Analysis of real world data to support regulatory decision-making

28 November 2024

Session 2 of the HMA/EMA Big Data Forum: Evidence generation to advance regulatory excellence, here and now

Presented by Patricia McGettigan - Clinical Pharmacologist, PRAC and BDSG Member

Analysis of RWD to support regulatory decision-making

- Where RWD potentially supports decision-making
- Where it has – some examples, benefits / limitations
- Achieving intentions?

Where might Big Data help regulatory decision making?

Pre-authorisation

- Current landscape: Existing therapies; Use patterns; Patient populations – age, morbidities, concomitant therapies; Gaps /needs
- Rare diseases: Multiple datasets → optimise numbers of patients available for studies to support authorisation application

Authorisation

- Rare disease studies

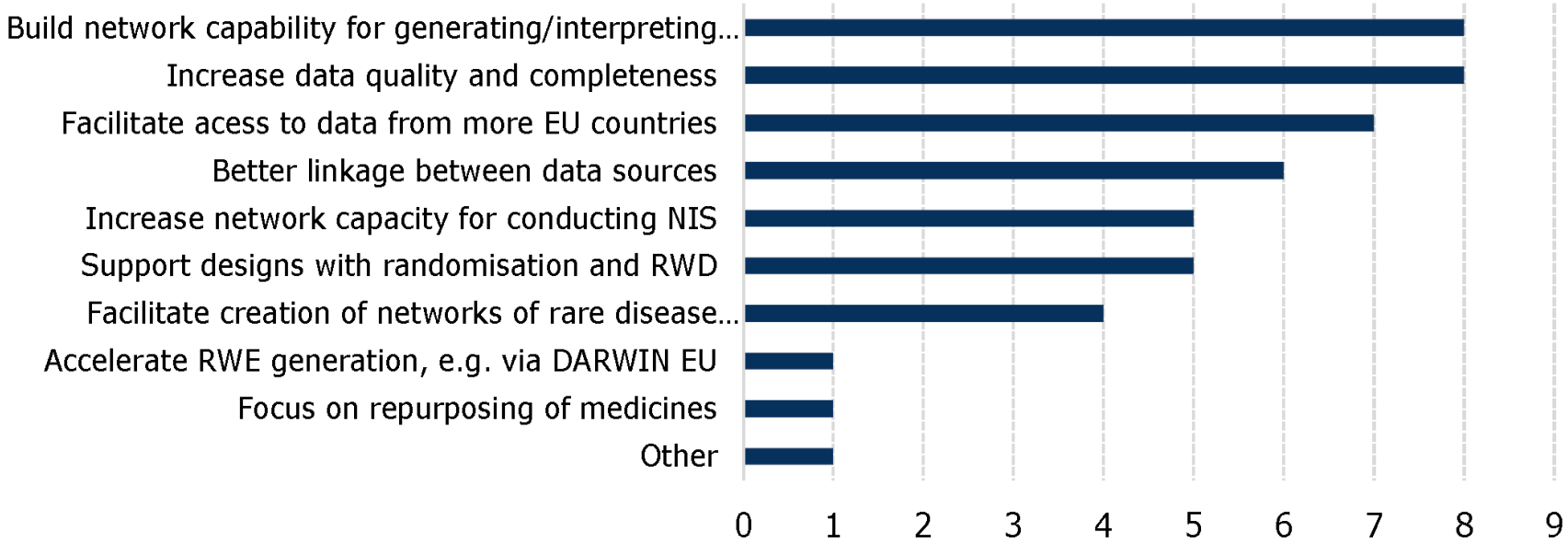
Post-authorisation

- Outcomes: PAES; PASS;
  - Clinical benefits (surrogate endpoint based authorisations);
  - Harms (anticipated / new / signal evaluation)
  - Impacts of warnings / communications
- Uptake; Use patterns (New products; Existing products - new indications); Switches

Future planning

- Supply problems → substitutions

What do National Competent Authorities (NCAs) want / need from RWE based on big data?



Survey on the use of RWD by NCAs: Priorities to further enable the use and establish the value of RWE in regulatory decision making. NIS = non-interventional studies

Source: Real-world evidence framework to support EU regulatory decision-making. HMA EMA 2nd Report
Respondents: Croatia, Czechia, Finland, France, Germany, Italy, Luxembourg, Norway.

Pre-authorisation / Authorisation
Big Data informing current therapy landscape

Paediatric systemic lupus erythematosus (SLE): How are young patients with SLE treated currently *v* adult patients?

- **Question:** For new drug (marketing authorisation) applications (MAAs), what are similarities / differences in current therapeutic practices? Limited good quality evidence (EUPAS106436)
- **Study:** patient-level characterisation and drug utilisation study; 2013-2022

→New diagnosis cohorts; Common Data Model

Patients with >/=365 days of prior observation

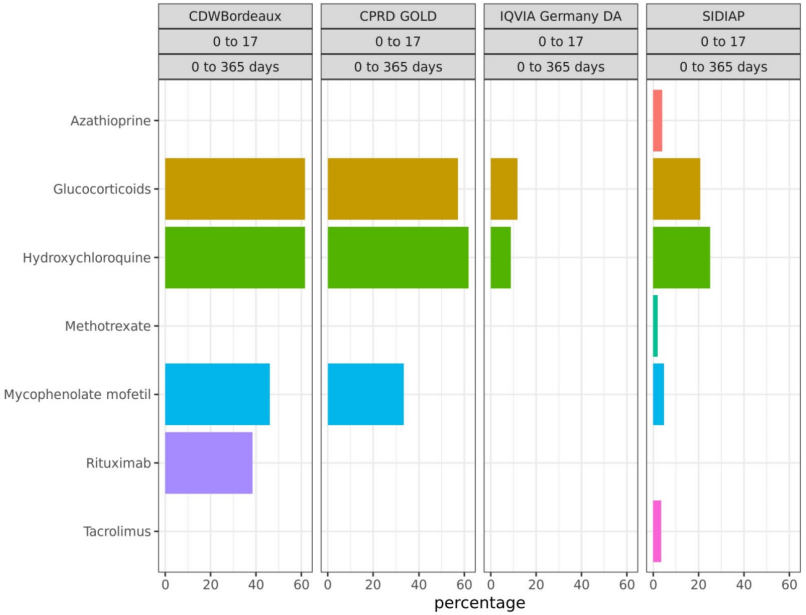
- **Paediatric:** 378 patients (<18y): CDW Bordeaux; CPRD GOLD UK; IQVIA Germany; SIDIAP Spain
- **Adult**: 11,257 patients; CDW Bordeaux; CPRD GOLD UK; IMASIS Spain; IQVIA Germany; SIDIAP Spain

Source: DARWIN EU® Treatment patterns of drugs used in adult and paediatric population with systemic lupus erythematosus EUPAS106436

SLE therapy currently: Paediatric v Adult populations

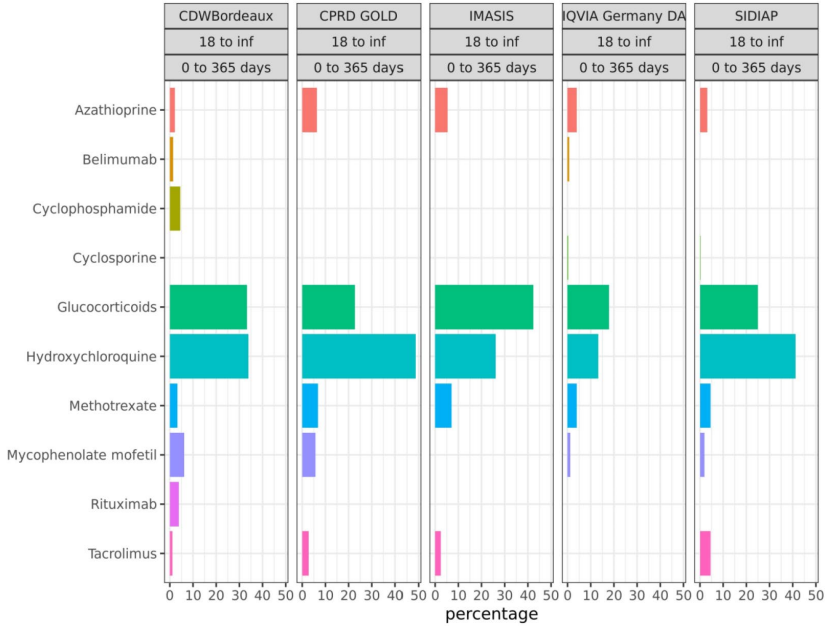
Paediatric

Figure 5 New users of SLE treatment within 365 days of diagnosis, stratified by database (paediatric)



Adult

Figure 7 New users of SLE treatment within 365 days of diagnosis, stratified by database (adult)

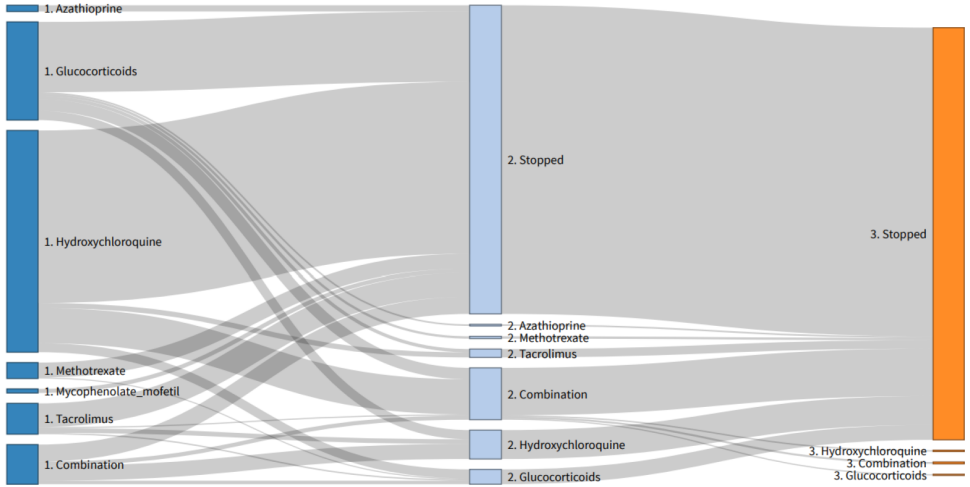


- **Between-country (dataset) differences; Most marked in paediatric group**
- **Patient with new SLE diagnosis ≠ New SLE therapy user**

Figure Source: EUPAS106436 Study Report

Therapy continuity: adults + children

Figure 13 Sankey diagram of SLE treatment pathway (SIDIAP)



Note: Stopped refers to patient stopping treatment without initiation of another study medication within their observation period

Figure Source: DARWIN EU® - Treatment patterns of drugs used in adult and paediatric population with systemic lupus erythematosus EUPAS106436 Study Report

Valuable study

- Quality-assessed datasets; quantitative, descriptive information
- Initial therapeutic choices; Trajectories of therapy; Guidelines alignment

But

- No insight on therapeutic reasoning, patient responses / choices / preferences

Raises questions/ hypotheses potentially of value to explore further

- *Inform further focused efforts: S*eek data via, e.g., Registries, Framework Contract study → Insight on therapy initiations, cessations, switches, patient perspectives, outcomes, benefits, harms
- Characterise patients not treated.

Future planning: Public Health

EMA-European Centre for Disease Prevention and Control (ECDC) Collaboration Vaccine Monitoring Platform (VMP)

- Enabling EMA & ECDC to coordinate vaccine use, safety, effectiveness studies

Research agenda

- Short-term: Influenza, Pneumococcal, COVID; vaccine effectiveness, safety according to types, regimens, brands, patient characteristics, other
- Medium Term: RSV, HPV, M-Pox

Vaccine Adverse Events of Special Interest (AESIs) ongoing DARWIN-EU study

- Building on EMA ACCESS project – Background rates of vaccine AESIs
- Aims to support safety monitoring endeavours via VMP (EUPAS1000000254)

Future planning: Public Health Emergencies

Drugs at risk of (future) shortages - Antibiotics

- Completed (EUPAS107932)
- Data-sets from 4 countries: Belgium, Germany, Spain, UK

Two sets of analyses: Findings

1. *Population-level drug utilisation study on antibiotics*
   - **Confirmed knowns:** Seasonality, older users
   - **New observations:** Declining use of some antibiotics after COVID spikes
   - **Highlighted patterns**: women (community) v men (hospital, OPD)

2. *Time series modelling; 6-month and 12-month forecasts*
   - Models fitted to time series prescribing data → forecast future use / demand
   - 6-month models most accurate; artefacts & exogenous variables (e.g., COVID) impacted

Forecasts were not generalisable across countries

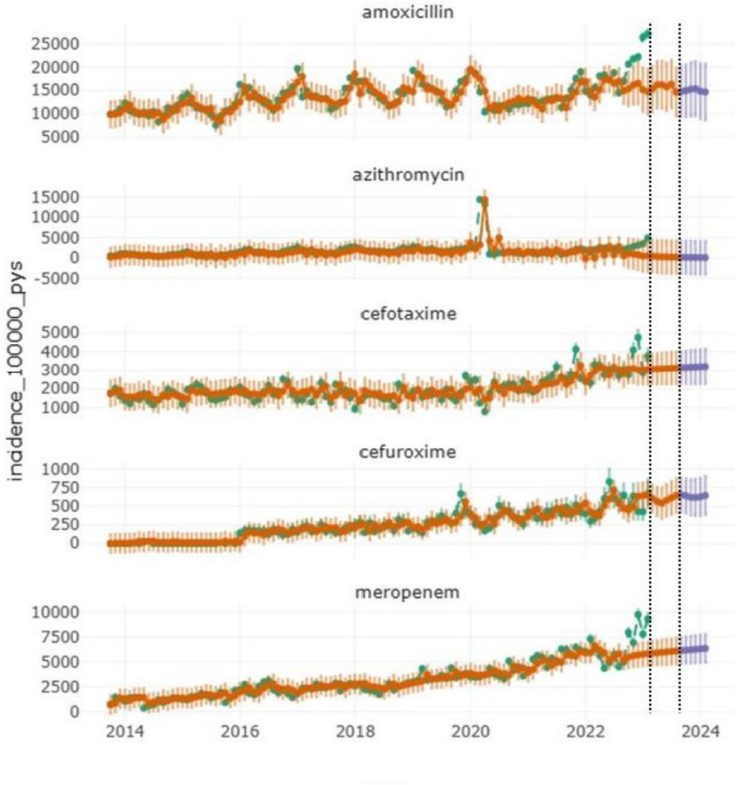
Potentially inform planning for emergencies / shortages

EMA Emergency Task Force, ECDC, NCAs

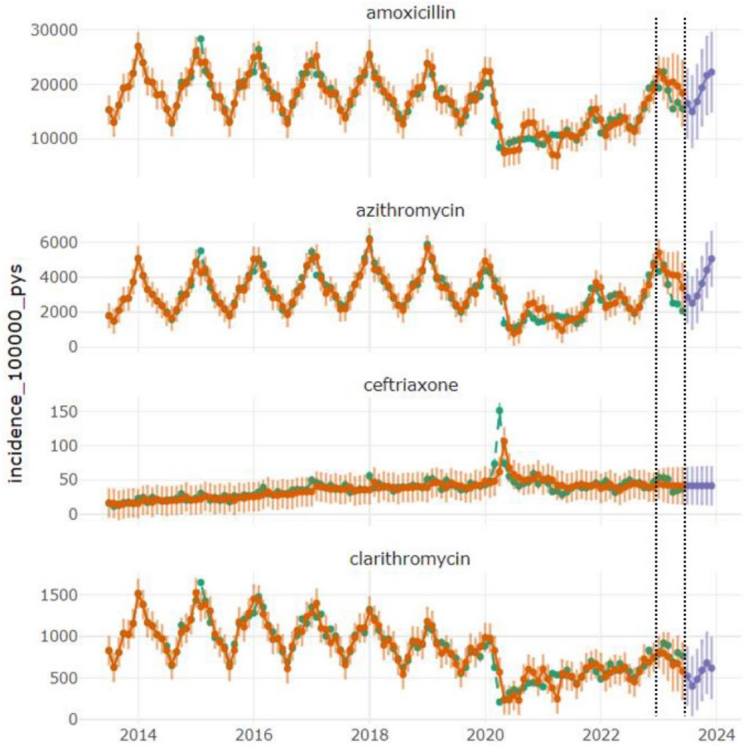
Source: DARWIN EU® Monitoring prescription of medicines for public health emergencies at risk of shortages, EUPAS107932

Antibiotics: Observe, Train & Tune, Forecast

UK: CPRD GOLD



Spain: SIDIAP



CPRD_GOLD - Observed | CPRD_GOLD - Train and Tune | CPRD_GOLD - Forecast

SIDIAP - Observed | SIDIAP - Train and Tune | SIDIAP - Forecast

Ongoing PRAC plenary, December 2024
RWD supporting decision-making

RWD complementing other sources, e.g. EudraVigilance, published literature

Azathioprine

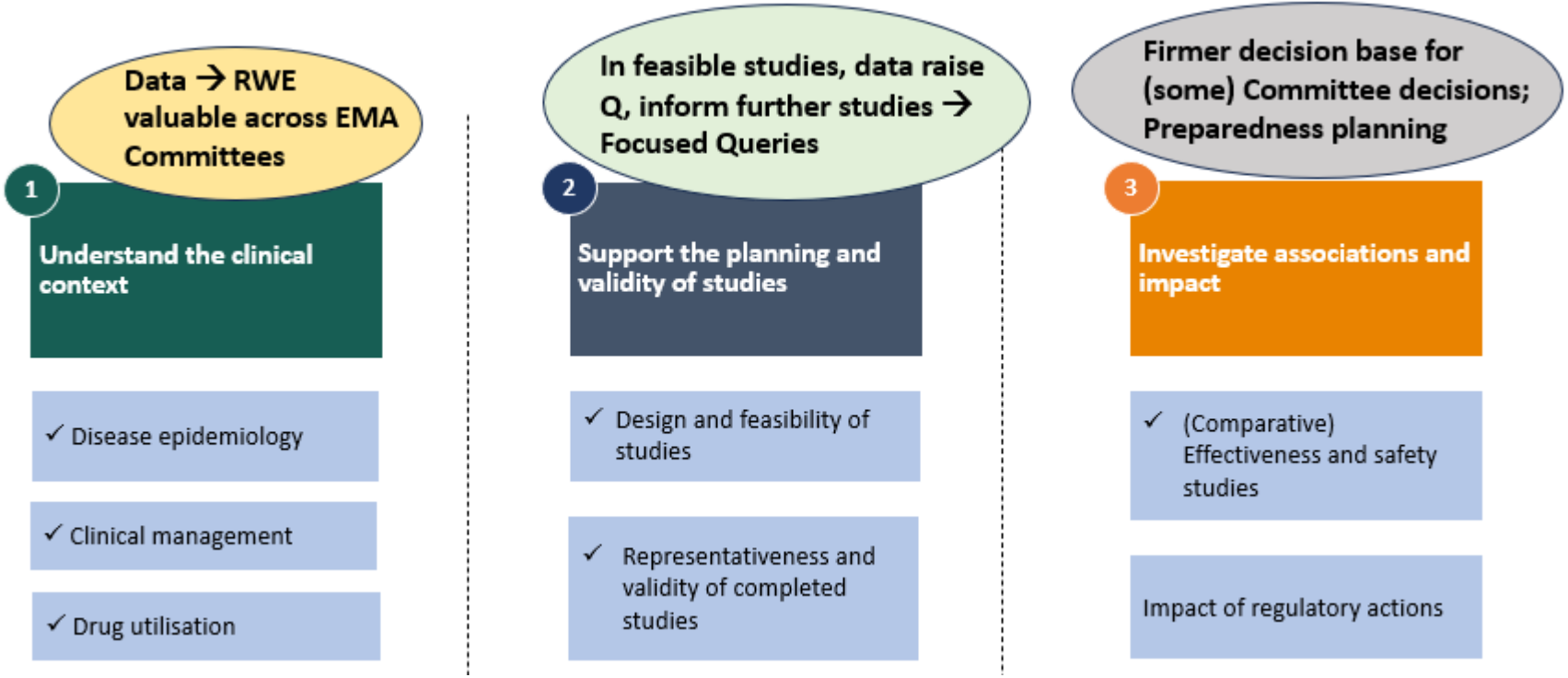
- Informed the Committee on indications / users potentially at risk of the adverse event in question

Doxycycline

- Evaluation - suicidality signal; Informed on strength of this doxycycline - adverse event association

Both will be published in wrap-up

RWE routinely supporting regulatory decision-making



Early positive steps on meeting (some) wants and needs from RWE based on big data

Source: Andrej Segec, ENCePP plenary, November 2024

Thank you for listening

See websites for contact details

Heads of Medicines Agencies www.hma.eu
European Medicines Agency www.ema.europa.eu

The European Medicines Agency is an agency of the European Union

Acknowledgements

Thank you to EMA Real World Evidence team experts for discussions and insights

GLP-1 RA shortages study

- Shortage since 2022, EUPAS1000000223
- Dulaglutide, liraglutide, semaglutide,
- Common Data Model, 5 databases; Belgium, Germany, Netherlands, Spain, UK
- Study ongoing
  - GLP-1 receptor agonists, EUPAS1000000223
  - 5 datasets (11 networks), Common Data Model
  - Aim: Characterise patients prescribed GLP-1 RA products over the past ten years → contextualise demand drivers vis-à-vis the observed shortage of medicines, including exploring comparative trends of prescription of other medicinal products used in diabetes and for weight management as well as patterns of off-label use.

https://catalogues.ema.europa.eu/node/4124/administrative-details

Vaccine Monitoring Platform LINK

EMA/ECDC **extended mandates** → **joint evidence generation** on vaccine use, effectiveness and safety

- Identification and prioritisation of **evidence gaps** (from regulatory procedures, national public health needs, or independent research)
- Facilitation, coordination, registration of **post-authorisation studies**
- **Independent** studies using EMA and ECDC scientific/operational infrastructures and procurement + DARWIN EU for EMA
- Identification of gaps and opportunities in the EU **infrastructure** for studies (e.g., data discoverability and use)
- **Communication** - to EU regulatory & public health decision makers (work plan, study results)
- **Funding** - contribution from the European Commission to the budget of ECDC and EMA
- **Governance** - Steering Group and Joint Secretariat

EU Immunisation and Vaccine Monitoring Board (IVMAB)

- Advice on **strategy, data sources, feasibility, methods**
- And on **interpretation** and **use** of vaccine real-world evidence (RWE)

6 regulatory experts from **EMA** Committees & ETF

National Competent Authorities

National Focal Points from all 29 EU/EEA public health authorities on vaccine-preventable diseases and immunisation (**ECDC** network)

Link to IVMAB meeting summaries

Classified as public by the European Medicines Agency

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