EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

From EMIF to EHDEN: scaling up the big data ecosystem across Europe

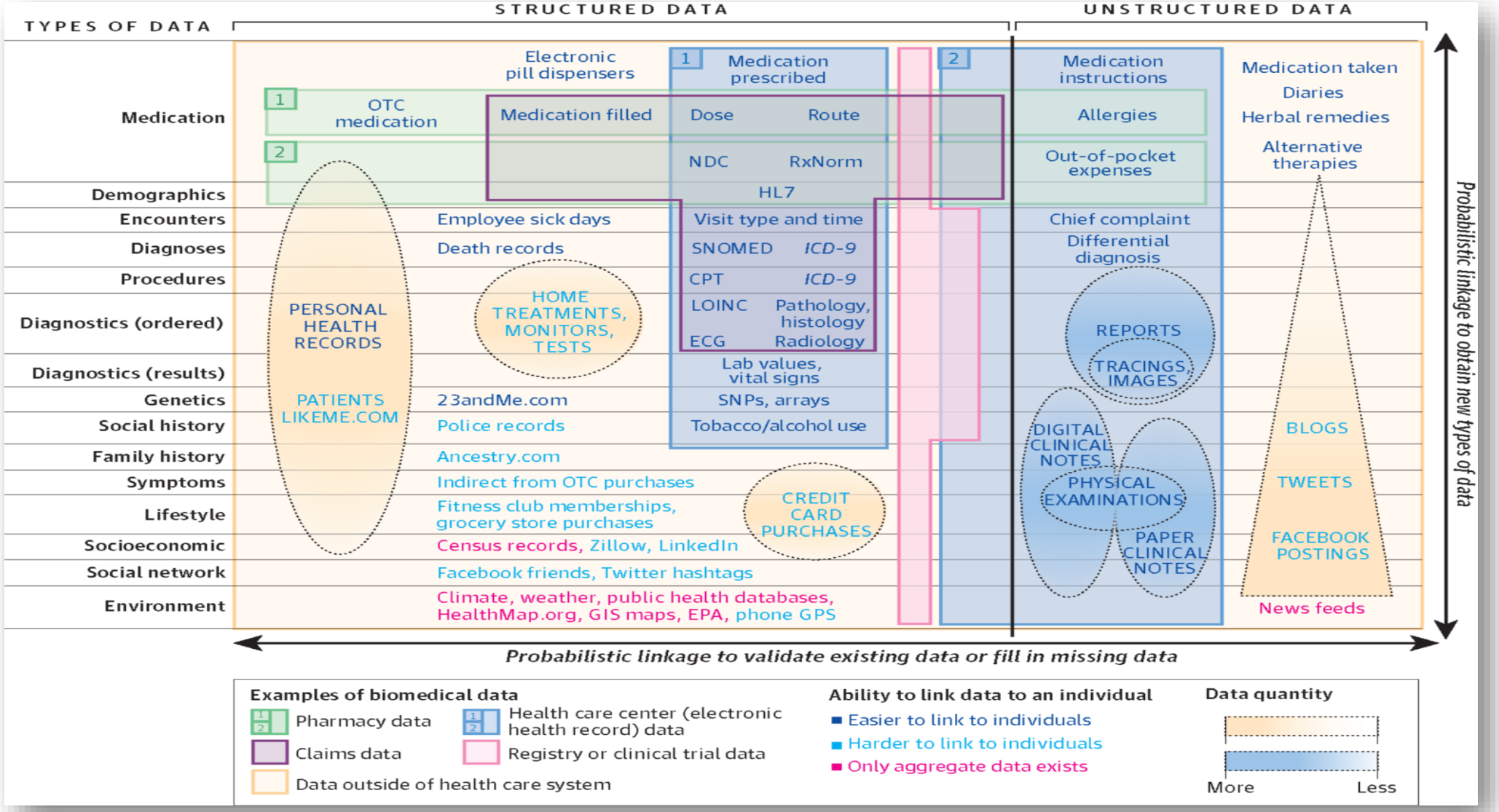
Nigel Hughes

EHDEN Project Leader/Co-Coordinator
Scientific Director, JCI Patient Data for Research, Janssen

imi efpia

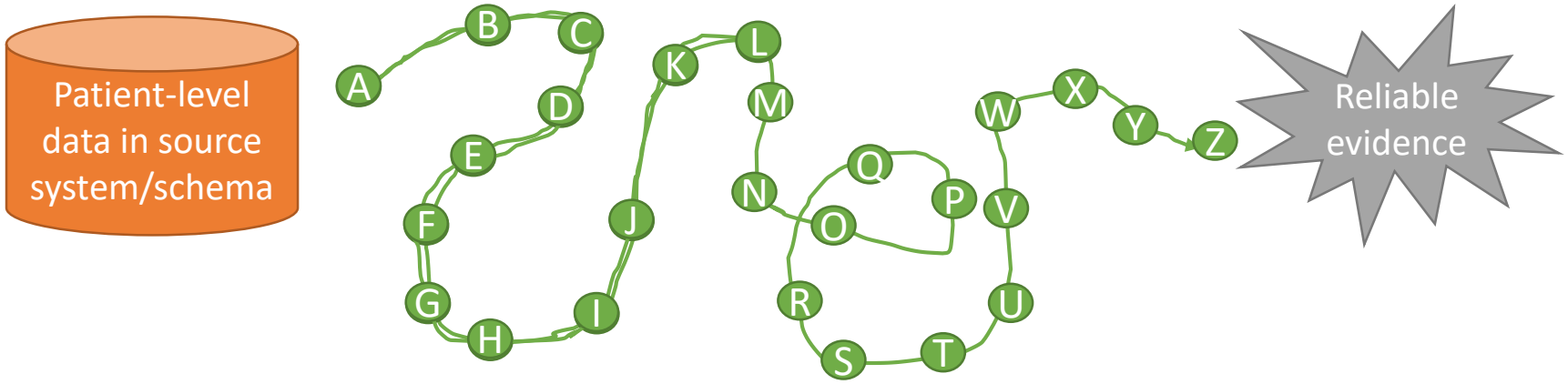
ALL TOO OFTEN REAL WORLD RESEARCH IS A CHALLENGING JOURNEY….

It's Going to Take All Sorts of Data....



JAMA. 2014;311(24):2479-2480. doi:10.1001/jama.2014.4228

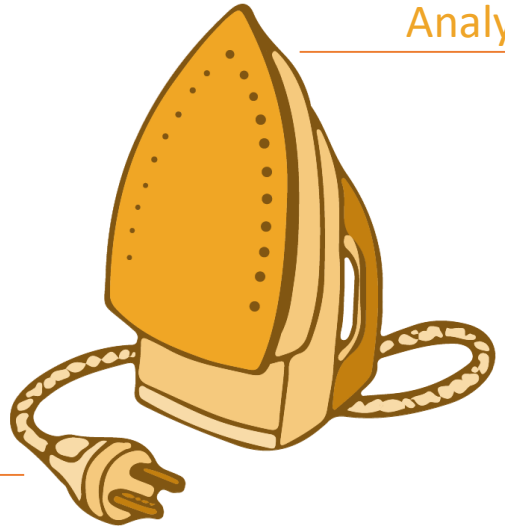
Generating Reproducible and Reliable Evidence



We need fully transparent and reproducible pipelines that enable large-scale federated analyses across Europe.

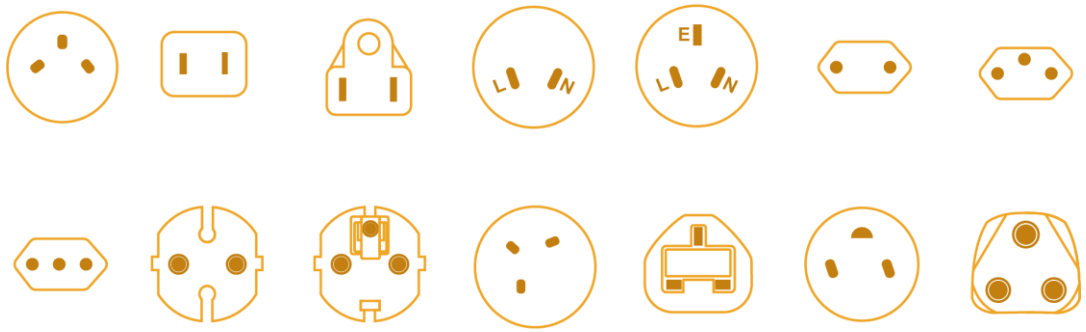
WHY IS THIS NOT CURRENT PRACTICE?

Analytical method



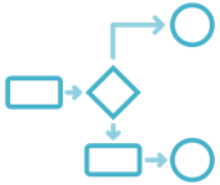
Link to data

The data…



What will it require?

Data interoperability

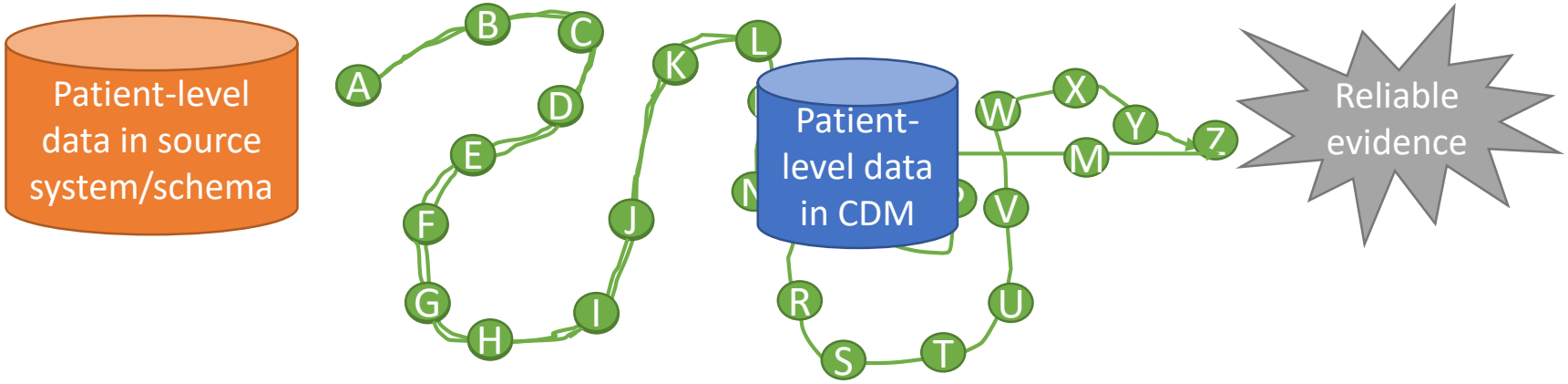


Standardised analytics

Data network

Strong community

GENERATING RELIABLE EVIDENCE USING THE OMOP CDM



EHDEN will build on expertise and tools from prior IMI projects, such as EMIF, and will collaborate intensively with the global OHDSI community.

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

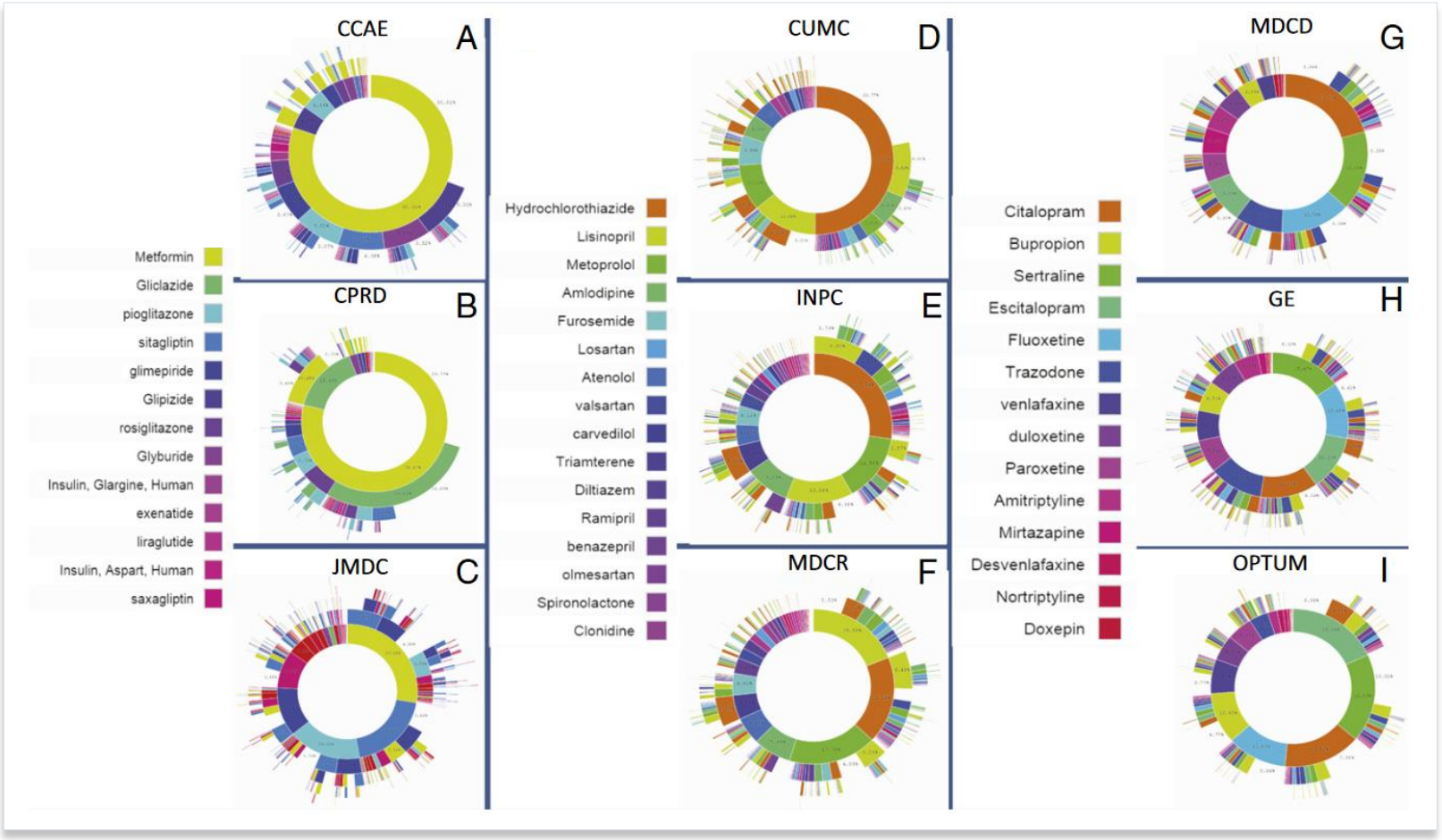
What we need is infrastructure and a network to conduct real world research in the 21st Century….

'We have more pilots than an airline....'

Anon, Conference Participant, 2019

LARGE-SCALE OBSERVATIONAL RESEARCH IS FEASIBLE

T2 Diabetes Mellitus | Hypertension | Depression



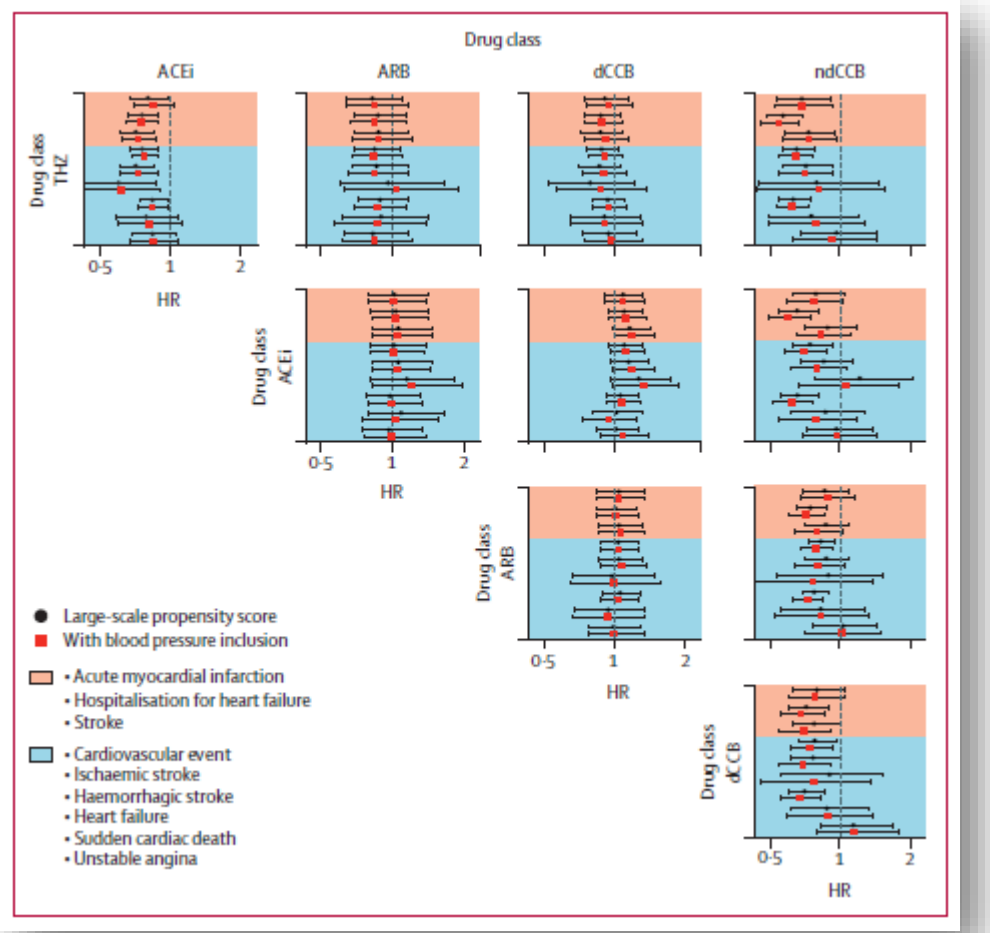
11 Data sources

4 Countries

> 250 million patients

"Characterizing treatment pathways at scale using the OHDSI network."
George Hripcsak et al. - PNAS (2016)27:7329–7336

LARGE-SCALE OBSERVATIONAL RESEARCH TO INFORM GUIDELINES



Uncertainty remains about the optimal monotherapy for hypertension, and RCT data is lacking

LEGEND-HTN – a systematic, large-scale study under a new-user cohort design; 3 primary outcomes (AMI, Heart Failure hospitalisation, CVA), 6 secondary outcomes & 46 safety outcomes

1st first line role of thiazide or thiazide-like diuretics under appreciated in current guidelines

Estimated 1.3 CVS events avoided for every 1000 patients THZ vs ACEi

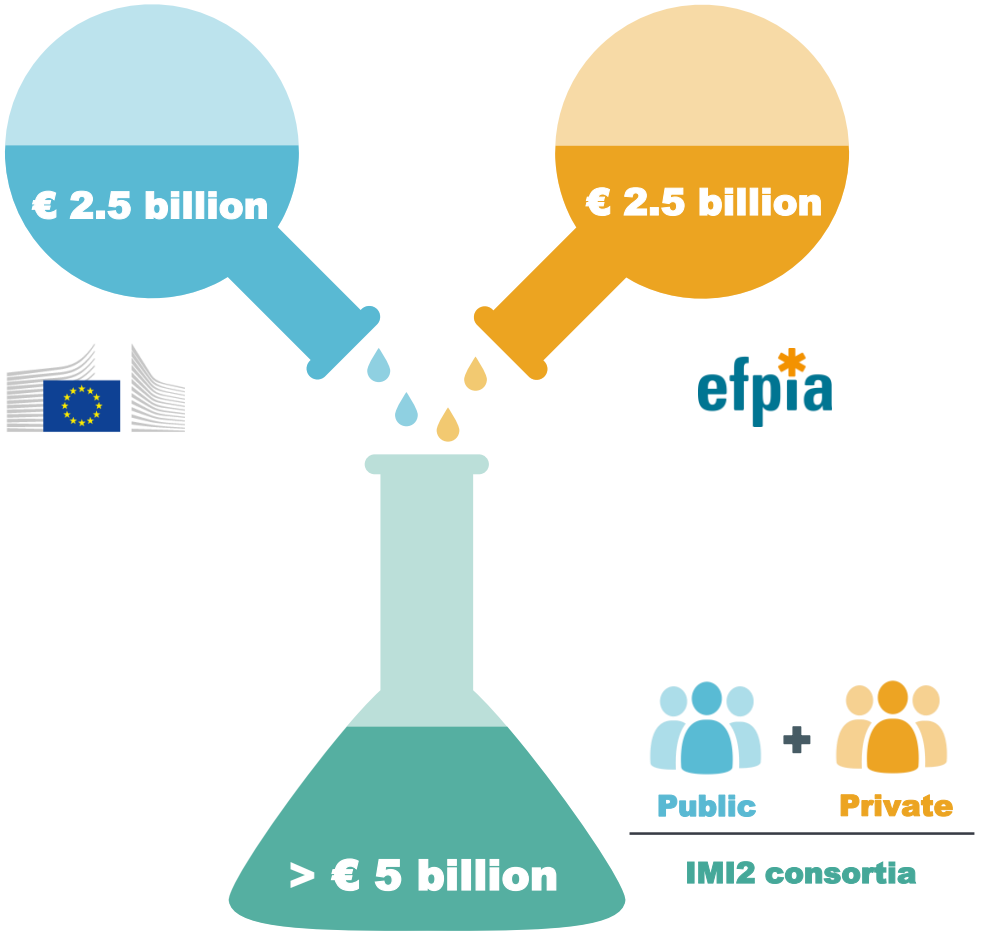
9 Data sources
6 Claims
3 EHR

4 Countries

4.9 million patients

Equivalent to 22,000 observational studies

" Comprehensive comparative effectiveness and safety of 1st line antihypertensive drug classes."
Suchard MA, et al. – Lancet (2019): online 24 Oct



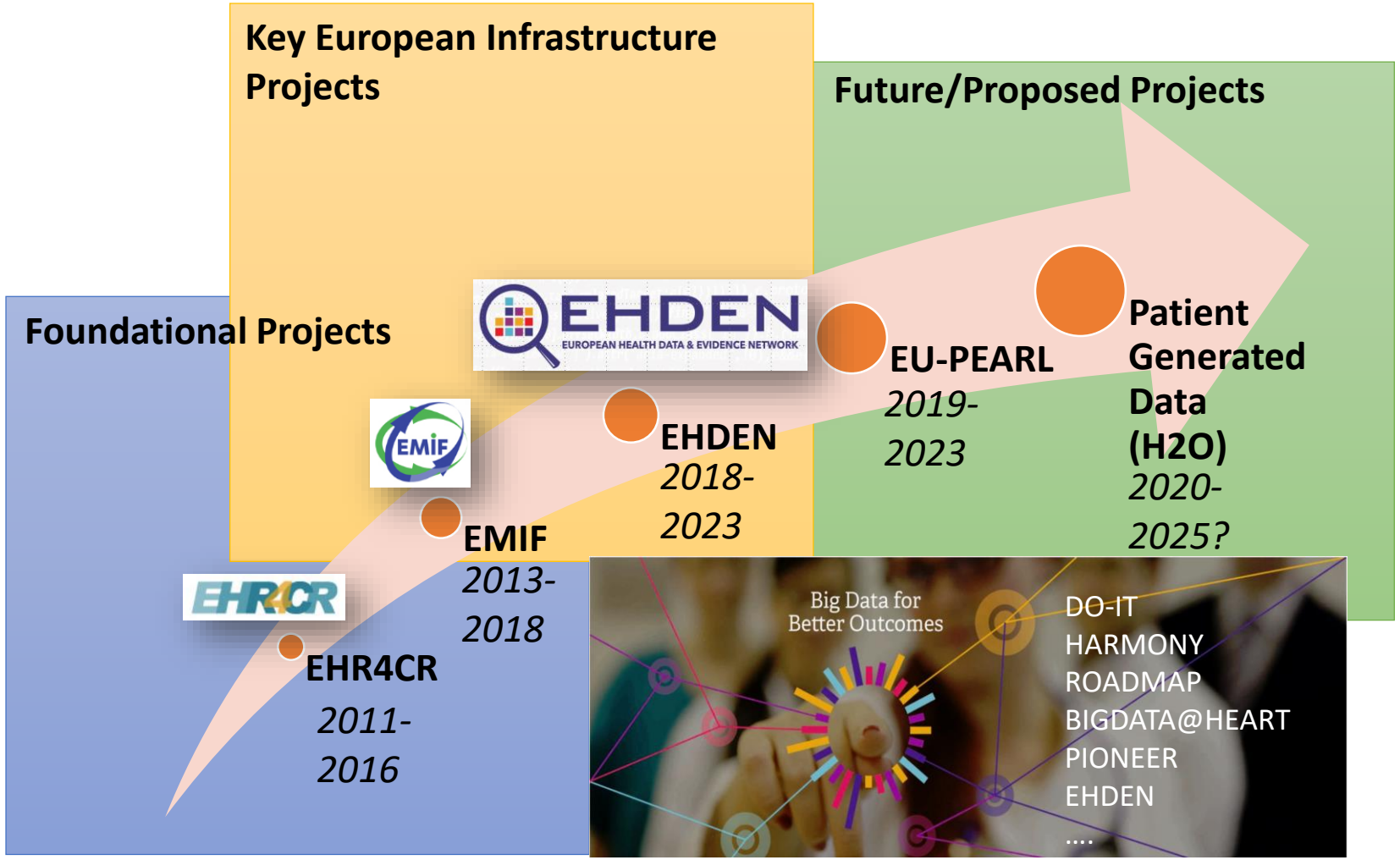
Carlos Moedas

EU commissioner for research, science and innovation

*"**Radical collaboration** where multinational companies work together and share data instead of keeping it secret is helping to change the model of the pharmaceutical industry and solve problems more quickly." (Source)*

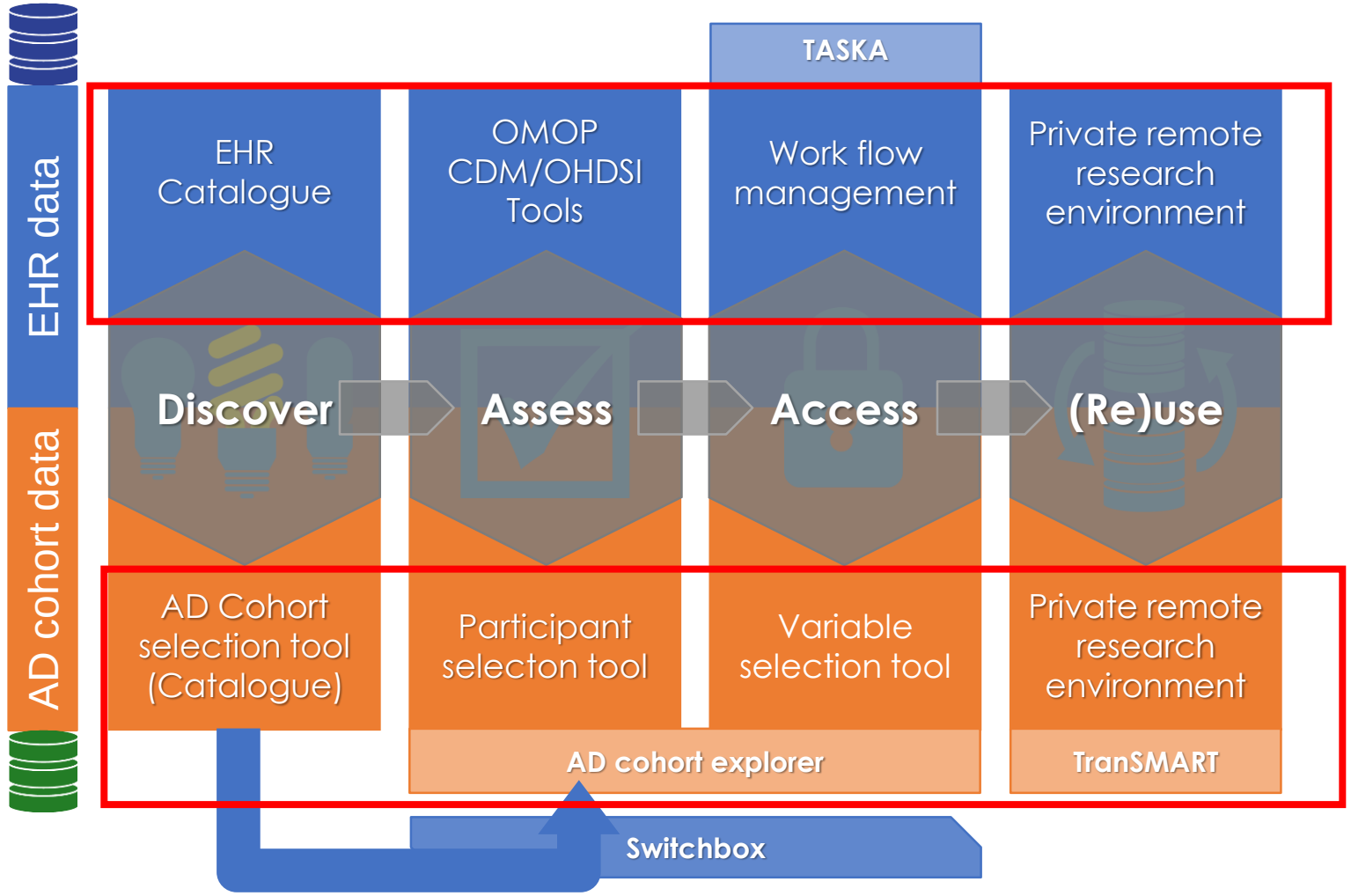
- Accelerate research and development.
- Speed up patient access to innovative treatments.
- Improve patient outcomes and safety of medicines.

IMI EU Real World Project Timeline 2011 - 2025



EMIF Contributing to Sustainable Elements in Other Projects

- EHDEN will utilise the technology framework from IMI1 EMIF, with key partners in both projects
- Innovation will continue to scale the architecture, develop new tools and incorporate the OMOP CDM and OHDSI tools more extensively
- Open science, open source technology is a main driver for IMI projects, inclusive of EHDEN



Elements of the EMIF EHR Platform will be used for the EHDEN architecture

EMIF-AD will be a spin-out from EMIF in 2019, supporting the AD research community

EHDEN: Vision and Mission

EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Vision

The European Health Data & Evidence Network (EHDEN) aspires to be the trusted observational research ecosystem to enable better health decisions, outcomes and care

Mission

Our mission is 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 standardized to a common data model

EHDEN CONSORTIUM

Start date: 1 Nov 2018
End date: 30 Apr 2024
Duration: 66 months

22 partners

Almost €29 million

Universities, public bodies and research organisations

Erasmus MC – Academic coordinator

Uppsala Monitoring Centre

universidade de aveiro

NICE National Institute for Health and Care Excellence

Tartu Ülikool

University of Oxford

SME & Mid-sized companies

SYNAPSE Research Management Partners

thehyve

Odysseus Data Services Inc

Non-profit organisations

EPF European Patients Forum

ICHOM

EFPIA & Associated partners

Janssen – EFPIA Lead

Bayer

Celgene

Pfizer

Lilly

abbvie

AstraZeneca

Sanofi

UCB

Novartis

Servier

WHY IS EHDEN NEEDED?

Regulators

Continuous effectiveness & safety assessment

Payers

Assess cost effectiveness

Determine reimbursement

Patients

Understanding benefits and risks

Improvement of care

Better patient outcomes

Research

Understanding diseases

New indications

Development

Trial design and feasibility

Demonstrating value

EHDEN IS ABOUT ...

FEDERATION

Creation of an EU-wide architecture for federated analyses of real world data

HARMONISATION

Harmonise more than 100 million anonymised health records to the OMOP common data model

COMMUNITY

Establish a self-sustaining open science collaboration in Europe, supporting academia, industry, regulators, payers, government, NGOs and others

OUTCOMES

Enabling outcomes driven healthcare at a European level

EDUCATION

The establishment of an EHDEN Academy, webinars and face-to-face training sessions to train all stakeholders

FOUNDATIONAL PILLARS

Infrastructure

Creation of an **EU-wide** federated network architecture

Privacy by design

Data harmonisation to the OMOP common data model

Training & certification of **SMEs**

Research & Outcomes

Use cases to evaluate the EHDEN federated network

Collaboration on consistent **methodologies**

Collaboration with the global **OHDSI** research network

Incorporation of the **ICHOM** health outcome standards

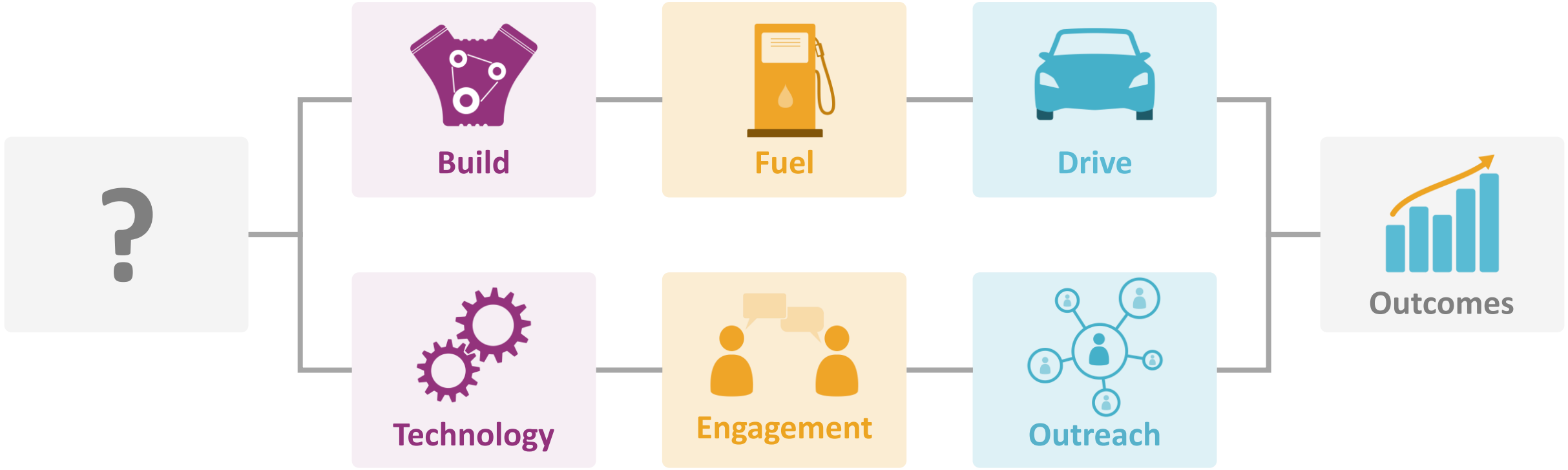
Education & Community

Establishment of an **EHDEN Academy**

Expansion of the **OHDSI network** in Europe

Collaboration on **collective memory** for research use cases

KEY COMPONENTS FOR EHDEN



Work Package Structure

WP1: Evidence Workflow Development

Incorporating the use cases for supporting development and validation of the EHDEN socio-technical approach, inclusive of BD4BO projects

WP2: Outcome Driven Healthcare

Related to all activities specific to e.g. BD4BO projects outcome focus, and ICHOM standards incorporation

WP3: Personalized Medicine

Focusing on the support of outcomes/value based healthcare, inclusive of clinical prediction models, with the incorporation of 'novel' patient data

WP4: Technical Implementation

Key priority is socio-technical development of the EHDEN federated framework and relevant services

WP5: Data Workflow Implementation & Service Deployment

Development, oversight and evaluation of the ecosystem development from SME qualification/ certification to data source engagement, OMOP CDM mapping and evaluation

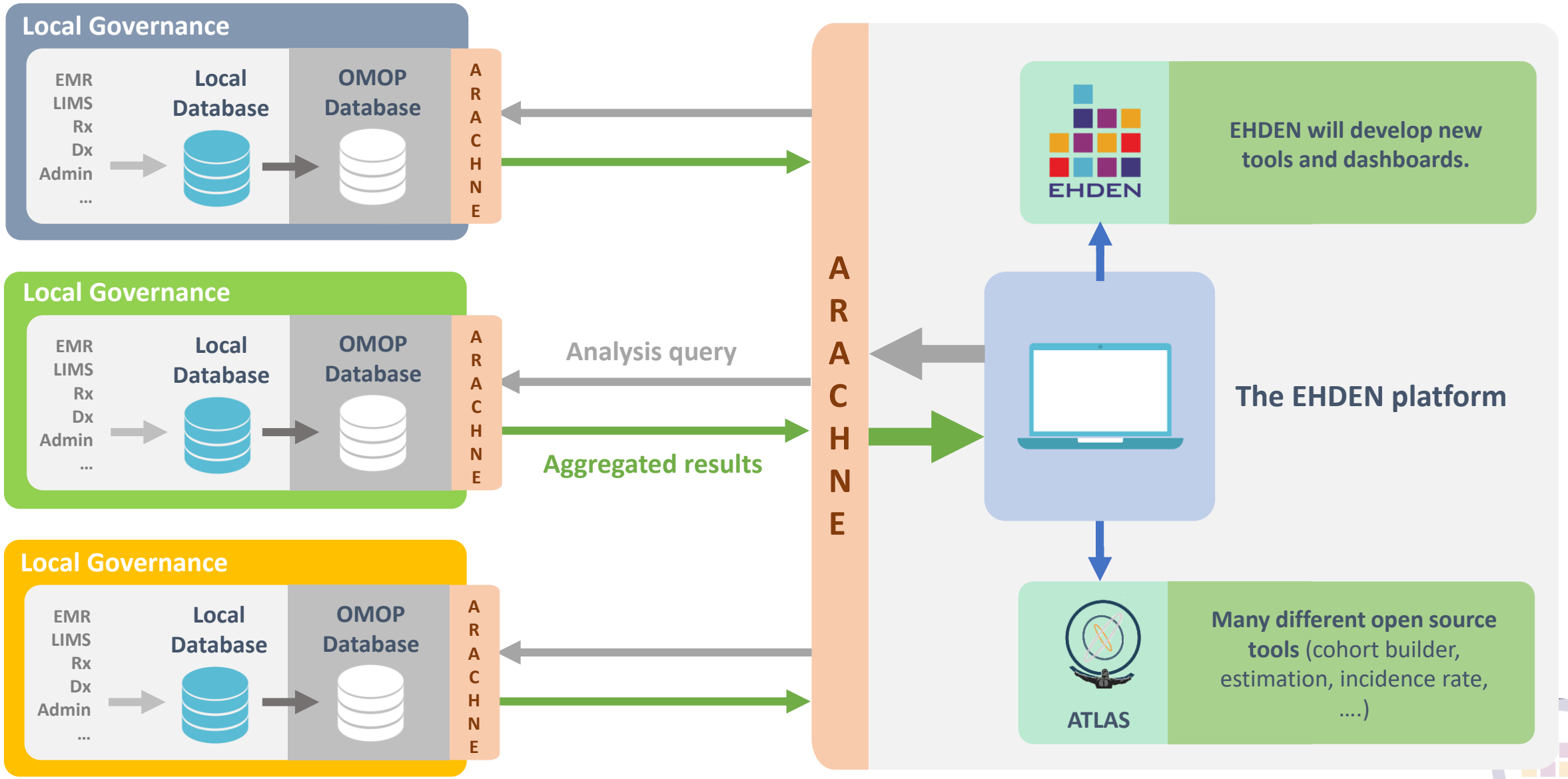
WP6: Outreach and Sustainability

Ensuring the development of value propositions for key stakeholders, and developing the sustainable operational model for EHDEN during and post IMI phase

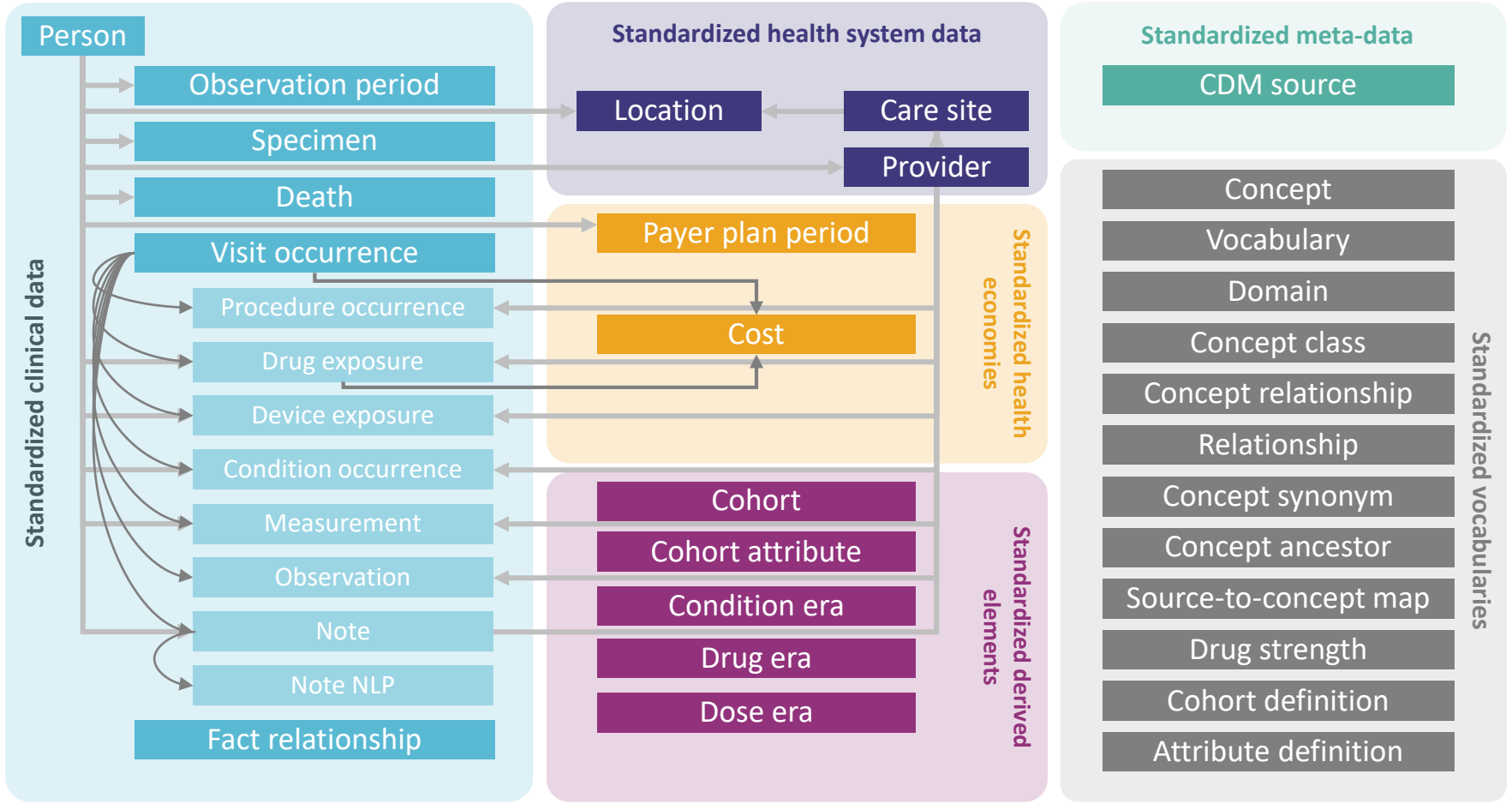
WP7: Project Management and Dissemination

Concentrating on intra-project project management, internal communications and external dissemination, and responding to IMI deliverables

The EHDEN Federated Data Network



THE OMOP COMMON DATA MODEL



Patient-centric

Tabular

Extendable

Built for analytics

Relational design

v 5.0.1

EHDEN HIT THE GROUND RUNNING

Collaborators	Findable	Accessible	Interoperable	Reusable
Main developers of many of the OHDSI tools are EHDEN partners OHDSI	EHR Catalogue	WHITE RABBIT RABBIT IN A HAT USAGI Jerboa ARACHNE enabling network research Ethical code of practice	ATHENA ICHOM OMOP cdm	Private remote research environment ATLAS

CALL PROCESS OVERVIEW

Harmonisation fund

Data sources

Open calls

Tailored for project objectives and sustainability

Grant awarding

Evaluated via a pre-defined set of criteria by the Data source prioritisation committee

Data sources can choose the SME from the pool of EHDEN certified SMEs

SMEs are paid via grants from the harmonisation fund

Payments are milestone based

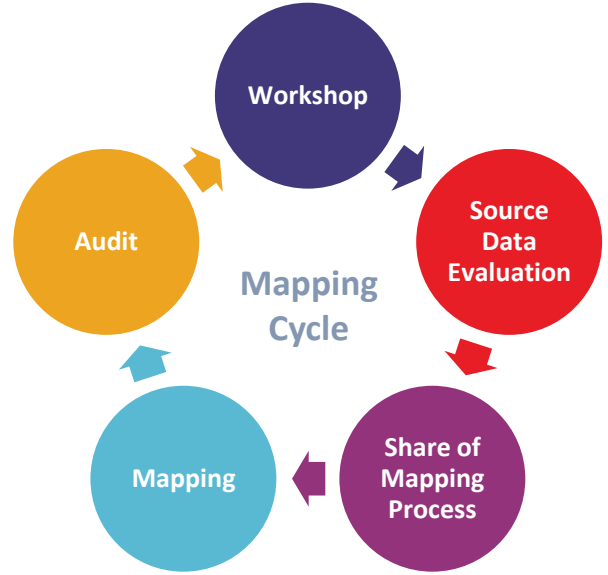
Supporting SMEs

Open calls

Focusing on SMEs able to support mapping and sustainability

Training & Certification

SME certification committee prioritizes SMEs for training and certification



Mapped data sources are encouraged to be active members of the **EHDEN community**, participating in **research studies**.

SME Pilot Call

Open Call

Submission of applications for the open call for SMEs from the 1st of April until the 1st of May (17h00) via the EHDEN website.

Evaluation

Following an eligibility check, applications were evaluated by the SME certification committee.

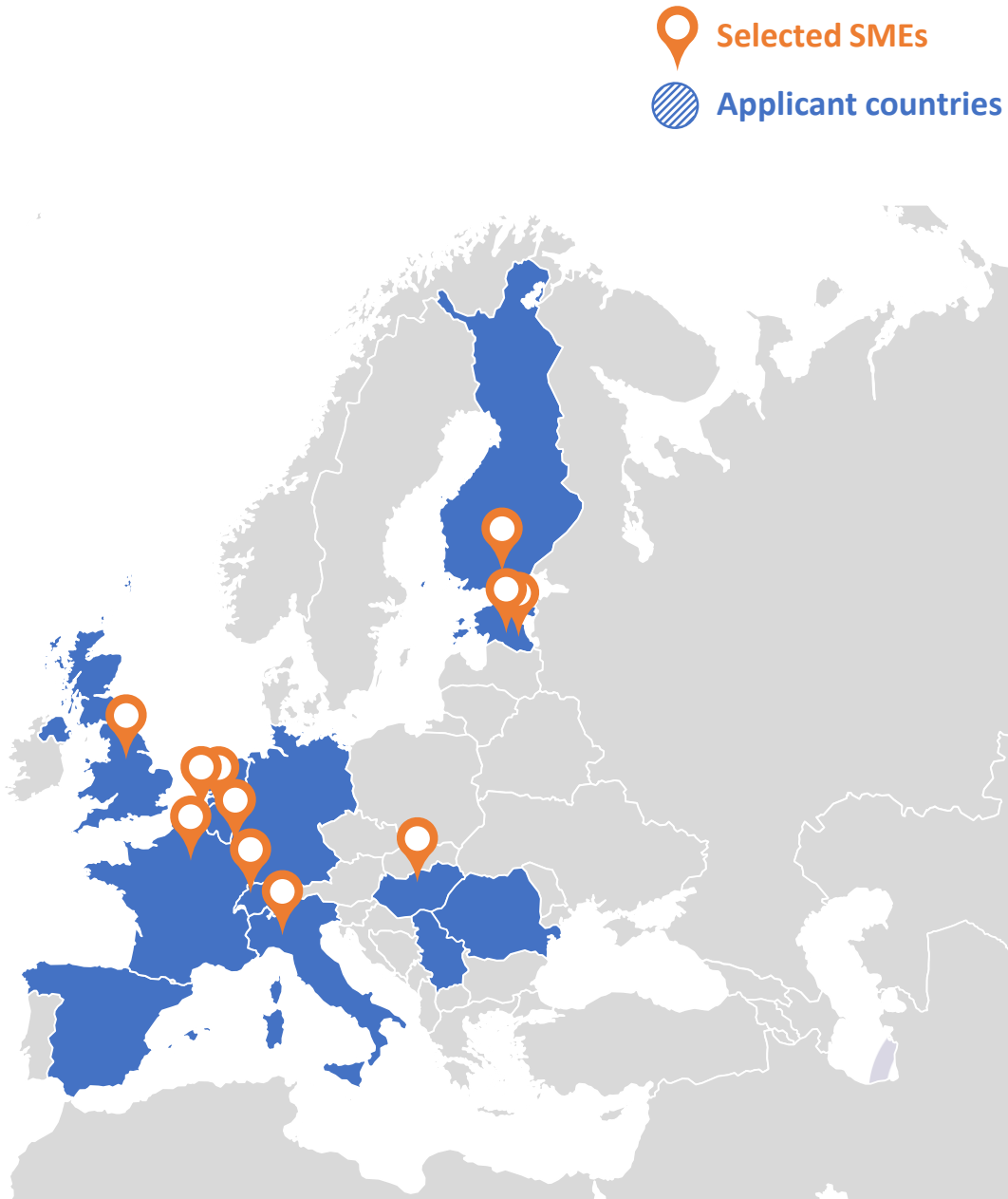
Training & Certification

Certification and training of selected SMEs in all necessary competencies.

34 SME profiles made

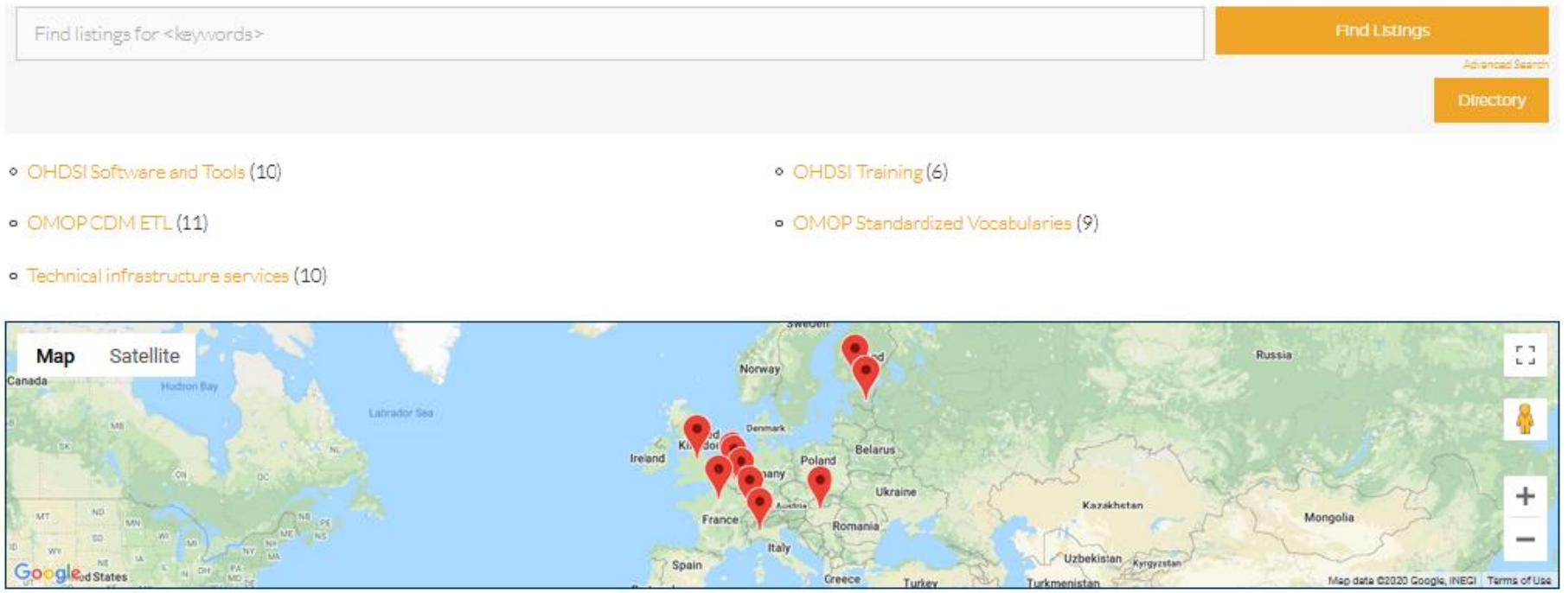
28 Eligible applications

11 SMEs initially selected



SME CATALOGUE

www.ehden.eu/service-provider-catalogue/



Certified SMEs:

- edenceHealth NV
- Easter-eggs
- Biomeris
- Clinerion Ltd
- B2i Healthcare
- ITTM S.A.
- MediSapiens Ltd
- P-95
- Imosphere
- Quretec OÜ
- Stacc OÜ

Data Partner Pilot Call

(Preliminary results)

Public review of the call
Initial phase during which all interested data partners can review the call description, ask questions and comment on the call description (July 15 – August 15).

Grant application portal open
Open call for data partners (September 1 – September 15)

Evaluation
Evaluation of all applications by our committee of both internal and external experts.

Agreement
Grant awarding and signing of grant agreement.

SME linking
Identification and linking up with the SME of choice.

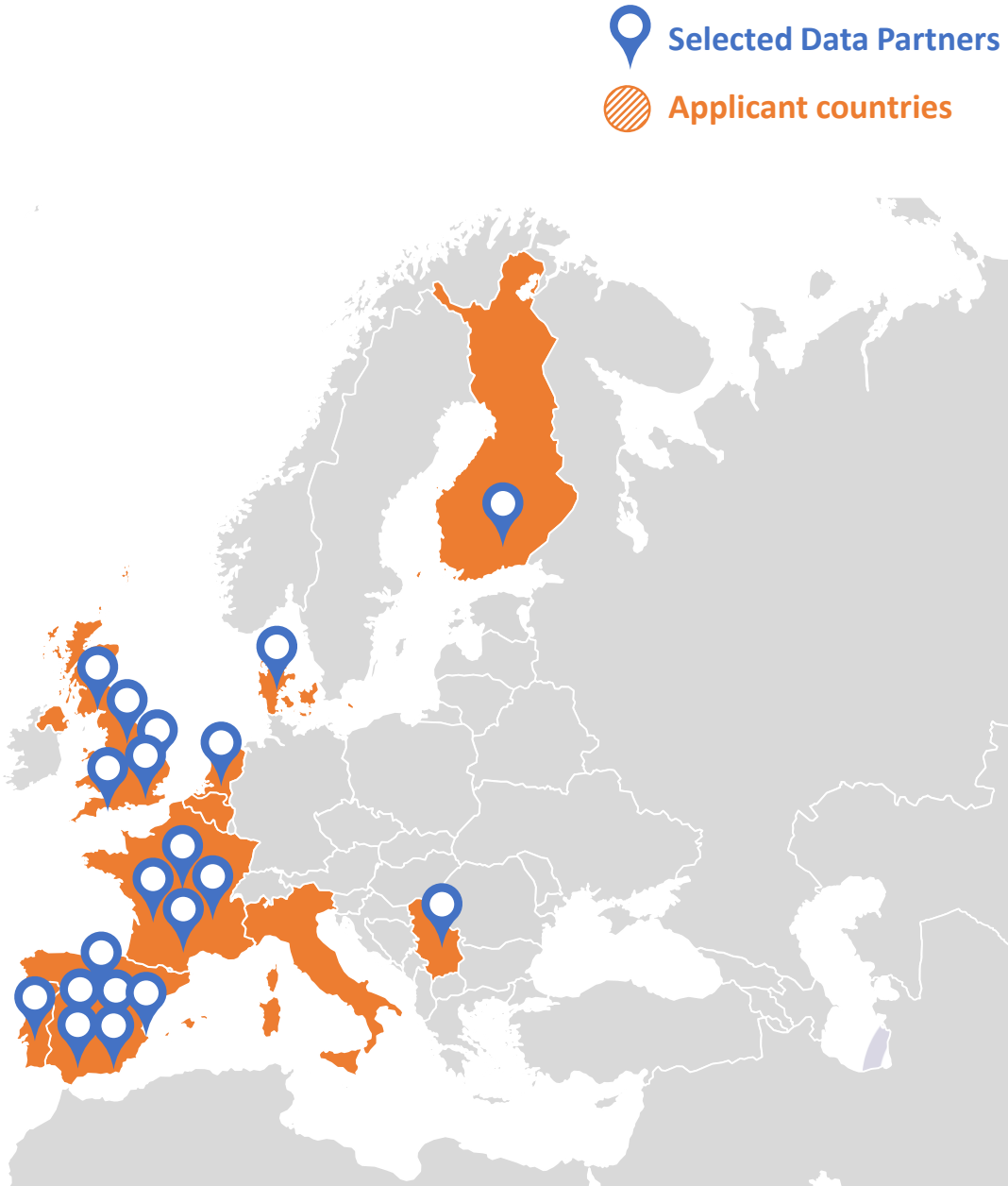
Harmonisation
Initiation of the data harmonisation.

(Timelines are provisional)

48 Data partner profiles made

29 Eligible applications

20 Selected Data Partners



2020 CALL TIMELINES

SME
The second open call for SMEs.

SME
The third open call for SMEs.

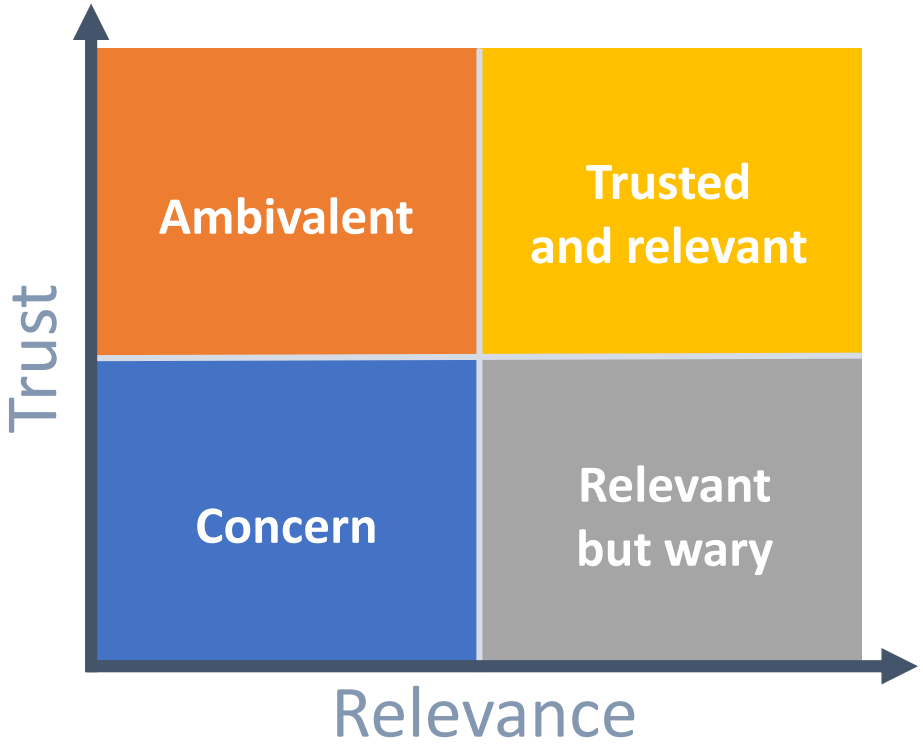
2020

JAN | FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC

Data partner
The second open call for Data partners.

Data partner
The third open call for Data partners.

A Research Quid Pro Quo for Sustainability



The success of EHDEN will only be based on **trust** and **relevance**

Openness, **transparency** and **collaboration** will be key drivers for trust

Relevance needs to be based on relative **usefulness** of data, research **outputs** and **accessible** technology

Ultimately, trust and relevance are based on **successful outputs**

EHDEN WILL ENSURE COMPLIANCE WITH E.G. GDPR

Compliance with citizen and data protection regulations

Further development of the EMIF Ethical Code of Practice

Ethical Advisory Board

Privacy by design
(data remains local)

Evolving framework for data protection

USE-CASE DRIVEN

Use Case 1 – Drug utilisation study

Validate the OMOP CDM in European data sources comparing results from source versus OMOP data

Use Case 2 – Drug and device safety study

Test and further develop existing (OHDSI) population-level estimation and population-level prediction packages in EU Data sources

Use Case 3 – HTA study

Assess whether data commonly used for HTA purposes can easily be measured and analysed using the OMOP CDM

FAST OBSERVATIONAL RESEARCH IS FEASIBLE (STUDY-A-THON)

"To compare the **risk** of post-operative **complications** and **mortality** between unicompartmental *vs* total knee replacement."

Monday

Group consensus on the **problem**
Draft cohort definitions

Tuesday

Review clinical characterisation
Draft patient-level prediction design

Wednesday

Review patient-level prediction results
Externally validate prediction model

Thursday

Draft population-level effect estimation design
Review population-level effect estimation diagnostics

Friday

Review of results
Plan for completing **publications**

(EHDEN 1st Study-a-thon, Oxford, December 2018)

ACADEMY

Aim

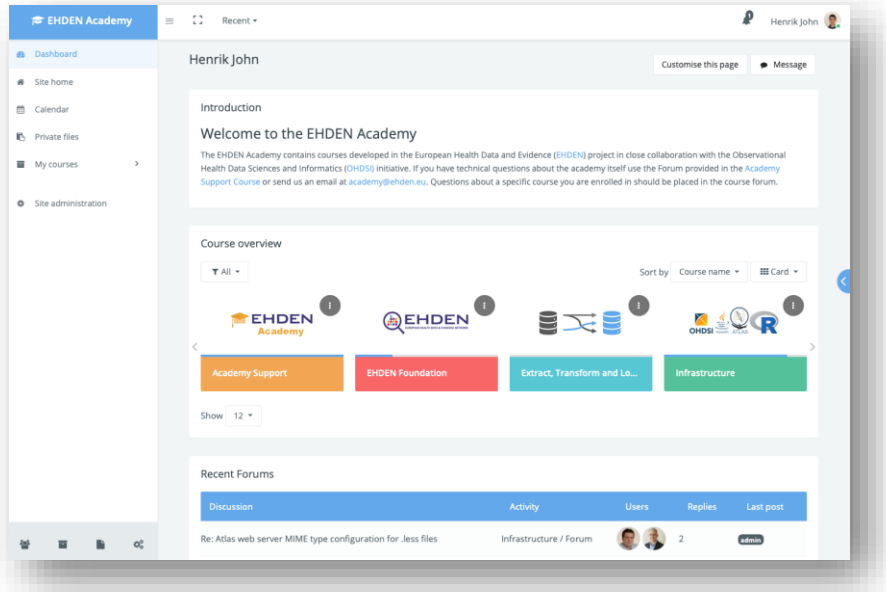
To develop an **e-learning** environment **to train all stakeholders** on the use of the tools and processes that are being adopted within EHDEN and OHDSI.

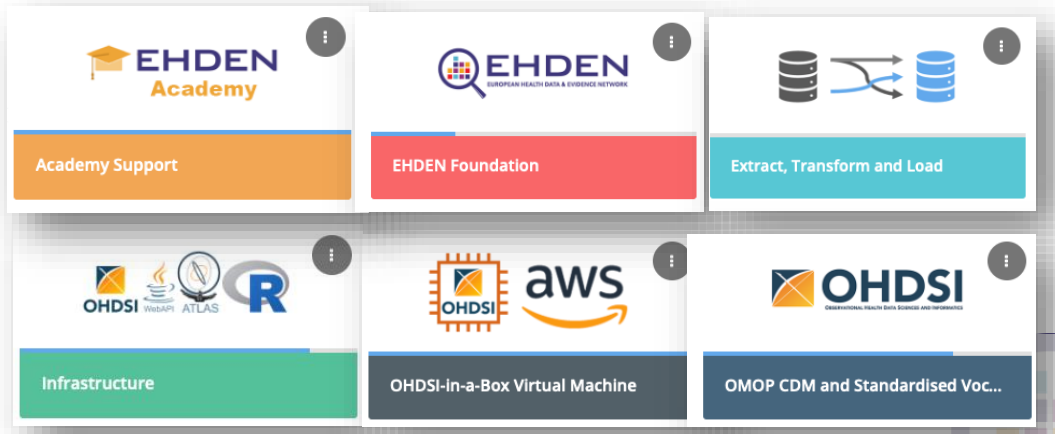
Collaboration

Course development on the OMOP Common Data Model and the rich set of OHDSI tools that are being developed in collaboration with the **OHDSI community.**

Infrastructure

The EHDEN Academy is developed in **Moodle** and is hosted in the **Amazon AWS cloud.** We use virtual machines for assignments.





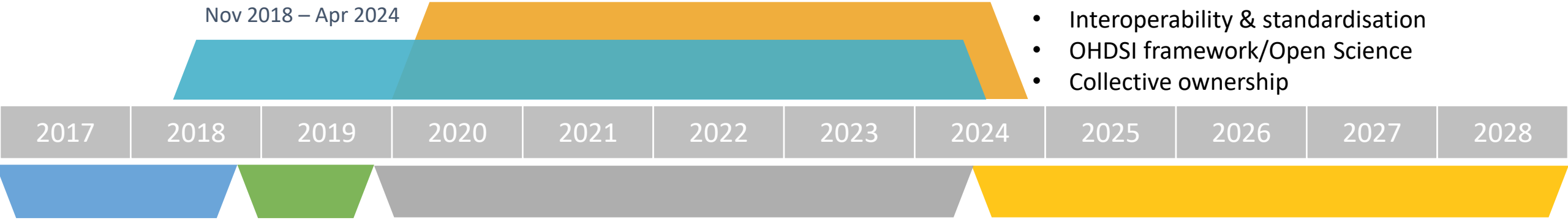
The Development & Milestones of the EHDEN Project

EHDEN needs to be sustainable

- European project supported by IMI
- Building research infrastructure for coming decades
- Interoperability & standardisation
- OHDSI framework/Open Science
- Collective ownership

OHDSI
Symbiotic Relationship/Global Linkage

IMI Duration
Nov 2018 – Apr 2024



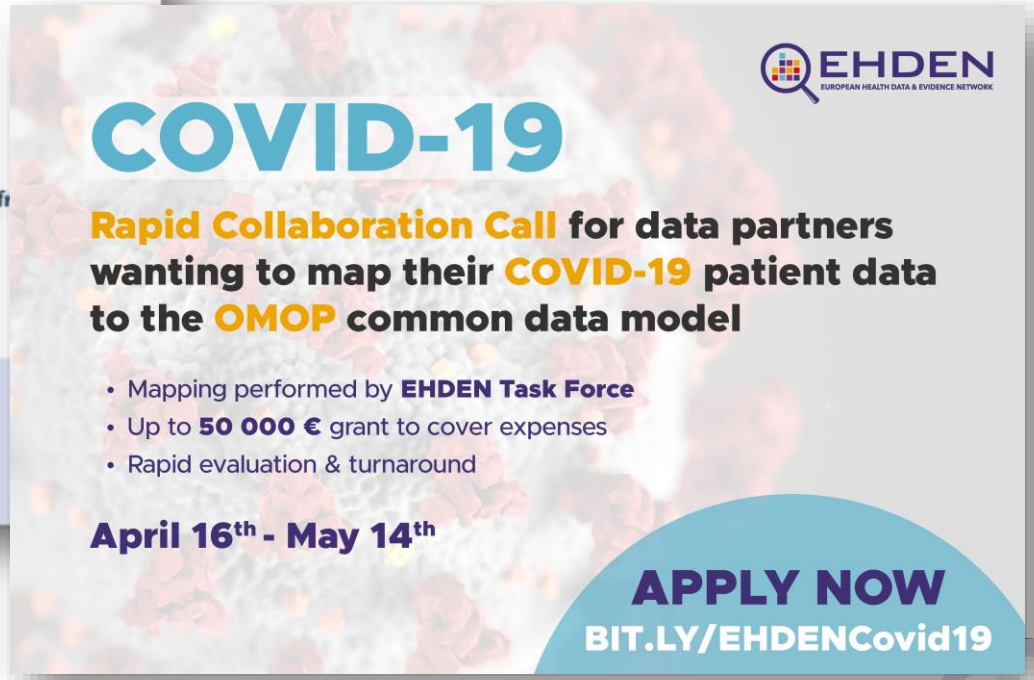
Inception
Creation of IMI Project

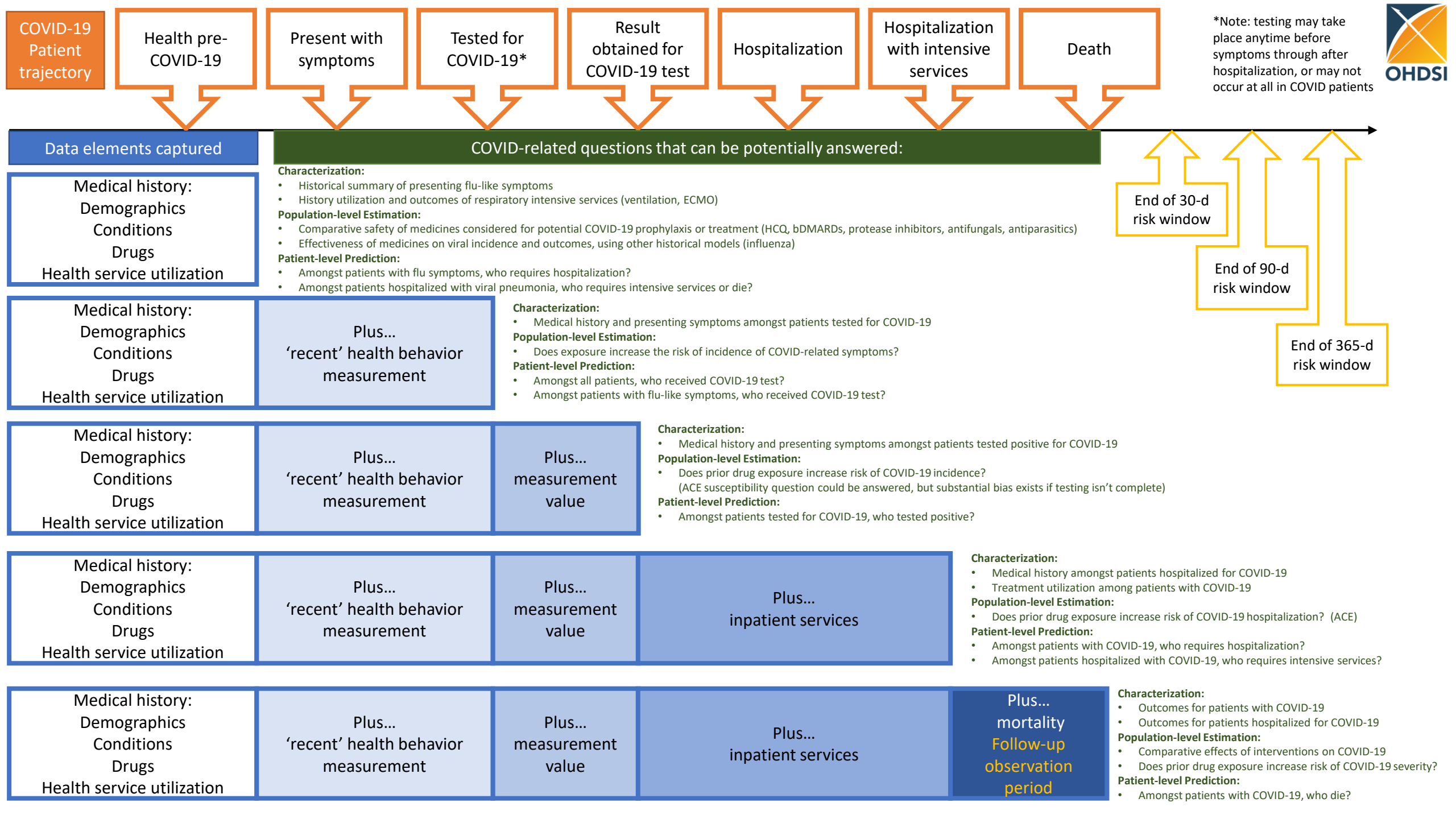
Pilot Year
Initial:
- SME & Data Calls
- Research Use Cases
- Technology Architecture
- Stakeholder Engagement

Scale Up
Expansion:
- SME & Data Calls
- ETL/Mapping (OMOP CDM)
- Research Use Cases
- Technology Architecture
- Community Building
- Evidence Generation

Sustainability
Scalability
- Open Science Community
- OHDSI Framework & Network Evolution
- Research Use Cases
- Pharmaco-surveillance
- Evidence Generation
- Discovery & R&D

COVID-19, OHDSI & EHDEN and the Need For Data & Insights




COVID-19 Patient trajectory
Health pre-COVID-19
Present with symptoms
Tested for COVID-19*
Result obtained for COVID-19 test
Hospitalization
Hospitalization with intensive services
Death
*Note: testing may take place anytime before symptoms through after hospitalization, or may not occur at all in COVID patients
OHDSI
Data elements captured
COVID-related questions that can be potentially answered:
End of 30-d risk window
End of 90-d risk window
End of 365-d risk window
Medical history:
Demographics
Conditions
Drugs
Health service utilization
Characterization:
• Historical summary of presenting flu-like symptoms
• History utilization and outcomes of respiratory intensive services (ventilation, ECMO)
Population-level Estimation:
• Comparative safety of medicines considered for potential COVID-19 prophylaxis or treatment (HCQ, bDMARDs, protease inhibitors, antifungals, antiparasitics)
• Effectiveness of medicines on viral incidence and outcomes, using other historical models (influenza)
Patient-level Prediction:
• Amongst patients with flu symptoms, who requires hospitalization?
• Amongst patients hospitalized with viral pneumonia, who requires intensive services or die?
Plus…
'recent' health behavior measurement
Characterization:
• Medical history and presenting symptoms amongst patients tested for COVID-19
Population-level Estimation:
• Does exposure increase the risk of incidence of COVID-related symptoms?
Patient-level Prediction:
• Amongst all patients, who received COVID-19 test?
• Amongst patients with flu-like symptoms, who received COVID-19 test?
Plus…
measurement value
Characterization:
• Medical history and presenting symptoms amongst patients tested positive for COVID-19
Population-level Estimation:
• Does prior drug exposure increase risk of COVID-19 incidence?
(ACE susceptibility question could be answered, but substantial bias exists if testing isn't complete)
Patient-level Prediction:
• Amongst patients tested for COVID-19, who tested positive?
Plus…
inpatient services
Characterization:
• Medical history amongst patients hospitalized for COVID-19
• Treatment utilization among patients with COVID-19
Population-level Estimation:
• Does prior drug exposure increase risk of COVID-19 hospitalization? (ACE)
Patient-level Prediction:
• Amongst patients with COVID-19, who requires hospitalization?
• Amongst patients hospitalized with COVID-19, who requires intensive services?
Plus…
mortality
Follow-up observation period
Characterization:
• Outcomes for patients with COVID-19
• Outcomes for patients hospitalized for COVID-19
Population-level Estimation:
• Comparative effects of interventions on COVID-19
• Does prior drug exposure increase risk of COVID-19 severity?
Patient-level Prediction:
• Amongst patients with COVID-19, who die?

EHDEN: 21ST CENTURY NETWORK FOR 21ST CENTURY REAL WORLD RESEARCH

- EHDEN is a bold step in recognising that a flagship project is needed to address conducting real world research for the 21st Century
- At its heart is the acknowledgement that we need to develop a community via a federated network, within an ecosystem, all based on a *quid pro quo* around data for research use
- The Open Science/Open Source community of OHDSI, and the OMOP CDM are critical enablers and partners for EHDEN in this endeavour
- Watch out for *#DataSavesLives*….

Some Useful Sites

- EHDEN Coordinator: Assoc Prof Peter Rijnbeek, Erasmus Medical Centre: p.rijnbeek@erasmusmc.nl
- EHDEN Coordinator: Nigel Hughes, Janssen: nhughes@its.jnj.com

- EHDEN project website: https://www.ehden.eu
- IMI website: https://www.imi.europa.eu
- IMI2 BD4B0 programme: https://bd4bo.eu
- OHDSI website: https://ohdsi.org
- List of converted ('OMOPd') databases: http://www.ohdsi.org/web/wiki/doku.php?id=resources:2018_data_network
- OHDSI Europe website: https://www.ohdsi-Europe.org/

Key Contact Points

EHDEN
EUROPEAN HEALTH DATA & EVIDENCE NETWORK

https://forum.ehden.eu

enquiries@ehden.eu

www.ehden.eu

@IMI_EHDEN

IMI_EHDEN

github.com/EHDEN

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 806968. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.