EHDEN
EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Annual Report 2021

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PREFACE

On behalf of the Consortium, we are delighted with EHDEN's progress after year three, and also on welcoming a 23rd Partner, Boehringer Ingelheim. To already have created an initial network across 26 countries, with broad collaboration across a diverse community of Data Partners, SMEs and Researchers, supporting evidence generation at scale has been remarkable. Our Data Partner community is progressing the mapping of their source data to the OMOP CDM, serviced now by 47 SMEs in 19 countries, a unique, international resource. Furthermore, the EHDEN Portal technical architecture is getting closer to 'beta' and will become more widely available in year four in and outside of the project.

Meanwhile, evidence generation, the second 'E' in EHDEN, has expanded beyond our aspirations. This is based on the success of the wider project's aims, unfortunately the COVID-19 pandemic, our growing Data Partner community, collaboration with IMI BD4BO sister projects and many others, as well as our evidence-a-thon, and study-a-thons to accelerate time from hypothesis to evidence. This will be core to our work in years four and five, and indeed our sustainable future. And in year three we have also created a not-for-profit legal entity in The Netherlands to shadow and takeover from the IMI project in 2024. Methods development from HTA to federated learning have all mirrored progress made generally in supporting how we generate evidence.

Finally, we have been in the COVID-19 pandemic for two years, and all hope to see its abatement and a return to some sense of normality. EHDEN, and the world, have learned much, and the pandemic has been a catalyst for accelerating the use of RWD and RWE generated, which we need to ensure raises the bar across healthcare and for all diseases. At the time of writing, Ukraine is fighting for its survival against Russian invasion, and we stand with our Ukrainian colleagues.

Peter Rijnbeek
EHDEN Coordinator
Professor of Medical Informatics
Erasmus Medical Center, The Netherlands

Nigel Hughes
EHDEN Project Leader
Scientific Director RWD/RWE
Janssen R&D, Belgium

OPEN CALLS

- Processes and tools for the open calls are being fine tuned following each call.
- 140 Data Partners across 26 countries.
- 47 SMEs selected, trained, and certified in 19 countries.
- The Data Selection Prioritisation Committee (DSPC) and SME Certification Committee (SMECC) have additional/new expert members.

EDUCATION & COMMUNITY

- EHDEN Academy has more than 1,800 participants in over 60 countries and offers 14 different courses.
- Value propositions have expanded across stakeholders.
- We actively engaged with sister BD4BO projects, IMI, the EU Commission and EMA on areas of mutual relevance.

INFRASTRUCTURE

- Establishment of the EHDEN architecture (expansion of Data Partners metadata in EHDEN Database Catalogue, advancement data source dashboards)
- Contributed to ETL and mapping tools, further developed the ARACHNE tool, integrated ELIXIR authentication (AAI) mechanisms, publication data quality dashboards and advanced multiple analytical pipelines.

RESEARCH & OUTCOMES

- EHDEN and OHDSI collaboration on the COVID-19 resulted in multiple publications that directly impacted decision making by EMA.
- We ran a series of evidence-a-thons to onboard new Data Partners
- Collaborative study-a-thon organised by PIONEER with EHDEN and OHDSI on prostate cancer (March 2021).
- Extensive methodological research on personalised medicine resulted in multiple preprint publications.

MAJOR ACHIEVEMENTS

We are proud of the project's progress thus far, and on behalf of the consortium, thank everyone who has collaborated with us on our journey – it has been remarkable!

Certainly, the historic year of 2020 and the ongoing global pandemic have reinforced the need to ensure the *right data* is in the *right place* to answer the *right question*, within the appropriate socio-technical framework and governance.

We have met all major milestones on time, as anticipated.

An overview of the deliverables can be found on our Zenodo page.

2021 OPEN CALLS

THIRD SME CALL

(March-April 2021)

**40 APPLICATIONS
23 SELECTED**

FOURTH DATA CALL

(April-May 2021)

**55 APPLICATIONS
41 SELECTED**

FIFTH DATA CALL

(October-November 2021)

**90 APPLICATIONS
49 SELECTED**

SME CATALOGUE

Following our three SME open calls, we now have a total of **47 SMEs** in our SME Catalogue. Each of these SMEs was selected by our independent **SME Certification Committee**, received training via the EHDEN Academy and was validated during a two-day certification meeting.

EHDEN continues to build and strengthen this community via monthly update calls, an SME forum where experiences and knowledge can be shared, etc., to further reinforce this collaboration.

A last SME call will be launched in 2022 to further expand EHDEN's community.

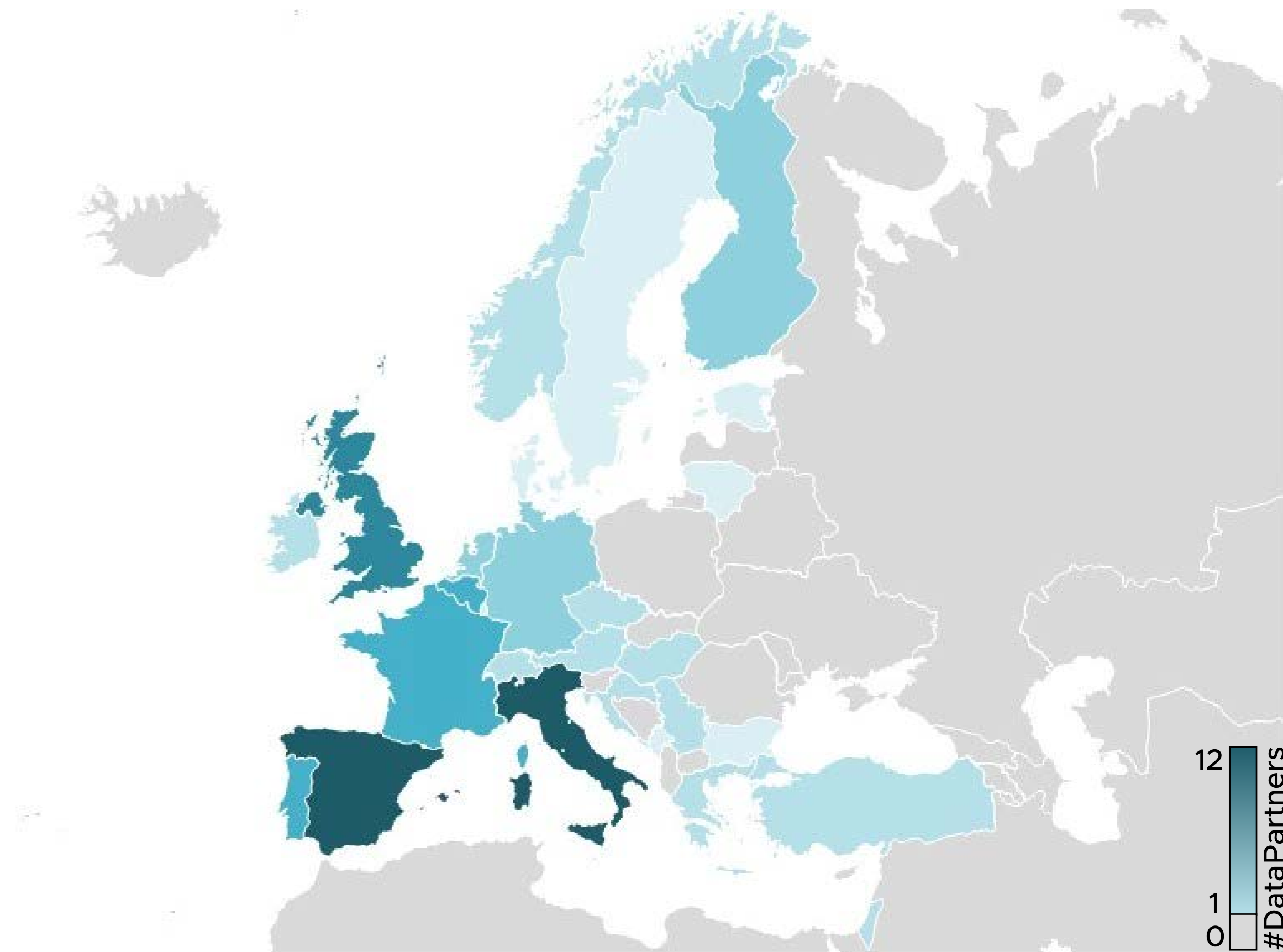Access the catalogue via ehden.eu/business-directory

FEDERATED NETWORK OF DATA PARTNERS

The EHDEN project aims to collaborate with diverse institutions and data custodians across the EU, with a goal of harmonising source data to the OMOP common data model locally, within a federated network.

Following the five open calls to date, we currently have **140 Data Partners** from **26 different countries** which are mapping their data to the OMOP common data model. This includes a few EHDEN project partners who have also mapped their data to the OMOP CDM for use in the federated network.

The most up-to-date overview is available at any time via ehden.eu/datapartners

FEDERATED NETWORK OF DATA PARTNERS

AUSTRIA (2)
- Medical University of Vienna
- Syndena

BELGIUM (10)
- Lynxcare
- Medaman
- AZ Klina
- University MS Center
- AZ Damiaan Oostende
- AZ Delta
- AZ Maria Middelares
- Universitaire Ziekenhuizen KU Leuven
- Icometrix
- Ziekenhuis Oost-Limburg

BULGARIA (1)
- Technical University of Sofia

CROATIA (3)
- Clinical Hospital Dubrava
- Hierarchia d.o.o.
- MCS Grupa d.o.o. & Health Care Center of Primorje-Gorski Kotar County

CZECH REPUBLIC (2)
- Institute of Rheumatology
- OAKS Consulting s.r.o.

DENMARK (1)
- Center for surgical science

ESTONIA (1)
- University of Tartu

FINLAND (6)
- Hospital District of Southwest Finland
- BCB Medical Ltd
- Prostate Cancer Registry of South West Finland
- Pirkanmaa Hospital District
- Hospital District of Helsinki and Uusimaa
- Finnish Institute for Health and Welfare (THL)

FRANCE (9)
- APH de Marseille
- Bordeaux Hospital
- Bordeaux PharmacoEpi
- Cegedim Health Data
- CHU de Toulouse
- Health Data Hub
- Lille University Hospital
- CHU de Montpellier
- APHP-EDS

GERMANY (8)
- Charité - Universitätsmedizin
- MS Forschungs- und Projektentwicklungs
- Hanover Medical School
- European Rare Kidney Disease Registry (ERKReg)
- University Medicine Dresden
- University of Ulm, ZIBMT
- CancerDataNet GmbH
- Krebsregister Rheinland-Pfalz

GREECE (2)
- Innovative Medical Research SA
- General Hospital of Kavala

HUNGARY (2)
- Semmelweis University
- University of Pécs

ITALY (21)
- Fondazione IRCCS Istituto Neurologico Carlo Besta
- AUSL Reggio Emilia
- Fondazione Poliambulanza Istituto Ospedaliero
- Azienda Policlinico Universitaria di Modena
- Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
- SIMG
- IRCCS Policlinico San Donato
- Fondazione Istituto Nazionale de Tumori
- Casa di Cura Privata del Policlinico (CCPP)
- Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo
- Fondazione IRCCS Policlinico San Matteo
- Fondazione Toscana Gabriele Monasterio per la Ricerca Medica e di Sanità pubblica (FTGM)
- ASL Roma 1
- Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli"
- Basilicata Cancer Registry
- AO Card. G. Panico - Center for Neurogenerative Diseases and Aging Brain
- IRCCS Azienda Ospedaliero-Universitaria di Bologna Policlinico di Sant'Orsola
- University Hospital of Parma
- Azienda Ospedaliera Universitaria

- Integrata Verona
- ATS Bergamo
- ISMETT

IRELAND (1)
- Trinity St Jame's Cancer Institute

ISRAEL (2)
- The Directorate of Government Medical Centers at the Israeli Ministry of Health
- Hadassah OBGYN

LUXEMBOURG (1)
- Registre National du Cancer du Luxembourg

MONTENEGRO (1)
- Clinical Center of Montenegro

NORWAY (2)
- University of Oslo
- The Norwegian Cancer Registry

PORTUGAL (8)
- Rosa Maria Príncipe
- 2CA-Braga
- Registo Portugues de Doentes Reumaticos
- Instituto de Medicina Molecular
- CUF
- Unidade Local de Saúde de Matosinhos
- Hospital do Espírito Santo de Évora
- ADPD

SERBIA (3)
- Clinical Center of Serbia
- Clinical Centre of Nis
- Clinical Hospital Center Zvezdara

SPAIN (22)
- Biocruces Bizkaia Health Research Institute
- Parc Salut Mar Barcelona
- Fundación de Investigación Biomédica del Hospital Universitario 12 de Octubre
- HULAFE
- FIIBAP
- Servicio Cántabro de Salud and IDIVAL
- The Information System for Reseach in Primary Care
- Vall d'Hebrón Hospital Marina Salud S.A.
- Parc Sanitari Sant Joan de Déu
- Virgen Macarena University Hospital
- Consellería de Sanidade
- INCLIVA
- Fundació Institut d'Investigació Sanitària Illes Balears

- Healthcare Service of the Principality of Asturias
- Instituto Aragonés de Ciencias de la Salud (IACS)
- Institut Català d'Oncologia
- Consorci Corporació Sanitària Parc Taulí
- Research Institute - Hospital de la Santa Creu i Sant Pau
- Rioja Salud
- Servicio Madrileño de Salud (SERMAS)
- FIMIM
- PSMAR

SWITZERLAND (3)
- Geneva Cancer Registry
- University Hospital Geneva
- Institute of Social and Preventive Medicine, University of Bern

SWEDEN (1)
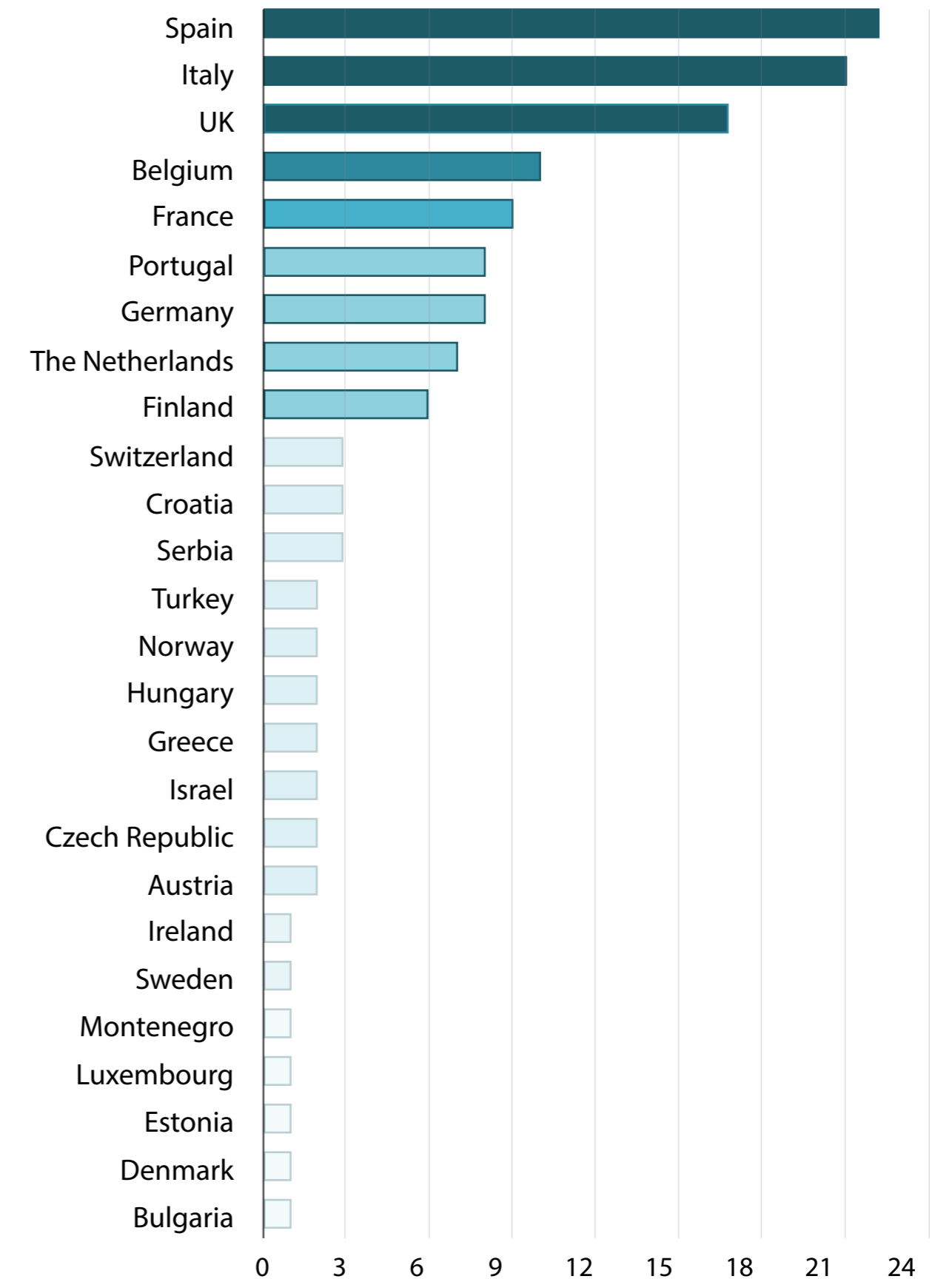- MEB Karolinska Institutet

THE NETHERLANDS (7)
- NICE Foundation
- Amsterdam UMC
- EMC
- STIZON
- IKNL
- EBMT
- Harm Slijper

TURKEY (2)
- Istanbul University - Faculty of Medicine
- IUC Cerrahpaşa TIP Fakületesi

UNITED KINGDOM (17)
- CPRD
- University of Edinburgh
- Health Informatics Centre
- King's College London
- Royal College of General Practitioners Research and Surveillance Centre
- SAIL Databank
- Akrivia Health
- Barts Health NHS Trust
- Harvey Walsh Ltd
- Leeds Teaching Hospitals
- UK National Neonatal Research Database
- Optimum Patient Care
- Queen Mary University of London
- University College London Hospitals
- Connected Bradford
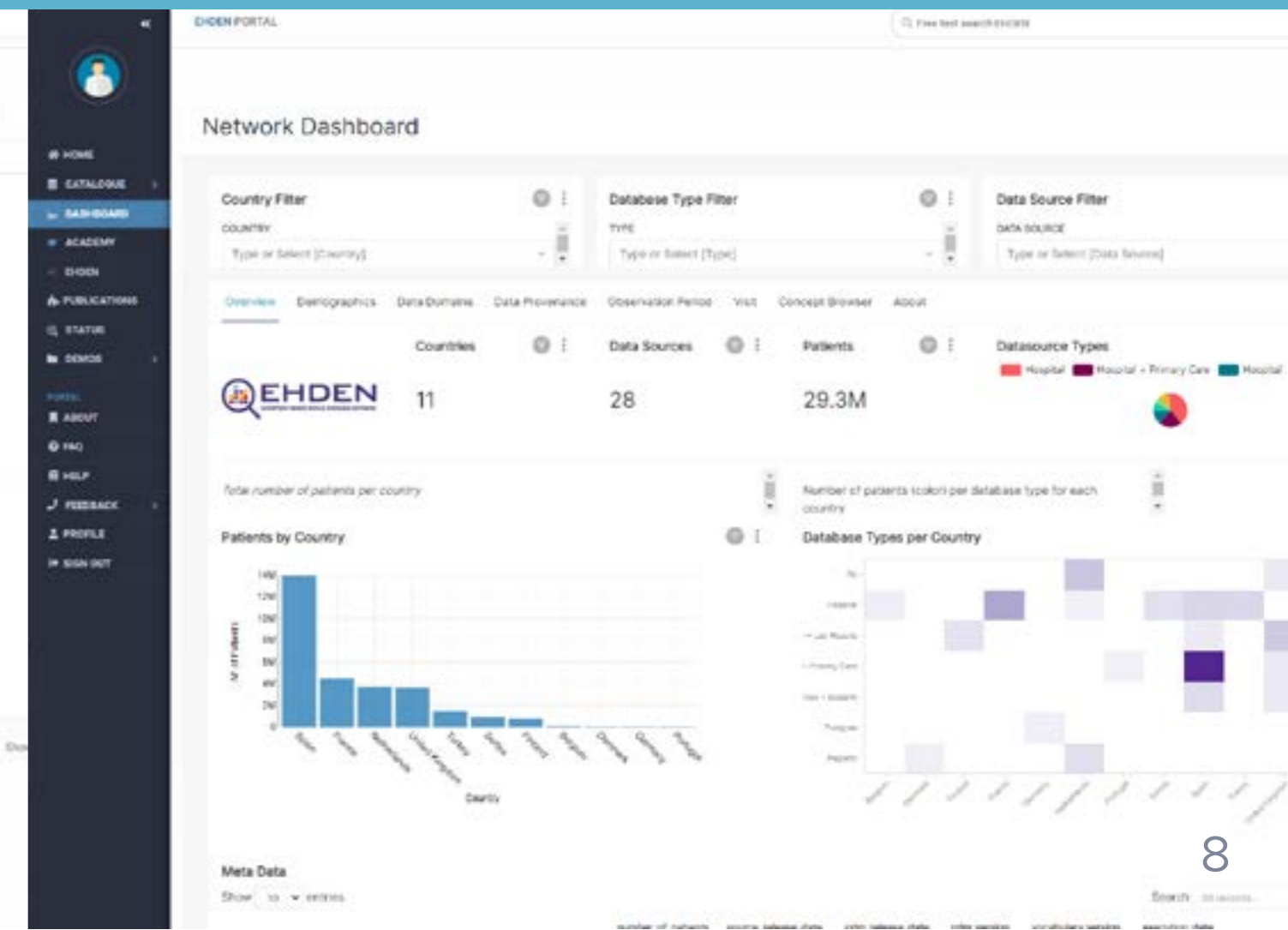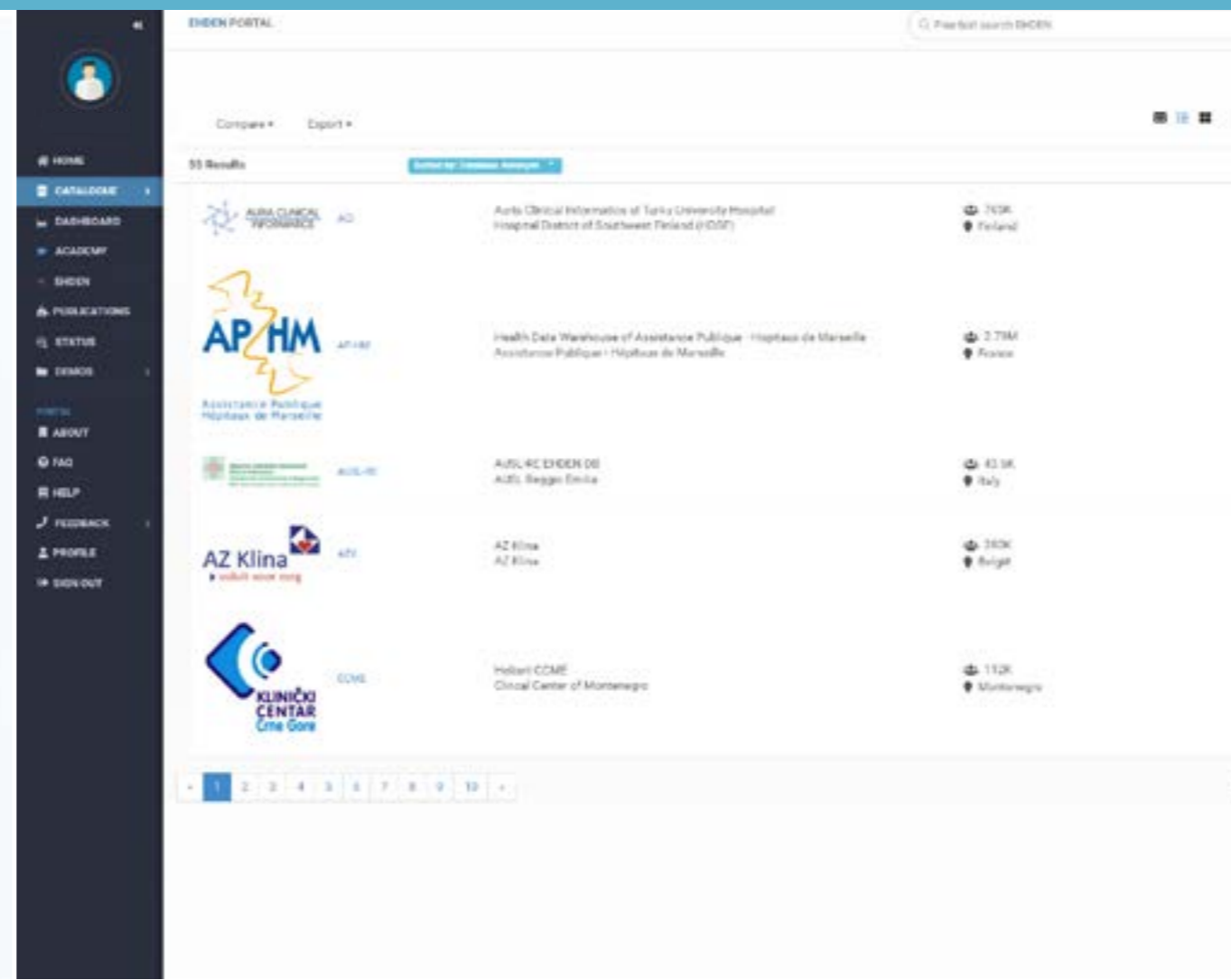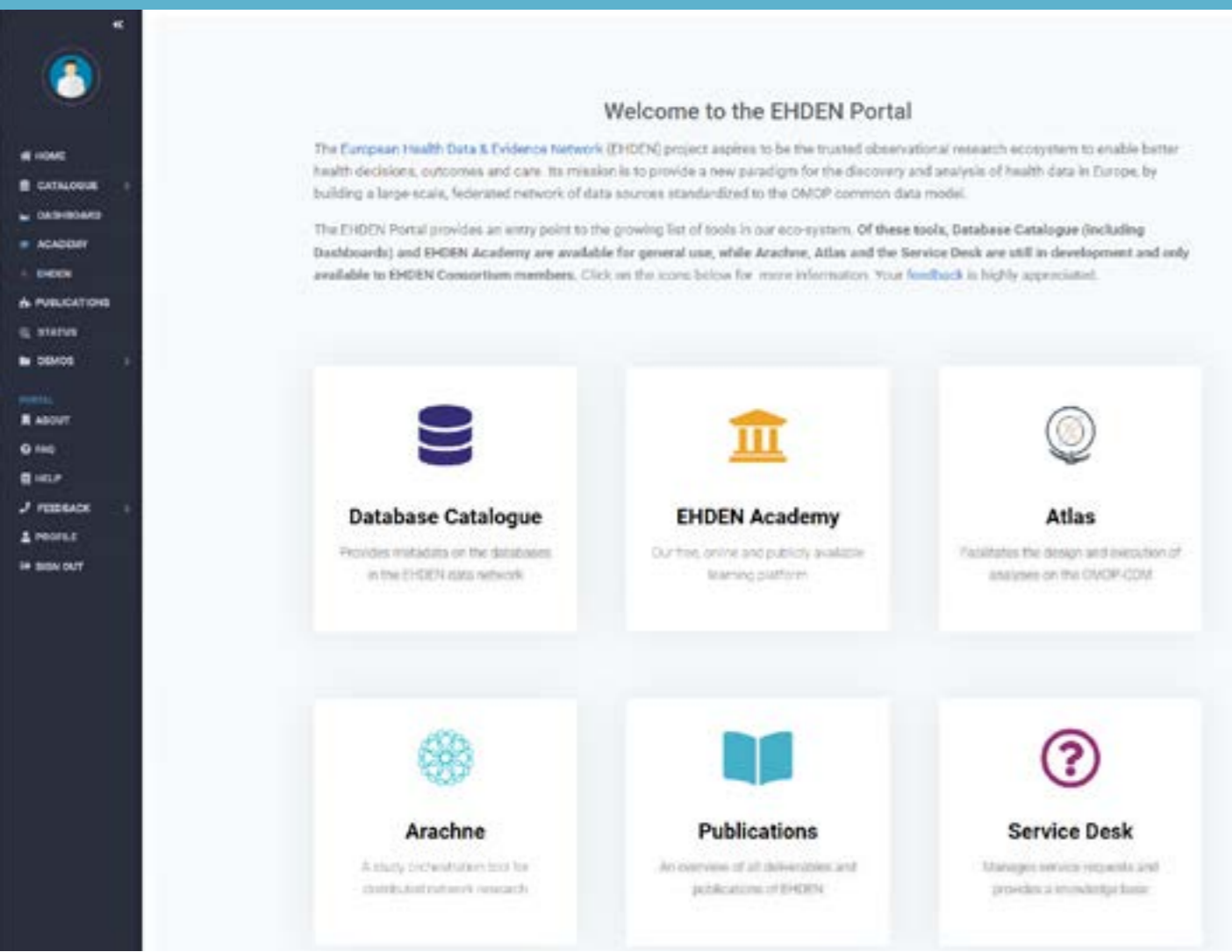- GOSH

OF DATA PARTNERS

EHDEN PORTAL

The EHDEN infrastructure is envisioned as a one-stop shop for connecting researchers with Data Partners to answer real world research questions and execute upon them.

The EHDEN Portal has been set up as the high level point of entry for researchers looking for high quality real world data from a broad range of European data sources, while the database catalogue and the network dashboards allow a deeper dive into data sources to explore study feasibility more in-detail.

Since the Portal has been launched internally for EHDEN consortium members, helpful feedback has been collected through useability studies. The public launch of the EHDEN Portal, which will allow non-EHDEN members to leverage the database catalogue is planned for early summer 2022.

(Left to right) The images at the bottom show the homepage, the Data Catalogue and some of the dashboards available via the EHDEN Portal.

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TOOLS AND METHOD DEVELOPMENT

In the course of year three of EHDEN, an ever growing number of data sources have been added to the EHDEN Portal. A rich set of (meta) data was added to the database catalogue, allowing researchers to identify and leverage relevant data sets for the generation of reliable evidence. The onboarding of new data sources is facilitated by the EHDEN community manager, who welcomes data sources and provides support during the process

Release of Arachne 1.19 including additional functionality as identified during the Arachne workshop 2021

New features were developed for USAGI, e.g., collaborative review code mapping, and new mapping relations (Maps to Value and Maps to Unit)

ATHENA tool 1.12.2 was released, which mainly contains fixes for the vocabulary download process and improved security for dependencies
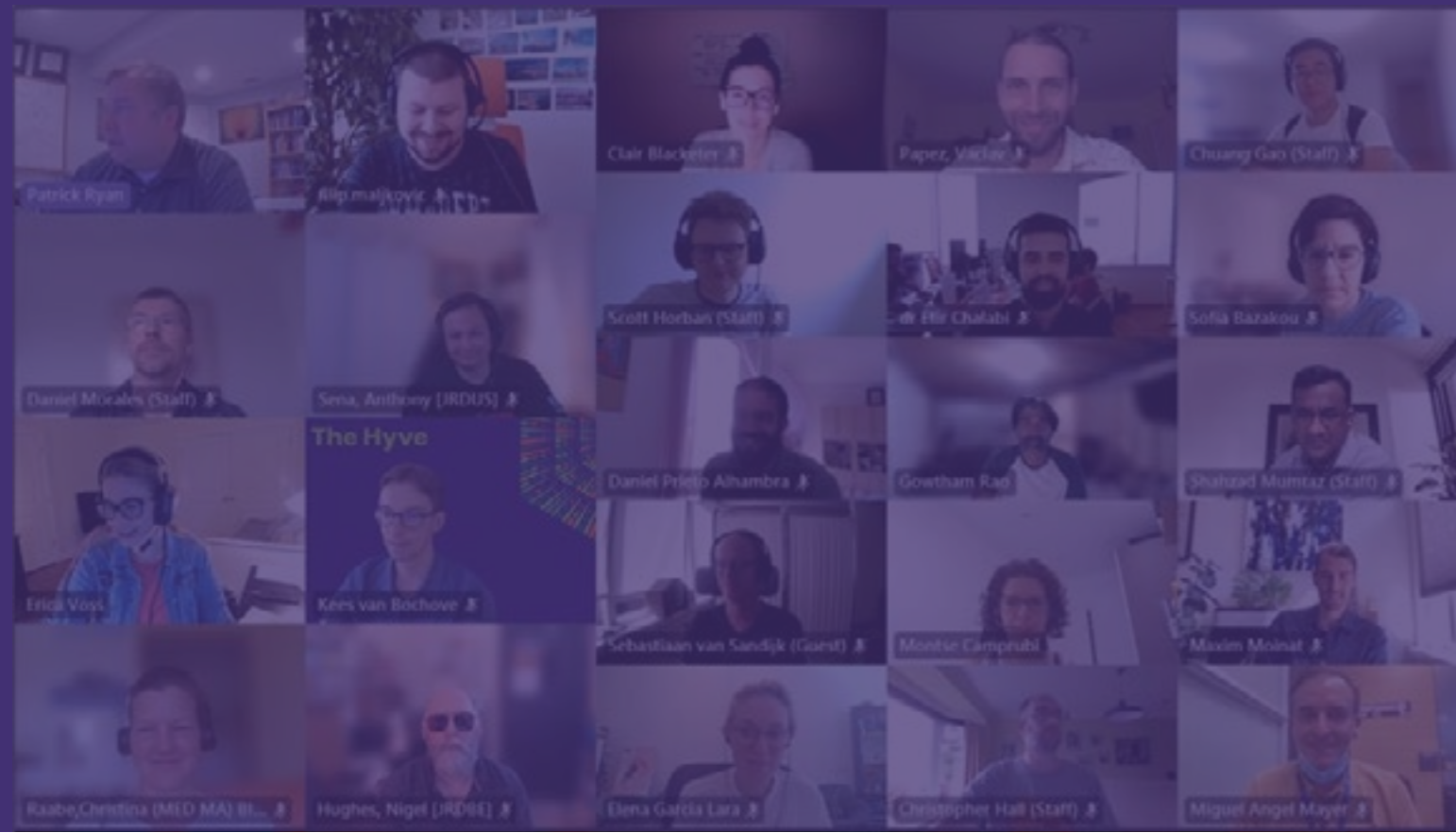
Integration with Elixir AAI and definition of roles and corresponding permissions of users in applications such as the EHDEN portal, EHDEN Academy and Arachne

FIRST EHDEN EVIDENCE-A-THON ("E-THON")

We have created an 'Evidence Taskforce' to facilitate a focus on evidence generation through use cases and network studies, as well as expanding our educational activities via 'e-thons', or focused evidence generation events to work with newly mapped Data Partners (DPs) in learning to work with their OMOP-mapped datasets.

A particular aspect helpful to all was the granularity of understanding afforded by this event in exploring the mappings to the OMOP CDM and the specific nuances per DP's dataset.

Below: group photo of the e-thon participants. The group is composed of EHDEN COVID-19 ETL Task Force members, colleagues from OHDSI and 4 Data Partners - APHM, CC Serbia, FIMIM, HIC and UK Biobank.

OUR SCIENTIFIC OUTPUT IN YEAR THREE

PEER REVIEWED STUDIES
- Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study (BMJ)
- Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study (BMJ)
- The natural history of symptomatic COVID-19 during the first wave in Catalonia (Nature Communication)

PREPRINTS
- Characteristics and outcomes of 118,155 COVID-19 individuals with a history of cancer in the United States and Spain
- Using the OHDSI network to develop and externally validate a patient-level prediction model for Heart Failure in Type II Diabetes Mellitus
- Alpha-1 blockers and susceptibility to COVID-19 in benign prostate hyperplasia patients : an international cohort study

MORE INFO
- Visit our EHDEN Zenodo page for the latest publications
- The first EHDEN "e-thon"
- EHDEN Website newsposts

USE CASE 1
DRUG UTILISATION

We have completed and published an analysis of the use of medicines to treat COVID-19 amongst hospitalised patients, released in the BMJ on 11th May 2021: "Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study".

This work received media attention, was mentioned by eight news outlets, and remains in the top 5% of all publications compiled by Altmetric (for more details see here).

Work was performed in the domain of drug utilisation for Asthma medication of which results were presented at the 2021 symposium of the European Respiratory Society (link).

USE CASE 2
DRUG AND DEVICE SAFETY

We have collaborated with the European Medicines Agency (EMA) and contributed to the generation of key evidence on the safety of COVID-19 vaccines:

• Firstly, we collaborated with previously mapped EHDEN Data Partners and OHDSI international collaborators to estimate "expected" (background) incidence rates of a list of fifteen pre-specified adverse events of special interest for the monitoring of COVID-19 vaccine safety. This work was published in June 2021 in the BMJ: "Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study". These data have been used and cited by many international regulators and stakeholders, including the EMA and the Australian Government Department of Health

• Secondly, we estimated the incidence of thrombosis and thrombosis with thrombocytopenia syndrome/s in people with COVID-19 and following vaccination with BNT162b2 or ChAdOx1 COVID vaccines. The outcome has been cited as a key source of information during the evaluation of Vaxevria by the European Medicines Agency: see full report here.
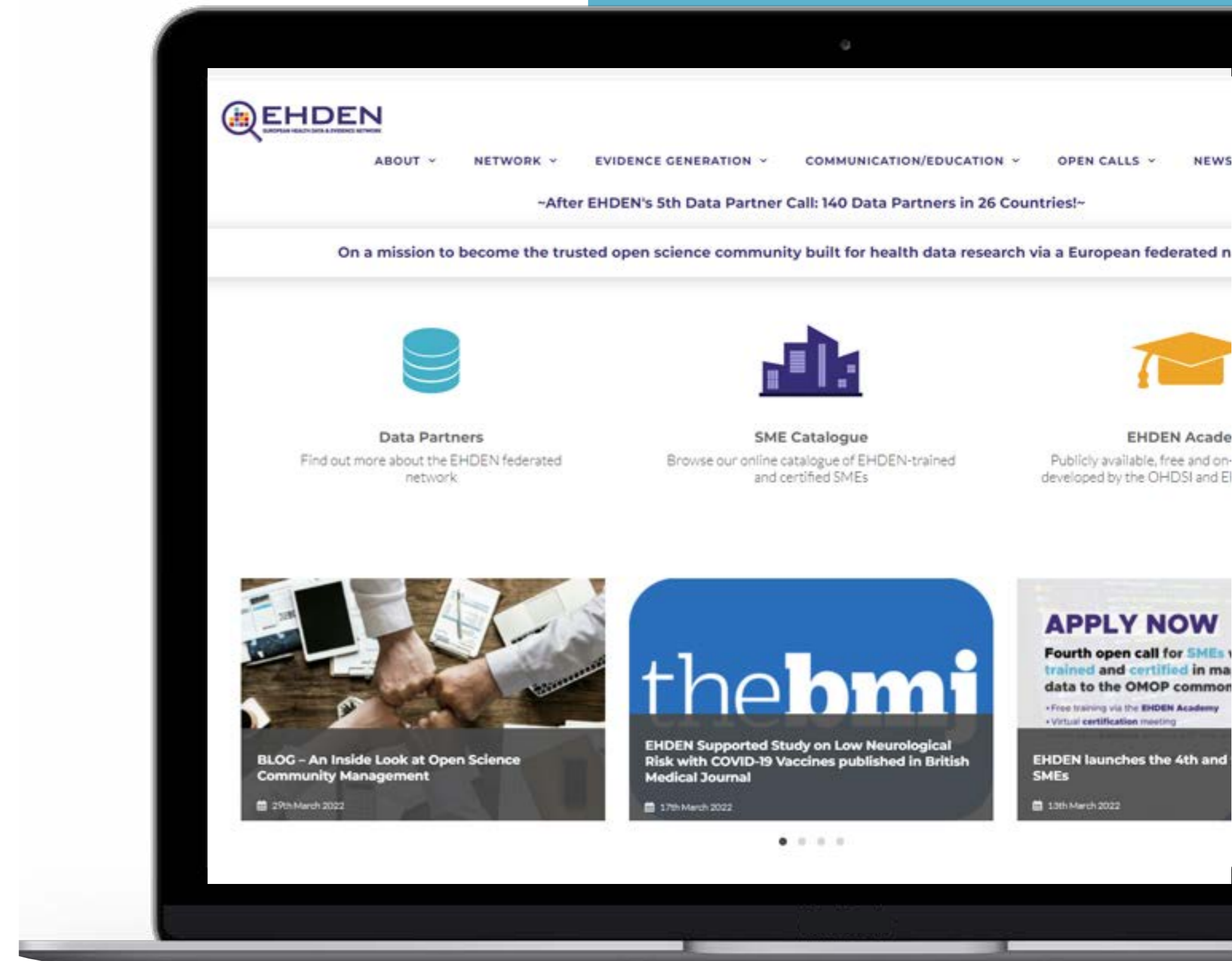
DISSEMINATION

EHDEN aims to be at the forefront of open science, making healthcare data more accessible for research. Our dissemination activities reflect this vision and as such, all our papers, preprints and public deliverables are available via the EHDEN Zenodo page.

COMMUNICATION

Our communication aims at building an open science community that will endure and use the project outcomes long after the project has ended. This has resulted in an average of 17,000 visitors to the EHDEN website each month and a steady increase in followers on Twitter and LinkedIn. A complete overview of all newsposts, newsletters, webinars, podcasts, videos, etc., can be accessed via our website.

We are also proud to have launched the "Voice of EHDEN" podcast series in September 2021. These podcasts bring together a diverse range of experts to discuss key aspects of working with real world data in large scale observational research, network studies and building 21st century architecture.

EHDEN ACADEMY

The **EHDEN Academy** has grown to be a significant educational and collaborative resource for EHDEN, OHDSI and the global community with regards to training and upskilling.

At the end of the third year, **approximately 1,800 users** from over **60 countries** have started their learning journey in the Academy.

With **14 courses** currently available, the Academy continues to update its curriculum and number of expert trainers, with specific focus on more HTA and regulatory science trainings planned for launch in year four.

Getting started

Phenotype Definition, Characterisation and Evalu-

EHDEN Foundation

OMOP CDM and Stand-ardised Vocabularies

OHDSI-in-a-box

Infrastructure

Extract, Transform and Load

Patient-Level Prediction

Population-level Effect Estimation

ATLAS

NEW COURSES LAUNCHED IN YEAR THREE

Introduction to Real World Data & Real World Research

R for Patient-level Predic-tion

Introduction to Data Quality

ETL Learning Pathway: Data Partner & SME Real World Use

COLLABORATIONS

BD4BO

- EHDEN has provided consultative support to HARMONY and BIGDATA@HEART regarding technical aspects of using the OMOP CDM, study-a-thons, through to sustainability.
- PIONEER and EHDEN have a co-working group to explore opportunities to collaborate around Data Partners, SMEs, research uses cases/study-a-thons, and educational support via the EHDEN Academy.
- We have MoUs in place with BD4BO sister projects, but also H2020 projects such as HTx.

EUROPEAN COMMISSION & EMA

- We have been actively collaborating with the TEHDAS Joint Action as part of the European Health Data Space initiative by the European Commission, also positioning EHDEN within the proposed legislative changes (2022).
- We held initial meetings with H2020 funded project COMED to gain insight into challenges using RWE on medical devices for HTA purposes.
- We have had numerous engagements with applicant consortium for IMI projects, as well as contributing to EU-PEARL, FAIRPLUS, H2O, HARMONY, NEURONET, VALUE-Dx, SOPHIA, HIPPOCRATES.
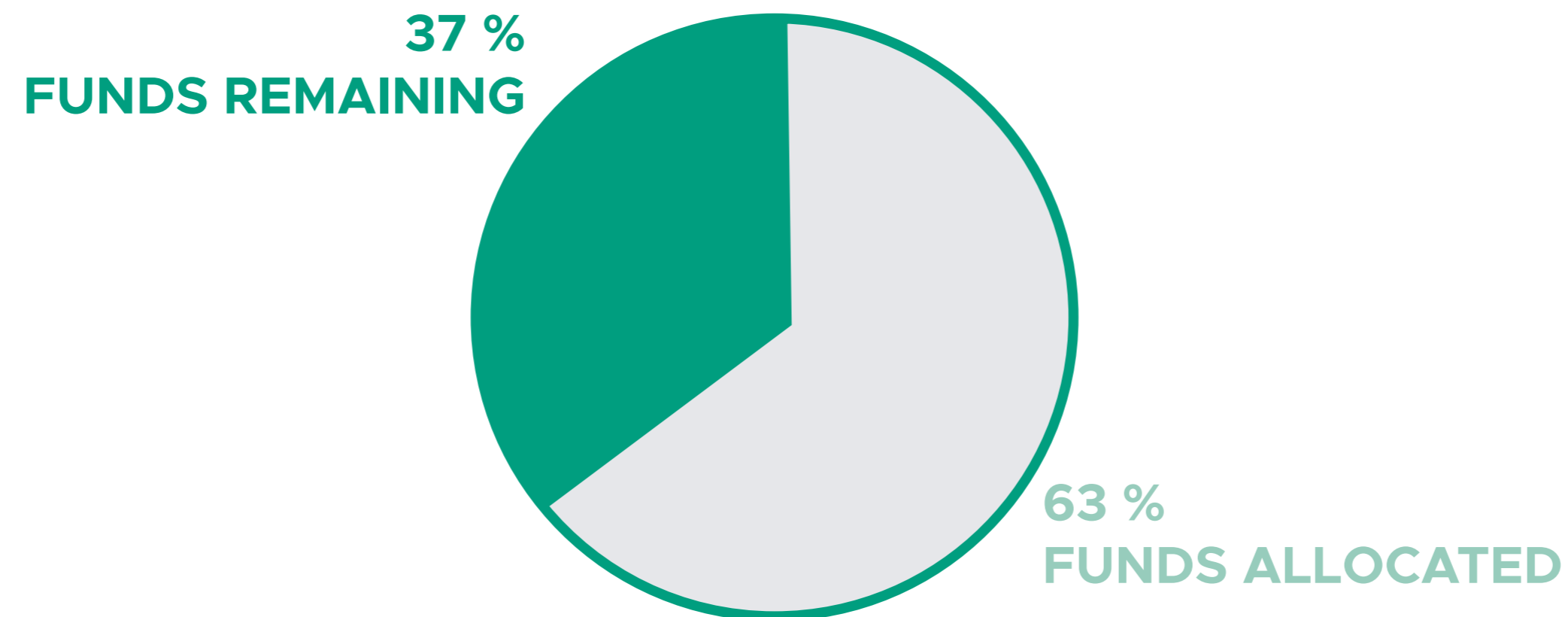
OHDSI

- EHDEN and OHDSI further intensified their collaboration on the COVID-19 research and initiated new studies in this domain. This includes work that directly impacted regulatory decision making by European Medicines Agency.
- EHDEN and OHDSI continue to collaborate (effectively symbiotic) with reference to open source tooling, skills, methods development and evidence generation.

HARMONISATION FUND

The project originally set aside a €17 million Harmonisation Fund (HF) for the harmonisation of data to the OMOP common data model through article 15: 'Financial Support to Third Parties.' The EHDEN project has allocated €7.77 million from the first four Data Partner (DP) Open Calls, and will allocate a further €3 million in the recently closed Open Call #5. We will have then allocated €10.77 million (63%) of the €17 million HF.

As highlighted above, the original EHDEN objectives in terms of number of patient records under harmonisation have already been **exceeded by more than three-fold,** reaching **more than 500 million anonymous records**.

In 2022 it is planned to have two final open calls, focusing on specific types of data sources, geographies and meeting evidence generation use case gaps.

37 %
FUNDS REMAINING

63 %
FUNDS ALLOCATED

SUSTAINABILITY

Our vision remains steadfast: a Europe where harmonised real world data is used by the healthcare community to more rapidly generate high quality insights that improve outcomes for patients, revolutionising how treatment and care are implemented and evaluated.

Building on EHDEN's foundation, **a new legal entity is being launched as a not-for-profit incorporated** in The Netherlands, that will transition the project into a long-term, sustainable operation from 2024. It will facilitate the developing ecosystem, operationalise the research operating model post-project, working in parallel on the transition and cross-fade between the project and the legal entity.

As a sustainable entity it will service research in the EHDEN network and wider research community, supporting studies, study-a-thons, methodological and technical developments, and research programmes.

LOOKING FORWARD

The EHDEN Consortium is delighted with progress made by end of year three, and looking forward beyond a pivot point in year four and five as we focus more heavily on the second 'E' in EHDEN, evidence, as well as our sustainability developments around a new legal entity.

It has thus far been a remarkable journey already in terms of the rapid expansion of our Data Partner and SME network, deployment of the mapping work, and creation of our technical and governance architecture.

EHDEN has already been submitting publications across disease areas, inclusive of COVID-19, and we look forward to an expanding portfolio of use cases, study-a-thons, and e-thons. We remain committed to maximising the transformational potential of real world data by generating real world evidence, at scale, that improves patient treatments and outcomes.

As an open science research community, we're looking forward to adding more EHDEN Academy courses and collaborating with all our partners across Europe as we build our sustainable future.