Prevalence of Multiple Sclerosis in the Lazio region, Italy: use of an algorithm based on Health Information Systems

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Introduction Italy is considered a high prevalence country for Multiple Sclerosis (MS) (estimated prevalence: 110 per 100,000).[1,2] Limited epidemiological data are available for Central Italian regions with prevalence estimates available for some small urban or provincial areas only. In the Lazio region Health Information Systems (HIS) are comprehensive and contains high-quality information; consequently, health administrative data are largely used to measure the occurrence of acute and chronic diseases.[3,4] The principal aims of this study were to estimate the prevalence of MS in the Lazio region using population-based health administrative databases and to describe the geographical distribution of MS. Additionally, we evaluated the validity of the case-finding algorithm based on administrative data using a cohort of patients enrolled at MS treatment centers as the gold standard.

Materials and Methods

Study area
Lazio is the third most populated region of Italy and comprises Rome, capital and largest Italian city. The population on the prevalence day, December 31, 2011, was 5,500,022 inhabitants.[5]

Data sources
Health administrative data
Data from different regional HIS were used to identify people affected by MS. The *Hospital Discharge Registry (HDR)* routinely collects data from all regional hospitals. The *PHARMED* database contains individual records for each drug prescription. The *Regional Mortality Registry* (ReNCaM) lists the causes of death. The *Ticket Exemption Registry* (TER) includes data on all residents who are entitled to co-pay fee exemption for some particular conditions, e.g. disability, chronic diseases etc. The *Regional Health Assistance File* comprises all resident individuals registered with the Regional Health Service.

Clinical data
We used a cohort of MS patients recruited from five specialized high-volume centers to evaluate the validity of the algorithm based on health administrative data. Socio-demographic and clinical data of patients were extracted from medical charts according to a common protocol and using a customized software.

Case ascertainment
We used the HDR, the PHARMED and the TER to identify MS cases in the period from 01/01/2006 to 31/12/2011. From the HDR we selected all patients who were hospitalized in the Lazio Region with a primary or a secondary diagnosis of MS; from the PHARMED we selected all patients with at least one pharmacy claim in the study period for at least one among Interferon beta-1a , Interferon beta-1b, Glatiramer Acetate and Natalizumab; finally, from the TER we selected all patients registered with the MS specific code (046.340).

Statistical analysis
The prevalence day was December 31, 2011. Age and gender specific prevalence rates per 100,000 were calculated using the number of MS patients that were alive on the prevalence day as numerator and the population of residents in the Lazio region the same day as denominator.
To explore the geographic pattern of MS prevalence within the region, standardized prevalence ratios were calculated for each of the 12 LHU and 56 districts. We used a multivariate Poisson regression with no intercept and centered covariates, in which in addition to gender and age, were included n dummy variables that represent the areas being compared. All statistical analyses were conducted using SAS, version 9.2.

Validity of the case ascertainment algorithm
Data of MS patients recruited at the treatment centers were linked to prevalent cases identified through HIS. Considering clinical data as the gold standard, we calculated the proportion (and 95% confidence intervals) of individuals correctly identified as MS cases.

Figure 1. Flow chart of MS cases selection from regional health care administrative databases

Results
Through the regional HIS we identified a total of 7377 MS patients residing in the Lazio region on the prevalence day, 2427 males and 4950 females (figure 1). Figure 2 shows the contribution of different data sources to the identification of MS cases.
At prevalence day, mean age was 45.9 years (SD 12.9) without differences between genders. The crude regional prevalence was 130.5/100,000 (89.7/100,000 for males and 167,9/100,000 for females) with a male to female ratio of 1:1.9. Age- and gender-specific prevalence rates are reported in table 1. Table 2 shows crude and standardized prevalence rates and prevalence ratios by LHU. The standardized prevalence rates ranged from 96.3 (95% CI: 86.4-107.3) for Latina to 169.6 (95% CI: 147.6-194.9) for Rieti with statistically significant variations among LHU. Distribution of MS showed a large variation between districts even within the same LHU (figure 3). Most districts close to the coast showed lower prevalence estimates compared to those situated in the eastern mountainous area of the region.

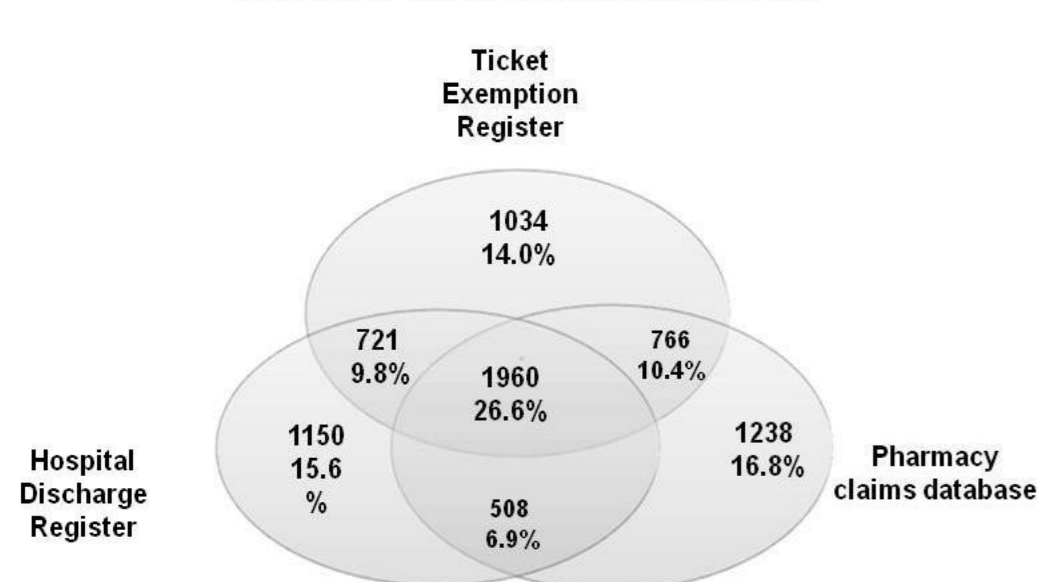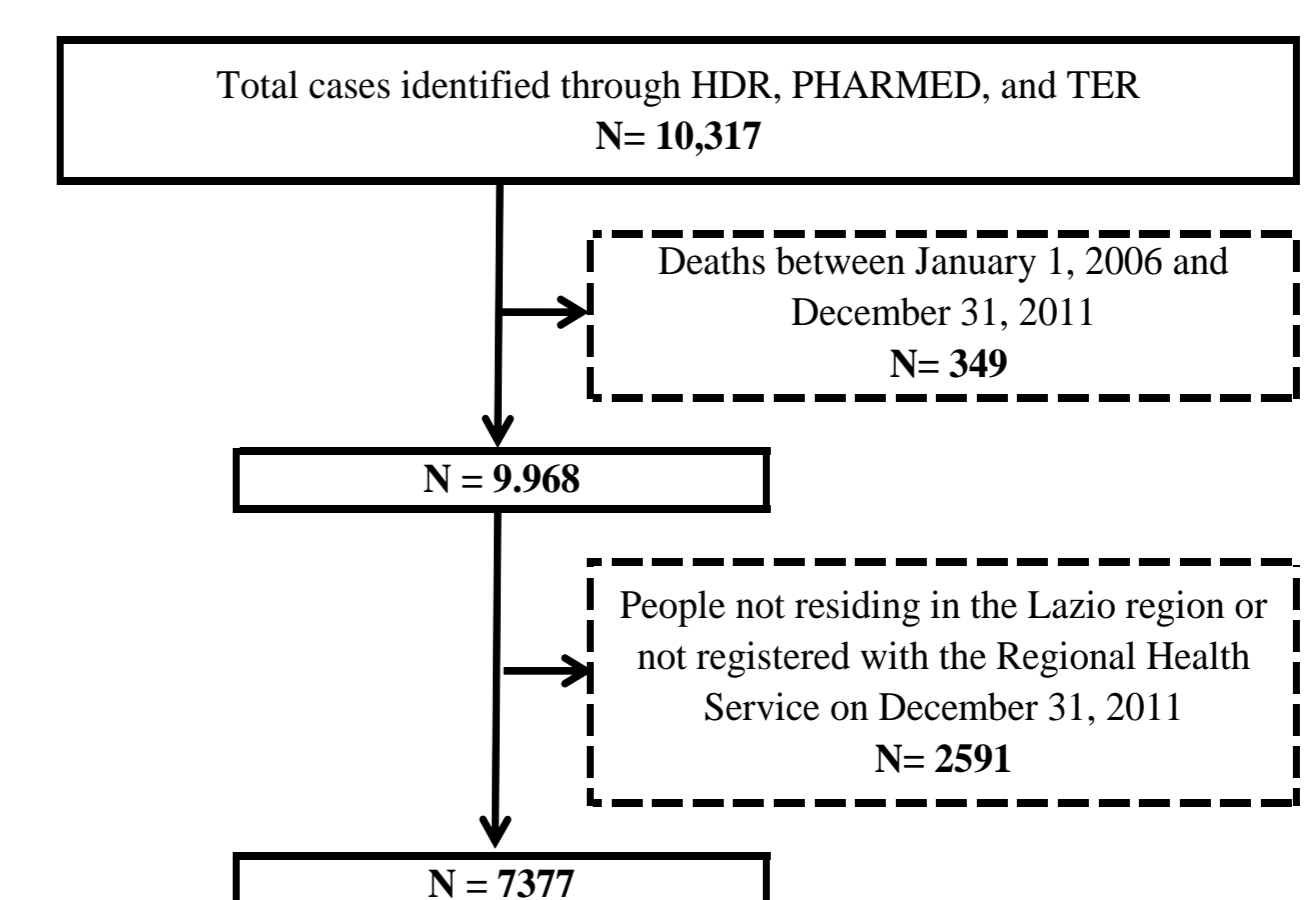Figure 2. Contribution of regional administrative health care databases to MS cases identification

Table 1 - Age and gender-specific prevalence rates per 100,000 inhabitants on December 31, 2011. Lazio region, Italy

Age classes	Female			Male			Total		
	Cases	Population*	Prevalence	Cases	Population*	Prevalence	Cases	Population*	Prevalence
0-14	10	377117	2,7	8	400174	2,0	18	777291	2,3
15-24	161	258499	62,3	86	272381	31,6	247	530880	46,5
25-34	786	337250	233,1	386	327865	117,7	1172	665115	176,2
35-44	1444	480267	300,7	687	451034	152,3	2131	931301	228,8
45-54	1335	458242	291,3	628	429264	146,3	1963	887506	221,2
55-64	814	370602	219,6	400	337570	118,5	1214	708172	171,4
65+	400	665683	60,1	232	487060	47,6	632	1152743	54,8
TOT	4950	2947660	167,9	2427	2705348	89,7	7377	5653008	130,5
*Standardized rate**			155,5			81,4			119,6

*Population of residents in the Lazio region and alive on the prevalence day (December 31, 2011)

**Prevalence standardized to the European Standard Population

Conclusions The Lazio region is a high risk area for MS, although an uneven geographical distribution within the region was observed.
This is the first Italian study using administrative data to estimate MS prevalence and the first to produce prevalence estimates at the regional level. Although some limitations must be considered including possible prevalence underestimation, administrative database represent an attractive source information to measure the burden of SM allowing for periodic updates of prevalence estimates, useful for monitoring prevalence trends at population level and to ensure appropriate healthcare resources allocation Using data from HIS.

Table 2 - Crude and standardized prevalence and prevalence ratios by Local Health Unit per 100,000 inhabitants. Lazio region, Italy

Local Health Unit	Cases	Crude prevalence	Standardized prevalence	95% C.I.	PR	p value
RM A	742	137,3	134,0	121,4 - 147,9	1,03	0,604
RM B	1008	147,5	147,5	134,6 - 161,6	1,13	0,009
RM C	783	147,4	147,6	133,9 - 162,6	1,13	0,013
RM D	714	129,2	129,5	117,3 - 143,1	0,99	0,885
RM E	704	140,7	140,8	127,4 - 155,6	1,08	0,136
RM F	349	114,1	112,9	99,7 - 127,9	0,87	0,023
RM G	658	136,9	136,8	123,6 - 151,5	1,05	0,363
RM H	599	110,5	110,0	99,1 - 122,1	0,84	0,001
VITERBO	345	111,0	112,1	98,9 - 127,1	0,86	0,017
RIETI	260	165,5	169,6	147,6 - 194,9	1,30	0,000
LATINA	533	95,9	96,3	86,4 - 107,3	0,74	0,000
FROSINONE	682	138,3	140,5	127,0 - 155,4	1,08	0,151
TOT	7377	130,50				

Figure 3. Age- and gender- adjusted MS prevalence rates, per 100,000 population by district in the Lazio region, Italy
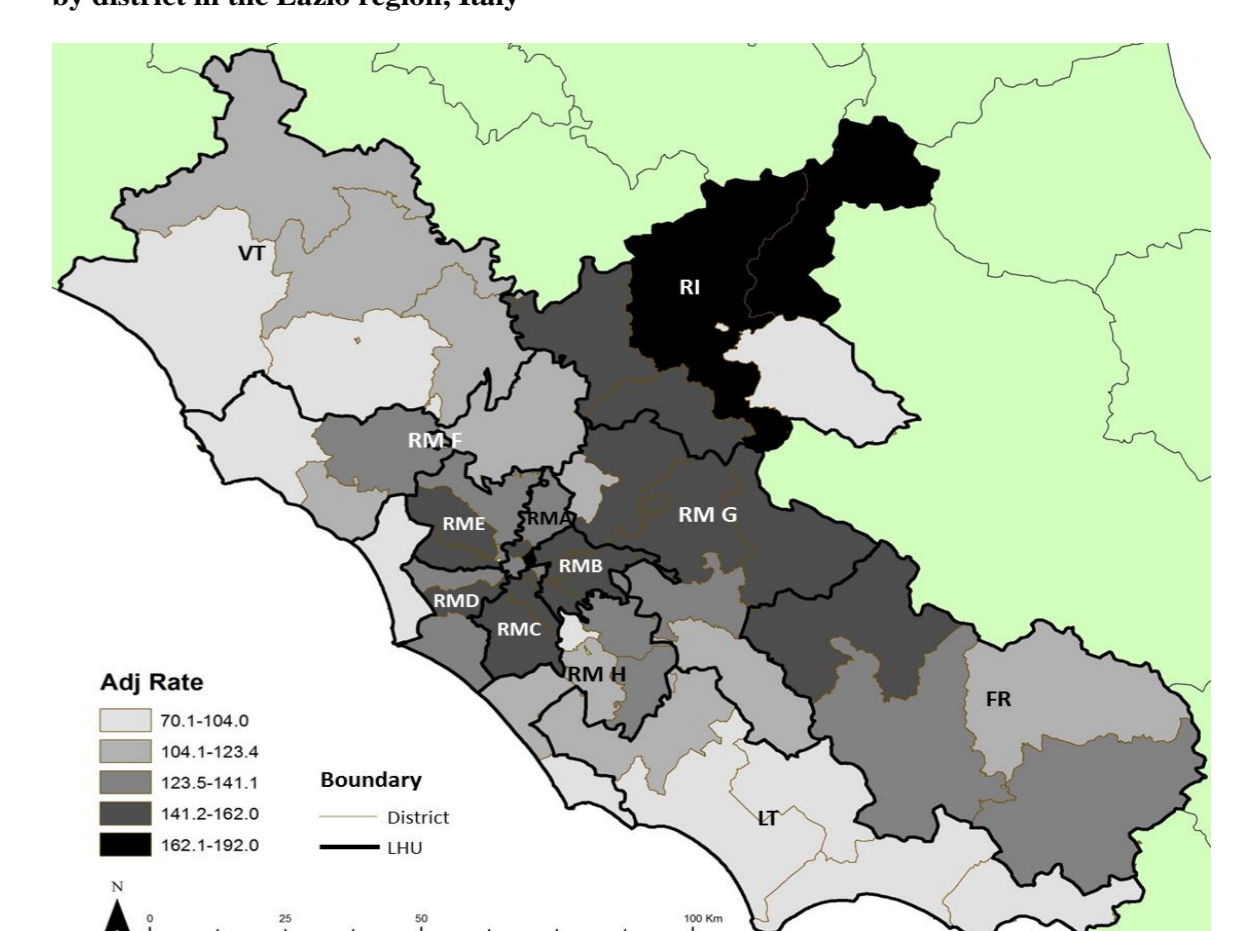
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