EMA
EUROPEAN MEDICINES AGENCY

DARWIN EU and RWE use throughout medicinal product life cycle

Experience so far and impact on regulatory decision making

PCWP/HCPWP 2 April 2025
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Disclaimer

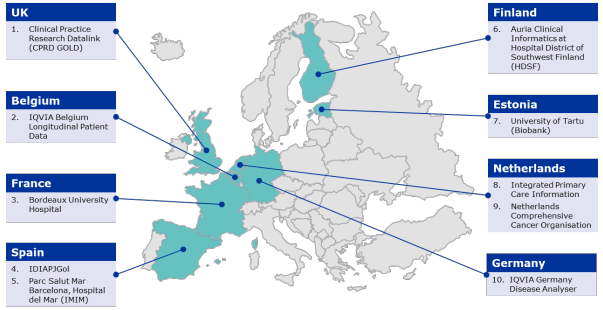
The presenter does not have any conflict of interests.

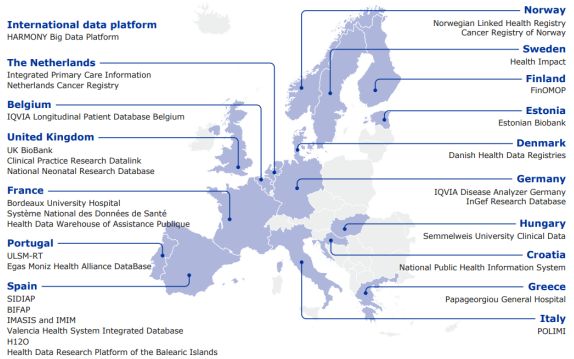
DARWIN EU® vision

The vision that the EMA had when DARWIN EU® was designed is really now in action to support core medicine regulation, as well as public health in the EU

For this, we will continue to optimise the way we generate and deliver evidence to the EMA, its committees, the network and other stakeholders, to make it even **better, faster and smarter** and with more and more data from the majority of the European countries

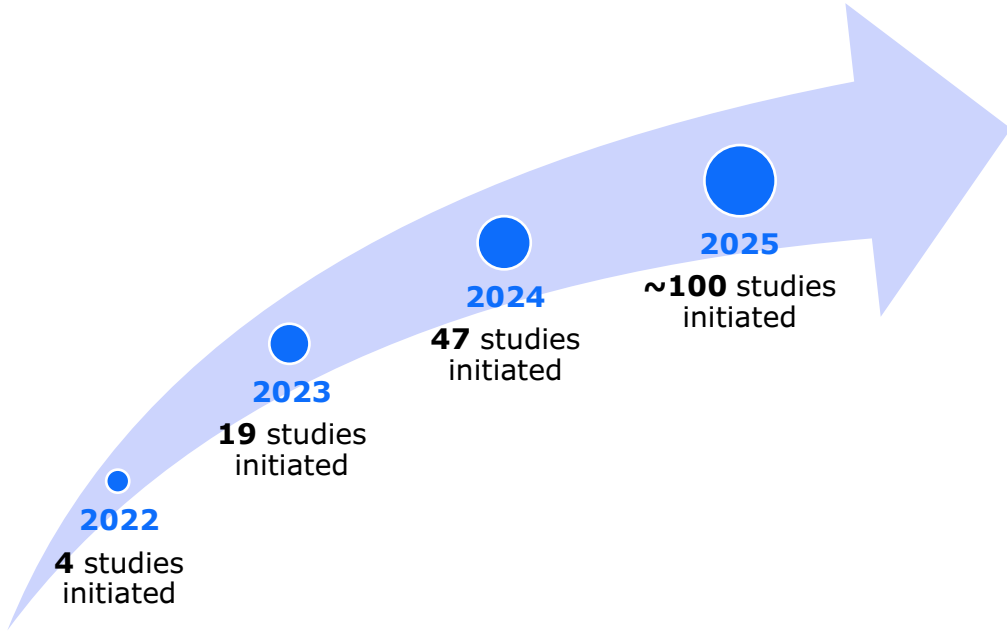
End of 2022



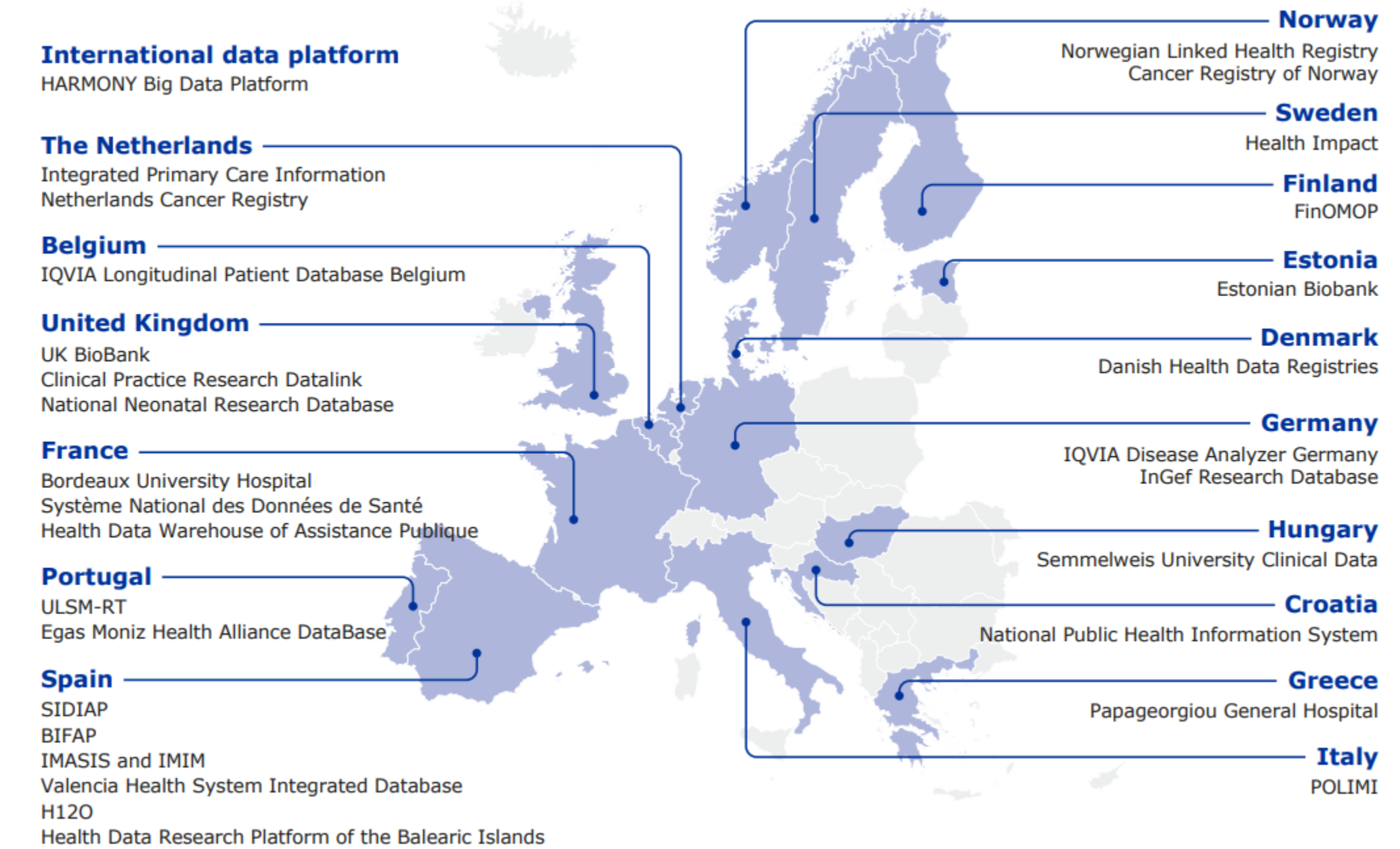


End of 2024

From **~26** to **~180** million active patients



DARWIN EU Network of Data Partners



International data platform
HARMONY Big Data Platform

The Netherlands
Integrated Primary Care Information
Netherlands Cancer Registry

Belgium
IQVIA Longitudinal Patient Database Belgium

United Kingdom
UK BioBank
Clinical Practice Research Datalink
National Neonatal Research Database

France
Bordeaux University Hospital
Système National des Données de Santé
Health Data Warehouse of Assistance Publique

Portugal
ULSM-RT
Egas Moniz Health Alliance DataBase

Spain
SIDIAP
BIFAP
IMASIS and IMIM
Valencia Health System Integrated Database
H12O
Health Data Research Platform of the Balearic Islands

Norway
Norwegian Linked Health Registry
Cancer Registry of Norway

Sweden
Health Impact

Finland
FinOMOP

Estonia
Estonian Biobank

Denmark
Danish Health Data Registries

Germany
IQVIA Disease Analyzer Germany
InGef Research Database

Hungary
Semmelweis University Clinical Data

Croatia
National Public Health Information System

Greece
Papageorgiou General Hospital

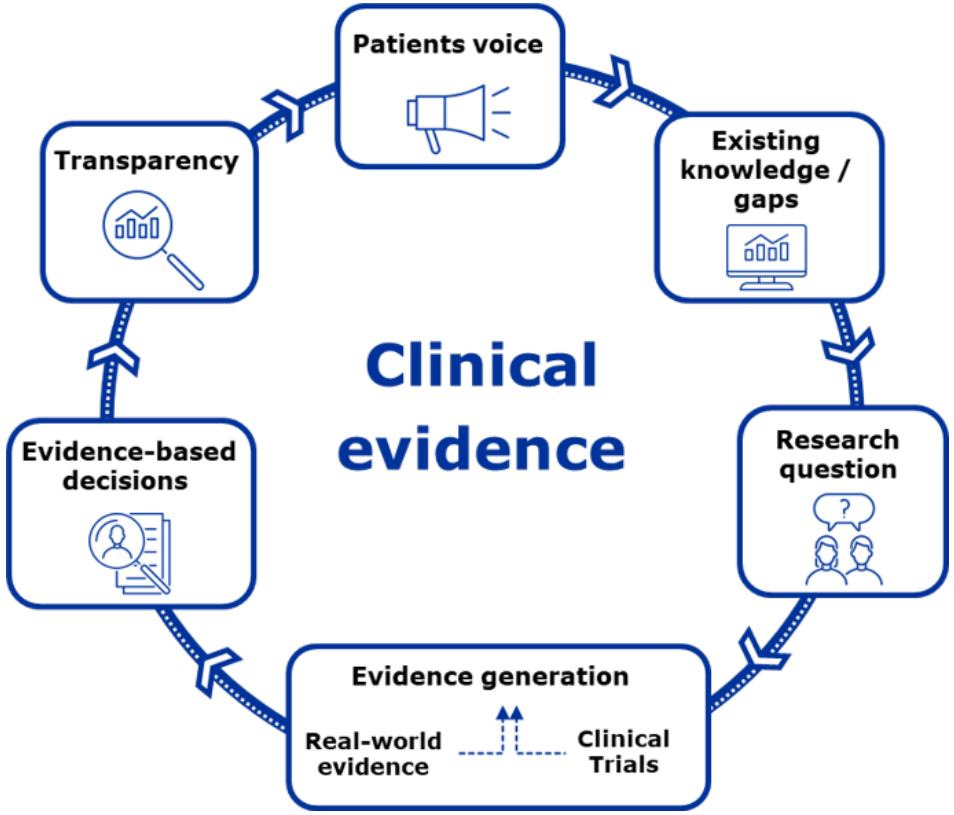
Italy
POLIMI

30 Data Partners as of Feb 2025 in **16 European countries** (~ +10 by end of Feb 2026)

EMA

DARWIN EU described by data partners

Generating clinical evidence: Shared vision towards 2030



- Patient voice guides every step of the way
- Evidence generation is planned and guided by purpose, data, knowledge and expertise
- Research question drives evidence choice and embraces spectrum of data and methods
- Clinical trials remain core but should be **better, faster** and **optimised**
- Real world evidence is **enabled**, and its value is **established**
- High transparency level underpins societal trust

Clinical Evidence 2030. Arlett P, Umuhire D, Verpillat P, Foggi P, Wändel Liminga U, Sepodes B, Lunzer M, Aylward B, Vamvakas S, Roes K, Pétavy F, Thirstrup S, Lamas M, Cooke E, Broich K. *Clin Pharmacol Ther*. 2025 Feb 14. doi: 10.1002/cpt.3596.

The continuum of evidence generation in regulatory decision making

Randomised clinical trials (RCTs) mainstay of drug efficacy and safety information for regulators

Value of Real World Data (RWD) is increasingly acknowledged

- Transform, accelerate and de-risk decision making
- Improve efficiency in design and conduct of trials
- Increase public health impact

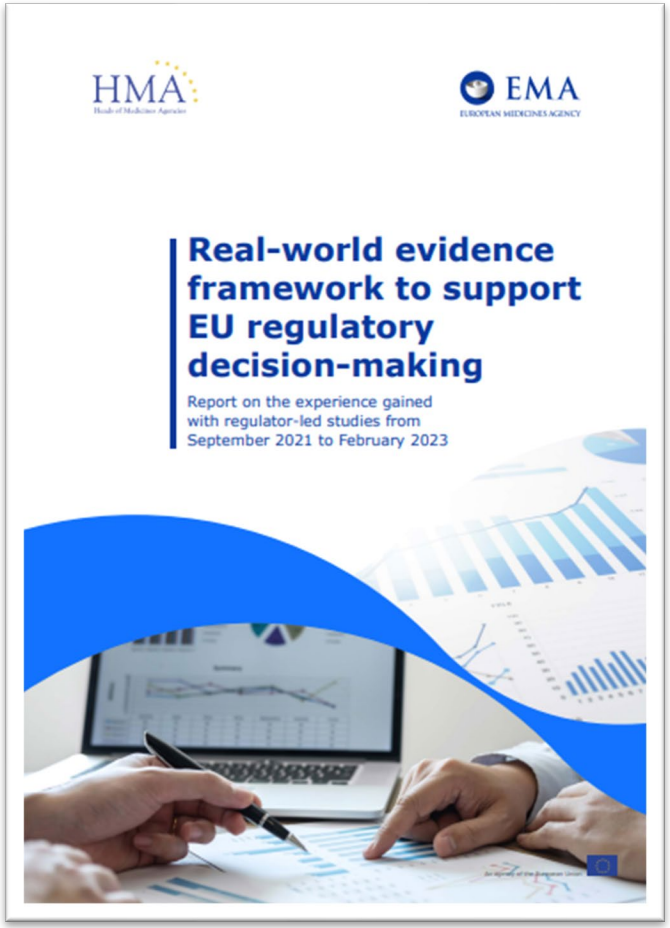
Marketing authorisation

- Contextualise study results
- Ensure generalisability of results to target population

Post-authorisation

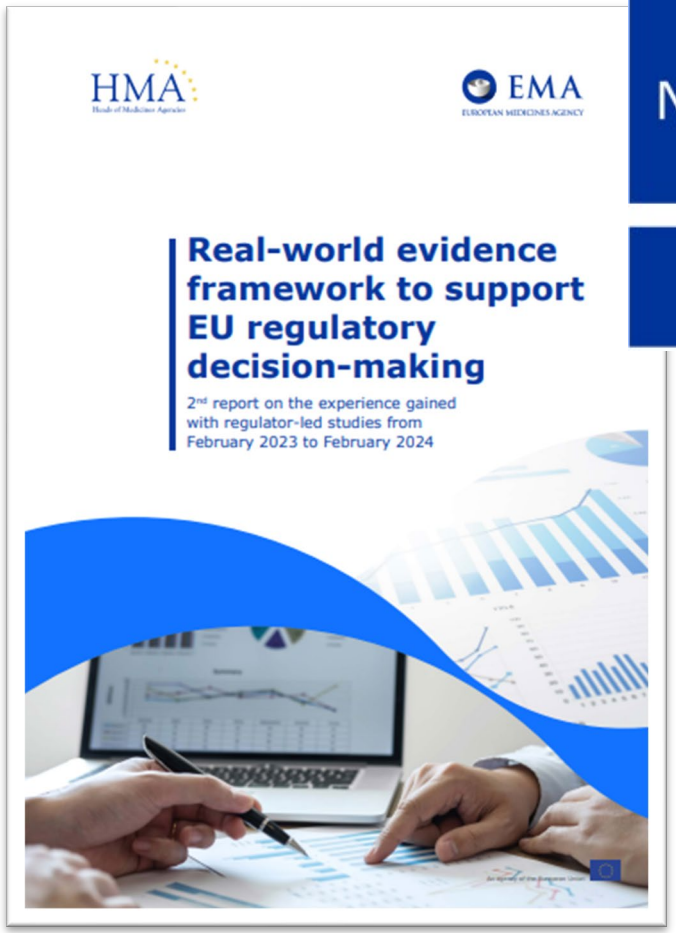
- Appreciate real-world value
- Long-term benefit-risk balance

Reports on RWE experience



Published in June 2023

Period covered: **Sep 2021 to Feb 2023**



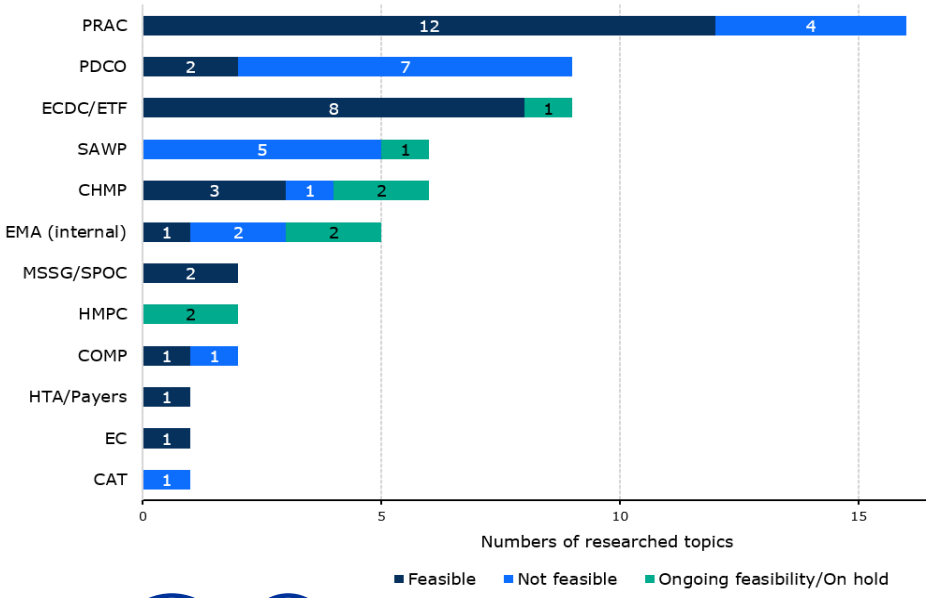
Published in July 2024

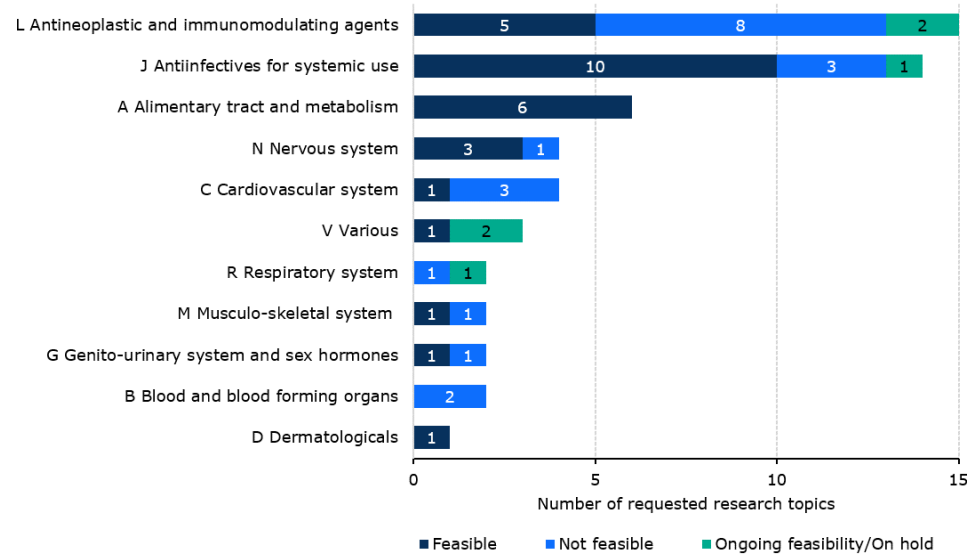
Period covered: **Feb 2023 to Feb 2024**

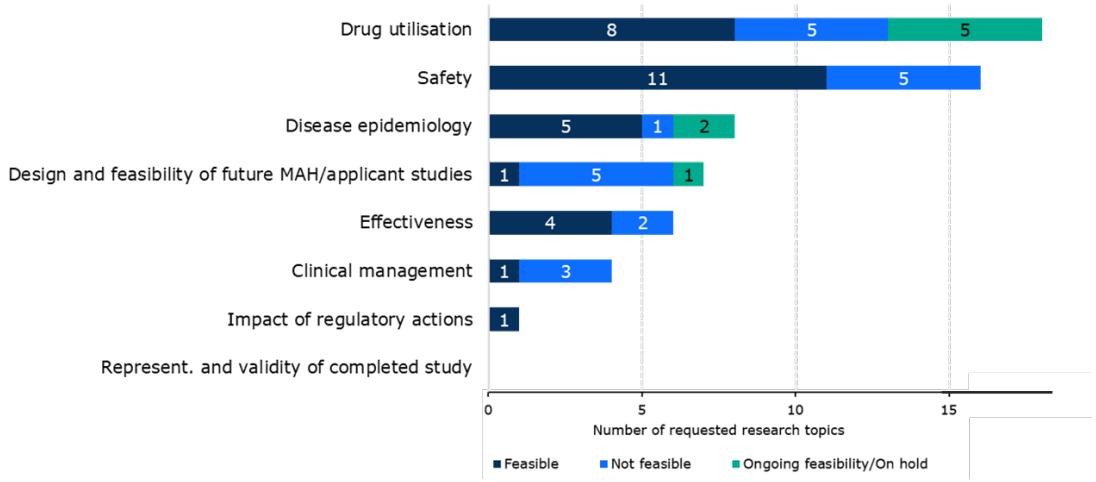
60
NEW research topics
(Feb '23 – Feb '24)

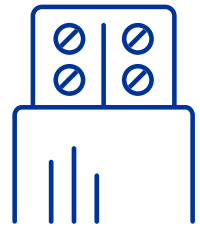
38	16	6
DARWIN EU	In-house	FWC

Study requests by…









What can we expect for the new report? Feb ’24 – Feb ’25

Total number of RWD studies per pathway				
	Newly requested (Feb 2023-Feb 2024)	Completed (Feb 2023 – Feb 2024)	*Newly requested (since Feb 2024)**	*Completed (since Feb 2024)**
DARWIN EU studies	38	9		
In-house studies	16	4		
Framework contract studies	6	9		
Total	**60**	**22**		

* From February to xxx 2024 (X-month period)

What can we expect for the new report? Feb ’24 – Feb ’25

Total number of RWD studies per pathway				
	Newly requested (Feb 2023-Feb 2024)	Completed (Feb 2023 – Feb 2024)	*Newly requested (since Feb 2024)**	*Completed (since Feb 2024)**
DARWIN EU studies	38	9	71	23
In-house studies	16	4	7	5
Framework contract studies	6	9	5	5
Total	**60**	**22**	**83**	**33**

* From February to January 2025

Examples of impactful studies

CHMP

Co-prescribing of **endothelin receptor antagonists (ERAs) and phosphodiesterate-5 inhibitors (PDE-5is)** in pulmonary arterial hypertension (PAH) (CHMP request to understand current practice of such combined treatment and unmet medical need)

Results included in the **clinical efficacy section of the assessment report (D120)** as supportive evidence to complement evidence provided by the MAH (application for a new marketing authorisation) and from the literature

Respiratory Syncytial Virus (RSV) vaccine and disease epidemiology (CHMP request to support discussion on unmet medical need)

Epidemiological data concerning RSV infection and hospitalization, especially for the 50-59 year-old age group, used by the MAH (extension of indication) **to answer one of the clinical questions**, and issue considered as solved by the Rapporteur as the MAH discussed the Darwin-EU data (as per Rapporteur assessment)

Examples of impactful studies

PDCO

Paediatric Systemic Lupus Erythematosus and treatment patterns (PDCO request to support review of upcoming Paediatric Investigation Plan (PIP) submissions in view of clinical trials in the paediatric SLE population being hampered by competitive recruitment)

Informed on the **paediatric SLE population potentially available for clinical trials** (being mainly naive to target therapies) and on the similarity between adults and children, which in turn informs the **extrapolation approach** to be applied

Juvenile polymyositis (JPM) and dermatomyositis (JDM) and disease natural history in adults and paediatric populations (PDCO request to better understand the disease context)

Largest European DM & PM study showing increased prevalence over time and clinical manifestations and treatments prescribed in line with most recent clinical criteria and recommendations

Used by PDCO in a PIP as results suggested sufficient patients available to perform a controlled clinical trial —> **Request made to the applicant**

Examples of impactful studies

PRAC

CGRP* antagonists and background rates (PRAC request to support 3 signal evaluations - **insomnia, erectile dysfunction, increased blood pressure**)

Signals assessment hard to conclude due to limited evidence on background rates in migraine patients

Results helped to reach a conclusion regarding the 3 different signals and a faster decision. The company had no comments and accepted the evidence provided —> **All signals closed**

Doxycycline and association with risk of **suicidality** (PRAC request to facilitate signal assessment)

Safety signal on “suicidality” raised based on cases reported to the Finnish national competent authority and EudraVigilance

Currently available evidence not supporting link between this antibiotic drug and risk of suicidality —> **No update to doxycycline product information warranted**

*Calcitonin gene-related peptide

Is the risk observed in patients taking doxycycline for acne indication linked to the disease itself* or is this risk increased by the intake of the medication?

*Separate DARWIN EU study assessed the risk of suicide-related events in patients with chronic skin conditions: the acne population showed a higher numbers of suicide-related events compared to the general population in Europe, even higher in the younger age groups (from 12 to 30 years of age) and in women.

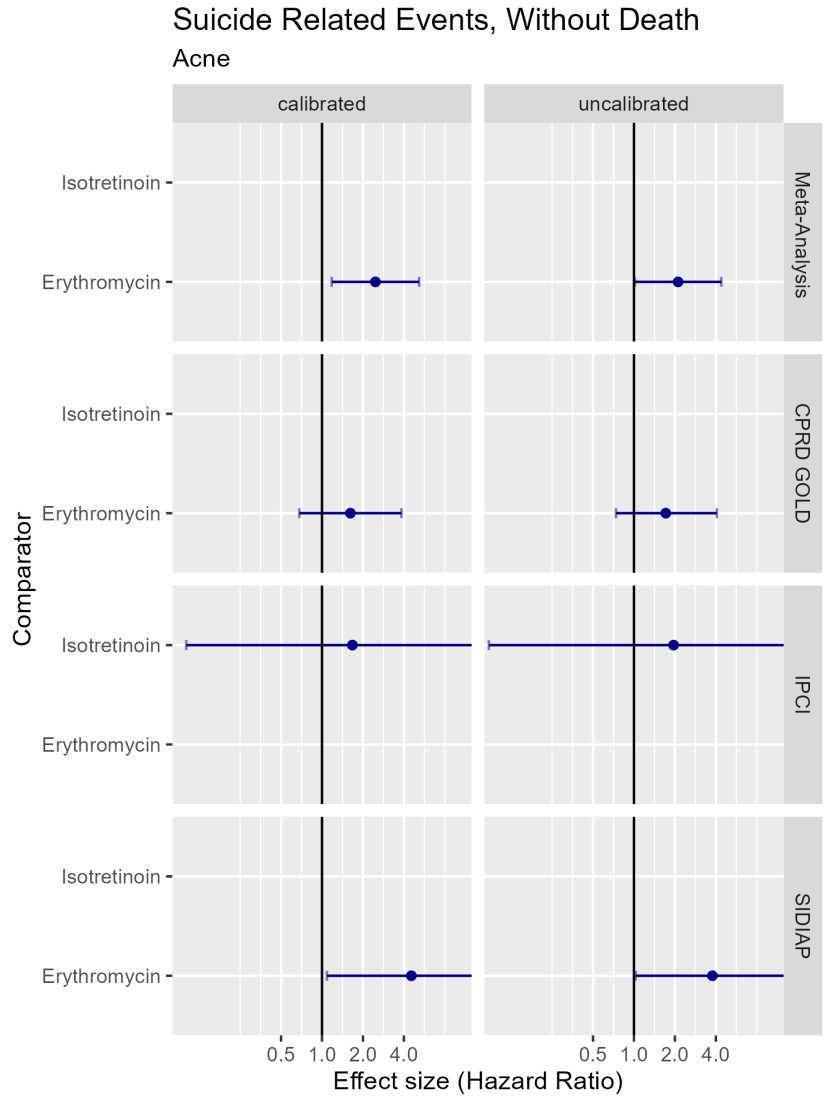
→ To use a **new-user cohort** study to assess the association between doxycycline and completed suicide, composite suicide-related events, depression and anxiety, compared to *active comparators*, stratified by indication of acne, rosacea, chlamydia and lower respiratory tract infection

→ To use a **self-controlled case series** study to assess the association between use of doxycycline and composite non-fatal suicide-related events, depression and anxiety in risk windows of -90,0 (-30,0) and 0-90 days (with smaller, 30D periods)

Indication Acne

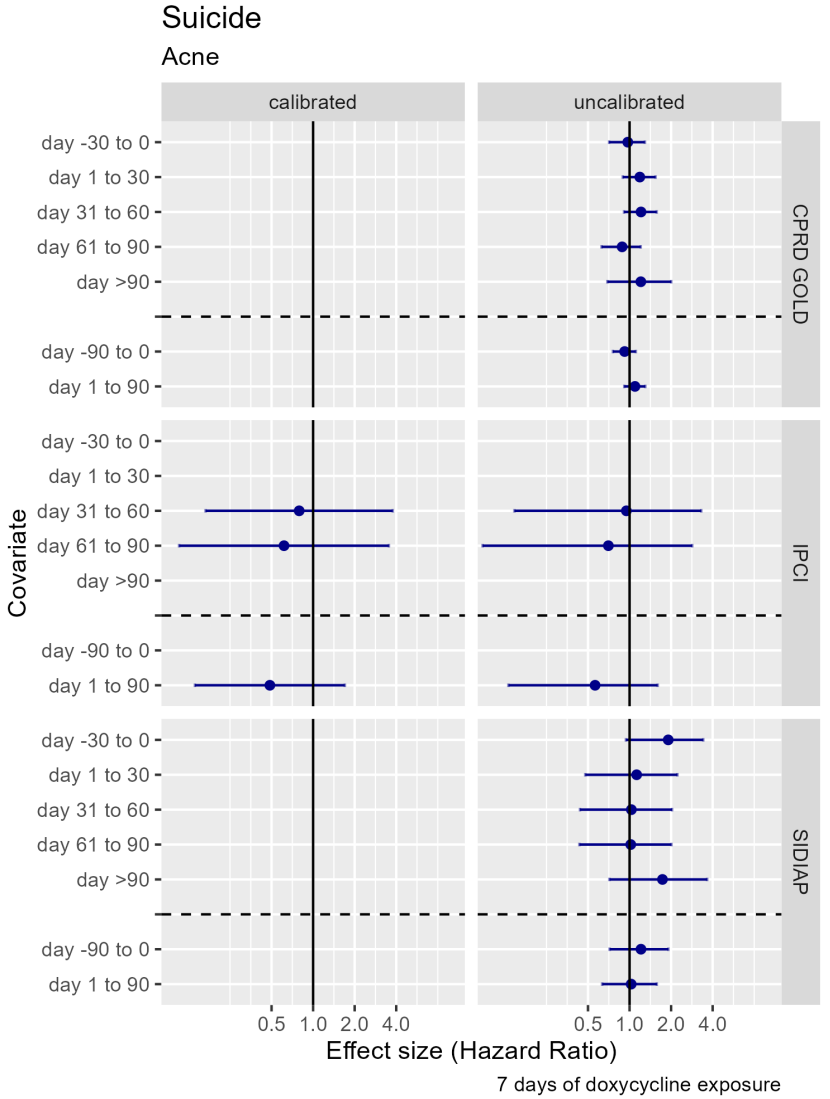
Cohort study: Doxycycline vs. Erythromycin

Meta-analysis: **Uncalibrated HR 2.11, 95% CI [1.01-4.39]**



SCCS: Doxycycline (same outcome)

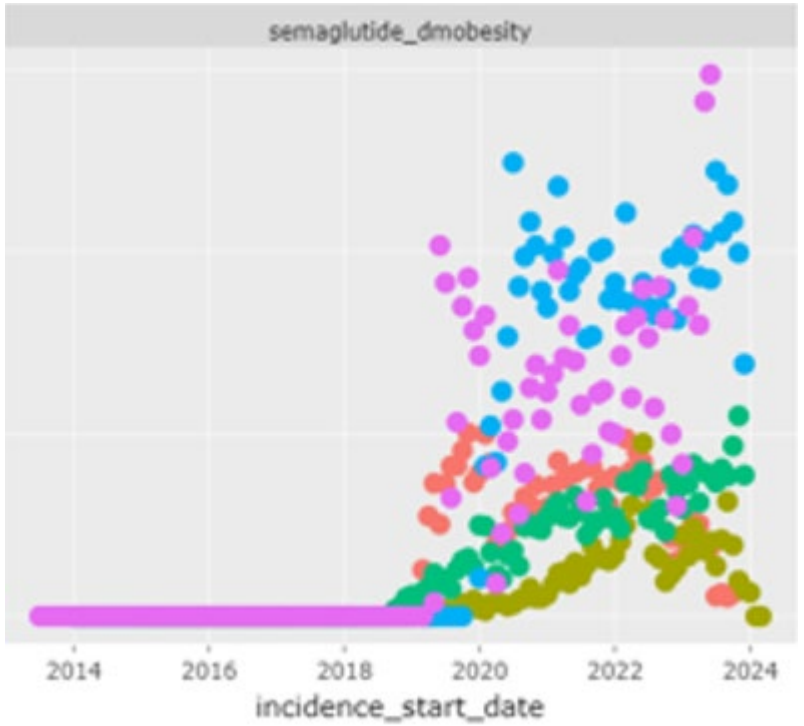
No significant association, IRRs around 1,CIs overlapping



More on the horizon…

Studies of antibiotic utilisation incl indication (all ATBs)

Utilisation of GLP-1 RAs



COVID-19 Vaccine effectiveness studies

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Thank you

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