HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Big Data Steering Group update

Delivering on the Network Strategy to 2025

For information

Enpr-EMA meeting 28 September 2021

DARWIN EU

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Topics

1. The Big Data Steering Group
2. Access to Real-World Evidence for Medicines Regulation in Europe: DARWIN EU

Today's objective is to introduce the work of the BDSG and DARWIN EU that will enable the use of Big data (starting with RWD) in the decision-making process of the EU Regulatory Network,

Looking forward

"By delivering the vision of a regulatory system able to integrate Big Data into its assessment and decision making, we can support the development of innovated medicines, deliver life-saving treatments to patients more quickly and optimise the safe and effective use of medicines through measurement of a products performance on the market."

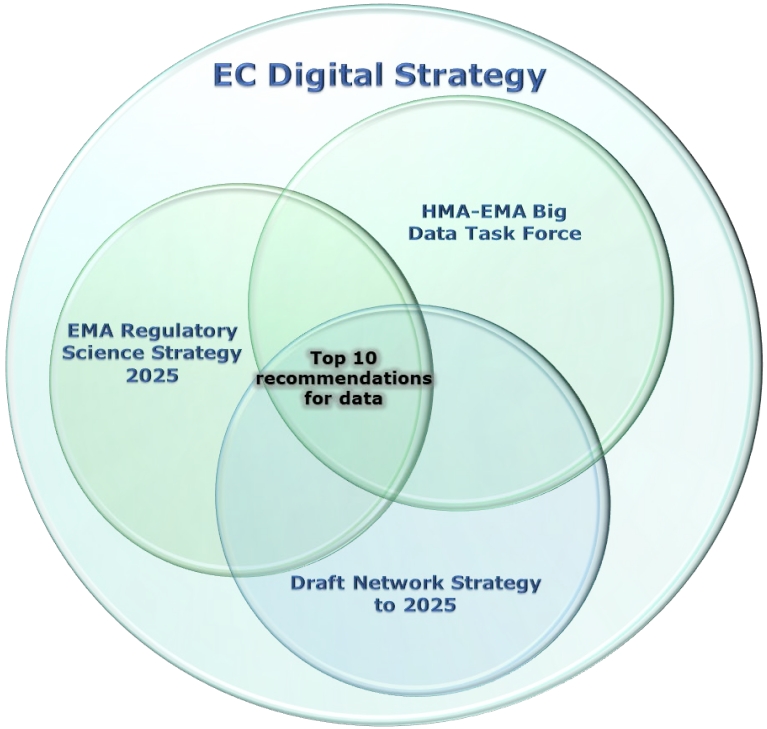
Big Data Task Force final report December 2019

Background - Big Data Task Force

The timing is now:

- Joint HMA EMA Big Data Task Force Top-ten data recommendations
- EU Network Strategy to 2025 includes data and analytics pillar
- EMA Regulatory Science Strategy to 2025 (stakeholders endorse these actions)
- Commission Health Union proposal includes access to healthcare data for EMA

Science and technology are evolving fast



HMA / EMA Big Data Steering Group

The European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) set up a **joint task force** to describe the big data landscape from a regulatory perspective and identify practical steps for the European Medicines Regulatory Network to make best use of big data in support of innovation and public health in the European Union (EU). This led to the creation of the **Joint HMA/EMA Big Data Steering Group** and **Big Data Steering Group Work Plan**.

Jan. 2020

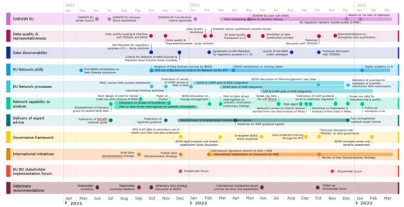
'Ten recommendations to unlock the potential of big data for public health in the EU'

Sep. 2020

Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21

July 2021

EMA MB and HMA informed of BDGS workplan 2021/2023



1st Big data steering group meeting in May 2020

May 2020

BDSG workplan 2022/2023

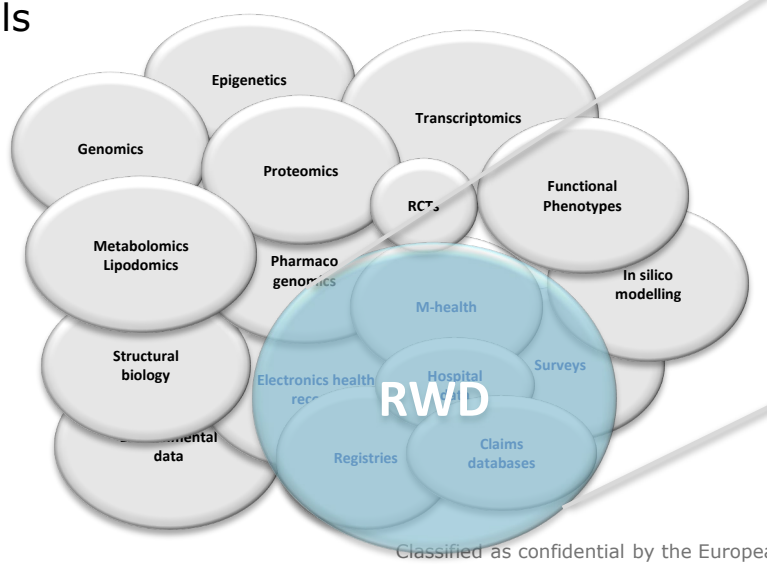
May and June 2021

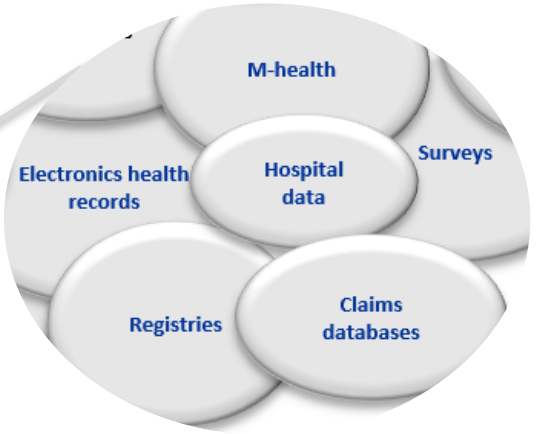
Publication of BDSG workplan 2021/2023

Aug. 2021

Real-World Data and Real-World Evidence

Real-World Data (RWD): routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials





Real-World Evidence (RWE): information derived from analysis of real-world data

Access to Real-World Evidence for Medicines Regulation in Europe

- Use of RWE in the development, authorisation and post-marketing surveillance of medicines to facilitate decision-making is increasing
- Several mechanism for obtaining Real-World Evidence are available to Scientific Committees. DARWIN EU will provide the breadth in access to data combined with speed of analysis to meet today's demand and in particular future demand:

Current way to obtain RWE	Requests or obligations to pharmaceutical companies	Analysis of public information including public scientific literature	Data analyses and studies conducted or initiated by NCAs
RWE provided through the Agency	**EMA studies** on the electronic health databases accessible in-house	**Studies procured** through the EMA framework contracts	**DARWIN EU** (starting from 2022)

DARWIN EU® - Vision

- 1st of the priority HMA/EMA BDTF recommendations + anchored in the Network Strategy to 2025
- DARWIN EU vision:
  - Establish a **network of data, expertise, and services**, the **D**ata **A**nalysis and **R**eal-**W**orld **I**nterrogation **N**etwork (DARWIN EU®), to supports better decision-making throughout the product lifecycle with reliable evidence from real-world healthcare data.
- DARWIN EU will:
  - Provide **scientific expertise** in formulating and executing studies and analysis;
  - Maintain a **catalogue of known, relevant data holders**, continually ensuring the quality of the data held by data holders and conformance to metadata (e.g. maintain the federated network);
  - **Expand the federated network**, assisting potential new data holders in conforming the standards necessary for a data source to be used in the regulatory context;
  - Deliver **training**, and support for business services;
  - **Enable the EMRN, EMA and the scientific committees to make use of the future EHDS** in the context of medicines regulation.

DARWIN EU project

- To begin the assembly of DARWIN EU, EMA published a **call for tender** in June 2021 for a service provider to:
  - establish the **DARWIN EU Coordination Centre**, related contractual services and connectivity with the EHDS and its initial pilot;
  - conduct scientific studies and answer research questions supporting regulatory decision-making by EMA scientific committees and the European medicines regulatory network;
  - maintain a catalogue of real world data sources for use in the regulatory context and their metadata.
- Appointment of the Coordination Centre on track for early 2022
- DARWIN EU webpage has been launched

Actors and key characteristics

EU Medicines Regulatory Network

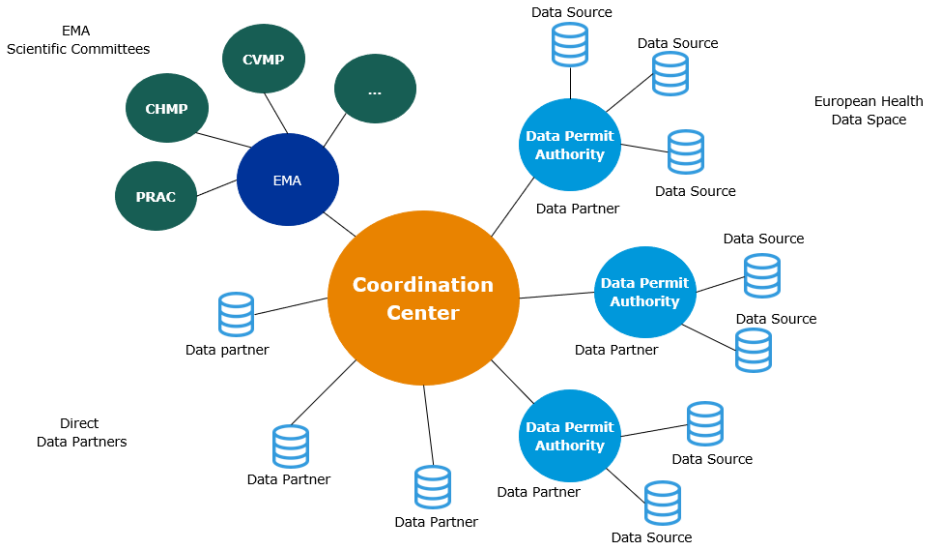
- **EMA** - provides leadership, setting standards, contracting studies,
- **EMRN -** including EMA scientific committees and working parties, national competent authorities (NCAs) and the European Commission: **request studies** via EMA

The Coordination Centre

- **Establishes** and **maintains the network** (including onboard/maintain data sources), manage the **execution of scientific studies**

Data Partners, incl. Data Permit Authorities

- **Partners** who have access to data, or who may request analyses in a data source and provide results to the Coordination Centre
- This includes **Data Permit Authorities** (DPAs), already existing or to be created as part for the EHDS



Key characteristics

- Distributed network for fast access and analysis
- Data
  - Stays local
  - Queried remotely
  - Includes use of a common protocol and common data model for fast analysis
- Data exchanged within the network is anonymous

DARWIN EU® - high level timelines

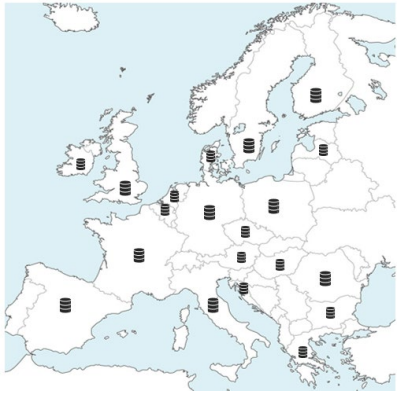
- **2021:**
  - Selection of the Coordination Centre provider
- **2022/2023:**
  - Coordination centre set-up, inc. operational processes and governance
  - Establish connectivity with EHDS and existing Data Permit Authorities
  - First catalogue of standard data analyses available
  - Start recruiting and onboarding the data partners
  - Start running pilot studies to support EMA committees - **first benefits delivered.**
- **2024:**
  - DARWIN EU® to be operational and routinely supporting the scientific evaluation work of EMA's scientific committees and NCAs by delivering studies and maintaining data sources.
- **2025/2026:**
  - DARWIN EU® to be fully operational and yearly evolves to meet the need from the EU regulatory network
  - Full integration with the EHDS

Over the course of the 5 year contract an estimated 380 observational studies can be delivered

Evolution: from early delivery to fully leverage of the EU Health Data Space

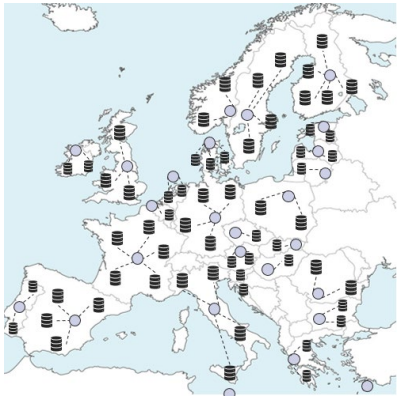
DARWIN EU **2023**

- Coalition of existing datasets with medicines regulators
- Federated access to data holders



DARWIN EU **evolution**

- DARWIN EU integral to the EHDS
- Access to data via Data Permit Authorities ( )



EHDS promotes health data exchange and supports research and innovation on new preventive treatments, medicines, medical devices

- Access of citizens to health data and portability of data
- Access of regulators to health data for policy making and regulatory purposes
- Study on regulatory gaps in cross border digital healthcare (eHealth, AI in health)
- Joint Action to provide rules, governance structures, guidelines, data quality framework, infrastructure

Why do we need real-world evidence: regulatory use-cases

RWE

Generate prevalence data to support orphan designation

RWE

Advise companies on use of RWE in product development based on feasibility and relevance of studies

RWE

Identify needs in children to support waivers/deferrals (i.e. for diseases that only affect the adult population)

Establish and regularly update an inventory of paediatric medicine needs

RWE

Supplement, validate and contextualise clinical trial results to inform benefit-risk decision making

Inform decision-making on post-authorisation studies (e.g. feasibility of imposed PASS)

RWE

Monitor performance on the market and inform decision-making:

Assess benefit and risks in real world when imposing studies on specific MAHs is not appropriate

Assess extension of indication and repurposing of medicines

Monitor safety and effectiveness in special populations, off-label use

Characterise safety profile and monitor the effectiveness of risk minimisation measures.

DARWIN EU® - RWE use cases for PDCO

Work is underway at EMA to identify more areas where independent RWE provided by EMA could support the assessment during a procedure:

- Support evaluation of incidence and prevalence of diseases
  - Assess applications for waiver and/or deferrals when development of a medicine in pediatric can be delayed or it is not needed (e.g. are there enough patients for paediatric clinical trials?)
- Natural history of disease
  - Support a better understanding of the disease progression in pediatrics, by generating evidence on disease characteristics (procedures, lab values,…) and comorbidities over time
- Clinical management of the disease of interest
  - Generate evidence on the actual clinical standard of care (e.g. are medicines used according to the authorised indication or off-label?)
  - Characterise severe adverse events occurring in the treated population

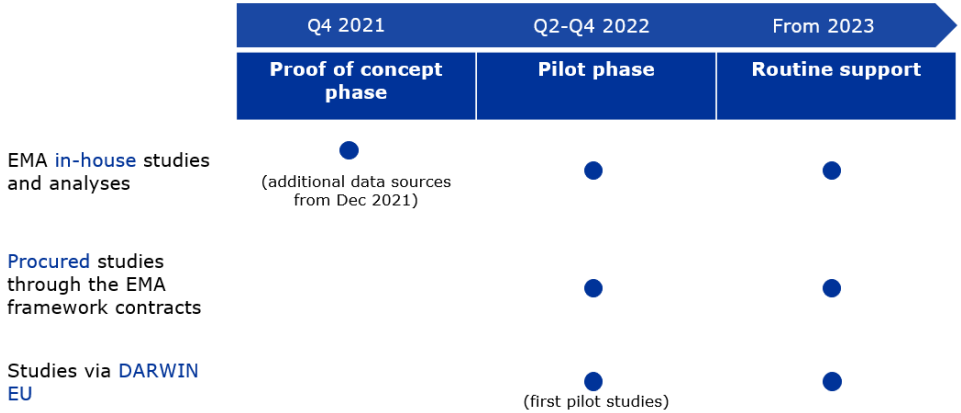
DARWIN EU® - Benefits

- **Additional benefits** as EU partners participate and access the platform:
  - **European Commission** – key use case for the European Health Data Space
  - **National governments** to support health policy and delivery of healthcare systems
  - **HTA bodies and payers** to support better quality decisions on cost-effectiveness
  - **EU health agencies** - use cases specific for EFSA, ECDC, ECHA, JRC
  - **EU patients** - faster access to innovative medicines and safe and effective use

- Increase access to the adequate data sources and expertise
  - Data sources used by DARWIN EU will also feed into the European Health Data Space, and will ultimately become available to some extent to other stakeholders in a FAIR (findable, accessible, interoperable and reusable) manner,
- Contribution to the acceptability of RWE for decision making

Next steps: Proof of concepts (PoC) and pilots (1/2)

- Interacting with committees to agree PoC and pilots
  - PRAC: implementing the lessons learnt from the pilot run in 2019-21
  - COMP, PDCO, SAWP: PoC in 2021, pilot in 2022
  - CAT, CHMP: PoC and pilot in 2022
  - CMDh: initiate discussions on use cases and processes in 2022
- Later on, requests/processes will also be looked at (e.g. HTAs, payers, national competent authorities…)



Aim to support the majority of Committees in their decision-making with reliable RWE by 2023

Next steps: other activities (2/2)

- Evaluate the impact of RWE in the decision-making process and to promote the provision of recommendations for best practice
- Refine methodologies for the use of RWE collaborating with DG Research
  - Call published for the Horizon Europe Cluster 1 Health, submission from Oct. 21 to Apr 22.
  - HORIZON-HLTH-2022-TOOL-11-02: New methods for the effective use of real-world data and/or synthetic data in regulatory decision-making and/or in health technology assessment
- Big Data learning initiative workshop in November 2021

DARWIN EU® - Summary of the future model

- **DARWIN EU** will support better decision-making throughout the product lifecycle via its network of expertise/partnerships and databases
- **RWE will be an established (and understood) source of evidence**
- **Data will be discoverable and of known quality and representativeness** allowing choice of optimal data source, enabling regulators to expertly assess study results
- **EMRN will have knowledge and experience in data science, methods and analytics** to advise companies developing products and to expertly assess application dossiers. **Committee decision-making will be enriched** with expert advice across the spectra of analytic and methodological approaches.
- **Learning initiatives will enable continuous learning** and evolve to rapidly be able to address new regulatory needs, including response to future health crisis.
- **Suite of EU and international guidelines and standards available** to help industry and regulators develop and supervise medicines (built on learnings from submissions of Big Data and enhanced study transparency (EU PAS Register)
- **Full compliance with data protection and ethics of data sharing**
- **Collaboration** with all stakeholders, incl. patients and healthcare professionals

Any questions?

Further information

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Background - Big Data Task Force

- Technology and methodology advances are driving digitisation of large volumes of research and clinical data (Big Data).
- The acceptability of evidence from Big Data for regulatory decision-making is uncertain.
- Major investment in Big Data from U.S. FDA (Sentinel), Health Canada (CNODES), Japan (MIHARI & MID-NET), China, and others. E.g. recent $220 million 5-year FDA contract with Harvard Pilgrim for the Sentinel program.
- The EU regulatory network:
  - has limited capacity to access and analyse large, unstructured data sets; and
  - is not best prepared to guide the use of emerging technologies or to interpret analyses based on big data or novel analytical approaches.

Challenge: capitalise on the promise of novel new datasets of unknown quality and provenance and still reach a robust position on the benefit risk of a medicine.

Background - Big Data Task Force

Phase I report: endorsed by HMA & EMA management board end 2018:

- Characterisation of data sources
- Survey of NCAs and industry
- Set of core recommendations
- Annexes including reports from 7 subgroups (now published)

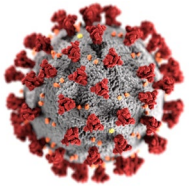
Phase II report

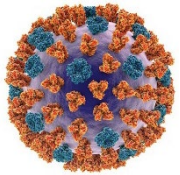
- Extend the taskforce mandate until end of 2019:
  - Top ten recommendations
  - Regulatory prioritisation and implementation of recommendations

Key progress and future highlights

	2021	2022
DARWIN EU	**Procurement launched -** 1st meeting of the **Advisory board**	**Coordination Centre appointed** – Support EHDS2 pilot – **Start conducting pilot/studies** for decision making
Data quality & representativeness	**Procurement launched** for academic consortium to deliver a data quality framework	**EU Data quality Framework v1.0 available - 2 workshops** on data quality and data qualification
Data discoverability	Progress on **selection of metadata for RW**	**Agreement on RW Metadata for regulatory purpose** (v.1.0) - **Launch of RWD public catalogue**
EU Network skills	**Data science curriculum** finalised – **Survey of skills** completed - **Training delivery outsourcing** finalised	**Roll out** of Big data curricula (content outsourced and delivered through EU-NTC)
EU Network processes	**RWE use cases developed** with PRAC, PDCO, COMP – **Learnings initiative workshop**	**RWE integration pilots** (PDCO, COMP, SAWP, CAT, CHMP)
Network capability to analyse	1st discussion on **Cluster of Excellence** **Advisory group on CT raw data** established	**Workshop on Raw Data in MAAs** (including CHMP pilots) **Draft guideline on AI**
Delivery of expert advice	**ENcEPP RWE methods guide published**	Publication of **registries guidance** - **Roadmap for RWE guidance agreed**
Governance framework	**BDSG recommendations on ethics advice**	**EHDS** legal proposal and impact assessment study supported – publish Q&A on **data protection**
International initiatives	**Data standardisation strategy** adopted – Progress on **RWE Collaboration Roadmap** with FDA and HC	International **regulators summit on data and RWE**
EU BD stakeholder implementation forum	**Multi stakeholder forum on Big Data**	Stakeholder forum
Veterinary recommendations	**Workshop on the** Veterinary **Data Strategy**	**International** cooperation **forum** and the **Vet Data Hub** established

DARWIN EU: a central pillar for health crisis planning and response



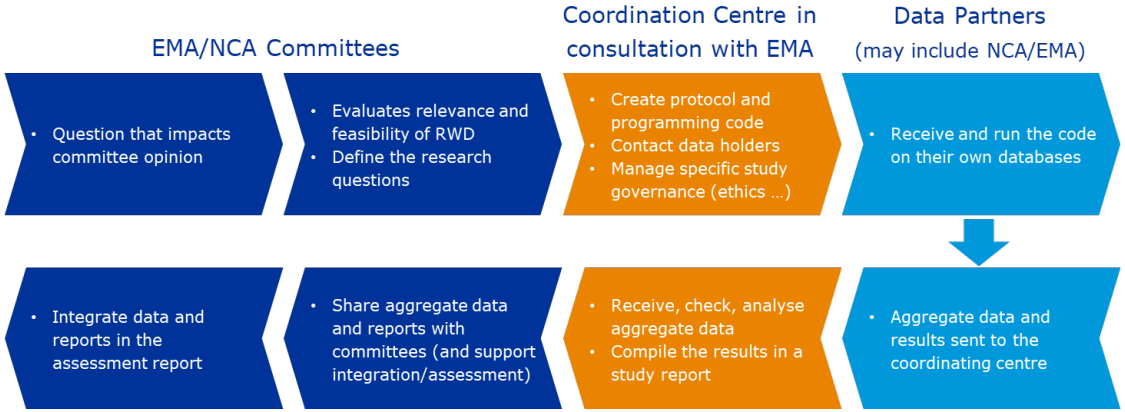


Use cases include:

- Monitoring the use of medicines to predict demand and shortages
- Understanding the disease natural history to support development of vaccines and therapeutics
- Provide evidence for repurposing existing medicines
- Monitor the safety and effectiveness of vaccines and therapeutics post-authorisation

DARWIN EU will support future crisis responses with an operational infrastructure for conducting studies

DARWIN EU® - Conducing Studies and Analysis



Routine repeated analyses

- Routine analyses based on a **generic study protocol**.
- Example: Periodical estimation of drug utilization of a class of medicinal products in several European countries, safety monitoring of a medicinal product or the estimation of the incidence of a series of adverse events of interest.

Off-the-shelf studies

- Studies for which **a generic protocol may be developed or adapted** to a descriptive research question.
- Example: A study aiming to estimate the prevalence, incidence or characteristics of exposures or health outcomes in defined time periods and population groups or to describe population characteristics.

Complex Studies

- Studies requiring development or customization of **specific study designs**, protocols and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data.
- Example: Etiological studies measuring the strength and determinants of an association between an exposure and the occurrence of a health outcome in a defined population considering sources of bias, potential confounding factors and effect modifiers.

Very Complex Studies

- Studies which cannot rely only on electronic health care databases, or which would require **complex methodological work**, for example due to occurrence of events that cannot be defined by existing diagnoses codes including events that do not yet have a diagnosis code, where it may be necessary to combine a diagnosis code with other data such as results of laboratory investigations.

The databases that will support such analyses and EU regulatory use cases should be representative and cater to different needs e.g. **primary care**, **specialist care**, **hospital care data** from electronic health records (EHRs), **claims databases**, **disease registries**, and **longitudinal drug prescription**, **dispensing or other drug utilisation databases** and geographical settings.