Update on RWE including DARWIN EU®

PCWP and HCPWP plenary - 28 June 2023

Presented by Andrej Segec, Kelly Plueschke, Denise Umuhire
Data Analytics and Methods Taskforce – Real World Evidence

Towards delivering the 2025 RWE vision

A tale with three pathways…

Countdown to 2025

Enabling use

EMA studies using in-house databases

- **Primary care** health records from the **France**, **Germany, UK, Italy, Spain** and **Romania.** Some data sources include data on specialist.

DARWIN EU®

- Coordination Centre launched February 2022
- Onboarded first **10 data partners**
- **First studies** finalised
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Studies procured through EMA FWCs

- New framework contract (FWC) since September 2021: services of **8 research organisations** and academic institutes
- Access to **wide network of data sources**: 59 data sources from 21 EU countries
- Ability to leverage external **scientific expertise**

Regulatory authorities also have access to national databases e.g., Nordic registries, SNDS, BIFAP, …

RWE report published, with infosheet

61
research topics

49	8	4
In-house	DARWIN EU	FWC

RWE needs

- the **needs** for RWE of CxMP and SAWP;
- the **ability** and **capacity** of the current RWE framework;
- the **usefulness** of the RWE provided.

Suitability of data sources

- the **suitability** of available **RWD sources** and **pathways**;
- the **methodological challenges** of data collection, study design and reporting.

Process for RWE studies

- receiving **study requests**;
- **proactively offering** and **conducting** RWE studies;
- identify **opportunities for improvements.**

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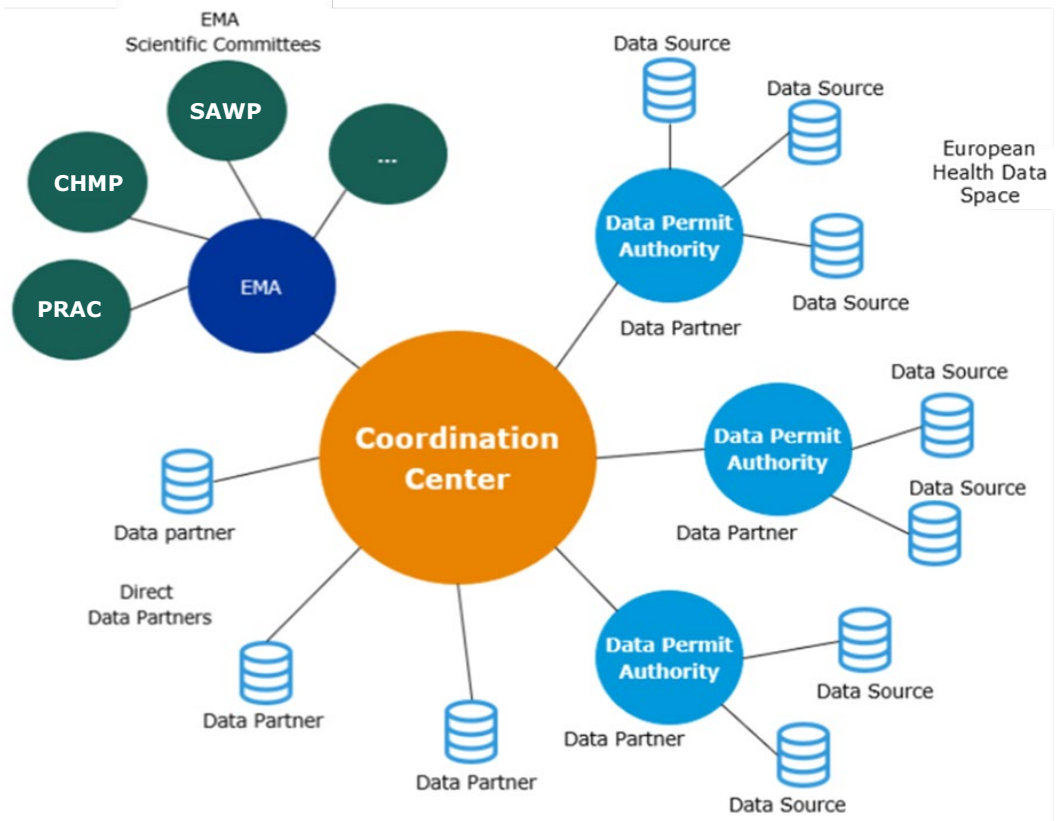
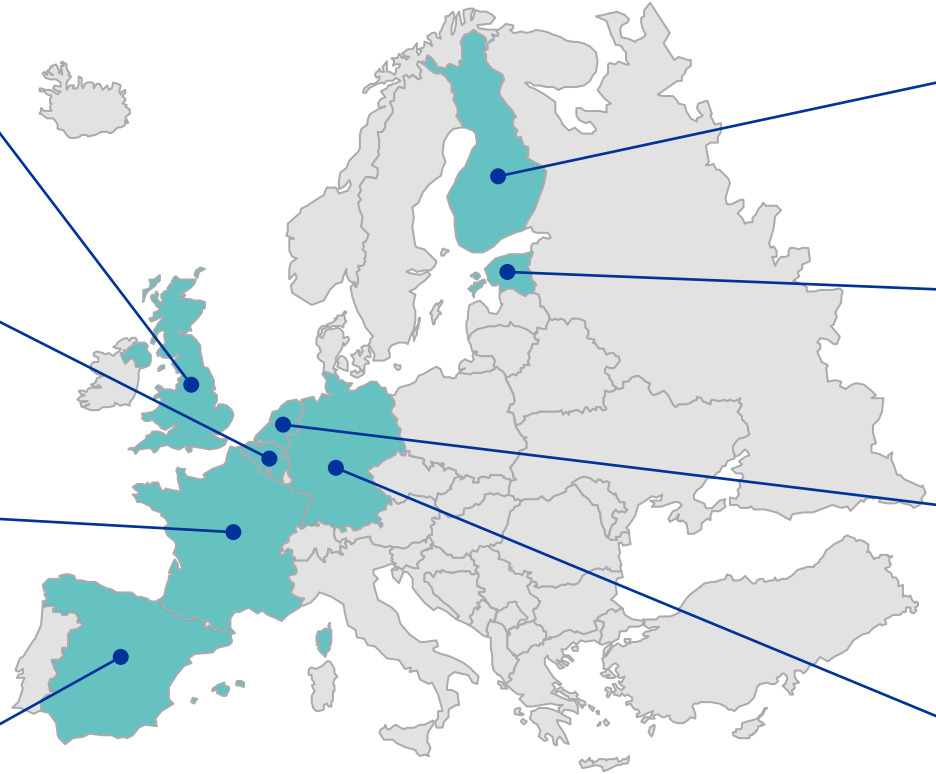
DARWIN EU® is a federated **network** of **data**, **expertise** and **services** that supports better decision-making throughout the product lifecycle by generating reliable **evidence from real world healthcare data**



FEDERATED NETWORK PRINCIPLES

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

Data Partners – Phase I



UK

1. Clinical Practice Research Datalink (CPRD GOLD)

Belgium

2. IQVIA Belgium Longitudinal Patient Data

France

3. Bordeaux University Hospital

Spain

4. IDIAPJGol
5. Parc Salut Mar Barcelona, Hospital del Mar (IMIM)

Finland

6. Auria Clinical Informatics at Hospital District of Southwest Finland (HDSF)

Estonia

7. University of Tartu (Biobank)

Netherlands

8. Integrated Primary Care Information
9. Netherlands Comprehensive Cancer Organisation

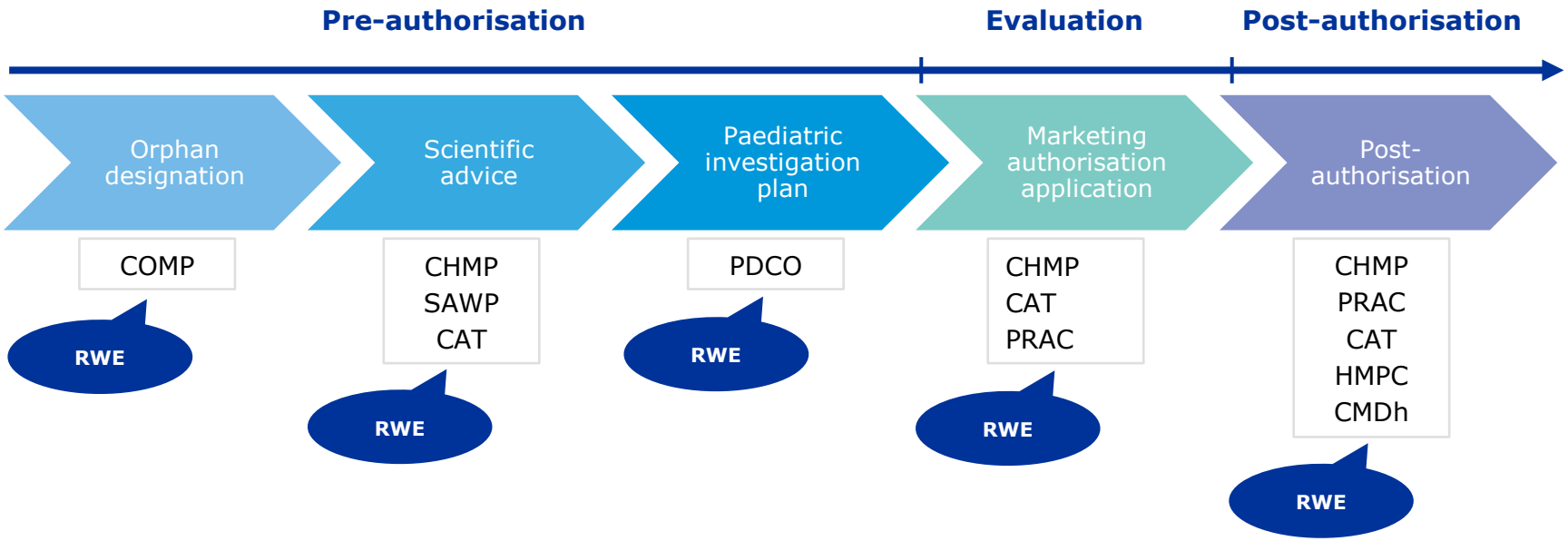
Germany

10. IQVIA Germany Disease Analyser

~26 million active patients

Currently selecting Phase II DPs after open call for expression of interest

RWE use across the medicinal product lifecycle



Milestones completed in 2023

- ✓ Phase II in progress, delivery on target, according to plan
- ✓ Focus on selection of further DPs and study conduct (various use cases)
- ✓ Establishment of analytical pipelines and codes

		Phase I	Phase II	Phase III	Option I	Option II
Studies	**Off the shelf**	2	6	30	60	60
	Routine repeated	1	6	30	60	60
	Complex study	1	4	12	24	24
	Very complex	0	0	0	1	1
Data Partners (total)		10	20	30	40	40

DARWIN EU 'ramping up quickly' with more partners coming on board

Regulatory News | 22 March 2023 | J

BASEL, Switzerland – DARWIN EU i
adherents as an increasing number
Arlett, head of the European Medici

EMA unveils first projects as data partners join DARWIN EU project

Two years ago, the EMA proposed a set of recommendations to unlock the potential of big data for public health, headlined by the creation of a platform to access and analyse healthcare data from across the bloc.

High Ambitions For EU DARWIN Pla
Delivery Of First RWE Studies

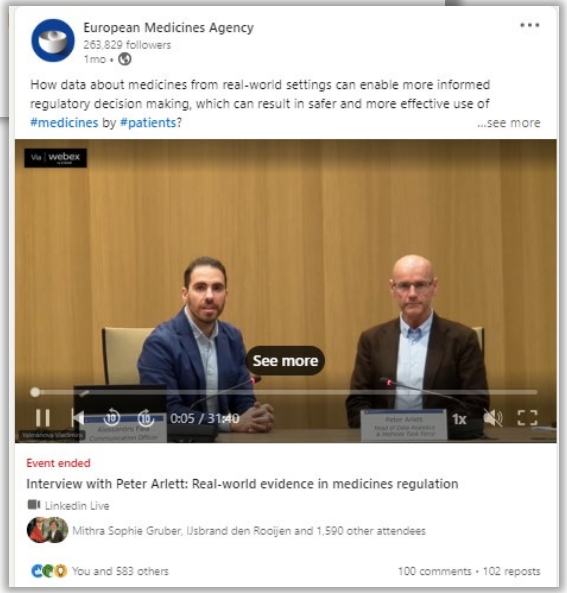
29 Mar 2023 | NEWS

by Vibha Sharma

@ScripRegVibha | vibha.sharma@informa.com

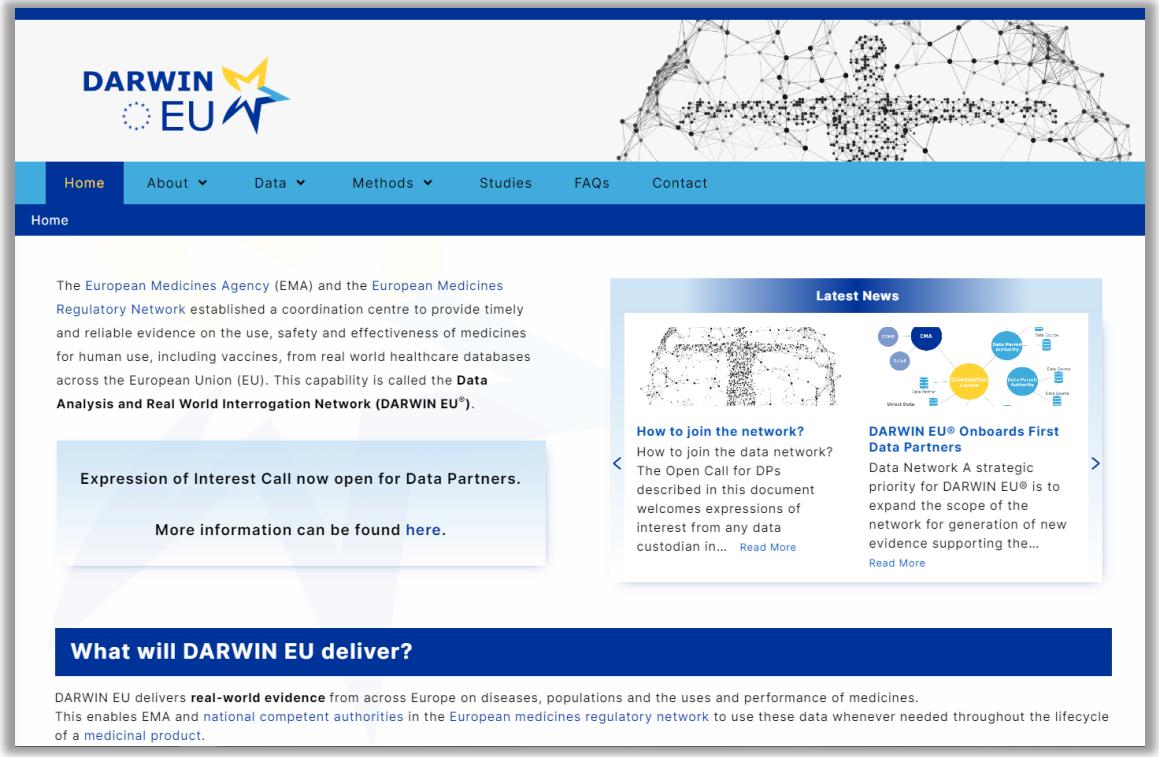
Executive Summary

Within one year of its establishment, DARWIN EU has started reap
regulators commissioning studies using real-world data to better u
and the uses and effects of medicines. The studies can be performed faster, cheaper and at
increased capacity.



DARWIN EU Coordination Centre website launched

www.darwin-eu.org



Catalogue of standard data analyses

Off-the-shelf studies

These are mainly characterisation questions that can be executed with a generic protocol. This includes disease epidemiology, for example the estimation of the prevalence, incidence of health outcomes in defined time periods and population groups, or drug utilization studies at the population or patient level.

- Patient-level characterisation
- Patient-level DUS analyses

Cohort of newly diagnosed patients or new users of a medicine followed over time. Studies used to characterise disease, patients or use of medicines

- Population-level DUS analyses
- Population-level descriptive epidemiology

Used for incidence/prevalence studies. All subjects in the database are eligible based on minimal inclusion criteria.

Catalogue of standard data analyses

Complex

These are studies requiring development or customisation of specific study designs, protocols, analytics, phenotypes. This includes studies on the safety and effectiveness of medicines and vaccines.

- Prevalent user active comparator cohort studies
- New user active comparator cohort

Studies comparing risk of health outcome in exposed vs unexposed cohorts

- Self-controlled case risk interval
- Self-controlled case series

Studies comparing risk of health outcome in exposed vs unexposed periods in cohort of cases

- Time series analyses and Difference-in-difference studies
- RMM effectiveness

Studies to assess the impact of restrictions in the use of medicines

Studies started in 2022 (year 1/ phase I)

Additional 16 studies to start in 2023 (Phase II) – including HTA/payers, ECDC, EHDS2 pilots

Off the Shelf	**Population level epidemiology** study on prevalence of **rare blood cancers** from 2010 EUPAS50800	NL, ES, UK, BE, DE	Support COMP in orphan designation decision making & useful as background rates for other committees
Off the Shelf	Patient level **drug utilization** study of **valproate-containing medicinal products** in women of childbearing potential from 2010 EUPAS50789	NL, ES, UK, BE, DE, FI	Assess the use of valproate after safety referral
Off the Shelf	Patient level **drug utilisation** study of **antibiotics** on the Watch list of the WHO AWaRe classification, 2010-2021 EUPAS103381	NL, FR, ES, DE, UK	Inform PRAC/CHMP decision making, AMR strategy
Complex	Background all-cause **mortality rates in patients with severe asthma aged ≥12 years** old EUPAS103936	NL, ES x2, UK, EE	Support CHMP post-authorisation inform future decision making

More detail in protocols + study reports in EU PAS Register

+shiny apps

Table of contents

DARWIN EU

Study Report for C1-003

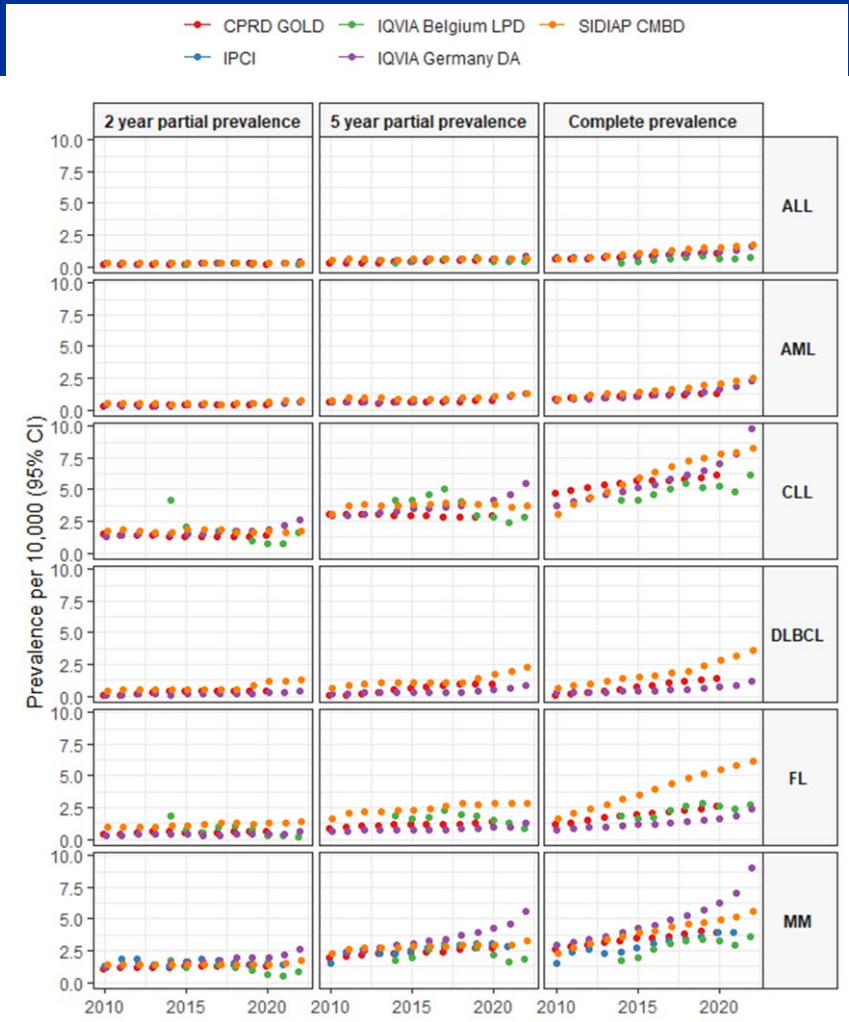
Author(s): Katia Verhamme, Maria de Ridder, Talita Duarte Salles, Dani Prieto Alhambra, Miguel-Angel Mayer, Romain Griffier

Version: v3.1

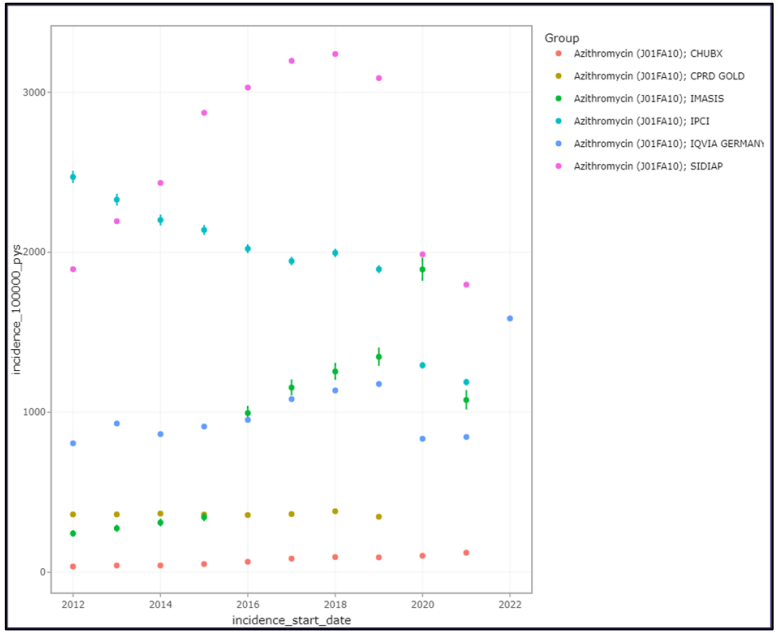
Dissemination level: Public

Document History

Version	Date	Description
V1.0	23/01/2023	First Version for EMA review
V2.0	06/02/2023	Second Version for EMA review
V3.0	15/02/2023	Final version incorporating EMA comments
V3.1	27/03/2023	Link to Shiny App added



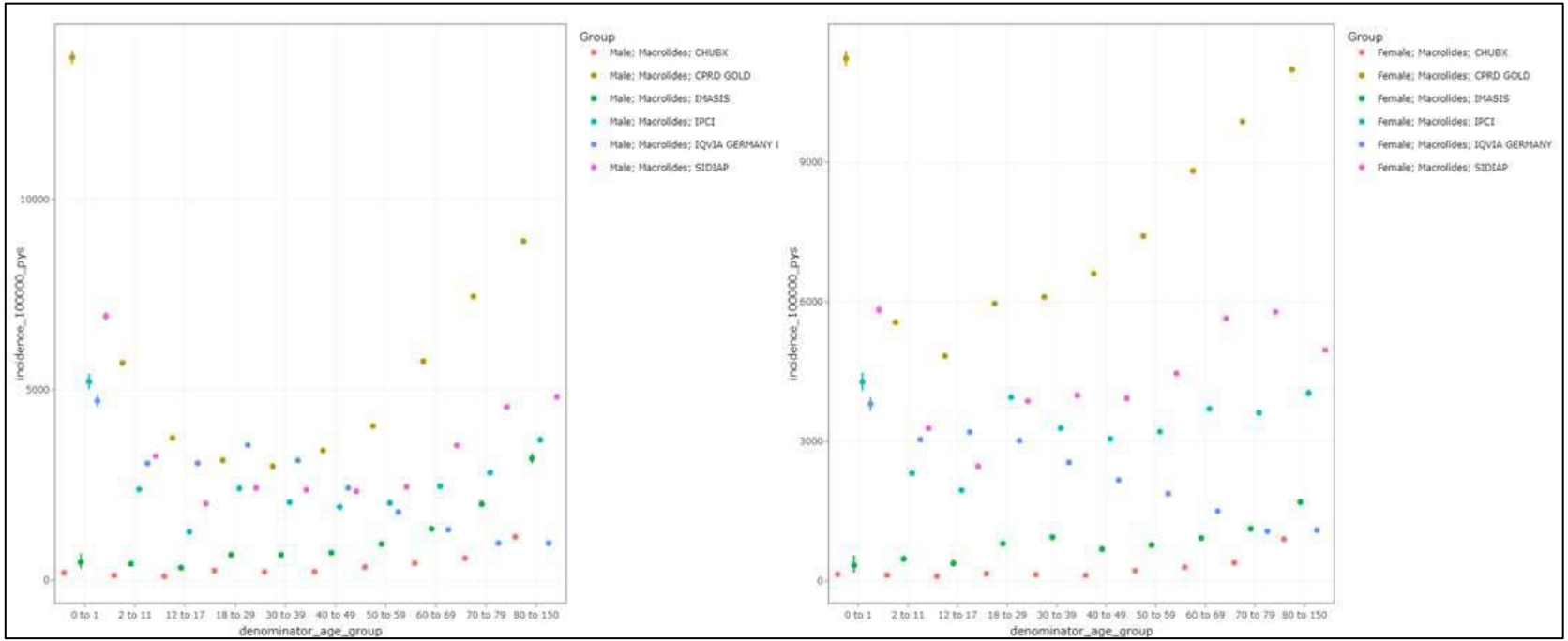
Incidence rates of azithromycin



Ref. EUPAS50800
and EUPAS103381

Macrolide (ATB group) use stratified by age/gender

See also shiny app: https://data-dev.darwin-eu.org/EUPAS103381/



EUPAS50789

New user valproate use incidence in women 12 to 55 yrs

Studies in progress (various stages)

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

CHMP
Complex

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

HTA/Payers
OTS

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

ECDC/VMP
Complex

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

CHMP
OTS

Naloxone use in treatment of opioid overdose.

CHMP
OTS

Erythomycin use as prokinetic

NCA
OTS

EHDS coagulopathy of COVID-19

EC/EHDS
Complex

Drug utilisation study of prescription **opioids**.

PRAC
OTS

OTS = off-the-shelf study

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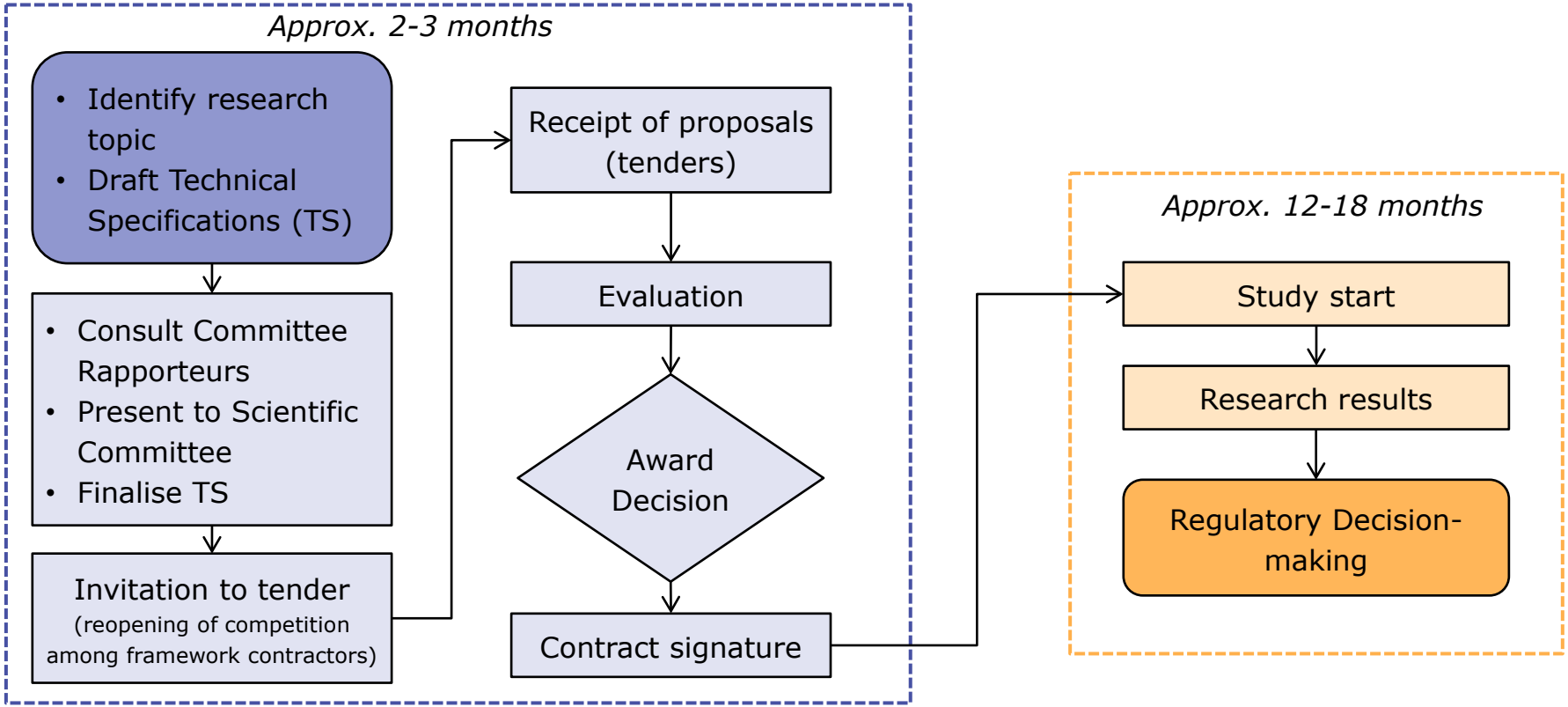
EMA-funded studies – the process

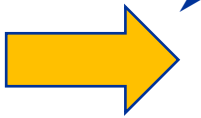


EMA funded study based on registry data in collaboration with Aetion and TREAT NMD

EMA priority topics on Registries for 2023/2024

Priority topics

- Leverage the existing CHMP guideline on registry-based studies (Oct 2021)
- Assess needs for further guidance on registries (Methodology Working Party)
- Better understand the barriers to data access and collaboration
- Promote data quality and discoverability
- SAWP qualification procedure on registries
- Multi-stakeholder workshop Q1 2024

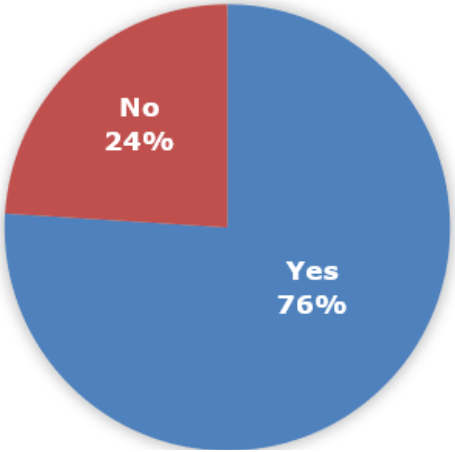


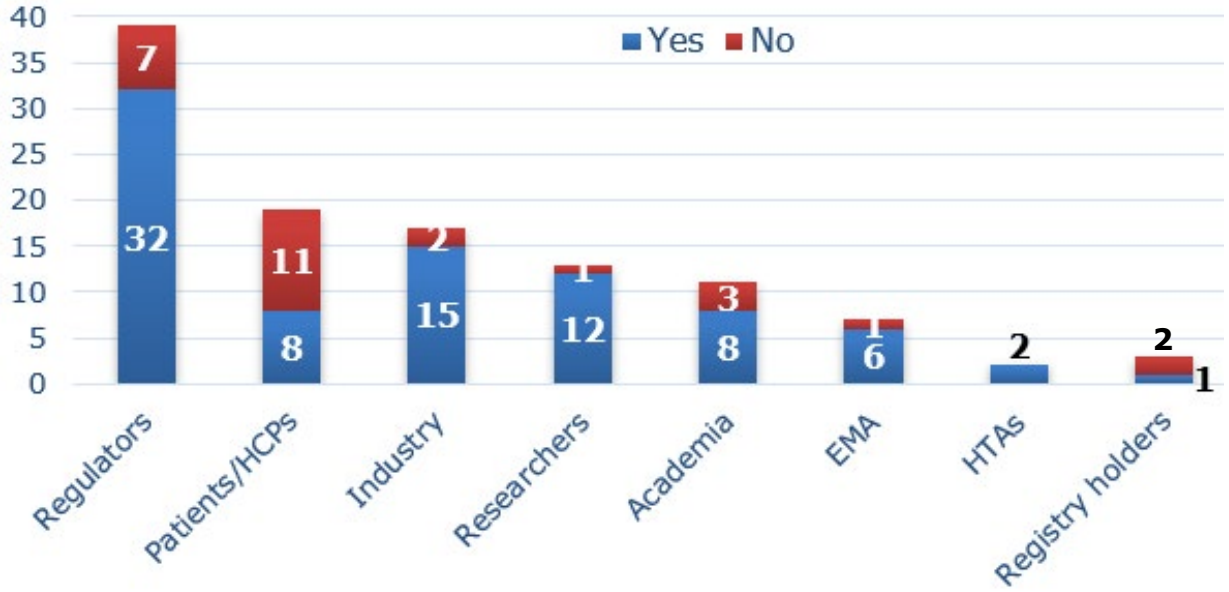
Direct actions

- **Survey on Guideline on registry-based studies**
  - To assess stakeholders' awareness on guideline
  - To identify specific topics requiring clarification
  - To understand training needs
- **Stakeholder communication, engagement and training** through webinars/educational videos with concrete use cases; Q&A
- **PCOs/HCPs to be consulted** on annexes to DQF and engaged in populating the EMA catalogue
- **Patient angle and patient-experience data** to be a central theme of the workshop

Main results of survey on Guideline on registry-based studies

Awareness of the guideline (total: 111)



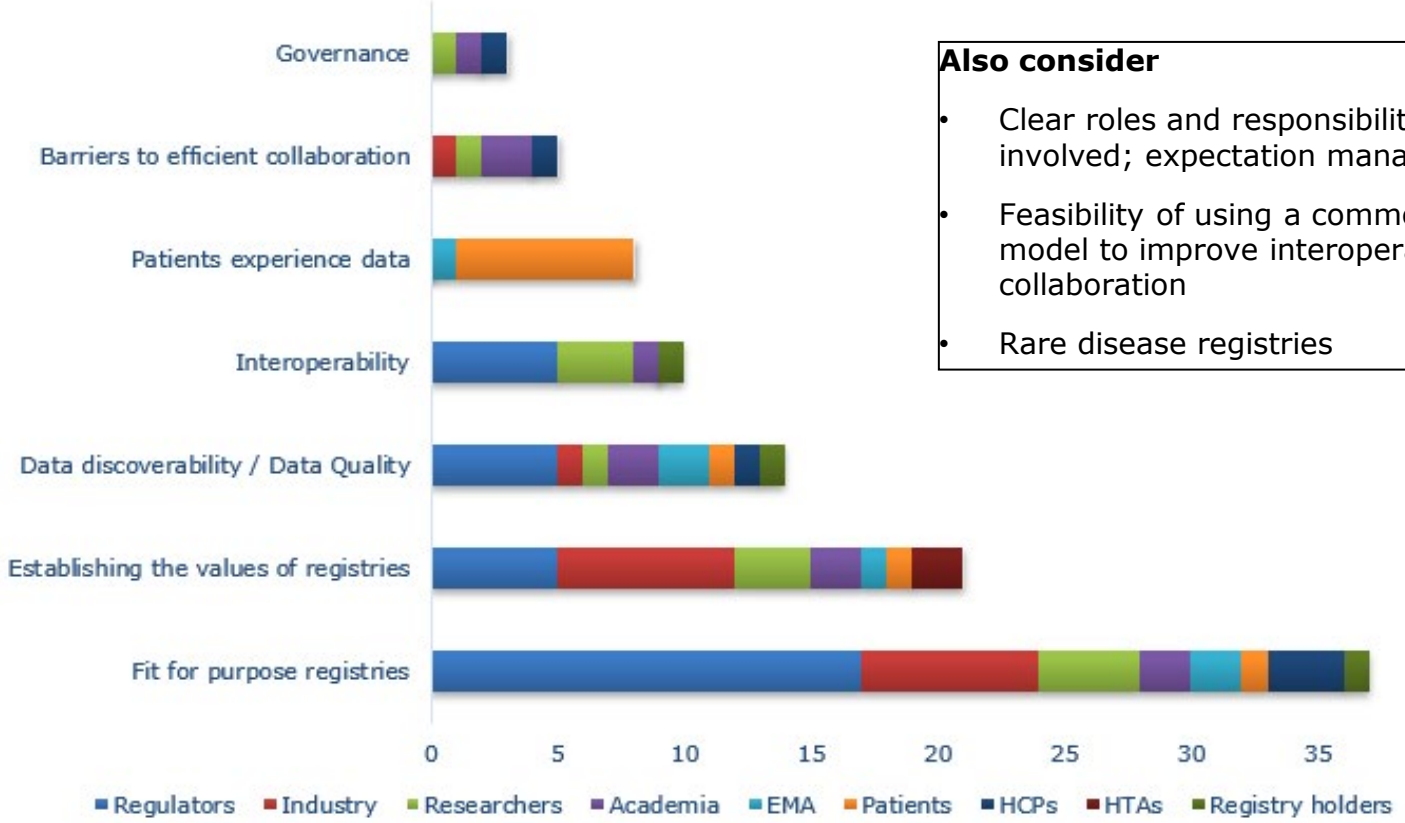


How?: EMA website and through interactions with EMA

Who?: Regulatory, epidemiology and research teams

Who else should know?: Clinical (medical/operational) + analysts

Priority topics for multi-stakeholder workshop on registries (denominator 111)



Also consider

- Clear roles and responsibilities of all involved; expectation management
- Feasibility of using a common data model to improve interoperability and collaboration
- Rare disease registries

Take home messages

- Patients and HCPs are the end-users of medicines and are experts on their disease / condition / treatments → **Patient data are instrumental** in optimising medicines development and regulatory decision-making
- Need to increase patient/HCP involvement at each step of the way → Reinforcing patient relevance in evidence generation is **a key priority** in EMA's **Network Strategy** and the **Regulatory Science Strategy**
- **Understand patient/HCP needs** in terms of training, **consult / integrate their input** on key deliverables → **Identify challenges / opportunities** for enhancing optimal and impactful use of PED and establishing their value in regulatory assessment and decision-making
- Priority topics on Registries: volunteers to collaborate in development of patient communication and engagement strategy + preparation of workshop

Any questions?

Further information

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Coordination Centre website: www.darwin-eu.org

For questions to the Coordination Centre, please contact: enquiries@darwin-eu.org

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