A Randomized Pilot Study of Naturopathic Medicine in Multiple Sclerosis

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ABSTRACT

Background: Complementary and alternative medicine (CAM) use is high in people with multiple sclerosis (MS), yet there are limited reports on safety and effectiveness of CAM in MS. Naturopathic medicine encompasses a broad range of CAM modalities and may improve quality of life in patients with MS.

Objective: To assess quality of life in MS subjects who received interventions designed to “model” the “whole practice” of naturopathy.

Design: A pilot, randomized, controlled study with a 6-month intervention period.

Participants: Participants who met criteria for clinically definite MS.

Interventions: The 3 intervention arms were usual care, naturopathic medicine plus usual care, and MS education plus usual care.

Outcome measures: The primary outcome measure was quality of life (36-item short form health survey [SF-36]). Secondary outcome measures included fatigue (Modified Fatigue Impact Scale); depression (Beck Depression Inventory); cognition battery (Stroop test and Paced Auditory Serial Addition Test 3), and neurologic impairment (Expanded Disability Status Scale [EDSS] and Multiple Sclerosis Functional Composite). Adverse event reporting and laboratory measures were used to assess safety.

Results: Forty-five (45) participants (15 per group) were randomized and all completed the 6-month intervention. There were no significant differences between groups on any outcome measure. There was a trend in favoring the naturopathic group in the General Health subscale of the SF-36 ($p = 0.11$), Timed Walk ($p = 0.11$), and neurologic impairment (EDSS) ($p = 0.07$). There was a trend favoring the Education group in the Stroop attention test ($p = 0.07$). There was no difference between groups in adverse events or laboratory changes.

Conclusions: Naturopathic medicine combined with usual care for MS showed a trend in improvement in the General Health subscale of the SF-36, Timed Walk, and neurologic impairment. Evaluation of naturopathic medicine, as a multimodality regimen, warrants further investigation.

INTRODUCTION

Multiple sclerosis (MS) is the most common disabling neurologic disease of young and middle-aged adults in North America and Europe and affects over 350,000 Americans.¹ It is an immune-mediated disease in which T

cells, macrophages, and soluble mediators of inflammation cause multifocal demyelination and axonal injury in the central nervous system (CNS).^{2,3} While MS is rarely fatal, it is often disabling, with about one third of patients losing the ability to walk 15–20 years after onset. MS symptoms vary, depending on the location and severity of lesions within the

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CNS. Common symptoms include generalized fatigue, partial or complete paralysis of the legs and arms, spasticity, imbalance, urinary urgency and incontinence, constipation, sexual dysfunction, tremor, loss of vision, double vision, cognitive impairment, and depression.

Conventional treatments for MS are divided into disease-modifying therapies, which seek to alter the course or progression of the illness, and therapies designed to control specific symptoms (e.g., modafinil for fatigue). Although the availability of these therapies has improved the disease course in MS, there are still a significant number of MS patients who do not benefit from these therapies. Some patients do not respond to these treatments, many experience significant side-effects, and at an average cost of \$25,000 per year, cost of therapy may be prohibitive.⁴ Identifying therapies that have the potential to alter the disease course with a low side-effect profile are needed.

Complementary and alternative medicine (CAM) use is high among people with MS,^{5,6} and MS patients who use CAM generally report that these therapies are beneficial, improve symptoms, and improve quality of life with few side-effects.^{5,7–10} Common CAM therapies utilized include massage, specific diets, and nutritional supplements.^{5,7–10} The majority of MS patients use CAM along with their conventional MS medications.^{5,10} Although CAM use is high in MS, there are few studies assessing the safety and effectiveness of these therapies, and none on combination treatment delivered by qualified CAM practitioners. There are also limited studies evaluating the effects of CAM therapies in conjunction with conventional MS medications.

In the United States, naturopathic medicine is a primary health care profession that functions to promote health, and to prevent, diagnose, and treat disease. The intent of a naturopathic doctor is to stimulate the self-healing capacities of the individual by using therapeutic modalities including clinical nutrition/diet counseling, herbs, nutritional supplements, homeopathy, physical medicine (physiotherapy, hydrotherapy, manipulation), and psychologic counseling. Naturopathic medicine is practiced as either a complement or an alternative to conventional medicine. Treatment is individualized for the particular patient's condition and capacities rather than for just a disease entity. A combination of treatments is frequently applied and is adjusted over time as a patient's condition changes.¹¹

Naturopathic medicine shares key characteristics with other whole systems of medicine such as Traditional Chinese Medicine, Ayurvedic medicine, homeopathy, and other traditional systems that include a holistic approach to diagnosis and treatment. The inherent complexity of these systems makes them difficult to evaluate scientifically. Because the majority of patients with MS use CAM as complementary rather than an alternative approach^{5,12} and naturopathic physicians use a multimodality, individualized approach to treating MS,¹³ the purpose of this study was to evaluate quality of life in MS participants receiving interventions that

“modeled” whole-practice naturopathic care along with conventional care. We hypothesized that MS participants receiving naturopathic treatments plus conventional care would have improved quality of life compared to those receiving MS education plus conventional care or conventional care alone.

METHODS

Study design

A national survey and a Delphi panel were used to develop a “best” naturopathic treatment model. The survey asked naturopathic practitioners about their patients' demographics, recommended therapies, and their own perceptions of effectiveness.¹³ The survey data indicated that naturopathic physicians believed that their treatments were most effective during an early disease phase (minimal neurologic impairment) and very effective for improving quality of life. The three most frequently recommended therapy types included diet, essential fatty acids, and vitamins/minerals.¹³

The Delphi panel, consisting of 4 naturopaths from Portland, Oregon and 1 from Seattle, Washington, were considered experts in MS by their professional community. The panel used results from the practitioner survey, their clinical experience, and scientific evidence to design the naturopathic treatment model. Along with the survey results, the panel members were given written instructions on considerations for choosing a core treatment that they would implement for all patients with MS. Considerations included the following: frequency of treatment use (from clinical experience and/or survey results), experimental evidence for efficacy of treatment (from current literature), and empirical evidence of treatment effectiveness (from clinical experience and/or survey results). These were only suggested considerations for panel members; members were free to pick a core regimen based on other considerations. Each panel member received the survey results and instructions 1 month before the panel convened. The Delphi panel meeting took place at Oregon Health & Science University (OHSU), Portland, OR for 8 hours. Consensus decision making was used to determine the core regimen therapies. When consensus could not be reached on a specific therapy, majority vote determined its inclusion.

The study designed was a pilot 3-arm, parallel-group, randomized clinical trial. After baseline assessments, participants were randomized to 1 of 3 arms: (1) naturopathic treatments plus usual care; (2) usual care alone; or (3) MS-focused educational visits with a nurse plus usual care (Table 1). The intervention period was 6 months. The primary outcome measure was quality of life (36-item short form health survey [SF-36]). Secondary measures included fatigue, depression, cognitive impairment, and neurologic impairment. Although it was not possible to blind partici-

TABLE 1. DESCRIPTION OF STUDY GROUPS

<i>Naturopathic intervention</i>	<i>Educational sessions^a</i>	<i>Usual care</i>
8 Visits with naturopath	8 Visits with nurse trained in MS care	Conventional/usual care for MS
I. Supplements Multivitamin and mineral without iron Buffered ascorbic acid, 1000 mg/day Vitamin E, 400 IU/day Fish oil, 2000 mg/day α -lipoic acid, 200 mg/day	Education on the following: Fatigue Mood Cognitive problems Bowel and bladder problems Exercise	
II. Vitamin B ₁₂ , intramuscular, 1000 μ g/1 $\times$ per wk	Stress	
III. Diet intervention	Nutrition	
IV. Counseling during naturopathic visit	Vitamins, minerals, and herbs	

^aAt each visit, the participants received an educational pamphlet published by the National MS Society containing information about multiple sclerosis (MS).

pants to treatment, they were instructed not to disclose their treatment intervention to the neurologists and research assistants performing end-of-study assessments. Blinding was evaluated by having study assessors fill out a short questionnaire at the end of the study. Safety was measured by comprehensive metabolic panel, complete blood count with differential, and adverse event reports. Study measures were collected at baseline (prior to randomization) and at 6 months.

Naturopathic intervention. All participants randomized to the naturopathic treatment intervention received their usual MS care plus 8 visits with the naturopath following their baseline assessments. The naturopathic intervention included daily supplementation of the following: multivitamin/mineral without iron, vitamin C, vitamin E, fish oil, and α -lipoic acid (Pure Encapsulations, Sudbury, MA) and intramuscular vitamin B₁₂ once a week (Apothecure, Dallas, TX) (Table 1). The intervention also included 4 diet levels (Table 2). Participants filled out a 4-day Diet Recall before the second “naturopathic” visit. This diet recall was used by

the naturopath to assess diet and choose 1 of the 4 diet levels for the participant to follow (Table 2). The participant was instructed to follow the chosen diet level guidelines for 6 months and was counseled by the naturopath at each of the subsequent naturopathic study visits. A 4-day Diet Recall was completed prior to each naturopathic study visit so that both the naturopath and participant could track diet compliance and identify areas where diet could be improved. These diet records were filled out in addition to the baseline diet record (prior to randomization) and the 6-month diet record (end of study).

Education sessions. This group was implemented as a “time and attention” control, the number of visits and time spent with the nurse matched the naturopathic visits. Participants randomized to this group received their usual care for MS plus 8 visits with a nurse that specialized in MS care. At each visit, the participant received an educational pamphlet published by the National MS Society containing information about MS (Table 1). The nurse instructed each participant that the intent of the session was to focus on the

TABLE 2. DESCRIPTION OF DIET INTERVENTION FOR THE NATUROPATHIC GROUP

<i>Level I. Simple intervention</i>	<i>Level II. Moderately simple intervention</i>	<i>Level III. Moderate intervention</i>	<i>Level IV. Advanced intervention</i>
Limit <i>trans</i> fatty acids	Level I intervention plus the following:	Level II intervention plus the following:	Hypoallergenic diet (Brennamen’s food elimination and challenge)
Decrease intake of artificial sweeteners	Reduce intake of red meat to two 4–6-oz servings/week	No refined sugar	
Decrease intake of coffee and alcohol	Increase intake of fresh fruits and vegetables to ≥ 6 1/2-cup servings/day	No fried foods	
Decrease cigarette use Increase intake of water to 6–8 cups/day		No processed/packaged foods No coffee or alcohol	

information contained within the pamphlets. If participants had questions about other aspects of their care, such as advice on medications, specific interventions for MS-related symptoms, or alternative therapies, the nurse instructed the subjects to contact their physicians for answers to these types of questions. The "Fatigue," "Mood," "Bowel and Bladder Problems," and "Stress" pamphlets gave general recommendations to help cope with these MS-specific symptoms. The "Exercise" pamphlet gave general recommendations of exercises that were not strenuous or overheating. The "Nutrition" pamphlet included general nutritional guidelines (e.g., recommending a well-balanced diet, 5 servings of fruits and vegetable a day, lower saturated fat by trimming fat off meat). There was very little overlap with the naturopathic diet levels II, III, and no overlap with diet level IV. The "Vitamins, Minerals, and Herbs" pamphlet recommended Recommended Daily Allowance values for vitamins A, C, and E, and cautioned against the use of most herbs except for the use of cranberry for urinary tract infections. There was no overlap with the information recommended in this pamphlet with the naturopathic intervention.

Usual care

After randomization the usual care only group continued their standard medical care for 6 months.

Participants

This study was approved by the OHSU Institutional Review Board. All participants gave informed consent prior to entering the study. Participants were recruited from the general public, MS Society Oregon Chapter Newsletter, and the MS Center of Oregon at OHSU. Inclusion criteria were definite MS as defined by Poser criteria¹⁴; relapsing–remitting course of MS; and Expanded Disability Status Score (EDSS) ≤ 6.0 indicating the ability to ambulate 100 m (mild–moderate neurologic impairment).¹⁵ Participants were excluded if they had corticosteroids or an MS relapse within 30 days of enrollment; serious medical problems (e.g., cancer, uncontrolled diabetes mellitus, congestive heart failure, severe psychiatric disorder); pregnancy; or recent visits to a CAM practitioner. Participants in all arms were allowed to continue their conventional treatment for MS, including disease-modifying therapies and prescription symptomatic therapy.

MEASURES

Quality of life

Quality of life was measured by the Multiple Sclerosis Quality of Life Inventory (MSQLI), which is a modular MS-specific quality-of-life instrument consisting of the SF-36 and supplemented by 9 symptom-specific measures (fatigue, pain, bladder function, bowel function, emotional status, perceived cognitive function, visual function, sexual satis-

faction, and social relationships). The reliability and construct validity of this measure has been evaluated by a field test of MS subjects with a broad range of impairment (EDSS 0–8.5), and its content has been validated by MS specialists (neurologists and allied health professionals), Health Related Quality of Life experts, patients, and caregivers.¹⁶

Neurologic impairment

Neurologic impairment was measured by the EDSS and the Multiple Sclerosis Functional Composite (MSFC). The EDSS score was determined by a neurologist at the MS Center of Oregon. EDSS is a measure of impairment that is scaled between 0 (normal neurologic examination) to 10.0 (dead). Scores in the 0–4.0 range indicate mild impairment with the ability to walk at least 500 m without aid or rest; scores in the 4–6.0 range, indicate increasing limitations in the ability to walk.¹⁵

The MSFC includes a timed 25-foot walk, upper extremity function (9-hole peg test), and cognitive performance (Paced Auditory Serial Addition Test [PASAT]).¹⁷ The MSFC correlates moderately with the EDSS and is more sensitive to detecting change in disability than the EDSS.^{17,18}

Cognitive impairment

Cognitive impairment was measured by the PASAT 3 and the Stroop. The PASAT 3 assesses attention, rate of complex information processing, and working memory.¹⁹ The participant is required to comprehend auditory input, respond verbally, inhibit encoding of one's own response while attending to the next stimulus in a series, and perform at an externally determined pace. The Stroop is a selective attention task that assesses the ability to attend to a relevant stimulus while inhibiting responses to an irrelevant stimulus.²⁰

Depression

Depression was assessed by the Beck Depression Inventory which is a brief, frequently used self-report measure of depression.²¹

Fatigue

Fatigue was measured by using the Multidimensional Fatigue Inventory and the Modified Fatigue Impact Scale (part of MSQLI). Both are self-report questionnaire designed to assess the impact of fatigue on daily function.^{22,23}

Diet

Diet was assessed by using the 4-day Diet Recall (Nutrition Data System for Research, Nutrition Coordinating Center, University of Minnesota). This is a well-validated measurement of food intake that is often used as the standard of comparison when evaluating the validity of specific food

frequency questionnaires.²⁴ It requires a person to record their diet for an entire day throughout the week on alternate days (e.g., Monday, Wednesday, Friday, and Sunday). Average daily servings of fruits and vegetable and average weekly servings of red meat were used to assess diet compliance for the naturopathic intervention group.

Data analysis

Statistical analysis was performed using SPSS version 14.0 (SPSS Inc., Chicago, IL). Descriptive statistics were used to summarize demographic information. Analysis of variance (ANOVA) and χ^2 analyses were used to determine differences between groups at baseline. ANOVA was used to evaluate differences between groups in change from baseline on all outcome variables. Tukey's highly significant difference was used to determine differences between any two groups.

RESULTS

Participant characteristics

All of the 45 participants enrolled completed the study (Fig. 1). Table 3 summarizes the participants' characteristics at baseline.

Primary outcome measure: Quality of life

There was no significant difference between groups on the physical or mental component summary (PCS or MCS) of the SF-36 (Table 4). A trend in groups differences was found in the General Health Subscale of the SF-36 ($p = 0.11$). This trend favored the naturopathic group. There was no significant difference found between groups on the other SF-36 subscales (data not shown, all p values > 0.20).

Secondary outcome measures: fatigue, depression, disability, cognitive impairment

Table 4 summarizes the results of the mean change from baseline between all groups on all outcome measures. Mean change scores were adjusted so that a positive number reflects an improvement and a negative number reflects a worsening.

The Modified Fatigue Impact Scale (part of MSQLI) showed no difference between groups ($p = 0.68$). The Multidimensional Fatigue Inventory showed no differences between groups on 4 of the 5 subscales (all p values $> .20$) and a trend in improvement favoring the usual care group of the mental fatigue subscale ($p = 0.14$).

FIG. 1. Study design.

TABLE 3. SUBJECT BASELINE CHARACTERISTICS: COMPARISON OF GROUP DIFFERENCE AT BASELINE

Characteristic	Mean (SD) or %	p value
Age	43.5 (9.2)	$p = 0.45$
Female	87%	$p = 0.56$
White	96%	$p = 0.59$
Education (college degree or greater)	47.8%	$p = 0.42$
MS duration in years	10.0 (7.6)	$p = 0.64$
EDSS	2.5 (1.1)	$p = 0.45$
Relapses (2 years prior)	1.2 (1.2)	$p = 0.96$
Disease-modifying therapy	84%	$p = 0.84$

SD, standard deviation; EDSS, Expanded Disability Status Scale.

Disease-modifying therapy included interferon β -1a, interferon β -1b, and glatiramer acetate.

There was no significant difference between groups on the Beck Depression Inventory ($p = 0.76$).

Neurologic impairment was measured by EDSS and MSFC. EDSS showed a trend in improvement for the “naturopathic group” ($p = 0.07$). Although the total MSFC score was not different between groups ($p = 0.24$), the naturopathic group showed a trend in improvement for the Timed Walk portion ($p = 0.11$) of the MSFC.

Cognitive impairment was measured by the PASAT 3 and Stroop. There were no trends observed between groups on the PASAT 3 ($p = 0.34$). There was a trend in improvement for the “education” group on the Stroop ($p = 0.07$).

Safety, compliance, and blinding

Over the 6-month intervention time, there were no serious adverse events reported by any participant. Seven per-

cent of the “usual care” group, 20% of the naturopathic group, and 13% of the education group reported an MS relapse ($p = 0.56$). Sixty-seven percent (67%) of the usual care group, 60% of the naturopathic group, and 40% of the education group reported MS symptoms ($p = 0.31$). Laboratory values for complete blood count with differential and comprehensive metabolic panel remained within normal limits at the end of the study in all subjects and were not different between groups (data not shown).

For the naturopathic group, compliance for all oral supplementation (9 capsules/day) was 93.1% (standard deviation $\pm 5.6\%$). Compliance on intramuscular vitamin B₁₂ was 100%. Thirteen (13) participants were on diet intervention II, 1 participant was on diet intervention III, and 1 participant was on diet intervention IV (Table 2). Diet compliance for the goal of ≥ 6 half-cup servings of fresh fruits

TABLE 4. MEAN CHANGE FROM BASELINE BETWEEN GROUPS ON ALL OUTCOME MEASURES

Measure	Usual care mean (SD)	Naturopathic mean (SD)	Education mean (SD)	p value
Quality of Life (SF-36)				
General Health	−3.1 (18.1)	7.9 (10.6)	4.8 (13.2)	0.11
MCS	−1.2 (9.0)	0.10 (6.5)	0.40 (9.7)	0.85
PCS	−0.30 (6.4)	1.5 (5.9)	1.5 (5.0)	0.64
Fatigue				
MFIS (MSQLI)	−.20 (4.2)	.93 (3.0)	.29 (3.0)	0.68
MFI				
Mental fatigue	3.00 (4.8)	0.53 (2.8)	−0.47 (6.2)	0.14
Depression				
BDI	0.9 (5.28)	1.9 (5.89)	2.3 (5.3)	0.76
Neurologic impairment				
EDSS	−0.33 (0.6)	0.20 (0.4)	−0.07 (0.8)	0.07
MSFC				
Timed Walk	−0.05 (.70)	0.07 (.38)	−0.67 (1.6)	0.11
PASAT-3	0.15 (.31)	0.18 (.44)	0.32 (.38)	0.45
9-hole peg	0.13 (.52)	0.03 (.93)	−0.08 (.51)	0.71
Total score	0.09 (.37)	0.09 (.39)	−0.14 (.53)	0.24
Cognitive impairment				
Stroop	−2.0 (3.8)	−2.7 (5.7)	1.0 (3.8)	0.07

Positive value reflects improvement and negative value reflects worsening.

SD, standard deviation; SF-36, 36-item short form health survey; MCS, mental component summary; PCS, physical component summary; MFIS, Modified Fatigue Impact Scale; MSQLI, Multiple Sclerosis Quality of Life Inventory; MFI, Multidimensional Fatigue Inventory; BDI, Beck Depression Inventory; EDSS, Expanded Disability Status Scale; MSFC, Multiple Sclerosis Functional Composite; PASAT-3, Paced Auditory Serial Addition Test 3.

and vegetables was 27% and for the goal of red meat servings ≤ 2 4–6-ounce servings per week after 6 months was 30%. Blinding remained at 93%, and 1 participant in each arm revealed treatment status.

DISCUSSION

This study is the first to evaluate a model of “whole systems” naturopathic medicine in MS. Participants accepted the randomization to the 3 intervention groups and all completed the 6-month trial. Although there were no statistically significant improvements to naturopathic treatments in any of the outcome measures in this small pilot study, trends favoring this group as observed in General Health, Timed Walk, and EDSS may indicate a generalized trend in clinical benefit. The naturopathic group showed an 8-point improvement in the General Health subscale of the SF-36. It is interesting that the naturopathic group showed a slight improvement in the mental and physical health components (MCS, PCS) of the SF-36 and a slight improvement in EDSS and timed walk over 6 months, while the usual care group showed a slight worsening in both MCS and PCS and had a slight worsening in EDSS and Timed Walk. Lower baseline MCS scores have been reported to be significantly associated with a worsening of EDSS scores over time.²⁵ The naturopathic group was the only group that showed any improvement over time in both EDSS and timed walked, while the usual care group and education group showed a slight worsening over time. Since EDSS is heavily weighted by the ability to walk, we would expect to see these scores showing the same trends in each group. The trend observed in EDSS reflects an improvement in the naturopathic group when compared to the usual care group ($p = 0.06$). The difference in mean change in EDSS between these groups is 0.53 points, about half an EDSS point in 6 months. It is possible that this might translate into a significant clinical difference over a longer time frame. The education group showed a trend in improvement for the Stroop, whereas the other 2 groups had a worsening of this score. The Stroop is a measure of directed attention. It may be that having to read specific material over 6 months in order to have a topic-focused discussion with the nurse was an exercise that improved focus and attention.

There is very little known about the safety of combining multimodality complementary therapies with conventional medications in MS. Eighty-seven percent (87%) (13/15) of the participants in the naturopathic intervention were on MS disease-modifying therapy. Combining diet changes with 5 different oral supplements and intramuscular vitamin B₁₂ injections showed no significant increase in MS-related adverse events nor significant changes in blood chemistry or complete blood count over the 6-month intervention. The preliminary safety findings show that this intervention is safe when used with conventional MS disease-modifying ther-

apy for 6 months. Long-term safety of this intervention still needs to be assessed.

There were several study limitations. First, the study's small sample size was a limitation because it was powered to detect a >7 -point change in quality of life. Except for the General Health subscale, changes in quality of life were small in all groups. Fan et al. observed a trend for a decreased risk of morbidity and hospitalizations in ambulatory outpatients with small increases of 1–5 points in the PCS. This trend became significant if the change in PCS was >10 points.²⁶ The small increases in quality-of-life scores observed in the naturopathic group may reflect a generalized trend in improvement in MS-related health.

This study was not double-blinded and not placebo-controlled. It is a methodological challenge to design studies evaluating whole-systems medicine because blinding every factor of a “system” is not as simple as blinding for a single drug. Assessor blinding was maintained for 93% of patients. We randomized after baseline measures and then assessed for end-of-study blinding of assessors by asking them whether they had knowledge of treatment group. We controlled for time and attention factors by including the MS-education group. This group was required to read MS-related education materials that were then discussed with a nurse who was a MS specialist. Visits with the nurse were matched for frequency and visit-length time to the naturopathic visits. Having these controls allows for more confidence that the trends in improvements observed for the naturopathic group were not solely a placebo or other non-specific effects.

It is recognized that this is a simplified model of naturopathic care with limitations on the breadth of possible treatments and that does not reflect truly individualized and comprehensive naturopathic care. The intervention model evaluated was a standardized regimen of the most “effective” treatments with limited individualization. The model was chosen because it is reproducible and can be retested in future studies. There was consensus from licensed naturopaths (survey data) and the Delphi panel on the treatment intervention to ensure that the treatments evaluated were representative of the “best” of naturopathic MS care for effect, safety, and adherence. For the participants in the naturopathic group, adherence was 100% for weekly intramuscular B₁₂ injections and 93% for oral supplementation and 30% or less for diet. This is an interesting finding and may reflect a general hierarchy of adherence in multimodality interventions. It appears that a once-a-week treatment is easier than daily oral supplementation and that daily oral supplementation is easier than dietary change. The majority of this group (87%) was on MS-disease-modifying medication that often involves self-administration of subcutaneous or intramuscular injections daily to weekly. The 100% compliance on B₁₂ may reflect a perception that an injected medication will have high benefit coupled with a familiarity with this type of administration. Even with poor adherence to di-

etary change, trends in improvement were observed in the naturopathic group. For future studies, strategies to encourage diet compliance should be incorporated in the design.

This study showed that naturopathic treatments plus conventional care over 6 months may have benefit in MS and may be safe to use with MS-disease-modifying therapies. The results from this study warrant further evaluation of naturopathic medicine in MS so that its effectiveness and safety can be more thoroughly assessed.

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