Perspectives on use of clinical data in the regulatory review process and scientific advice by regulatory authorities

Jesper Kjær, Director of Data Analytics Centre, Danish Medicines Agency

The vision

A world class data analytics centre that…

"Through use of clinical trial and real world data and advanced analytical methods
we want to increase the accessibility of safe and effective medicines and medical devices"

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Denmark: National Genome Centre

Personalised / Precision medicines

"Over the next 4 years, up to 60,000 patients will be able to look forward to better diagnostics and more tailor-made treatment, which is also known as personalised medicine."

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Source: https://sum.dk/Media/7/C/Personalised%20medicine%20for%20the%20benefit%20of%20patients%20publikation.pdf

Denmark: National Biobank

Personalised / Precision medicines

DANMARKS NATIONALE BIOBANK

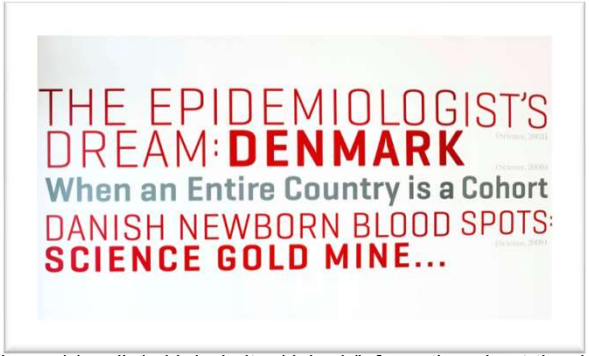
INFORMATION ABOUT THE DANISH NATIONAL BIOBANK

”25 million biological samples

• An unbiased sampling of the Danish population such as the PKU blood samples from all newborns since 1982

• Samples from more than 800,000 potential controls

• Uniquely, sample groups link to vast amounts of donor information in the Danish registers - e.g. medical history, school performance, place of living etc.”



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Source: https://www.danishnationalbiobank.com/-/media/arkiv/subsites/dnb-uk/information-about-the-danish-national-biobank.pdf?la=en

Denmark: Life Science Strategy

38 initiatives including:

Initiative 15 Establishment of a secure national analytics platform for health data

To support these needs, the government, in collaboration with central authorities and stakeholders in the field, will explore potentials for establishing a common national analytics platform that can support data users to access health data and other relevant data from different data controllers in a secure analytics environment. with extensive storage and computing capacity (supercomputer facilities).

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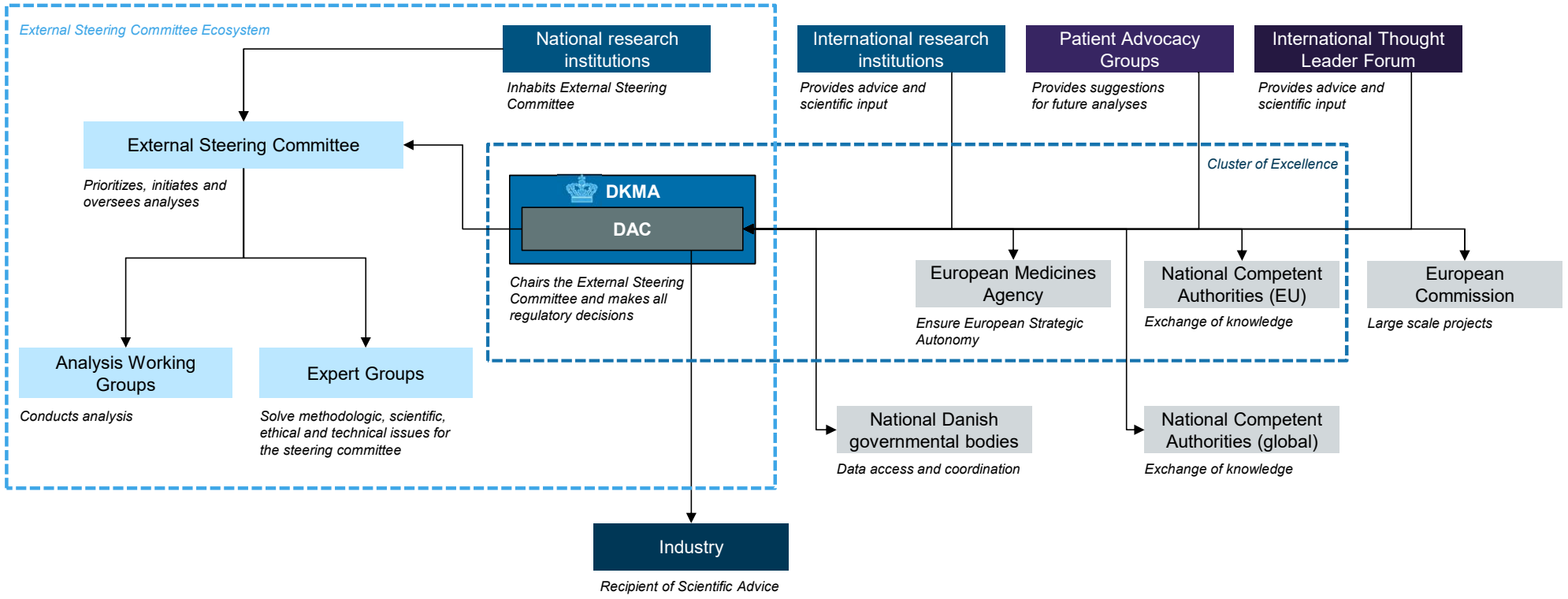
Translated from source: https://sum.dk/Media/637541521670727421/Strategi%20for%20life%20science.pdf

Governance structure and ecosystem of DAC



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EU: EMA and HMA - the European strategies

Data analytics at EMA and the network

Source: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf
https://www.ema.europa.eu/en/documents/report/european-union-medicines-agencies-network-strategy-2025-protecting-public-health-time-rapid-change_en.pdf

EMA Regulatory Science to 2025

Source: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

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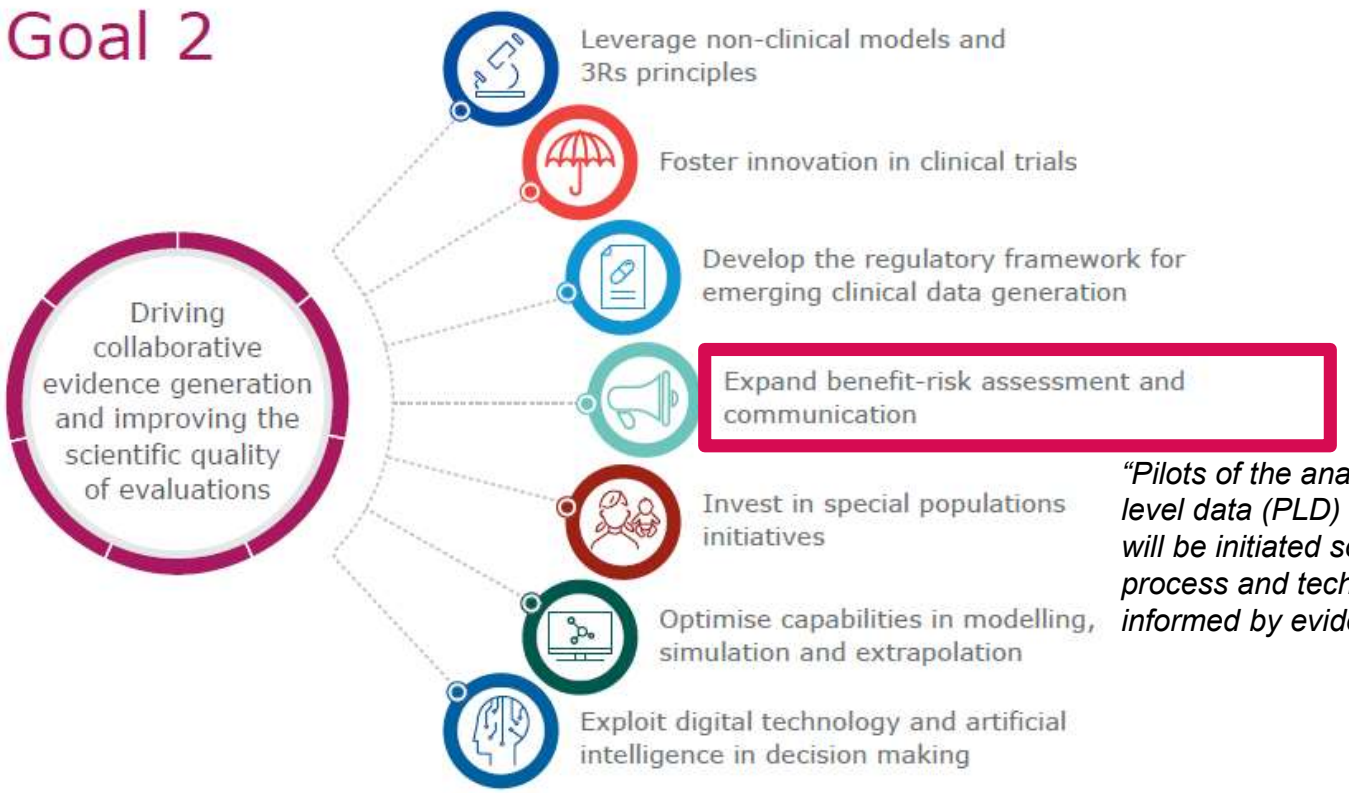
EMA Regulatory Science to 2025



"Pilots of the analysis of patient level data (PLD) from clinical trials will be initiated so that policy, process and technology choices are informed by evidence."

Source: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

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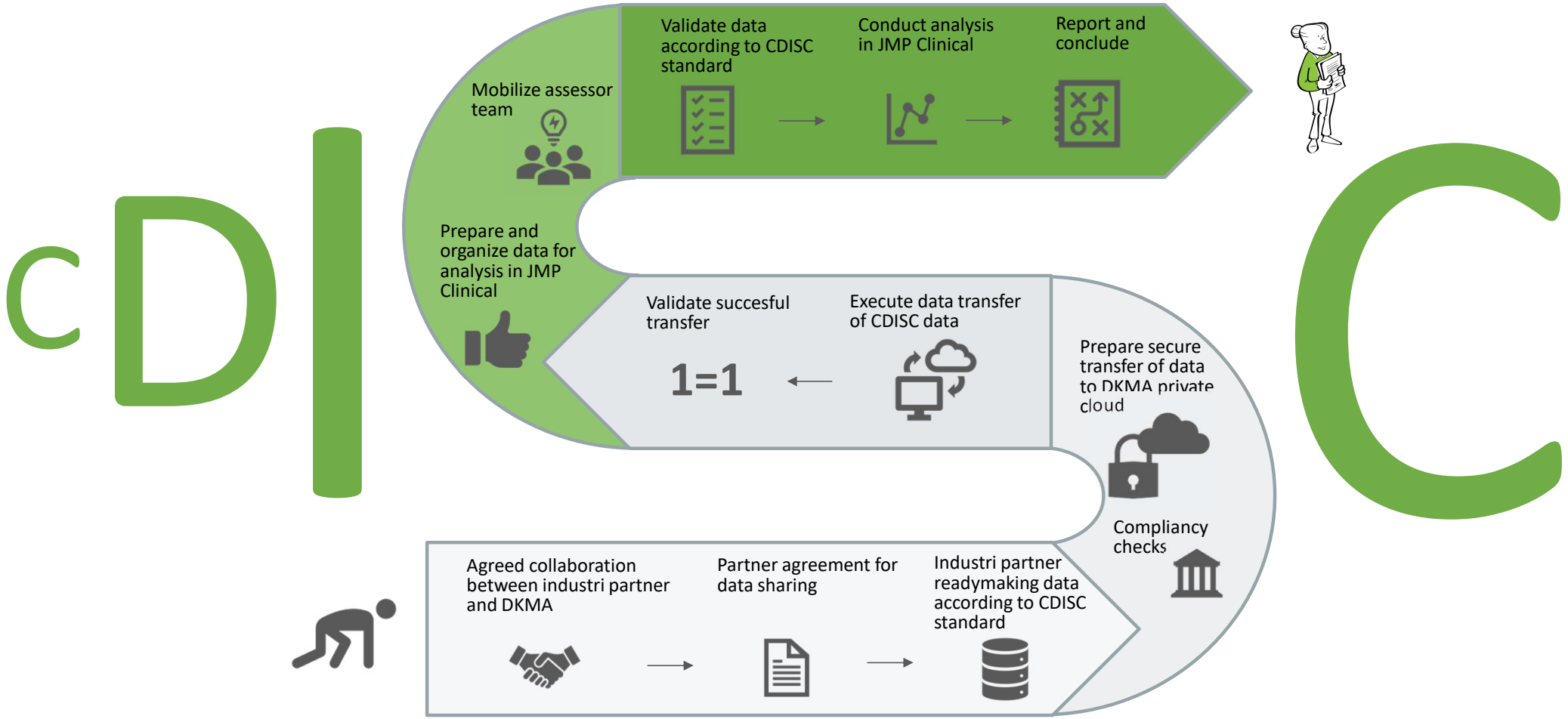
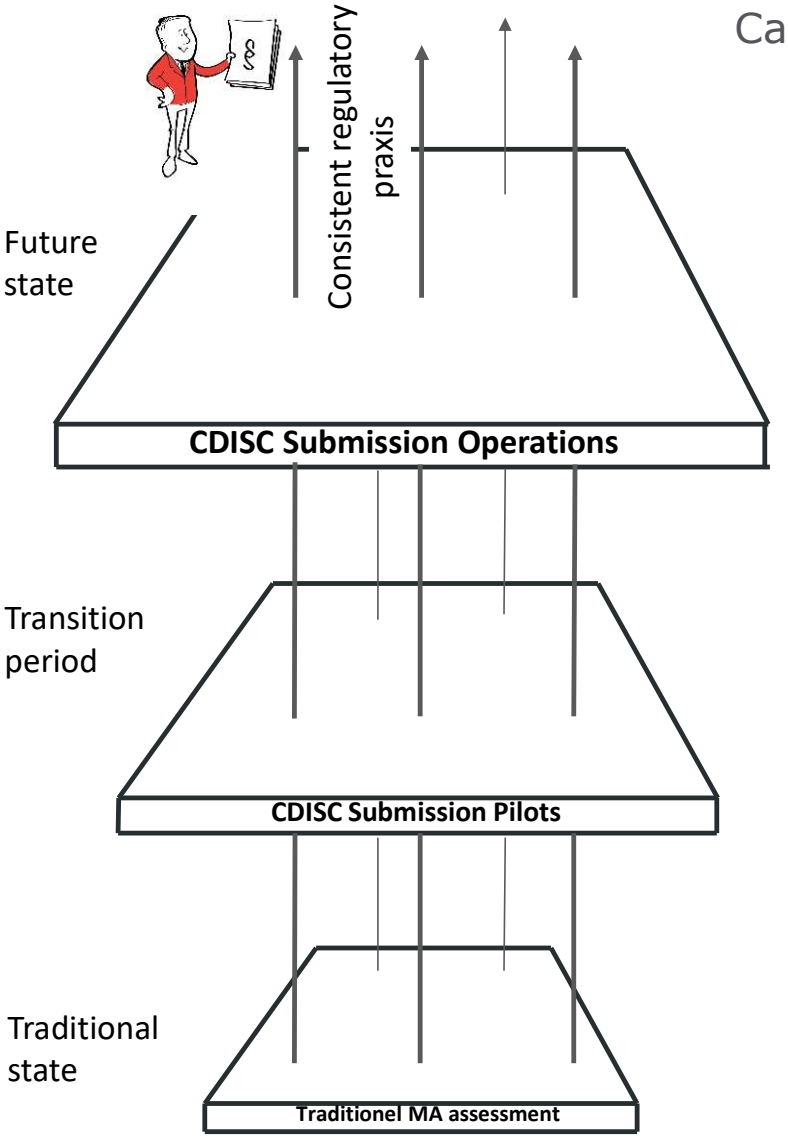
Big data - Network capability to analyse





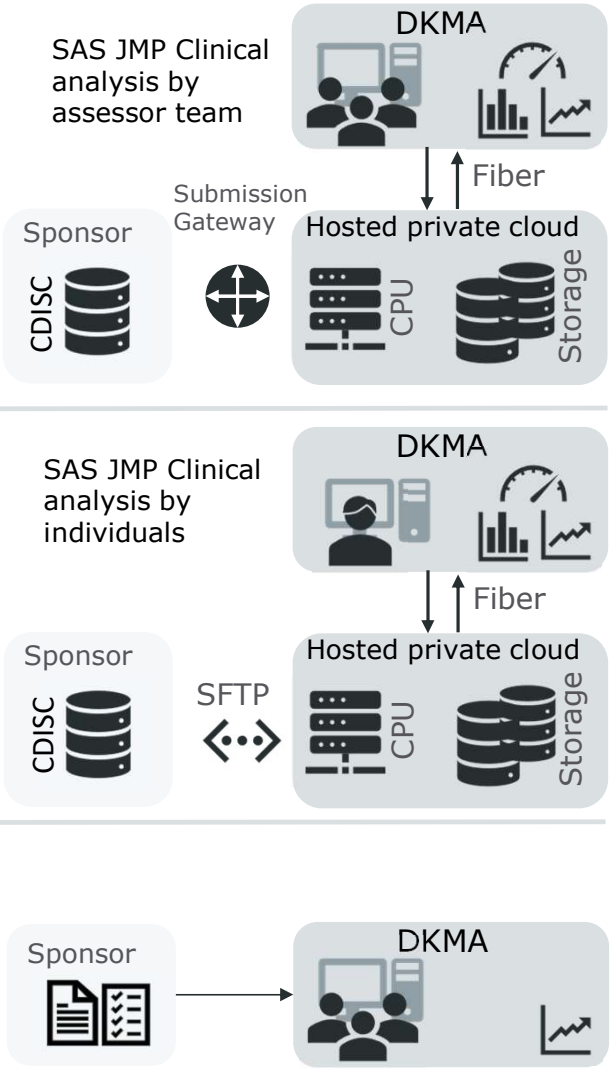
Capabilities and Characteristics

- **Data-driven MA assessment**
- Improved decision support
- **Processed optimized approval cycles**
- Routine JMP Clinical analysis
- Tailored analysis
- Sophistication of tools
- Electronic submission gateway
- Sponsor opt-in to CDISC submission

- Pilot projects
- Feasibility studies
- Repeated analysis and studies from sponsor
- Learning CDISC standard
- Competency building
- Process understanding
- Opportunity mapping

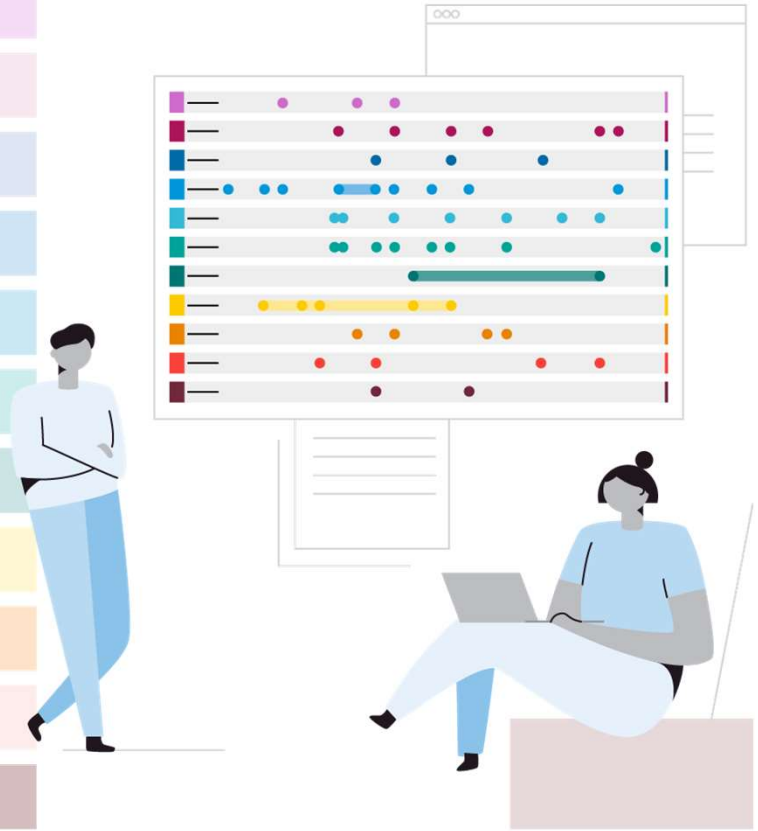
- Conventional MA approval process
- Decisions based on data summaries and text based applications

Process and System



HMA / EMA road map – Big Data Workplan

- DARWIN EU
- Data quality & representativeness
- Data discoverability
- EU Network skills
- EU Network processes
- Network capability to analyse
- Delivery of expert advice
- Governance framework
- International initiatives
- EU stakeholder implementation forum
- Veterinary recommendations



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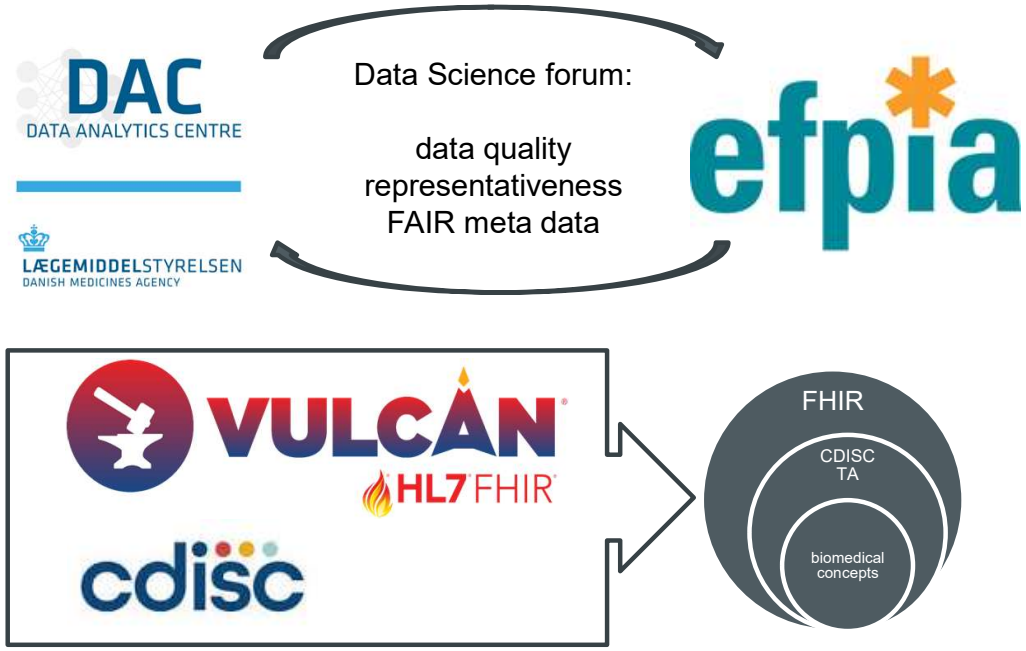
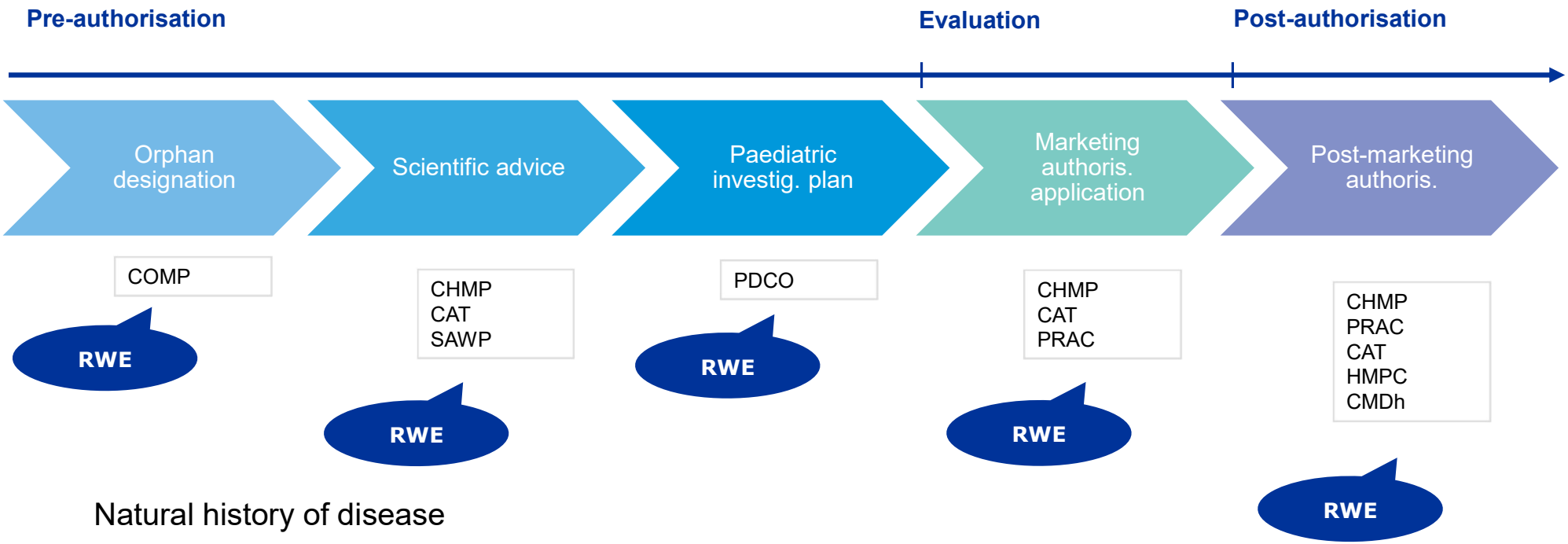
Big Data Workplan
Data quality & representativeness + Data discoverability



- Engagement with stakeholders and leveraging the ongoing work of external parties will be critical to delivering a data quality framework for the EU Regulatory Network.
- It is therefore proposed to contract an external study to analyse existing data quality initiatives and to discuss data quality with a wide range of stakeholders.
- The aim is to deliver the first version of the framework in early 2022. It is proposed to review the Scientific Advice qualification process and this review should start in mid-2021.

Source: https://www.ema.europa.eu/en/documents/work-programme/workplan-hma/ema-joint-big-data-steering-group_en.pdf

Real world data in scientific advice



Natural history of disease

Clinical management of the disease of interest / standard of care

Trial design, inform recruitment

\+ Better understand data sources and their representativeness

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Scientific advice based on RWD

Developing an eco-system for differentially private analysis of Danish health data

This project seeks to **develop** and **apply differential privacy techniques** in the context of **disease progression** by building an eco-system for **access to data** and secure environments to **perform analysis**, allowing **research institutions and industry** to develop useful models while ensuring **appropriate data protection** and privacy of the patients.

The developed methods have the **potential to be generalized** to other use cases of medical research as well as research in other fields that would **benefit from access to sensitive data** that requires a higher degree of privacy protection.

Project team

IT University of Copenhagen
Computer Science, University of Copenhagen
Data Analytics Centre, Danish Medicines Agency

request to collaboration has gone out to EFPIA

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Scientific advice PK/PD modelling

Personalised treatment with direct oral anticoagulants (DOACs):

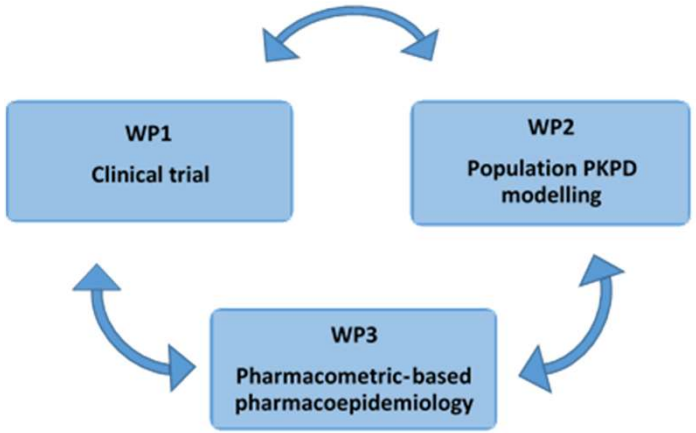
a multidisciplinary approach to optimise effectiveness and safety

- By using machine learning techniques, which risk factors can then be found in real-world data for patients at high risk of adverse events from DOACs?
- How does these risk factors influence pharmacokinetics and pharmacodynamics of DOACs in a clinical trial setting?
- How to tailor dosing for personalised treatment with DOACs? e.g., by taking into account covariates for biological aging, accurate measures of organ function, especially for renal function, and measures of body composition in addition to other risk factors found by studying real world data?

Project team

Pharmacometrics Research Group, University of Copenhagen
Pharmacovigilance Centre, University of Copenhagen
Hvidovre and Amager Hospitals
Data Analytics Centre, Danish Medicines Agency

Request for collaboration has gone out to EFPIA



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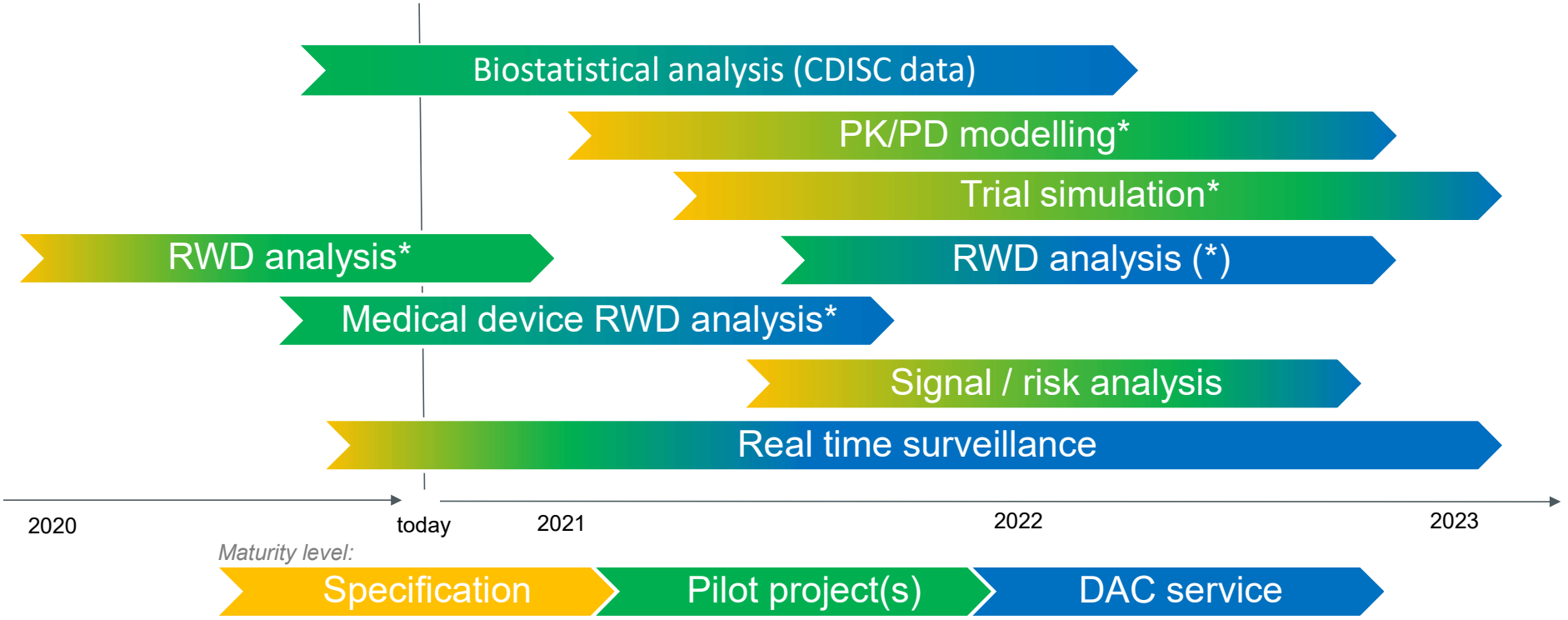
DAC product catalogue road map

Iteratively and through collaboration expanding the analytical capabilities



** Collaboration with academia*

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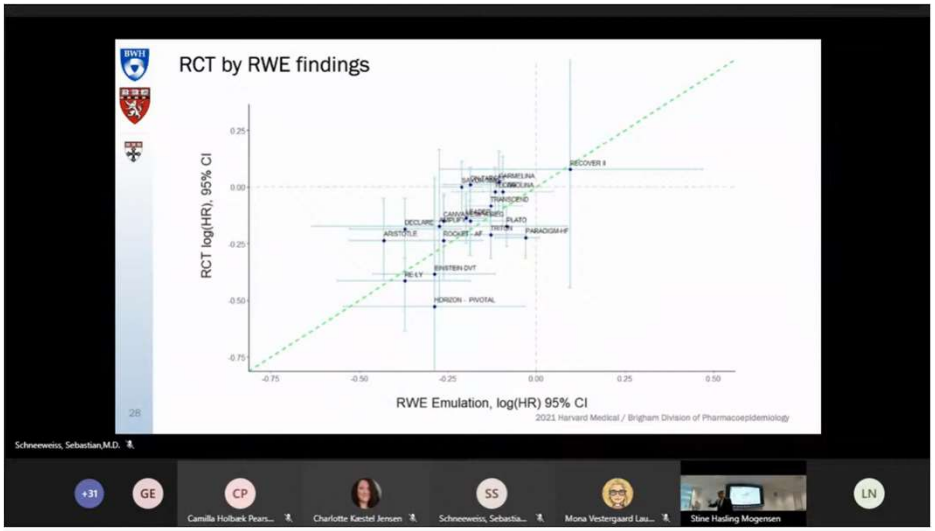
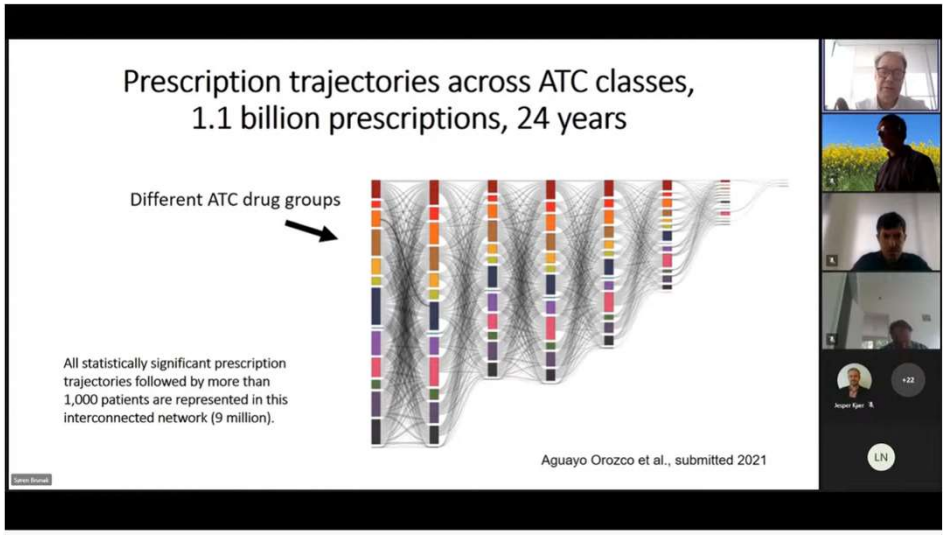
For more information…

lmst.dk/DAC

DAC InnovationTalks and MasterClass webinars on youtube:



DAC MASTER CLASS: Pharmacovigilance 2.0 – real world signal generation



INNOVATION TALKS @ DAC feat. PROFESSOR SØREN BRUNAK

https://www.youtube.com/watch?v=0s0-WByTmb4

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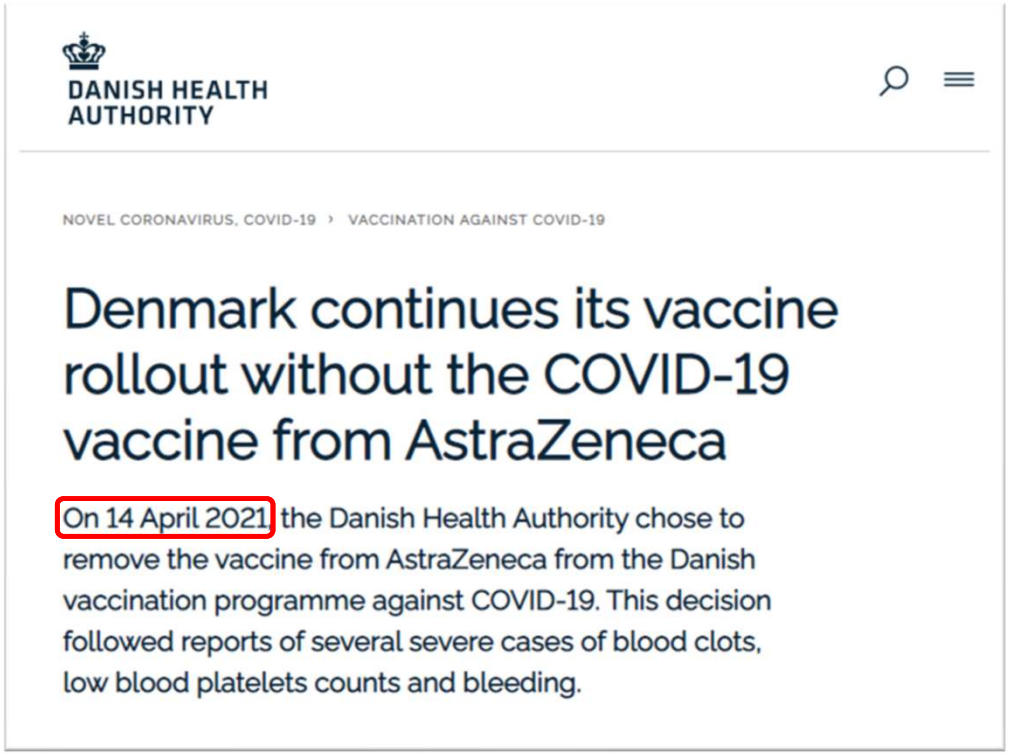
April 14th

AZ-vaccine is removed from the Danish vaccination program



DANISH HEALTH AUTHORITY

NOVEL CORONAVIRUS, COVID-19 › VACCINATION AGAINST COVID-19

Denmark continues its vaccine rollout without the COVID-19 vaccine from AstraZeneca

On 14 April 2021 the Danish Health Authority chose to remove the vaccine from AstraZeneca from the Danish vaccination programme against COVID-19. This decision followed reports of several severe cases of blood clots, low blood platelets counts and bleeding.

https://www.sst.dk/en/english/corona-eng/vaccination-against-covid-19/astrazeneca-vaccine-paused

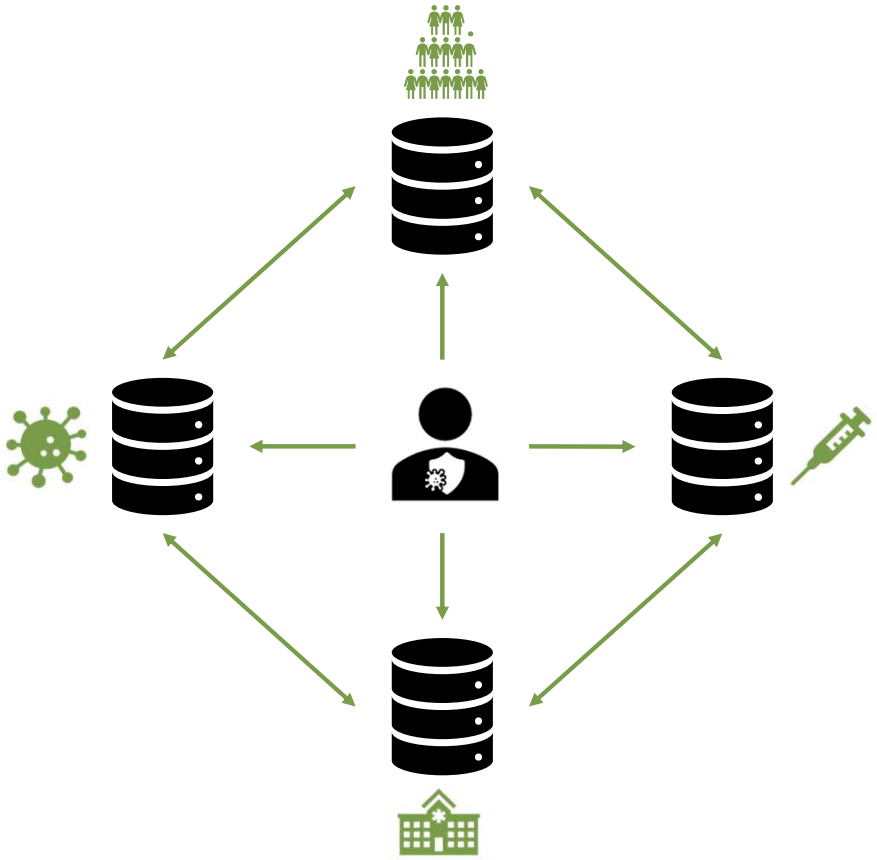
The Danish Health Authority decides to complete the vaccination with a **mRNA-vaccine**, If you have received 1. vaccination with the **AstraZeneca-vaccine**

https://www.sst.dk/en/english/corona-eng/vaccination-against-covid-19/astrazeneca-vaccine-paused

Monitoring off-label cross vaccination in Danish cohorte

- **Objective:** Monitor effect and side effects of **off label use** of cross vaccinations between AstraZeneca and mRNA vaccines
- **Design:** Cohorte study
- **Setting:** Nationwide Danish healthcare registers
- **Participants:**
  I. All people receiving 1. vaccination with Astrazeneca vaccine, excl. death, emigration and SARS-CoV-2 positive test (N~140.000)
  II. A comparativ cohorte of people receiving 1. and 2. vaccination with Pfizer-vaccine

Danish data sources



Central person registry

- Person identifier, age gender, civil status, emigration, death

Microbiology Database

- Test results from microbiological departments

Danish Vaccination Registry

- Vaccination status and vaccination dates

National Patient Registry

- Contacts and admissions to hospital, diagnoses, examinations, treatments

RWD as a important tool in vaccine rollout

- Cross-vaccination has not been studied in the clinical trials for which the AstraZeneca and mRNA vaccines have been approved
- Cross-vaccination is characterized as **off-label use** by the Danish Medicines Agency.
- The off-label follow-up study allows the Danish Medicines Agency to follow the **effects of off-label use** of the vaccines incl. lack of efficacy and side effects after cross-vaccination
- **RWD is an important tool** in the pandemic control and monitoring of COVID-19 vaccine rollout and surveillance