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Excess Treatment Costs of Multiple Sclerosis: What Can We Learn From Longitudinal Population-Based Data?

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Multiple sclerosis (MS) is a chronic disorder affecting 0.1% to 0.2% of the population in North America and Western Europe[1]. People with MS are often diagnosed during their working age, and the diagnosis adversely impacts their earning ability, quality of life and functional capability[2]. Caring for people with MS has enormous financial costs for healthcare systems, patients, and their caregivers. In the United States, the average excess direct and indirect cost of MS has been estimated at $65,612 per patient per annum (pppa)[3]. In the United Kingdom, the median medical cost has been estimated at $3,729 pppa, and the non-medical cost at $1,079 pppa[4]. In Sweden, the median medical cost of MS is approximately $9,937 pppa[2]. The heterogeneity in cost estimates reflects different countries' medication prices and health system financing models.

Studies that look at costs associated with specific conditions are an important because they provide a summary of the financial burden of that disease to individuals and society and, by identifying patterns in health expenditures, optimize the use of limited resources[5]. To date, many costing studies in MS have shared many limitations that reduce their utility: a cross-sectional design, small sample sizes, and short follow-up[6].

In this issue of *Neurology*, Khakban et al.[7] publish a study where they estimate direct healthcare costs associated with

MS using population-based administrative health data in the Canadian province of British Columbia. The strength of the study is that it utilises a longitudinal data set from January 1997 until December 2020. The MS cohort is comprised of patients who had 3 or more MS-related health claims within one year, with a claim defined as an inpatient admission, outpatient attendance or a disease-modifying therapy (DMT) prescription. The claims were identified using ICD-9 and ICD-10 codes. As this was an administrative data set, only direct healthcare costs for inpatient stays, outpatient services and prescriptions were included. The dataset did not contain information on lab work or imaging studies done in the private sector. The primary outcome was the excess cost in people with MS compared to a cohort of matched controls, identified based on sex, age, and cohort entry date. All costs were reported in 2020 Canadian dollars. 17,071 MS patients were matched to 85,355 controls. Overall, 72% women, average age at entry 46.1 (±13.4) years, average follow-up time 12.3 (±6.9) years. The excess direct health care cost of MS was CAD$6,881 pppa (95% CI CAD$6,713 to CAD$7,049); it was CAD$644 higher in men than women (95% CI CAD$260 to CAD$1,027). This difference was potentially due to men in the cohort being slightly older than women as within each age group there was no difference between sexes. The excess cost of MS decreased with age: the average excess cost of MS was CAD$10,126 in patients <29 years, compared to an average of CAD$5,159 in patients >60 years old. Although the direct cost of inpatient and outpatient services was higher for MS patients than for matched controls (excess cost of CAD$723 pppa (95% CI

CAD$706 to CAD$741) and CAD$1,683 pppa (95% CI CAD$1,582 to CAD$1,784) respectively), the majority of excess costs were due to medications, which were associated with a mean excess cost of CAD$4,474 pppa (95% CI CAD$4,354 to CAD$4,595), representing 65% of total excess costs. The excess cost of medications was higher in younger patients compared to older patients. To further explore the impact of medication costs, the MS cohort was divided into two groups based on the use of DMT: DMT users (one DMT prescription during the study period) and non-DMT users. DMT users had higher excess costs than non-DMT users; however the use of DMT contributed to a reduced rate of inpatient stays.

The limitations of the study included potential misclassification of MS cases due to the sensitivity of the identification algorithm (the algorithm has been validated in Canada and has a sensitivity of 96% and specificity of 99%), lack of data on patients' characteristics, geographic location as a proxy for access to care, and comorbidities. Another important limitation is that there were no data on disease severity. The lack of information about disease severity limits the conclusions that may be drawn from this study. Disease severity is associated with higher costs, and specifically indirect/non-medical costs. Non-medical costs were beyond the scope of the study but existing studies highlight the need to account for productivity loss, informal care, and out-of-pocket costs[8]. These costs are considerable for people with MS and outweigh medical costs as disability level increases[1].

DMTs are the main cost driver in MS care but there is extensive evidence that they are cost-effective and improve health-related quality of life[8], something this study was unable to evaluate. Although DMTs are expensive in the short-run, they provide benefits in the long-run; therefore, there is a need to create the right balance between incentives to achieve health gains and financial constraints. The rising cost of MS requires innovation in service models, accounting for patients' needs and individualised care.

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