Healthcare costs for treating relapsing multiple sclerosis and the risk of progression: a retrospective Italian cohort study from 2001 to 2015

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Introduction and Purpose. Disease Modifying Treatments (DMTs) are nowadays the main responsible for direct healthcare costs in Multiple Sclerosis (MS), and are expected to have a further expansion among overall expenses as a consequence of the introduction of newer and more effective drugs characterized by high healthcare costs for administration and management. Therefore, the present study aims to explore the relationships between the expenditure for MS treatments, and the risk of relapses and of disability progression during 10-year observation.

Methods. The present observational cohort study is a retrospective analysis of prospectively collected data. 544 newly diagnosed Relapsing Remitting MS (RRMS) patients were included and prospectively followed up for 10.1±3.3 years. Details of the study population and included/excluded patients are reported in Table 1 and Figure 1.
Economic resources included the healthcare costs for DMTs, for staff involved in DMT administration, for neurological and other specialist visits related to DMT safety procedures, for MRI, for laboratory exams, for psychological and neuropsychological evaluations. Healthcare costs were inflated to the most recent values, from the National Drug Formulary for DMT costs (Italian Drug Agency), and from the National Tariffs for Healthcare of the Italian National Health System for resource utilization costs (Italian Ministry of Health) Following clinical endpoints were recorded: time to first relapse, annualised relapse rate (ARR), 1-point EDSS progression, reaching EDSS 4.0, reaching EDSS 6.0, and conversion to secondary progressive MS (SP). Covariates for statistical analyses were age, gender, disease duration and EDSS at diagnosis.

Results. After adjusting for different covariates, 10% increase in the annual healthcare costs was associated with 1.1% reduction in the rate of 1-point EDSS progression (HR=0.897; 95%CI=0.820-0.981; Figure 2B), with 0.7% reduction in the reaching of EDSS 6.0 (HR=0.925; 95%CI=0.862-0.992; Figure 2D), and with 1.0% reduction in the conversion to SP (HR=0.902; 95%CI=0.838-0.971; Figure 2E), but not with the occurrence of the first relapse (HR=0.993; 95%CI=0.890-1.109; Figure 2A), and with the reaching of EDSS 4.0 (HR=0.929; 95%CI=0.859-1.005; Figure 2D). Overall annual healthcare costs were positively associated with the ARR (Coef=2.770; 95%CI=1.056-4.483; and Coef=2.468; 95%CI=0.629-4.307 at the adjusted model) (Figure 3).

Conclusions. Healthcare costs are driven by the use of DMTs, which are prescribed depending on the initial severity of MS and on its subsequent evolution. However, the costs for DMT management are usually determined on the basis of their clinical efficacy as evaluated in clinical trials, whereas they have never been tested in long-term real-life scenarios. Therefore, the present study showed that patients who received more expensive DMTs, specifically indicated for a more aggressive disease evolution, presented better long-term outcomes, compared to subjects with relatively milder symptoms who received "low-cost" DMTs. Thus, highly active and, possibly, expensive DMTs can delay disease progression and its long-term burdensome economic consequences.

Figure 1. Patient disposition flow diagram.

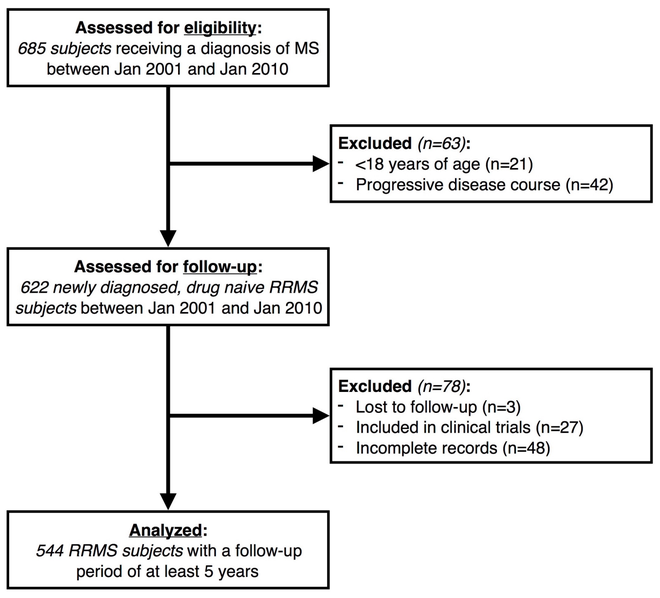
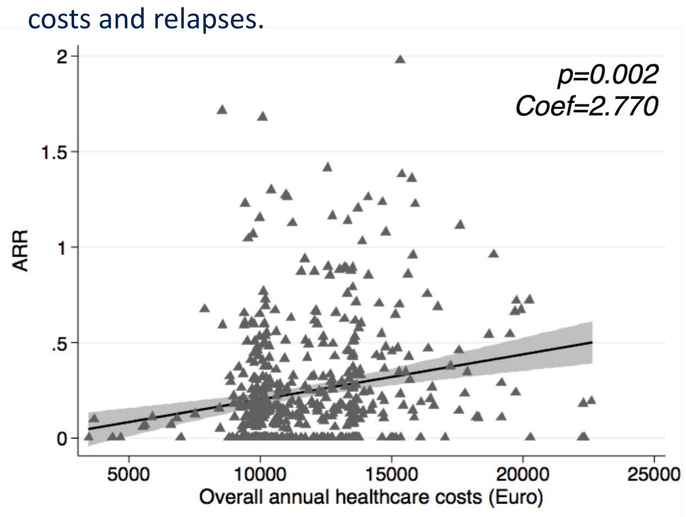


Table 1. Demographic features, clinical findings and healthcare costs.

	MS population (n=544)
Age, *average years±SD*	33.7±8.7
Gender, *number of females (percent)*	345 (63.5%)
Disease duration at diagnosis, *average years±SD*	3.1±3.3
EDSS at diagnosis, *median (IQR)*	2 (1.5-2.5)
Observation period, *average years±SD*	10.2±3.4
Overall annual healthcare costs, *€±SD*	11785.35±2718.76
Relapse occurrence, *number (percent)*	415 (76.2%)
Time to the first relapse, *average years±SD*	2.7±2.5
1-point EDSS progression, *number (percent)*	448 (82.3%)
Time to 1-point EDSS progression, *average years±SD*	4.5±4.0
Reaching of EDSS 4.0, *number (percent)*	256 (47.0%)
Time to EDSS 4.0, *average years±SD*	7.0±3.7
Reaching of EDSS 6.0, *number (percent)*	59 (10.8%)
Time to EDSS 6.0, *average years±SD*	10.3±3.6
Conversion to SP, *number (percent)*	102 (18.7%)
Time to SP conversion, *average years±SD*	8.6±3.3

Figure 2. Kaplan-Meier curves for the probability of relapse occurrence, of 1-point EDSS progression, of reaching of EDSS 4.0, of reaching of EDSS 6.0, and of SP conversion, in relation to annual healthcare costs before the specific study endpoint was reached.

Figure 3. Scatter plot for overall annual healthcare costs and relapses.



Selected References.

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