Prevalence and incidence of multiple sclerosis estimated in European Register for Multiple Sclerosis (EUReMS): Study protocol of the Epi-1d study

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EUReMS project and studies

With the general aim of establishing a European-wide platform for systematic analysis and comparison of longitudinally collected MS data in Europe, the European Register for Multiple Sclerosis (EUReMS) project was set up in 2010 by an international and interdisciplinary consortium. It is co-funded by the European public health program and involves both scientists and patient organisations.

Based on the assumption that a comprehensive approach to and harmonization of MS data collection at a European level is needed, a consensus statement on EUReMS' vision, mission and strategies was approved [1]. Based on the defined areas of action, four studies were defined:

EPI1-d Study: Estimating Prevalence and Incidence of MS in Europe from EUReMS data collection, coordinated by Prof. M Pugliatti;

EPI1-s Study: Comparison of the effect of the month of birth across Europe, coordinated by D Ellenberger and Prof. M Pugliatti;

DMD1 Study: Comparison of access and effectiveness of DMD treatment for people with MS across Europe, coordinated by Prof. J Hillert;

PRO1 Study: Assessment of people with MS' quality of life, the burden of disease and influence of employment from the patient's perspective across European countries, coordinated by Prof. P Flachenecker.

EUReMS study	DMD1	EPI1-d	EPI1-s	PRO1
Number of patients	**15788**	**13004**	**61848**	**4507**
Countries of participating registers				
Croatia			■	
Czech Republic			■	
Finland		■	■	
Germany	■	■	■	■
Italy	■	■	■	
Norway			■	
Poland		■	■	■
Serbia		■	■	
Spain		■	■	
Sweden	■	■	■	■
QR-Code				

Background

The attempt to define the burden of MS in Europe is hampered by the variability of the surveyed populations and the different ascertainment across studies. To overcome this, epidemiological indices should be derived based on standardized procedures for data collection. This requires a consolidated collaborative network, harmonizing data structure and capturing, designing a registry system for both existing and prospective longitudinally collected data as well as shared analytical plans and interpretation of results.

Objectives

To fulfill one of EUReMS missions: MS epidemiological and clinical surveillance across European countries, including the assessment of the MS burden in Europe;
To test the ultimate research hypothesis:

"MS in Europe is changing over time and in space"

Methods

A survey was conducted between July 2013 and February 2014 by administering an ad hoc questionnaire (EPI-Q) to the leaders of eligible existing European databases, to collect data on database management and governance, contents (demographics, MS course, year of onset/diagnosis, diagnostic validation through lab and instrumental tests, EDSS), format and quality of data. Specific focus was given to detect the possibility for generating population-based estimates on better-ascertained sub-areas [2].

Main Research Questions (EUReMS short-term activity):
Q1: What is the number of new MS cases per year in Europe (incidence), by gender and age groups?
Q2: Are there differences in the MS incidence in the countries included?
Q3: Is there evidence that MS incidence has increased over time (eg., over the last two decades)?
Q4: Has MS incidence increased in women as equally as in men?
Q5: What is current gender specific MS age at onset?
Q6: Has MS age at onset changed over time?
Q7: What is the current diagnostic delay (i.e., time elapsing from clinical onset to diagnosis)?
Q8: Has the diagnostic delay changed over time?
Q9: What is the current gender and age specific proportion of PwMS (prevalence) over the general population in Europe?
Q10: Are there differences in the MS prevalence in the countries included?

Additional Research Questions (EUReMS short-term, long-term activity):
Q11: Has MS incidence changed by cohort of year of birth (i.e., is there a calendar cohort effect)?
Q12: Has MS incidence changed by cohort of year of onset?
Q13: Has the type of clinical onset (relapsing vs. progressive) changed over time?
Q14: Has MS prevalence increased over time? In both genders?
Q15: Has MS prevalence trends over time been similar in all countries?

Results

Out of 18 databases contacted, EPI-Q was successfully administered to Croatia, Czech Republic, Denmark, Finland, Germany, Italy (Liguria, Tuscany, iMED), Norway, Poland, Serbia, Spain, Sweden and United Kingdom.
Overall population-based epidemiological data collected since 2003 was integrated into a database of ca. 17,000 MS patients over a total population of 18,000,000 for sub-areas in Catalunya/Spain, Italy, Sweden, UK, Norway, Finland and Serbia, despite some heterogeneity across regions.
As of beginning of September 2014, we are able to present preliminary data on MS incidence and prevalence estimates in some of the populations participating to EUReMS (Table 1 and Table 2).

Table 1. EUReMS: Estimated mean annual incidence (per 100,000/year) of MS in Europe

	Serbia[a]	Finland[b]	Spain[c]	Sweden[d]
N. total cases (N. women)	285 (187)	513 (358)	187 (117)	776 (531)
Incidence period	2000-2013	2000-2010	2009-2013	2000-2013
Mean annual incidence rate				
Total (95%CIs)	1.23 (-1.62-4.08)	13.44 (10.22-16.65)	4.97 (3.18-6.77)	5.31 (1.88-8.73)
Men (95%CIs)	0.89 (-0.95-2.73)	8.33 (6.50-10.17)	3.69 (1.22-4.91)	3.34 (1.41-5.27)
Women (95%CIs)	1.53 (-0.70-3.76)	18.28 (15.60-20.96)	6.29 (4.88-7.68)	7.28 (4.41-10.15)
Women:Men ratio	1.72	2.19	1.70	2.18
Peaking age group(s)				
Men	25-29 years	25-29 years	35-39 years	25-29 years
Women	25-29 years	25-29 years	20-24 years	25-29 years
			35-39 years	45-49 years

Table 2. EUReMS: Estimated prevalence (per 100,000) of MS in Europe

	Serbia[a]	Sweden[d]	Italy[e]
N. total cases (N. women)	1634 (1107)	2032 (1415)	7239 (4686)
Prevalence year	2013	2013	2013
Prevalence estimate (crude)			
Total (95%CIs)	98.47 (94.35-102.59)	194.55 (190.66-198.45)	178.63 (169.60-187.66)
Men (95%CIs)	67.06 (64.77-69.36)	117.81 (115.75-119.88)	130.01 (124.84-135.17)
Women (95%CIs)	126.72 (123.25-130.18)	271.73 (268.40-275.06)	224.34 (216.91-231.76)
Prevalence estimate (stand.*)			
Total	97.52	203.88	177.42
Men	68.08	123.03	129.94
Women	122.93	285.70	221.01
Women:Men ratio	1.89	2.31	1.73
Peaking age group(s)			
Men	85+ years	50-54 years	40-44 years
Women	60-64 years	55-59 years	45-49 years

a Belgrade Region
b Tampere, Vaasa, Seinäjoki
c Girona province, Catalunya
d Östergötland, Uppsala, Västerbotten
e Apulia Region
* Standardized to 2011 European population (28 Countries)

In conditions of ensured standardized procedures, quality of data and harmonized nomenclature, the disclosed differences in estimates across populations reflect (i) population-specific distribution of the disease and the concentration of its determinants, as well as (ii) the original main aim and design of the source existing datasets.

Conclusions

Benefitting from EUReMS architectural infrastructure, and from previous work on purposes and constructs of existing MS databases in Europe, population-based sex- and age-specific incidence and prevalence from well-defined geographic sub-areas and over time, temporal trends of gender-ratio, age at onset and diagnostic delay can be computed. This will ensure the current '**best estimate**' of **the MS burden in Europe**, as well as indicators of **registry accuracy**.

References

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2. Flachenecker P, Buckow K, Pugliatti M et al. Multiple sclerosis registries in Europe – results of a systematic survey. Mult Scler 2014; doi: 10.1177/1352458514528760

EUReMS Consortium

Disclosure

european register eurems multiple sclerosis

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Executive Agency for Health and Consumers

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