



# EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

## *Basel Biometric Society Seminars 2024*

---

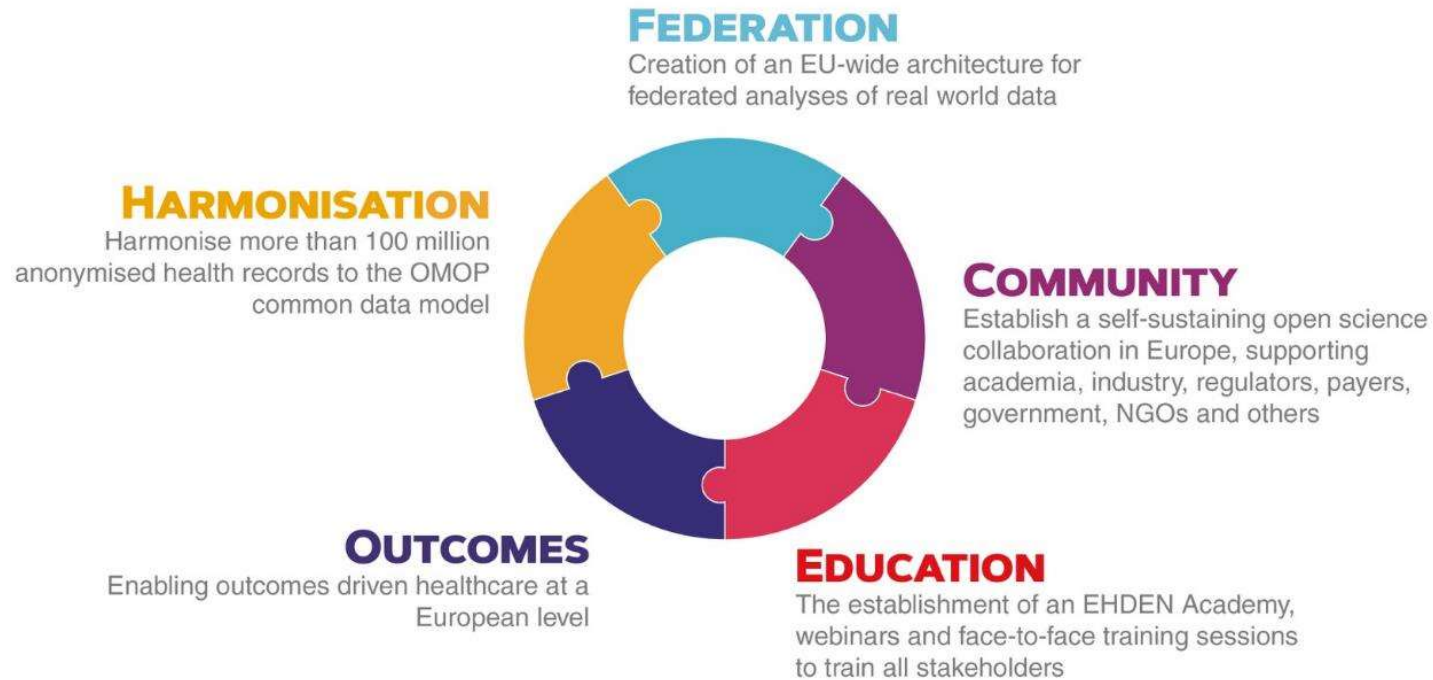
Dani Prieto Alhambra  
University of Oxford - EMC Rotterdam





## EHDEN IS ABOUT...

Providing 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 (OMOP), significantly speeding up the generation of reliable evidence.





# EHDEN BASICS



**Start date:** 1 Nov 2018  
**End date:** 30 Oct 2024  
**Duration:** 72 months



**25 partners**



**~€30 million**

## Universities, public bodies and research organisations



**Academic coordinator**



## Small & Mid-sized companies



## Other organisations



## EFPIA & Associated partners

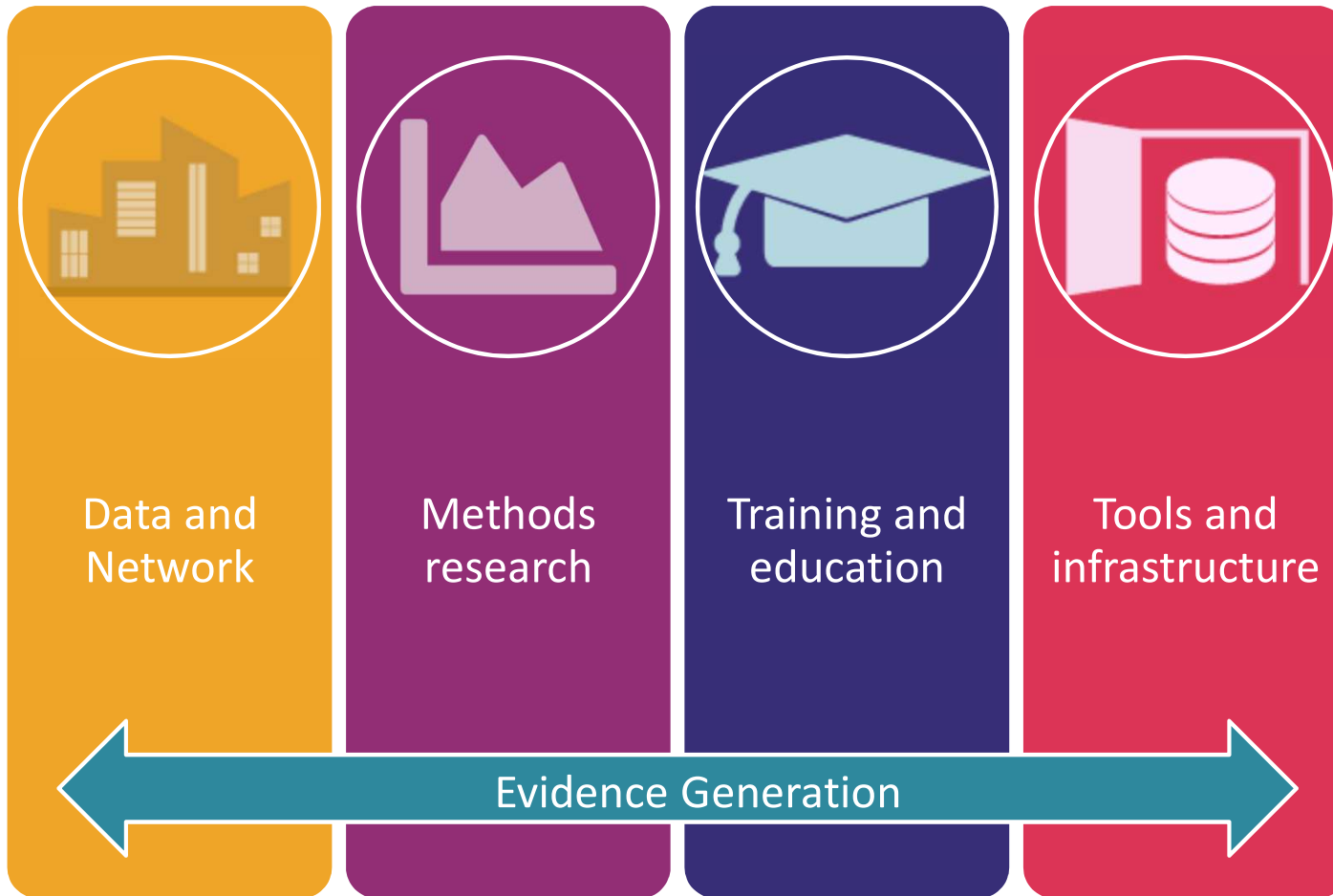


**EFPIA Lead**





# EHDEN BASICS

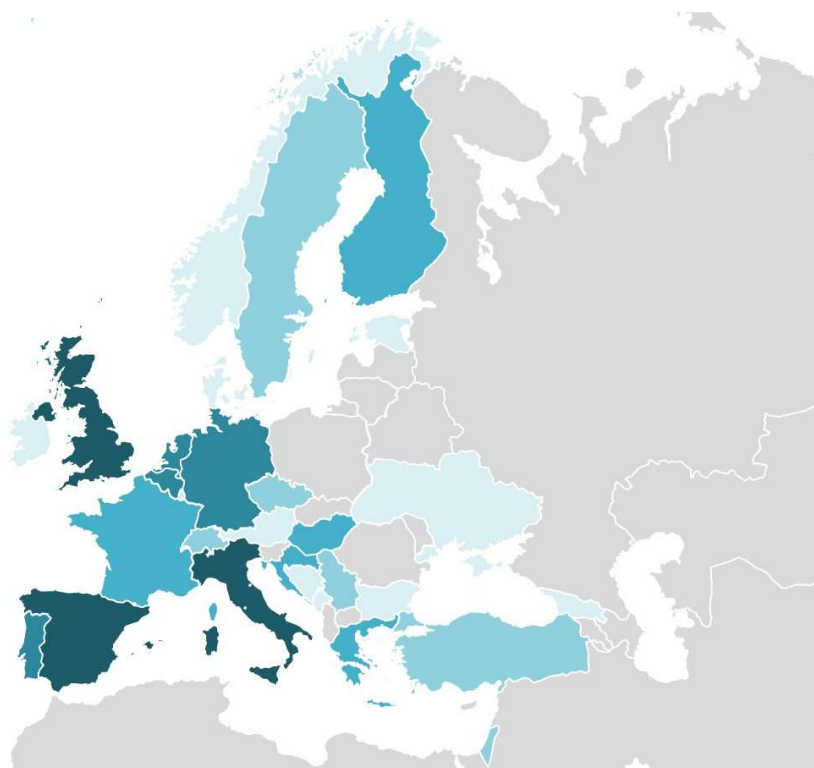




# DATA PARTNER NETWORK [AFTER 7 CALLS]



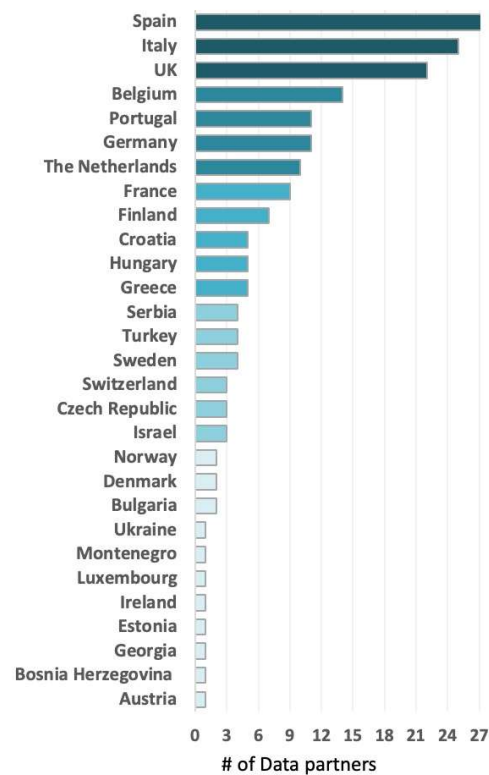
<https://www.ehden.eu/datapartners/>



Geographic spread of data partners. The shade of blue indicates the # of data partners in that country (darker = more)

Applications (n=563)

 Awarded applications (n=187)

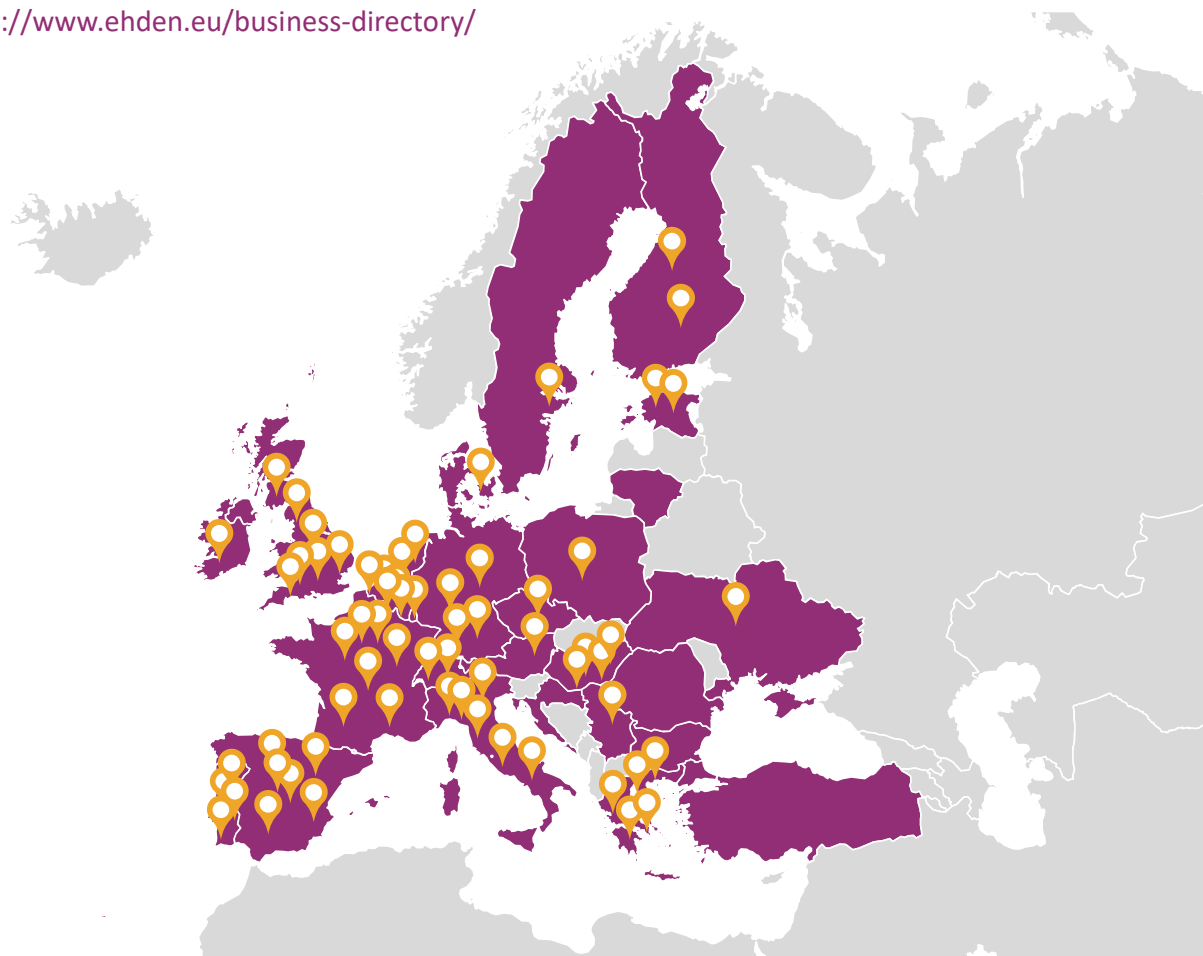


~850 million records being mapped to OMOP CDM in 29 European countries



# SME NETWORK [AFTER 4 CALLS]

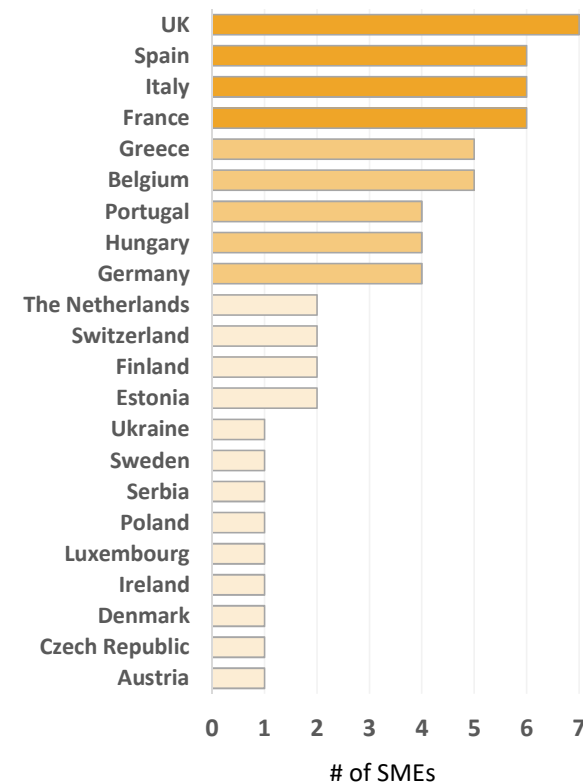
 <https://www.ehden.eu/business-directory/>



Certified SMEs (n=64)



Applications (n=143)





# METHODS: MANY PUBLICATIONS. SOME EXAMPLES...



Computer Methods and Programs in Biomedicine

Volume 225, October 2022, 107081



TreatmentPatterns: An R package to facilitate the standardized development and analysis of treatment patterns across disease domains

Aniek F. Markus <sup>1</sup>, Katia M.C. Verhamme <sup>2, b</sup>, Jan A. Kors <sup>2</sup>, Peter R. Rijnbeek <sup>2</sup>

Show more

Meta-Analysis > J Am Med Inform Assoc. 2022 Jun 14;29(7):1292-1302.

+ Add to Men doi: 10.1093/jamia/ocac058.

https://doi.org/10 Under a Creative

Use of unstructured text in prognostic clinical prediction models: a systematic review

Tom M Seinen <sup>1</sup>, Egill A Fridgeirsson <sup>1</sup>, Solomon Ioannou <sup>1</sup>, Daniel Jeannot <sup>1</sup>, Luis H Joh Jan A Kors <sup>1</sup>, Aniek F Markus <sup>1</sup>, Victor Pera <sup>1</sup>, Alexandros Rekkas <sup>1</sup>, Ross D Williams <sup>1</sup>, Cynthia Yang <sup>1</sup>, Erik M van Mulligen <sup>1</sup>, Peter R Rijnbeek <sup>1</sup>

Affiliations + expand

PMID: 35475536 PMCID: PMC9196702 DOI: 10.1093/jamia/ocac058

Highli

> Drug Saf. 2022 May;45(5):563-570. doi: 10.1007/s40264-022-01161-8. Epub 2022 May 17.

Using Iterative Pairwise External Validation to Contextualize Prediction Model Performance: A Use Case Predicting 1-Year Heart Failure Risk in Patients with Diabetes Across Five Data Sources

> Int J Med Inform. 2022 Jul;163:104762. doi: 10.1016/j.ijmedinf.2022.104762. Epub 2022 Apr 12.

Ro: Kai Aff PM Fre

Logistic regression models for patient-level prediction based on massive observational data: Do we need all data?

Luis H John <sup>1</sup>, Jan A Kors <sup>2</sup>, Jenna M Reps <sup>3</sup>, Patrick B Ryan <sup>3</sup>, Peter R Rijnbeek <sup>2</sup>

Affiliations + expand

PMID: 35429722 DOI: 10.1016/j.ijmedinf.2022.104762

Proceedings of Machine Learning Research 182:1-25, 2022

Machine Learning for Healthcare

Why predicting risk can't identify 'risk factors': empirical assessment of model stability in machine learning across observational health databases

Aniek F. Markus

Department of Medical Informatics Erasmus University Medical Center Rotterdam, The Netherlands

Peter R. Rijnbeek

Department of Medical Informatics Erasmus University Medical Center Rotterdam, The Netherlands

Jenna M. Reps

Janssen Research and Development Raritan, New Jersey, United States

A.MARKUS@ERASMUSMC.NL

P.RIJNBEEK@ERASMUSMC.NL

JREPS@ITS.NJ.COM

> BMC Med Inform Decis Mak. 2022 May 25;22(1):142. doi: 10.1186/s12911-022-01879-6.

Learning patient-level prediction models across multiple healthcare databases: evaluation of ensembles for increasing model transportability

Ross D Williams <sup>1, 2</sup>, Martijn J Schuemie <sup>3</sup>, Patrick B Ryan <sup>3</sup>

> BMC Med Res Methodol. 2022 Jan 30;22(1):35. doi: 10.1186/s12874-022-01505-z.

models that are accurate could help aid medical decision making. However, models that are accurate often contain temporal medical data for large and diverse populations. This study aims to learn prognostic models using the large observational data that are available in a distributed setting. In this study we investigate different ensemble learning methods to learn prognostic models using the large observational data that are available in a distributed setting. In this study we investigate different ensemble learning methods to learn prognostic models using the large observational data that are available in a distributed setting. In this study we investigate different ensemble learning methods to learn prognostic models using the large observational data that are available in a distributed setting.

Stavrou <sup>4</sup>

> BMC Med Res Methodol. 2022 Jan 30;22(1):35. doi: 10.1186/s12874-022-01505-z.

Seek COVER: using a disease proxy to rapidly develop and validate a personalized risk calculator for COVID-19 outcomes in an international network

Ross D Williams <sup>1</sup>, Aniek F Markus <sup>1</sup>, Cynthia Yang <sup>1</sup>, Talita Duarte-Salles <sup>2</sup>, Scott L DuVal <sup>3</sup>, Thomas Falconer <sup>4</sup>, Jitendra Jonnagaddala <sup>5</sup>, Chungsoo Kim <sup>6</sup>, Yeunsook Rho <sup>7</sup>,

> Semin Arthritis Rheum. 2022 Oct;56:152050. doi: 10.1016/j.semarthrit.2022.152050. Epub 2022 Jun 15.

Development and external validation of prediction models for adverse health outcomes in rheumatoid arthritis: A multinational real-world cohort analysis

Cynthia Yang <sup>1</sup>, Ross D Williams <sup>2</sup>, Joel N Swerdel <sup>3</sup>, João Rafael Almeida <sup>4</sup>, Emily S Brouwer <sup>5</sup>, Edward Burn <sup>5</sup>, Loreto Carmona <sup>6</sup>, Katarina Chatzidinacou <sup>7</sup>, Talita Duarte-Salles <sup>8</sup>, Walid Fakhouri <sup>9</sup>, Antj

> JAMA Open. 2022 Mar 16;5(1):eoac021. doi: 10.1093/jamaopen/oaac021. eCollection 2022 Apr. Lembe Kullamaa <sup>13</sup>, J Henry Morgan Stewart <sup>14</sup>, Carmen O Torre <sup>17</sup>, Ki Daniel Prieto-Alhambra

Affiliations + expand

PMID: 35728447

Free article

Abstract

Background: Identifying a variety of adverse health outcomes remains a challenge in the era of precision medicine. We developed a framework for identifying temporal clinical event trajectories from observational medical outcomes Partnership-formatted observational healthcare data.

Abstract Objective: To develop a framework for identifying temporal clinical event trajectories from observational medical outcomes Partnership-formatted observational healthcare data. Materials and methods: A 4-step framework based on significant temporal event pair detection is described and implemented as an open-source R package. It is used on a population-based Estonian dataset to first replicate a large Danish population-based study and second, to conduct a disease trajectory detection study for type 2 diabetes patients in the Estonian and Dutch databases as an example.

Trends in the conduct and reporting of clinical prediction model development and validation: a systematic review

Cynthia Yang <sup>1</sup>, Jan Alexandros Rekkas <sup>1</sup>, Peter R Rijnbeek <sup>1</sup>

Affiliations + expand

PMID: 35045179

Free PMC article

> Knee Surg Sports Traumatol Arthrosc. 2022 Sep;30(9):3068-3075. doi: 10.1007/s00167-021-06799-y. Epub 2021 Dec 6.

90-Day all-cause mortality can be predicted following a total knee replacement: an international network study to develop and validate a prediction model

Ross D Williams <sup>1</sup>, Jenna M Reps <sup>2</sup>, OHDSI/EHDEN Knee Arthroplasty Group;



# TRAINING: EHDEN ACADEMY – FREE ONLINE TRAINING FOR ALL

19 courses covering:

EHDEN  
Academy

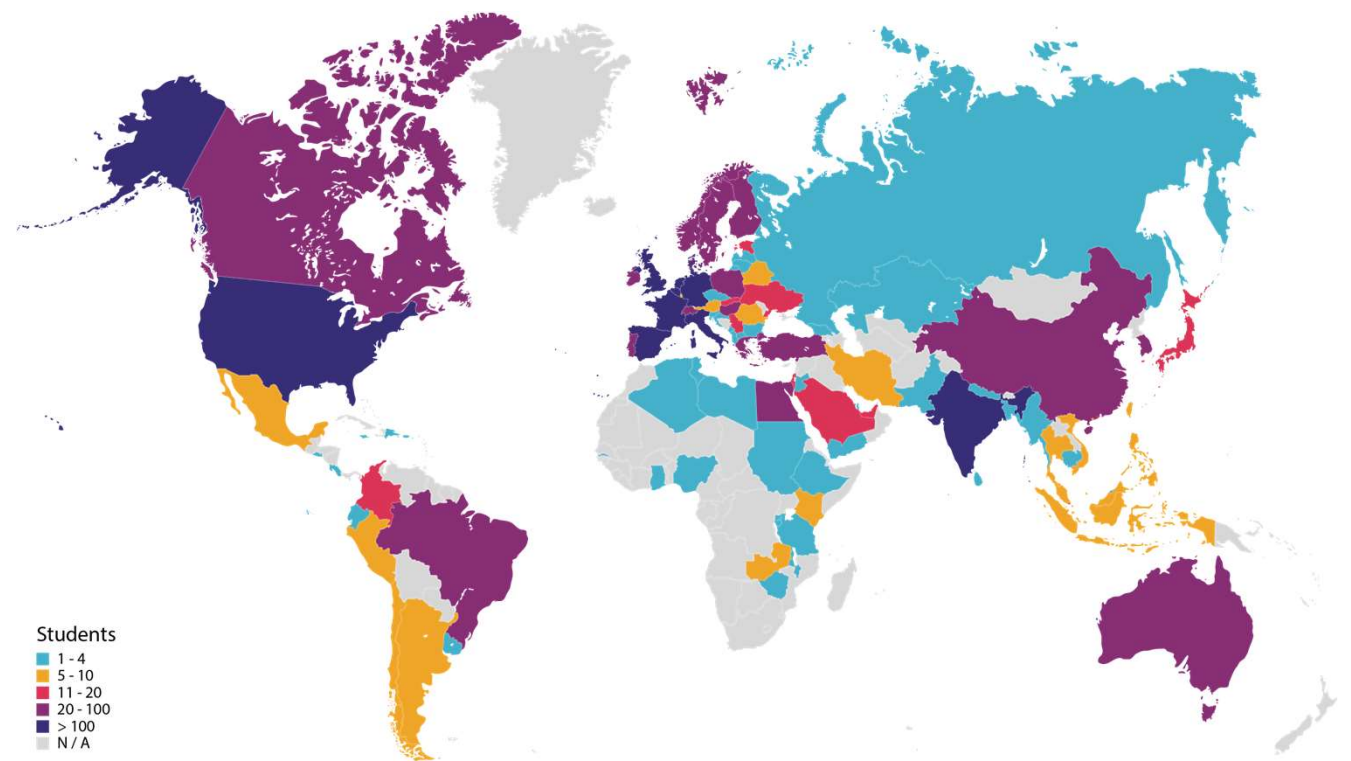
SKILLS

TOOLS

METHODS

and a course for **non-experts**

> 4,000 students



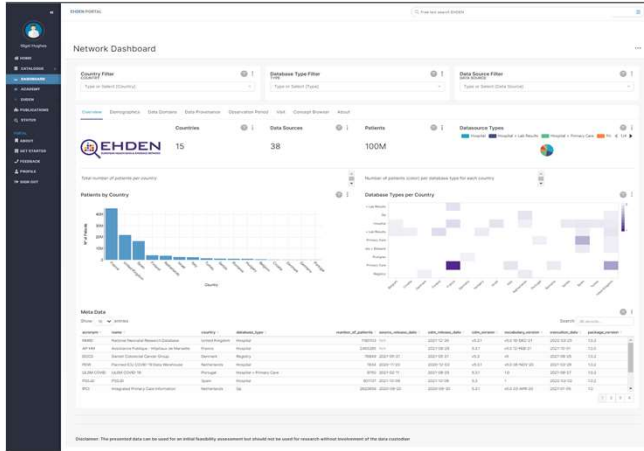
Also used as a training program for certification of SMEs to support Data Partners mapping their data to the OMOP CDM





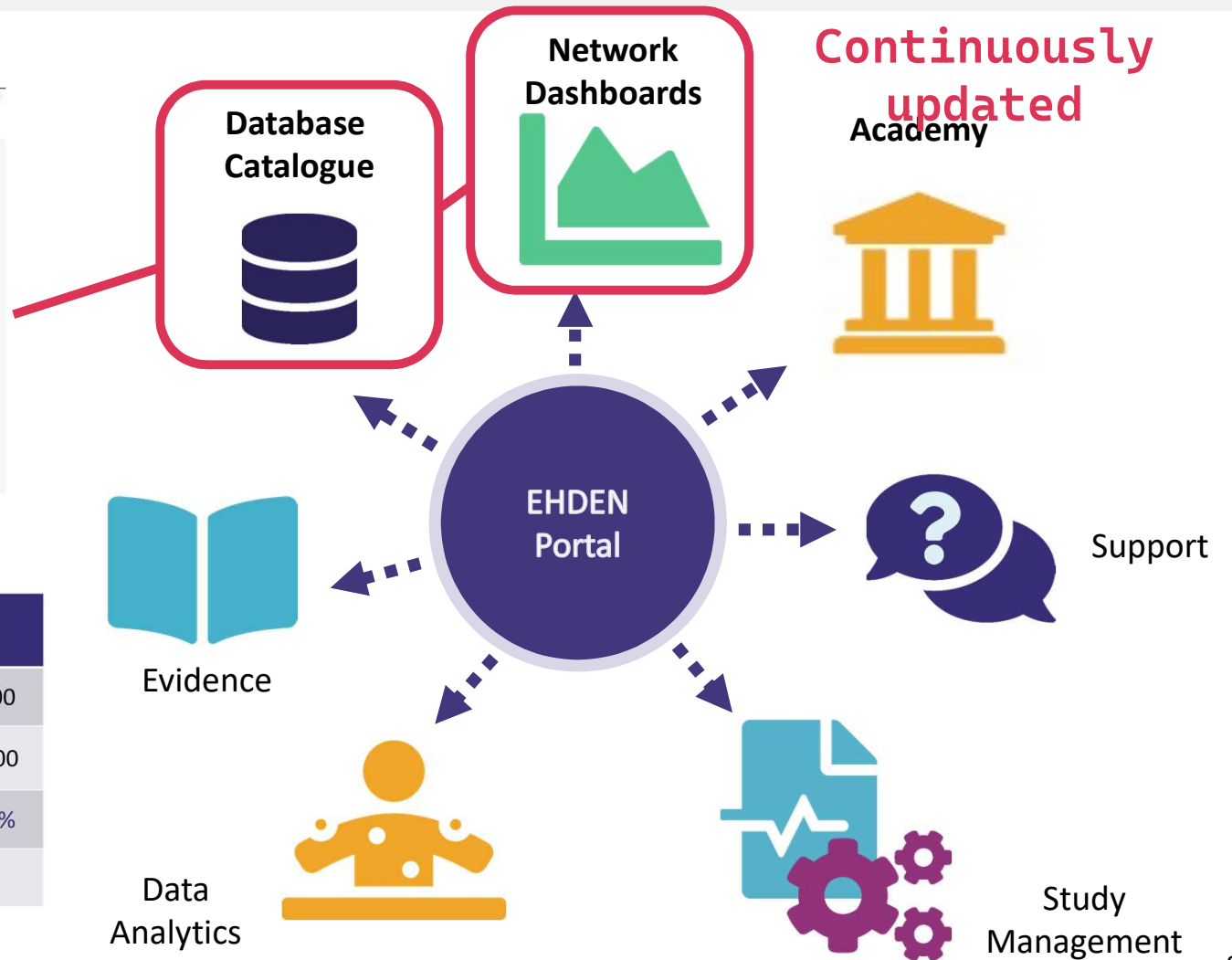
# TOOLS: THE EHDEN PORTAL – ONE-STOP-SHOP LAUNCHED 24 JUNE 2022

<https://www.ehden.eu/ehden-portal/>



**Free Enrolment!**

	# databases in Database Catalogue	# databases in Network Dashboard	# countries	# patients	# users
OHDSI EU 2022	67	35	15	~ 44 Mio	~ 400
OHDSI EU 2023	118	90	23	~ 149 Mio	~ 900
	76%	157%	53%	238%	125%
Total number at end of project	187	187	29		



# EVIDENCE GENERATION EXAMPLE: LONG-COVID STUDY-A-THON

## 13 Data Partners



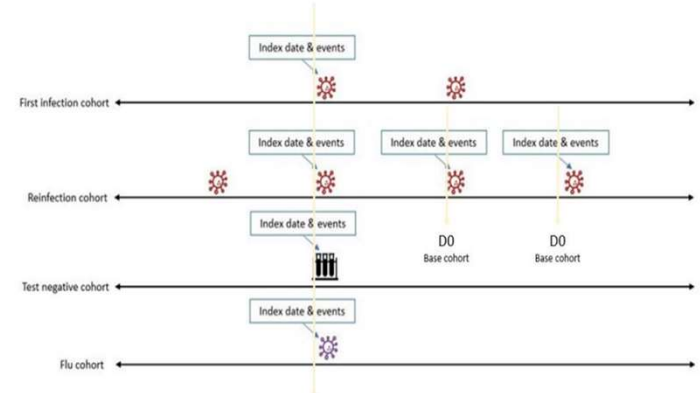
- GOLD  
- AURUM



UiO : Department of Pharmacy  
University of Oslo

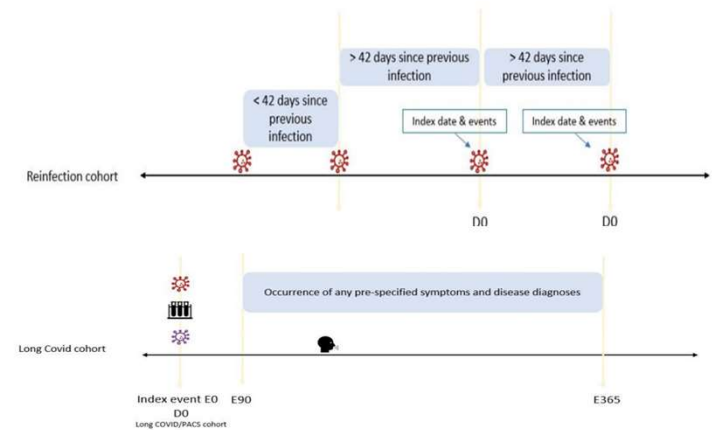


ADDITIONAL DPs (online) Pharmetrics+, IQVIA (USA), HSD (Italy), Ajou University (S Korea)



	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
8.45-9.00			COFFEE		
9.00- 10.30		9.00-9.30 Intro to Github (Data Scientists) All: Presentation of Results for 1 DB	Break out session in 3 groups	Break out session in 3 groups	All: Review results from additional analyses and manuscripts together
10.30-11.00	Technical Help desk	Coffee break			
11.00-13.00		Break out in 3 groups: (1) Descriptive epi (2) Drug utilisation (3) Clusters and trajectories	Break out session in 3 groups	Break out session in 3 groups	All: Closure; Next steps beyond this study-a-thon (publication) Lunch from 12.00
13.00-14.00	LUNCH				
14.00- 15.30	Welcome and Introductions	Manuscript discussion Break out session in 3 groups	All: Progress update	All: Progress update	
15.30- 16.00	Coffee break				
16.00- 17.00	Introduction of the databases Form expert teams for the rest of the week	All: Update and Summary of Plan for the next days	Break out session in 3 groups	Break out session in 3 groups	
		Evening: Dinner		Evening: Dinner	

	Team 1	Team 2	Team 3	Team 4
Work Package	Incidence	Characterisation and DUS	Clustering and Trajectories	Technical Experts
Lead	FRANK	ANNIKA	KIM	MARTI and ED
Long COVID Experts	Roger	Cora	Lourdes	
Clinical Experts	[Dani]	Miguel-Angel	Raúl	
			[Dani]	
Data Sciences	Juan Manuel	Núria	Raivo	Aki
	Jaime	Dominique	Alvaro	
	[Ed]	Laura	[Martí]	
Pharmacists		Nhung		
		Theresa		
Epidemiologists	Kristin	Johnmary	Talita	
	Alicia	Bernardo	Daniel	
	Anneli		Gregoire	
	Jessie			





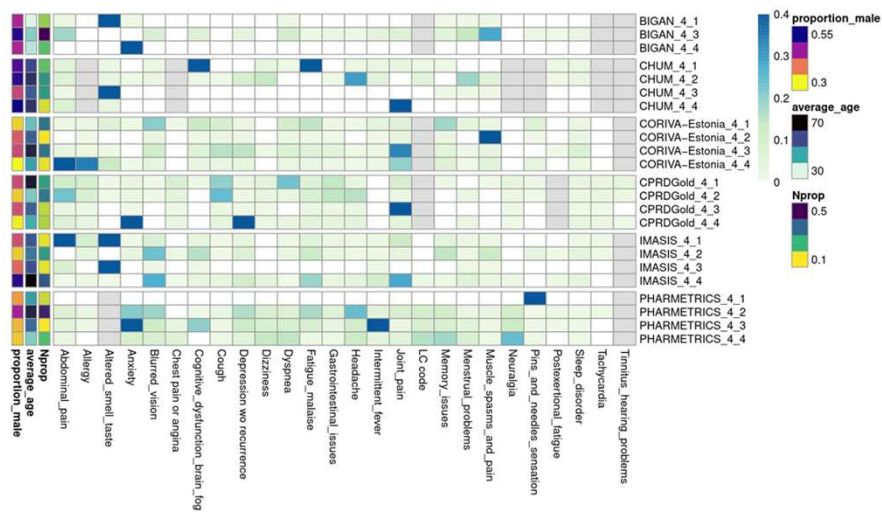
# EVIDENCE GENERATION: EXAMPLE OUTPUTS

## Long COVID characterisation

- Background
- Large scale characterisation
- Health conditions: individual cohorts**
- Health conditions: cohort comparison
- Drug utilisation: individual cohorts
- Drug utilisation: cohort comparison
- Health care resource utilisation
- Health care resource utilisation
- Vaccination data
- Vaccination data
- Treatment Patterns
- Treatment Patterns



## Preliminary clusters identified using Latent Class Analyses across 4 databases



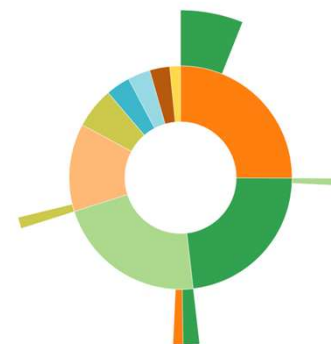
## SUNBURST PLOTS

Treatments after COVID-19 diagnosis in the NL and the UK



- Corticosteroids
- Antithrombotic\_agents
- Antibiotics
- Anti\_inflammatory\_drugs
- ACEI
- ARB
- Metmorfin
- HMG\_CoA\_inhibitors
- H\_2\_receptor\_antagonists
- Others

## CPRD GOLD

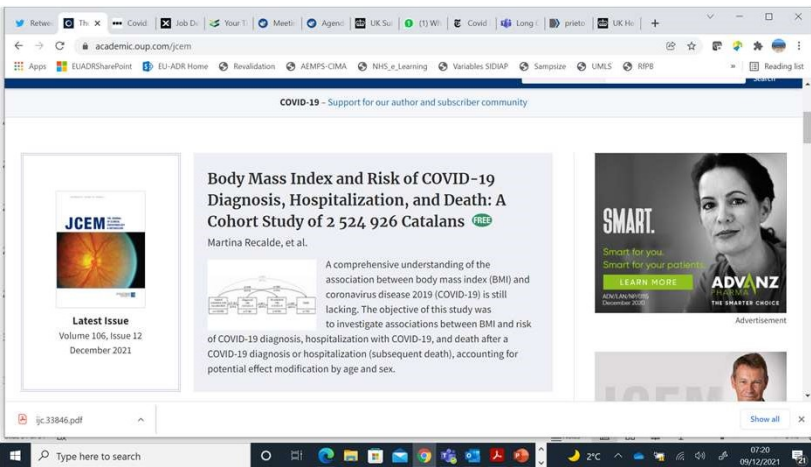


- Anti\_inflammatory\_drugs
- Corticosteroids
- Antibiotics
- Antithrombotic\_agents
- ACEI
- Metmorfin
- ARB
- Ivermectin
- Others

## IPCI



# ACADEMIC/SCIENTIFIC IMPACT: ~70 METHODOLOGICAL & SCIENTIFIC PUBLICATIONS



BMI in COVID-19: JCEM pick of the week!!

RESEARCH

OPEN ACCESS Check for updates

For numbered affiliations see end of article.  
Correspondence to: P Ryan  
ryan@ohdsi.org  
<http://orcid.org/0000-0002-9727-2138>  
Additional material is published online only. To view please visit the journal online  
Cite this as: *BMJ* 2021;373:n1038  
<http://dx.doi.org/10.1136/bmj.n1038>  
Accepted: 16 April 2021

## Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study

Albert Prats-Urbe,<sup>1</sup> Anthony G Sena,<sup>2,3</sup> Lana Yin Hui Lai,<sup>4</sup> Waheed-Ul-Rahman Ahmed,<sup>5,6</sup> Heba Alghoul,<sup>7</sup> Osaid Alser,<sup>8</sup> Thamir M Alshammari,<sup>9</sup> Carlos Areia,<sup>10</sup> William Carter,<sup>11</sup> Paula Casajust,<sup>12</sup> Dalia Dawoud,<sup>13</sup> Asieh Golzar,<sup>15,16</sup> Jitendra Jonnagaddala,<sup>17</sup> Paras P Mehta,<sup>18</sup> Mengchun Gong,<sup>19</sup> Daniel R Morales,<sup>20</sup> Fredrik Nyberg,<sup>22</sup> Jose D Posada,<sup>23</sup> Martina Recalde,<sup>24,25</sup> Elena Roel,<sup>24,25</sup> Karishma Shah,<sup>5</sup> Nigam H Shah,<sup>23</sup> Lisa M Schilling,<sup>11</sup> Vignesh Subbian,<sup>26</sup> David Vizcaya,<sup>27</sup> Lin Zhang,<sup>28,29</sup> Ying Zhang,<sup>19</sup> Hong Zhu,<sup>30</sup> Li Liu,<sup>30</sup> Jaehyeong Cho,<sup>31</sup> Kristine E Lynch,<sup>32</sup> Michael E Matheny,<sup>33,34</sup> Seng Chan You,<sup>35</sup> Peter R Rijnbeek,<sup>3</sup> George Hripcsak,<sup>36</sup> Jennifer CE Lane,<sup>5</sup> Edward Burn,<sup>1,24</sup> Christian Reich,<sup>37</sup> Marc A Suchard,<sup>38</sup> Talita Duarte-Salles,<sup>24</sup> Kristin Kostka,<sup>37,39</sup> Patrick B Ryan,<sup>2,40</sup> Daniel Prieto-Alhambra<sup>1</sup>

RESEARCH: SPECIAL PAPER

OPEN ACCESS Check for updates

**FAST TRACK**

## Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study

Xintong Li,<sup>1</sup> Anna Ostropelets,<sup>2</sup> Rupa Makadia,<sup>3</sup> Azza Shoaibi,<sup>3</sup> Gowtham Rao,<sup>3</sup> Anthony G Sena,<sup>3,6</sup> Eugenia Martinez-Hernandez,<sup>4</sup> Antonella Delmestri,<sup>1</sup> Katia Verhamme,<sup>6,7</sup> Peter R Rijnbeek,<sup>6</sup> Talita Duarte-Salles,<sup>5</sup> Marc A Suchard,<sup>8,9</sup> Patrick B Ryan,<sup>2,3</sup> George Hripcsak,<sup>2</sup> Daniel Prieto-Alhambra<sup>1,6</sup>

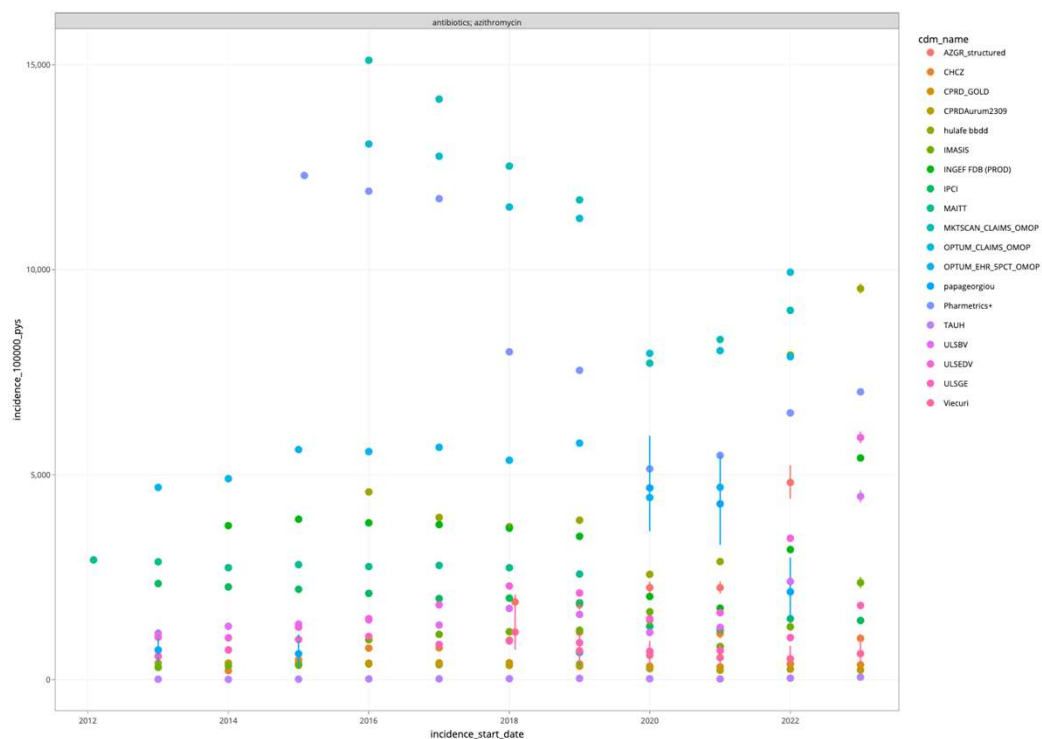


# EVIDENCE GENERATION: A STRIKING UPCOMING STUDY

## • EH DEN Mega-St udy

- To describe the incidence and prevalence of medicines with suggested shortages between 2015 and 2023
- To characterise incident users of medicines with suggested shortages between 2015 and 2023

Database name	Persons in the database	Number of observation periods	OMOP CDM vocabulary version
AZGR_structured	68,918	67,532	v5.0 16-JAN-23
BARDENA	1,972,272	1,972,272	v5.0 23-JAN-23
BG	501,065	501,065	v5.0 04-FEB-22
CHA CAN	214,443	208,183	v5.0 16-JAN-23
CHCZ	588,650	779,119	v5.0 04-FEB-22
CPRD_GOLD	17,267,137	17,267,137	v5.0 31-AUG-23
CPRDAurum2309	44,851,398	44,851,398	v5.0 31-AUG-23
CPRDAurum50	1,377,783	1,377,783	v5.0 23-JAN-23
hulafe bbdd	2,371,896	1,920,548	v5.0 23-OCT-21
IMASIS	1,066,675	1,066,675	v5.0 31-MAY-23
IncPrev_UZB_structured	19,218	19,048	v5.0 16-JAN-23
INGEF FDB (PROD)	9,111,064	9,111,064	v5.0 29-FEB-24
IPCI	2,817,331	2,817,331	v5.0 31-AUG-23
ITF_CDM	899,515	899,515	v5.0 17-JUN-21
MAITT	149,364	149,364	v5.0 23-JAN-23
MEGA	49,011	49,011	v5.0 20-APR-21
MEGA	49,011	49,011	v5.0 16-JAN-23
MKTSCAN_CLAIMS_OMOP	176,890,290	202,823,163	v5.0 23-JAN-23
NCR	2,514,888	2,514,888	v5.0 31-AUG-23



# EHDEN AS A CONNECTED COMMUNITY

## 1 Webpage with all the latest news

The screenshot shows the EHDEN website homepage with a navigation menu at the top including 'ABOUT', 'EHDEN Foundation', 'WORK PACKAGES', 'NETWORK', 'EVIDENCE GENERATION', 'COMMUNICATION/EDUCATION', 'NEWS', and 'CONTACT'. A prominent article titled 'Becoming the trusted open science community built with standardised health data via a European federated network' is featured. Other sections include 'Annual report of year 4 now available', 'EHDEN Portal', 'SME Catalogue', and 'EHDEN Academy'. A footer section welcomes visitors to the European Health Data & Evidence Network (EHDEN) as an IM2 consortium with 25 partners operating in Europe.

## 2 Monthly BLOG

The screenshot shows the EHDEN website blog page. The first article is titled 'BLOG - Concentric Circles View (CCV) - What does this mean for how we protect patients when using their health data' and is dated May 2023. The second article is titled 'BLOG - Contextualising adverse events of special interest to characterise the baseline incidence rates in 24 million patients with COVID-19 across 26 databases: a multinational retrospective cohort study' and is dated April 2023. Both articles include a 'Read more' link.

## 3 Podcast

THE VOICE OF EHDEN  
EUROPEAN HEALTH DATA & EVIDENCE NETWORK  
Ethics, Legal & Social Implications

## 4 Social media

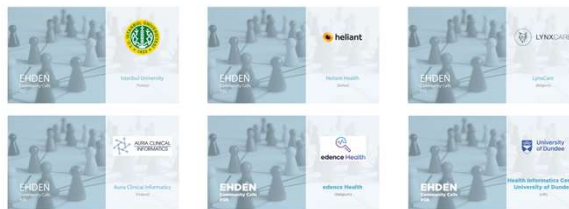


## 5 Meetings dedicated to our Community Community Calls

Behind the scenes of our Community, there is an important role of management and coordination, from the onboarding of Data Partners and SMEs to the mapping of data to the OMOP Common Data Model, and evidence generation thereafter. Listen to Monica Campbell as she explains her role and how the EHDEN Community is growing with time.



EHDEN is very pleased to support our Data Partner and SME community via a bi-monthly call to discuss topics of interest, and for them to share their experiences, learnings and recommendations related to mapping their data to the OMOP Common Data Model, and evidence generation thereafter. The video outputs from some of these calls also provide excellent educational materials for anyone with an interest in these domains, and we are grateful to our collaborators for their permission in making them publicly available.



THE VOICE OF EHDEN  
EUROPEAN HEALTH DATA & EVIDENCE NETWORK  
season 4



## FUTURE OF EHDEN



- Need for high-quality RWE increasing and recognised by all stakeholders.
- Project's legacy needs to be sustained and further developed.
- IMI consortium construct creates huge opportunities to fuel and build this system but enabling it for external collaborations requires a different focus of resources.
- Acting on sustainability now is the best way to ensure smooth and progressive transition to a project after-life.
- Legal entity in the Netherlands established in late 2021 (EHDEN Foundation)
- Consistent with the EHDEN project's vision, workplan and results
- Flexible and scalable by design to prepare for the future