Large Scale Evidence Generation in EHDEN and DARWIN EU®

Moderators: Daniel Prieto Alhambra and Katia Verhamme

Department of Medical Informatics, Erasmus MC

Introduction to EHDEN

Daniel Prieto Alhambra

Predicting long term cancer survival for Health Technology Assessment: A Multinational Cohort Study Across Europe

Jeremy Dietz

National Institute for Health and Care Excellence, UK

EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Predicting long term cancer survival for Health Technology Assessment: A multinational Cohort Study Across Europe

Jeremy Dietz (he/him)

with thanks to Danielle Newby, Ravinder Claire, James Koh, Ian Koblbauer, Dalia Dawoud and everyone else who contributed to this study

imi innovative medicines initiative

efpia NICE UNIVERSITY OF OXFORD

WORK PACKAGE 2 AIMS

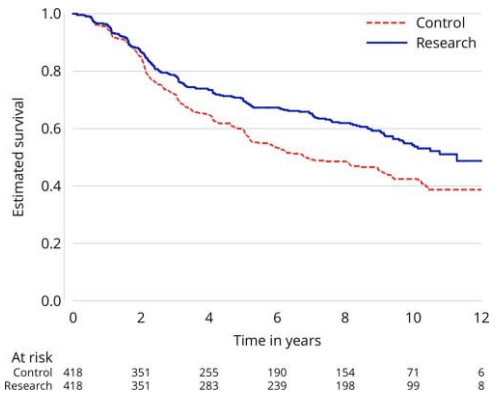
- Enable the transition towards outcomes-driven healthcare systems in Europe

- Extend the OMOP-CDM and vocabularies to include PROM standard outcomes sets (e.g. ICHOM)

- **Test whether OMOP-CDM can be used in the context of regulatory approval, health technology assessment (HTA), and for payer purposes**

HTA use case: Cancer survival

- Extrapolation of time-to-event outcomes beyond trial data is a critical input for cost-effectiveness models used in HTA
  - How do long-term projections based on trial controls compare with the real world?



HTA use case:

- Retrospective observational cohort study
- Population: 8 cancer phenotypes
- Intervention: current care
- Outcome: overall survival
- Output: accessible dashboard allowing easy examination of outcomes
- Data: CPRD (UK) for initial development, then extend across EHDEN network

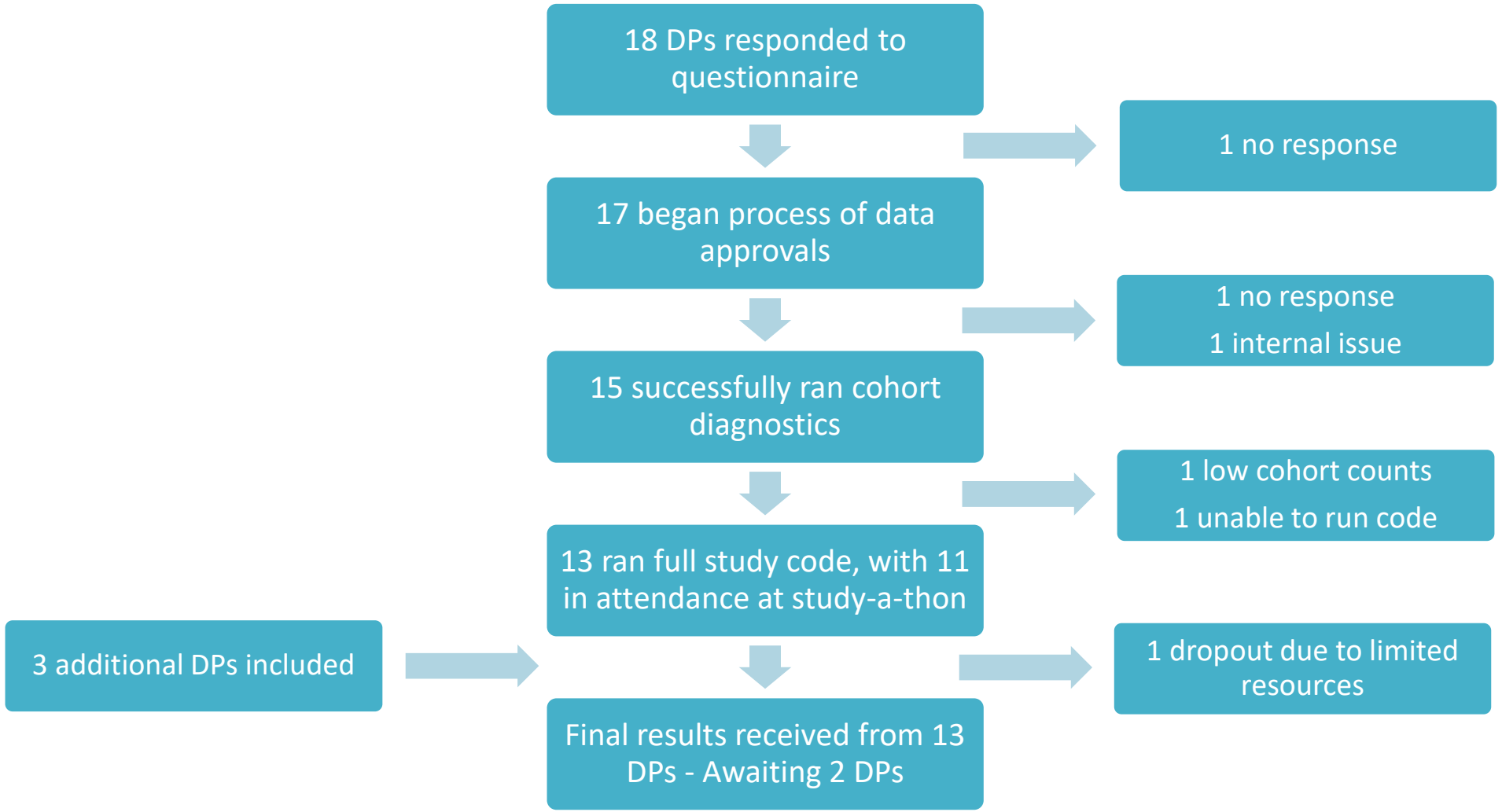
OBJECTIVES

1. To create a dashboard prototype for multiple data sources so users can easily examine natural history data and common extrapolation models for a range of cancers

2. To describe the overall survival of multiple cancers across multiple data sources

3. To compare long term survival versus predicted survival of multiple cancers across multiple data sources

DATA PARTNERS



STUDY PACKAGE WORKFLOW

STEP 1

Instantiate cancer cohorts
Apply exclusion criteria

STEP 2

Calculate survival statistics, risk tables, hazards using KM method

STEP 3

Predict KM results using parametric and flexible parametric methods

STEP 4

Repeat step 2 for sex and age group and sex*age group stratification

STEP 5

Repeat step 3 for sex and age group stratification and adjustment

STEP 6

Characterisation of patient populations

Total number of models for study:

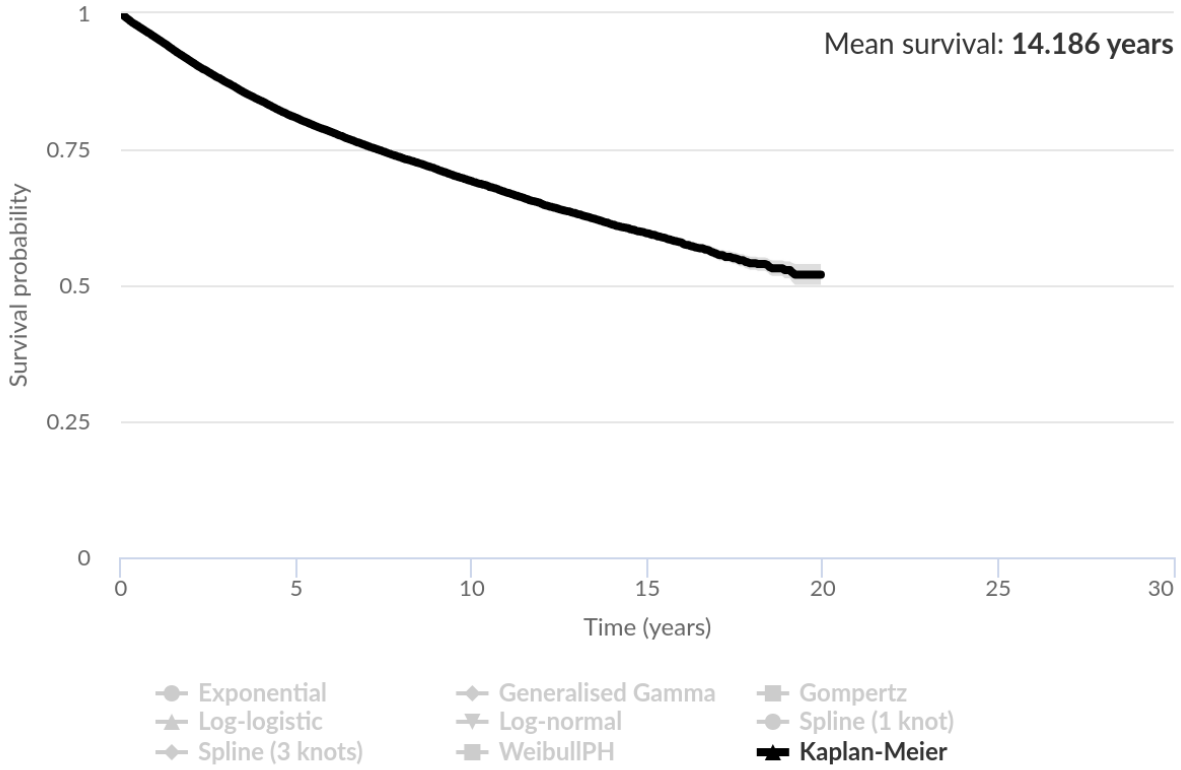
1210!

Write – test - repeat

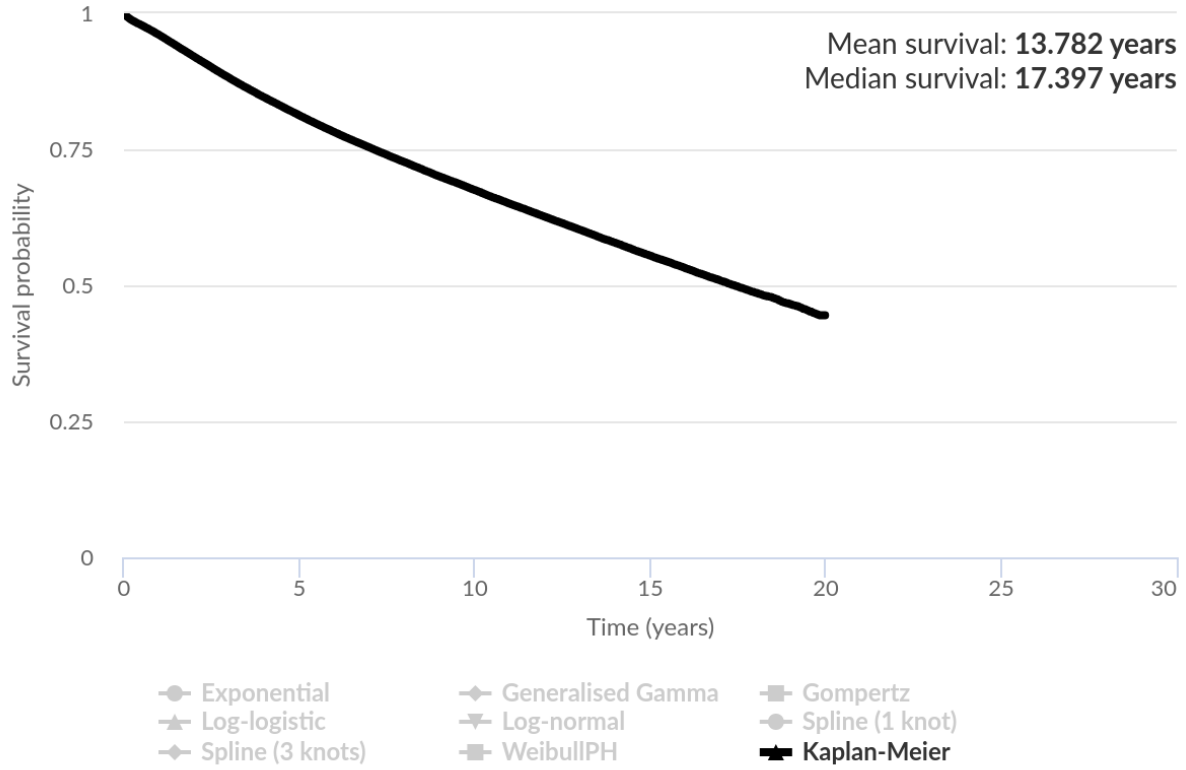
RESULTS - DASHBOARD

1. To create a dashboard prototype for multiple data sources so users can easily examine natural history data and common extrapolation models for a range of cancers

2. To describe the overall survival of multiple cancers across multiple data sources

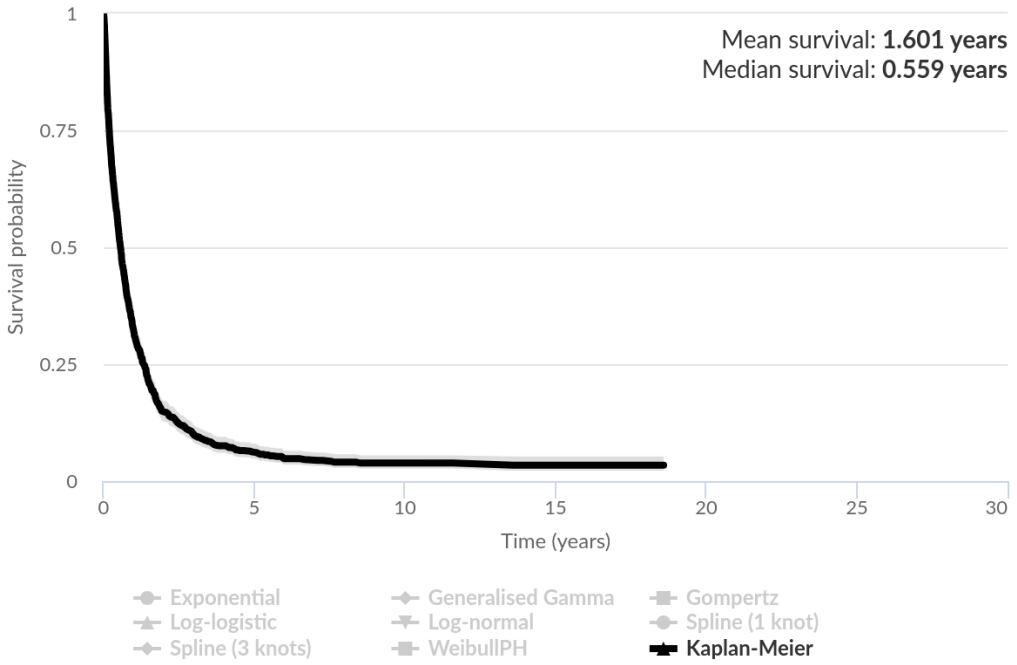


CPRD

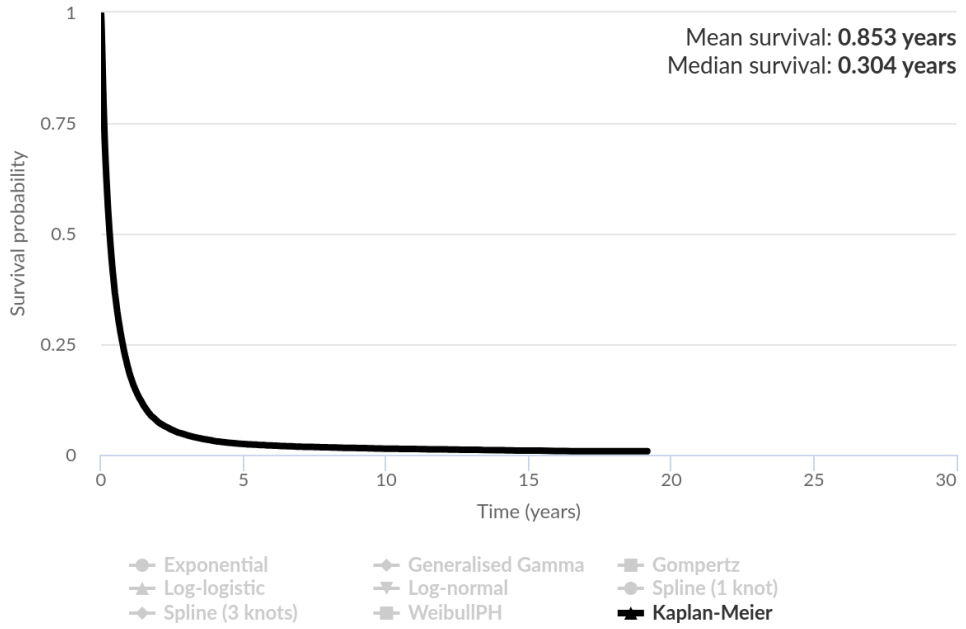


Netherlands Cancer Registry

2. To describe the overall survival of multiple cancers across multiple data sources



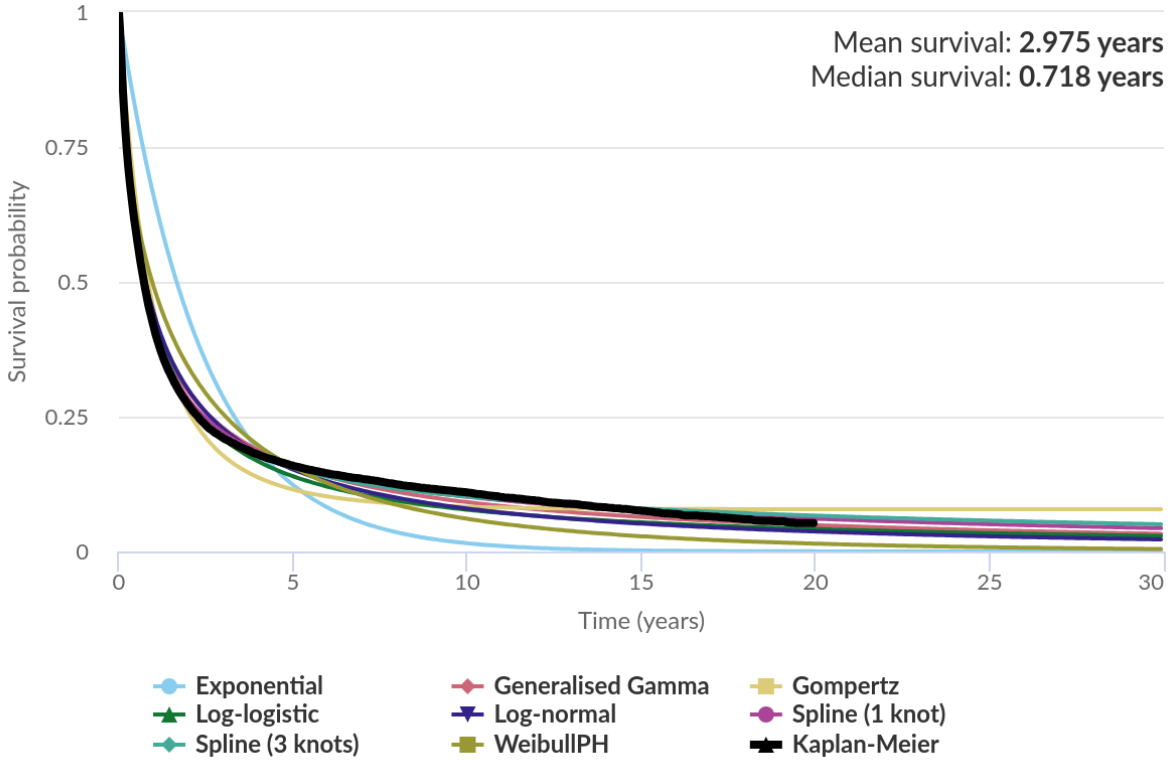
Geneva cancer registry



Netherlands Cancer Registry

STOMACH CANCER - NCR

3. To compare long term survival versus predicted survival of multiple cancers across multiple data sources



Goodness of fit

Method	logLik	AIC	BIC
Gompertz	-41040.619	82085.239	82101.958
WeibullPH	-42153.474	84310.949	84327.668
Exponential	-50306.962	100615.924	100624.284
Log-logistic	-39732.49	79468.98	79485.7
Log-normal	-39707.181	79418.362	79435.081
Generalised Gamma	-39580.283	79166.567	79191.646
Spline (1 knot)	-39423.76	78853.521	78878.6
Spline (3 knots)	-39345.501	78701.002	78742.8

DISSEMINATION

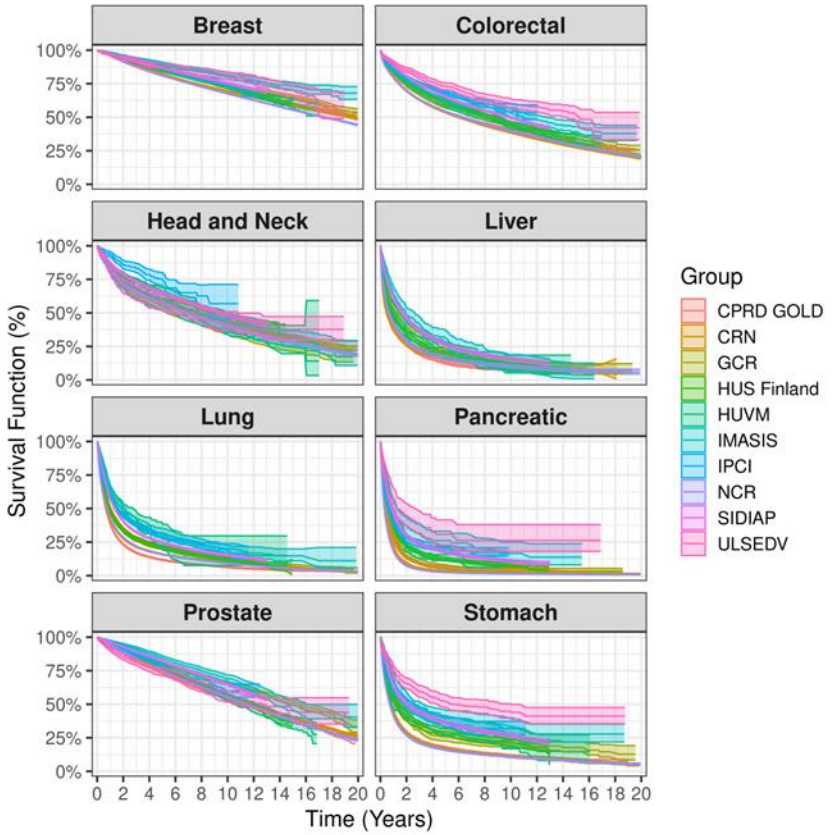
Three manuscripts underway:

1) **Survival of cancers across databases**
2) **Modelling long term survival for health technology assessment**
3) **Federated data-analyses for HTA: An Oncology Dashboard**

Abstracts written with plans to showcase at:

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ISPOR
Improving healthcare decisions



STUDY-A-THON

THANKS GO TO…

AURIA CLINICAL INFORMATICS

Cancer Registry of Norway

SIDIAP

NICE National Institute for Health and Care Excellence

IDIAP JORDI GOL

CPRD

HUS

Erasmus MC

THE UNIVERSITY of EDINBURGH

Hospital del Mar Research Institute Barcelona

EGAS MONIZ SCHOOL of HEALTH & SCIENCE

Trends over time in medicines with suggested shortages in Europe

Marta Pineda Moncusí

Oxford University, UK

EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Trends over time in medicines with suggested shortages in Europe

Lead by:

Dr Marta Pineda Moncusí

Postdoctoral Research Assistant In Health Data
Pharmaco- and Device Epidemiology Group – Planetary Health Informatics
Centre for Statistics in Medicine (CSM) | NDORMS
University of Oxford

Dr Theresa Burkard

Postdoctoral Data Scientist
Pharmaco- and Device Epidemiology Group
Centre for Statistics in Medicine (CSM) | NDORMS
University of Oxford

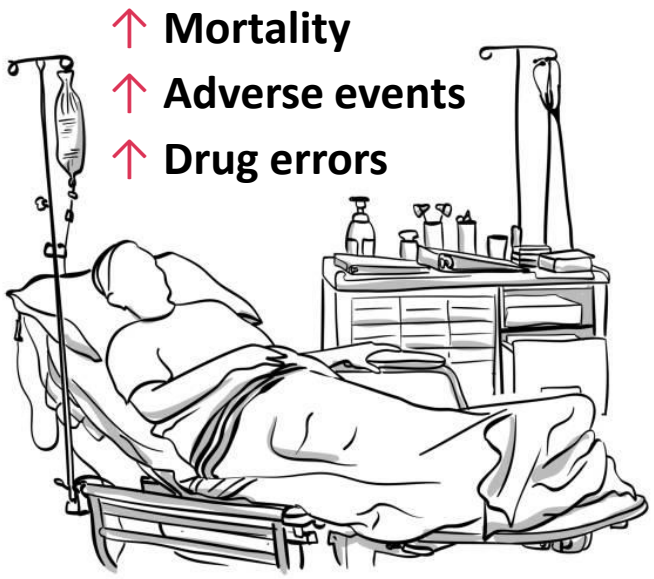
UNIVERSITY OF OXFORD

imi

efpia

WHY DRUG SHORTAGES?

Drug shortages[1]



Exacerbated during COVID-19 outbreak

During lockdown [2]:

- Reduction or cessation of local/global transportations
- Supply chain disruption (including drugs production and distribution)

COVID-19 vaccines as an example [3]:

- High demand, insufficient to cover the worldwide
- Unequal distribution (economically driven)

[1] *Phuong, J.M., et al., The impacts of medication shortages on patient outcomes: A scoping review. PLoS One, 2019. 14(5): p. e0215837.*
[2] *Ayati, N., P. Saiyarsarai, and S. Nikfar, Short and long term impacts of COVID-19 on the pharmaceutical sector. Daru, 2020. 28(2): p. 799-805.*
[3] *Klobucista, C. A Guide to Global COVID-19 Vaccine Efforts. 2022 [cited 2023]. Available from: https://www.cfr.org/backgrounder/guide-global-covid-19-vaccine-efforts.*

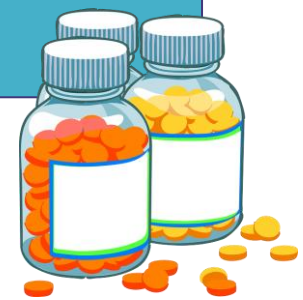
AIMS OF THE STUDY

- To study incidence and prevalence of medicines with suggested shortages and its alternatives
- To describe incident and prevalent users of medicines with suggested shortages

STEPS OF THE STUDY

1) Feasibility check
2) Incidence-Prevalence
3) Drug utilisation study (e.g. Characterisation)

Medicines under suggested shortage: n= 25
Alternatives: n= 32



EHDEN
EUROPEAN HEALTH DATA & EVIDENCE NETWORK

EMA drug shortages catalogue, information on website (publicly available)

Drug shortages MEGASTUDY

Additional alternatives from literature

>50 medicines in shortages and alternatives

DARWIN EU R code packages (publicly available)

>70 Data Partners

Analytical code
1) Feasibility
2) Incidence/ Prevalence
3) DrugUtilisation

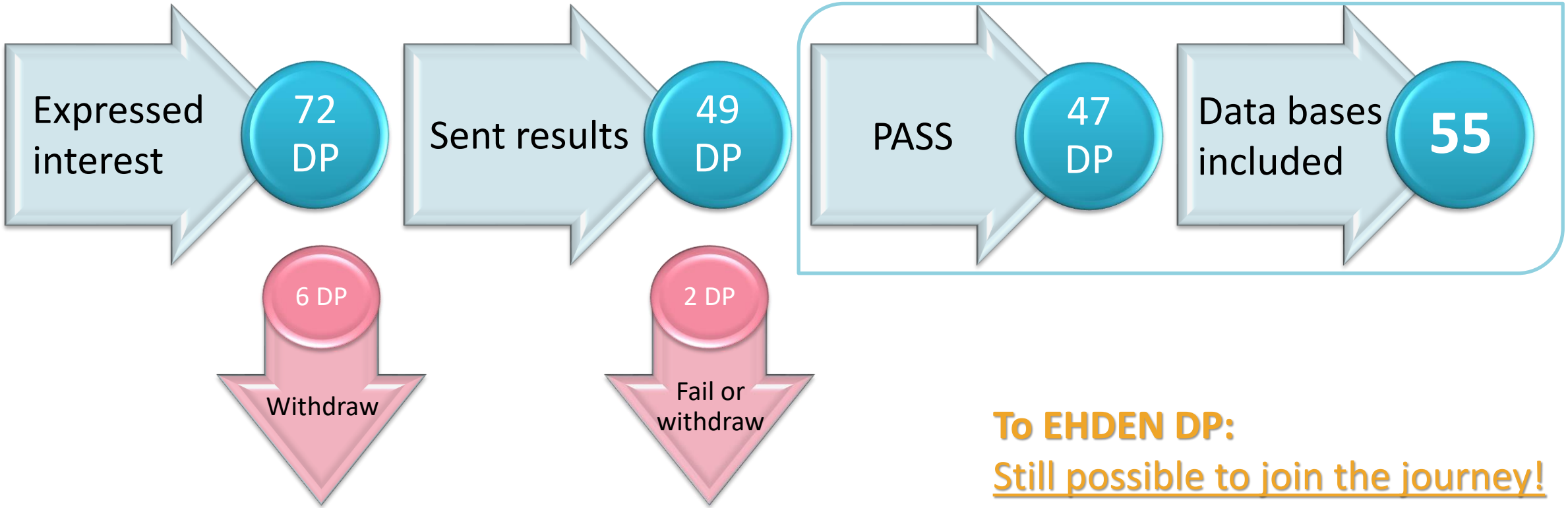
Results

- Publications
- Conferences
- EFPIA
- EMA

DATA PARTNERS INVOLVED

Requirement to Pass:
minim 1 drug and >100 patients within study period (2010 – 2023)

1) Feasibility Step

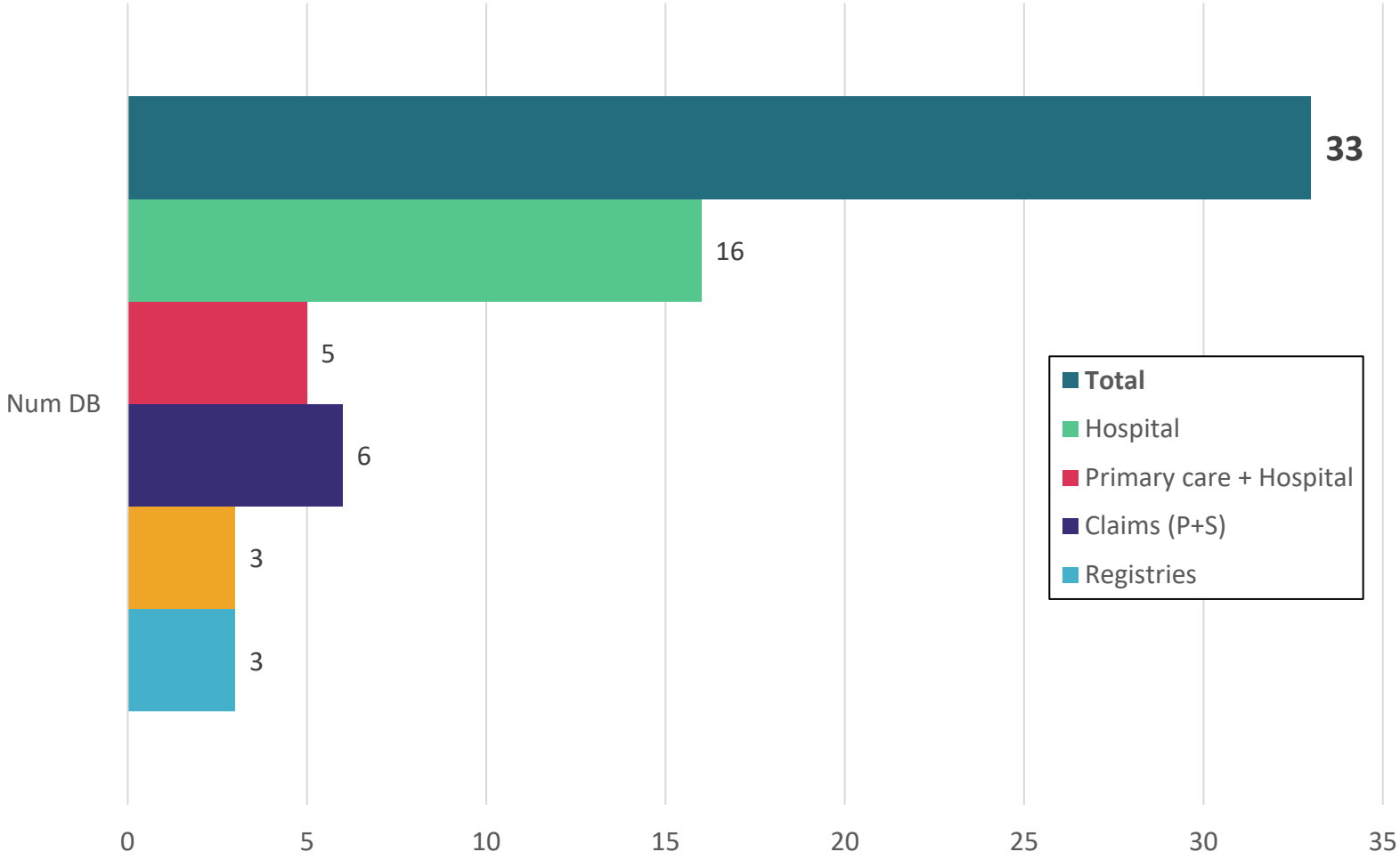


To EHDEN DP:
Still possible to join the journey!

*DP = data partner

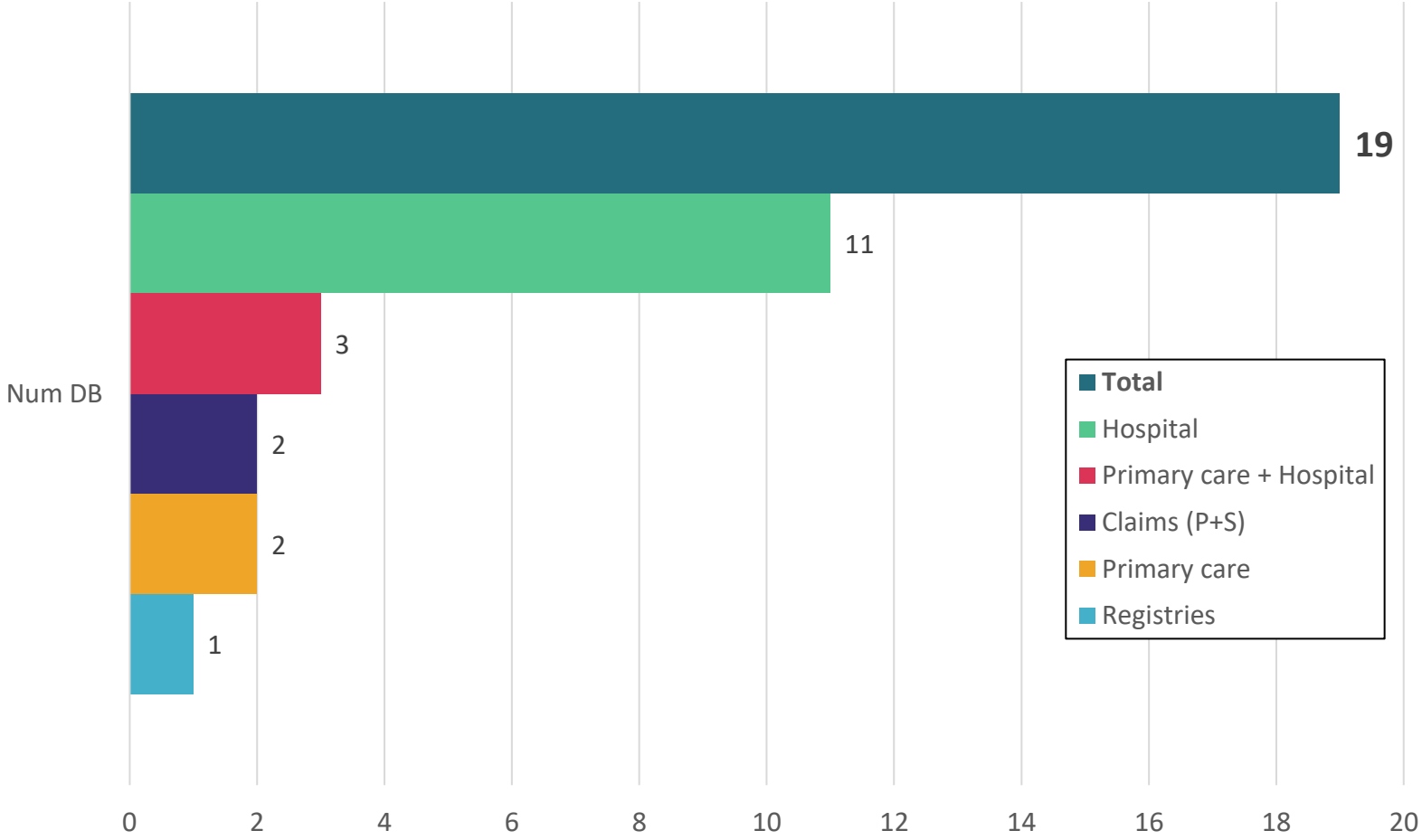
DATA PARTNERS INVOLVED

2) Incidence-Prevalence Step



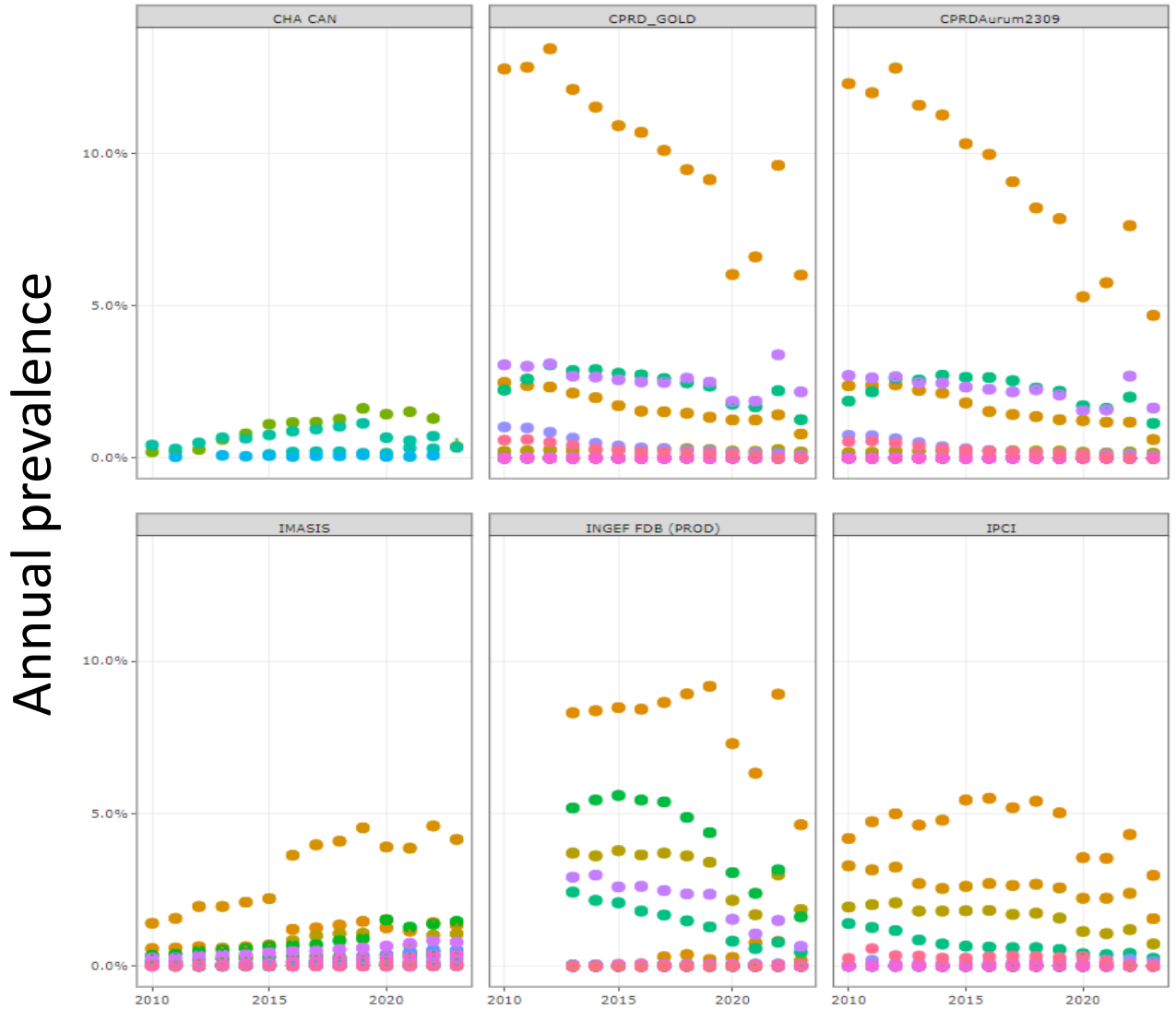
Country	DB per Country
Belgium	3
Bulgaria	1
Estonia	1
Finland	2
Germany	3
Greece	1
Netherlands	3
Portugal	5
Serbia	1
Spain	5
Turkey	1
UK	3
US	4
Grand Total	**33**

3) Drug Utilisation Study



Country	DB per Country
Estonia	1
Finland	1
Germany	1
Greece	1
Italy	1
Netherlands	3
Portugal	3
Serbia	1
Spain	4
Turkey	1
UK	2
Grand Total	**19**

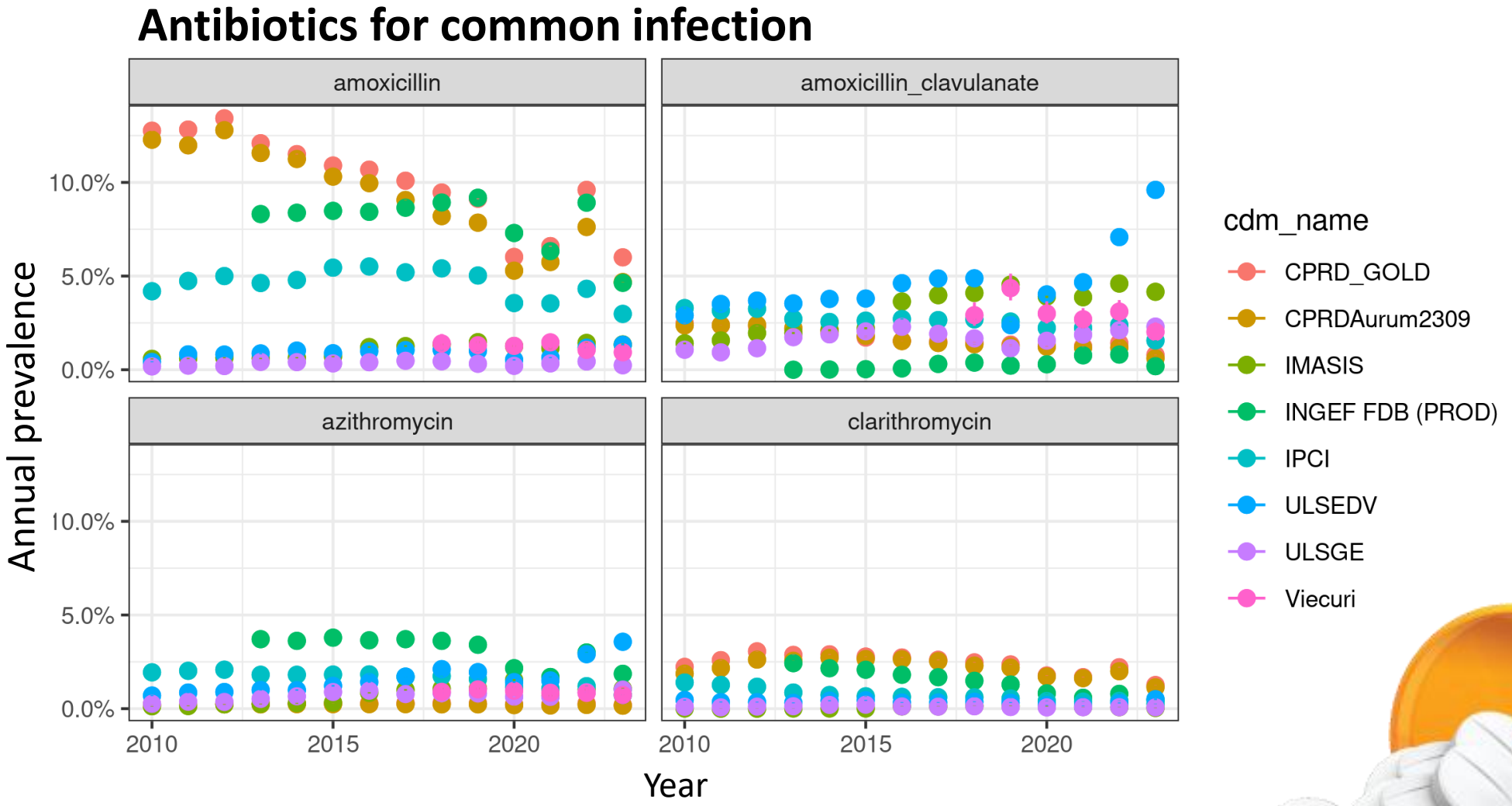
PRELIMINARY RESULTS* IN INCIDENCE/PREVALENCE



- abatacept
- agalsidase_alfa
- agalsidase_beta
- alteplase
- amoxicillin
- amoxicillin_clavulanate
- anakinra
- arsenic_trioxide
- azithromycin
- baricitinib
- belatacept
- berotralstat
- bevacizumab
- c1_esterase_inhibitor
- cefotaxime
- ceftriaxone
- cefuroxime
- certolizumab
- cetrorelix
- clarithromycin
- cyclosporine
- cytarabine_any
- daunorubicin
- etanercept
- ganirelix
- golimumab
- icatibant
- idarubicin
- imiglucerase
- infliximab
- lanadelumab
- meropenem
- mycophenolic_acid
- nicotine
- penicillin_g
- penicillin_v
- piperacillin_tazobactam
- ranibizumab
- sarilumab
- sirolimus
- tacrolimus_no_topical
- tocilizumab
- tofacitinib
- upadacitinib
- urokinase
- varenicline
- verteporfin

* Subset of results including only those with an IRB approval to share

PRELIMINARY RESULTS* IN INCIDENCE/PREVALENCE



* Subset of results including only those with an IRB approval to share

CHALLENGES

- Scaling up
  - Project management task
  - Timelines
  - Outputting a lot of results
    - Community effort to digest and disseminate (webinar)

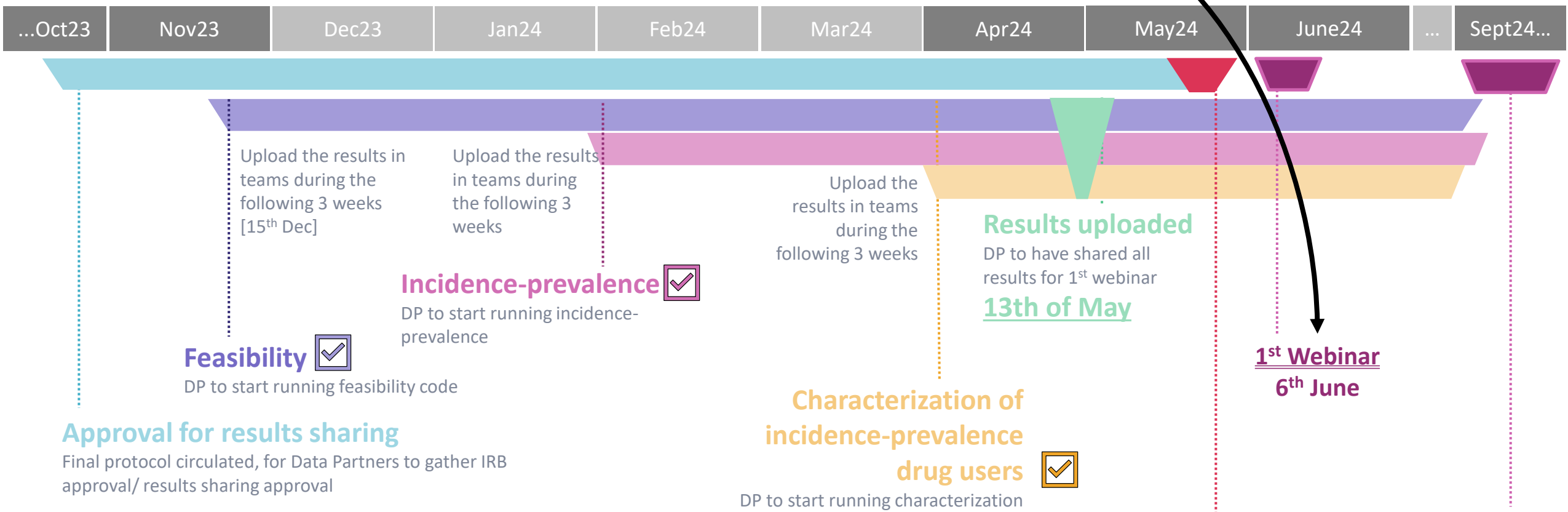
- New data partners participating with their first study
  - Much help needed with R and running study code

Timelines and Webinar

Data Partners timelines

Registration ends today!

Code released in GitHub



To EHDEN DP:

Still possible to join the journey!

EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

Thank you!

UNIVERSITY OF OXFORD

imi

efpia

Introduction to DARWIN EU®

Katia Verhamme

Coordination Centre

Large Scale Evidence Generation in Darwin EU®

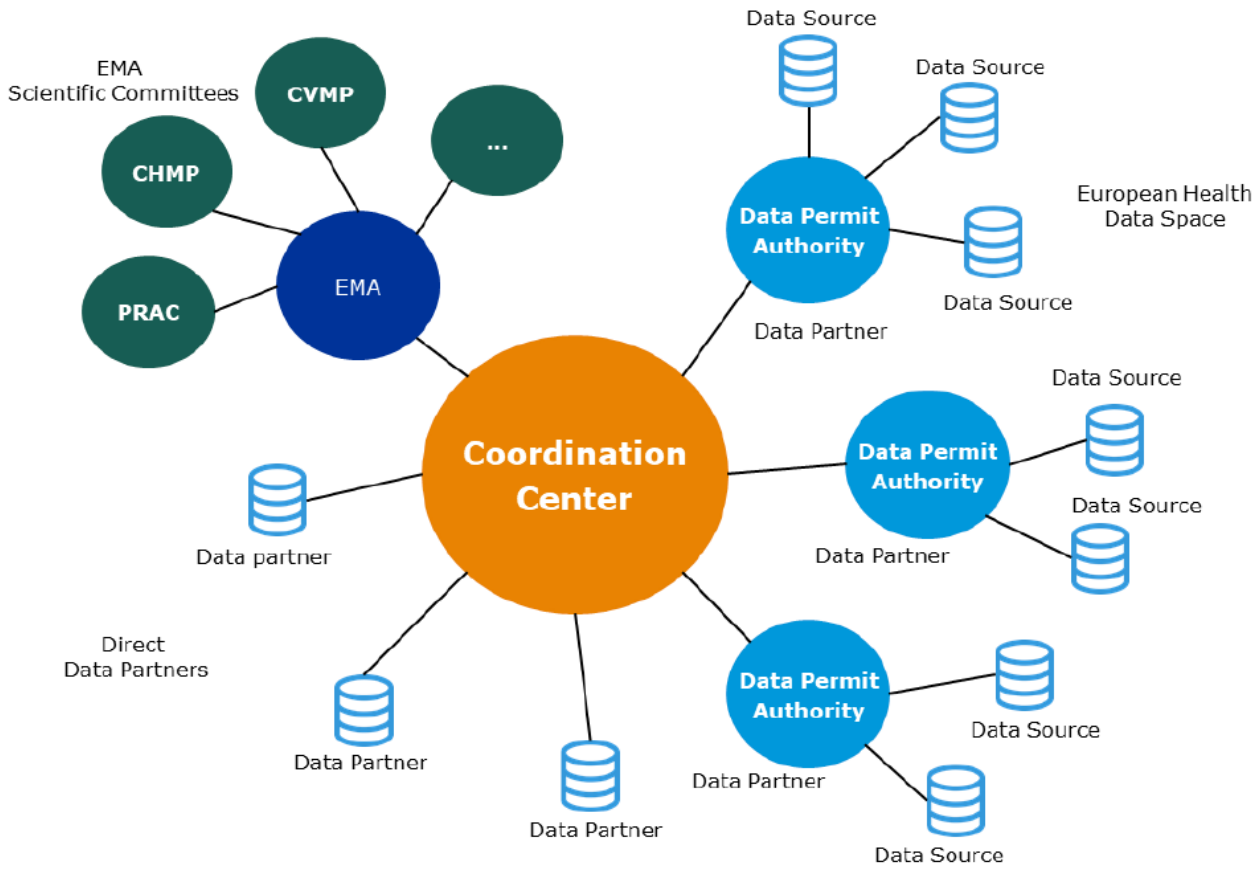
Katia Verhamme

The OHDSI EU Symposium 2024-06-03

Disclosure

This presentation represents the views of the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the European Medicines Agency or the European Medicines Regulatory Network.

DARWIN EU® is a federated **network** of **data**, **expertise** and **services** that supports better decision-making throughout the product lifecycle by generating reliable **evidence from real world healthcare data**



FEDERATED NETWORK PRINCIPLES

- Data stays **local**
- **Use of Common Data Model** to perform studies in a timely manner and increase consistency of results

Welcome DARWIN EU® Data Network

UK
- Clinical Practice Research Datalink (CPRD GOLD)
- UK Biobank

Netherlands
- Integrated Primary Care Information
- Netherlands Comprehensive Cancer Organisation

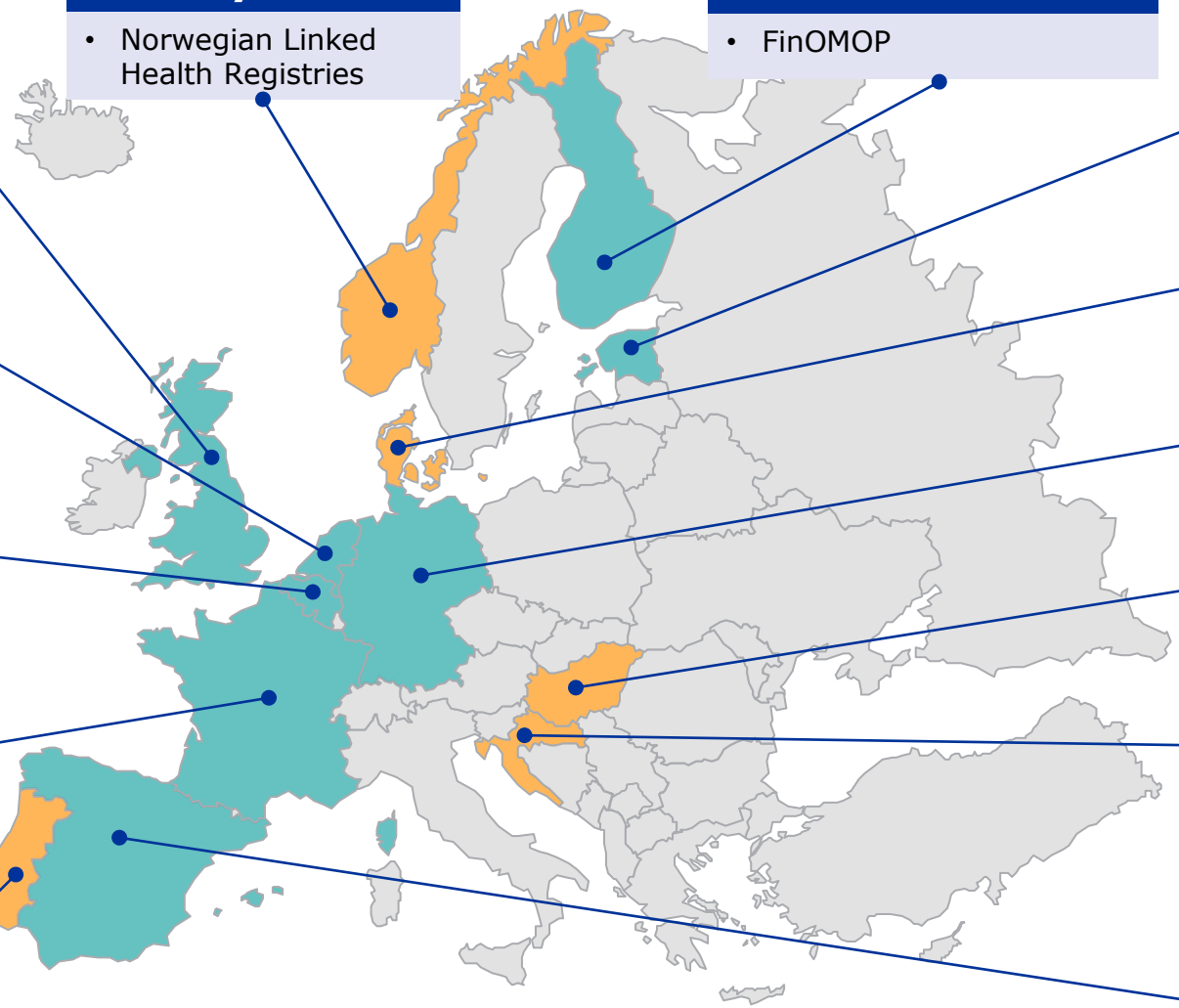
Belgium
- IQVIA Belgium Longitudinal Patient Data

France
- Bordeaux University Hospital
- Système National des Données de Santé

Portugal
- Unidade Local de Saúde de Matosinhos
- Egas Moniz Database

Norway
- Norwegian Linked Health Registries

Finland
- FinOMOP



Estonia
- University of Tartu (Biobank)

Denmark
- Danish Health Data Registries

Germany
- IQVIA Germany Disease Analyser

Hungary
- Semmelweis University

Croatia
- Croatian National public health information system

Spain
- IDIAPJGol
- Parc Salut Mar Barcelona, Hospital del Mar (IMIM)
- BiFAP
- Valencia Health System Integrated Database

How to join the data network?

The Open Call for DPs described in this document welcomes expressions of interest from **any data custodian in Europe wishing to be considered as a candidate DP for DARWIN EU®**. These include primary and secondary care data sources, claims databases, biobanks, etc. Being open to any data source, the Open Call is an instrument to facilitate a level playing field to any interested institution to participate in DARWIN EU® and aims to compile relevant information from candidate Data Partners to support decision making by the EMA to determine which DPs will be formally invited to join the initiative.

How to express interest?

The first step is to add an entry for your data source(s) on the HMA-EMA Catalogue of Real-World Data (RWD) sources.

Required steps:

1. Go to https://catalogues.ema.europa.eu/catalogue-rwd-sources and click on the 'Login' button (in the top-right hand side of the header).
2. You will be directed to the EU Login webpage. On this page, choose the 'Create an account' option. After providing your personal information (First name, Last name and Email), you will receive an email with instructions to activate your account. For more guidance on how to log in to the RWD Catalogues, please refer to the Support section of the Catalogues website.
   Note: If you already have an EU Login, you can login to the RWD Catalogues with those credentials.
3. Go to 'My dashboard' > 'Add content' > '+ Data Source' and fill out the webform page. When you have uploaded the desired information, click on 'Save'. When finalised, submit the Data Source entry by changing the state of the entry from 'Draft' to 'Submitted'. In case of multiple data sources, you need to submit separate entries for each data source, one at a time.
   Note: This document contains all question fields included in the webform page for offline review (if needed).
4. Go to 'My dashboard' and click on the title of the Data Source entry that you have just submitted (the moderation state of the entry should be 'Submitted'). Once you enter the Data Source entry page, click on the 'Download as PDF' button (in the light blue title banner of the entry). Also, make a note of the link appearing in the **PURI** field in your entry (see 'Administrative details' section).

HMA-EMA Catalogues of RWD sources and studies

Public **metadata repositories** that describe **RWD sources** and **studies that utilise such data to generate RWE.** They help pharmaceutical companies, researchers and regulators **identify** and **utilise RWD data** in investigating the use, safety and effectiveness of medicines.

Launched February 2024, https://catalogues.ema.europa.eu/

- One step closer to data-driven medicines regulation!
- Enhance **discoverability** of data sources and studies facilitating **collaboration and research**
- **Link RWD sources to studies** conducted which can support **study design**, **protocol evaluation**, and **results interpretation**
- **'FAIR'** data principles supported
- Promote **transparency** in observational research
- Ongoing activities on data **interoperability** and **integration** with other catalogues (e.g. EHDS, EHDEN)
- Advanced **user-friendly platform**

Help us foster the discoverability of RWD sources!

Add information on your data source directly to the Catalogues or send us an email at metadata@ema.europa.eu

Benefits of including your data source in the Catalogue

- Increased identification and utilisation of your data source which can promote collaborations and studies
- Increased visibility to regulators, researchers and pharmaceutical companies
- Respond to the DARWIN EU Open Call to become a DARWIN data partner via the Catalogues

Expected number of studies

PHASE I Establishment – 1st year → PHASE II Establishment – 2nd year → PHASE III Operation – 1st year → Operation 2nd year → Operation 3rd year

	Year 1	Year 2	Year 3	Year 4	Year 5
Phases	Phase I	Phase II	Phase III	Option 1	Option 2
Routine Repeated analysis	At least 1 study	-	30	60	60
Off the shelf studies	At least 2 studies	6 + 8	30	60	60
Complex Studies	1	4	12	24	24
Very Complex Studies	0	0	0	1	1

Use cases: How RWE can support decision-making?

1 Understand the clinical context

- ✓ Disease epidemiology
- ✓ Clinical management
- ✓ Drug utilisation

2 Support the planning and validity of studies

- ✓ Design and feasibility of studies
- ✓ Representativeness and validity of completed studies

3 Investigate associations and impact

- ✓ (Comparative) Effectiveness and safety studies
- Impact of regulatory actions

Slides: Courtesy of Andrej Segec (Darwin EU® Project Manager) - EMA

Examples of recently completed studies

a. Background all-cause **mortality rates in patients with severe asthma aged ≥12 years** old [EUPAS103936]

CHMP
Complex

b. Drug utilisation study on co-prescribing of **endothelin receptor antagonists** (ERAs) and **phosphodiesterate-5 inhibitors** (PDE-5is) in pulmonary arterial hypertension. [EUPAS106052]

CHMP
OTS

c. Naloxone use in treatment of opioid overdose. [EUPAS105644]

CHMP
OTS

d. Drug utilisation study of prescription **opioids**. [EUPAS105641]

PRAC
OTS

e. Drug utilisation study of **medicines with prokinetic properties** in children and adults diagnosed with gastroparesis

NCA
OTS

f. EHDS coagulopathy of COVID-19

EC / EHDS
Complex

g. Multiple myeloma: patient characterisation, treatments and survival in the period 2012-2022 [EUPAS105033]

HTA / Payers
OTS

h. Age-specific incidence rates of **RSV-related disease** in Europe [EUPAS107708]

ECDC
OTS

i. Use of antivirals for the treatment of chronic **hepatitis B and C.** [EUPAS107650]

ECDC
OTS

j. Natural history of **dermatomyositis** (DM) and **polymyositis** (PM) in adults and paediatric populations [EUPAS107454]

PDCO
OTS

k. Treatment patterns of drugs used in adult and paediatric population with **lupus** [EUPAS106436]

PDCO
OTS

OTS = off-the-shelf study

completed

l. Polypharmacy among adults aged 65 and above with cancer at the time of diagnosis

EMA/CHMP workplan (geriatrics)
OTS

m. Effectiveness of **COVID-19** vaccines against severe COVID-19 and post-acute outcomes of SARS-CoV-2 infection.

ECDC - VMP
Complex

n. Effectiveness of HPV vaccines against cervical cancer

ECDC - VMP
Complex

o. Overall survival in patients with advanced or metastatic non-small cell lung (**NSCLC**) cancer treated with selected **immunotherapies as first line** of treatment.

HTA Payer
Complex

p. DUS of medicines at risk of **shortages**

EMA TRS
OTS

q. Monitoring prescription of essential **medicines administered in ICU**

EMA TRS
OTS

r. Comparing **direct and indirect** methods to **estimate prevalence** of chronic diseases using real-world data

EMA
OTS

s. Rates of occurrence of treatment-related intercurrent events in patients with **major depressive disorder** [EUPAS106685]

EMA TA
OTS

OTS = off-the-shelf study **completed**

List of studies can be consulted at: https://darwin-eu.org/index.php/studies
https://catalogues.ema.europa.eu/catalogue-rwd-studies

DARWIN EU® - Trend of prescription opioid use in Europe

Annika Jödicke

Oxford University, UK

DARWIN EU

Coordination Centre

DARWIN EU® - Trend of prescription opioid use in Europe

Junqing Xie, Mike Du, Yuchen Guo, Cesar Barboza, James Brash, Antonella Delmestri, Talita Duarte-Salles, Jasmin Gratton, Romain Griffier, Raivo Kolde, Wai Yi Man, Nuria Mercade-Besora, Marek Oja, Sarah Seager, Katia Verhamme, Dina Vojinovic, Edward Burn, Daniel Prieto-Alhambra, Martí Català, Annika Jödicke

OHDSI Europe Symposium: Large Scale Evidence Generation in EHDEN and DARWIN EU®
Monday, June 3rd 2024

Disclosure

This presentation represents the views of the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the European Medicines Agency or the European Medicines Regulatory Network.

Data partners' role was only to execute code at their data source. Data partners do not have an investigator role.

Rationale and Objectives

Background

- Opioids are a highly effective for managing severe pain.
- Increased (inadequate) opioid prescriptions have led to a public health crisis particularly in North America.
- Concerns have been growing in Europe due to increasing opioid use and related mortality.

Objective

1) To evaluate the trends of prescription opioid use
2) Characterise new opioid users in European countries

Multinational network cohort study

IPCI

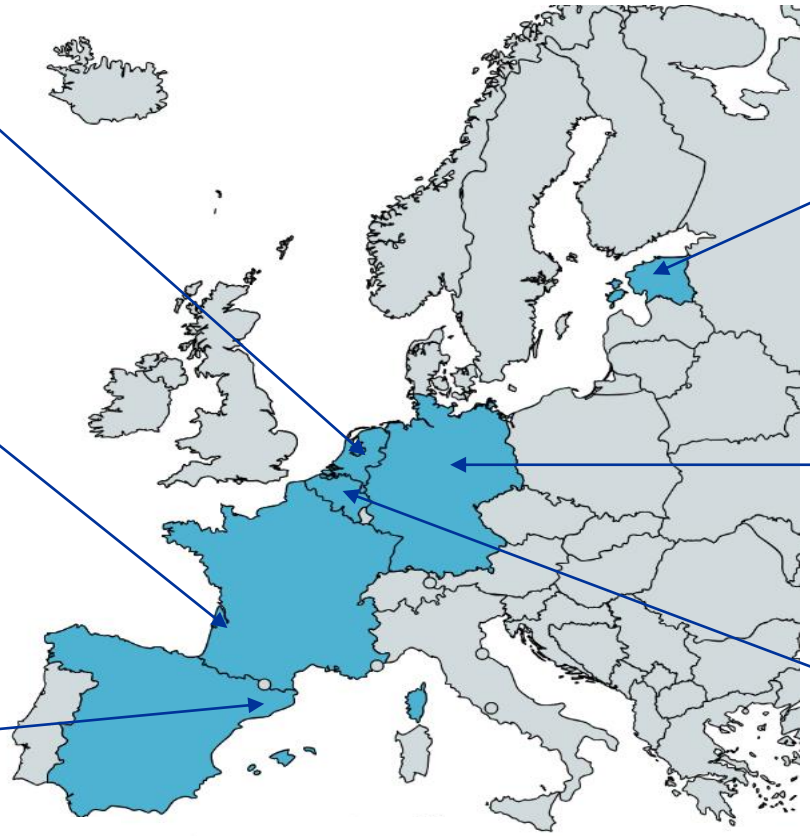
Integrated Primary Care Information Project

CHUBX

Clinical Data Warehouse of Bordeaux University Hospital

SIDIAP

Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària



EBB

Estonian Biobank

IQVIA DA Germany

IQVIA Disease Analyzer Germany

IQVIA LPD Belgium

IQVIA Longitudinal Patient Database Belgium

Study Population and Exposure definition

Study Population

All people registered in the respective databases on 1st of January of each year in the period 2012-2022, with at least 1 year of prior data availability.

Exposure definition

- All opioids
- By strength (weak/potent)
- By route of administration (oral, injection, transdermal)
- By active drug substance (N = 35)

New user definition

No previous use of respective opioid (substance/class) in the last 365days [180 days]

Population-level opioid utilisation

DARWIN EU® standardized analyses

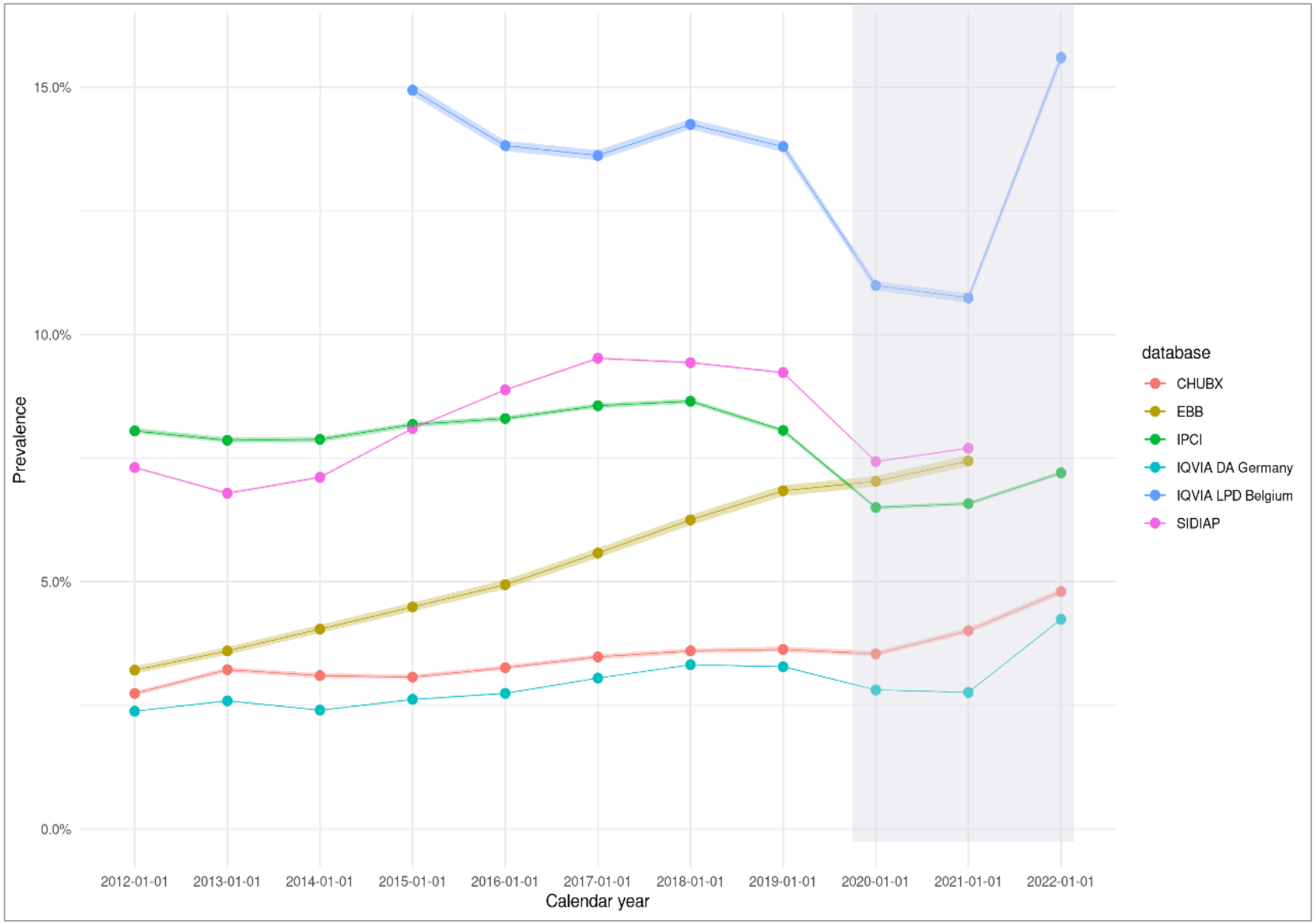
Annual period prevalence calculated as the number of opioid users in the study population

Annual incidence rates calculated as the number of new opioid users in the study population (excl. prevalent opioid users) per 100’000 person-years

Stratification by calendar year (2010-2022),

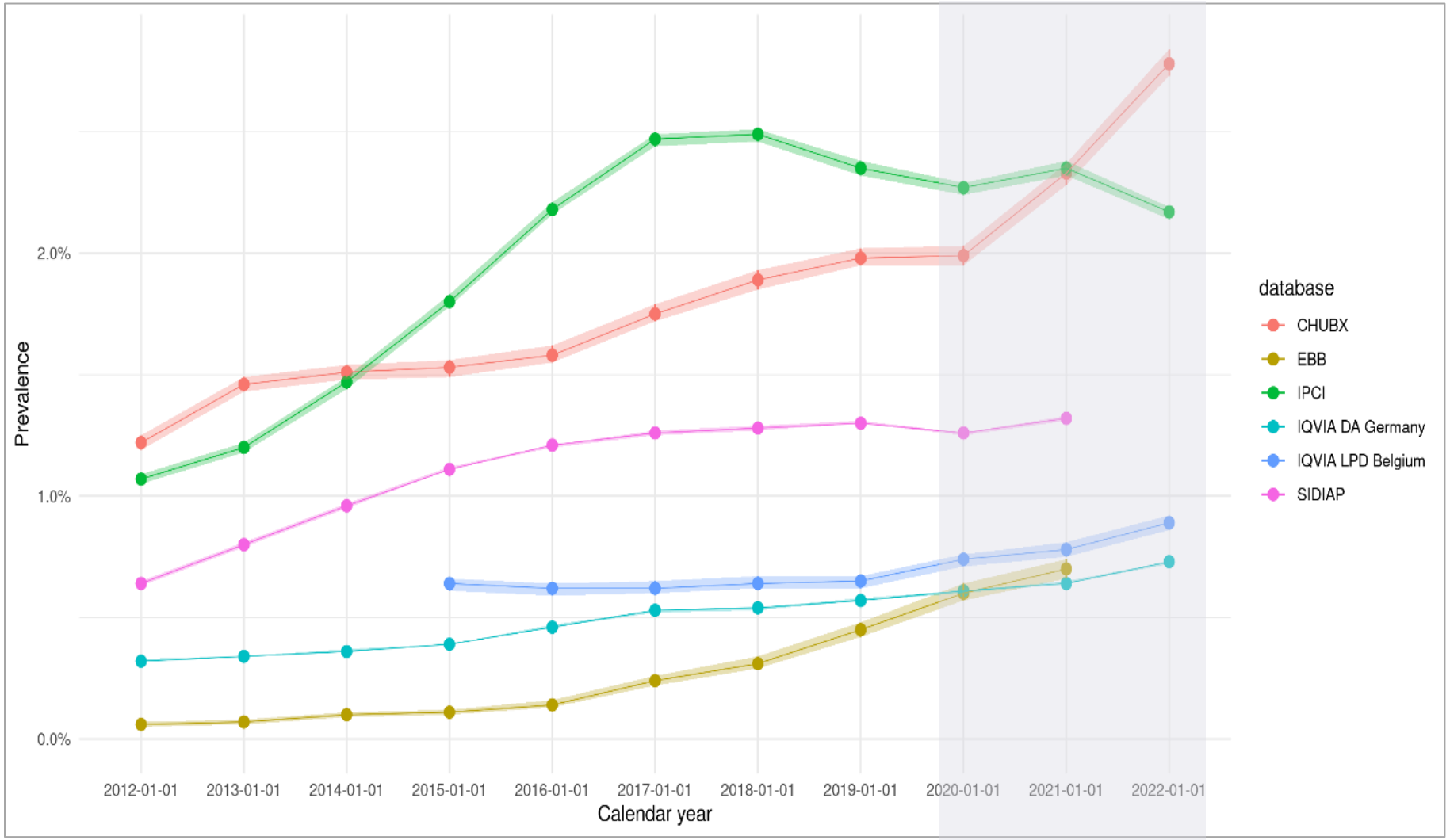
age groups (10-year age bands), sex (male/female)

Prevalence of overall prescription opioid use in 2010-2022



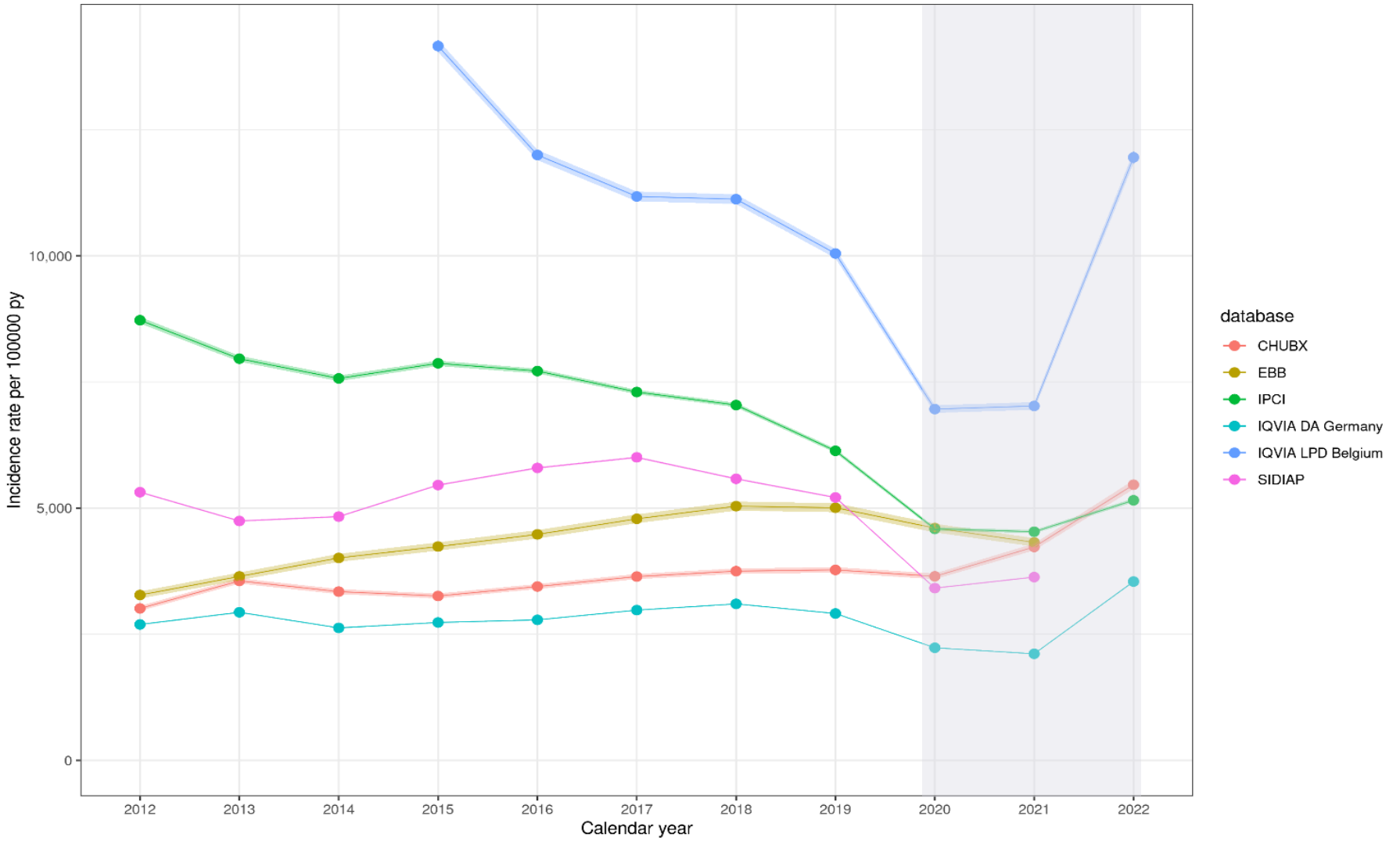
- Prevalence largely stable over time
- Increase in EBB in line with previous literature
- Largely driven by oral opioids

Prevalence of strong opioids in 2010-2022



- Prevalence of oxycodone, morphine, fentanyl, and hydromorphone increased

Incidence of overall prescription opioid use in 2010-2022



- Incidence substantially decreased in LPD Belgium, IPCI and SIDIAP over time
- Opioid use was highest in older adults
- New prescriptions of codeine and tramadol decreased over time

Patient-level opioid utilisation

DARWIN EU® standardized analyses

- Large-scale patient-level characterization including patient demographics, and history of comorbidities and comedication at and before treatment initiation
- Frequency of potential indications based on condition concept_ids recorded at index date, and in the 7 and 30days before.
- Treatment duration for the first treatment era.

A minimum cell count of 5 was used when reporting results, with any smaller counts reported as <5.

New user characterisation

	SIDIAP	IPCI	IQVIA DA Germany	IQVIA LPD Belgium	CHUBX	EBB
N (New opioid users)	2,023,867	440,849	1,248,388	207,754	138,171	53,344
Age (Median, IQR)	55 [40 - 70]	57 [43 - 70]	54 [32 - 70]	50 [34 - 64]	57 [37 - 72]	54 [42 - 65]
Sex (Female)	1,773,685 (59%)	366,540 (60%)	936,414 (57%)	163,545 (56%)	84,635 (51%)	52,659 (69%)
Proxy for indication*	Common cold (10·9%) Cough (5·4%) Low back pain (3·0%)	Cough (21·5%) Acute upper respiratory tract infection (6·0%) Low back pain (3·7%)	Acute upper respiratory tract infection (15·6%) Cough (14·4%) Nerve root disorder (4·4%)	Cough (26·9%) Common cold (13·7%) Low back pain (10·3%)	Complication of surgical procedure (6·4%) Complication of procedure (6·2%) Headache (5·5%)	Nerve root disorder (11·6%) Pain in spine (9·0%) Cough (8·6%)

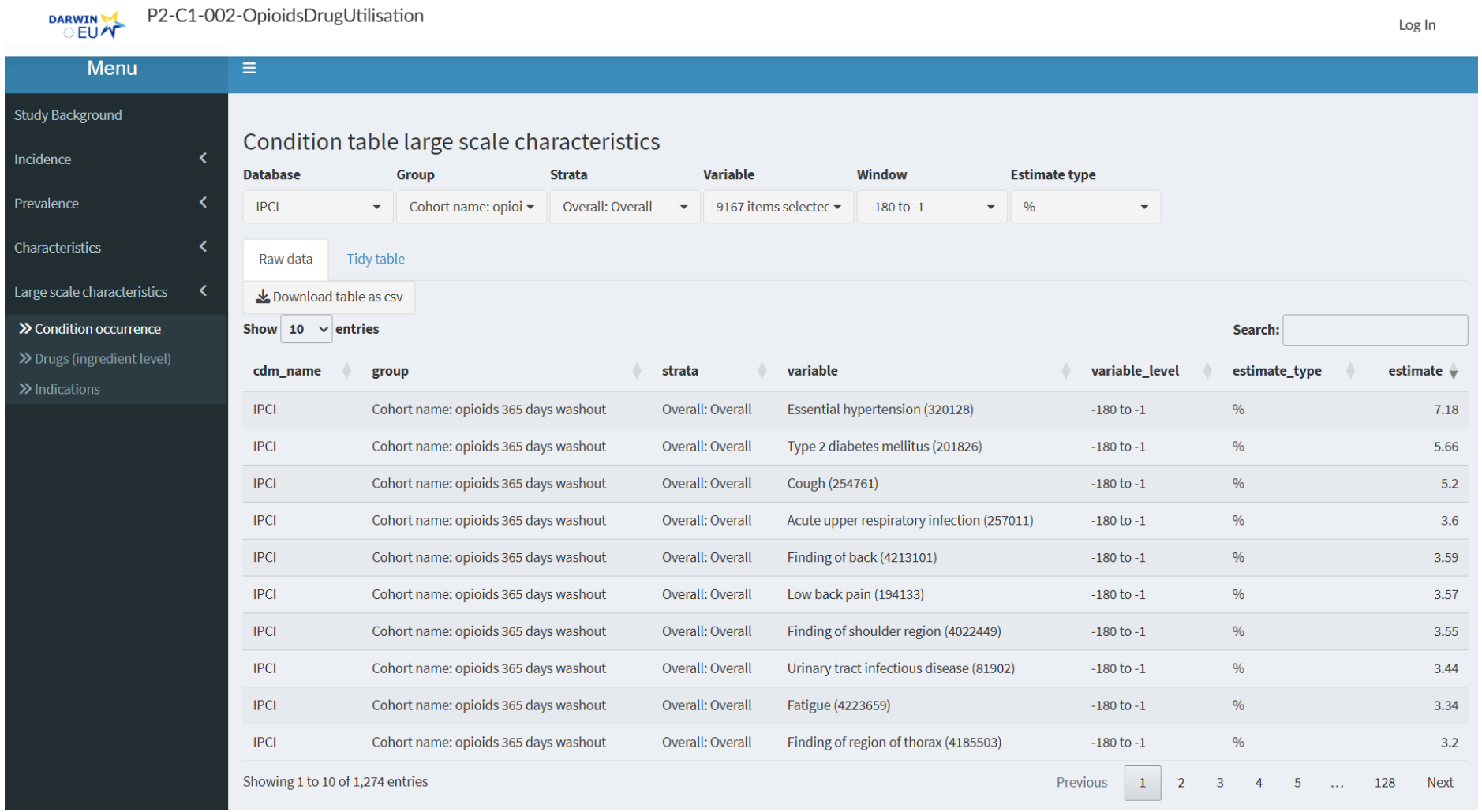
*Most frequent conditions recoded in 7 days before and on the day of treatment start

Treatment duration

	SIDIAP	IPCI	IQVIA DA Germany	IQVIA LPD Belgium	CHUBX
All Opioids	**11 [7 - 31]**	**10 [7 - 15]**	**20 [7 - 30]**	**9 [5 - 25]**	**2 [1 - 5]**
Codeine	7 [6 - 11]	10 [8 - 15]	8 [1 - 20]	7 [4 - 20]	3 [1 - 6]
Tramadol	21 [10 - 61]	10 [8 - 17]	15 [7 - 25]	20 [10 - 34]	2 [1 - 4]
Hydromorphone	81 [31 - 260]	28 [14 - 52]	50 [25 - 76]	30 [15 - 34]	6 [3 - 10]
Fentanyl	89 [31 - 225]	23 [14 - 50]	30 [30 - 60]	10 [5 - 30]	4 [1 - 9]
Morphine	33 [11 - 91]	15 [7 - 34]	13 [4 - 30]	15 [7 - 56]	1 [1 - 3]
Oxycodone	69 [29 - 175]	12 [6 - 24]	25 [20 - 50]	28 [9 - 30]	3 [1 - 8]

*median (q25 – q75) in days

More results in shiny web-application



Summary

- Prevalence of opioid use largely stable over the last decade
- Decrease in new opioid prescriptions in many European countries
- Opioid use highest among older adults.
- Most common indications: Respiratory conditions and pain-related conditions
- Treatment duration varied greatly by setting and opioid substances

Thank you very much
Study team,
Data partners,
EMA colleagues!

Thank you for your attention!!

DARWIN EU®- Treatments of multiple myeloma in Europe from 2012-2022: a population-based network cohort study

Talita Duarte Salles

Erasmus MC, The Netherlands

DARWIN EU

Coordination Centre

DARWIN EU® - Multiple myeloma: patient characterisation, treatments and survival in the period 2012-2022

Talita Duarte-Salles, Department of Medical Informatics, EMC Rotterdam, The Netherlands

OHDSI Europe Symposium - 2024

Disclosure

This presentation represents the views of the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the European Medicines Agency or the European Medicines Regulatory Network.

Rationale

- Multiple myeloma is a plasma cell malignancy which represents from 1-1.8% of all cancers and nearly 10% of all hematological malignancies.

- Survival rates have improved in the past decades due to the better management of the disease and the development of new medicines. However, still only 10%-15% of patients achieve or exceed expected survival compared with the matched general population.

- The rarity of multiple myeloma makes it challenging to have a clear picture across Europe of the characteristics of these patients at the time of diagnosis, the different therapies they receive and their overall survival.

Objectives

1. To describe demographic and clinical characteristics of patients with multiple myeloma at the time of diagnosis.

2. To describe multiple myeloma treatments and treatment sequences.

3. To estimate the overall survival of incident multiple myeloma patients during the study period (2012-2022).

Methods

Study design: Cohort study

Study population: all individuals with a first diagnosis of multiple myeloma between 2012 and 2022 (no prior history of cancer) ->3 cohorts were created

Data sources:

- IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
- Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain
- Institut Municipal d'Assistència Sanitària Information System (IMASIS), Spain
- Estonian Biobank, Estonia
- Clinical Data Warehouse of Bordeaux University Hospital (CDWBordeaux), France
- Netherlands Cancer Registry (NCR), The Netherlands

Methods – Data analyses

Large-scale patient-level characterisation – number and % of all comorbidities and medications recorded in different time periods (anytime –and up to 365 days before index date, 365 to 31 days before index date, for 30 to 1 day before index date, and at index date).

Cancer treatments - the number and % of patients receiving each of a pre-specified list of multiple myeloma treatments (at index date, 1 to 30, 1 to 90, and 1 to 365 days post index date).

Survival - calculated using data on time at risk of death from any cause and the Kaplan-Meier (KM) method. Results are reported as plots of the estimated survival curves and the estimated probability of survival at 1, 3, and 5 years.

Results were reported by database, overall and stratified by age and sex, and study period.

R-packages: CohortDiagnostics, PatientProfiles, TreatmentPatterns, and CohortSurvival.

Study population

	IQVIA DA Germany	SIDIAP	IMASIS	EBB	CWDBordeaux	NCR
Database population	41,974,403	8,265,343	1,051,862	209,457	2,371,226	2,383,827
with a diagnosis of multiple myeloma identified in the database between 01/01/2012 and 31/12/2022	14,218	4,687	386	182	1,930	13,579
without a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of multiple myeloma	12,360	3,993	329	111	1,7811	11,745
with at least 365 days of prior history available before date of multiple myeloma diagnosis (**Cohort 1**)	6,080	3,895	254	111	867	-
with a minimum follow-up time of 30 days (**Cohort 2**)	-	-	275	107	1,587	11,289
with a minimum of 1 year of potential follow-up time (**Cohort 3**)	-	3,558	301	90	1,639	11,745

Study population – Demographic characteristics

	CDWBordeaux	IQVIA DA Germany	EBB	IMASIS	NCR	SIDIAP
Number	1,781	12,360	111	329	11,745	3,993
Age, median, IQR	67 [59 - 76]	71 [61 - 78]	66 [57 - 73]	75 [64 - 83]	70 [62 - 77]	71 [59 - 79]
Age group, N (%)						
0 to 17	<5	19 (0%)	<5	<5	<5	101 (3%)
18 to 44	51 (3%)	412 (3%)	8 (7%)	12 (4%)	227 (2%)	226 (6%)
45 to 59	428 (24%)	2,192 (18%)	30 (27%)	34 (10%)	2,069 (18%)	687 (17%)
60 to 69	559 (31%)	3,015 (24%)	27 (24%)	70 (21%)	3,346 (28%)	878 (22%)
>=70	760 (42%)	6,722 (54%)	46 (41%)	210 (64%)	6,103 (52%)	2,101 (53%)
Sex, N (%)						
Female	823 (46%)	6,017 (49%)	65 (59%)	164 (50%)	4,918 (42%)	2,043 (51%)
Male	976 (54%)	6,332 (51%)	46 (41%)	165 (50%)	6,827 (58%)	1,950 (49%)

Study population – Large-scale characterisation

	IQVIA DA Germany	SIDIAP	IMASIS	EBB	CWDBordeaux	NCR
Database population	41,974,403	8,265,343	1,051,862	209,457	2,371,226	2,383,827
with a diagnosis of multiple myeloma identified in the database between 01/01/2012 and 31/12/2022	14,218	4,687	386	182	1,930	13,579
without a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of multiple myeloma	12,360	3,993	329	111	1,7811	11,745
with at least 365 days of prior history available before date of multiple myeloma diagnosis (**Cohort 1**)	6,080	3,895	254	111	867	-
with a minimum follow-up time of 30 days (**Cohort 2**)			275	107	1,587	11,289
with a minimum of 1 year of potential follow-up time (**Cohort 3**)	-	3,558	301	90	1,639	11,745

Results – Large-scale characterisation – Comorbidities

Comorbidity	CDWBordeaux (n=3895)	EBB (n=107)	IQVIA DA Germany (n=6080)	IMASIS (n=254)	SIDIAP (n=3895)
Hypertension	309 (35.44%)	65 (58.56%)	2898 (47.66%)	116 (45.67%)	1051 (26.98%)
Osteoarthritis	39 (4.47%)	65 (58.56%)	1998 (32.86%)	52 (20.47%)	1073 (27.55%)
Hyperlipidemia	94 (10.78%)	26 (23.42%)	1538 (25.3%)	77 (30.31%)	544 (13.97%)
Renal impairment	183 (20.99%)	26 (23.42%)	868 (14.28%)	86 (33.86%)	698 (17.92%)
Diabetes mellitus	95 (10.89%)	16 (14.41%)	1164 (19.14%)	32 (12.6%)	446 (11.45%)
Urinary tract infection	32 (3.67%)	19 (17.12%)	739 (12.15%)	47 (18.5%)	765 (19.64%)
Depressive disorder	50 (5.73%)	34 (30.63%)	1027 (16.89%)	28 (11.02%)	434 (11.14%)
Obesity	11 (1.26%)	16 (14.41%)	681 (11.2%)	23 (9.06%)	706 (18.13%)
Anxiety	89 (10.21%)	32 (28.83%)	625 (10.28%)	10 (3.94%)	659 (16.92%)
Pneumonia	71 (8.14%)	24 (21.62%)	420 (6.91%)	36 (14.17%)	414 (10.63%)
COPD	38 (4.36%)	16 (14.41%)	645 (10.61%)	28 (11.02%)	213 (5.47%)
Asthma	24 (2.75%)	24 (21.62%)	527 (8.67%)	14 (5.51%)	144 (3.7%)

* - Displayed conditions are those with a proportion > 5% and a count >5 in each individual database.

Results – Large-scale characterisation – Comorbidities

Comorbidity	CDWBordeaux (n=3895)	EBB (n=107)	IQVIA DA Germany (n=6080)	IMASIS (n=254)	SIDIAP (n=3895)
Hypertension	309 (35.44%)	65 (58.56%)	2898 (47.66%)	116 (45.67%)	1051 (26.98%)
Osteoarthritis	39 (4.47%)	65 (58.56%)	1998 (32.86%)	52 (20.47%)	1073 (27.55%)
Hyperlipidemia	94 (10.78%)	26 (23.42%)	1538 (25.3%)	77 (30.31%)	544 (13.97%)
Renal impairment	183 (20.99%)	26 (23.42%)	868 (14.28%)	86 (33.86%)	698 (17.92%)
Diabetes mellitus	95 (10.89%)	16 (14.41%)	1164 (19.14%)	32 (12.6%)	446 (11.45%)
Urinary tract infection	32 (3.67%)	19 (17.12%)	739 (12.15%)	47 (18.5%)	765 (19.64%)
Depressive disorder	50 (5.73%)	34 (30.63%)	1027 (16.89%)	28 (11.02%)	434 (11.14%)
Obesity	11 (1.26%)	16 (14.41%)	681 (11.2%)	23 (9.06%)	706 (18.13%)
Anxiety	89 (10.21%)	32 (28.83%)	625 (10.28%)	10 (3.94%)	659 (16.92%)
Pneumonia	71 (8.14%)	24 (21.62%)	420 (6.91%)	36 (14.17%)	414 (10.63%)
COPD	38 (4.36%)	16 (14.41%)	645 (10.61%)	28 (11.02%)	213 (5.47%)
Asthma	24 (2.75%)	24 (21.62%)	527 (8.67%)	14 (5.51%)	144 (3.7%)

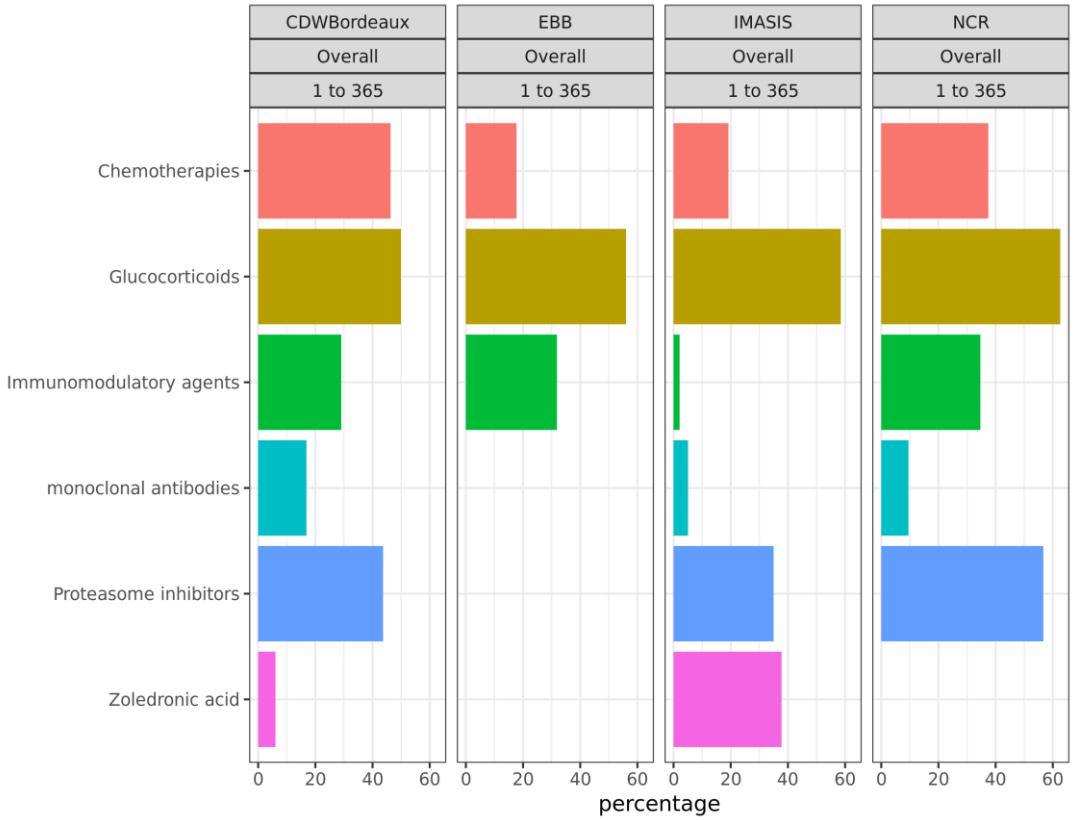
* - Displayed conditions are those with a proportion > 5% and a count >5 in each individual database.

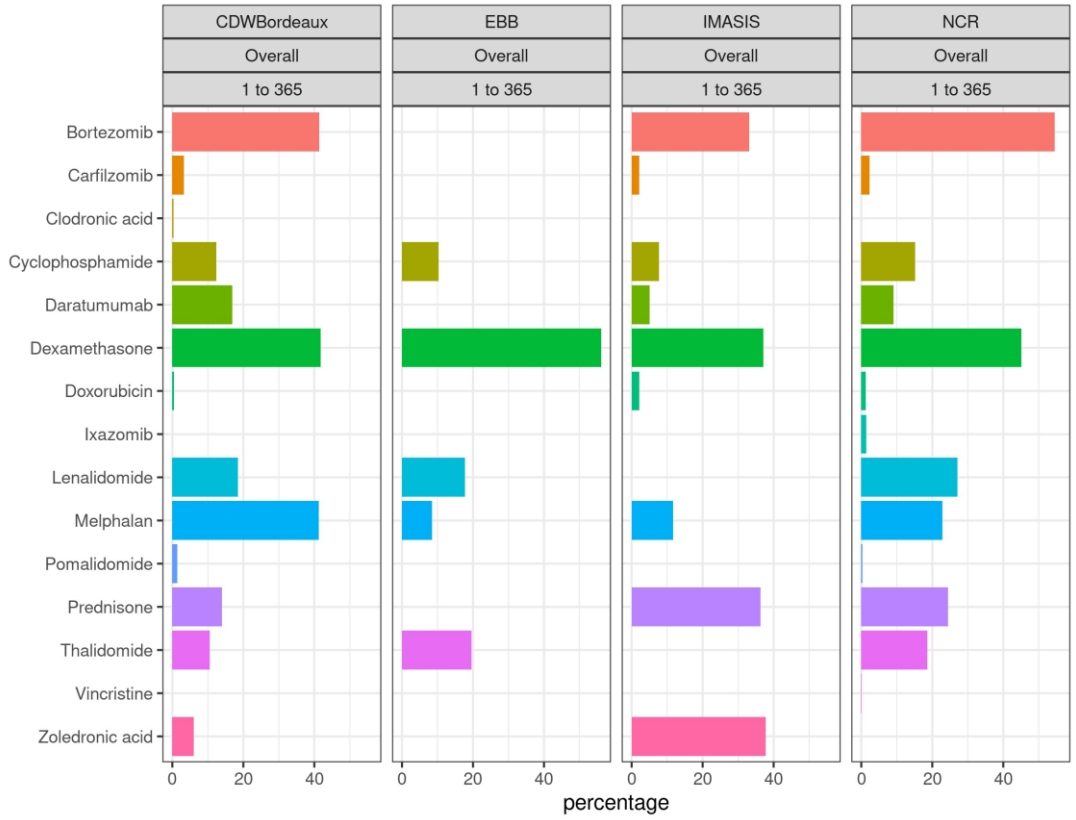
- No differences by sex
- By age group
  - Younger age groups (18-59 years) also included anxiety, depression, and asthma
  - Among those aged >=70 years, renal impairment was one of the most frequent co-morbidities

Study population – Cancer Treatments

	IQVIA DA Germany	SIDIAP	IMASIS	EBB	CWDBordeaux	NCR
Database population	41,974,403	8,265,343	1,051,862	209,457	2,371,226	2,383,827
with a diagnosis of multiple myeloma identified in the database between 01/01/2012 and 31/12/2022	14,218	4,687	386	182	1,930	13,579
without a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of multiple myeloma	12,360	3,993	329	111	1,7811	11,745
with at least 365 days of prior history available before date of multiple myeloma diagnosis (**Cohort 1**)	6,080	3,895	254	111	867	-
with a minimum follow-up time of 30 days (**Cohort 2**)	-	-	275	107	1,587	11,289
with a minimum of 1 year of potential follow-up time (**Cohort 3**)	-	3,558	301	90	1,639	11,745

Results – Cancer Treatments





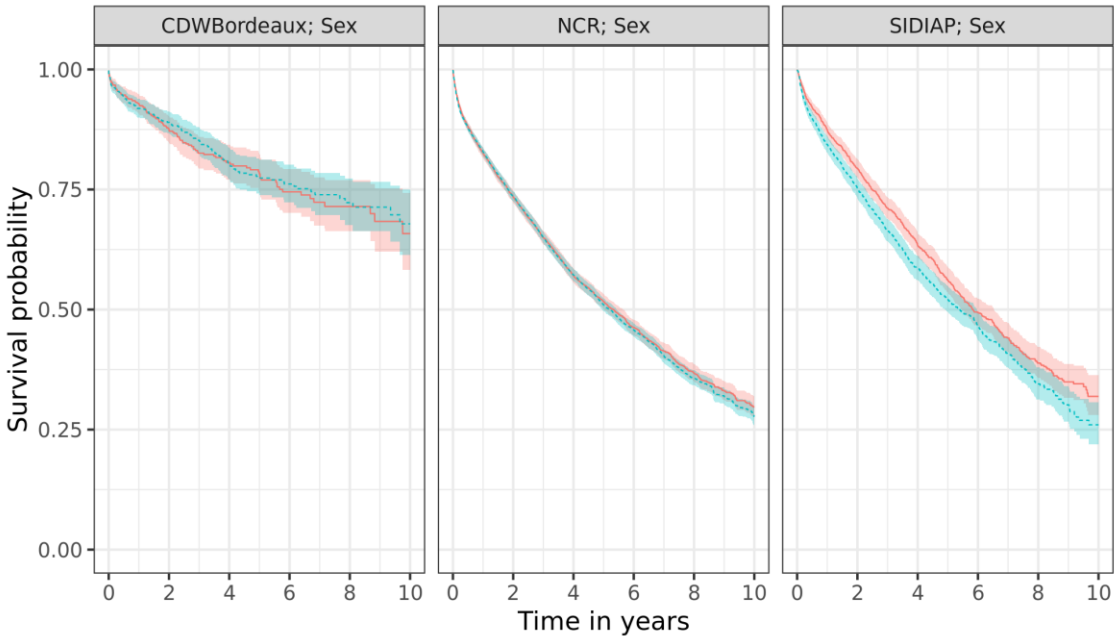
Study population - Survival

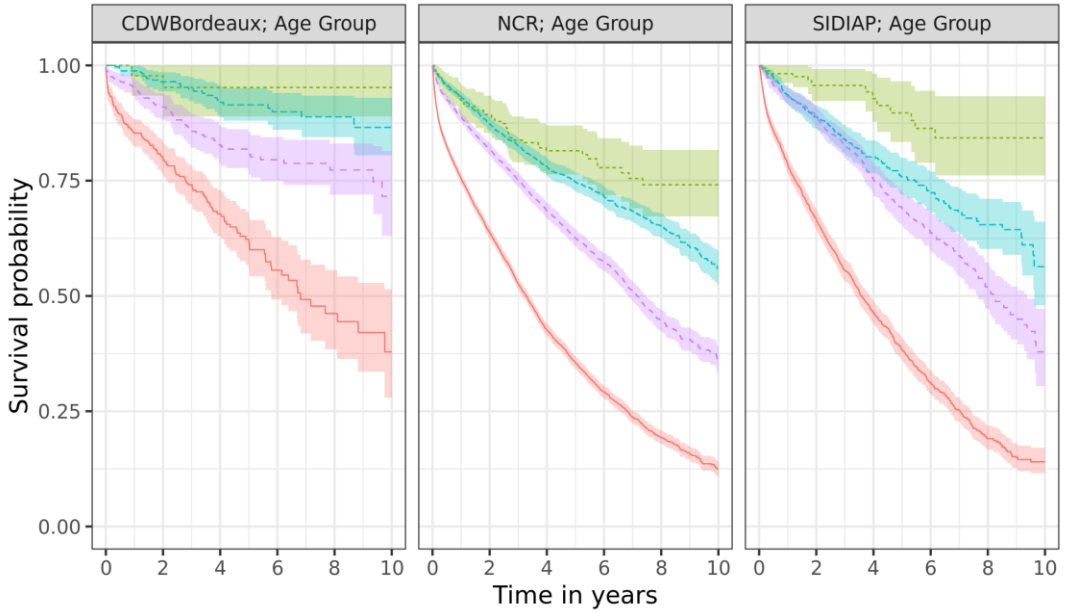
	IQVIA DA Germany	SIDIAP	IMASIS	EBB	CWDBordeaux	NCR
Database population	41,974,403	8,265,343	1,051,862	209,457	2,371,226	2,383,827
with a diagnosis of multiple myeloma identified in the database between 01/01/2012 and 31/12/2022	14,218	4,687	386	182	1,930	13,579
without a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of multiple myeloma	12,360	3,993	329	111	1,7811	11,745
with at least 365 days of prior history available before date of multiple myeloma diagnosis (**Cohort 1**)	6,080	3,895	254	111	867	-
with a minimum follow-up time of 30 days (**Cohort 2**)	-	-	275	107	1,587	11,289
with a minimum of 1 year of potential follow-up time (**Cohort 3**)	-	3,558	301	90	1,639	11,745

Results – Overall Survival

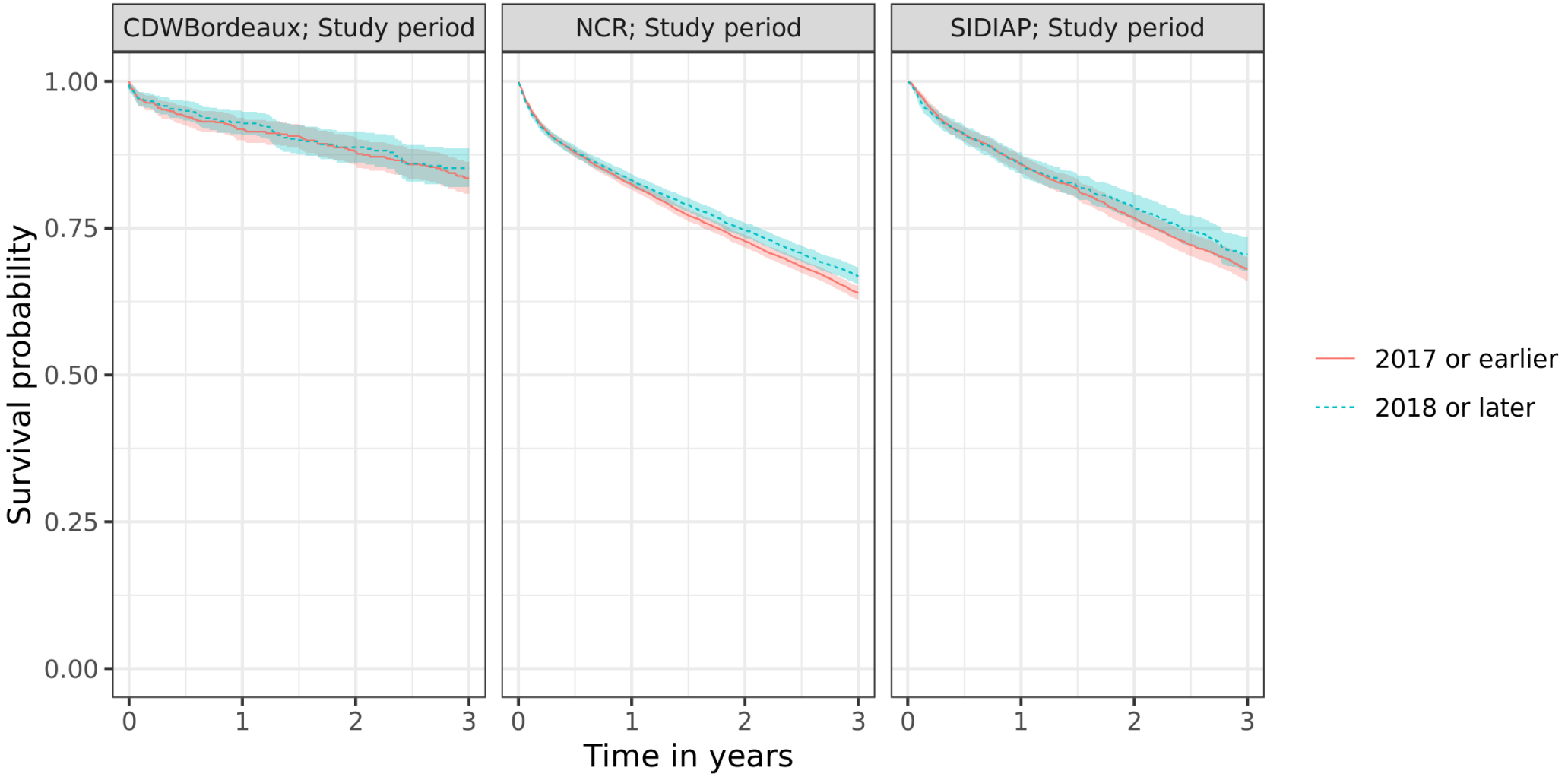
Database	N start	Events	Restricted mean survival (years)	1 year survival	3 year survival	5 year survival
CDWBordeaux	1644	262	7.96	0.92 (0.91 to 0.94)	0.84 (0.82 to 0.86)	0.78 (0.75 to 0.81)
EBB	90	26	6.96	0.92 (0.87 to 0.98)	0.79 (0.71 to 0.89)	0.76 (0.67 to 0.86)
IMASIS	301	114	5.16	0.79 (0.74 to 0.84)	0.62 (0.56 to 0.69)	0.49 (0.42 to 0.58)
NCR	11745	5964	5.47	0.83 (0.82 to 0.83)	0.65 (0.64 to 0.66)	0.51 (0.5 to 0.52)
SIDIAP	3558	1615	5.70	0.86 (0.85 to 0.87)	0.69 (0.67 to 0.7)	0.54 (0.52 to 0.56)

Results – Survival by Sex and Age





Results – Survival by Study Period



Conclusions

- We provided a characterisation of 30,319 patients newly diagnosed with multiple myeloma in between 2012 and 2022 across Europe.
- The most frequently used treatments were glucocorticoids, followed by proteasome inhibitors, chemotherapies and immunomodulatory agents.
- Immunomodulatory agents and proteasome inhibitors were used less in older individuals.
- Survival probabilities varied substantially by age groups, with a decrease in survival observed with older age.

Acknowledgements

Healthcare professionals and patients

Data Partners

Names	Organisation
James Brash	IQVIA - DA Germany
Jasmine Gratton	IQVIA - DA Germany
Dina Vojinovic	IQVIA - DA Germany
Núria Mercadé	IDIAPJGol - SIDIAP
Miguel-Angel Mayer	PSMAR - IMASIS
Angela Leis	PSMAR - IMASIS
Juan Manuel Ramirez	PSMAR - IMASIS
Raivo Kolde	University Tartu - Estonian Biobank
Romain Griffier	University of Bordeaux - CDWBordeaux
Peter Prinsen	Netherlands Cancer Registry - NCR

Study team

Names	Organisation
Daniel Prieto-Alhambra	Erasmus MC/University of Oxford
Katia Verhamme	Erasmus MC
Maarten van Kessel	Erasmus MC
Ross Williams	Erasmus MC
Edward Burn	University of Oxford

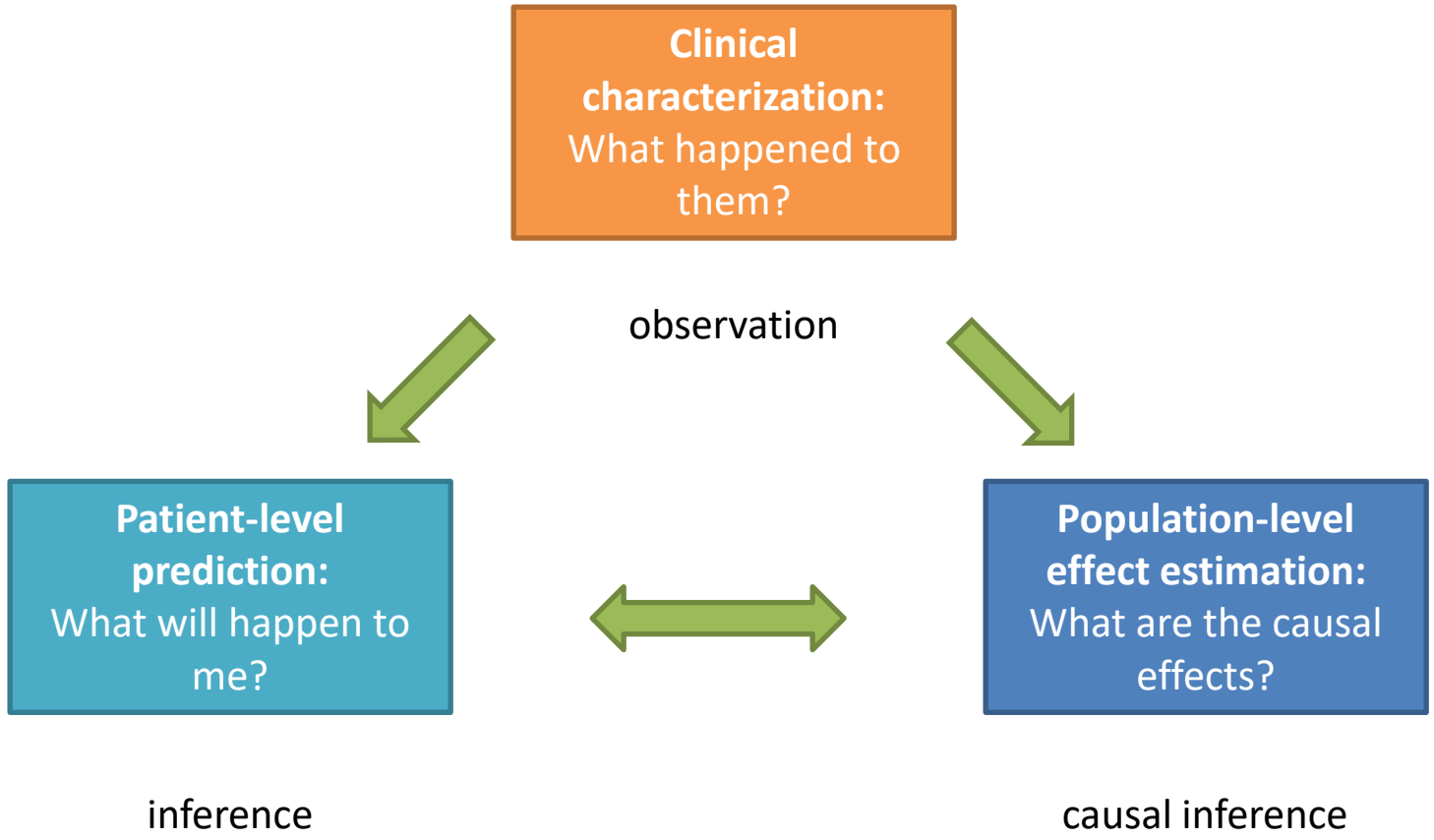
What evidence are we going to showcase at OHDSI Europe in 2025?

Patrick Ryan PhD

Johnson & Johnson

Columbia University Irving Medical Center

Complementary evidence to inform the patient journey

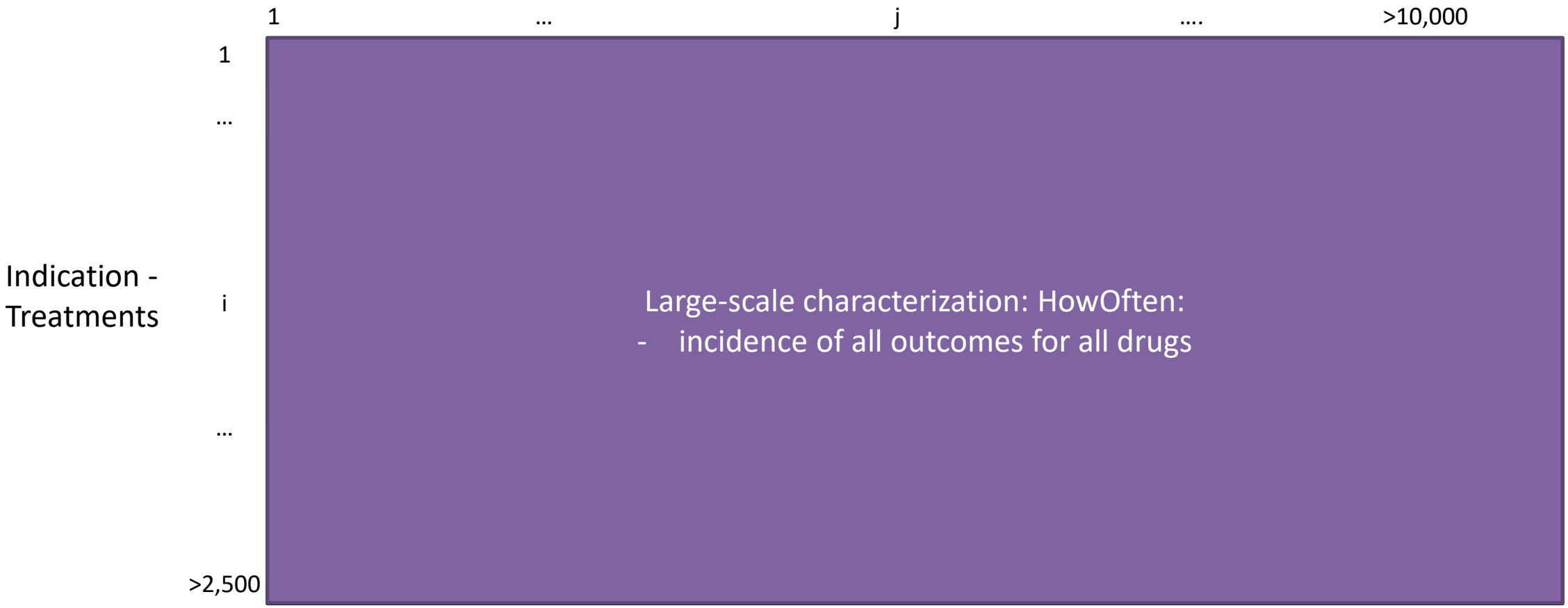


Standardized questions → Standardized analytics → Standardized evidence

Analytic use case	Type	Structure	Example
Clinical characterization	**Disease Natural History**	Amongst patients who are diagnosed with **<insert your favorite disease>**, what are the patient's characteristics from their medical history?	Amongst patients with **rheumatoid arthritis**, what are their demographics (age, gender), prior conditions, medications, and health service utilization behaviors?
	Treatment utilization	Amongst patients who have **<insert your favorite disease>**, which treatments were patients exposed to amongst **<list of treatments for disease>** and in which sequence?	Amongst patients with **depression**, which treatments were patients exposed to **SSRI, SNRI, TCA, bupropion, esketamine** and in which sequence?
	Outcome incidence	Amongst patients who are new users of **<insert your favorite drug>,** how many patients experienced **<insert your favorite known adverse event from the drug profile>** within **<time horizon following exposure start>**?	Amongst patients who are new users of **methylphenidate,** how many patients experienced **psychosis** within **1 year of initiating treatment**?
Population-level effect estimation	**Safety surveillance**	Does exposure to **<insert your favorite drug>** increase the risk of experiencing **<insert an adverse event>** within **<time horizon following exposure start>**?	Does exposure to **ACE inhibitor** increase the risk of experiencing **Angioedema** within **1 month after exposure start**?
	Comparative effectiveness	Does exposure to **<insert your favorite drug>** have a different risk of experiencing **<insert any outcome (safety or benefit) >** within **<time horizon following exposure start>**, relative to **<insert your comparator treatment>**?	Does exposure to **ACE inhibitor** have a different risk of experiencing **acute myocardial infarction** while **on treatment**, relative to **thiazide diuretic**?
Patient level prediction	**Disease onset and progression**	For a given patient who is diagnosed with **<insert your favorite disease>**, what is the probability that they will go on to have **<another disease or related complication>** within **<time horizon from diagnosis>?**	For a given patient who is **newly diagnosed with atrial fibrillation**, what is the probability that they will go onto to have **ischemic stroke** in **next 3 years**?
	Treatment response	For a given patient who is a new user of **<insert your favorite chronically-used drug>**, what is the probability that they will **<insert desired effect>** in **<time window>**?	For a given patient **with T2DM who start on metformin** , what is the probability that they will **maintain HbA1C<6.5%** after **3 years**?
	Treatment safety	For a given patient who is a new user of **<insert your favorite drug>,** what is the probability that they will experience **<insert adverse event >** within **<time horizon following exposure>**?	For a given patients who is a **new user of warfarin**, what is the probability that they will have **GI bleed** in **1 year**?

Where in the universe of real world evidence opportunities should we work together?

RWE “all-by-all” matrix



When poll is active respond at **PollEv.com/patrickryan800**

What evidence should we generate together and showcase at OHDSI Europe in 2025?


EUROPEAN OHDSI
SYMPOSIUM
EUROPE
Scaling up reliable evidence
across Europe
June 1 - 3 2024
Rotterdam

Closing Remarks

Peter R. Rijnbeek

Chair Department of Medical Informatics

Erasmus MC, The Netherlands

ODYSSEUS' TEN-YEAR JOURNEY HOME

(POSSIBLE ROUTE ACCORDING TO PETER STRUCK, UNIVERSITY OF PENNSYLVANIA)

WORLD HISTORY ENCYCLOPEDIA

Characters from Odyssey to OHDSI

- Achilles
- Aegis
- Aeolus
- Andromeda
- Aphrodite
- Apollo
- Arachne
- Ares
- Argos
- Artemis
- Athena
- Atlas
- Broadsea
- Calypso
- Castor
- Centaur
- Charybdis
- Chronos
- Circe
- Cyclops
- Eunomia
- Eumaeus
- Hades
- Helios
- Hera
- Heracles
- Hermes
- Hestia
- Homer
- Hydra
- Icarius
- Koios
- Laertes
- Nostos
- Olympus
- Penelope
- Perseus
- Strategus
- Sisyphus
- Scylla
- Tantalus
- Themis
- Ulysses
- ???

What's Next: OHDSI Workgroups

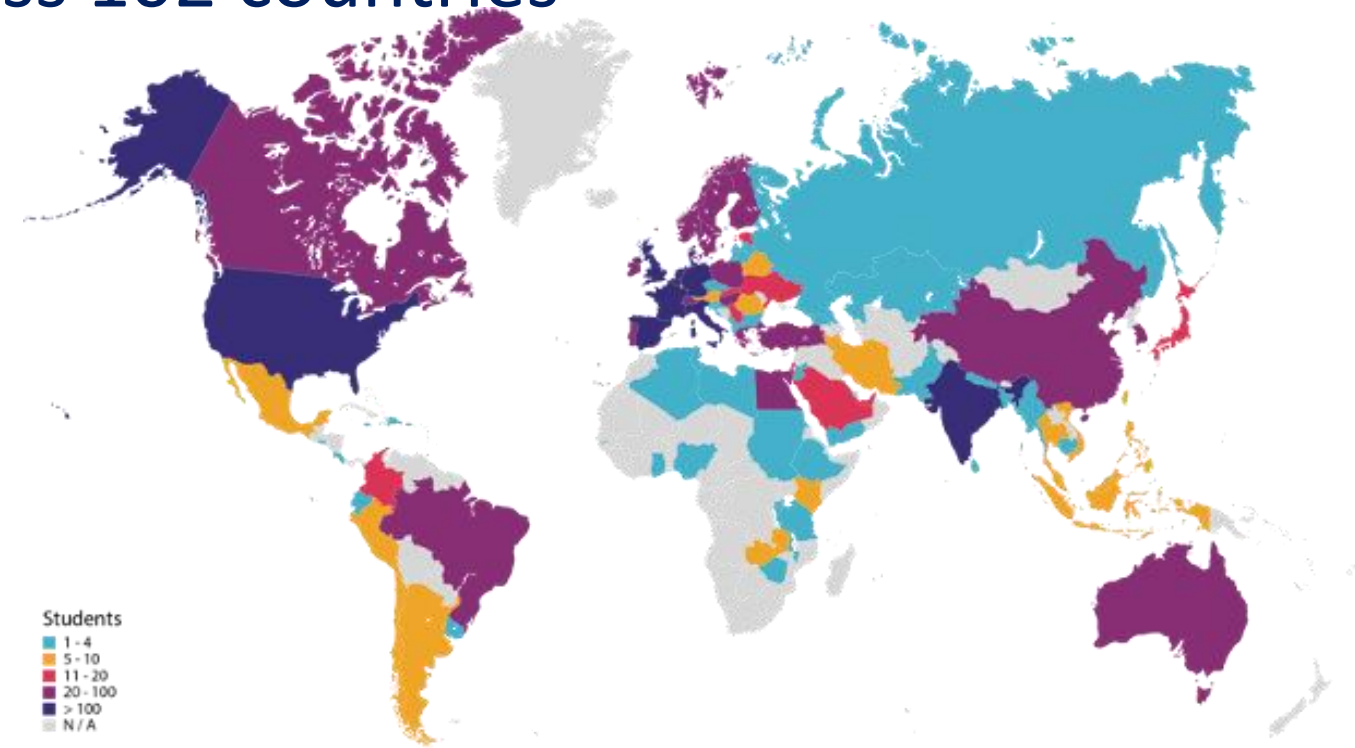
Upcoming Community Calls

Date	Topic
April 9	April Olympians Update | Presentation: Vocabulary for ETL
April 16	April Olympians Update | Presentation: Tools to Evaluate ETL
April 23	April Olympians Update | Presentation: Themis & CDM Process Overview
April 30	April Olympians Update | Presentation: What We Achieved & How You Can Use It
May 7	DevCon 2024 Review
May 14	10-Minute Tutorials
May 21	Open Studies in the OHDSI Community
May 28	Collaborator Showcase Brainstorm
June 4	NO CALL – EUROPEAN SYMPOSIUM
June 11	European Symposium Review
June 18	Application of LLMs In Evidence Generation Process
June 25	Recent OHDSI Publications

EHDEN Academy

- Free online-educational resource
- Publicly available since March 27, 2020
- 5,256 active learners across 102 countries
- 24 course offerings

https://academy.ehden.eu



As of June 1, 2024

#OHDSI2024 Registration Is Open!

Registration is OPEN for the 2024 OHDSI Global Symposium, which will be held **Oct. 22-24** at the **Hyatt Regency Hotel in New Brunswick, N.J., USA**.

Tuesday: Tutorials
Wednesday: Plenary/Showcase
Thursday: Workgroup Activities

ohdsi.org/OHDSI2024

This is the Moment to increase our Impact

- We are in a perfect storm to impact better health decisions and better care.
- In Europe we have a strong focus on Findable Interoperable Accessible Reusable Data -> European Health Data Space
- We have the uptake and capacity in place in Europe to further improve our data model and analytics together as one community

This is our moment to:

- publish many methodological publications to improve or establish best practices;
- make major steps in improving semantic interoperability;
- sustain and maintain the largest federated network in Europe;
- generate reliable evidence in Europe and at a global scale.

A fantastic journey to be on together!!

EUROPEAN OHDSI SYMPOSIUM


EUROPEAN OHDSI
SYMPOSIUM
EUROPE
Scaling up reliable evidence
across Europe
June 1 - 3 2024
Rotterdam

EUROPEAN OHDSI SYMPOSIUM


EUROPEAN OHDSI
SYMPOSIUM
EUROPE
Let’s make a group picture!
June 1 - 3 2024
Rotterdam