ENCePP and Covid-19: How does ENCePP contribute to the monitoring of therapeutics and vaccines?

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Professor of Pharmacoepidemiology, CSM, University of Oxford

CONTENTS

- Distributed networks: building from the community
- ENCEPP and COVID-19 therapies: E-Core
- ENCEPP and vaccines: ACCESS
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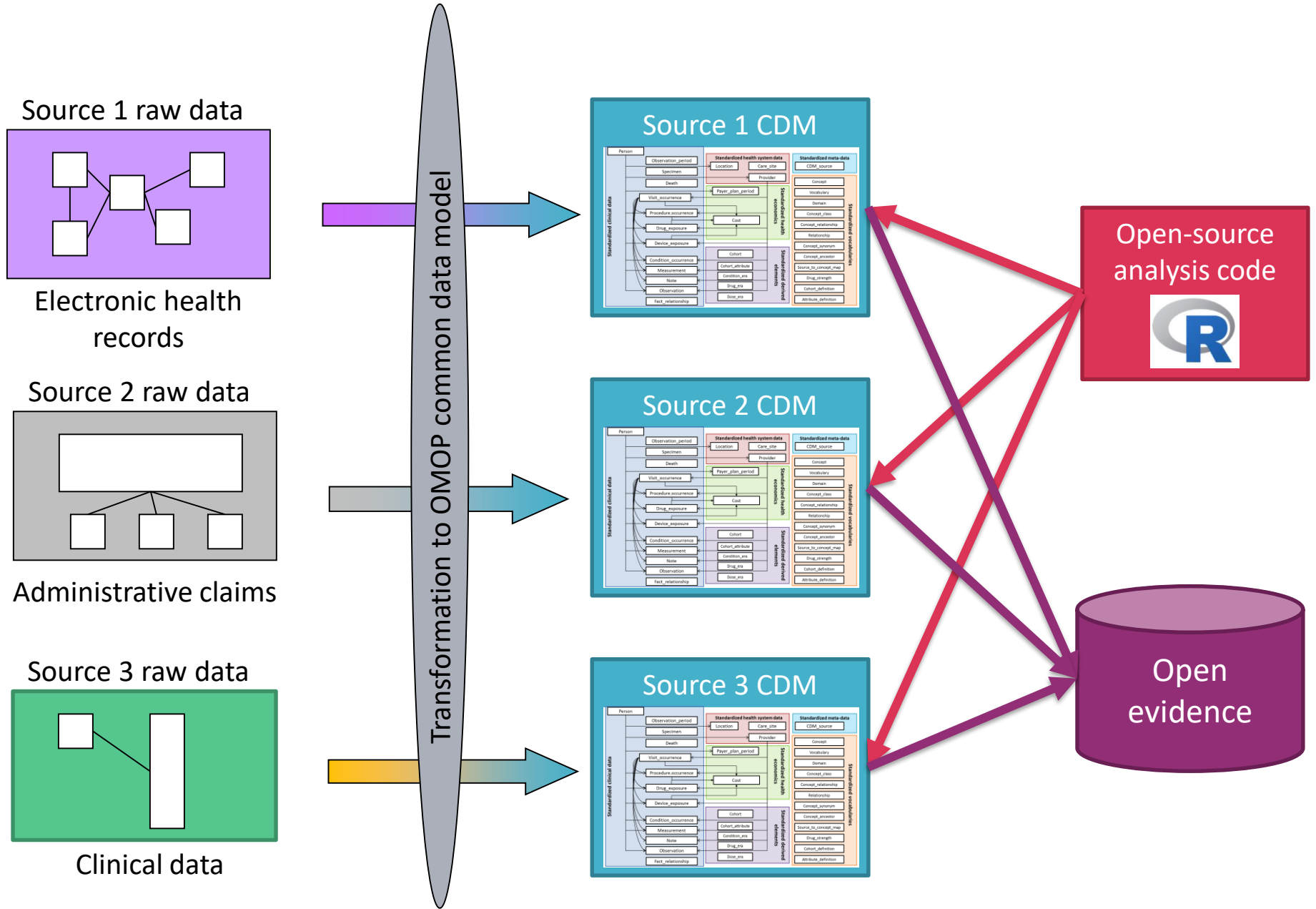
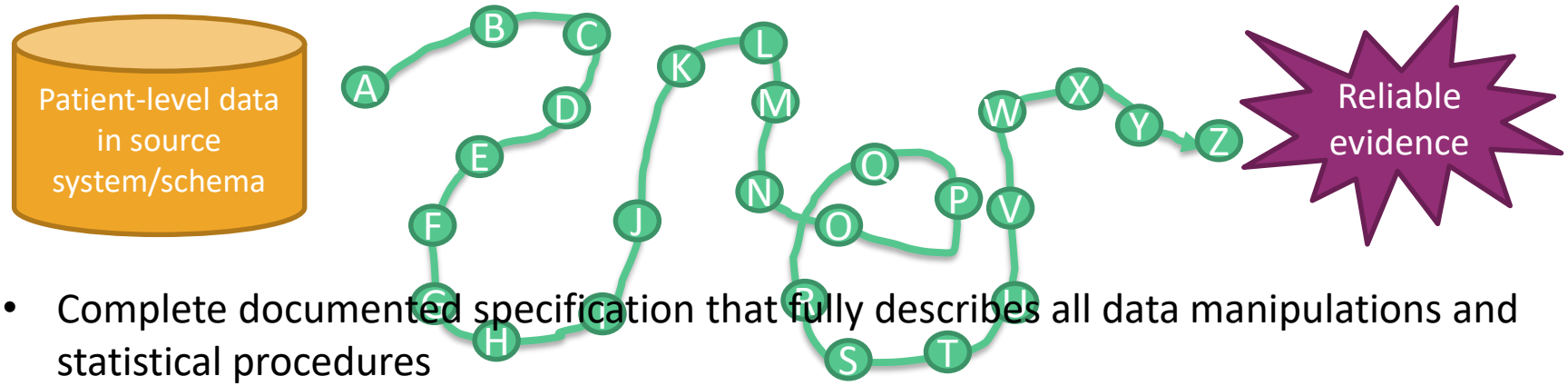
COMMON DATA MODEL TO ENABLE STANDARDIZED ANALYTICS



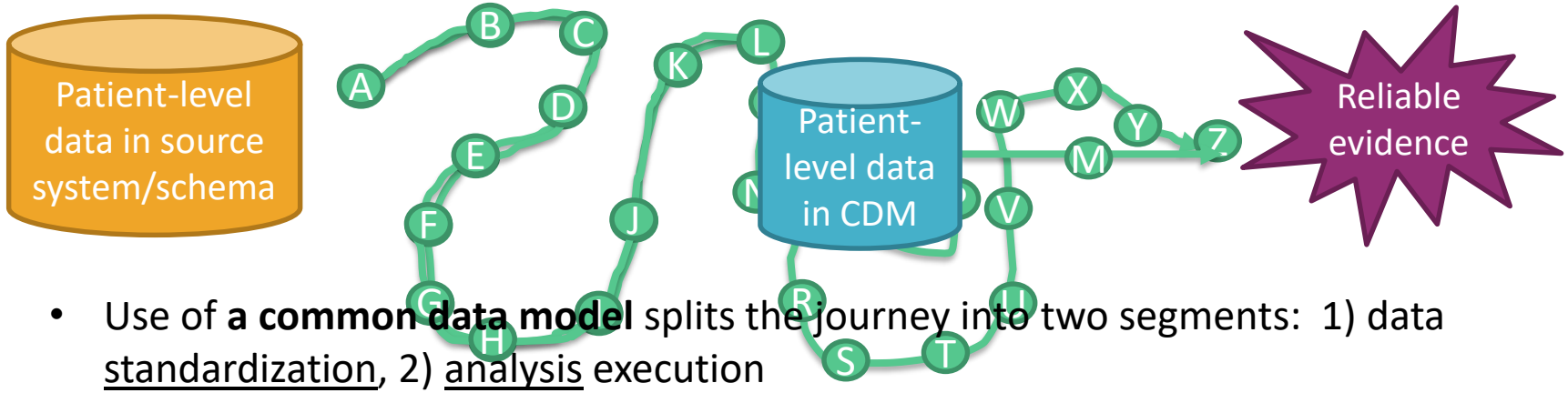
THE JOURNEY TO REAL-WORLD EVIDENCE: A FULLY REPRODUCIBLE DATA FLOW



- Complete documented specification that fully describes all data manipulations and statistical procedures
- Full analysis code that executes end-to-end (from source to results) without manual intervention

GOAL: to implement a **large sustainable** data **network** (+100m records) in Europe to generate **reliable evidence** for patient care that is **transparent** and fully **reproducible**

A Common Data Model and Standardized Vocabularies



- Use of **a common data model** splits the journey into two segments: 1) data standardization, 2) analysis execution
- **CDM** creates opportunity for re-use of data curation and analysis step

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E-CORE

EUROPEAN COVID-19 OBSERVATIONAL RESEARCH EXCHANGE

EMA tender for multicentre collaboration

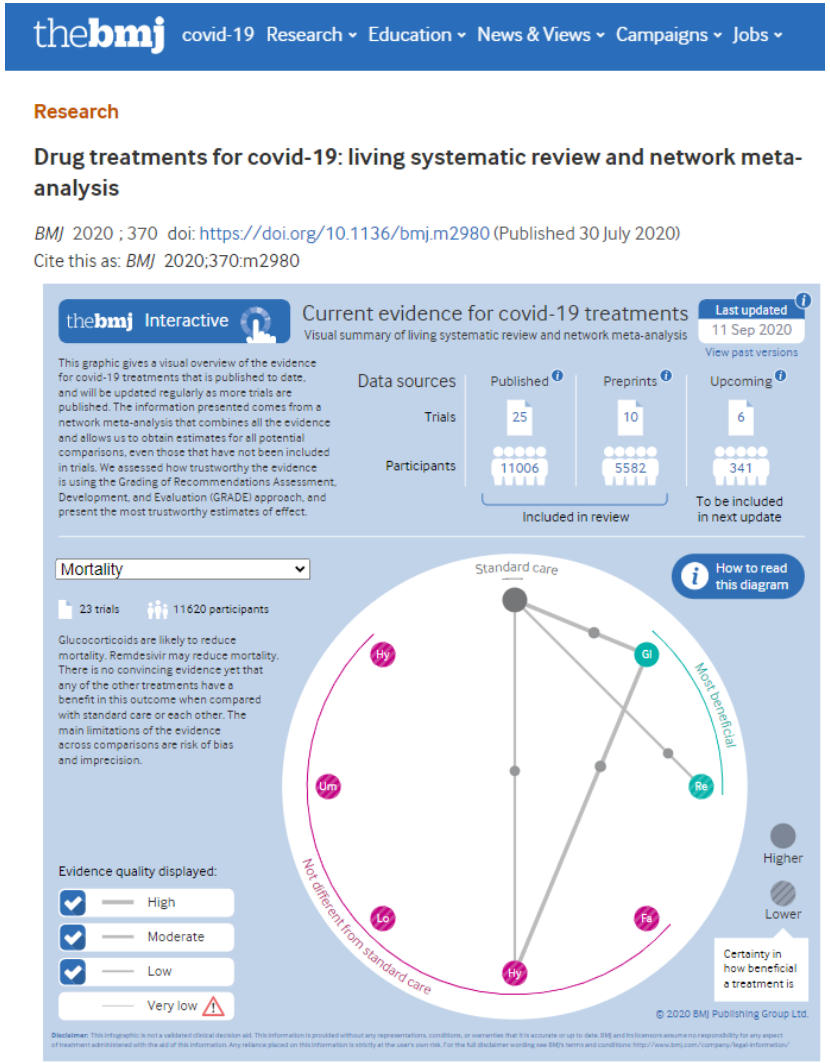
for COVID-19 pharmaco-epidemiology research

RATIONALE

- Many trials ongoing
- Many already published
- Most in some ‘living’ meta-analysis

- Most or all vs placebo or ‘standard’

- But …
  - Are all corticosteroids = safe?
  - Are anticoagulants > anti-agg?
  - …

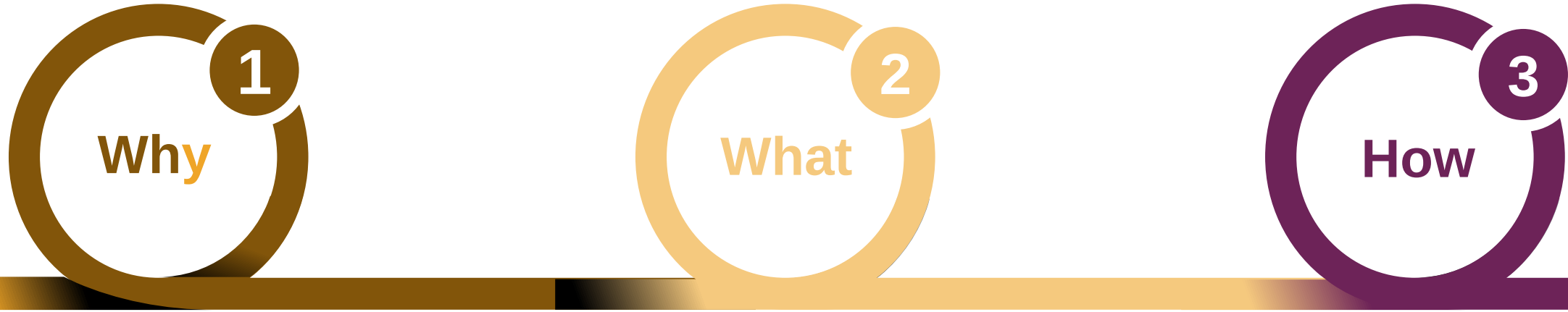


Overarching Aim

- "In the context of the COVID-19 pandemic, the Agency considers that it requires **a framework that will support collaborations for conducting multicentre observational studies related to the utilisation, safety and effectiveness of medicines used by COVID-19 patients"**

E-CORE: European COVID-19 Observational Research Exchange

A framework that will support collaborations for conducting multi-centre observational studies related to the utilisation, safety and effectiveness of medicines used by COVID-19 patients



The Challenge

- Observational database studies are under way across Europe and in the world employing a wide range of study methodologies and patient populations.
- These studies are challenged with problems around sample size, design, quality and generalisability to European populations

Our offer

Set up a European network designed to deliver high-quality COVID-19 observational studies.

Deliverables:

1. A library of cohorts of COVID-19
2. A collaborative framework across the network supporting the use of this
3. A large multinational pilot study

Characteristics

- Geography: 7 European countries
- Timeline: Jun-20 to Jun-21
- Inspired by the **OHDSI-EHDEN COVID-19 collaboration**

MILESTONES AND DELIVERABLES

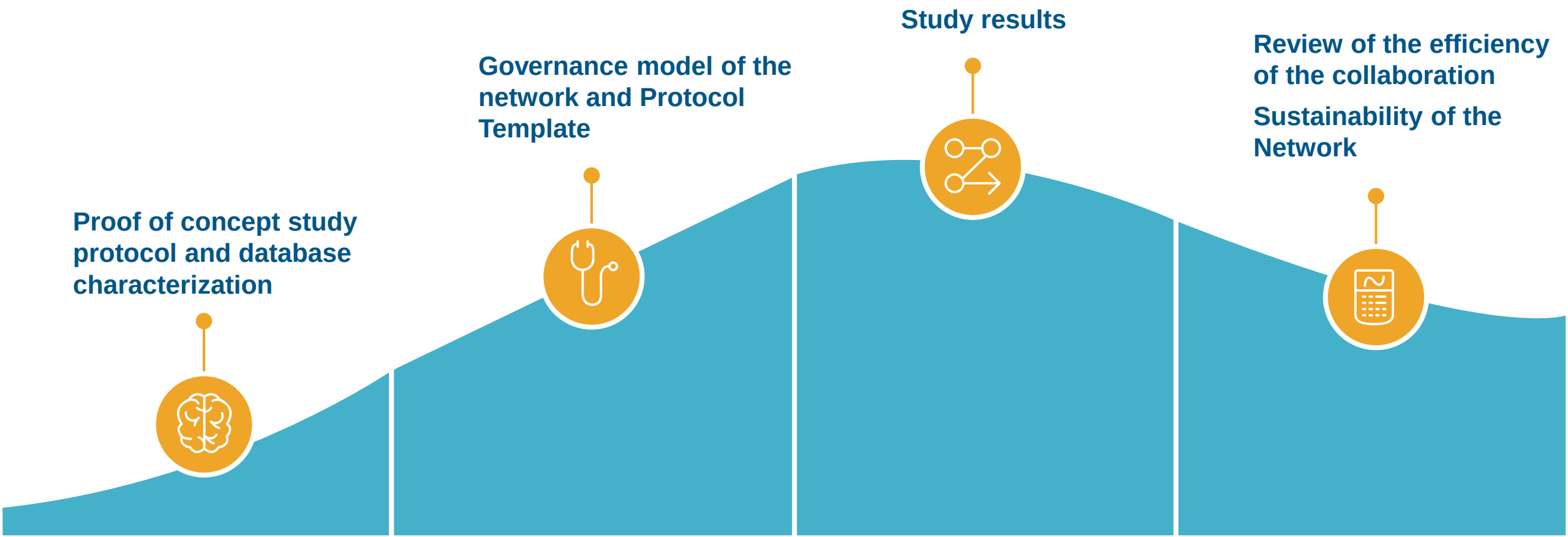
Proof of concept study protocol and database characterization

Governance model of the network and Protocol Template

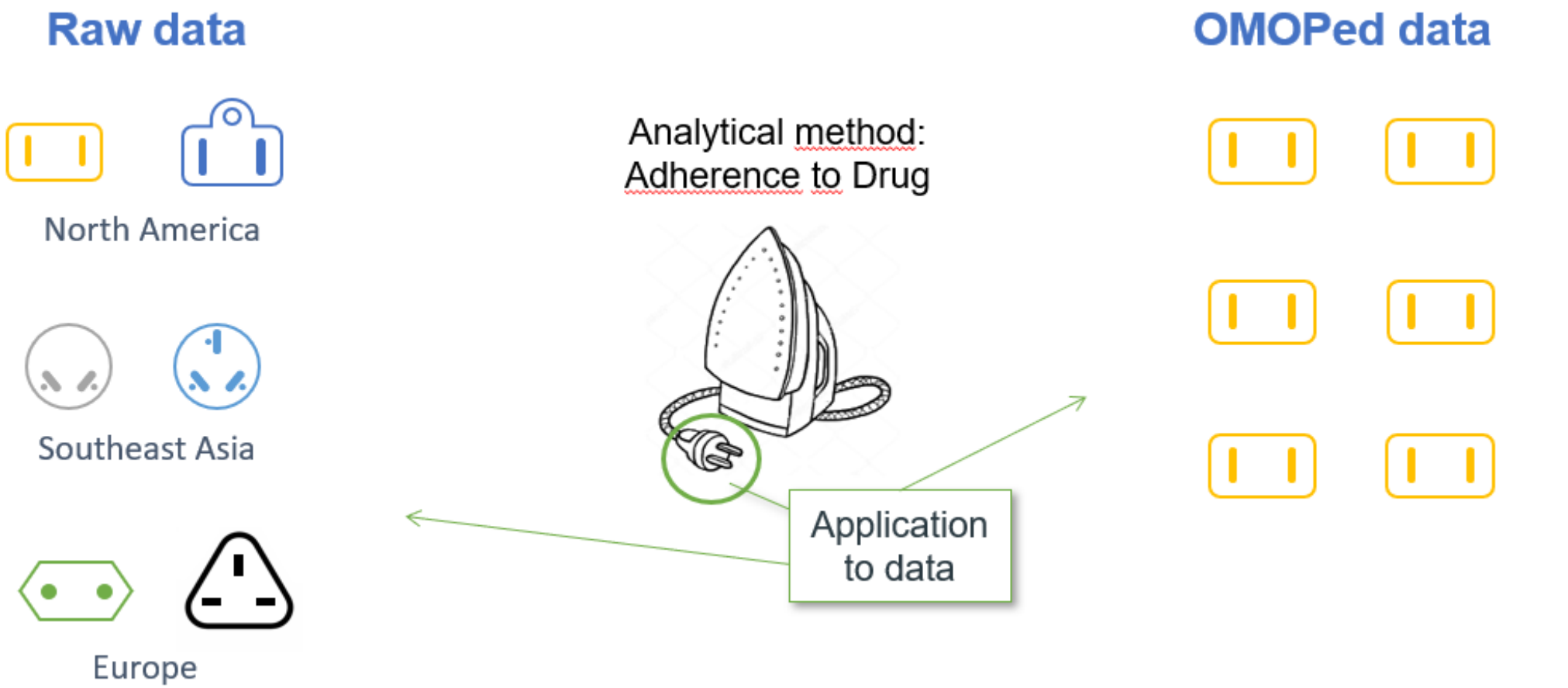
Study results

Review of the efficiency of the collaboration

Sustainability of the Network



OMOP Common Data Model



How partners are being enrolled

Contracting - Transformed in OMOP CDM - Quality Checks

- HM Hospitales
- LPD Belgium
- *LPD France*
- *DA Germany*
- *UK – IMRD*
- *LPD Italy*
- *IPCI*
- *SIDIAP*

Contracting

Transformed in OMOP CDM Ongoing

Quality checks

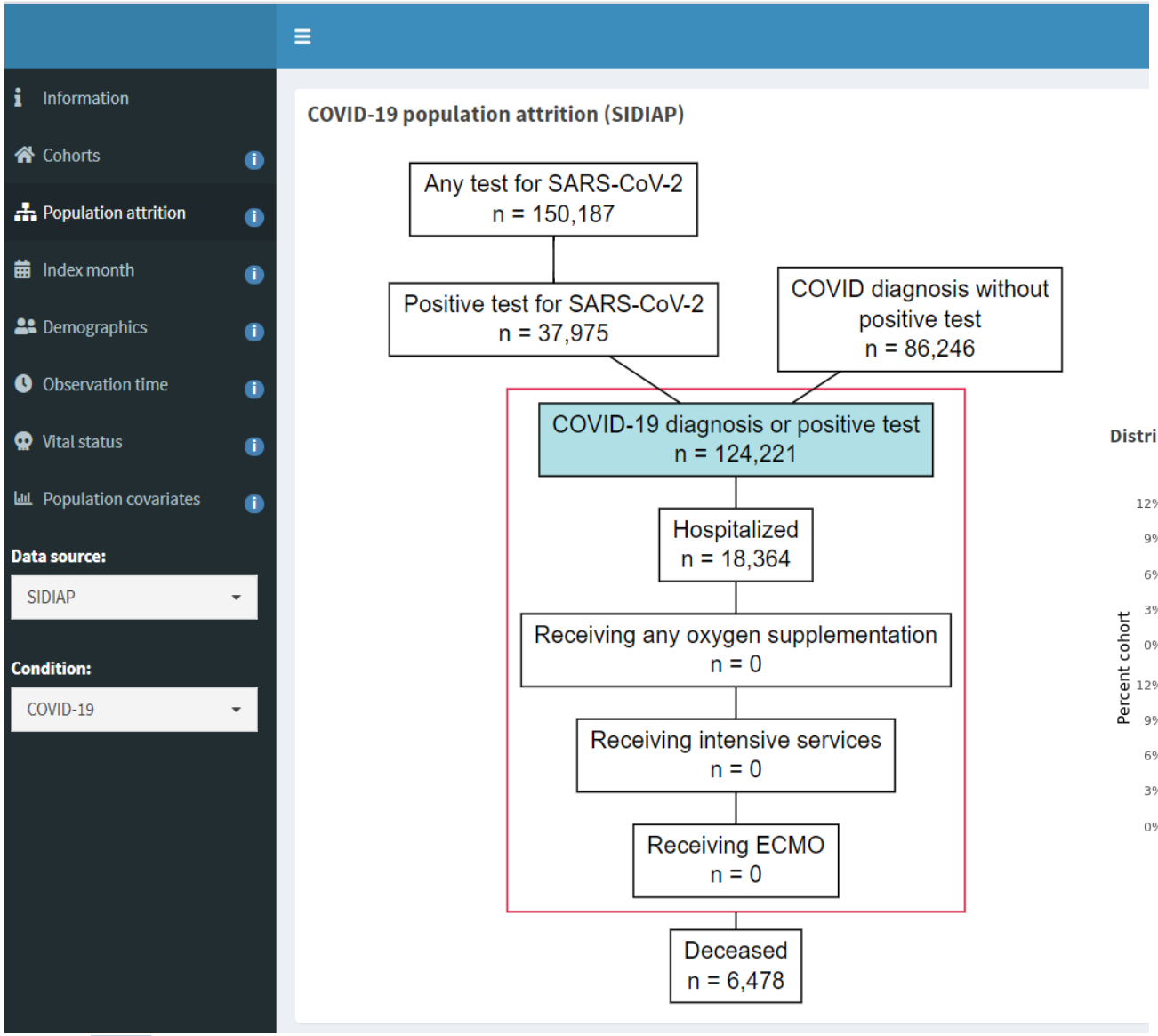
- *Technical University Dresden*
- *Clinerion Serbia*

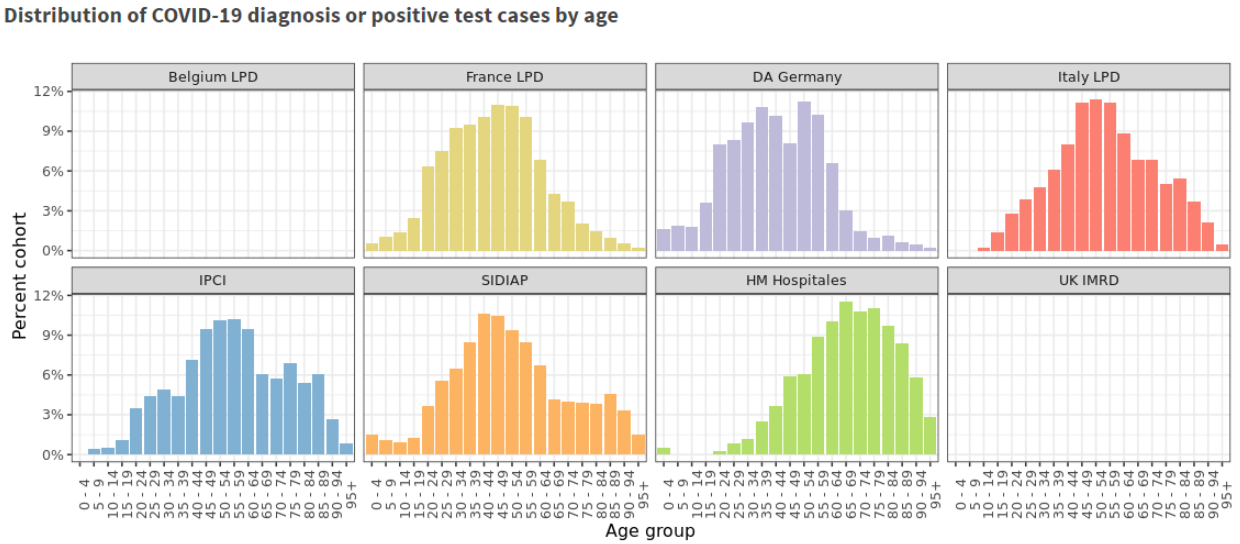
Contracting Ongoing

- Lyon SNDS Claims
- EDS APHP France Paris

Expected deadline Jan 2021

CHARACTERISATION DASHBOARD





PROOF OF CONCEPT STUDY – AIMS

Aims

- To describe the utilisation of systemic glucocorticoids in COVID-19
- To investigate the risks of adverse outcomes including non-fatal complications and deaths occurring within the first 6 months following COVID-19 diagnosis in patients treated with systemic glucocorticoids
  - … as observed in ambulatory and hospital inpatient care settings
  - … including seven European countries

DIFFERENT CODING DEFINITIONS FOR COVID-19

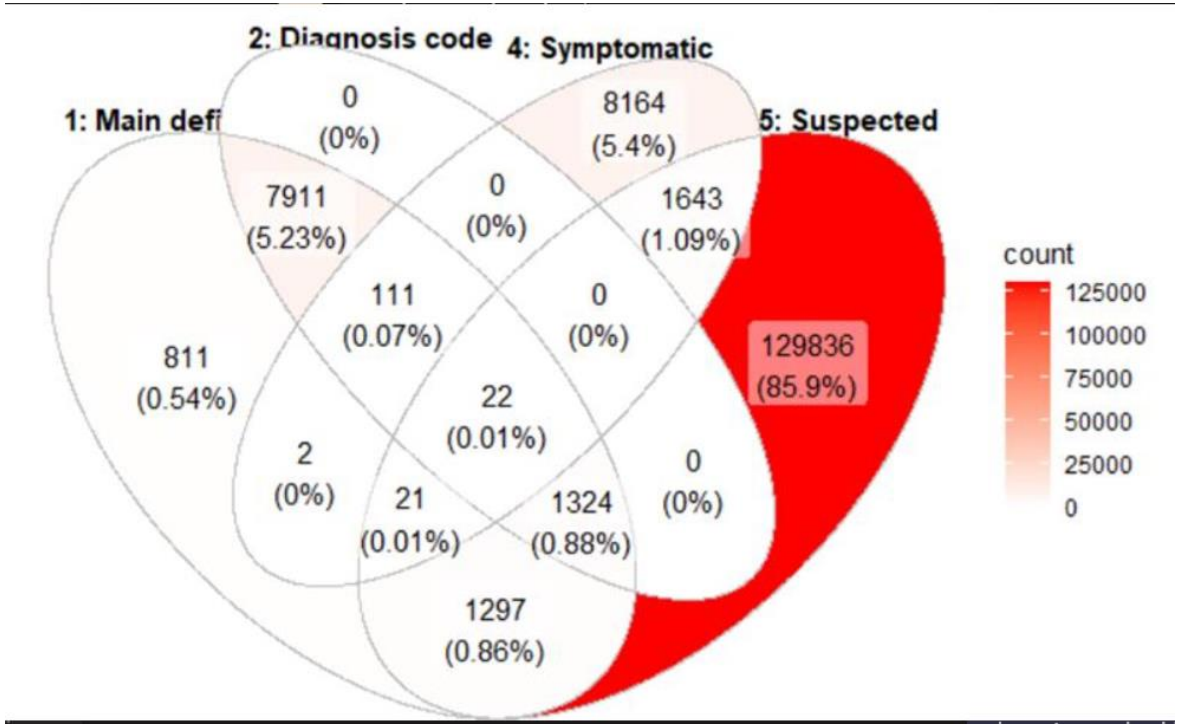
1. **Catch-all** (main definition)
Defined either as the first confirmed diagnosis for COVID-19 OR the first SARS-CoV-2 positive PCR test, if both present the earliest date will be considered.

2. **Diagnosis confirmed (diagCOVID-19)**
- U07.1 COVID-19, virus identified
- U07.2 COVID-19, virus not identified

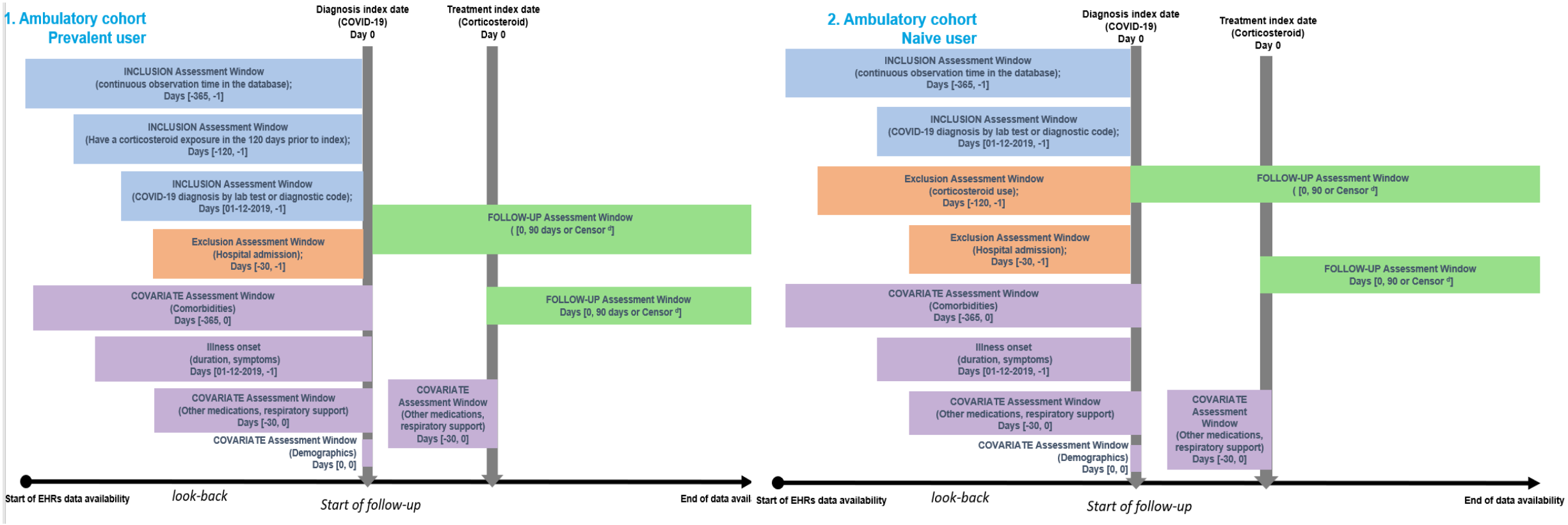
3. **Laboratory confirmed (labCOVID-19)**
Defined as a record of SARS-CoV-2 positive PCR (cCOVID-19) as performed on nasopharyngeal swabs and/or on respiratory tract secretions and aspirates.

4. **Symptomatic COVID-19.**
At least two symptoms of the following
Cough, Dyspnoea, Fever, Malaise and fatigue, Myalgia
Anosmia, Hyposmia or Dysgeusia episodes

5. **Suspected COVID-19**



PROOF OF CONCEPT STUDY DESIGN



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EMA commissions independent research to prepare for real-world monitoring of COVID-19 vaccines

Share

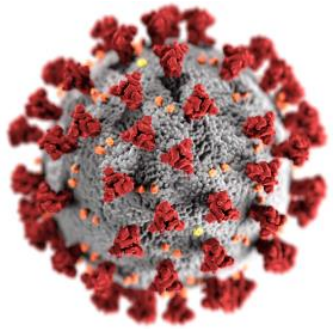
Press release 27/05/2020

EMA is engaging early with researchers to ensure that a European infrastructure will be in place to effectively monitor COVID-19 vaccines in the real world, once these are authorised in the European Union. The Agency has signed a contract with Utrecht University as coordinator of the EU Pharmacoepidemiology and Pharmacovigilance Research Network, a public-academic partnership of 22 European research centres, to conduct preparatory research into data sources and methods that can be used to monitor the safety, effectiveness and coverage of COVID-19 vaccines in clinical practice. The ACCESS (vACcine Covid-19 monitoring readinESS) project will be led by the University Medical Center Utrecht (UMCU) and Utrecht University.

eu2020.de

Courtesy of Prof H Gardarsdottir et al

ACCESS

vACCine covid-19  monitoring readinESS

Prof. dr. Miriam Sturkenboom, prof. dr. OH Klungel

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

VAC4EU
VAccine monitoring Collaboration for Europe

Universiteit Utrecht

sciensano

Lareb
Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Ce

PHARMO

agencia española de medicamentos y productos sanitarios

BIPS Leibniz Institute for Prevention Research and Epidemiology - BIPS

Tampere University

RTI (h)(s)
Health Solutions

AARHUS UNIVERSITY

STUDIORUM UNIVERSITAS MESSANAE

Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana

Bordeaux PharmacoEpi BPE

IDIAP Jordi G

PEDIANET

ARS TOSCANA
agenzia regionale di sanità

ISTITUTO SUPERIORE DI SANITÀ

UiO : University of Oslo

UMC Utrecht

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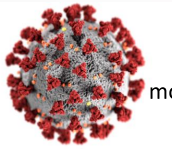
Courtesy of Prof H Gardarsdottir et al

What will ACCESS do for EMA?

ACCESS
vACCine covid-19 monitoring readinESS



- Create readiness as much as possible
- Event definitions, codes and algorithms to identify and measure Adverse Events of Special Interest **(AESI)**
- Create **common protocols and tools, and identify data sources** for
  - Background rate using electronic health care data
  - Post-licensure
    - Safety assessment
    - Effectiveness assessment
    - Coverage monitoring
    - Integration of benefit/risk
- Generate **background rates for AESI in 7 countries**

Courtesy of Prof H Gardarsdottir et al

ACCESS
vACCine covid-19 monitoring readinESS

Available data for calculation of background rates

Country	Organization	Name Data source	Active population	Type of data source
Germany	BIPS	GePaRD	16 million	Health insurance
Netherlands	PHARMO	PHARMO	6 million	Record linkage
Denmark	Aarhus University	Danish Registries	5.8 million	Record linkage
Spain	AEMPS	BIFAP	8 million	GP Medical records
Spain-Valencia	FISABIO	FISABIO	5 million	Record linkage
Spain-Catalunya	IDIAP-Jordi Gol	SIDIAP	5.7 million	Record linkage
Italy	SoSeTe	PEDIANET	0.3 million	Pediatric medical record
	ARS	ARS data	5 million	Record linkage
United Kingdom	University Utrecht	CPRD	13 million	GP medical record
Norway	University Oslo	Norwegian registries	5.3 million*	Record linkage
France	University of Bordeaux BPE	SNDS	69 million	Health insurance
Total			138.6 million	

Courtesy of Prof H Gardarsdottir et al

BACKGROUND RATES (1) – COMMON AESI

Tableau depiction of published data. Source: http://www.encepp.eu/phact_links.shtml

BACKGROUND RATES (2) – RARE AESI

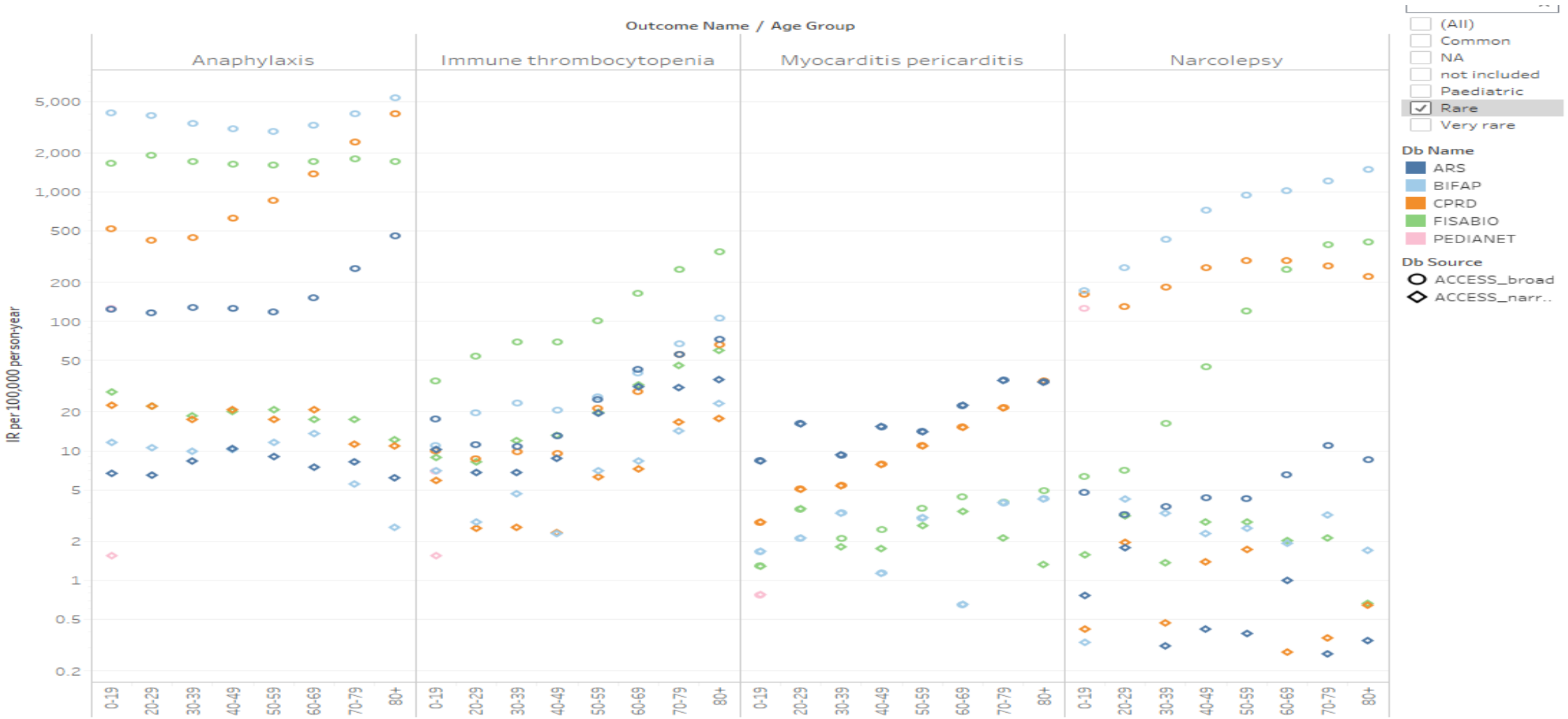


Tableau depiction of published data. Source: http://www.encepp.eu/phact_links.shtml

BACKGROUND RATES (2) – VERY RARE AESI

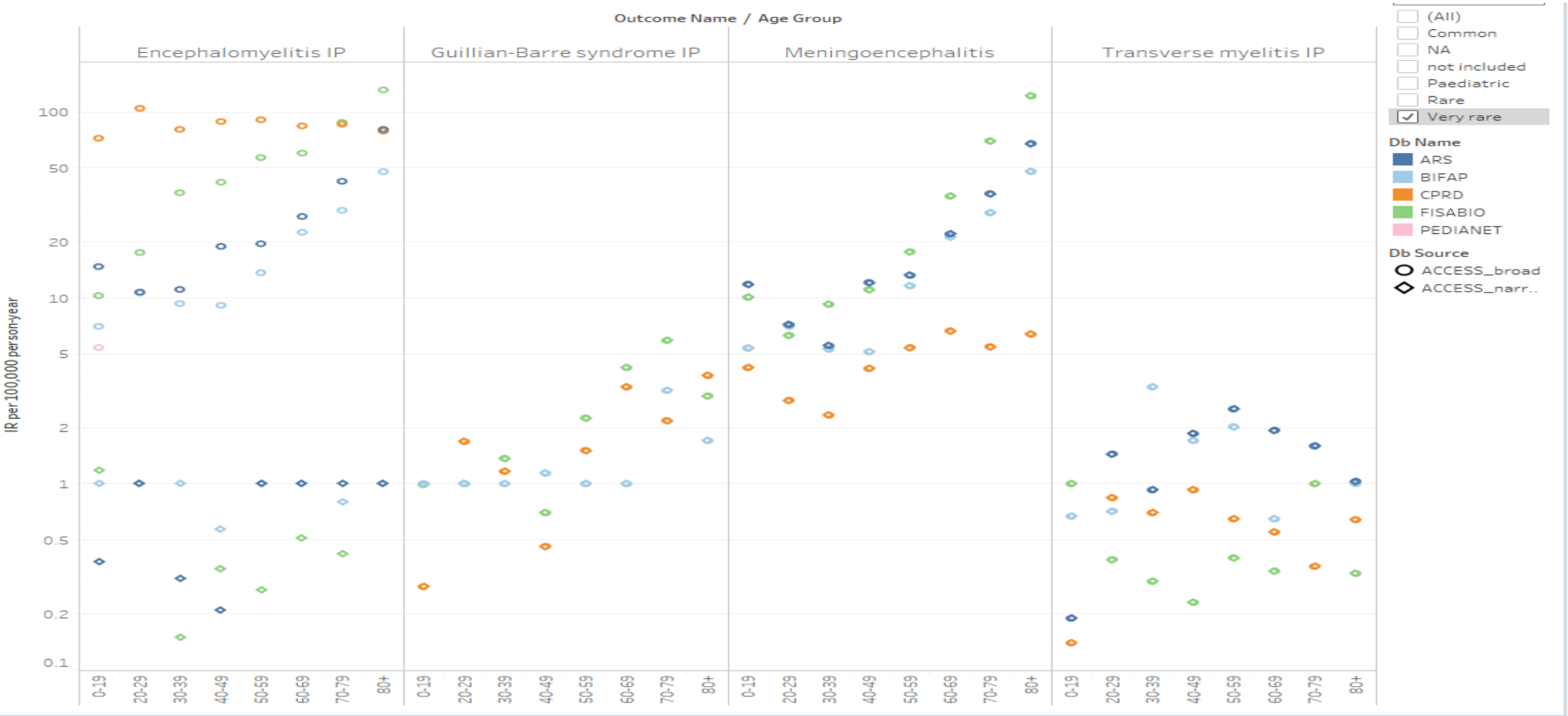


Tableau depiction of published data. Source: http://www.encepp.eu/phact_links.shtml

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EHDEN & OHDSI COLLABORATION ON COVID-19 RESEARCH

EHDEN-OHDSI International Collaboration for COVID-19 research

Kostka K et al. ResearchSquare preprints

EUROPE (9)		
CPRD (EHR)	3,864	NR
IQVIA DA Germany (EHR)	11,500	NR
HM Hospitales (Hospital Billing)	NR	2,544
Hospital del Mar (EHR)	NR	2,686
Integrated Primary Care Information (EHR)	3,306	60
IQVIA LPD France (EHR)	23,592	NR
IQVIA LPD Italy (EHR)	4,816	NR
Information System for Research in Primary Care (SIDIAP) (EHR)	124,305	18,369
SIDIAP-H (EHR Hospital linkage)	43,441	7,197

USA (13)		
Columbia University Irving Medical Center (EHR)	10,437	3,439
Department of Veterans Affairs (EHR)	57,937	10,951
HealthVerity (Claims with diagnostic testing)	587,683	22,887
IQVIA Open Claims (Claims)	2,875,812	533,997
IQVIA Hospital Charge Data (Hospital Billing)	153,477	57,062
Optum EHR (EHR)	217,772	36,717
Optum SES (EHR with socio-economic data)	7,863	4,336
Oregon Health & Sciences University (EHR)	11,187	627
Premier (Hospital Billing)	417,650	156,187
Stanford University (EHR)	4,788	744
Tufts Medical Center (EHR)	1,250	326
University of Colorado Anschutz Medical Campus-Health Data Compass(EHR)	9,481	1,874
University of Washington School of Medicine (EHR)	3,245	733

ASIA-PACIFIC (3)		
Health Insurance Review & Assessment Service (Claims)	NR	7,599
Daegu Catholic University Medical Center (EHR)	559	46
Nanfang Hospital (EHR)	403	304

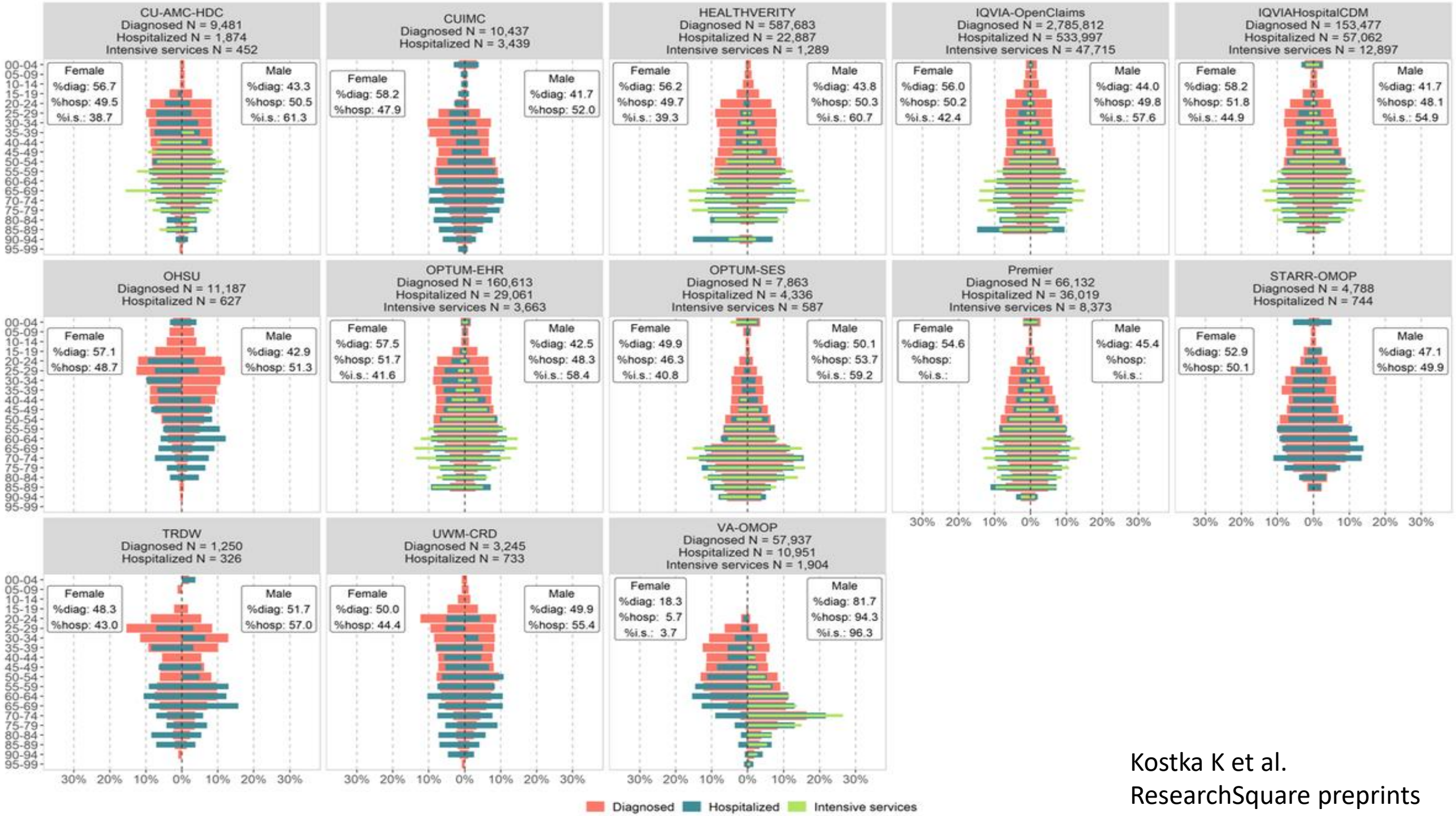
KEY

Persons diagnosed with COVID-19 or lab confirmed tested positive (no prior observation required)

Persons hospitalized with diagnosed with COVID-19 or lab confirmed tested positive (no prior observation required)

NR = Not Reported

- > 4.5 m tested+
- > 1.2 m hospitalized
- 9 EU countries
- 13 US, 3 Asian nodes



Kostka K et al.
ResearchSquare preprints

BACKGROUND RATES ACCESS-OHDSI-EHDEN– COMMON AESI

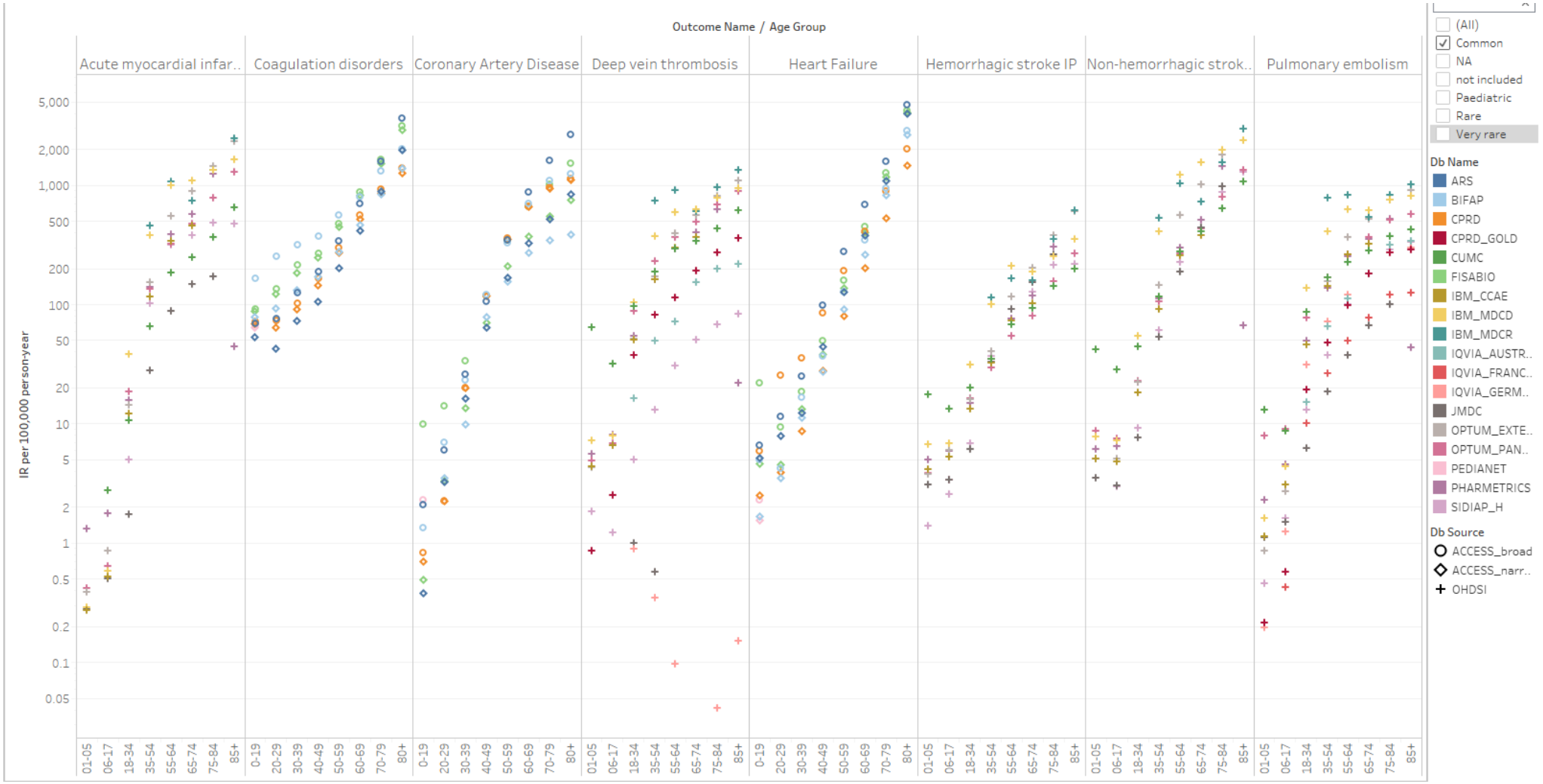


Tableau depiction of published data. Source: http://www.encepp.eu/phact_links.shtml

+ Unpublished OHDSI-EHDEN estimates using the OMOP CDM

BACKGROUND RATES – NARROW VS BROAD, DIFFERENT DATA MODELS

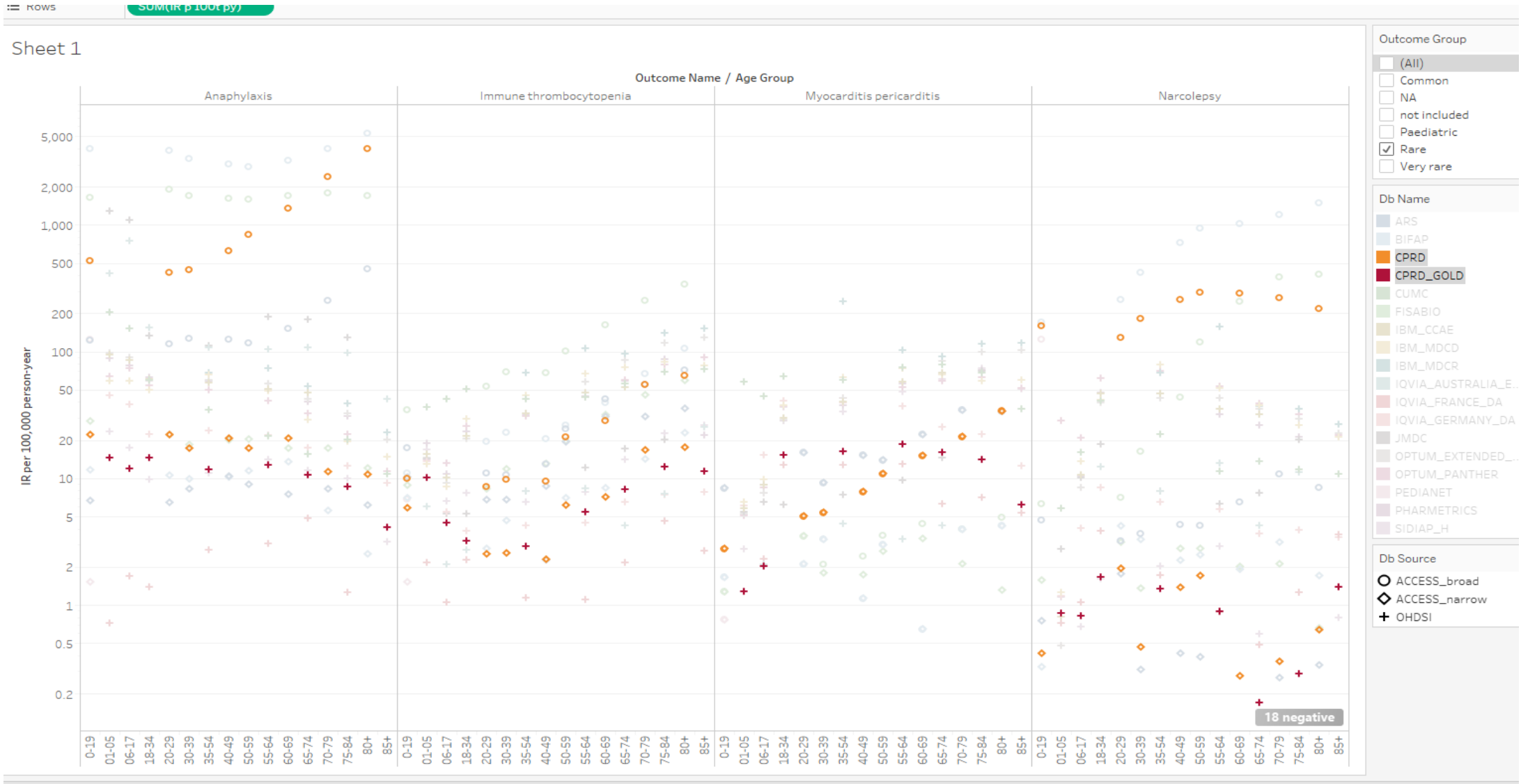


Tableau depiction of published data. Source: http://www.encepp.eu/phact_links.shtml

+ Unpublished OHDSI-EHDEN estimates using the OMOP CDM

EMA-FDA-Health Canada collaboration

EMA tender for the study of covid-related coagulopathy

led by emc Rotterdam,

in collaboration w uoxf, sidiap, iqvia

RESEARCH QUESTION AND OBJECTIVES

1. To estimate the incidence of venous thromboembolic events among patients with COVID-19 at 30-, 60-, and 90-days.
2. To calculate the risks of COVID-19 worsening stratified by the occurrence of a venous thromboembolic event.
3. To assess the impact of risk factors on the rates of venous thromboembolic events among patients with COVID-19.
4. To develop and externally validate patient-level prediction models for venous thromboembolic events for patients with COVID-19.

RESEARCH QUESTION AND OBJECTIVES

5. To estimate the incidence of arterial thromboembolic events among patients with COVID-19 at 30-, 60-, and 90-days.
6. To calculate the risks of COVID-19 worsening stratified by the occurrence of an arterial thromboembolic event.
7. To assess the impact of risk factors on the rates of arterial thromboembolic events among patients with COVID-19.
8. To develop and externally validate patient-level prediction models for arterial thromboembolic events for patients with COVID-19.

Q&A