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# Financial burden of out of pocket nonpharmacological therapies in an Austrian multiple sclerosis cohort

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Given the financial constraints in public healthcare, we investigated the monthly out-of-pocket expenses for non-pharmacological treatments among individuals with multiple sclerosis (MS), a chronic neurological disorder that primarily affects individuals of working age. This crosssectional study employed an online questionnaire to evaluate the expenses and utilization of non-pharmacological treatments, as well as the weekly working hours among 104 individuals with relapsing-remitting MS (RRMS, 79%), secondary progressive MS (SPMS, 12%), and primary progressive MS (PPMS, 10%). Non-pharmacological treatments were used by 82% of participants (vitamin D (43%), physiotherapy (31%), massage (21%), magnesium (19%)). The average monthly out-of-pocket expenses were 136 EUR (SD ± 218) and significantly higher among individuals with PPMS (337 EUR SD $\pm$ 354) compared to RRMS (110 EUR SD $\pm$ 195; p=0.01). The average weekly working hours were 26 and significantly lower among individuals with PPMS (11 h/week, SD ± 16; p = 0.008) and SPMS (13 h/ week, SD  $\pm$  16; p = 0.001) compared to the RRMS cohort (30 h/week, SD  $\pm$  15). Working hours were not related to individual monthly costs. This study reveals substantial expenses incurred by individuals with MS in Austria, particularly those with PPMS, highlighting the willingness to actively participate in their disease management. Physicians should be aware of the financial resources and inform about available evidence on non-pharmacological treatment approaches.

**Keywords** Multiple sclerosis, Dietary supplements, Alternative therapies, Financial burden, Health economics

Multiple Sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS) and a common cause of non-traumatic disability. MS stands out as chronic disorder predominantly affecting young, working-age adults. Symptoms including chronic fatigue, motor and gait impairment, sensory loss and urinary dysfunctions result in considerable disability for individuals with MS but also impact family life and social interactions, work and ultimately society<sup>1,2</sup>.

To alleviate symptoms and impairments, in addition to immunomodulatory drugs, many individuals with MS turn to various dietary supplements and alternative therapies, whose costs often fall directly on the individuals. Even though many such approaches lack high-quality evidence to support their efficacy $^3$ , usage of complementary and alternative medicines (CAMs) in MS is substantial and higher compared with other chronic diseases such as hypertension and diabetes $^{4-8}$ .

While the expenses for the healthcare system have been extensively studied and primarily result from the prescription of disease-modifying therapies (DMTs)9, the financial implications on individuals with MS and their families receive little attention. Financial constraints, including limited employment opportunities and out-

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of-pocket expenses for non-pharmacological treatments, may contribute to economic challenges for individuals with MS. These economic threats can exacerbate the limitations and disabilities imposed by the chronic disorder itself.

The primary objective of this study was to explore the usage of non-pharmacological treatments among an Austrian MS cohort and to estimate the monthly out-of-pocket costs incurred by the individual participants.

# Results Demographics

Of the 104 participants recruited for the MS And DisAbility Improvement (MADAI) study, 67 (64%) were women, the mean age was 44 years (SD  $\pm$  12) and the mean disease duration 11 years (SD  $\pm$  9). The cohort consisted of 82 individuals with relapsing remitting multiple sclerosis (RRMS), 12 with secondary progressive multiple sclerosis (SPMS) and 10 with primary progressive multiple sclerosis (PPMS). No significant differences between MS types regarding sex were observed (p=0.49). The most often used DMTs were ocrelizumab (21%), followed by ofatumumab (18%); 13% of participants had no DMT (suppl. Figure 1). Among the cohort, 98 participants (94%) correctly completed the online survey, whose results are analyzed in this paper. Demographics of survey respondents are summarized in Table 1.

# Usage and expenses of non-pharmacological MS treatments

Non-pharmacological treatments were defined as dietary supplements and services provided by therapists (e.g., physiotherapists, massage therapists), in contrast to pharmacological treatments such as DMTs and symptomatic medications (e.g., antispastic formulations). Overall, 80 survey participants (82%) reported using non-pharmacological treatments on a regular basis (Table 1). Usage was comparable between individuals with PPMS (89%), SPMS (82%) and RRMS (81%) as well as among women (80%) and men (85%). The mean monthly expenses were 136 EUR (SD $\pm$ 218), ranging from 0 to 1210 EUR and are summarized in Table 2. Monthly expenditure among individuals with PPMS were significantly higher (337 EUR SD $\pm$ 354) compared to RRMS individuals (110 EUR SD $\pm$ 195; p=0.01; Fig. 1A). We found no gender-related differences on total monthly expenses (p=0.71).

In regards to dietary supplements, 74 respondents (76%) reported taking any kind of oral supplements on a regular basis. Supplements were more frequently reported by individuals with PPMS (89%) as compared with RRMS (75%) and SPMS (73%). The mean monthly expenditures for the supplements were 44 EUR (SD $\pm$ 70; range 0–505 EUR). The most frequently used oral supplements were vitamin D (43%), followed by magnesium (19%) and vitamin B (12%, Table 3 and Fig. 2A). In total, over 60 different supplements were mentioned by the participants, including Vitamin A, iron, calcium, various aminoacids, folic acid, homeopathic globuli and different types of herbal teas (suppl. Table 1).

Overall, 50 participants (51%) reported visiting at least one of the following therapists regularly: physiotherapy (n=30), massage therapy (n=21), osteopathy (n=9), dietitian (n=3), acupuncture (n=3), homeopathy (n=2),

	All participants (n)	Non-pharmacological treatment users (n)	Non-pharmacological treatment non-users (n)		
Total	98	80	18		
Gender					
Male	34	29	5		
Female	64	51	13		
Diagnosis					
RRMS	78	63	15		
SPMS	11	9	2		
PPMS	9	8	1		
Age [years; mean (±SD)]	44 (± 12)	45 (± 12)	39 (± 12)		
Disease duration [years; mean (±SD)]	11 (±9)	10 (± 10)	11 (±8)		
EDSS [mean (±SD)]	2.1 (±2)	2.3 (± 2)	1.5 (±2)		
Distribution by ranges					
0-3.5	76	61	15		
≥4	22	19	3		
BMI [mean (±SD)]	27 (±7)	26 (± 6)	26 (±8)		
Distribution by ranges					
<18.5	4	3	1		
18.5-24.9	52	42	10		
25–29.9	25	20	5		
>30	16	14	2		
Weekly working hours [hours; mean (±SD)]	26 (±17)	25 (± 17)	32 (± 14)		

**Table 1**. Demographics of the survey respondent group (n = 98). *RRMS* relapsing–remitting multiple sclerosis, *SPMS* secondary progressive multiple sclerosis, *PPMS* primary progressive multiple sclerosis, *SD* standard deviation, *EDSS* expanded disability status scale, *BMI* body mass index.

	Total expenses [EUR (SD)]	Expenses for supplements [EUR (SD)]	Expenses for therapists [EUR (SD)]
Total (n = 98)	136 (±218)	44 (±70)	93 (± 198)
Gender			
Male (n = 34)	147 (±228)	50 (±64)	98 (±217)
Female (n=64)	130 (±214)	41 (±72)	90 (± 187)
Diagnosis			
RRMS (n = 78)	110 (±195)	42 (±73)	70 (± 173)
SPMS (n = 11)	154 (±159)	35 (±39)	119 (±152)
PPMS (n = 9)	337 (±354)	79 (±62)	257 (±326)

**Table 2**. Mean monthly expenses of the individual survey respondents for non-pharmacological therapies. *RRMS* relapsing–remitting multiple sclerosis, *SPMS* secondary progressive multiple sclerosis, *PPMS* primary progressive multiple sclerosis, *EUR* Euros (currency), *SD* standard deviation.

chiropractic (n=1) and others (n=10). This information is summarized in Table 3 and Fig. 2B. The majority (62%) reported using the services of only one of these professionals, while 24% reported using two and 14% reported visiting three or more different therapists. These treatments were more commonly reported by the PPMS group (89%) than by the SPMS (64%) and RRMS (45%) cohort. Mean monthly expenditures for visiting these therapists were 93 EUR  $(SD\pm198)$ , ranging from 0 and 1200 EUR.

Usage of both, oral supplements and therapists on a regular basis was more frequent among PPMS (89%) compared to SPMS (55%) and to RRMS (39%).

#### **Employment**

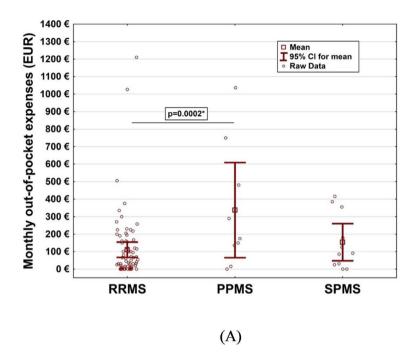
The mean weekly working hours were 26 (SD  $\pm$  17). Participants with RRMS reported to be working significantly more hours per week (30 h/week; SD  $\pm$  15) compared to individuals with PPMS (11 h/week; SD  $\pm$  16; p = 0.008) and with SPMS (13 h/week; SD  $\pm$  16; p = 0.001; Fig. 1B); we found no differences in the weekly working hours between SPMS and PPMS (p = 0.86) and no gender-related differences (women 25 h/week SD  $\pm$  16 and men 27 h/week SD  $\pm$  18; p = 0.59) but significant correlations with age (p = 0.000157, Spearman r = -0.37). Working hours were not related to individual monthly costs for non-pharmacological treatments.

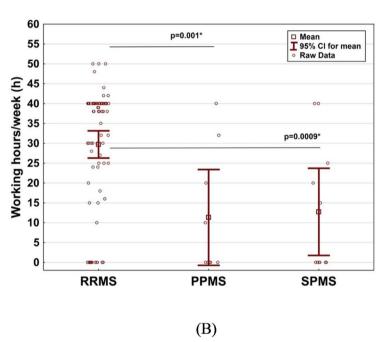
#### Discussion

Our study provides insight into the financial burden faced individuals with MS due to the use of non-pharmacological treatments. On average, participants from our cohort spend 136 EUR per month out-of-pocket on supplements and other non-DMT approaches. Notably, the expenses assessed in this study represent out-of-pocket costs incurred by participants, including expenditures for physiotherapy and speech therapy, beyond the coverage provided by the healthcare system. Expenses were substantially higher for individuals with PPMS, who spend an average of 337 EUR monthly. These individuals not only face higher costs but also reported fewer working hours per week, thereby exacerbating their financial strain. Considering that the average annual gross income for full-time employees in Austria was 57,731 EUR in 2023<sup>10</sup>, the expenses faced by individuals with PPMS, who work on average 11 h per week, seem disproportionately high.

Interestingly, few studies have thoroughly examined the individual costs outside the full health care coverage and carried individually in MS. Our findings reveal significantly higher costs compared to an Italian study from the early 2000s, which reported mean annual expenses of 483 EUR for CAMs<sup>11</sup>. These increased expenses cannot be attributed solely to inflation or to the fact that, compared to the aforementioned study, we encompassed all non-pharmacological therapies and therefore also physiotherapy. Instead, the higher costs likely reflect a shift in perceptions and utilization of CAMs over the past years, as supplements, exercise, and mind-body therapies have gained more attention since then<sup>12</sup>. Of note, the majority of non-pharmacological approaches lack higher-quality evidence supporting their safety and efficacy in MS<sup>3</sup>. Nevertheless, approximately 80% of individuals with MS use CAMs<sup>6,7,12</sup>, which aligns with the high rate (82%) of non-pharmacological treatments among our Austrian cohort. According to our data, the most commonly used therapies were Vitamins D and B as well as magnesium, physiotherapy and massage treatments. However, the use of alternative therapies is widespread encompassing regular intake of trace elements and incense, and visits to osteopaths and acupuncturists. Usage of supplements (76%) among our cohort was comparable to previous data<sup>6</sup>, and also the utilization of therapists was similar to a cohort of 524 American people with MS who reported visiting chiropractors (22%), acupuncturists (10%), and massage therapists (15%) primarily for symptom relief, back problems, and pain management 13.

The expenses for and the frequent use of CAMs in MS however underscore the peoples' willingness to explore all possible options to manage their condition and their desire to actively participate in their recovery through a holistic therapeutic approach. Yet, there seems to be a gap between the knowledge of individuals with MS about CAMs efficacy on one hand and the information physicians have about the usage of CAMs of their clients on the other hand. Reasons may include that practicing neurologists and primary care physicians often do not engage in discussions about CAMs, but also a lack of time in visits. Conversely, individuals with MS may be reluctant to disclose their use of CAMs, fearing negative reactions from their conventional healthcare providers<sup>14</sup>. Therefore, it is crucial for physicians to foster open communication, providing accurate information about the efficacy and tolerability of CAMs based on scientifically valid data.





**Fig. 1.** Monthly expenses (**A**) and weekly working hours (**B**) among participants with RRMS, PPMS and SPMS. PPMS individuals spend significantly more for non-pharmacological therapies compare to RRMS (**A**) but work significantly less hours per week (**B**). Individuals with RRMS work more hours a week than participants with SPMS (**B**). RRMS: relapsing–remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis.

MS is an expensive disease, with total lifetime costs exceeding 4 million dollars per affected individual<sup>15</sup>. Compared to many alternative therapies, mounting evidence highlights the effectiveness of DMTs in reducing disease activity in MS, primarily by targeting T and B cells<sup>1,9,16,17</sup>. DMTs represent a large financial component in MS treatment, and their annual costs amount to approximately 70,000 dollars<sup>17–19</sup>. Additionally, MS imposes considerable indirect costs, including loss of productivity and unemployment. An American study estimated that the indirect and non-medical costs per individual with MS amounted to 18,542 dollars in 2019, with a majority of these expenses attributed to productivity losses in the workplace<sup>9</sup>. Indeed, the employment rate drops soon after receiving a diagnosis of MS, and more than 30% of individuals with MS experienced early retirement, with an average retirement age of 43.6 years<sup>20</sup>. Among 462 Spanish individuals with MS with an EDSS score between

	All Supplements (n)	Vitamin D (n)	Magnesium (n)	Vitamin B (n)	Omega 3 (n)	Vitamin Complexes (n)	Vitamin K (n)	Selenium (n)	Zink (n)	Probiotics (n)	Incense (n)
Total (n = 98)	74	42	19	12	12	9	8	6	5	5	5
Gender	Gender										•
Male (n = 34)	24	16	11	7	5	2	3	2	2	3	3
Female (n=64)	50	26	8	5	7	7	5	4	3	2	2
Diagnosis											
RRMS (n=78)	58	30	10	10	7	4	7	6	4	4	3
SPMS (n = 11)	8	7	7	1	4	3	1	-	1	-	-
PPMS (n = 9)	8	5	2	1	1	2	-	-	-	1	2
PPMS (n = 9)	8	5	2	1	1	2	-	-	-	1	2

	All therapists (n)	Physiotherapy (n)	Massage therapy (n)	Osteopathy (n)	Dietitian (n)	Accupuncture (n)	Homeopathy (n)	Chiropractic (n)	Miscellaneous (n)		
Total (n = 98)	50	30	21	9	3	3	2	1	10		
Gender	Gender										
Male (n = 34)	18	8	9	4	-	1	1	1	3		
Female (n=64)	32	22	12	5	3	2	1	-	7		
Diagnosis											
RRMS (n = 78)	35	19	13	5	2	2	1	-	6		
SPMS (n = 11)	7	5	3	1	-	-	-	-	2		
PPMS (n = 9)	8	6	5	3	1	1	1	1	2		

**Table 3**. Usage of nutritional supplements (top) and therapists (bottom) by survey respondents. *RRMS* relapsing–remitting multiple sclerosis, *SPMS* secondary progressive multiple sclerosis, *PPMS* primary progressive multiple sclerosis.

0 and 3, the employment rate was as low as of  $45\%^{21}$ . In our cohort, with a mean age of 44 years and a mean EDSS of 2.1, the average weekly working hours were 26, significantly below the extent of full-time employment. Weekly working hours were particularly low among participants with progressive MS, underscoring the socioeconomic impact of the disease on individuals with these MS courses.

Our study is limited by a relatively small sample size among the different MS types. Additionally, the nature of participation in the MADAI study, a placebo-controlled trial on supplements, may have introduced selection bias, including individuals who are more attracted to non-pharmacological MS treatments. The limited scope of the questionnaire might have missed specific therapies, and the absence of clear definitions for CAMs, dietary supplements, and alternative therapies could complicate interpretation. Furthermore, the study focused on direct costs, neglecting indirect costs such as unpaid caregiving by family members, which have however been investigated in other studies. As Austria falls within the mid-range of European countries in terms of out-of-pocket spending on medicine for people with chronic conditions, our data may serve as an example for other high-income nations<sup>22</sup>.

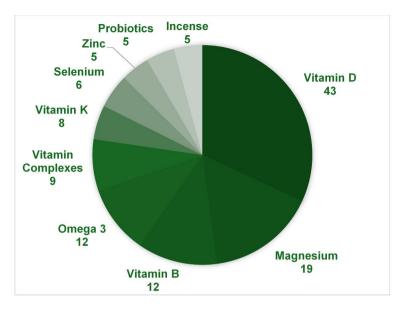
To conclude, our study highlights high out-of-pocket costs for individuals with MS in Austria, particularly for those with progressive forms of the disease, who are more likely to face financial hardships due to reduced employment. Our data encourages communication between individuals with MS and healthcare providers regarding evidence and usage of non-pharmacological treatments.

#### Methods

#### Recruitment and assessments

Participants for this cross-sectional study were recruited in May 2024 from the MADAI trial that is conducted at the University Hospital for Neurology, in Salzburg, Austria. MADAI is a prospective, placebo-controlled study involving individuals with MS, that are randomized in a 1:2 ratio to receive either a placebo or oral propionic acid (1000 mg/day) over a 90-day period. Detailed inclusion and exclusion criteria for the MADAI study can be found in suppl. Table 2. Demographics and data on the MS history were extracted from participants' records.

After providing written informed consent to participate in the study, all participants received a structured online questionnaire via email, which they were asked to complete at home. The questionnaire consisted of seven sections and three of them were analyzed for the aim of this study (suppl. File 1). The second section of seven, entitled "Nutritional Supplements," included questions about the use of nutritional supplements. This section consisted of closed questions, where participants were asked whether they used any nutritional supplements, vitamins, or natural remedies and herbs, which could only be answered with "yes" or "no". If answered with yes, participants could provide details about the types of supplements taken, including specific products, daily dosages, and brands, and reported their approximate monthly expenditure for each category in Euro (EUR) in open questions. The third section, titled "Other Healing Methods and Therapies," focused on practices administered by therapists. This section again consisted of closed questions, and participants were asked to report whether they used professional support such as physiotherapy, chiropractic care, osteopathy, massage therapy, speech therapy, homeopathy, acupuncture, dietologist consultations, or other therapies, which could



(A)

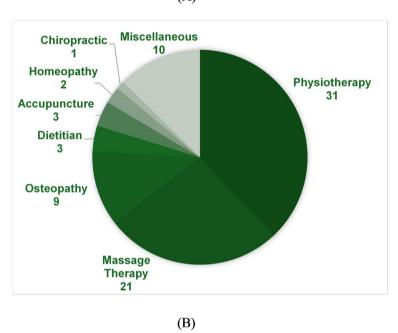


Fig. 2. Most commonly used supplements (A) and therapists (B) reported by individuals with MS (%).

analogously to the previous section only be answered with "yes" or "no". If answered with "yes", they also were asked about their monthly expenditure for each therapy in EUR. Finally, participants were asked about their weekly working hours.

In addition to gathering information on usage and monthly expenditure on non-pharmacological MS treatments, the questionnaire collected general data about the participants, essential for analyzing the placebocontrolled MADAI study. The remaining sections covered various aspects such as quality of life, self-reported EDSS, lifestyle, and family history. Overall, completing the questionnaire was estimated to take 30–60 min.

The questionnaire was administered using *Evasys*, and the responses were collected as .csv files and subsequently edited using Excel. Descriptive statistics were employed to summarize the expenditure data, with results presented as means (± standard deviation (SD)) and ranges across different categories.

### Statistical methods

Data were checked for consistency and normality using Saphiro-Wilks tests. Pearson's Chi-Squared test was used to analyze cross tabulations. Depending on deviations from normality, generalized linear models (GLMs) based on log-normal distributions or randomization tests with and without the assumption of variance homogeneity based on 4000 Monte Carlo simulations were used to test means between groups. GLMs were used to compare

the mean expenses for non-pharmacological treatments among the PPMS, RRMS, and SPMS groups. In all other cases, randomization tests were applied. Variance homogeneity was tested using the F-test and Levene's tests. Spearman correlation coefficients were computed and tested for association analyses. Whisker plots with 95% CI for means were used to illustrate results. All reported tests were two-sided, and *p*-values < 0.05 were considered statistically significant. All statistical analyses in this report were performed by use of NCSS (NCSS 2022, NCSS, LLC. Kaysville, UT) and STATISTICA 13 (Hill, T. & Lewicki, P. Statistics: Methods and Applications. StatSoft, Tulsa, OK).

#### **Ethics**

This study has been performed in accordance with the Declaration of Helsinki. The MADAI study received ethical approval from the *Ethikkommission Land Salzburg* (Approval Number: 1026/2024), and all participants provided written informed consent. The MADAI trial is registered at ClinicalTrials.gov with the identifier NCT06402487.

# Data availability

Data supporting the findings of this study are available within the paper and its Supplementary Information.

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#### References

- 1. Dobson, R. & Giovannoni, G. Multiple sclerosis—A review. Eur. J. Neurol. 26, 27-40. https://doi.org/10.1111/ene.13819 (2019).
- Kobelt, G., Berg, J., Lindgren, P., Fredrikson, S. & Jonsson, B. Costs and quality of life of patients with multiple sclerosis in Europe. J. Neurol. Neurosurg. Psychiatry 77, 918–926. https://doi.org/10.1136/jnnp.2006.090365 (2006).
- 4. Mbizo, J. et al. Complementary and alternative medicine use among persons with multiple chronic conditions: Results from the 2012 National Health Interview Survey. *BMC Complement Altern. Med.* 18, 281. https://doi.org/10.1186/s12906-018-2342-2 (2018)
- 5. Claflin, S. B., van der Mei, I. A. F. & Taylor, B. V. Complementary and alternative treatments of multiple sclerosis: A review of the evidence from 2001 to 2016. *J. Neurol. Neurosurg. Psychiatry* 89, 34–41. https://doi.org/10.1136/jnnp-2016-314490 (2018).
- O'Connor, K. et al. Patterns of dietary and herbal supplement use by multiple sclerosis patients. J. Neurol. 259, 637–644. https://doi.org/10.1007/s00415-011-6226-3 (2012).
- 7. Gotta, M., Mayer, C. A. & Huebner, J. Use of complementary and alternative medicine in patients with multiple sclerosis in Germany. *Complement Ther. Med.* 36, 113–117. https://doi.org/10.1016/j.ctim.2017.12.006 (2018).
- 8. Nayak, S., Matheis, R. J., Schoenberger, N. E. & Shiffett, S. C. Use of unconventional therapies by individuals with multiple sclerosis. Clin. Rehabil. 17, 181–191. https://doi.org/10.1191/0269215503cr604oa (2003).
- 9. Bebo, B. et al. The economic burden of multiple sclerosis in the united states: Estimate of direct and indirect costs. *Neurology* 98, e1810–e1817. https://doi.org/10.1212/WNL.0000000000200150 (2022).
- 10. https://www.stepstone.at/e-recruiting/blog/durchschnittsgehalt-oesterreich-stepstone-gehaltsreport/#h-durchschnittsgehalt-in-osterreich-2023, <a href="https://www.stepstone.at/e-recruiting/blog/durchschnittsgehalt-oesterreich-stepstone-gehaltsreport/#h-durchschnittsgehalt-in-osterreich-2023">https://www.stepstone.at/e-recruiting/blog/durchschnittsgehalt-oesterreich-stepstone-gehaltsreport/#h-durchschnittsgehalt-in-osterreich-2023> (2024).</a>
- 11. Pucci, E., Cartechini, E., Taus, C. & Giuliani, G. Why physicians need to look more closely at the use of complementary and alternative medicine by multiple sclerosis patients. *Eur. J. Neurol.* 11, 263–267. https://doi.org/10.1046/j.1468-1331.2003.00758.x (2004)
- 12. Silbermann, E. et al. Cross-sectional survey of complementary and alternative medicine used in Oregon and Southwest Washington to treat multiple sclerosis: A 17-Year update. *Mult. Scler. Relat. Disord.* 41, 102041. https://doi.org/10.1016/j.msard.2020.102041
- 13. Kim, S. et al. Complementary and alternative medicine usage by multiple sclerosis patients: Results from a prospective clinical study. *J. Altern. Complement Med.* **24**, 596–602. https://doi.org/10.1089/acm.2017.0268 (2018).
- 14. Winterholler, M., Erbguth, F. & Neundorfer, B. The use of alternative medicine by multiple sclerosis patients—patient characteristics and patterns of use. Fortschr. Neurol. Psychiatr. 65, 555–561. https://doi.org/10.1055/s-2007-996363 (1997).
- 15. Owens, G. M. Economic burden of multiple sclerosis and the role of managed sare organizations in multiple sclerosis management. *Am. J. Manag. Care* 22, s151-158 (2016).
- 16. Newsome, S. D., Binns, C., Kaunzner, U. W., Morgan, S. & Halper, J. No evidence of disease activity (NEDA) as a clinical assessment tool for multiple sclerosis: Clinician and patient perspectives [Narrative Review]. *Neurol. Ther.* 12, 1909–1935. https://doi.org/10.1007/s40120-023-00549-7 (2023).
- 17. Hartung, D. M. Economics and cost-effectiveness of multiple sclerosis therapies in the USA. *Neurotherapeutics* 14, 1018–1026. https://doi.org/10.1007/s13311-017-0566-3 (2017).
- 18. Moser, T., Akgun, K., Proschmann, U., Sellner, J. & Ziemssen, T. The role of TH17 cells in multiple sclerosis: Therapeutic implications. *Autoimmun. Rev.* 19, 102647. https://doi.org/10.1016/j.autrev.2020.102647 (2020).
- Greenfield, A. L. & Hauser, S. L. B-cell therapy for multiple sclerosis: Entering an era. Ann. Neurol. 83, 13–26. https://doi.org/10.1 002/ana.25119 (2018).
- 20. Garcia-Dominguez, J. M. et al. Economic burden of multiple sclerosis in a population with low physical disability. *BMC Public Health* **19**, 609. https://doi.org/10.1186/s12889-019-6907-x (2019).
- 21. Oreja-Guevara, C. et al. New insights into the burden and costs of multiple sclerosis in Europe: Results for Spain. *Mult. Scler.* 23, 166–178. https://doi.org/10.1177/1352458517708672 (2017).
- 22. Palladino, R. et al. Multimorbidity and out-of-pocket expenditure on medicine in Europe: Longitudinal analysis of 13 European countries between 2013 and 2015. Front Public Health 10, 1053515. https://doi.org/10.3389/fpubh.2022.1053515 (2022).

### **Author contributions**

TLC has made substantial contributions to the acquisition, analysis, and interpretation of data and has drafted the work. He has also prepaired the tables. SH has made substantial contributions to the acquisition of data and substantively revised the manuscript. JS has made substantial contributions to the acquisition of data and substantively revised the manuscript. LB has made substantial contributions to the acquisition of data and

substantively revised the manuscript. KD has made substantial contributions to to the acquisition of data and substantively revised the manuscript. MG has made substantial contributions to the acquisition of data and substantively revised the manuscript. WH has made substantial contributions to the analysis and interpretation of data and substantively revised the manuscript. He has also prepared the Figs. 1–2. ET has made substantial contributions to the interpretation of data and substantively revised the manuscript. PW has made substantial contributions to the conception and design of the work and substantively revised the manuscript. TM has made substantial contributions to conception and design of the work, interpretation of data and has drafted the work. All authors have approved the submitted version and to have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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# **Declarations**

# Competing interests

E.T. has received consultancy fees from Arvelle Therapeutics, Argenx, Clexio, Celegene, UCB Pharma, Eisai, Epilog, Bial, Medtronic, Everpharma, Biogen, Takeda, Liva-Nova, Newbridge, Sunovion, GW Pharmaceuticals, and Marinus; speaker fees from Arvelle Therapeutics, Bial, Biogen, Böhringer Ingelheim, Eisai, Everpharma, GSK, GW Pharmaceuticals, Hikma, Liva-Nova, Newbridge, Novartis, Sanofi, Sandoz and UCB Pharma; research funding (directly, or to his institution) from GSK, Biogen, Eisai, Novartis, Red Bull, Bayer, and UCB Pharma outside the submitted work. He has received grants from Austrian Science Fund (FWF), Österreichische Nationalbank, and the European Union. E.T. is the CEO of Neuroconsult Ges.m.b.H. P.W. has participated in meetings sponsored by, received honoraria (lectures, advisory boards, consultations) or travel funding from Alexion, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme, Teva-Ratiopharm, Janssen-Pharmazeutika, Bristol-Myers SQUIBB and Horizon Therapeutics. T.M. received travel support, honoraria for presentations or participation on advisory boards from Biogen, BMS, Novartis, Roche, Sanofi, Merck and Teva. The remaining authors report no conflict of interest.

### Additional information

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