Conclusions: Organising this study-a-thon was a major collaboration between the IMI's PIONEER and EHDEN projects and demonstrated that the OHDSI and EHDEN network study approach using the OMOP CDM can be reproduced quickly in communities that are new to this, such as the urologists and clinical researchers in PIONEER. It was also a very multi-disciplinary event, bringing together clinicians, researchers, and software developers, and as a highlight, patients sharing their stories and key questions about our understanding of the disease.

Protocol publications:

<https://protocolexchange.researchsquare.com/article/pex-1468/v1>

<https://protocolexchange.researchsquare.com/article/pex-1525/v1>

The following [podcast](#) and [blog](#) offer more information about this case.

COVID-19 Study a-thon

Objectives: Four-day study-a-thon with 330 colleagues from 30 countries in March 2020 to work on characterisation, effect estimation and prediction studies, supported by deep literature review. A key study output was the determination of the safety of Hydroxychloroquine (HCQ) and AZ (azithromycin) and how this impacted on Regulatory decisions. The event marked an unprecedented level of global collaboration: there were 17 concurrent channels that hosted more than 100 collaborator calls and 12 global huddles. More than 10,000 publications were reviewed and +13,000 chat messages helped design 355 cohort definitions and nine protocols, as well as the release of 13 study packages. As of August 2021, the OHDSI community has published ten COVID-19 studies and more are in the pipeline, with ongoing protocols.

Conclusions: HCQ alone is generally safe, but in combination with AZ it shows a doubling of risk of 30-day cardiovascular mortality; psychiatric safety of HCQ: no increased risk of depression, suicidal ideation or psychosis for new users of HCQ with RA. One example of the results can be found here in [The Lancet Rheumatology](#).

Study: Background Rates of AESI for Vaccines

Objective: The largest, most extensive global network study (~126mio people in 8 countries) on background rates for AESIs (Adverse Events of Special Interest) identifies important age, sex and database differences to inform future surveillance efforts.

Conclusions: This study found large variations in the observed rates of AESIs by age group and sex, showing the need for stratification or standardisation before using background rates for safety surveillance. Considerable population heterogeneity in AESI rates was found between databases.

Link to [this paper](#) for detailed results.

Health Technology Assessment (HTA) Use Case: Chronic Obstructive Pulmonary Disease (COPD)

Health Technology Assessment (HTA) Use Case: Chronic Obstructive Pulmonary Disease (COPD)

Objectives:

-Understand the extent to which the OMOP common data model and standardised analytical tools support evidence generation for HTA of chronic diseases.

-Assess the extent to which current ETL processes support common HTA use cases.

-Assess the ability to generate reliable evidence for multiple jurisdictions.

-Identify priority areas for further developments to the common data model or analytical tools to support such applications.

Conclusions:

-Ensure use of data for HTA purposes is reflected in data processing and mapping processes and ensure HTA experts are involved in the ETL process.

-Map visits in a way that reflects the specificity of healthcare delivery in different settings, e.g., distinguishing between primary and secondary care.

-Development of analytical tools to support common analyses for HTA purposes.

Complete results can be found in this [abstract](#).

Evidence-a-thon

Objective: Five EHDEN Data Partners who had mapped their data to the OMOP CDM from a previous COVID-19 call came together with nineteen ETL Taskforce members and OHDSI colleagues came together virtually in July 2021 for EHDEN's first evidence-a-thon. The premise was running the R packages from the study [published](#) as a special paper in the BMJ (British Medical Journal) on characterising the background incidence rates of adverse events of special interest (AESIs) for COVID-19 vaccines in eight countries. This would enable EHDEN Data Partners (DPs) to familiarise themselves with running analyses on top of their OMOP mapped datasets, and for EHDEN and OHDSI colleagues to both evaluate the veracity of those mappings, as well as providing educational support to the DPs.

Conclusions: More details can be found [here](#).

Other achievements

Methods Research & Analytical Tool Development:

An accelerated achievement in methods development in the fields of characterisation, patient level prediction, and population-level effect estimation:

- Exhaustive search for optimal decision rules
- Treatment patterns
- Association rule & frequent pattern mining
- Predictive analytics using unstructured data
- Deep learning – attention models
- Risk minimisation measures effectiveness
- Risk-based assessment of treatment effect heterogeneity
- Disease trajectories
- Trends in prediction model development & validation

Infrastructure

- EHDEN architecture development (EHDEN Database Catalogue, data characterisation tools & dashboards) to be launched early in year four.
- Contributions to ETL and mapping tools further developed by the ARACHNE tool, integrated security framework and advanced multiple analytical pipelines.

EHDEN Academy

- The [Academy](#): currently over 1,800 courses completed, 1,400 course enrollees, and offers fourteen free, on-demand courses led by industry experts. 93% of enrollees rated their experience as good to excellent.
- [Value propositions](#) are available for key stakeholders and sustainability learnings of past and current projects have been analysed.
- We continue to actively engage with sister BD4BO projects, the IMI, the EU Commission and EMA on areas of mutual relevance.

Open calls

- Five open calls for Data Partners have been conducted resulting in the network expanding to 143 Data Partners from twenty-seven countries.
- A Rapid Collaboration call was held in 2020 for Data Partners in response to the COVID-19 pandemic.
- Three open calls for SMEs were conducted resulting in forty-seven SMEs from nineteen countries being selected, trained and certified to work with Data Partners in mapping their data to the OMOP common data model.

Looking ahead...

With such a solid foundation now in place, EHDEN is transitioning to the next phase of its evolution, and its aspirations are no less bold as it enters its fourth year. While the Data Partner and SME network is deep and geographically diverse, we will seek to expand it with open calls in 2022 and are keen to have stronger representation in central, eastern and south-eastern Europe. In terms of upcoming key priorities, EHDEN will continue focusing on:

- **First and foremost: improving patient treatments and outcomes by increasing the number of research use cases among the Data Partners within the EHDEN network and beyond – the foundational principle of EHDEN;**
- Launching the EHDEN Portal, which will initially contain the Data Partner Catalogue and feasibility tools;
- Creating new analytical research tools & methodologies;
- Promoting OHDSI & community education via the EHDEN Academy with more instructors and an expanded curriculum of free, online courses;
- Launching a new legal entity and operating model that will sustain the EHDEN project beyond 2024.

4,000

avg. monthly number of visits to EHDEN's website

>1,000

followers on LinkedIn and on Twitter



Reflections

Here's what some of our colleagues had to say about EHDEN's three-year anniversary



Innovative Medicine Initiative (IMI)

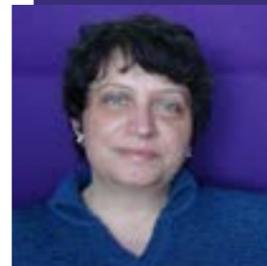
"EHDEN has excelled in the first half of the project. By building a network with 143 Data Partners across Europe and training researchers to use it, EHDEN has already provided important evidence to improve patient care. We are really looking forward to even greater success as the project continues to empower the digitisation of healthcare research."

Colm Carroll, Scientific Project Manager & IMI Lead on Digital Health



European Federation of Pharmaceutical Industries and Associations (EFPIA)

"EHDEN is a great illustration of why collaboration is essential in setting up the European Health Data Space(s). Thanks to its collaborative approach, EHDEN builds scalable infrastructures and lays foundations for future healthcare research that meet the imperatives of public and private sectors and of the patients at the same time. EHDEN is not just an aspiration; through concrete use cases it is actively contributing to resolving public health challenges." Magda Chlebus, Executive Director, Science Policy & Regulatory Affairs, EFPIA



Consortium members



"EHDEN is implementing a paradigm shift for the use of real world data. It's inspiring to see the interest in the work that EHDEN is driving in Europe, the impressive growth of the data network, and the continuing interest of Small and Medium-Sized Enterprises to support the ecosystem. Coordinating the EHDEN project is a privilege, and I am very proud of the EHDEN Consortium. The next years in our journey will be even more exciting as we generate more reliable evidence and impact patient health and outcomes through our collaborative efforts."

Prof Peter Rijnbeek, Coordinator for the EHDEN Project & Head of the Department of Medical Informatics at the Erasmus MC, The Netherlands

"EHDEN is building a future for European open science research at scale, and our progress has been remarkable and encouraging. We could not have achieved this progress without our Consortium, Data Partners, SMEs and associated colleagues, with collaboration being at the root of our work together. COVID-19 has made the last 18 months difficult for everyone worldwide, and we should be rightfully proud of being able to contribute to the better understanding of the pandemic, also as an example of what is feasible across all diseases. Lots to do still, but lots we can achieve in improving evidence generation, supporting R&D, and ultimately patient outcomes."

Nigel Hughes, EHDEN Project Lead and Scientific Director, Observational Health Data Analytics/Epidemiology Janssen R&D, Belgium



"EHDEN is very much about the second 'E', for evidence, and we should be very proud of the contribution we have already worked on in the first half of the project, with almost 40 publications, across therapeutic areas, but in particular in response to the COVID-19 pandemic. As Research Coordinator I am very much looking forward to ongoing collaboration with our Data Partners in supporting them in evidence generation, and to research outputs that have a demonstrable impact on management, care and outcomes for our patients." Dani Prieto-Alhambra, EHDEN Research Coordinator and Professor of Pharmacology and Device Epidemiology, Centre for Statistics in Medicine, NDORMS, University of Oxford, UK

"For the digital transformation of health to bring real value, it must be co-developed with patients to reflect what matters to them. That is why we are pleased to be part of the EHDEN project – working with our partners to produce educational and lay language material to support patients and non-expert audiences with the digital health literacy tools to engage meaningfully in this transformation, and in EHDEN."

Valentina Strammello, Head of Programmes, European Patients' Forum, Belgium





“EHDEN is helping us map the complex labyrinth of real world data in Europe. And by use of the OMOP-CDM it has given us the necessary ball of thread to navigate it.”

Jimmy Toulas, Real World Data Acquisition & Partnership Lead, Pfizer Digital, Greece

“Over the past three years, we have been part of the diverse international EHDEN team that is building a solid footprint of the OHDSI-based research capability with 143 partners across Europe. It was a great inspiration to work directly with the ‘fresh’ Data Partners in the COVID

Task Force, helping them to convert their data to the OMOP-CDM and to build up a mature community at the same time.”

Sebastiaan van Sandijk, Health Informatician, Odysseus Data Services & SME,

Czechia

“EHDEN is a truly ground-breaking project that, in only a few years, is already providing a quantum leap for observational data research in Europe. The network of Data Partners and SMEs, together with the educational value of the EHDEN Academy, are creating an indispensable “fabric” that’s raising awareness, creating capacity, and hands-on training in health data standardisation and use, allowing for faster evidence-based

decision making on matters that directly affect all citizens.”

Carlos Díaz, CEO, Synapse Research Management Partners & SME, Spain



“For an electronically advanced country like Estonia, it is extremely important to see that data from our small nation and unique language can still be relatively easily comparable to other countries and cohorts. With EHDEN we get several steps closer in understanding our data - the strengths, as well as weaknesses. Our ambition is to develop a national genetic data infrastructure for healthcare; the lessons from EHDEN will help us develop vision on what some of the next steps shall be.”

Jaak Vilo, Professor of Bioinformatics, Institute of Computer Science, University of Tartu, Estonia



“ Data Partners

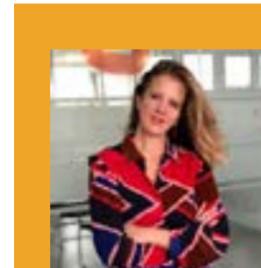


“EHDEN provides us with the opportunity to join a team of pioneers when it comes to overcoming socio-technical challenges that arise when scaling-up health data. It feels like coming home for us.”

Liesbet M. Peeters, Professor Biomedical Data Sciences, Hasselt University, Belgium

“While massive amounts of health-related data are generated every second, the possibility for data-driven research is obstructed by isolated data silos. Together with EHDEN and Partners of the EHDEN community, the Department of Anaesthesia, Intensive Care Medi-

SMEs



“We are very proud to have been selected as a trusted SME partner by a number of Italian Data Providers, such as SIMG – Società Italiana di Medicina Generale to guide them in the process of mapping their patient data to OMOP. Thanks to this

European partnership, the Datawizard technical team will be able to bring and improve all its expertise in the field of health data and RWD mapping, for the purposes of Research & Innovation and Product Development of standardised data analysis technologies.”

Lucia Comnes, Director of Innovation Programs, Digital Health, Datawizard, Italy

“The work with EHDEN and the implementation of OMOP with data owners such as hospital districts has opened a new window into standardised

cine and Pain Medicine at the Medical University of Vienna, will be able to provide standardised access to billions of health records for new research questions at the frontier of intensive-care medicine.”

Daniel Laxar, Researcher, Medical University of Vienna, Austria

“Together with EHDEN, we’ll go faster and further.”

Nhung Trinh, postdoc, University of Norway



data models and compatibility for MediSapiens. In addition, it has significantly influenced how we implement RWE in our own data IT solution and opened up new means of cooperation with partners.”

Hans Garritzen, VP of Sales & Marketing, MediSapiens, Finland

“EHDEN offers valuable resources, networking events and training materials. As an SME deeply involved in the EHDEN community, what you don’t do is as important to your success as what you do.”

José Ramón Varela, Project Director, Bahia Software, Spain





EHDEN

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