

Use of complementary therapies is associated with expectations of treatment effectiveness among persons with multiple sclerosis

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To cite: Stanikić M, Steinemann N, López-Alcalde J, *et al.* Use of complementary therapies is associated with expectations of treatment effectiveness among persons with multiple sclerosis. *BMJ Neurology Open* 2026;8:e001499. doi:10.1136/bmjno-2025-001499

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/bmjno-2025-001499>).

Received 04 December 2025
Accepted 18 March 2026



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ABSTRACT

Background Complementary therapies (CTs) are widely used among persons with multiple sclerosis (MS). Patients' expectations of treatment effectiveness are linked to CT use in the general population. However, little is known about how such expectations vary among people with MS or whether they are associated with CT use.

Objectives To identify expectation-based clusters among adults with MS, describe their characteristics and assess associations with current CT use.

Methods We conducted a cross-sectional analysis of Swiss MS Registry follow-up survey data collected between October 2022 and October 2023, exploring expectations regarding manual, mind–body, natural product-based and dietary therapies. K-means clustering was applied to eight variables assessing participants' expectations of each therapy's effectiveness for physical and psychological symptoms. Clusters were described, and associations with current CT use were analysed using log-binomial regression.

Results A total of 753 participants were classified into three expectation clusters: low (20.3%), moderate (47.6%) and high (32.1%). The low-expectation cluster included more individuals with progressive MS, severe gait disability and lowest CT use. Expectation clusters were significantly associated with current CT use. In unadjusted analyses, inclusion of the cluster variable significantly improved model fit (likelihood ratio test (LRT)=31.25, $p<0.001$), and participants in the moderate-expectation and high-expectation clusters were more likely to use CT compared with the low-expectation cluster (relative risk (RR) 1.60, 95% CI 1.26 to 2.04; RR: 1.80, 95% CI 1.42 to 2.30). After adjustment, the association remained significant (LRT=29.01, $p<0.001$), with higher likelihoods of CT use in the moderate-expectation and high-expectation clusters (adjusted RR: 1.58, 95% CI 1.24 to 2.00; RR: 1.80, 95% CI 1.41 to 2.30, respectively). Sensitivity analyses using an alternative CT outcome variable yielded consistent results.

Conclusions Expectation profiles are independently associated with CT use in MS. Addressing misalignments between patient expectations and evidence may help

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Many persons with multiple sclerosis use complementary therapies (CTs) alongside or instead of conventional treatments, particularly women, those with higher education, longer disease duration and those not disease-modifying therapies. Whether expectations of CT effectiveness play a role in CT use remains unexplored.

WHAT THIS STUDY ADDS

⇒ We found that current CT use is independently associated with higher expectations after accounting for past CT use, disease-modifying therapy use and disease severity. Expectations often diverged from evidence: in the low expectation cluster, mind–body therapies were undervalued for psychological symptoms despite robust support, while natural product-based therapies were overvalued in the high expectation cluster despite limited evidence.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings should prompt clinicians to proactively elicit and calibrate patient expectations through targeted education that addresses both unwarranted pessimism and overoptimism about CTs, enabling evidence-informed choices aligned with individual needs.

promote informed, evidence-based decision-making about CTs.

INTRODUCTION

Disease-modifying therapies (DMTs) have considerably advanced multiple sclerosis (MS) management, yet symptoms such as fatigue, pain and spasticity remain a challenge for many persons with MS (pwMS).^{1,2} Consequently, a substantial proportion of pwMS use complementary therapies (CTs) as adjunctive

or alternative approaches to conventional treatment, seeking enhanced symptom control, relief from DMT side effects and quality of life improvement.^{3–7}

In general, CT use is understood to reflect a combination of demographic, sociocultural, psychological and disease-related influences.⁸ Previous research indicates that CT use in MS is more common among women, individuals with higher educational attainment, those with longer disease duration and those not using DMTs.^{4 9 10} In addition, pwMS who adopt CTs often employ distinct coping strategies, seeking greater understanding of their condition, more control over treatment and holistic approaches to care.^{11 12} Beyond these factors, expectations of treatment effectiveness have been shown to shape CT choices in health contexts outside MS.^{8 13 14} However, the role of treatment effectiveness expectations in relation to CT use among pwMS remains largely unexplored. Consequently, it remains unclear how such expectations relate to CT use or whether pwMS who use CTs differ in their expectations from non-users. Examining perceptions of CT effectiveness among pwMS may help clarify patterns of CT adoption and support more informed clinical discussions about CT use, including management of patient expectations and the alignment of treatment decisions with available evidence.

This study explored the expectations of pwMS regarding the CT effectiveness in alleviating MS symptoms. We aimed to: (1) classify adult pwMS into clusters based on differing levels of expectations about CT effectiveness; (2) describe and compare these expectation clusters across sociodemographic and health-related characteristics; and (3) explore the relationship between expectation clusters and current CT use.

METHODS

Data source and study population

We used data from the Swiss Multiple Sclerosis Registry (SMSR), an ongoing longitudinal study that recruits adults with MS or clinically isolated syndrome (CIS) living or receiving care in Switzerland. Participation in the SMSR is voluntary and requires submission of a signed informed consent form. Participants complete baseline and follow-up surveys, which are available online and in paper format in Switzerland's three official languages: German, French and Italian. The SMSR is a citizen-science project; survey instruments are co-developed with participants. Further information about the SMSR can be found elsewhere.^{15 16}

We used data from the annual SMSR follow-up survey, distributed to 2332 participants beginning in October 2022, with data collection concluding in October 2023. This survey included a supplementary questionnaire on CT use, co-developed by the Institute for Complementary and Integrative Medicine, University Hospital Zurich, as part of the Participatory Evidence Synthesis in Multiple Sclerosis and Complementary Therapies project. The questionnaire assessed participants' past, current and

potential future use of CTs for specific reasons (eg, to alleviate MS symptoms, improve quality of life) or symptoms (eg, spasms, depression, tremor). It also explored participants' expectations regarding the effectiveness and safety of different CTs in alleviating physical and psychological MS-related problems. The questionnaire focused on CT modalities identified through relevant literature and input from stakeholders, including researchers, CT practitioners, conventional medicine providers and SMSR participants. Further details on its development are provided in the online supplemental material and in a separate publication.¹⁷

Sociodemographic information, MS-related and other health-related data, was also collected from the same annual follow-up survey and supplemented with data from previous follow-up surveys or baseline records. All used questions from the follow-up survey, including those from the supplementary CT questionnaire, are provided in the online supplemental material.

Variables for clustering

Participants were clustered based on their expectations regarding the effectiveness of CTs in managing MS symptoms. These expectations were assessed using eight variables derived from the supplementary CT questionnaire. For each of four predefined CT categories—manual therapies, mind–body therapies, natural product-based therapies and specific diets¹⁷—participants rated two statements: one regarding expected effectiveness for physical symptoms (eg, 'I expect that physical complaints will improve significantly through manual therapies') and one for psychological symptoms (eg, 'I expect that psychological complaints will improve significantly through manual therapies'). All items were rated on an 11-point Likert scale from 0 ('Don't agree at all') to 10 ('Completely agree'), with responses analysed as quantitative variables (values ranging from 0 to 10). Definitions and examples were provided to clarify each CT and symptom category. Inclusion in the analysis required data for at least six of the eight clustering variables. Participants with data for all eight variables were included in the complete cases sample.

Variables for describing expectation clusters

Expectation clusters were described using baseline sociodemographic data, including sex (binary: female or male), age (continuous: calculated from birth year to follow-up questionnaire completion year), highest education level (categorical: university/applied university, higher professional education or mandatory school/high school/apprenticeship) and Swiss citizenship (binary: yes or no). Other variables for describing expectation clusters included: MS duration (continuous: calculated from diagnosis year reported at baseline to follow-up questionnaire year), and characteristics assessed at follow-up, such as MS subtype (categorical: CIS, relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS or transitioning from RRMS to SPMS),

DMT use in the past 6 months (binary: yes or no), gait disability (categorical: mild, moderate, severe) measured with the self-reported disability status scale,¹⁸ fatigue measured by the Modified Fatigue Impact Scale-21¹⁹ and presence of MS symptoms in the past 6 months (binary: yes or no). The presence of a chronic comorbidity was assessed using baseline and follow-up data, with a multiple-choice question on conditions like diabetes, hypertension, cancer, rheumatoid diseases, musculoskeletal disorders, depression and skin diseases (binary: yes or no).

Current and past CT use

Current CT use was assessed using two binary (yes or no) variables. The primary regression analysis used a variable derived from two questions regularly included in all SMSR follow-up surveys: one consisting of a multiple-choice list of CTs (eg, traditional Chinese medicine, vitamins, osteopathy) with an additional open text field for other therapies (online supplemental material, survey item H1) and another on cannabis-based product use within the past 6 months (online supplemental material, survey item H4). Reporting use of any listed CTs or cannabis-based products was coded as 'yes'. For sensitivity regression analysis, a second variable was created based on items from the supplementary CT questionnaire, which asked about past, current and potential future CT use for any reason or symptom—any reported current use was coded as 'yes'. The same supplementary CT questionnaire items were used to assess past CT use (binary: yes or no; online supplemental material, survey item K1 and K2).

Analysis

To address the first study aim, we conducted an exploratory k-means cluster analysis on the complete cases sample. Clustering was performed with 50 starting points to reduce the risk of suboptimal partitions. Simple Euclidean distance was used as the similarity measure. The initial range of plausible cluster numbers was determined using an elbow plot and refined using the Pseudo-F statistic.²⁰ The final number of clusters was selected based on interpretability, while ensuring a reasonable number of clusters for subsequent analysis.²¹ This constituted the primary analysis. For the sensitivity cluster analysis, we repeated the clustering on a sample of participants with up to two missing values in the clustering variables, henceforth referred to as the imputed sample. Missing data were addressed using multiple imputation, following the framework by Basagaña *et al.*²² We generated 100 imputed datasets, applied k-means clustering to each and identified the optimal number of clusters (k) using the CritCF criterion.²³ If the optimal k differed from that identified in the primary analysis, clustering was also performed using the k value from the primary analysis. Finally, we pooled results across the imputed datasets, assigning each person to their most frequently occurring cluster.

To address the second aim, we characterised the identified expectation clusters using sociodemographic

and health-related variables. Continuous variables were presented as means with SD and/or medians with IQRs. Categorical variables were presented as counts and percentages. We performed this characterisation for both the primary and sensitivity cluster analyses.

For the third aim, we explored the association between expectation clusters and current CT use in the complete case sample, hypothesising that higher expectations of CT effectiveness would be significantly and positively associated with current CT use. Associations were estimated using log-binomial regression, which provides more accurate risk estimates than logistic regression when the outcome is highly prevalent,²⁴ as was the case in this study. We first fitted an unadjusted model with expectation cluster as the only predictor and evaluated its contribution via a likelihood ratio test (LRT) against an intercept-only model. Next, we fitted an adjusted base model including age, sex, MS subtype, education level, DMT use and past CT use as fixed independent variables.^{4 7 9 25}

The expectation cluster variable was subsequently added, and its independent contribution was evaluated via LRT comparing models with and without it. In addition, we tested whether the association between expectation clusters and CT use was moderated by MS subtype, positing that disease characteristics may influence the relationship between expectations and CT use. To evaluate the interaction effect, an interaction term between the cluster variable and MS subtype was added, and model fit was again assessed via LRT. A sensitivity regression analysis was performed using the alternative current CT use variable derived from the supplementary CT questionnaire.

All analyses were carried out using R (V.4.4.1),²⁶ R studio (V.2024.09.0+375) and packages tidyverse, table1, factoextra, stats, cluster, miclust and lbm.

RESULTS

A total of 896 SMSR participants responded to the follow-up survey (38.4% response rate). After excluding 143 participants with missing data on three or more clustering variables, the final sample included 753 participants. Of these, 704 had complete data for all clustering variables, forming the complete case sample (figure 1). Their characteristics are summarised in table 1, while the online supplemental tables 1 and 2 provide a summary of the characteristics of the imputed sample, those excluded due to missing data and follow-up survey non-responders.

Current CT use was reported by 414 (58.8%) when responding to the follow-up SMSR survey question and by 450 (63.9%) participants in the supplementary CT questionnaire. Past CT use was reported by 379 (53.8%) participants (table 1). Overall, participants had the highest expectations of manual therapies for alleviating physical problems, with a mean score of 6.72 (SD: 2.93). In contrast, diet was perceived as the least effective CT, particularly for addressing psychological problems (mean score 4.23, SD: 3.15). A summary of all effectiveness

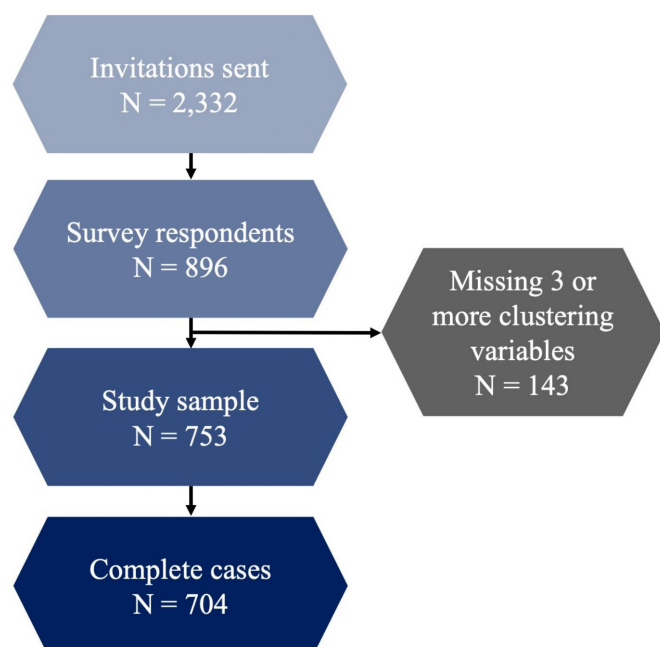


Figure 1 Study design flow chart.

expectation ratings is provided in the online supplemental table 3.

Expectation-based clusters

A three-cluster solution was selected based on statistical measures of fit and considerations of interpretability, with a comprehensive rationale for this decision provided in the online supplemental material and online supplemental figure 1. The three clusters were defined by their average expectations of the effectiveness of CTs in alleviating physical and psychological symptoms: *low* (mean scores around 1–2), *moderate* (mean scores around 5) and *high* (mean scores around or above 8). Out of 704 participants in the complete case sample, 143 (20.3%) were clustered in the low, 335 (47.6%) in the moderate and 226 (32.1%) in the high expectation group. **Figure 2** depicts the density distributions of the expectation clusters across four CT categories.

Table 1 presents participant characteristics across the expectation clusters in the complete case analysis, demonstrating a gradient across several characteristics. Namely, the low expectation group was oldest, had the longest disease duration, most comorbidities, highest prevalence of progressive MS and the lowest CT use, both current and past. In contrast, the high expectation group was youngest, had the shortest disease duration, most frequently had RRMS and reported the highest CT use. The moderate expectation group showed intermediate traits, with more pronounced differences between the low and moderate expectation clusters than between the moderate and high expectation clusters.

Sensitivity cluster analysis

Of the 753 participants in the imputed sample, 49 had 73 missing values across the eight clustering variables.

After data imputation, 155 (20.6%) participants were clustered in the low expectation cluster, 303 (40.2%) in the moderate and 295 (39.2%) in the high expectation cluster. The distributions of the clustering variables (online supplemental table 4) were comparable to the primary analysis. Current CT use was most prevalent in the high expectation cluster ($n=206$, 69.8%), followed by the moderate ($n=176$, 58.1%) and low expectation clusters ($n=70$, 40.6%). Past CT use was reported by $n=239$ (81.0%) of participants in the high expectation cluster, $n=218$ (71.9%) in the moderate and $n=97$ (62.6%) in the low expectation cluster (online supplemental table 5).

Association of expectation clusters with CT use

Regression modelling was performed on data from 642 participants due to missing confounder data (**table 1**). In the unadjusted analysis, the addition of the cluster variable significantly improved model fit ($LRT=31.25$, $df=2$, $p<0.001$). Participants in the moderate and high expectation clusters were more likely to use CT compared with the low expectation cluster (unadjusted relative risk (RR)=1.60, 95% CI 1.26 to 2.04, and RR=1.80, 95% CI 1.42 to 2.30, respectively). The addition of the cluster variable to the adjusted base model significantly improved model fit ($LRT=29.01$, $df=2$, $p<0.001$), with higher likelihoods of CT use in the high and moderate expectation clusters compared with the low expectation cluster (adjusted RR: 1.58, 95% CI 1.24 to 2.00, and RR: 1.80, 95% CI 1.41 to 2.30, respectively, online supplemental table 6).

Sensitivity analyses using the CT outcome derived from the supplementary questionnaire showed consistent findings. Inclusion of the cluster variable significantly improved model fit in both unadjusted ($LRT=20.84$, $df=2$, $p<0.001$) and adjusted models ($LRT=18.13$, $df=2$, $p<0.001$). In both models, participants in the moderate and high expectation clusters were more likely to report CT use compared with the low expectation cluster (unadjusted RR=1.43, 95% CI 1.17 to 1.74 and RR=1.49, 95% CI 1.22 to 1.83; adjusted RR=1.39, 95% CI 1.14 to 1.69 and RR=1.46, 95% CI 1.19 to 1.78, respectively, online supplemental table 7).

The interaction term between clusters and MS subtypes did not improve model fit in either the main or sensitivity analysis.

DISCUSSION

This study explored the expectations of pwMS regarding the effectiveness of CTs in alleviating MS symptoms, identifying three expectation-based clusters: low, moderate and high. These clusters differed not only in expectations but also in demographic and health-related characteristics. Participants in the low expectation cluster were generally older, more often male, had lived with MS longer, reported higher levels of disability and physical fatigue, and the lowest rates of both current and past CT use. While expectations varied across CT categories—being lower for diet-based interventions and higher for physical

Table 1 Characteristics of complete case sample by cluster

	Low n=143	Moderate n=335	High n=226	Overall N=704
Sex, N (%)				
Male	49 (34.3)	66 (19.7)	53 (23.5)	168 (23.9)
Female	94 (65.7)	269 (80.3)	173 (76.5)	536 (76.1)
Age in years, median (IQR)	59.0 (50.0–66.0)	52.0 (43.0–60.0)	49.0 (41.0–57.0)	52.0 (43.0–60.0)
Highest education level, N (%)				
Mandatory, high school or apprenticeship	71 (49.7)	177 (52.8)	111 (49.1)	359 (51.0)
Higher professional education	12 (8.4)	53 (15.8)	31 (13.7)	96 (13.6)
University or university of applied sciences	49 (34.3)	82 (24.5)	71 (31.4)	202 (28.7)
Missing	11 (7.7)	23 (6.9)	13 (5.8)	47 (6.7)
Swiss citizenship, N (%)				
No	18 (12.6)	26 (7.8)	24 (10.6)	68 (9.7)
Yes	124 (86.7)	303 (90.4)	201 (88.9)	628 (89.2)
Missing	1 (0.7)	6 (1.8)	1 (0.4)	8 (1.1)
MS subtype, N (%)				
CIS	1 (0.7)	3 (0.9)	3 (1.3%)	7 (1.0)
PPMS	27 (18.9)	35 (10.4)	19 (8.4%)	81 (11.5)
RRMS	71 (49.7)	227 (67.8)	162 (71.7%)	460 (65.3)
SPMS	41 (28.7)	58 (17.3)	31 (13.7%)	130 (18.5)
Transition	3 (2.1)	12 (3.6)	10 (4.4%)	25 (3.6)
Missing	0 (0)	0 (0)	1 (0.4%)	1 (0.1)
MS duration since diagnosis in years, median (IQR)	15.0 (8.0–23.0)	13.0 (6.2–19.8)	10.0 (5.0–18.0)	12.0 (6.0–20.0)
Missing	2 (1.4%)	5 (1.5%)	5 (2.2%)	12 (1.7)
Gait disability, N (%)				
Mild	74 (51.7)	234 (69.9)	163 (72.1)	471 (66.9)
Moderate	48 (33.6)	72 (21.5)	42 (18.6)	162 (23.0)
Severe	17 (11.9)	25 (7.5)	15 (6.6)	57 (8.1)
Missing	4 (2.8)	4 (1.2)	6 (2.7)	14 (2.0)
Presence of MS symptoms, N (%)				
No	49 (34.3)	111 (33.1)	82 (36.3)	242 (34.4)
Yes	94 (65.7)	222 (66.3)	142 (62.8)	458 (65.1)
Missing	0 (0)	2 (0.6)	2 (0.9)	4 (0.6)
Current DMT use, N (%)				
No	39 (27.3)	93 (27.8)	68 (30.1)	200 (28.4)
Yes	99 (69.2)	239 (71.3)	151 (66.8)	489 (69.5)
Missing	5 (3.5)	3 (0.9)	7 (3.1)	15 (2.1)
MFIS total score, median (IQR)	33.5 (19.2–48.0)	28.0 (11.0–43.0)	25.0 (9.0–43.0)	28.0 (12.0–44.0)
Missing	17 (11.9)	26 (7.8)	13 (5.8)	56 (8.0)
MFIS cognitive subscale score, median (IQR)	12.0 (6.0–19.8)	11.0 (5.0–20.0)	11.0 (4.0–18.0)	11.0 (5.0–19.0)
Missing	13 (9.1)	15 (4.5)	5 (2.2)	33 (4.7)
MFIS psychosocial subscale score, median (IQR)	3.0 (2.0–5.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (1.0–4.0)
Missing	3 (2.1)	7 (2.1)	5 (2.2)	15 (2.1)
MFIS physical subscale score, median (IQR)	17.0 (8.5–24.0)	13.0 (4.5–19.0)	12.0 (4.0–20.0)	13.0 (5.0–20.0)
Missing	8 (5.6%)	16 (4.8)	5 (2.2)	29 (4.1)
Comorbidity, N (%)				

Continued

Table 1 Continued

	Low n=143	Moderate n=335	High n=226	Overall N=704
No	48 (33.6)	144 (43.0)	93 (41.2)	285 (40.5)
Yes	94 (65.7)	191 (57.0)	133 (58.8)	418 (59.4)
Missing	1 (0.7)	0 (0)	0 (0)	1 (0.1)
Current CT use, N (%)				
No	88 (61.5)	130 (38.8)	71 (31.4)	289 (41.1)
Yes	55 (38.5)	205 (61.2)	154 (68.1)	414 (58.8)
Missing	0 (0)	0 (0)	1 (0.4)	1 (0.1)
Current CT use, sens.*, N (%)				
No	76 (53.1)	110 (32.8)	66 (29.2)	252 (35.8)
Yes	66 (46.2)	224 (66.9)	160 (70.8)	450 (63.9)
Missing	1 (0.7)	1 (0.3)	0 (0)	2 (0.3)
Past CT use, N (%)				
No	78 (54.5)	149 (44.5)	96 (42.5)	323 (45.9)
Yes	64 (44.8)	185 (55.2)	130 (57.5)	379 (53.8)
Missing	1 (0.7)	1 (0.3)	0 (0)	2 (0.3)

*Variable created for sensitivity analysis using the items from supplementary CT questionnaire.
CIS, clinically isolated syndrome; CT, complementary therapy; DMT, disease-modifying therapy; MFIS, Modified Fatigue Impact Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

therapies—cluster analysis of aggregated effectiveness expectations offers a useful framework for identifying clinically and demographically meaningful subgroups of pwMS. Importantly, identified expectation clusters were independently associated with current CT use: individuals in the moderate and high expectation clusters were significantly more likely to be current CT users compared with those in the low expectation cluster.

In MS care, preferences for holistic healthcare and dissatisfaction with conventional treatments are often cited as key drivers of CT use.¹⁰ However, the underlying motivation may stem from patients' perceived or expected benefits of CTs,⁸ despite limited and often inconclusive scientific evidence supporting CT's effectiveness in MS.²⁷ Our findings highlight a striking divergence between patient expectations and available evidence, which can manifest in opposing ways. First, participants in the low expectation cluster demonstrated exceptionally low expectations for mind-body therapies in alleviating psychological symptoms, even though recent robust evidence shows their benefits for psychological well-being and quality of life in pwMS.^{28–29} Second, participants in the high expectation cluster maintained high expectations of the effectiveness of natural product-based therapies (such as homeopathy and ginkgo biloba) for psychological symptoms, despite the lack of robust evidence supporting their use for anxiety or mood disorders in MS.³⁰ Even cannabis-based therapies, while well-established for reducing spasticity and pain,^{27–31–32} lack strong evidence for reducing anxiety in pwMS.³⁰ This

consistent misalignment suggests that patient expectations of CT effectiveness are not primarily shaped by scientific evidence. Instead, as indicated by research from both general populations and studies of other chronic diseases, these expectations develop through a complex interplay of personal beliefs, illness perceptions, self-efficacy and healthcare professional communication.^{33–36}

Our study demonstrates that current CT use is significantly associated with expectations of CT effectiveness among pwMS, independently of past CT use, DMT use or disease severity. While causal conclusions cannot be drawn given the study's cross-sectional design, the observed associations point to the potential role of expectation profiles in shaping CT use among pwMS and the value of addressing these in clinical practice. The lowest expectations and CT use rates were most common among older individuals, particularly males, with the highest disease burden, characterised by progressive disease, gait disability and physical fatigue. Notably, this group also reported minimal past CT use, suggesting their low expectations likely developed through factors beyond personal experiences with CTs. In contrast, those with the highest expectations typically had milder disease and demonstrated greater CT adoption. This dichotomy suggests a bidirectional challenge: individuals with severe MS may avoid potentially beneficial therapies due to misconceptions about effectiveness in progressive disease, while those with milder disease may pursue multiple CTs simultaneously, including those with limited evidence support. Healthcare providers should therefore proactively

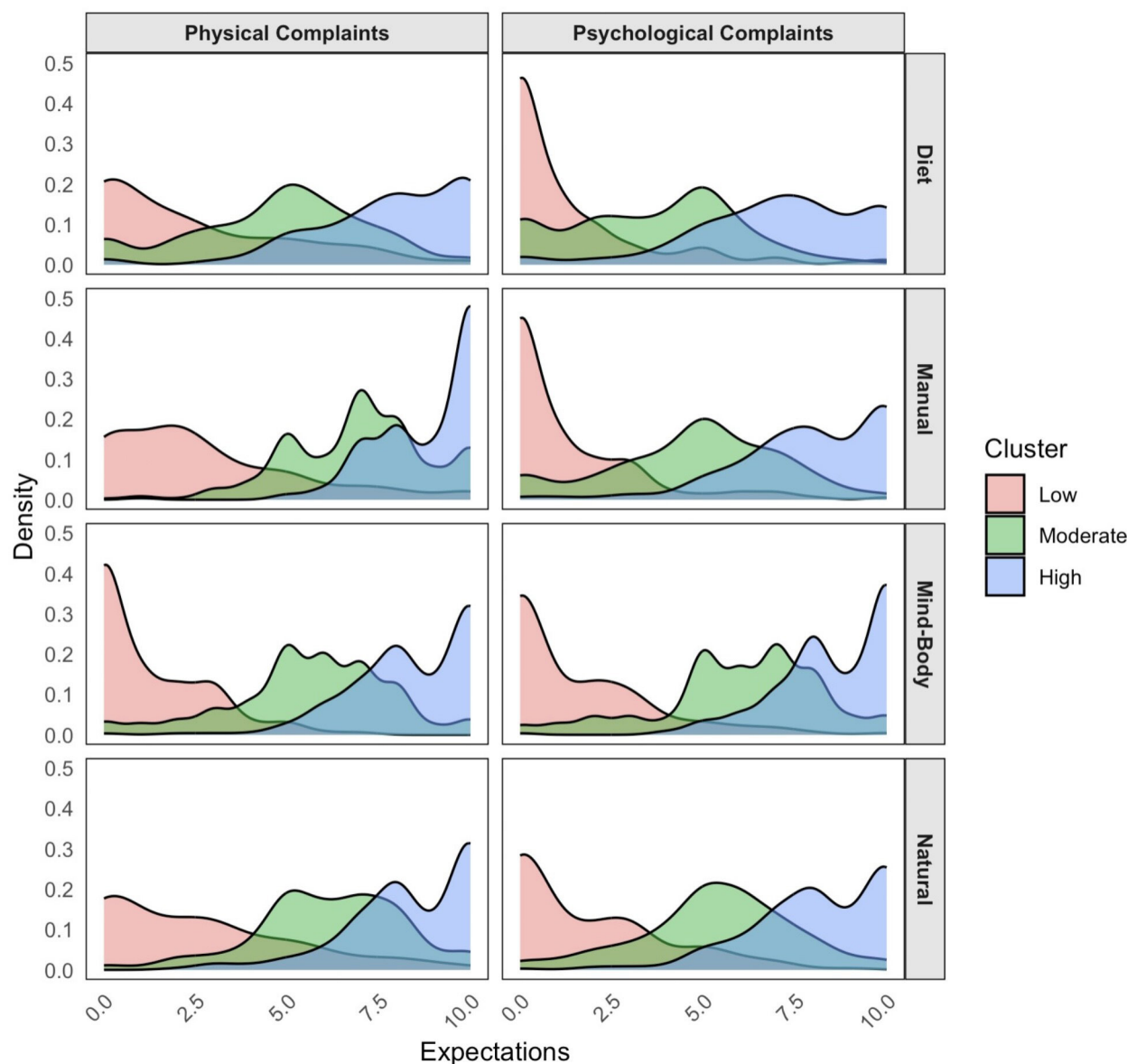


Figure 2 Density distributions of the three identified clusters (low, moderate and high expectations) across four CT categories—diet, manual, mind–body and natural therapies—and two dimensions: expectations for alleviating physical problems (left column) and psychological problems (right column) in the complete case analysis.

manage patient expectations through targeted education that addresses both unwarranted pessimism and overoptimism regarding CTs. Such an approach would enable pwMS to make evidence-informed choices about CT use aligned with their specific needs.³⁶

Strengths and limitations

To our knowledge, this is the first study to apply clustering techniques to investigate expectations of CTs in MS. Clustering enabled a data-driven classification of participants based on their multidimensional expectations regarding the CT effectiveness, capturing the heterogeneity of individual belief patterns without relying on arbitrary cut-offs or single-item analyses. However, several limitations should be noted. First, CT definitions vary widely, and debates persist over which interventions qualify as complementary versus conventional. Our inclusion of

diets may not align with narrower definitions, limiting comparability with studies using different classifications. Second, the analysis was cross-sectional and exploratory. As such, the findings cannot establish causal relationships between expectations and CT use, and the identified clusters should be interpreted as descriptive patterns rather than definitive subgroups. Third, although response rates were comparable to other SMSR follow-ups and missing data were imputed, the analytical sample represented only a subset of the SMSR cohort. Non-responders were slightly younger with shorter disease duration, whereas excluded responders were older, had more severe disease and reported lower CT use. Consequently, individuals with lower CT use and potentially different expectations may be under-represented,¹⁷ which may limit generalisability of the findings. Fourth, the supplementary

questionnaire did not assess which health professionals delivered CTs. In Switzerland, CTs can be provided by physicians, nurses or other practitioners, and expectations may differ by provider type. Finally, CT use was assessed using predefined, non-exhaustive options and self-report, which may limit validity and reliability given varying CT definitions and participants' individual interpretations. To mitigate this, we employed an additional CT use measure in sensitivity analysis; however, some measurement variability may have persisted as CT groups in supplementary questionnaire were broad and heterogeneous, with different modalities grouped together for pragmatic reasons. Results should be interpreted cautiously for CTs not explicitly mentioned in our measures. Future studies may benefit from more granular therapy categorisation, including distinctions by regulatory status, evidence base, symptom-specific applications or individual therapeutic modalities.

CONCLUSIONS

Our study identified distinct clusters of pwMS based on their expectations regarding CT effectiveness. These expectation profiles were associated with current CT use, independent of past CT use, DMT use or disease severity. We also found a mismatch between patient expectations and the available evidence on CT effectiveness. Our findings highlight the role of expectations in shaping treatment choices and underscore the need to address them in order to promote informed, evidence-based decision-making about CTs.

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Acknowledgements The authors thank all participants who contributed to the SMSR.

Collaborators On behalf of Swiss Multiple Sclerosis Registry: Mina Stanikić, Nina Steinemann, Jesús López-Alcalde, Claudia Canella, Jürgen Barth, Andrew Chan, Patrick Roth, Pasquale Calabrese, Chiara Zecca, Claudio Gobbi, Zina-Mary Manyali,

Claudia Baum, Sabin Ammann, Susanne Kägi, Christian P Kamm, Milo A Puhan, Claudia M Witt and Viktor von Wyl.

Contributors On behalf of Swiss Multiple Sclerosis Registry: MS contributed to conceptualisation, methodology, formal analysis, visualisation and drafting of the original manuscript, and contributed to reviewing and editing the manuscript. NS, JLA, CC and JB contributed to conceptualisation and methodology and to reviewing and editing the manuscript. AC, PR, PC, CZ, CG, ZMM, SA, SK, CPK, CB and MAP contributed to conceptualisation and to reviewing and editing the manuscript. CMW contributed to conceptualisation, methodology, funding acquisition and reviewing and editing the manuscript. VvW contributed to conceptualisation, methodology, supervision and reviewing and editing the manuscript. All authors read and approved the final manuscript. VvW is the guarantor.

Funding This study is funded by 'Schweizerische Multiple Sklerose Gesellschaft'.

Competing interests MS, NS, JLA, CC, ZMM, CB, SA, SK, MAP, CMW and VvW declare no competing interests. AC has received speakers'/board honouraria from Actelion (Janssen/J&J), Alexion, Almirall, Bayer, Biogen, Celgene (BMS), Genzyme, Merck KGaA (Darmstadt, Germany), Novartis, Roche and Teva all for hospital research funds. He received research support from Biogen, CSL Behring, Genzyme and UCB, the European Union and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience and as topic editor for the Journal of International Medical Research. CPK has received honouraria for lectures as well as research support from Biogen, Novartis, Almirall, Teva, Merck, Sanofi Genzyme, Roche, Janssen, Eli Lilly, Celgene and the Swiss MS Society. Ente Ospedaliero Cantonale (employer) received compensation for Chiara Zecca's speaking activities, consulting fees or grants from AbbVie, Alexion, Almirall, Biogen, Bristol Meyer Squibb, Eisai, Lilly, Lundbeck, Merck, Merz, Novartis, Organon, Pfizer, Sandoz, Sanofi, Teva Pharma, Roche. CZ is the recipient of a grant for senior researchers provided by AFRI (Area Formazione accademica, Ricerca e Innovazione), EOC. Ente Ospedaliero Cantonale (employer) received compensation for Claudio Gobbi's speaking activities, consulting fees or grants from AbbVie, Alexion, Almirall, Biogen, Bristol Meyer Squibb, Eisai, Lilly, Lundbeck, Merck, Merz, Novartis, Organon, Pfizer, Sandoz, Sanofi, Teva Pharma, Roche. Pasquale Calabrese has received honouraria for speaking at scientific meetings, serving at scientific advisory boards and consulting activities from AbbVie, Actelion, Almirall, Bayer-Schering, Biogen, Eisai, Lundbeck, Merck Serono, Novartis, Sanofi-Aventis and Teva. He also receives research grants from the Swiss Multiple Sclerosis Society (SMSG), and the Swiss National Research Foundation. PR has received honouraria for lectures, consulting or advisory board participation from Alexion, Bristol-Myers Squibb, Boehringer Ingelheim, Debiopharm, Galapagos, Laminar, Midatech Pharma, Novocure, QED and Roche, travel support from Sanofi and research support from Merck Sharp and Dohme and Novocure. JB received honouraria for workshops on digital health and academic writing.

Patient consent for publication Not applicable.

Ethics approval SMSR was approved by the Ethics Committee of the Canton of Zurich (PB-2016-00894; BASEC-NR 2019-01027). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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REFERENCES

- 1 Englund S, Frisell T, Qu Y, *et al.* Trajectories of self-reported fatigue following initiation of multiple sclerosis disease-modifying therapy. *J Neurol Neurosurg Psychiatry* 2024;95:1012–20.
- 2 Rommer PS, Eichstädt K, Ellenberger D, *et al.* Symptomatology and symptomatic treatment in multiple sclerosis: Results from a nationwide MS registry. *Mult Scler* 2019;25:1641–52.
- 3 Gotta M, Mayer CA, Huebner J. Use of complementary and alternative medicine in patients with multiple sclerosis in Germany. *Complement Ther Med* 2018;36:113–7.
- 4 Kim S, Chang L, Weinstock-Guttman B, *et al.* Complementary and Alternative Medicine Usage by Multiple Sclerosis Patients: Results from a Prospective Clinical Study. *J Altern Complement Med* 2018;24:596–602.
- 5 Leong EM, Semple SJ, Angley M, *et al.* Complementary and alternative medicines and dietary interventions in multiple sclerosis: what is being used in South Australia and why? *Complement Ther Med* 2009;17:216–23.
- 6 Carrillo-Mora P, Rodríguez-Barragán MA, Quinzanos-Fresnedo J, *et al.* Alternative and complementary medicine in neurological disorders and neurological disability patients: Prevalence, factors, opinions and reasons. *Complement Ther Med* 2023;72:102920.
- 7 Schwarz S, Knorr C, Geiger H, *et al.* Complementary and alternative medicine for multiple sclerosis. *Mult Scler* 2008;14:1113–9.
- 8 Tangkiatkumjai M, Boardman H, Walker D-M. Potential factors that influence usage of complementary and alternative medicine worldwide: a systematic review. *BMC Complement Med Ther* 2020;20:363.
- 9 Shinto L, Yadav V, Morris C, *et al.* Demographic and health-related factors associated with complementary and alternative medicine (CAM) use in multiple sclerosis. *Mult Scler* 2006;12:94–100.
- 10 Nayak S, Matheis RJ, Schoenberger NE, *et al.* Use of unconventional therapies by individuals with multiple sclerosis. *Clin Rehabil* 2003;17:181–91.
- 11 Rommer PS, König N, Sühnel A, *et al.* Coping behavior in multiple sclerosis-complementary and alternative medicine: A cross-sectional study. *CNS Neurosci Ther* 2018;24:784–9.
- 12 Hussain-Gambles M, Tovey P. The Experience of Complementary Alternative Medicine Use among People with Multiple Sclerosis. *Complement Health Pract Rev* 2004;9:21–30.
- 13 Kalauokalani D, Cherkin DC, Sherman KJ, *et al.* Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. *Spine (Phila Pa 1976)* 2001;26:1418–24.
- 14 Wilhelm M, Hermann C, Rief W, *et al.* Working with patients' treatment expectations - what we can learn from homeopathy. *Front Psychol* 2024;15:1398865.
- 15 Steinemann N, Kuhle J, Calabrese P, *et al.* The Swiss Multiple Sclerosis Registry (SMSR): study protocol of a participatory, nationwide registry to promote epidemiological and patient-centered MS research. *BMC Neurol* 2018;18:111:111:.
- 16 Puhan MA, Steinemann N, Kamm CP, *et al.* A digitally facilitated citizen-science driven approach accelerates participant recruitment and increases study population diversity. *Swiss Med Wkly* 2018;148:w14623.
- 17 Lopez-Alcalde J, Steinemann N, Moll H, *et al.* Characteristics and expectations of people with multiple sclerosis using complementary therapies: A cross-sectional survey from the swiss multiple sclerosis registry. *Mult Scler Relat Disord* 2025;96:106349.
- 18 Kaufmann M, Salmen A, Barin L, *et al.* Development and validation of the self-reported disability status scale (SRDSS) to estimate EDSS-categories. *Mult Scler Relat Disord* 2020;42:102148.
- 19 Fisk JD, Ritvo PG, Ross L, *et al.* Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clin Infect Dis* 1994;18 Suppl 1:S79–83.
- 20 Vogel MA, Wong AKC. PFS Clustering Method. *IEEE Trans Pattern Anal Mach Intell* 1979;1:237–45.
- 21 Liao M, Li Y, Kianifard F, *et al.* Cluster analysis and its application to healthcare claims data: a study of end-stage renal disease patients who initiated hemodialysis. *BMC Nephrol* 2016;17:25.
- 22 Basagaña X, Barrera-Gómez J, Benet M, *et al.* A framework for multiple imputation in cluster analysis. *Am J Epidemiol* 2013;177:718–25.
- 23 Breaban M, Luchian H. A unifying criterion for unsupervised clustering and feature selection. *Pattern Recognit DAGM* 2011;44:854–65.
- 24 McNutt L-A, Wu C, Xue X, *et al.* Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003;157:940–3.
- 25 Skovgaard L, Nicolajsen PH, Pedersen E, *et al.* Differences between users and non-users of complementary and alternative medicine among people with multiple sclerosis in Denmark: a comparison of descriptive characteristics. *Scand J Public Health* 2013;41:492–9.
- 26 R Core Team. R: a language and environment for statistical computing. 2013. Available: <https://www.R-project.org/>
- 27 Claflin SB, van der Mei IAF, Taylor BV. Complementary and alternative treatments of multiple sclerosis: a review of the evidence from 2001 to 2016. *J Neurol Neurosurg Psychiatry* 2018;89:34–41.
- 28 Carletto S, Cavallera C, Sadowski I, *et al.* Mindfulness-Based Interventions for the Improvement of Well-Being in People With Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Psychosom Med* 2020;82:600–13.
- 29 Nauta IM, van Dam M, Bertens D, *et al.* Improved quality of life and psychological symptoms following mindfulness and cognitive rehabilitation in multiple sclerosis and their mediating role for cognition: a randomized controlled trial. *J Neurol* 2024;271:4361–72.
- 30 Yadav V, Bever C, Bowen J, *et al.* Summary of evidence-based guideline: complementary and alternative medicine in multiple sclerosis: report of the guideline development subcommittee of the American Academy of Neurology. *Neurology (Ecricon)* 2014;82:1083–92.
- 31 Novotna A, Mares J, Ratcliffe S, *et al.* A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols® (Sativex), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. *Eur J Neurol* 2011;18:1122–31.
- 32 Sacco R, Riccitelli GC, Disanto G, *et al.* Effectiveness, Safety and Patients' Satisfaction of Nabiximols (Sativex®) on Multiple Sclerosis Spasticity and Related Symptoms in a Swiss Multicenter Study. *J Clin Med* 2024;13:2907.
- 33 Wilski M, Kocur P, Górny M, *et al.* Perception of Multiple Sclerosis Impact and Treatment Efficacy Beliefs: Mediating Effect of Patient's Illness and Self-Appraisals. *J Pain Symptom Manage* 2019;58:437–44.
- 34 Jeswani M, Furnham A. Are modern health worries, environmental concerns, or paranormal beliefs associated with perceptions of the effectiveness of complementary and alternative medicine? *Br J Health Psychol* 2010;15:599–609.
- 35 Mountfield R, Andrews JM, Mikocka-Walus A, *et al.* Doctor communication quality and Friends' attitudes influence complementary medicine use in inflammatory bowel disease. *World J Gastroenterol* 2015;21:3663–70.
- 36 Balneaves LG, Watling CZ, Hayward EN, *et al.* Addressing Complementary and Alternative Medicine Use Among Individuals With Cancer: An Integrative Review and Clinical Practice Guideline. *JNCI* 2022;114:25–37.