Multiple sclerosis lessons for AD registries

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Disclosures

Jan Hillert has received honoraria for serving on advisory boards for Biogen, Celgene/BMS, Merck KGaA, Novartis, Sandoz and Sanofi-Genzyme and speaker's fees from Biogen, Celgene, Novartis, Merck KGaA, Teva and Sanofi-Genzyme. He has served as P.I. for projects, or received unrestricted research support from, Biogen, Celgene, Merck KGaA, Novartis, Roche and Sanofi-Genzyme.

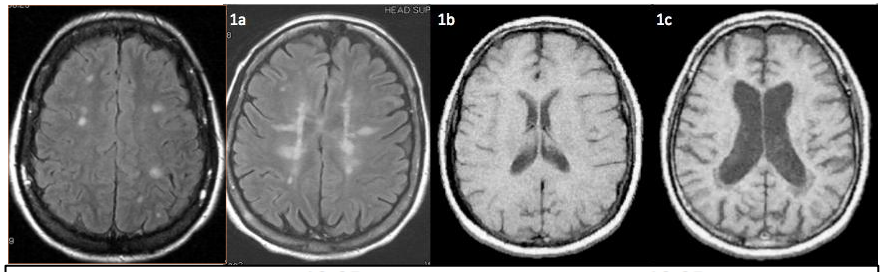
For this presentation, this should be of minor relevance

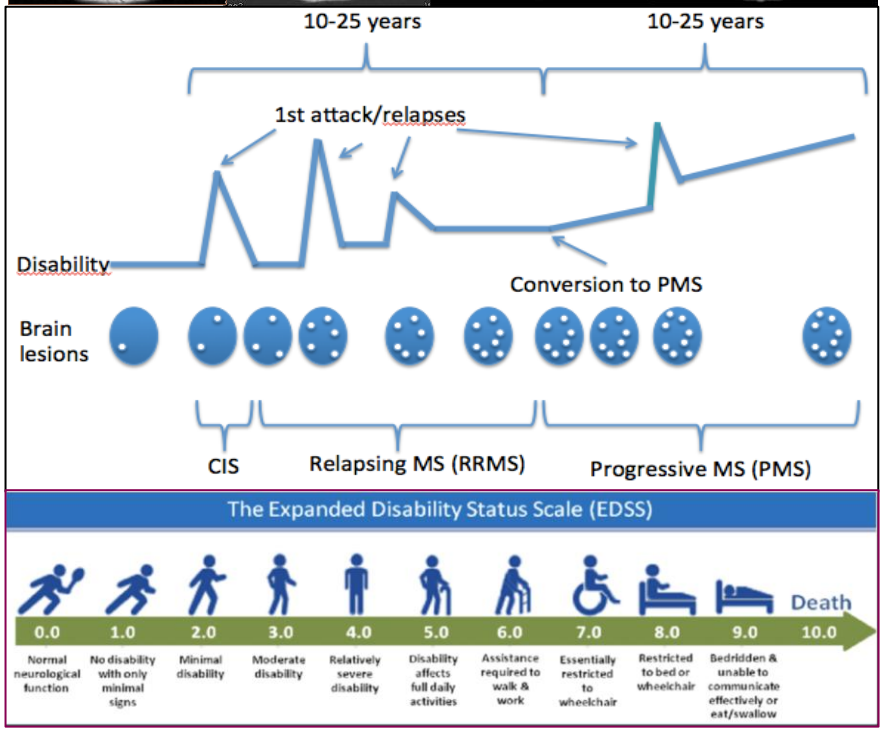
MS lessons for AD registries

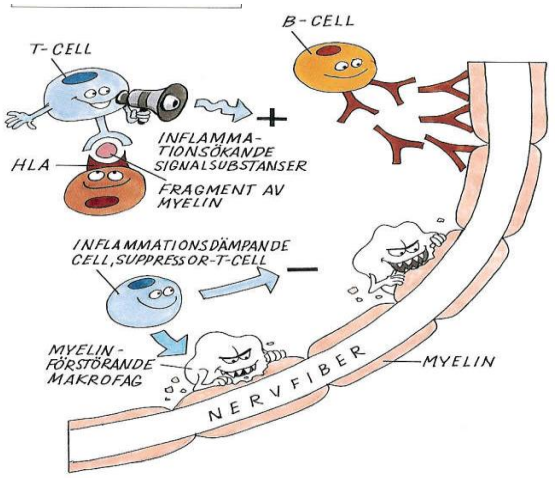
looking thru the retrospectoscope

- Prepare a proper informatics structure from start
- Establish an ADreg Common data model
- Base common data model on RCT standards
- Adapt to EMA Data Quality expectations
- Offer patient portals
- Establish a pharma consortium for support and advice

Multiple sclerosis
MS







1990:ies:
Disease modifying treatments
A dozen mechanisms

<u>MS epidemiology</u>
1/200 risk in Europe
Onset 20-40 yrs
Course 30-40 yrs
75% females

2025-12-17

Big MS Data Network since 2014

BIG MS
The big Multiple Sclerosis data network

The Danish Multiple Sclerosis Registry

OFSEP

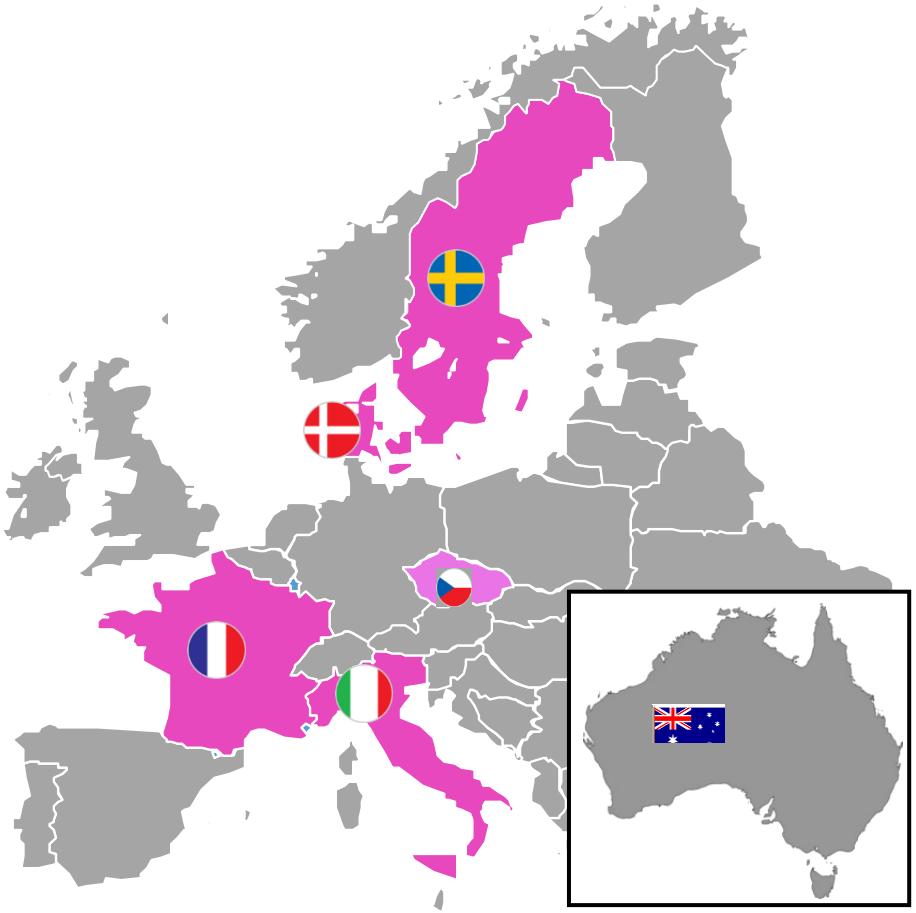
Nadační fond IMPULS

The Italian Multiple Sclerosis Register
Translating Research Into Health

ReMuS
MULTIPLE SCLEROSIS
PATIENT REGISTRY

MSBase
Neuro-Immunology Registry

Swedish
Neuro Registries



- Compatible variables
- Common data model
- Data sharing issues handled
  - Ethical aspects
  - Legal aspects
  - Governance aspects

    = Able to merge patient level data
- 6 joint papers on merged data (N=110,000)

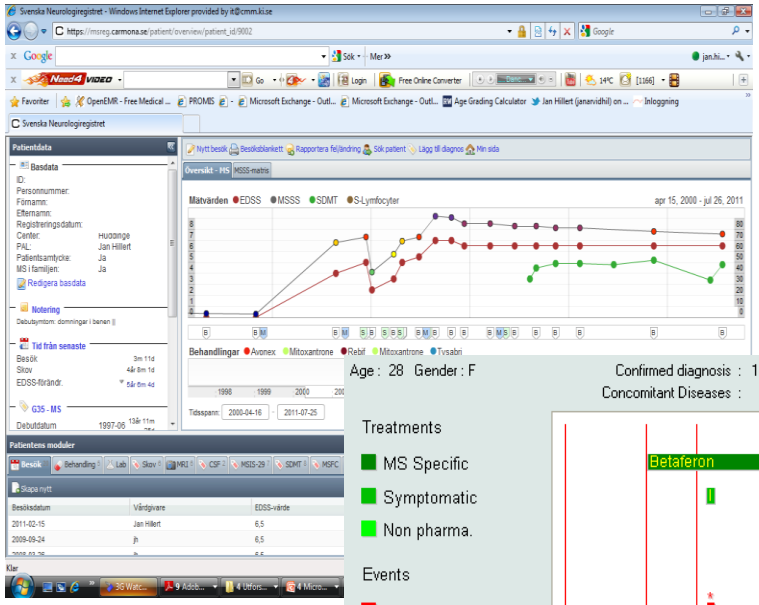
N=350,000

BigMS Registries > 10 % of the MS World

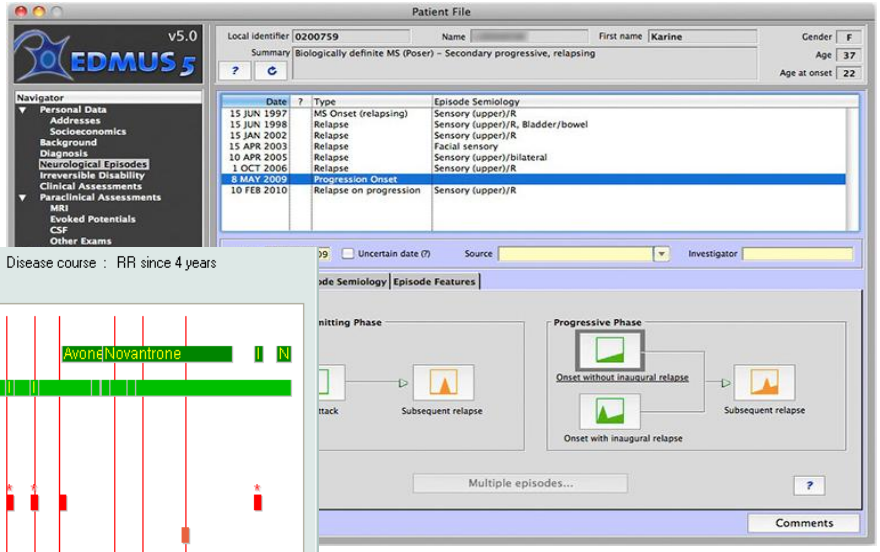
Registry	Estab-lished	Number of centres	Estimated number of patients	Number of publications
Danish MS Registry	1956	30	30,000	179
Swedish MS Registry	1998	64	22,000	280
OFSEP (France)	1980		67,000	155
Italian MS Database Network	2001	26	85,000	45
Czech Republic	2013	15	17,500	20
MSBase	2001	210	100,000	120
Total	**2014**	**355**	**350,000**	**< 620**

BigMS Registries – Patient overview as attractant

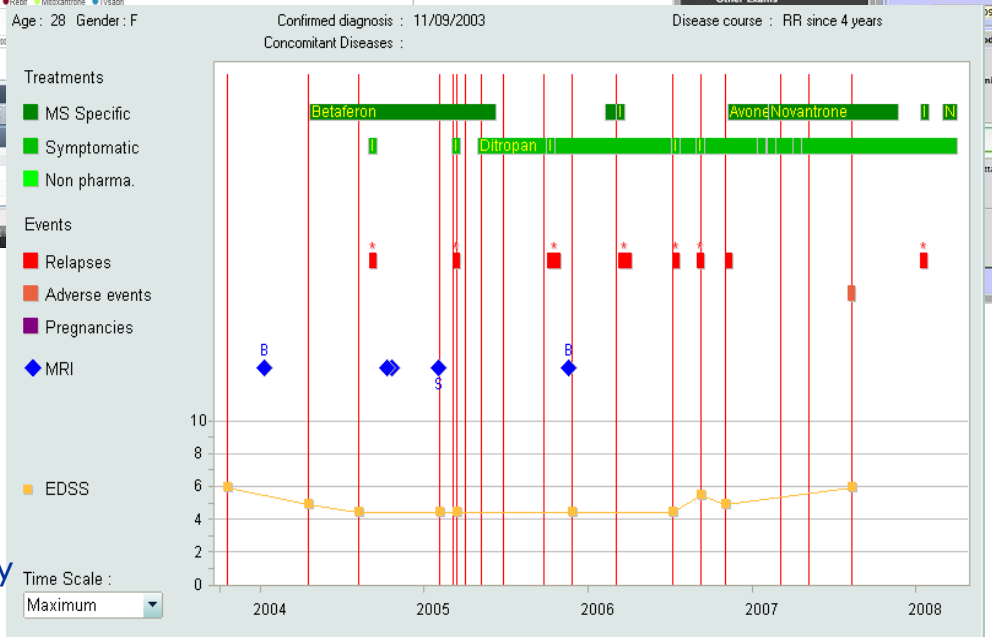
The big Multiple Sclerosis data network



Danish and Swedish - COMPOS



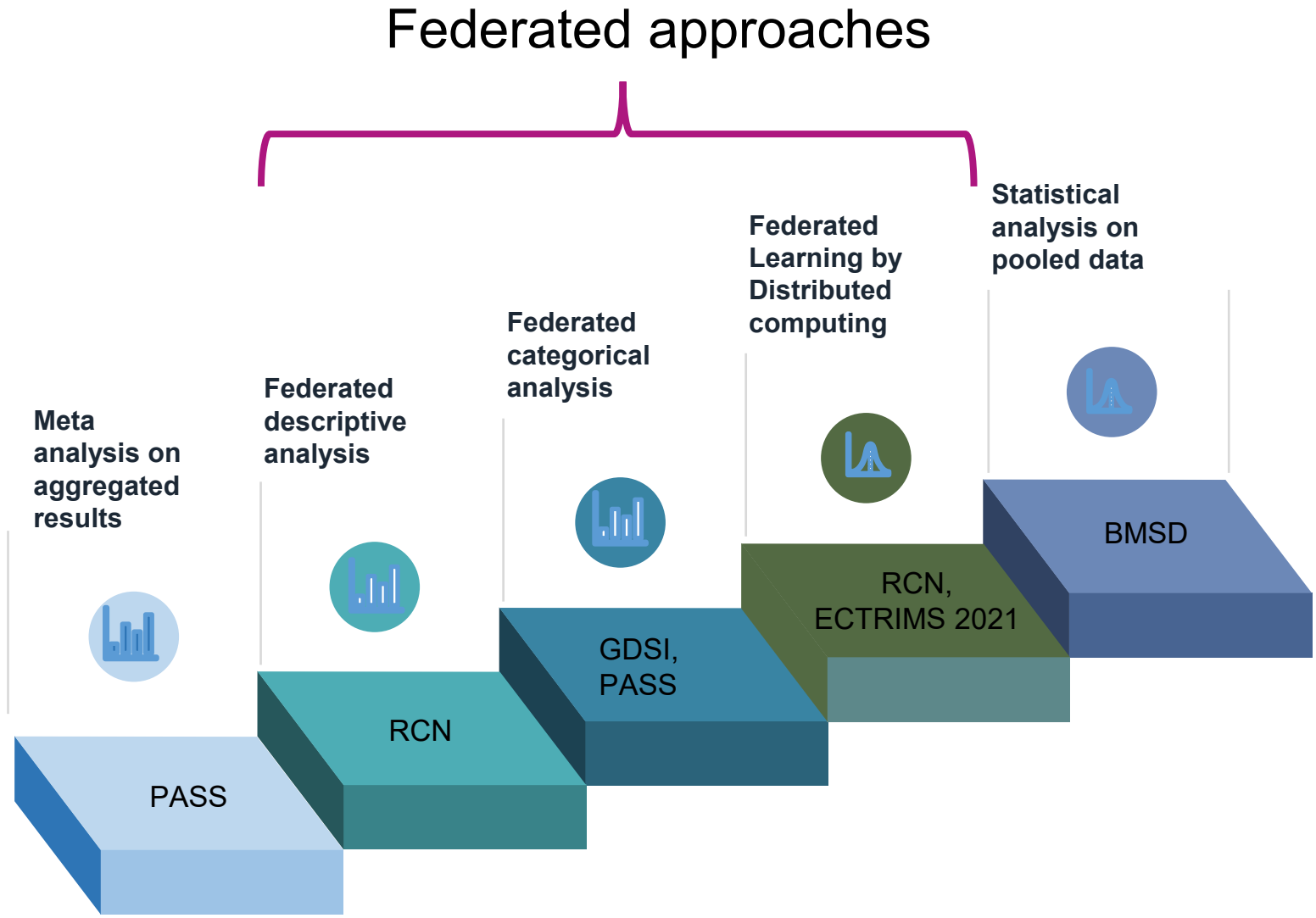
OFSEP - EDMUS



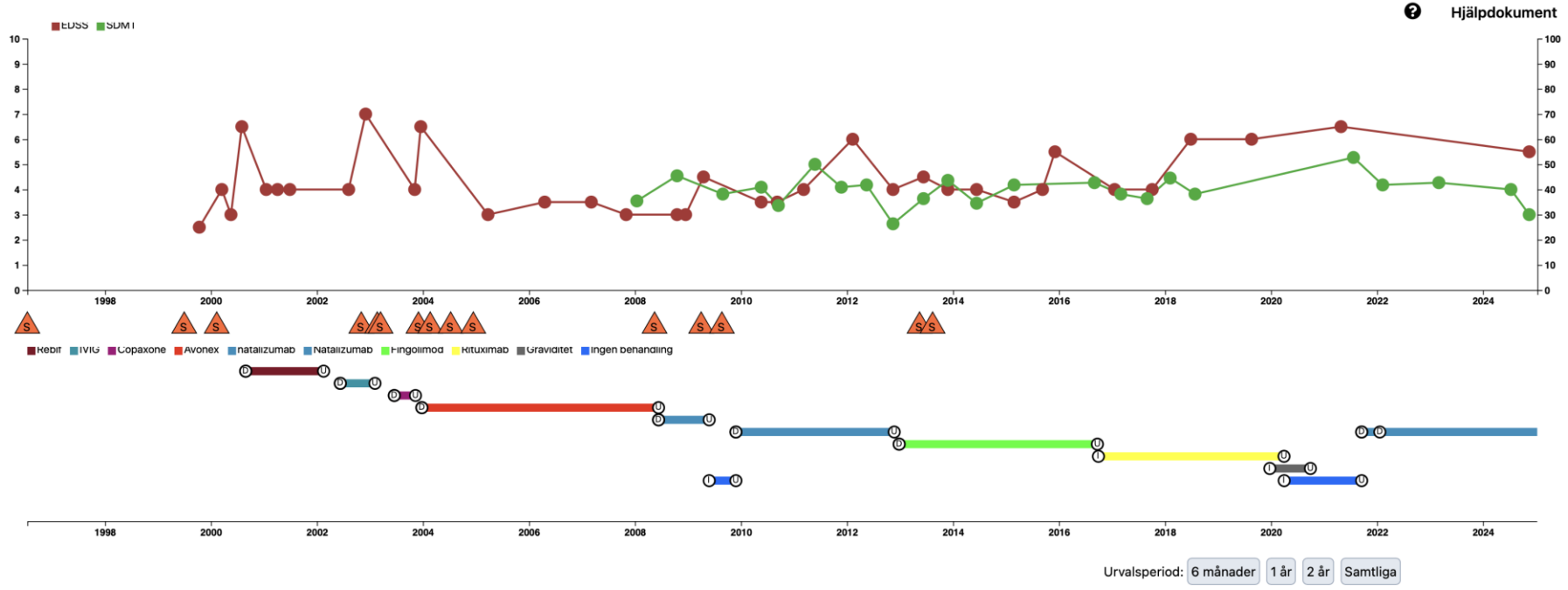
MSBase and Italian MS Registry - iMED

Alternatives to data pooling

BIG MS
The big Multiple Sclerosis data network



SMSreg Patient portal
- PROMS data collection
- Patient participation – shared treatment decisions



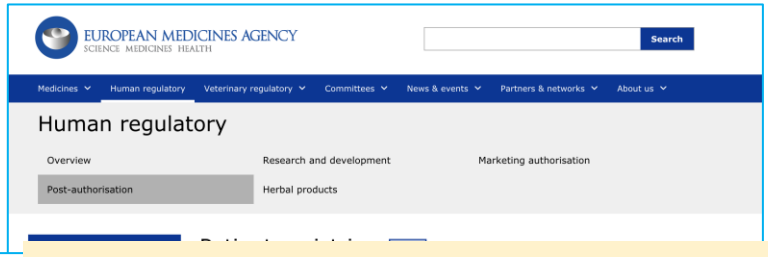
EMA (MS) registry initiative

Registries/RWD may offer:

→External validation at population level

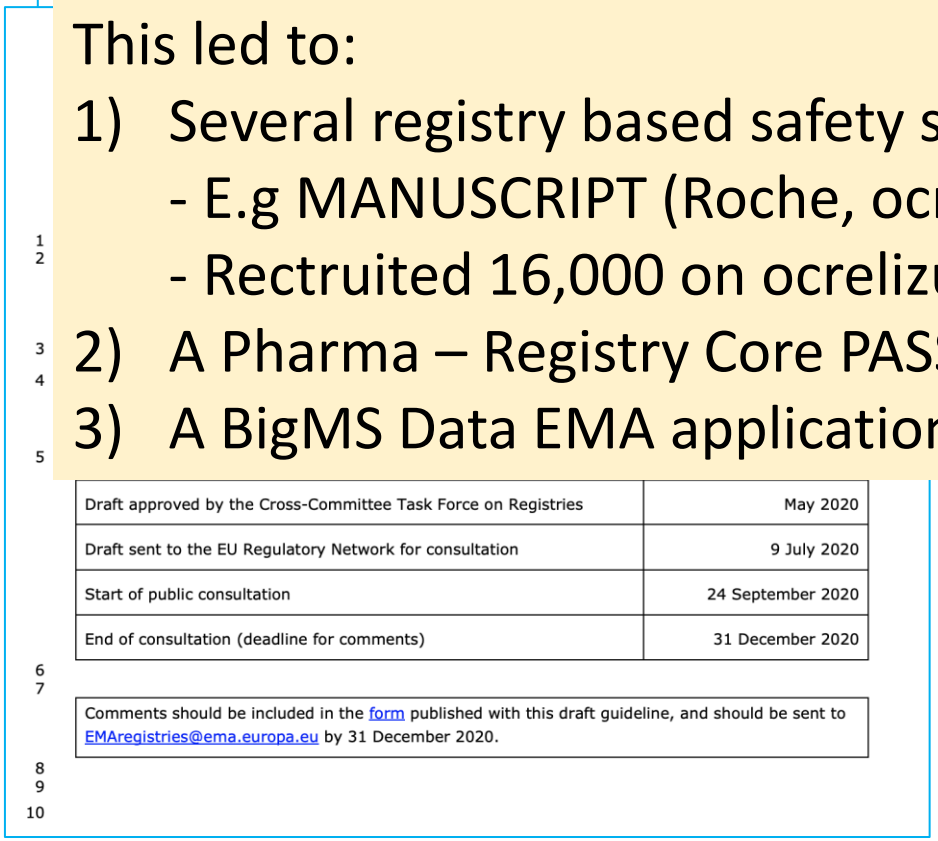
→Bigger numbers: Rare adverse events

→Cost-effectiveness



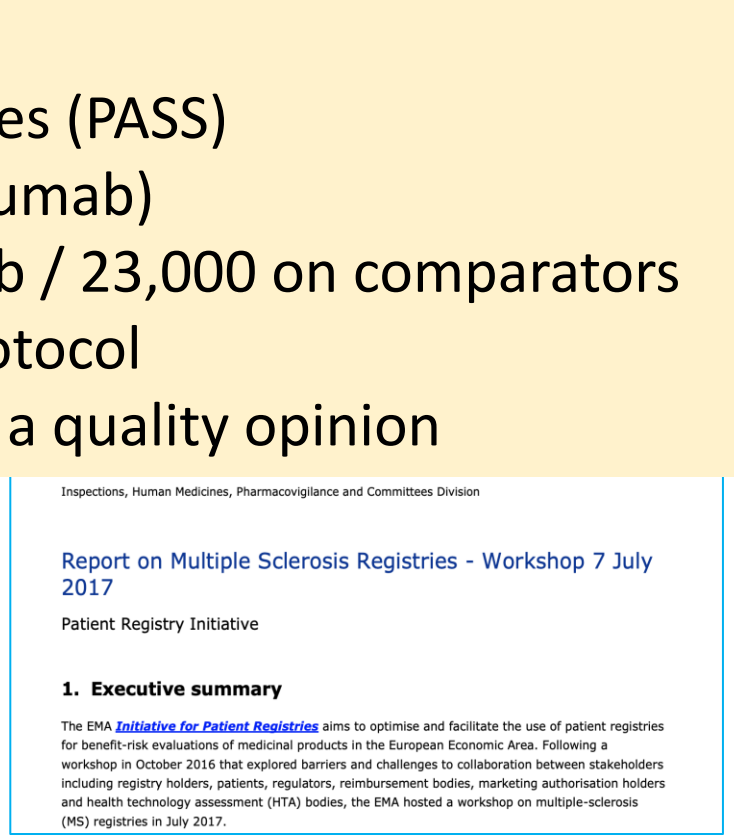
This led to:

1) Several registry based safety studies (PASS)
   - E.g MANUSCRIPT (Roche, ocrelizumab)
   - Rectruited 16,000 on ocrelizumab / 23,000 on comparators
2) A Pharma – Registry Core PASS Protocol
3) A BigMS Data EMA application för a quality opinion



Draft approved by the Cross-Committee Task Force on Registries	May 2020
Draft sent to the EU Regulatory Network for consultation	9 July 2020
Start of public consultation	24 September 2020
End of consultation (deadline for comments)	31 December 2020

Comments should be included in the form published with this draft guideline, and should be sent to EMAregistries@ema.europa.eu by 31 December 2020.



Inspections, Human Medicines, Pharmacovigilance and Committees Division

Report on Multiple Sclerosis Registries - Workshop 7 July 2017

Patient Registry Initiative

1. Executive summary

The EMA ***Initiative for Patient Registries*** aims to optimise and facilitate the use of patient registries for benefit-risk evaluations of medicinal products in the European Economic Area. Following a workshop in October 2016 that explored barriers and challenges to collaboration between stakeholders including registry holders, patients, regulators, reimbursement bodies, marketing authorisation holders and health technology assessment (HTA) bodies, the EMA hosted a workshop on multiple-sclerosis (MS) registries in July 2017.

Big MS Data Network
Qualification opinion application for PASS

BIG MS
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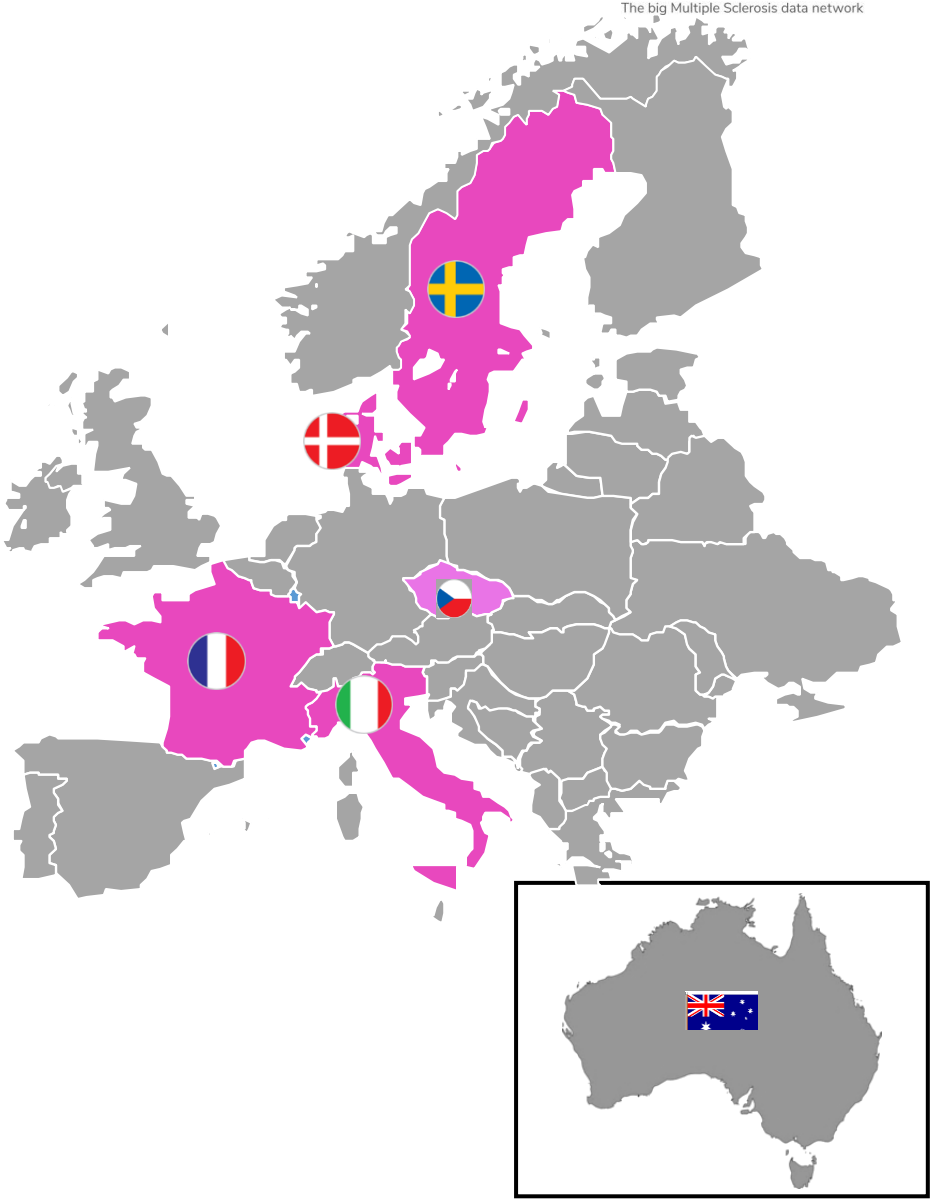


- Pre submission meeting Nov 2020
- Scientific Advice May 2021
- Letter of Support September 2021
- Re-application October 2025

2021: BigMSData seeking EMA's qualification opinion to run post authorization safety studies (PASS)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

BIG MS The big Multiple Sclerosis data network

CONFIDENTIAL
EMADOC-1700519818-684863
Case No.: EMA/SA/0000050512
Human Medicines Division

Amsterdam, 20/05/2021

Initial Qualification Procedure

Big MS Data Network (BMSD) and incorporated multiple sclerosis (MS)

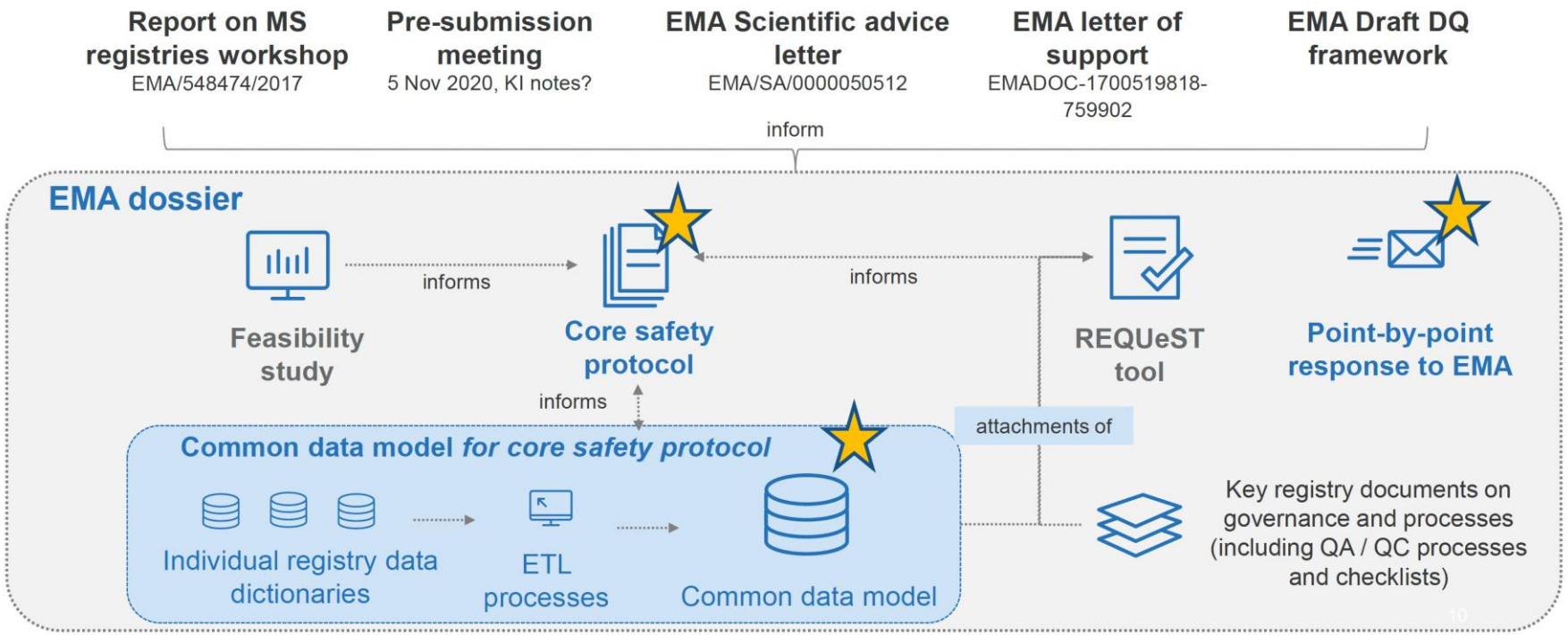
On 04/01/2021 the Applicant Karolinska Institute requested scientific advice for their network of registries Big MS Data network (BMSD) pursuant to Article 57(1)(n) of Regulation (EC) 726/2004 of the European Parliament and of the Council.

The Big MS Data network (BMSD), consisting of six participating multiple sclerosis registries, targets a context of use of performing registry-based post authorisation safety studies (PASS).

CHMP Qualification Advice - general feedback

The Applicant's proposal for the use of Big MS Data Network (BMSD) and six individual MS registries for future registry-based post authorisation safety studies (PASS) deserves support, but at this stage formal qualification is not possible for two major reasons: extent of safety data collected and central quality control (see further discussion below). In addition, within the current qualification procedure the EMA cannot agree on the qualification of future registries who are willing to join BMSD but are not yet included in the current procedure.

The submitted BigMS Data EMA dossier



BIG MS
The big Multiple Sclerosis data network

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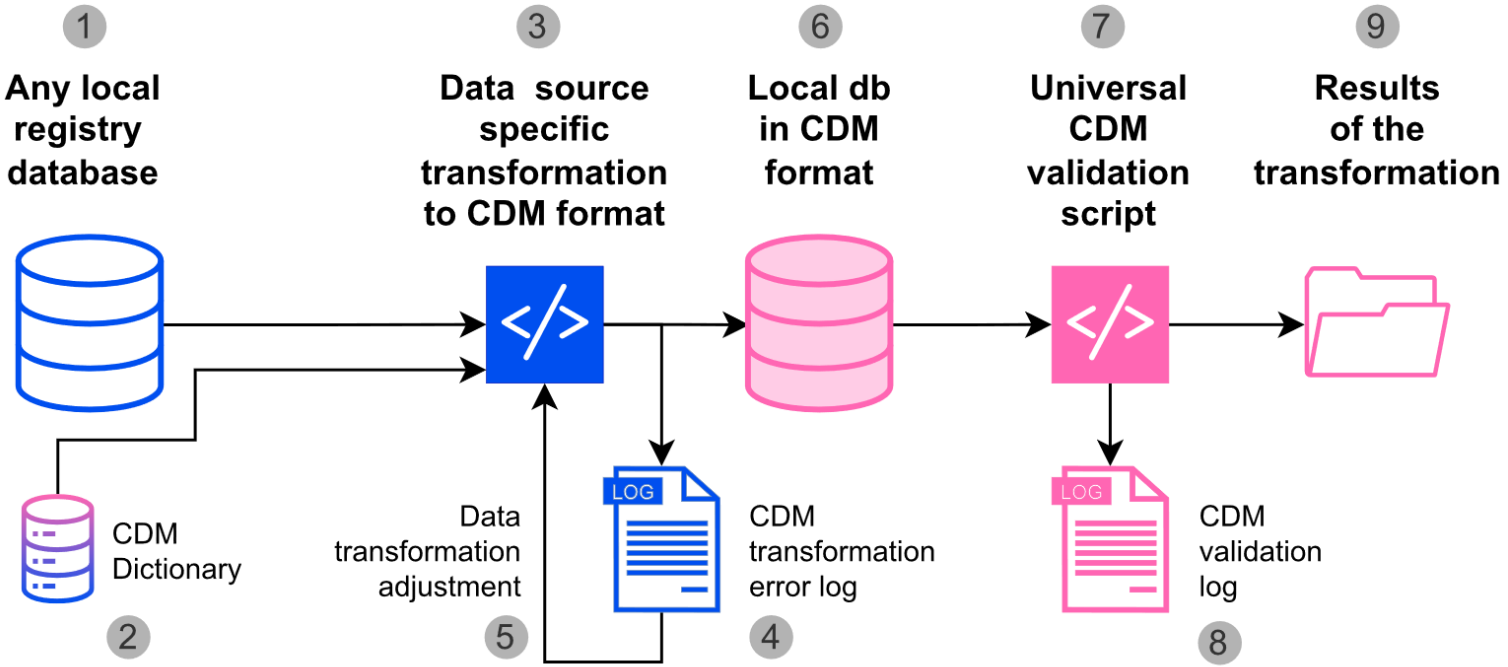
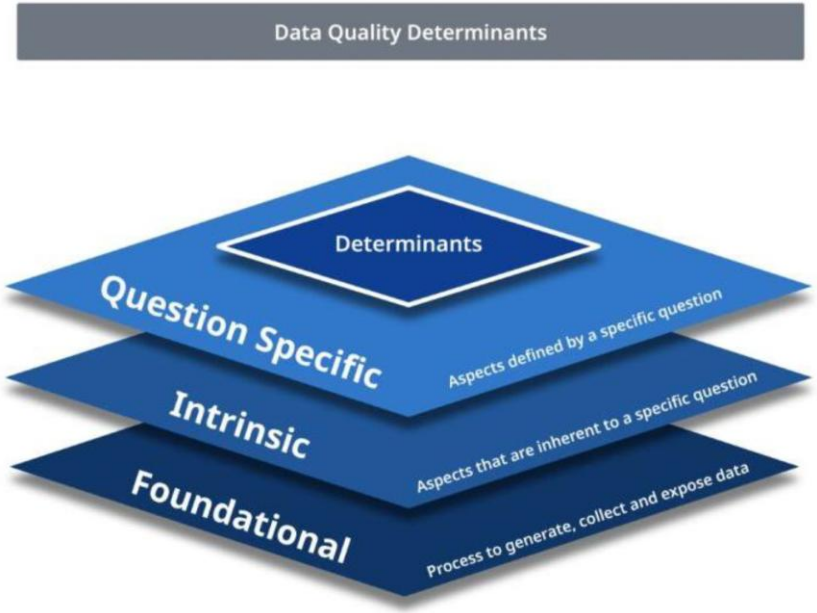
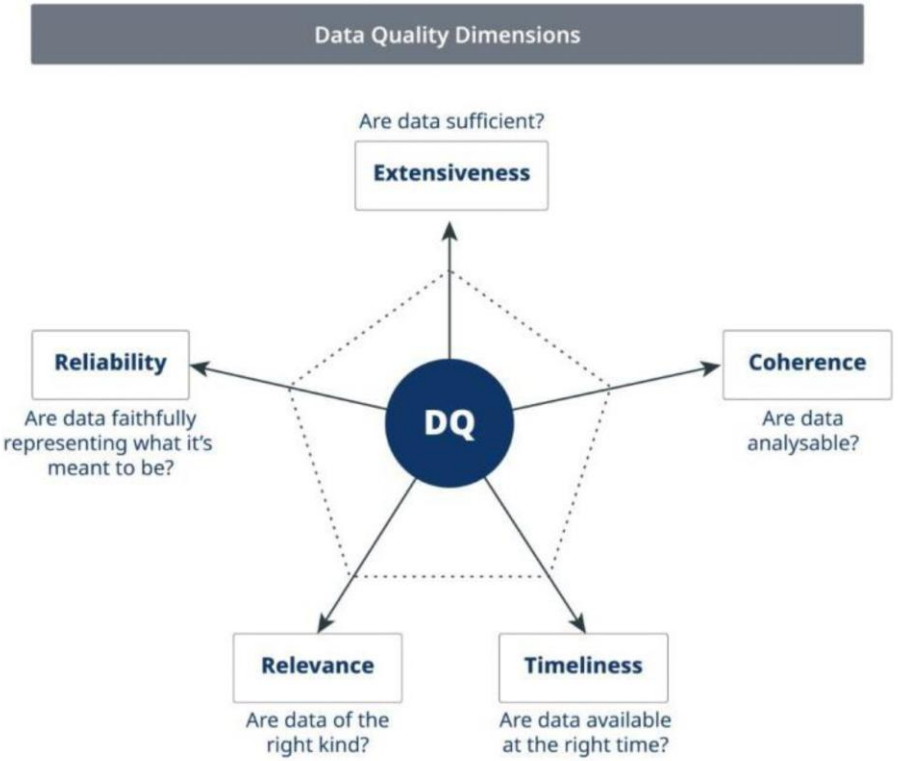
Common Data Model



EMA Data quality Framework:
- Determinants
- Dimensions





Application to real world data:

Framework for the categorisation and identification of metrics

	Reliability	Extensiveness	Coherence	Timeliness
Independent data checks				
Plausibility checks				
Conformance checks				
Comparison to other data sources				
Checks on dataset metadata				

Challenges for MS registry data to qualify with the EMA:

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- EMAs expectations are challenging:
  - → Old registries of various background
  - → Different platforms, stepwise developed
  - → Variable QA/QC routines
  - → Independent governance structures
  - → Different priorities

- Data elements difficult to collect include
  - → comorbidities
  - → concomitant medications

Industry support to MS registries

- Registry establishment, maintenance and development
- Data collection efforts
  → Clinician compensation
  → Monitoring
- Commissioned research
  → Post authorization safety studies (PASS)
  → Comparative effectiveness

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looking thru the retrospectoscope

- Prepare a proper informatics structure from start
- Establish an ADreg Common data model
- Base common data model on RCT standards
- Adapt to EMA Data Quality expectations
- Offer patient portals
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Finally:

- Registries/RWD may offer:
  - →External validation at population level
  - →Bigger numbers: Rare adverse events
  - →Cost-effectiveness
  - →A step towards universal safety assessment