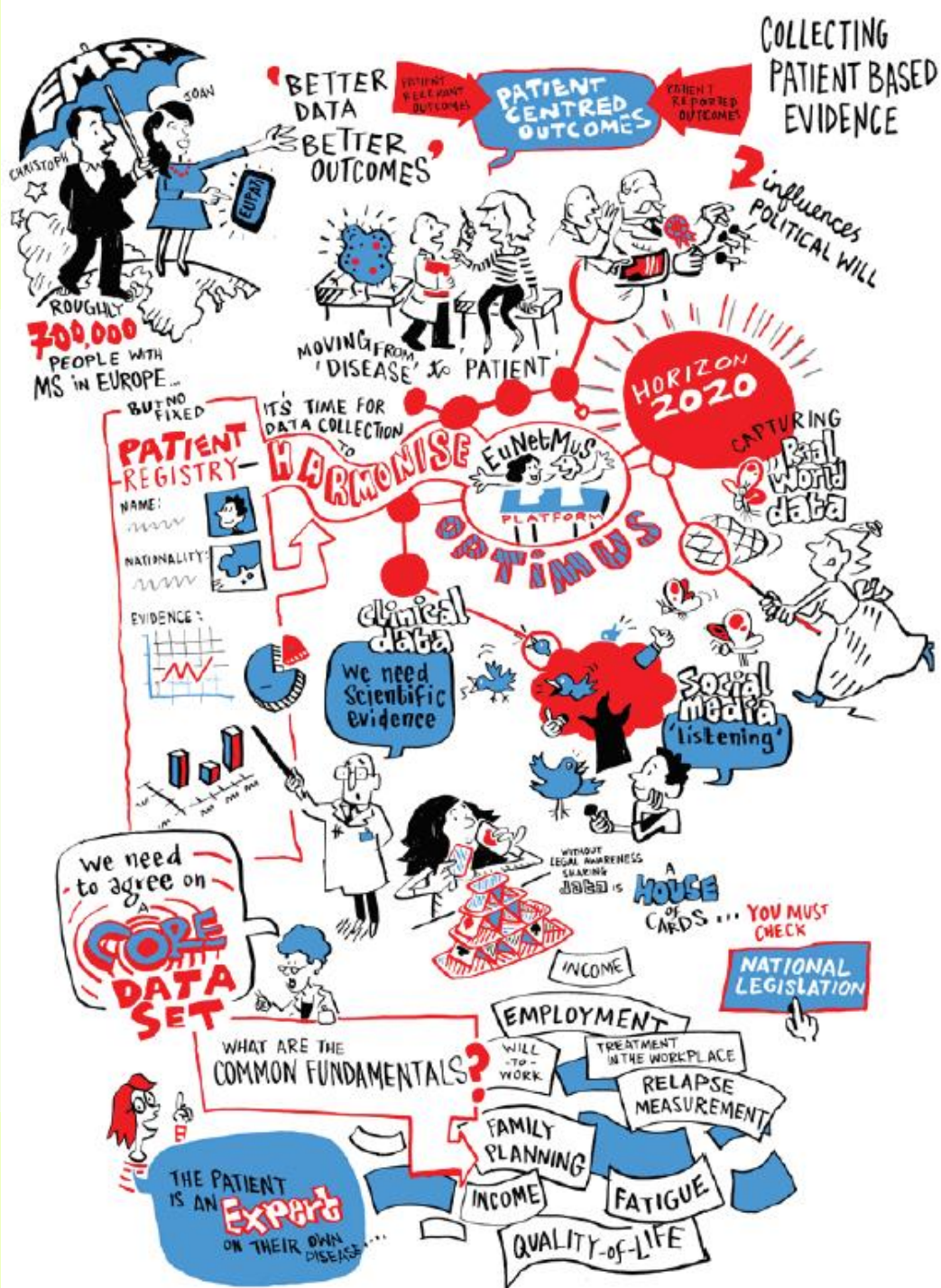


European Patient Innovation Summit – Milano, October 2016

Generating evidence and defining patient- relevant outcomes

Christoph Thalheim – Director External Affairs



EUROPEAN
MULTIPLE SCLEROSIS
PLATFORM

What is real world evidence?

Real world evidence is defined as data that are collected outside the constraints of conventional randomised clinical trials.

Electronic Health
Records

Patient Registries – ideally with

- Clinical data
- PCO/PRO data
- Socio-economic data

Digital phenotypes

Hospital data

Health Insurance Data

Genomes

Patient and physician
surveys

Biobanks

Evidence creating by Real World Data – a snapshot on current initiatives in Multiple Sclerosis

EMA patient
registries
taskforce



Work based on
PARENT

EUReMS Network

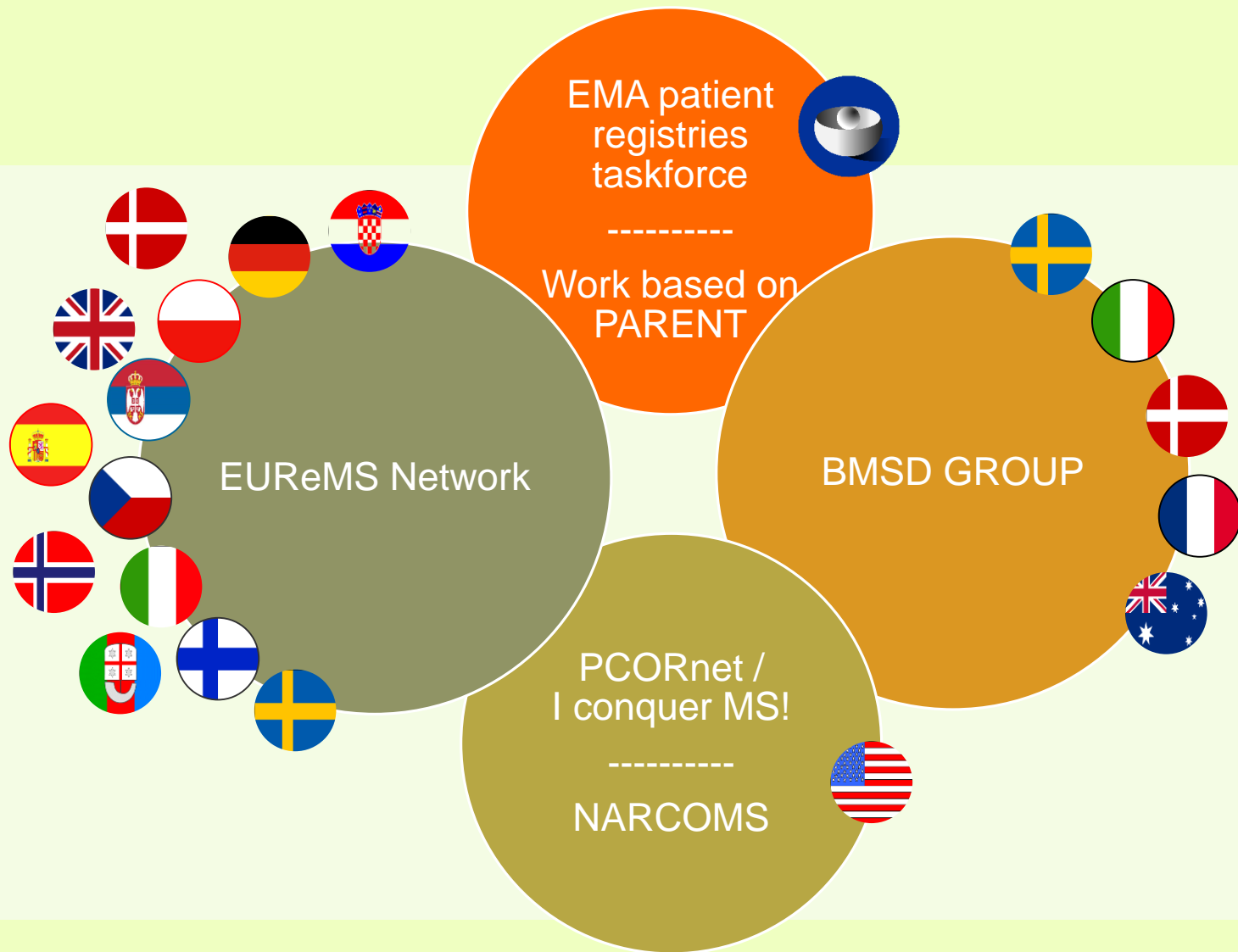
BMSD GROUP

PCORnet /
I conquer MS!

NARCOMS



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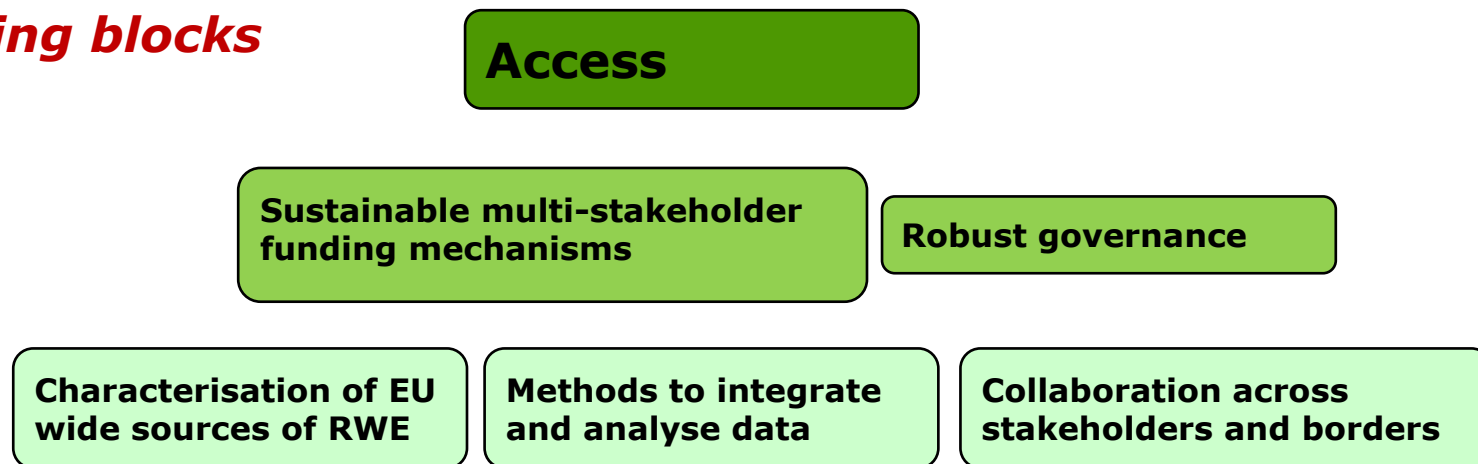
The view by the European Medicines Agency

(extract from a personal view by Dr. Xavier Kurz)

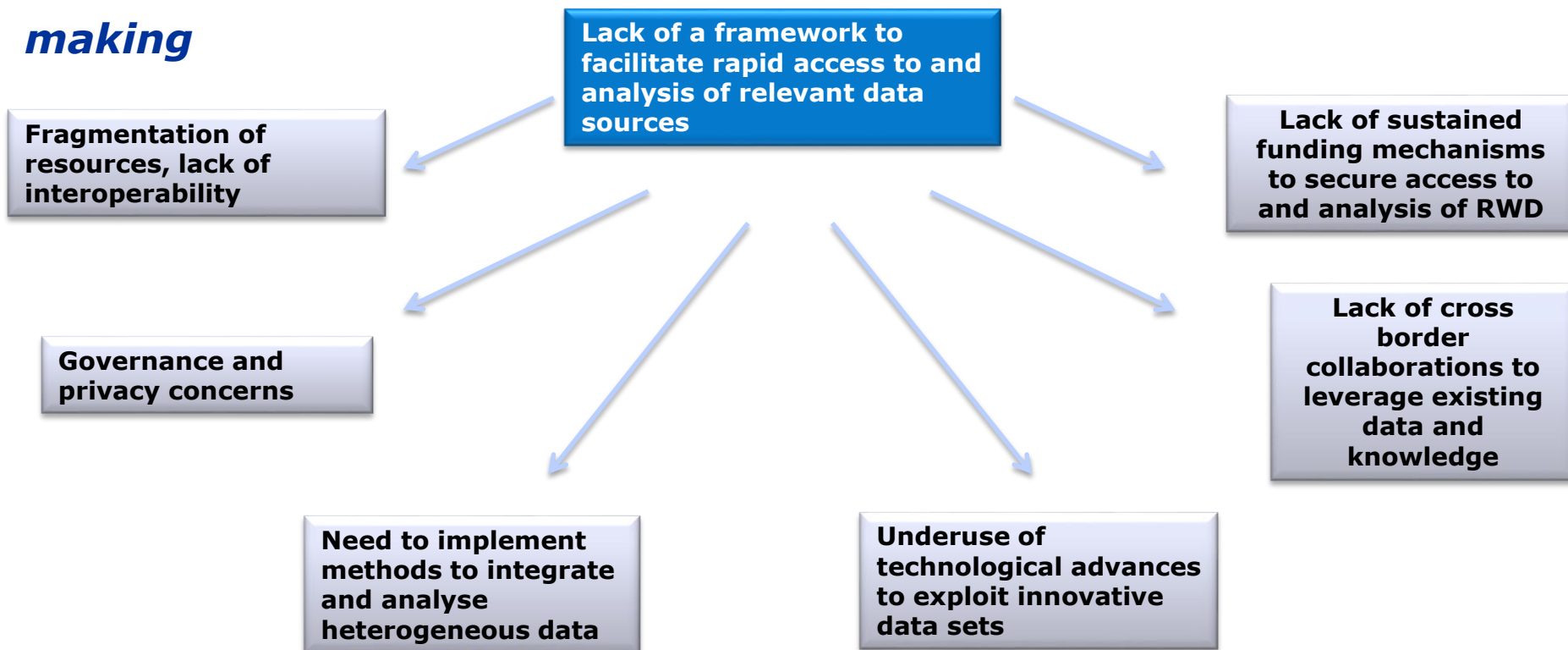
EMA's vision:

Access to and analysis of an extensive range of multinational real world data to optimise medicinal development and decision making

Building blocks



There is limited access to RWD across the EU to support decision making



RWD across the EU to support decision making could become very beneficial for HTA, EMA, researchers, industry & more...

**Improved access
to real world
data**

**Reducing cost of
development**

**Enabling
innovation**

**Optimise
indications**

**Safe,
accelerated
access to
medicines**

**New outcome
measures**

**Effectiveness
data**

**Improved EMA
and HTA decision
making**

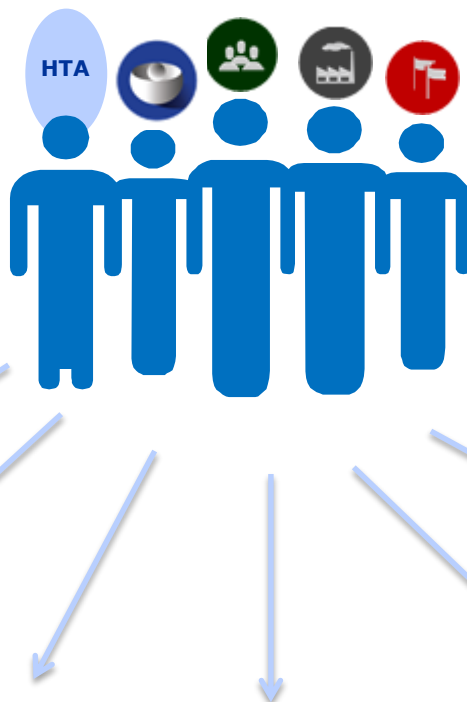
**Optimising use of
medicines through
ongoing monitoring**

**Ability to define the
impact of
regulatory/HTA
decisions**

**Determining safety
and efficacy in high
risk groups**

**Faster identification
and assessment of
safety issues**

**Patient
stratification for
benefit and risk**



RECENT EXAMPLE: Evaluation of risk of progressive multifocal leukoencephalopathy (PML)

Questions raised on clinical practice as regards:

- Use of magnetic resonance imaging (MRI) in identification of asymptomatic PML
- Use of anti-JCV antibody index as marker of PML risk
- Patient monitoring after treatment discontinuation

Registries with >1000 multiple sclerosis patients identified in 5 Member States

Questions to registry coordinators on availability of data and information to answer these questions

- The EMA Initiative on Patient Registries recognises that improvements in utilising existing registries in the context of existing procedures could be made
- Cross-Committee Task Force on Patient Registries in 2014
- Aims to explore better use of existing registries
- Pilot phase initiated Q4 2015

EMA website → Human regulatory → Pharmacovigilance → Patient registries

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000658.jsp&mid=WC0b01ac0580961211



Latest achievements

What we have...

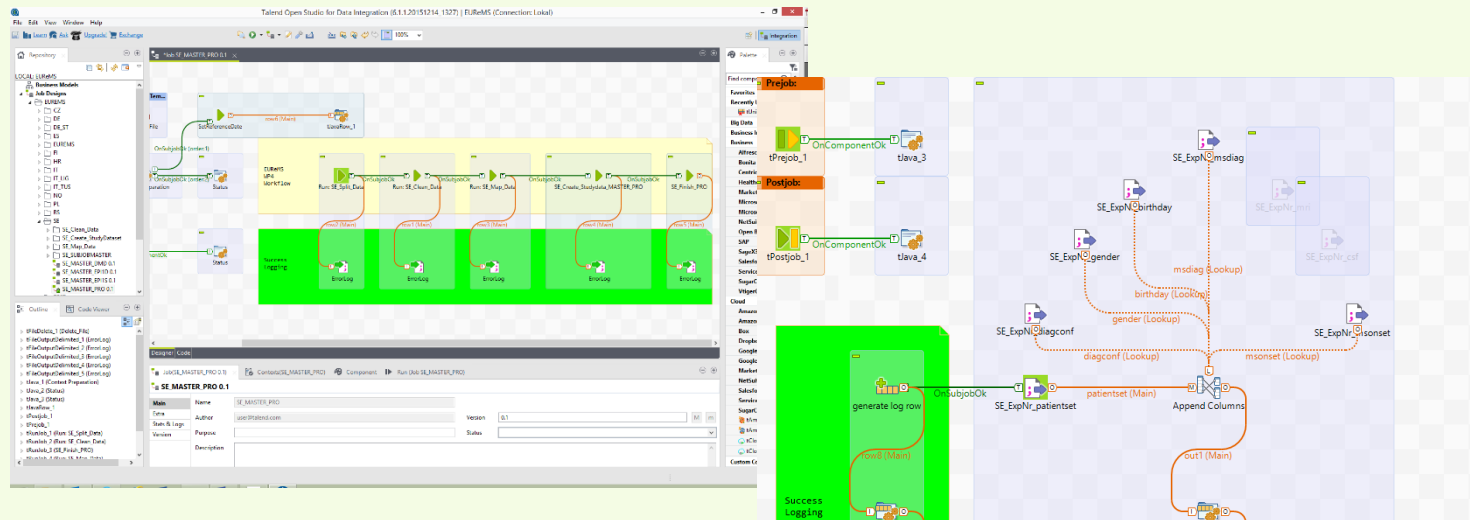
			Data is to be used for			
Country	Code	Date of Data Export	DMD2	EPI2-s	EPI2-d	PRO2
Czech	CZ	27.06.2014		x		
Germany	DE	01.08.2014	x	x		x
Spain – Catalonia	ES	13.03.2014 (correction of columns: 03.05.2016)	x			
Finland	FI	19.08.2014		x	x	
Croatia	HR	05.06.2014		x		
Italy	IT	18.07.2014	x	x	x	
Italy – Liguria	IT-LIG	17.06.2014		x		
Italy – Tuscany	IT-TUS	17.06.2014		x		
Norway	NO	30.06.2014		x		
Poland	PL	01.08.2014				x
Serbia	RS	31.07.2014		x	x	
Sweden	SE	11.08.2014	x	x	x	x
United Kingdom	UK	Access to SAIL Database in July 2016				x

What we achieved so far...

- We already made the network of European MS registers happen through EUREMS!
- Several countries have been working together in four studies, communicating and sharing ideas with each other, fed data into a central analysis center in Germany

What we achieved so far...

- We've developed data handling routines for the harmonisation of the heterogeneous data of the different registers into comparable study datasets - laying the groundwork for the IT network infrastructure.



What we have...

PRO2 – Work focussed analysis

The sample sizes are filtered data according to the following inclusion/exclusion criteria:

- Only patients with a given working status are considered
- Work must be income generating (if applicable)
- Date of working status assessment must be given
- Date of onset/diagnosis needs to be given

Currently:

- Integration of UK data
- Updates of the German and Polish registers

Tomorrow:

- Poster presentation here at the ECTRIMS

PRO WORK DATA	Country		
	GER	POL	SWE
Date of Data Export	01.08.2014	01.08.2014	11.08.2014
Number of PwMS	333	241	1338
% women	72.7 %	66.0 %	70.7 %
% RRMS	47.1 %	40.6 %	73.3 %
% PPMS	10.2 %	5.2 %	4.4 %
% SPMS	42.6 %	54.1 %	22.3 %
% working	30.3 %	27.0 %	73.0 %
Age of Onset (years)	32.5 (10.2)	34.8 (8.9)	31.5 (9.9)
Disease duration	15.4 (10.2)	13.5 (8.6)	12.9 (9.1)
MSIS-29 physical (median)	52.8	32.5	11.2
MSIS-29 psychol. (median)	50.0	38.9	19.4
EQ5D (median)	--	0.60	0.78
EDSS	4.8 (2.2)	4.0 (2.0)	2.8 (2.2)

EUREMS II Poster at ECTRIMS 2016



Assessing the employment status of people with MS across Europe

Meißner T¹, Ellenberger D², Buckow K¹, Flachenecker P³ and Hillert J⁴ for the EUREMS consortium

¹Department of Medical Informatics, University Medical Center Göttingen, Göttingen, Germany, ²Department of Department of Medical Statistics, University Medical Center Göttingen, Göttingen, Germany; ³Neurological Rehabilitation Center Quellenhof, Bad Wildbad, Germany; ⁴Karolinska Institute, Stockholm, Sweden

Background & Objectives

A challenging consequence of Multiple Sclerosis (MS) is the economic burden since many patients need to quit working early because of MS related challenges. The PRO (Patient-Reported Outcomes) study of the EUREMS (European Register for Multiple Sclerosis) project focusses on the identification of differences in quality of life and employment between the participating MS registers.

Methods

Three registers have been elected to participate in the PRO study: the MS-Register der DMSG (Germany), the REJSM – Polish MS register (Poland) and the SMSreg - Svenska

Discussion & Prospects

The data indicate how sensitive employment can be to underlying circumstances. A lot of progress has already been made to keep PwMS longer in employment, especially the Swedish MS register data show that high employment rates of PwMS are possible. One has to bear in mind, though, that Sweden has one of the lowest unemployment rates in the EU anyway and the collected data are from outpatients with a mostly RR-MS patient base. Findings of our study might also be slightly biased due to different definitions of income-generating work. Also selection biases may remain even after adjustment for covariates due to different data sources: E. g. in contrast to the Swedish

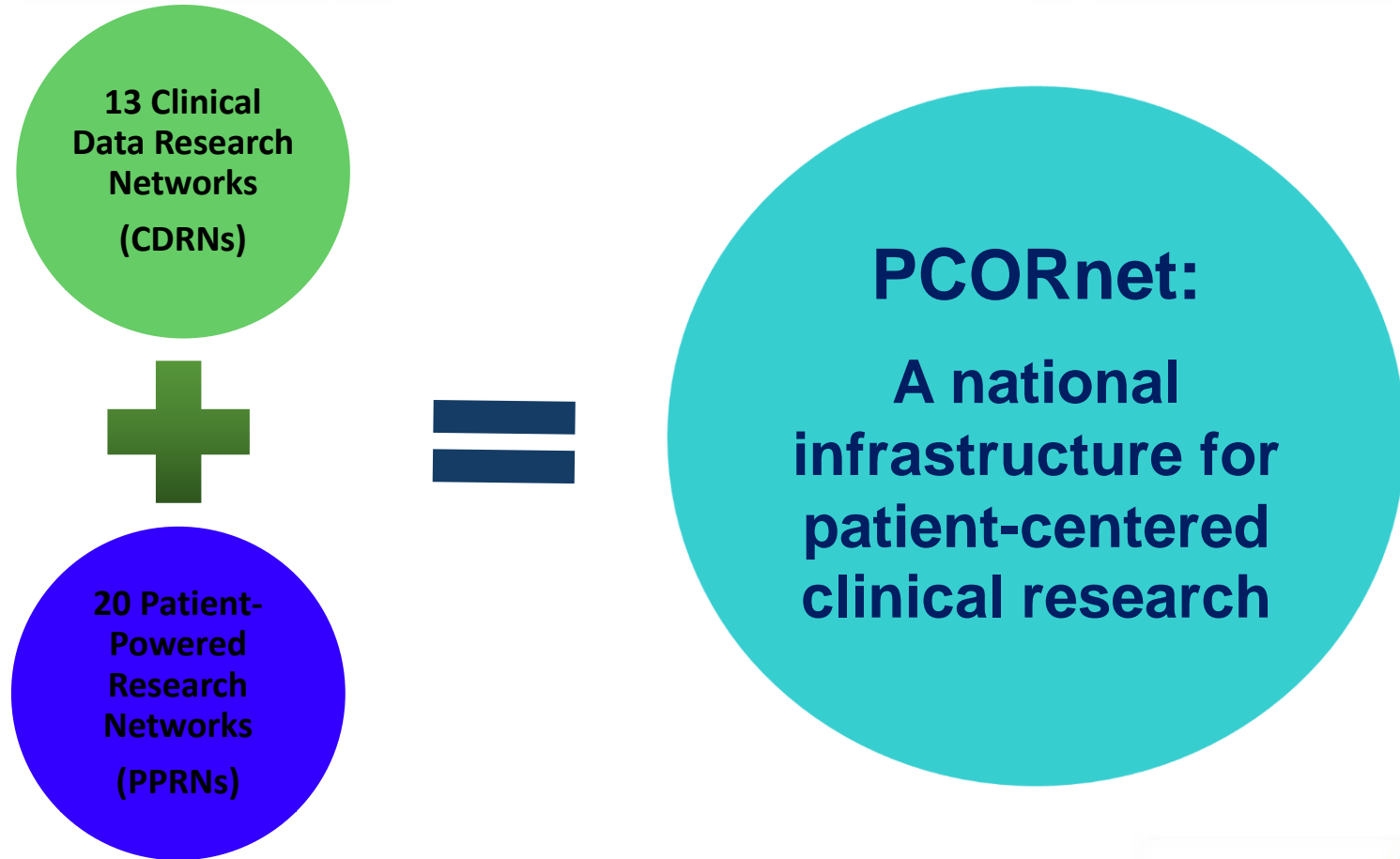
[http://www.emsp.org/wp-content/uploads/2016/09/Poster ECTRIMS A0 v03.pdf](http://www.emsp.org/wp-content/uploads/2016/09/Poster_ECTRIMS_A0_v03.pdf)

EMSP's vision for Real World Evidence in Multiple Sclerosis

- 1) **Temporary pooling and central analysis on European level** of all or some of those MS relevant data coming from multiple sources
- 2) **Coordinated by a European Network** of patient registries, cohorts and databases in MS
– run in close cooperation between academia and patient advocates
- 3) **Driven by specific queries** coming from
 - EMA and /or Healthcare Industry
 - HTA Agencies and Payers
 - Researchers and Health Care Providers
 - Patient Advocates
- 4) **Sustainably financed** - public/private partnership by industry & governments

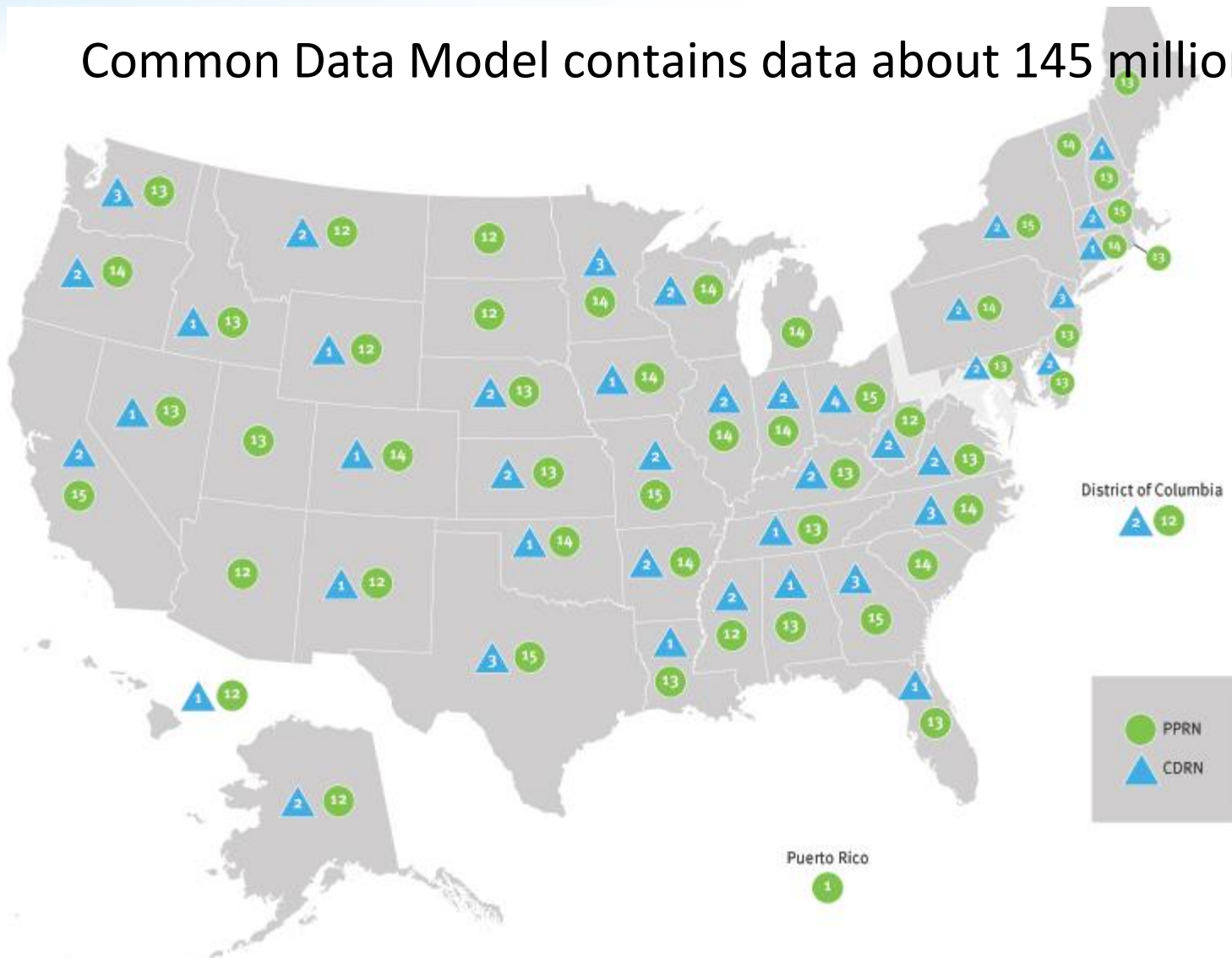
**THE US seems to be much
further then Europe:
PCORI, PCRnet & I Conquer MS!**

PCORnet



PCORnet is a National Research Network

Common Data Model contains data about 145 million Americans!



This map depicts the number of PCORI-funded Patient-Powered or Clinical Data Research Networks that have coverage in each state.

Neuro-QoL Adult Short Form - QoL Areas Covered

Physical Health	#	Mental Health	#	Social Health	#
Upper Extremity Function	8	Anxiety	8	Ability to Participate in Social Roles/Activities	8
Lower Extremity Function	8	Depression	8	Satisfaction with Social Roles/Activities	8
Fatigue	8	Positive Effect & Well-Being	8		
Sleep Disturbance	8	Emotional & Behavioral Dyscontrol	8		
Bowel Function	*	Cognitive Function	8		
Bladder Function	*	Communication	5		
Sexual Function	*	Stigma	8		

= number of questions * = not in Adult Short Form

Research and Evidence Generation Opportunities

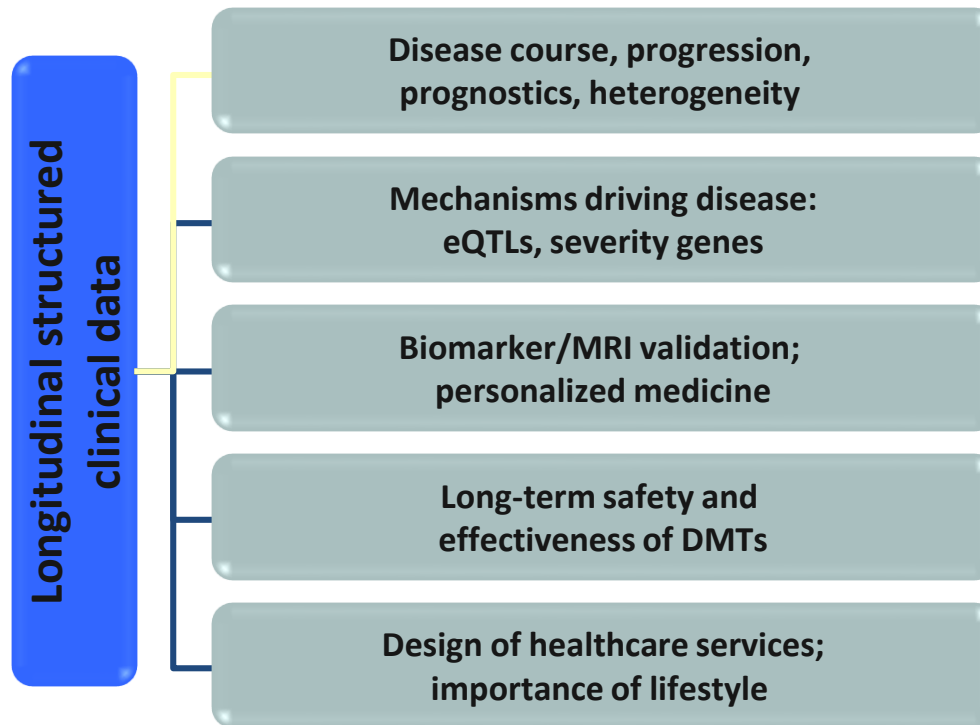
iConquerMS™ can:

- Facilitate input from people affected by MS on study design, topics of importance to them, etc.
- Provide 'core' longitudinal research data (MS History, Demographics, Neuro-QoL, PROMIS Global Health Scale, others)
- Conduct custom data collections for entire patient experience
- Provide home- or lab-based biosample collections (DNA piloted)
- Recruit participants, based on deep phenotype characteristics, for clinical trials & research studies
- Provide critical linkage of Patient-Reported Outcomes to EHRs
- Facilitate access to PCORnet participants or data via common data model data queries (MS Prevalence, comorbidities, etc.)



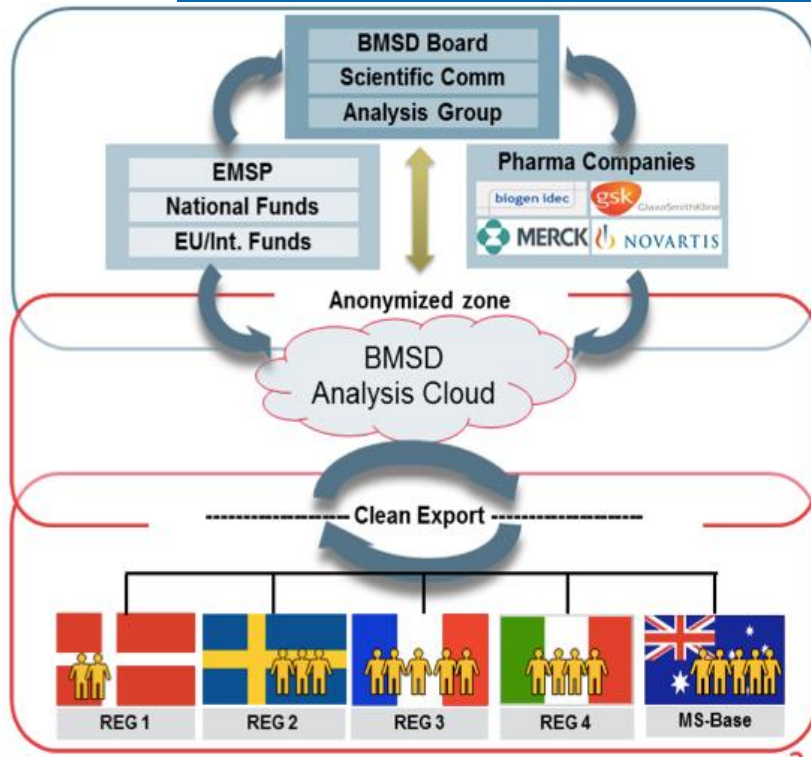
BIG MS Data network – the academia vision

Unmet needs in the understanding of MS require long term structured clinical data



eQTL, expression quantitative trait loci; MRI, magnetic resonance imaging.

Big MS Data network



- ❖ An opportunity to collaborate on research based on pooled data
- ❖ To be a multiplier for MS research for the member registries and external partners
- ❖ An opportunity for getting industry sponsorship, and to apply for EU funding

Participants:

Italian MS Registry (M Trojano), Swedish MS Registry (J Hillert), Danish MS (P Sorensen, M Magyari), Registry, OFSEP in France (S Vukusic), MSBase Registry (H Butzkueven)

Big MS Data network

Conclusion of the 2014 feasibility study

- ❖ The comparison of the five registries have shown that they are of different nature, have different histories, internal rules and external constraints
- ❖ However the common minimal data set has proven to be sufficiently present with all five and the data queries for data counts proved feasible bringing up worthwhile numbers
- ❖ It has been shown that data pooling and cooperation makes sense, **numbers likely to surpass anything available at the moment (>100.000 patients)**

www.emsp.org

**Interested in our next steps?
Just ask me! 😊**

Contact us:

European Multiple Sclerosis Platform

christoph.thalheim@emsp.org

Rue Auguste Lambiotte 144

B-1030 Brussels

+32 2 305 80 12



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