THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE AND NUTRIENT INTAKE AMONG INDIVIDUALS WITH MULTIPLE SCLEROSIS

by

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ABSTRACT

Background: Conventional treatments for multiple sclerosis (MS) are often ineffective and cause side effects. Many individuals with MS use complementary and alternative medicine (CAM); but the safety and efficacy of CAM are not well known.

Aims: The primary aim was to determine the prevalence of use for specific types of CAM among individuals with MS. The secondary aim was to assess nutrient intake for the MS population as a whole as well as for those following specific CAM diets.

Methods: In this descriptive, cross-sectional study, adults with MS were recruited to participate on a volunteer basis. Use of CAM was assessed by phone interview using a standardized survey, and nutrient intake was assessed using the Automated Self-Administered 24-hour Recall system. Frequencies and percentages were used to summarize prevalence of CAM therapies and demographic information, while means and percentiles were used for nutrient intake.

Results: A total of 35 subjects participated; 27 (77.1%) reported use of at least one CAM therapy. Vitamin/mineral supplements (n=24) and nonvitamin, nonmineral, natural products (n=12) were the most frequently reported. Special diets (n=8) included Swank, Paleo, and a combination of dietary modifications. Overall (n=33),

saturated fat and sodium intake were high, and vitamins E, C, D, and A, calcium, and magnesium were frequently below the EAR.

Conclusion: CAM use, especially biologically based therapies, are common within the MS population. The restrictive nature of special diets and high intake of certain supplements is concerning. Larger studies are needed to better understand the nutritional impact of special diets in this population.

Chapter 1

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) with an estimated prevalence of approximately 350,000 individuals in the United States (US).[1,2] The cause of MS is unknown; it is an autoimmune disease in which the myelin sheath that insulates the nerves within the CNS is attacked and damaged. Demyelination inhibits neurological transmission, which can have devastating effects on motor, sensory, and cognitive functioning.[1] Initial signs of MS typically present between ages 20 and 40, and may include numbness, tingling, muscle weakness, imbalance, difficulty walking, impaired vision, and poor coordination.[3] As the disease progresses, patients may experience pain, bowel and bladder problems, fatigue, cognitive impairment, and sexual dysfunction.[1,4] The type and severity of symptoms are unique to each case of MS, as they depend on the magnitude and location of lesions that form. Deterioration of neurological function may be gradual or progressive, and symptoms may manifest continuously or in acute episodes. No two MS patients will have the same experience, a characteristic that makes this idiopathic disease so unpredictable and complex to manage.

The ambiguous nature of MS prompted the Advisory Committee on Clinical Trials of New Agents in MS to standardize definitions for all of the clinical patterns observed.[5] They classified MS into four subtypes, which include primary-progressive

(PPMS), relapsing-remitting (RRMS), secondary-progressive (SPMS), and relapsing-progressive (RPMS).[6] Ten percent of MS cases are PPMS, in which neurological function deteriorates progressively from onset without distinct periods of new disease activity (ie, relapses) or remission. The rate of decline can fluctuate, but any plateau or improvement is merely temporary. Alternatively, RRMS is characterized by clearly defined relapses followed by periods of variable recovery and then stable remission.[3,4,6] Approximately 85% of patients are diagnosed with RRMS, but 50% of these cases develop into SPMS within 10 years, and 90% within 25 years.[5] Those who transition to SPMS begin to experience a steady decline in neurological function, which may or may not include minor relapses, remissions, or plateaus. The fourth and most rare form is RPMS, which accounts for 5% of cases and is characterized by progressive neurological decline from onset, but unlike PPMS, has distinct episodes of relapse without any remission periods.[1,4,6]

The cause of MS remains unknown, but certain risk factors have emerged from epidemiologic studies. White individuals are twice as likely to develop MS compared to their non-white counterparts, and in general, women are twice as likely as men to develop MS.[3] A recent review, which considered global MS incidence, found that the female to male MS ratio increased from an estimated 1.4 in 1955 to 2.3 in 2000.[7] A recent study of US women found that the incidence of MS has increased by approximately 50%.[3,8] This observation has not yet been explained, but a similar trend was found in Cretan women. The higher rate found in Crete was associated with lifestyle changes made after relocating from rural countryside to urban centers at a

young age. Specifically, an increase in alcohol consumption and smoking, the use of oral contraceptives, and switching from raw to pasteurized milk were related to increased MS incidence.[9] While associations do not imply causality, and there are limitations in generalizing the Cretan study to the US population, many epidemiologic studies have revealed patterns of MS incidence and prevalence that suggest its pathogenesis may have an environmental component. Early investigations found that the prevalence of MS followed a distinct geographic pattern, which subsequent studies have supported. Most notably, there exists a positive association between MS prevalence and distance from the equator (ie, latitude).[10-14] That is, as one moves higher in latitude, either north or south, the risk of MS increases. Another geographically based risk factor is the negative correlation between altitude and MS prevalence.[15-17] Both of these geospatial relationships have become a central theory in MS research, leading to the hypothesis that ultraviolet radiation (UR) may have a protective effect against the disease. Given that the synthesis of vitamin D in humans requires exposure to UR, a substantial amount of research has been conducted to better understand the role of vitamin D and MS incidence. The first prospective cohort study to investigate this relationship found that women who took supplemental vitamin D reduced the risk of MS by about 40% (RR 0.59, 95% CI = 0.38-0.91).[18] Unfortunately, the effects of vitamin D supplementation after the onset of MS are less promising.[19] Although the cause of MS remains to be elucidated, the positive associations observed with high latitude and low altitude suggest that its etiology may be related to these patterns.

Developing a cure for MS continues to be a challenge. Officially defined as a disease in the 1860s,[4] it was not until the 1990s that treatments for MS were developed. Several medications, known as disease-modifying agents (DMA), have been approved by the US Food and Drug Administration (FDA) to slow the progression of MS or reduce symptoms.[20] Unfortunately, DMA have only been approved for the relapsing forms of MS, and only certain injections (ie, interferons, glatiramer acetate) are effective if started after a demyelinating event. Another disadvantage of DMA is that they often cause side effects, some of which are extremely serious.[20,21] Side effects may be as mild as flu-like symptoms, nausea, fever, and reactions at injection site, while more serious effects include bradycardia, cardiac toxicity, leukemia, and alopecia.[20,21] Consequently, many patients turn to complementary and alternative medicine (CAM) to supplement or replace conventional medicine.[22-31]

The constant evolution of CAM makes it difficult to define, but the National Center for Complementary and Alternative Medicine (NCCAM) defines it as "a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine."[32] NCCAM acknowledges 36 types of CAM that are classified into five categories, including alternative medical systems (eg, acupuncture, traditional healers), manipulative and body-based therapies (eg, chiropractic care, massage, pilates), mind-body therapies (eg, meditation, yoga), energy healing therapies (eg, reiki), and biologically based therapies (eg, herbals, diets, vitamins). Diet-based therapies are considered CAM because there is no diet

recognized for the treatment of MS; the National MS Society (NMSS) advises that individuals with MS follow the same healthy dietary pattern recommended for the general US population.[33]

The efficacy and safety of CAM therapies remain unclear,[4] and many patients have been found to utilize these unconventional therapies without informing their physician.[34] Taken together, the prevalence of CAM use, and particularly diet-based CAM, warrants further investigation. Previous studies have examined CAM use in the MS population, but they did not elucidate the specific types of therapies used and have methodological limitations related to the thoroughness of CAM data collected. It is possible that certain CAM treatments are not innocuous in MS, whether they are megadoses of vitamins, unknown herbal remedies, or nutritionally inadequate diets. Therefore, it is crucial that clinicians and researchers are aware of the specific CAM therapies used in this population so that they are informed of unconventional health practices that may not be safe.

Chapter 2

REVIEW OF THE LITERATURE

2.1 Complementary and Alternative Medicine and Multiple Sclerosis

2.1.1 Prevalence of CAM Use

The prevalence of CAM use within the MS population varies widely.[22-30,35-37] Studies conducted in North America, Europe, and Australia have found that anywhere from 30% to 100% of individuals with MS subscribe to one or more forms of CAM (Table 1). Several US studies suggest that individuals with MS use CAM therapies more than the general population (38.3%).[32] The wide variation of CAM use from study to study may be related to the fact that each investigation employed different methods to assess CAM use and the studies were conducted in dissimilar populations. Methodological limitations include the use of varying data collection tools, different reference periods of CAM use, and inconsistent definitions of CAM. First, researchers used different surveys to collect data. Because the validity and reliability of these instruments were not addressed, the degree to which they assessed prevalence of CAM therapies in a systematic, reliable manner is unknown. In addition, the response formats varied; while one survey was entirely close-ended,[24] most allowed respondents to write in therapies not otherwise listed,[27,29,30] one included both close-ended and short answer,[38] a few other survey formats were simply not

explained,[25,26,28,35] one structured interview,[31] and semi-structured interviews were another means of data collection.[22,23]

An additional inconsistency among the surveys was the timeframe of CAM use. Although many studies inquired about current and past use,[24-27,30,36] others only considered CAM use within the past 6 months,[28] 1 year,[35] 2 years,[38] currently,[22,23] or ever in the past.[29] Longer reference periods for CAM use may have higher estimates compared to studies that inquire about more recent use; additionally, self-report of CAM therapies may be less accurate. It is important to note that there is no international consensus regarding the definition of CAM, so consequently, many studies only measured the use of certain categories of CAM therapies. For example, Leong and colleagues[26] examined usage patterns of products, supplements, and dietary interventions, but excluded physical and provider-based therapies such as acupuncture and yoga. In contrast, Nayak and colleagues[27] considered all forms of CAM, but excluded from analyses their results on prayer, vitamins, and exercise to make a more conservative estimate, given that some users may not consider these practices to be unconventional treatments. Finally, Schwartz and colleagues[28] only examined use of CAM providers (eg, herbalists) and did not consider use of herbal products (eg, ginkgo biloba).

Taken together, the wide range of CAM use found within the MS population may be attributed to the varying methods and measures utilized throughout the research to date. Marrie and colleagues,[25] who found that only 30% were current CAM users, were the only researchers that administered a close-ended survey. The

lack of write-in responses may have underestimated the prevalence of CAM use among respondents, which the authors acknowledged to be a limitation. That Schwartz and colleagues[28] also found a lower rate of 33% may be attributed to the fact that they only queried about use of provider-based therapies within the past 6 months. In contrast, a recent study by Stoll and colleagues[29] found that 100% of respondents used CAM therapies. However, this finding could be misleading as the survey did not differentiate between current and past use. Although their results may not be inaccurate, they are less meaningful for researchers and clinicians who are interested in the most common unconventional therapies patients are using currently. Finally, whether CAM use is more prevalent among individuals with MS compared to the general population remains unclear because the results are not directly comparable given the differences in methods employed.

2.1.2 Types of CAM Used in MS

Research to date shows that many different types of CAM therapies are used within the MS population, though some therapies and practitioners seem to be more common than others. The most commonly reported therapies among CAM users are listed in Table 1. Massage, chiropractic manipulation, and physical therapy were the most frequently reported manipulative and body-based therapies, while acupuncture was the most common alternative medical system. Overall, biologically based therapies were the most prevalent types of CAM used among respondents, including special diets, vitamin/mineral supplements, herbals, and other natural supplements.

The most commonly used biologic therapies were vitamin and minerals. Vitamin supplements reported included multivitamins,[24,31,38] B vitamins,[24,26,29,38] vitamin B12,[26,31] vitamin D,[29,31] vitamin C,[24,26,27,31] vitamin E,[24,26,31,38] and vitamin A.[38] Specific minerals reported were magnesium, calcium, zinc, selenium, and iron. That many of the reported nutrients (eg, vitamins A, C, E, selenium, zinc) have antioxidant functions is notable, as axonal injury and demyelination have been implicated as a consequence of oxidative stress.[39] Many studies only presented results on the use of vitamins/minerals in general without considering the specific nutrients;[22,27,30] therefore, whether the aforementioned results reflect typical usage patterns of the MS population as a whole is unknown.

Another common biologically based form of CAM is the use of supplements that the NCCAM identifies as "nonvitamin, nonmineral, natural products" (NP),[32] which are typically classified as herbal or natural remedies. Similar to the vitamin/mineral findings, the specificity of NP used by individuals with MS varies throughout the research. Based on the studies that inquired about specific products, essential fatty acids (EFA) were the most frequently reported NP and included evening primrose oil,[24,26,31,38] fish oil, flaxseed oil, alpha lipoic acid, and cod liver oil.[26,31] The less common NP used (ie, those reported by less than 20% of CAM users) included garlic, ginkgo biloba, ginseng,[26,38] valerian, St. John's Wort, grape seed extract, cranberry extract, coenzyme Q10, glucosamine/chondroitin, melatonin, and carnitine. In a more recent study conducted in the US, cranberry extract was among the most common (35.2%) NPs used by individuals with MS.[31] Given that many studies only

examined provider-based therapies or NP in general terms, it is possible that other NP are being used within the MS population unbeknownst to the scientific and medical communities.

Taken together, there is insufficient knowledge regarding the prevalence of specific CAM therapies used within the MS population. Few clinical trials have been undertaken to assess the safety and efficacy of CAM therapies. Considering the potential side effects and/or adverse interactions with MS medications, the use of these unconventional treatments is concerning. For example, administration of the coumarin-containing sweet clover has been shown to cause severe liver dysfunction when given in combination with the DMA interferon beta-1b.[40] Another herb, echinacea, can alter the metabolism of corticosteroids in the liver and thereby increase toxicity of the drug while concomitantly reducing its effectiveness.[41] With respect to vitamin and mineral use, high doses of certain nutrients (eg, vitamin D) can be toxic when taken in large doses on a regular basis. Although a few studies reported specific nutrients taken by respondents, only two[24,25] indicated that they took 'megadoses' of multivitamins, and the term megadose was not well defined. Whether other studies considered megadoses of vitamins and minerals is not known. Future studies should consider not only the specific vitamins and minerals used, but also the typical doses of these supplements.

2.1.3 Demographics of CAM Users

Certain individuals with MS are more likely than others to use CAM. Several studies found that patients with more severe cases of MS, which is typically quantified by the Expanded Disability Status Scale (EDSS), were more likely to use CAM than those with more benign cases.[22,23,25,27,28,30,35] Duration of disease was also a predictor of CAM use in two of these studies, which found that having lived with MS for a longer period of time increased the likelihood that subjects would use CAM to treat symptoms.[27,30] In contrast, one study in South Australia found that less severe cases predicted CAM use,[26] while another found that more recently diagnosed patients were more likely to use CAM.[28] All together the research suggests that that those who have had MS longer or have more severe cases are more likely to use unconventional therapies. These individuals may turn to CAM when conventional treatments are unsuccessful; Nayak and colleagues[27] found that those less satisfied with their physicians and traditional treatments were more likely to be CAM users (OR = 1.22, $p < 0.01$).

Additional predictors of CAM use are related to education and income. Schwartz and colleagues'[28] investigation of unconventional treatments among MS patients in Colorado found that those with a higher education and income were more likely to be CAM users. Similar results were observed in another US study, which found that CAM users were more educated than non-users and tended to have more adequate economic resources, though the latter finding did not reach significance.[30] These findings may be explained by the fact that unconventional treatments are rarely

covered by health insurance in the US, thus wealthier individuals are more likely to be able to pay for them out of pocket. While Nayak and colleagues[27] also found that education was positively associated with CAM use, they did not find any relationship with income.

2.2 Diet and Multiple Sclerosis

2.2.1 Nutrition and MS

There are several hypotheses that suggest nutrition is one environmental factor involved in the pathogenesis or exacerbation of MS. No definite link between nutrition and the etiology of MS has been established, but epidemiological studies have found nutrition-related risk factors. Of particular interest is the relationship between low vitamin D status and MS, as there is a higher prevalence of this disease in northern latitudes.[42] Although data are inconsistent, there are studies that support this hypothesis. The first prospective study to examine vitamin D intake and MS incidence involved women participating in the Nurses' Health Study (NHS) and NHS II, which found that intake of vitamin D from supplements was inversely associated with risk of MS.[18] The relative risk of women who took at least 400 IU/day of supplemental vitamin D compared with women who did not take vitamin D supplements was 0.59 (95% CI = 0.38 to 0.91). In a case-control study, Freedman and colleagues[43] examined the potential association of exposure to sunlight with mortality from MS (cases) and skin cancer (positive controls). For MS mortality, the OR at the

highest exposure level was 0.24 (95% CI = 0.15 to 0.38), whereas the OR for skin cancer mortality was 1.38 (95% CI = 1.12 to 1.69). These results suggest a protective effect of sunlight on MS mortality, thereby supporting the theory that vitamin D has a positive effect on MS.

Related to treatment of MS, there is some evidence that vitamin D may be beneficial, though the findings are inconsistent. In a prospective cohort study of 145 participants with RRMS, Simpson and colleagues[44] found that higher serum levels of 25-hydroxyvitamin D were associated with a reduced hazard of relapse. For each 10 nmol/L increase of 25-hydroxyvitamin D, there was up to a 12% reduction in risk of relapse (HR 0.88, 95% CI = 0.82-0.95, p = 0.001). However, the first clinical trial of methodological rigor to investigate this relationship found no benefit with vitamin D supplementation.[45] Although there may be a potential link, the Institute of Medicine recently came to the conclusion that there is not enough evidence to support the treatment of MS with vitamin D.[46]

Another dietary factor thought to have a deleterious effect on MS is the intake of saturated fatty acids of animal origin. Dr. Roy Swank[47] first suggested this relationship after observing an increased incidence of MS in conjunction with a saturated fat intake upwards of 100 to 150 g/d, in contrast to levels of 10 to 50 g/day in the non-industrialized countries where MS is low. Swank developed a special diet that limited saturated fat intake to 15 g/d, unsaturated fat to 20 to 50 g/d, and that recommended a daily multi-vitamin and mineral supplement plus 1 teaspoon of cod liver oil per day.[48] Individuals with MS followed this diet for 35 years, and the "good

dieters" (ie, those who kept fat below 20 g/d) experienced only slight deterioration and 31% death rate, in contrast to "poor dieters" who suffered more severe disability and had a higher death rate of about 80%. The results appear promising, but the study was not controlled, blinded, or randomized. Swank's rationale for restricting fat intake was the idea that large fat molecules would block small capillaries, leading to relapse.[49] Cod liver oil was advised in order to increase the ratio of omega-3 to omega-6 fatty acids, thereby reducing inflammatory responses and promote remission. Another rationale for the role of omega-3s in MS is that they may reduce the risk of new lesions via reduction in matrix metalloproteinase concentrations, which are thought to assist in migration of inflammatory cells into the CNS.[50] Despite these hypotheses, there remains inconsistent evidence regarding the role of dietary fat in the progression or pathogenesis of MS.

2.2.2 Diet Modification in MS

Many individuals with MS modify their diets as a means to control their disease. However, there is no diet currently recognized by conventional medical practitioners to treat MS. The National MS Society advises that patients should be following the same dietary guidelines that are recommended for the general public.[33] In contrast to conventional medical practitioners, naturopathic doctors often recommend specific diets to their patients, which they believe can be very effective in the earlier stages of MS.[51] Diet appears to be a rather common form of CAM used by this population, but few studies have identified the specific dietary modifications

employed. One US study found that 31.4% of subjects had previously used a "Special Diet," which was considered to be "any dietary practice that is altered from what was considered the normal diet of the person, [including] an exclusion or inclusion of fat, certain carbohydrates, or other nutrients," based on a definition used previously.[41,52]

The reported prevalence of diet therapy varies. In a study carried out in Spain, only 13.9% of the respondents who used an unconventional therapy in the past year reported using diet therapy.[35] Apel and colleagues[22,23] found that only 3% of MS patients from two clinics in Germany utilized diets, but again, no specific diets were noted. Finally, one study carried out in Colorado indicated that nutritionists were a common provider, who were seen by 9% of CAM users within the past six months.[28] Only a handful of studies elucidate the specific diets or dietary modifications utilized by individuals with MS. Nayak and colleagues[27] investigated the prevalence and patterns of CAM use in the US and found that 16% of individuals were currently following the Swank diet (a diet low in total fat/day, especially saturated fat of animal origin[48]) and 10.4% were making general dietary changes. Whether some subjects used more than one dietary therapy simultaneously was not clear. The primary reason for using these dietary changes was to treat overall MS-related symptoms, others reasons were to combat fatigue, loss of appetite, and pain. In a South Australian study that investigated current and past use of CAM products, supplements, and dietary interventions, the most common diet was low-fat (39.8%), followed by sugar-free or low-sugar (23.8%), wheat-free or gluten-free (16.4%), and then the Swank diet (11.1%). Finally, Berkman and colleagues[24] found that the Swank, Candida (low in

sugar, fermented foods, and refined carbohydrates designed to stunt oral yeast overgrowth[53]), McDougall (almost no fat, vegan diet high in starches, vegetables, and fruit[54]), and additive-free diets were followed by some of the CAM users; however, the frequency of use was not quantified, implying that dietary modifications were included in the different CAM modalities that comprised less than 5% of total therapies. Taken together, these studies indicate that dietary modifications are a relatively common form of CAM adopted by the MS population, particularly diets that are low in fat (ie, Swank, McDougall, general low fat). However, the specific dietary approaches taken are not fully elucidated and the nutrient composition associated with each diet has not be studied. Without knowing the specific dietary interventions used by these individuals, clinicians may not be prepared to advise their patients on potential inadequacies of their diet, or provide an informed response to inquiries about a particular diet.

2.2.3 Nutrient Intake of Individuals with MS

Only three investigations are known to have examined the dietary intake of individuals with MS. The studies to date have found mixed results, which may be attributed to the heterogeneous sample populations as well as methodological differences. Timmerman and colleagues[55] assessed the nutrient intake of 67 women with MS in the US and found that subjects had an inadequate intake of dietary fiber, vitamin E, calcium, and zinc. In contrast, saturated fat, protein, vitamin A, vitamin C, folate, and iron were more than adequate, and energy intake was 1863 Kcal ± 562.

Intake of each nutrient was compared to its respective recommended dietary allowance (RDA), and adequacy versus inadequacy for each nutrient were defined as more than 10% lower than the goal or 10% higher than the goal, respectively. The results should be interpreted with caution, however, because as of 1997, the RDA was replaced with the dietary reference intake (DRI) system, which can more accurately assess the prevalence of nutrient inadequacy and risk of excess at the group level. A more appropriate reference value is the Estimated Average Requirement (EAR), which is the DRI reference value for a particular nutrient that is estimated to meet the requirement for half the healthy individuals in a certain life stage and gender group.[56] Although the term "average" is used, the EAR actually represents the estimated median requirement. Therefore, given that dietary data is skewed, the means for each nutrient did not provide a meaningful picture of dietary intake. Also, only descriptive statistics were provided in this study, so the significant differences between intake and recommended intakes could not be determined. Finally, another limitation of analysis was that macronutrient intake was assessed based on weight instead of a percentage within the acceptable macronutrient distribution range (AMDR), which would have been a more appropriate means to assess protein, carbohydrate, and fat.

The two other studies that investigated nutrient intake among the MS population were not conducted in the US, and are therefore may not be generalized to the MS population in the US. One study focused on dietary intake of Dutch subjects with MS ($n = 80$) using 14-day food diaries.[57] Subjects with SPMS had a 20% lower intake of magnesium ($p = 0.009$) and 15% lower calcium intake ($p = 0.03$) compared

to PPMS and benign MS. The authors theorize that the neuroprotective qualities of magnesium may explain the inverse relationship found between intake of magnesium and tissue damage that is characteristic of SPMS. In an Iranian study, Shirazi and colleagues[58] studied the energy and macronutrient intake of Iranian subjects (n = 108) with RRMS, all with an EDSS score of 5.5 or less (ie, able to walk). Three 24-hour recalls and a semi-structured food frequency questionnaire (FFQ) were used to assess dietary intake. Similar to the study conducted among US women, female subjects had a lower intake of dietary fiber compared to the RDA and had a high saturated fat intake. Males also consumed inadequate fiber and excessive saturated fat. Mean percentage of calories coming from total fat was above recommended levels for both males and females, while only males consumed more cholesterol than recommended. Mean energy intake was 1602 Kcal ± 742 in females and 2473 Kcal ± 1079 in males. Compared to the general Iranian population, all subjects consumed a higher percentage of protein and fat, but less saturated fat and fewer carbohydrates. Calorie intake was also significantly lower than that of the general population. Again, the results of these studies should be interpreted with caution as nutrient intakes were not compared to the EAR. Because of this, the insufficiency of intake may be overestimated in these studies.

Research on the dietary intake and nutritional status of MS population in the US is lacking. In addition, the studies to date have methodological limitations, including the use of the older RDA to assess nutrient adequacy of a group. Because many theories of MS etiology involve a nutrition risk factor, the dietary intake of

individuals within this population should be investigated. Nutrition-related hypotheses associated with MS prevalence and progression have led to the adoption of biologically based CAM therapies, such as vitamins, minerals, and special diets, thus the dietary intake of the MS population is of particular interest.

Chapter 3

SPECIFIC AIMS

3.1 Statement of the Problem

MS is a complex, unpredictable disease for which there remains no cure. Only recently have treatments been developed to slow disease progression and reduce relapse rate, but they are often ineffective and cause side effects. Consequently, many patients turn to CAM as another form of treatment. The use of CAM is rather concerning, as there is a paucity of research addressing the safety and efficacy of these therapies, and many patients do not inform their conventional health care providers about their use of unconventional therapies. The prevalence of CAM use varies considerably throughout the literature, and few studies examine the specific types of therapies used. Therefore, further research on the prevalence of use for specific types of CAM is warranted. Additionally, research on the use of special diets and associated nutrient intake is needed, as diet-based therapies are a form of unconventional therapy used within the MS population. The specific diets and prevalence of use are not well known, and these diets may place individuals and nutritional risk. Additionally, there is limited research on the dietary intake of individuals with MS.

3.2 Specific Aims

AIM 1: The primary aim of this study is to determine the prevalence of use for specific types of CAM among individuals with MS.

AIM 2: The secondary aim of this study is to assess the nutrient intake profile for the MS population as a whole as well as for those following specific CAM diets.

Chapter 4

METHODS

4.1 Description of Participants

Male and female adults at least 18 years old who have MS were recruited for this study. To be eligible to participate, subjects were required to have been diagnosed with MS at least 1 year prior to the time of enrollment. Prospective study participants without access to high-speed Internet and telephone were deemed ineligible to participate, as they were required for data collection. Participants were recruited on a volunteer basis and were given a $25 gift card as compensation for their participation. All procedures were approved by the University of Delaware Institutional Review Board (IRB) (Appendix A). Subjects were informed about the purpose of the study, the risks and benefits associated with participating, the compensation provided, and the confidential and voluntary nature of the study. All subjects provided consent prior to enrollment (Appendix B).

4.2 Description of Measures

Use of CAM: The Complementary and Alternative Medicine Supplement (CAM-S) (National Center for Health Statistics, Hyattsville, MD, 2007) was administered to measure the prevalence of specific types of CAM used. The CAM-S

is administered every 5 years as part of the National Health Interview Survey (NHIS), which is a standardized survey conducted by telephone interview to a nationally representative sample of the US population. The validity and reliability of the CAM-S have not been established however it is a standardized survey used in national health surveillance studies in the US. The CAM-S includes questions on 36 types of CAM, 10 of which are provider based (eg, acupuncture, traditional healers, chiropractic manipulation) and 26 that do not require a provider (eg, supplements, special diets). For each therapy utilized, there were follow-up questions to gather more information about that therapy (eg, reasons for use). Because the survey has a branching design, there were 40 to 550 possible questions. Questions on the CAM-S were entered into Qualtrics Survey Software (Qualtrics Labs, Inc., Provo, UT, 2012) to allow for electronic data capture during the interview process.

Response formats include close-ended single response, close-ended multiple response, close-ended multiple responses with a write-in option for the "other," and open-ended. Close-ended questions have anywhere from 2 to 81 response choices. Responses with respect to CAM therapies were classified as categorical variables, while certain background questions were continuous (ie, anthropometrics, age, years since diagnosis). Minor changes were made to the CAM-S. First, a question that asks for the respondent's username was added, thereby allowing CAM survey responses to be matched to their corresponding diet recall. A background section was added to obtain subjects' demographics, medical and MS history, height, and weight. "Multiple

sclerosis" was added as an option for questions that inquired about the conditions or symptoms for which a particular therapy is utilized.

Nutrient intake: Nutrient intake was assessed using the Automated Self-Administered 24-hour Recall system, ASA24-2011 (ASA24) (National Cancer Institute, Bethesda, MD, 2011), which requires high-speed internet and the Microsoft Silverlight plugin. The format and design of the ASA24 system are based on a modified version of the interviewer-administered Automated Multiple Pass Method (AMPM) developed by the US Department of Agriculture (USDA), but unlike AMPM, ASA24 is self-administered by the respondent. Two validation studies for ASA24 are currently underway. ASA24 prompts respondents to report all food, drink, and supplement intake during the previous day. Nutrient intake reported by ASA24 includes macronutrients (proteins, carbohydrates, fats, alcohol) and micronutrients (vitamins, minerals), as well as intake of individual food groups including grains, vegetables, fruits, meats, milk, oils, and "extras" (ie, added sugars, discretionary solid fat, alcoholic drinks).

The Website is user-friendly, featuring an animated character that guides the respondents through the interview using audio and visual cues with an option to increase font size. These features enable respondents with low literacy, impaired hearing and/or vision to complete the recall. Based on pilot testing, respondents typically complete one dietary recall in 20-30 minutes. Each food and drink item reported by the respondent is linked to a food code in the USDA's Food and Nutrient

Database for Dietary Studies (FNDDS), while the dietary supplement intakes are based on supplements reported in the 2007-08 NHANES Dietary Supplement Database (NHANES-DSD). Subjects had up to 32 hours to finish their dietary recall before access was denied.

Procedures: To recruit participants, advertisements were posted on NMSS chapter Websites and/or e-blasts, via social media (eg, Facebook, Twitter), flyers posted on the University of Delaware campus, and in the classifieds section of local newspapers (Appendix C). Interested individuals contacted the principal investigator (PI) by phone or e-mail to determine their eligibility, obtain consent, and schedule the phone interview. Subjects were sent an interview confirmation by mail and email, which included the Web address, username, and password for ASA24, as well as handouts they could refer to during the CAM survey (Appendix D). Interviews took approximately 35 minutes. After subjects completed the CAM survey, they were directed to the ASA24 Website to complete the dietary recall. The interviewer remained on the phone to provide assistance as needed. Subjects were mailed a $25 gift card upon completion of their participation.

Design: Descriptive, cross-sectional

Analysis: All analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, 2012). Demographic, medical history, and CAM data were summarized using frequencies and percentages. Nutrient intake data were first assessed for

missing values and then summarized using the mean ± standard deviation. The 25th percentile, median, and 75th percentile were determined when the sample size was sufficient to produce a meaningful data summary. Percentage of subjects meeting the EAR and RDA/adequate intake (AI) for vitamins and minerals were determined, when available. Those who did not meet the EAR or exceeded the tolerable upper intake level (UL), for a particular nutrient were each expressed as a percentage of total subjects. To compare differences in nutrient intake between CAM users and non-users of CAM, the Mann-Whitney U test was performed to detect differences. To adjust for energy intake, an ANCOVA was also performed using calorie intake (kcal/day) as the covariate. Differences were considered significant when $p < 0.05$. Future analyses will consider the residual method[59] of energy adjustment.

Chapter 5

RESULTS

5.1 Recruitment

Out of 60 individuals who initially responded to the advertisement, 24 chose not to participate and one dropped out after a possible misdiagnosis of MS. Two subjects were excluded from nutrient analysis because they did not finish the ASA24 dietary recall. In total, 35 CAM surveys and 33 dietary recalls were analyzed.

5.2 Demographics

Characteristics of subjects are presented in Table 2. Females (91.4%) and whites (94.3%) comprised a majority of the sample, both of which were higher than the estimated ratio of about 2 for females and whites compared to male and non-whites, respectively. Age ranged from 24 to 74 years, with a mean of 49.9 ± 13.1 years. Overall, subjects were well educated, with 68.6% having at least a bachelor's degree. Annual household income ranged from below $25,000 to greater than $75,000. Two participants (5.7%) refused to report income; out of those who did, a majority (n=20) reported an income of at least $51,000 per year. Most resided in Florida (n=9) or the Mid-Atlantic states (n=23), predominately New Jersey (n=7) and New York (n=6).

5.3 Health-related factors

MS and other medical history is presented in Table 3. Consistent with national estimates, RRMS was the most prevalent form of MS (82.9%, n=29), followed by SPMS (n=4, 11.4%). One subject reported PPMS, while one other was not sure of MS type. Disease duration ranged from one to 28 years, with a mean duration of 9.7 ± 7.2 years. Subjects self-rated their disease severity by selecting one of six categories that ranged from "none/minimal" to "unable to walk." This severity rating scale has been found to be well correlated with the neurologist rated EDSS (r = 0.85),[37] which was not presented given that subjects were unaware of the EDSS or did not know their score. A higher frequency of subjects considered themselves mild (n=11,31.4%), but over half (n=18, 51.4%) reported at least moderate severity (ie, having many MS-related symptoms that affect daily activities). DMA were taken by about two-thirds (n=23, 65.7%) of all subjects, which included those with RRMS (n=22) and SPMS (n=1). For treatment of MS symptoms, commonly reported medications included antispasmodics (n=10, 28.6%), anticonvulsants (n=9, 25.7%), bladder control agents (n=5, 14.3%), potassium channel blockers (n=5, 14.3%), and wakefulness promoting agents (n=4, 11.4%).

With respect to other health factors, most were at an unhealthy weight, with12 (34.3%) and 9 subjects (25.7%) being overweight or obese, respectively. Cardiovascular-related conditions were common, with 10 (28.6%) subjects taking antihypertensives and 6 (17.1%) on antihyperlipidemic medications. Seasonal

allergies (n=10, 28.6%), arthritis (n=10, 25.7%), reflux (n=8, 22.9%), and hypothyroidism (n=5, 14.3%) were also prevalent.

5.4 Prevalence of specific CAM therapies

Overall, 77.7% (n=27) of participants used CAM for MS within the past 12 months (within 30 days for supplements). Frequency of CAM therapies used are presented in Table 4. The most common types employed by CAM users were biologically based (n=24, 88.9%), namely vitamin/mineral supplements (n=24, 88.9%) and NPs (n=12, 44.4%). Chelation therapy was the only biologically based therapy not used. Out of the vitamin/mineral and NP users who reported intake of supplements, a majority (n=14, 58.3%) took them in amounts containing vitamins and/or minerals in doses above the RDA and/or UL; however, data for 5 (20.8%) of the supplement users were not available as they did not report supplements in their dietary recall. The most common vitamin/mineral supplement taken was vitamin D (n=19, 70.4%), followed by vitamin B12 (n=6, 22.2%), and B complex (n=4, 14.8%). Others included vitamin C (n=3, 11.1%), multivitamin-mineral (n=3, 11.1%), calcium plus vitamin D (n=2, 7.4%), iron (n=1, 3.7%), and folate (n=1, 3.7%). With respect to NPs, fish oil/omega-3 fatty acid supplements were the most prevalent, taken by 33.3% (n=9) of CAM users. Evening primrose oil (n=2, 7.4%), flaxseed oil (n=2, 7.4%), pre- or probiotics (n=2, 7.4%), co-enzyme Q10 (n=1), cranberry pills (n=1), EGCG (n=1), lecithin (n=1), methylsulfonylmethane (n=1, 3.7%), S-adenosyl methionine (n=1), senna (n=1), and combination NPs (n=1) were also taken for MS.

Special diets were followed by 8 (29.6%) of CAM users, half of which were the Paleo (n=2) and Swank (n=2) diets. The other diet types were a combination of several modifications, which included gluten-free (n=3), Paleo (n=1), low sugar (n=1), low fat (n=1), low processed foods (n=1), soy-free (n=1), nitrate-free (n=1), juicing (n=1), fasting (n=1), limited in red meat (n=1), and vegetarian (n=1). There were a total of 4 combination dieters. It should be noted that some participants (n=9, 25.7%) were following diets for reasons other than MS, including low fat, weight loss, low sodium, vegetarian, lactose free/low residue, and wheat/soy/corn/dairy-free; reasons for use were predominantly for weight loss, general wellness or disease prevention, and to treat conditions other than MS.

Manipulative and body-based therapies comprised the next most common (n=13, 48.1%) type of CAM, especially massage (n=6, 22.2%) and chiropractic manipulation (n=5, 18.5%); movement therapies were used to a lesser degree, with only 3 and 1 participants reporting use of pilates and Alexander technique, respectively, and no participants using feldenkreis or trager psychophysical integration. Mind-body therapies were the next most frequent (n=12, 44.4%) type of CAM. Specifically, relaxation techniques (ie, meditation, guided imagery, progressive relaxation, and deep breathing exercises) were reported by one-third of CAM users, while 5 (18.5%) used yoga, tai chi, and/or qi gong. Interestingly, this was the only type of CAM therapy used by the one participant with PPMS. All male participants (n=3) used at least one CAM therapy, which included only those in the most commonly employed categories (ie, biologically based, manipulative and body based,

and mind-body), while none reported use of alternative medical systems or energy healing therapy.

With respect to alternative medical systems, the only therapies reported were acupuncture (n=1) and naturopathy (n=2), while none used ayurveda, homeopathic treatments, or traditional healers. The participants (n=3) who used alternative medical systems were well educated females with a long disease duration, two of whom were among the only three respondents with the highest disease severity in this sample. Users of energy healing therapy (n=2) had similar characteristics to those of alternative medical systems. Of the 8 participants who reported no use of CAM within the past 12 months for treatment of MS, all were female and most were within the 30-39 year age range—the only participant under age 30 did not use CAM. Type of MS or income did not appear to play a role in type of therapy used or use of CAM in general, though this cannot be confirmed given that only descriptive statistics were performed.

5.5 Nutrient intake of the MS population

Nutrient intake of all participants who completed the dietary recall (n=33) are presented in Table 6. The median energy intake was 1790 kcal, with percent calories from carbohydrate and protein within the AMDR; the median percent calories from fat was 36.8%, which was slightly higher than the AMDR. Percent of calories from saturated fat was 11.8%. Although there is no DRI for saturated fat, intake exceeded the guideline of <10% of total calories (<7% to reduce CVD risk) recommended by

the USDA Dietary Guidelines for Americans (DGA).[60] Overall, participants fell short of the AI for dietary fiber, meeting 87.3% of this DRI.

With respect to micronutrient intake, when evaluating all subjects as a group, many participants under consumed key vitamins and minerals. The number of participants who consumed below the EAR was 17 (51.5%) for vitamin E, 9 (27.3%) for vitamin C, 9 (27.3%) for vitamin D, 8 (24.2%) for vitamin A, 6 (18.2%) for folate, 7 (21.2%) for calcium, and 7 (21.2%) for magnesium. Interestingly, magnesium was also among the minerals consumed in relatively high amounts, with nearly half of participants (n=16) consuming it at a level above the UL. Many participants also consumed niacin and sodium at levels above the UL, 14 and 27, respectively. Intakes of thiamin and vitamin B12 were much higher than the EAR and RDA, but this was of less concern given that these nutrients do not have an established UL. For dietary intake, only servings of fruits and vegetables are presented. In general, participants consumed more vegetables than fruits, with mean daily intakes of 2.4 ± 1.8 cup equivalents and 0.9 ± 1.1 cup-equivalents per day, respectively.

5.6 Nutrient intake of supplement users and non-supplement users

Table 7 and Table 8 present nutrient intake of non-supplement users (n=1) and supplement users (n=32). Given that only one participant did not use supplements, the nutrient intake of all participants and supplement users is similar. The single non-supplement user was female and had a high calorie intake (3015 kcal), with 43.4% coming from fat. Both saturated fat (18.6% of kcal) and cholesterol (381 mg)

exceeded the DGA recommendations. These levels were higher than the mean and median intakes among supplement users. Dietary fiber was far below recommendations, meeting only 40.1% of the AI. Similar to many supplement users, this participant fell short in vitamins C, D, and E, with intakes of only 14.5%, 18.3%, and 39.6% of the RDA, respectively. Also consistent with many supplement users, niacin and sodium intake were both above the UL. However, this non-supplement user had the highest sodium intake (7627 mg) among all subjects, with an intake over three times the UL. This participant consumed 1.1 cup-equivalent/day of vegetables and no fruit.

5.7 Nutrient intake of CAM users

Nutrient intake of CAM users is presented in Table 9. There were few differences in median nutrient intakes between CAM users and non-users. Total carbohydrate ($p = 0.036$), percent calories from saturated fat ($p = 0.049$), and zinc intake ($p = 0.025$) were lower among CAM users, while riboflavin ($p = 0.08$) and calcium ($p = 0.09$) intake tended to be lower. When nutrients were adjusted for energy intake (Table 10), both saturated fat ($p = 0.011$) and percent calories from saturated fat ($p = 0.023$), as well as zinc intake ($p = 0.019$) were higher among non-users of CAM, The trend found with calcium intake was stronger after adjusting for calories ($p = 0.08$).

In Table 11, total nutrient intake of CAM users is broken down into the five NCCAM categories. Given the small sample size and because many participants used

more than one type of CAM therapy, nutrients were not compared statistically. Energy and macronutrient intakes of CAM users appeared similar across categories, though users of alternative medical systems and energy healing therapy seemed to consume less saturated fat and more dietary fiber than those who used other types of CAM. Interestingly, these subjects also had a higher intake of cholesterol. With respect to micronutrients, users of alternative medical systems and energy healing therapy appeared consumed substantially more vitamin A, while in general, the biologically based, manipulative and body-based, and mind-body therapy users had higher intakes of vitamin C, thiamin, riboflavin, vitamin B6, vitamin B12, and calcium compared to users of alternative medical systems and energy healing therapy. Vegetable and fruit intake were highest among those who used alternative medical systems and energy healing therapy.

5.8 Nutrient intake in special diets

Mean nutrient intake of participants of those following a special diet for MS are presented in Table 12. Intakes for Swank, Paleo, and combination diets are included, except for one combination diet (ie, low sugar and processed foods), which was not analyzed because the dietary recall was incomplete. Statistical tests were not performed given that each group had so few subjects. However, intakes of several nutrients should be noted. First, energy intake of Swank dieters was the lowest, followed by Paleo and combination, with non-dieters having the highest intake. Total fat and percent calories from fat were also lowest in the Swank diet, which was the

only group having an intake within the AMDR. The Paleo diet had the highest mean percentage (16.8 ± 2.7%) of calories from saturated fat, followed participants not on a diet for MS (12.3 ± 4.9%) and Swank (11.1 ± 1.3%). Those on a combination diet had the lowest intake of saturated fat (7.6 ± 1.1%), which was the only one to meet the DGA recommendation. One counterintuitive finding was these combination dieters had the highest intake of cholesterol (645 ± 87 mg) while all other groups had a mean intake below 300 mg.

There was no concern for deficiency with respect to minerals, as each group's mean intake for these nutrients was above the EAR. Swank dieters seemed to have the lowest intake of sodium and potassium, while combination dieters had the highest. Potassium intake for all groups fell short of the DGA recommendation of 4,700 mg, though those following a combination diet were closest (4193 ± 1575 mg). Swank and combination dieters had the highest and lowest mean calcium intakes, respectively. Two groups, Swank and Paleo, had mean intakes that were below the EAR. Specifically, Swank dieters' intake of vitamin C, folate, vitamin A, and vitamin E, and Paleo dieters' intake of vitamins E and D were below the EAR. In contrast, participants on the Swank diet had the highest intake of vitamin B12, well above the EAR.

Finally, vegetable and fruit intake varied substantially among the diet groups. Subjects on the Swank diet had the lowest intake of vegetables (1.5 ± 0.7 cup-equivalents/day) and fruit (0 cup-equivalents/day), while mean intake for combination dieters was the highest (5.5 ± 3.1 and 2.0 ± 2.1 cup-equivalents/day, respectively).

Subjects on the Paleo diet had the next highest intake of vegetables (3 ± 2 cup-equivalents/day) and fruits (1.9 ± 0.7 cup-equivalents/day), followed by non-dieters (2.1 ± 1.4 and 0.7 ± 0.9 cup- equivalents/day for vegetables and fruit).

Chapter 6

DISCUSSION

The prevalence of CAM in this sample was higher compared to previous studies (30 – 71.1%).[22-28,30,31,35,37,38] Although Stoll and colleagues[29] found that 100% of their respondents used CAM, their results considered lifetime use rather than current or recent use. The proportion of CAM use was also higher than in the general US population, in which 38.3% of adults reported use of at least one therapy in the past 12 months.[32] This may be due in part to the comprehensive nature of the CAM survey administered, the contemporary nature of the study, the small sample size of the study, or other measures. Similarities existed between the types of CAM used in the MS and general adult population, with biologically based, manipulative and body-based, and mind-body therapies being more common than use of energy healing therapy and alternative medical systems. NPs were the most frequently reported CAM by the general US population, while use of vitamin/mineral supplements were most common among participants in the present study, followed by NPs. However, it is possible that vitamin/minerals were taken as CAM among the general population, as "megavitamin therapy" was not reported in the most recent National Heal Statistics Report for CAM use. Based on data from the previous report, only 2.8% used megavitamin therapy, but what constitutes this CAM therapy is not clear. In contrast,

subjects in this study who reported use of vitamins/minerals for MS, regardless of micronutrient content, were considered CAM because they are not recognized as conventional treatment.

The relatively high prevalence of vitamin/mineral use among individuals with MS is consistent with previous investigations. Out of the few studies that elucidated specific nutrients, vitamin D, vitamin B12, and B vitamins in general were also commonly reported, though an interesting divergence was that vitamin D was not the most frequently reported nutrient. Rather, multivitamins[31,38] and vitamin C[38] were the most prevalent. Most participants taking vitamin D in this study reported that their physician recommended it (73.6%), which likely explains the high prevalence of use. The reason the proportion of vitamin D use was lower in previous studies is not clear, but perhaps there has been greater evidence since then that has made vitamin D supplementation more commonplace in conventional medicine. That 10.5% (n=2) of vitamin D users took doses above the UL without recommendation from a healthcare provider is of concern given risk for toxicity.

The high frequency that B vitamins were reported may be explained by the fact that fatigue is a common symptom of MS, and that vitamin B12 has been implicated in myelin synthesis.[61] Berkman and colleagues[24] found that one of the perceived benefits of B vitamins reported by subjects was strength and more energy. B vitamins are often advertised for their role in energy production, which could explain why users would take them for fatigue. The only B vitamin taken in doses above the UL was niacin. Although some participants took doses of vitamin B12 much higher than the

EAR and RDA, excessive consumption of this vitamin does not introduce the possible adverse reactions associated with high intakes of niacin or vitamin D. Taken together, healthcare providers should stress how important it is for patients to inform their physician about their use or potential use of any dietary supplements.

The use of NPs was consistent with previous literature. Essential fatty acids were the predominant NP, with fish oil/DHA/omega-3 being the most common, which supports previous studies that found fish oil to be used by a majority of CAM users.[26,31] Evening primrose oil was used less often compared to previous literature.[25,31,38] That use of these essential fatty acids by individuals with MS is not surprising, given that omega-3 fatty acids and alpha-linoleic acid have been examined extensively for their potential role in treatment and risk reduction of MS.[61] Interestingly, fish oil/DHA/omega-3 was also the most common NP reported by the general US population in 2007.[32] However, it is likely that US adults in general are taking them for different reasons due to the known cardioprotective effects of omega-3 fatty acids. With respect to special diets, there were few similarities with the general US population. One reason is that the CAM-S presents results on more mainstream dietary modifications and weight loss programs (eg, Atkins, South Beach, vegetarian), whereas "other" diets were reported in this study. Compared to the MS population, prevalence of special diets was similar; however, unique to this study was the Paleo diet, which was reported more than the Swank diet.

The prevalence of non-biologically based CAM therapies were similar to previous findings. Only two studies[23,35] found chiropractic manipulation to be one of

the least prevalent, used by only 1-3% of subjects. Perhaps these differences can be explained by the fact that those studies were conducted in Spain and Germany rather than in the US or Canada. Regarding demographics and MS history, the sample size was not large enough to find meaningful patterns of use.

In general, nutrient adequacy of this population was no more concerning than would be for the general US population. That is, nutrients typically under consumed in the general population are similar to those in this sample, including calcium, potassium, folate, vitamins A, C, D, and dietary fiber, while those often consumed in excess are fat, saturated fat, and sodium.[62] Low fruit and vegetable intake may be one reason for the shortfall in potassium, folate, vitamin A, C, and fiber. It is difficult to compare the results with those in previous studies due to the vast differences in the populations studied. However, similar findings included low dietary fiber and high saturated fat intake. Timmerman and colleagues,[55] who examined nutrient intake of adult US females, also found intakes of calcium (mean 676 ± 317 mg) and dietary fiber (mean 16.7 ± 6.8 g) to be less than recommended.

The higher intake of certain under consumed nutrients among non-users compared to CAM users may be a reflection of greater energy and food consumption. Additionally, most non-users took vitamin/mineral supplements (eg, calcium) for other reasons. However, when nutrients were energy-adjusted, calcium and zinc remained lower among CAM users. The most striking difference was saturated fat intake. One explanation may be the influence of special diets among these participants, but only four were following diets that may have influenced saturated fat intake (ie, Swank,

limited red meat, vegetarian). To better understand the differences in nutrient intake between CAM users and non-users, future analyses will employ the residual method of energy adjustment.[59]

Although statistical tests were not used to compare nutrient intake among special diets, there were some patterns that warrant future research in special diets and nutrient intake. It was not surprising that followers of the Swank diet had a low fat and saturated fat intake, as these are the main characteristics of the diet. Low-fat intake was likely the reason that mean vitamin E intake of Swank dieters only met 40% of the EAR, while low fruit and vegetable intake may explain why they fell short of the EAR for vitamin A, vitamin C, and did not meet the DGA recommendation for potassium. Considering the very small sample, whether the results closely resemble typical Swank dieters is not known. Given that two fruits per day are recommended as part of the diet,[48] these participants may not have been strict followers.

With respect to saturated fat intake, the Paleo diet appeared to have an opposite effect. The diet is designed to mimic the types of foods available to humans prior to the Agricultural Revolution, with an intake high in fruits, vegetables, protein, and moderate-to-higher amounts of fat, and exclusion of grains, legumes, dairy, salt, processed foods, and potatoes.[63] While vegetable and fruit intake likely contributed to higher intakes of nutrients below the EAR in the Swank diet, as well as a relatively high mean intake of dietary fiber, the percentage of calories from saturated fat was substantially higher than all other diets. Most notable was the low intake of vitamin D, which was the only diet with an intake below the EAR. The lack of dairy and other

foods fortified with vitamin D (eg, fortified cereals) excluded in the Paleo diet may pose a risk for inadequacy for this vitamin, but perhaps more so for calcium since it can only be obtained through the diet. Interestingly, the Paleo diet seems to embody the exact opposite of what many theorize to be nutrition risk factors for MS—high saturated fat intake and low vitamin D.

Participants in the Combination diet group were more difficult to assess, as there were several dietary modifications involved, though there existed some overlap. The two modifications that encouraged a plant-based diet may have contributed to the low saturated fat intake, though the cholesterol was substantially higher compared to other groups, perhaps due to intake of egg in lieu of meat. Participants following the Combination diet or no diet for MS were the only two groups without a mean below the EAR, which suggests the Swank and Paleo diets may be too restrictive to meet needs. However, it is possible that the small group samples do not represent nutrient intake typical of these diets, or that vitamin/mineral supplementation use is higher in the other groups.

Taken together, the use of CAM therapies among the MS population is common. Biologically based therapies are the most frequently used, especially supplementation with vitamins, minerals, and NPs. Also prevalent are special diets and dietary modifications, which may have a detrimental impact on nutrient intake. There is a paucity of data on the dietary and nutrient intake in the MS population, especially in the US. Considering the prevalence of these biologic therapies, larger studies that focus on nutrient intake and dietary modifications should be conducted.

Limitations to this study should be noted. The sample was small, therefore results may not be generalized to the general MS population. For example, females, whites, and the RRMS subtype were overrepresented. Another limitation was that participants only completed one 24-hour diet recall, which may not have been sufficient to reflect typical food and nutrient intake. There was also the potential for misreporting. Some participants who reported use of dietary supplements did not enter them into ASA24, so it is possible that the analyses did not reflect their long-term nutrient intake. The small sample size made interpretation of special diets difficult, as statistical tests could not be run. Also, adequacy of nutrient intake was based on the mean, rather than the median, which would have been more meaningful. Despite the limitations, there were strengths to this study. The use of the CAM-S allowed comparisons to be made between participants and the general US population. Previous studies did not use this standardized survey. Also, this is the first study to evaluate the nutrient intake of special diets among the MS population, and given the inadequacies found in the intake of some nutrients, this area of research warrants further investigation with a larger sample size.

TABLES

Table 1. Prevalence of CAM use in MS

Citation	Location	Sample Size	Prevalence of Overall CAM Use	Type and Prevalence of CAM (% of CAM users)
Schwartz et al, 1999[28]	US (CO)	N = 569	33% reported visiting CAM practitioner within past 6 months	Massage (42.9%) Chiropractic (36.5%) Nutritional (27.0%) Holistic (17.5%) Herbal (10.1%)
Stuifbergen et al, 2003[30]	US (Southwest)	N = 621	33.3% reported current use, 50.4% reported past use	Nutritional supplements (77.8%) Herbal treatment (26.6%) Special diet (26.1%) Massage (16.9%) Chiropractic (13.0%)
Marrie et al, 2003[25]	US (National)	N = 20,778	30% reported current or past use	*Therapies:* Evening primrose oil (53%) Megavitamin therapy (47%) Lecithin therapy (33%) *Practitioners:* Chiropractors (51.4%) Massage therapists (33.5%) Nutritionists (24.2%)
Berkman et al, 1999[24]	US (CA, MA)	N = 240	58.3% reported current or past use	Massage (33.6%) Chiropractic (29.3%) Vitamin C (29.3%) Acupuncture (27.9%) Meditation (22.9%) Vitamin E (22.9%)

Table 1. Prevalence of CAM use in MS (continued)

Citation	Location	Sample Size	Prevalence of Overall CAM Use	Type and Prevalence of CAM (% of CAM users)
Nayak et al, 2003[27]	US (National)	N = 3140	64.9% reported current or past use; 57.1% when excluding vitamins, prayer, and exercise	Vitamins (44.8%) Prayer (27.3%) Ingested herbs (26.6%) Chiropractic (25.5%) Massage (23.3%) Acupuncture (19.9%)
O'Connor et al, 2012[31]	US (NY)	N = 279	82.1% used dietary supplements 26.6% used herbal supplements	Multivitamin (78.1%) Vitamin D (64.5%) Calcium plus vitamin D (64.5%) Fish oil (61.7%) Evening primrose oil (40.4%) Cranberry extract (35.2%)
Shinto et al, 2005[36]	US (OR, WA)	N = 1913	68% reported current use 84% had ever used	Not specified (79% use therapies, 47% use providers)
Shinto et al, 2006[37]	US (OR, WA)	N = 1667	71.1% reported current use, 87.9% had ever used	Not specified
Stoll et al, 2012[29]	US (Philadelphia)	N = 111	100% reported past use	*Dietary supplements (100%):* Vitamin D (32.4%) B Vitamins (18.9%) Exercise activities (58.6%) *Other CAM (57.7%):* Physical therapy (47.7%) Massage therapy (18.0%)
Page et al, 2003[38]	Canada	N = 440	70% reported use within past 2 years	Multivitamin (61%) Vitamin C (48%) Massage (43%) Evening primrose oil (42%) Vitamin E (40%)

Table 1. Prevalence of CAM use in MS (continued)

Citation	Location	Sample Size	Prevalence of Overall CAM Use	Type and Prevalence of CAM (% of CAM users)
Apel et al, 2006[23]	Germany	N = 254	67.3% reported current use	Exercise therapy (73.7%) Vitamins (39.8%) Minerals and other supplements (33.9%) Phytotherapy (25.1%) Relaxation techniques (24.6%)
Apel et al, 2005[22]	Germany	N = 154	61.7% reported current use	Physiotherapy (55.8%) Vitamins (51.6%) Minerals and other supplements (32.6%) Phytotherapy (29.5%) Relaxation techniques (16.8%)
Sastre-Garriga et al, 2003[35]	Spain	N = 193	40.9% reported use within past year	Massage (24.1%) Diet therapy (13.9%) Homeopathy (6.3%) Acupuncture (5.1%) Chiropractic (1.3%)
Leong et al, 2009[26]	Australia	N = 416	64.7% reported current or past use	*Current and Past by Category:* Vitamins (81.8%) Essential fatty acids (80.7%) Minerals (62.5%) *Most frequently used "currently"* Fish oil (62.5%) Vitamin B12 (41.3%) Vitamin B1, 2, and/or 6 (38.3%) Calcium (36.1%) Magnesium (34.6%) Vitamin D (29.7%)

Table 2. Demographic characteristics of participants

	n	(%)
All subjects	35	(100)
Sex		
Male	3	(8.6)
Female	32	(91.4)
Age (y)		
18-29	1	(2.9)
30-39	9	(25.7)
40-49	7	(20.0)
50-59	8	(22.9)
60-69	8	(22.9)
70-85	2	(5.7)
> 85	0	(0)
Race		
American Indian or Alaska Native	0	(0)
Asian	0	(0)
Black or African American	1	(2.9)
Native Hawaiian or other Pacific Islander	0	(0)
White	33	(94.3)
Other	0	(0)
Refused	1	(2.9)
Ethnicity		
Hispanic	1	(2.9)
Non-Hispanic	34	(97.1)
Education		
Less than high school	0	(0)
High school diploma or equivalent	3	(8.6)
Some college, no degree	5	(14.3)
Postsecondary non-degree award	0	(0)
Associate's degree	3	(8.6)
Bachelor's degree	13	(37.1)
Master's degree	8	(22.9)
Doctoral or professional degree	3	(8.6)
Household income (US$)		
<$25,000	4	(11.4)
$25,000-$50,999	9	(25.7)
$51,000-$75,000	8	(22.9)
≥$75,000	12	(34.3)
Refused	2	(5.7)
Geographic Region		
Delaware	3	(8.6)
Florida	9	(25.7)
Illinois	2	(5.7)
Maryland	1	(2.9)

Table 2. Demographic characteristics of participants (continued)

	n	(%)
Missouri	1	(2.9)
New Jersey	7	(20.0)
New York	6	(17.1)
Pennsylvania	4	(11.4)
Virginia	2	(5.7)

Table 3. Medical history and health-related factors of participants

	All subjects	
	n	**(%)**
Form of MS		
Relapsing remitting	29	(82.9)
Primary progressive	1	(2.9)
Secondary progressive	4	(11.4)
Progressive relapsing	0	(0)
Unknown	1	(2.9)
MS duration (y)		
1-5	12	(34.3)
6-10	11	(31.4)
11-15	4	(11.4)
15+	8	(22.9)
MS severity		
None/minimal	6	(17.1)
Mild	11	(31.4)
Moderate	7	(20.0)
Some support needed for walking	8	(22.9)
Walker/two-handed crutch	3	(8.6)
Unable to walk	0	(0)
Medical history		
Cardiovascular	12	(34.3)
Hypertension	8	(22.9)
Heart disease	0	(0)
Irregular heartbeat	2	(5.7)
Pacemaker	0	(0)
Phlebitis/clots	2	(5.7)
Stroke/TIA	0	(0)
Renal	3	(8.6)
Kidney failure	0	(0)
Kidney stones	3	(8.6)
Immunologic	10	(28.6)
Seasonal allergies	10	(28.6)
Asthma	3	(8.6)
Endocrine	5	(14.3)
Diabetes	0	(0)
Hyperthyroidism	0	(0)
Hypothyroidism	5	(14.3)
Gastrointestinal	11	(31.4)
Irritable bowel syndrome	5	(14.3)
Reflux	8	(22.9)
Cancer	6	(17.1)
Liver disease	0	(0)
Glaucoma	1	(2.9)
Multiple sclerosis	35	(100)

Table 3. Medical history and health-related factors of participants (continued)

	All subjects	
	n	**(%)**
Arthritis	9	(25.7)
Fibromyalgia	0	(0)
Hemophilia	0	(0)
COPD	1	(2.9)
Other [a]	11	(31.4)
Medication		
Prescription	35	(100)
Analgesic	3	(8.6)
Antianxiety	4	(11.4)
Antiasthma	1	(2.9)
Antibiotic	1	(2.9)
Anticoagulant	1	(2.9)
Anticonvulsant	9	(25.7)
Antidepressant	9	(25.7)
Antihistamine	1	(2.9)
Antihyperlipidemic	6	(17.1)
Antihypertensive	10	(28.6)
Antimigraine	1	(2.9)
Antiparkinson	2	(5.7)
Antispasmodic	10	(28.6)
Antiviral	1	(2.9)
Allergies	2	(5.7)
Birth control	3	(8.6)
Bladder control agent	5	(14.3)
Corticosteroid	2	(5.7)
Disease modifying agents	23	(65.7)
Erectile dysfunction treatment	1	(2.9)
Hormone replacement	2	(5.7)
Opioid receptor antagonist	1	(2.9)
Osteoporosis treatment	1	(2.9)
Potassium channel blocker	5	(14.3)
Proton pump inhibitor	2	(5.7)
Pulmonary hypertension	1	(2.9)
Sedative	2	(5.7)
Stimulant	2	(5.7)
Thyroid hormone	4	(11.4)
Vitamin/mineral supplement	4	(11.4)
Wakefulness promoting agent	4	(11.4)
Over the counter	**14**	**(40)**
Analgesic	8	(22.9)
Antiemetic	1	(2.9)
Antihistamine	5	(14.3)
Proton pump inhibitor	4	(11.4)
Vitamin/mineral supplement	34	(97.1)

Table 3. Medical history and health-related factors of participants (continued)

	All subjects	
	n	**(%)**
Nonvitamin, nonmineral, natural products	23	(65.7)
Chewing/swallowing difficulty		
Solids only	3	(8.6)
Liquids only	3	(8.6)
Solids and liquids	2	(5.7)
No difficulty	26	(74.3)
BMI		
Underweight	1	(2.9)
Normal	13	(37.1)
Overweight	12	(34.3)
Obese	9	(25.7)
Vitamin/mineral supplement use for MS	24	(68.6)
On specific diet for MS	8	(22.9)

[a] anxiety (n=2, 5.7%), prostate, macular degeneration, optic neuritis (n=2, 5.7%), seizure disorder, anorexia nervosa (recovered), osteoporosis (n=3, 8.6%), pulmonary hypertension, lupus, sleep apnea, migraines

Table 4. Frequencies and percentages of participants who used CAM for MS in the past 12 months, by type of therapy

	CAM users		All subjects (n=35)
	n	(%)	(%)
Any	**27**	**(100)**	**(77.1)**
Alternative medical systems	**3**	**(11.1)**	**(8.6)**
Acupuncture	1	(3.7)	(2.9)
Ayurveda	0	(0)	(0)
Homeopathic treatment	1	(3.7)	(2.9)
Naturopathy	2	(7.4)	(5.7)
Traditional healers	0	(0)	(0)
Curandero	0	(0)	(0)
Espiritista	0	(0)	(0)
Hierbero or Yerbera	0	(0)	(0)
Shaman	0	(0)	(0)
Botanica	0	(0)	(0)
Native American Healer or Medicine man	0	(0)	(0)
Sobador	0	(0)	(0)
Biologically based therapies	**24**	**(88.9)**	**(68.6)**
Chelation therapy	0	(0)	(0)
Nonvitamin, nonmineral, natural products[a]	12	(44.4)	(34.3)
Diet-based therapies	8	(29.6)	(22.9)
Vegetarian diet	0	(0)	(0)
Macrobiotic diet	0	(0)	(0)
Atkins diet	0	(0)	(0)
Pritikin diet	0	(0)	(0)
Ornish diet	0	(0)	(0)
Zone diet	0	(0)	(0)
South Beach	0	(0)	(0)
Swank diet	2	(7.4)	(5.7)
Paleo diet	2	(7.4)	(5.7)
Combination	4	(14.8)	(11.4)
Supplements[a]	24	(88.9)	(68.6)
Vitamin mineral intake ≤RDA	5	(18.5)	(14.3)
Vitamin mineral intake >RDA and <UL	5	(18.5)	(14.3)
Vitamin mineral intake ≥UL	9	(33.3)	(25.7)
Vitamin mineral intake unknown	5	(18.5)	(14.3)
Manipulative and body based therapies	**13**	**(48.1)**	**(37.1)**
Chiropractic or osteopathic manipulation	5	(18.5)	(14.3)
Massage	6	(22.2)	(17.1)

Table 4. Frequencies and percentages of participants who used CAM for MS in the past 12 months, by type of therapy (continued)

	CAM users		All subjects (n=35)
	n	**(%)**	**(%)**
Movement therapies	4	(14.8)	(11.4)
Feldenkreis	0	(0)	(0)
Alexander Technique	1	(3.7)	(2.9)
Pilates	3	(11.1)	(8.6)
Trager Psychophysical Integration	0	(0)	(0)
Mind-body therapies	**12**	**(44.4)**	**(34.3)**
Biofeedback	0	(0)	(0)
Relaxation Techniques [b]	9	(33.3)	(25.7)
Hypnosis	0	(0)	(0)
Yoga, Tai chi, and/or Qi gong	5	(18.5)	(14.3)
Energy healing therapy	**2**	**(7.4)**	**(5.7)**

[a] Used within the past 30 days
[b] Meditation, guided imagery, progressive relaxation, and/or deep breathing exercises

Table 5. Characteristics of participants who used CAM for MS in the past 12 months, frequency by CAM category

	Alternative medical systems		Biologically based therapies		Manipulative and body based therapies		Mind body therapies		Energy healing therapies		Non-users of CAM	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
All subjects	3	(100)	24	(100)	13	(100)	12	(100)	2	(100)	8	(100)
Sex												
Male	0	(0)	2	(8.3)	1	(7.7)	2	(16.7)	0	(0)	0	(0)
Female	3	(100)	22	(91.7)	12	(92.3)	10	(83.3)	2	(100)	8	(100)
Age (y)												
18-29	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(12.5)
30-39	0	(0)	5	(20.8)	0	(0)	0	(0)	0	(0)	4	(50)
40-49	1	(33.3)	5	(20.8)	2	(15.4)	4	(33.3)	1	(50)	2	(25)
50-59	1	(33.3)	7	(29.2)	6	(46.2)	3	(25.0)	1	(50)	0	(0)
60-69	0	(0)	6	(25)	3	(23.1)	4	(33.3)	0	(0)	1	(12.5)
70-85	1	(33.3)	1	(4.2)	0	(0)	1	(8.3)	0	(0)	0	(0)
> 85	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Race												
American Indian or Alaska Native	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Asian	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Black or African American	0	(0)	1	(4.2)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
Native Hawaiian or other Pacific Islander	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
White	2	(66.7)	22	(91.7)	12	(92.3)	11	(91.7)	2	(100)	8	(100)
Other	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Refused	1	(33.3)	1	(4.2)	0	(0)	0	(0)	0	(0)	0	(0)
Ethnicity												
Hispanic	0	(0)	1	(4.2)	0	(0)	1	(8.3)	0	(0)	0	(0)
Non-Hispanic	3	(100)	23	(95.8)	13	(100)	11	(91.7)	2	(100)	8	(100)
Education												
Less than high school	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
High school diploma or equivalent	0	(0)	1	(4.2)	1	(7.7)	1	(8.3)	0	(0)	1	(12.5)
Some college, no degree	0	(0)	3	(12.5)	2	(15.4)	1	(8.3)	0	(0)	2	(25)
Postsecondary non-degree award	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Associate's degree	0	(0)	2	(8.3)	0	(0)	1	(8.3)	0	(0)	1	(12.5)

Table 5. Characteristics of participants who used CAM for MS in the past 12 months, frequency by CAM category (continued)

	Alternative medical systems		Biologically based therapies		Manipulative and body based therapies		Mind body therapies		Energy healing therapies		Non-users of CAM	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Bachelor's degree	1	(33.3)	10	(41.7)	6	(46.2)	4	(33.3)	1	(50)	3	(37.5)
Master's degree	1	(33.3)	5	(20.8)	3	(23.1)	4	(33.3)	1	(50)	1	(12.5)
Doctoral or professional degree	1	(33.3)	3	(12.5)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
Household income (US$)												
<$25,000	0	(0)	2	(8.3)	0	(0)	0	(0)	0	(0)	2	(25)
$25,000-$50,999	0	(0)	4	(16.7)	1	(7.7)	4	(33.3)	0	(0)	3	(37.5)
$51,000-$75,000	2	(66.7)	8	(33.3)	5	(38.5)	3	(25.0)	1	(50)	0	(0)
≥$75,000	1	(33.3)	8	(33.3)	6	(46.2)	4	(33.3)	1	(50)	3	(37.5)
Refused	0	(0)	2	(8.3)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
Geographic Region												
Delaware	1	(33.3)	2	(8.3)	1	(7.7)	1	(8.3)	1	(50)	1	(12.5)
Florida	0	(0)	7	(29.2)	4	(30.8)	3	(35.0)	0	(0)	2	(25)
Illinois	0	(0)	1	(4.2)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
Maryland	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(12.5)
Missouri	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	1	(12.5)
New Jersey	0	(0)	4	(16.7)	1	(7.7)	2	(16.7)	0	(0)	2	(25)
New York	2	(66.7)	5	(20.8)	3	(23.1)	2	(16.7)	1	(50)	0	(0)
Pennsylvania	0	(0)	3	(12.5)	2	(15.4)	2	(16.7)	0	(0)	1	(12.5)
Virginia	0	(0)	2	(8.3)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
Form of MS												
Relapsing remitting	2	(66.7)	20	(83.3)	10	(76.9)	9	(75)	1	(50)	7	(87.5)
Primary progressive	0	(0)	0	(0)	0	(0)	1	(8.3)	0	(0)	0	(0)
Secondary progressive	1	(33.3)	3	(12.5)	2	(15.4)	1	(8.3)	1	(50)	1	(12.5)
Progressive relapsing	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
Unknown	0	(0)	1	(4.2)	1	(7.7)	1	(8.3)	0	(0)	0	(0)
MS duration (y)												
1-5	0	(0)	10	(41.7)	7	(53.8)	3	(25)	0	(0)	2	(25)
6-10	0	(0)	5	(20.8)	3	(23.1)	5	(41.7)	0	(0)	4	(50)
11-15	1	(33.3)	3	(12.5)	2	(15.4)	1	(8.3)	1	(50)	1	(12.5)
15+	2	(66.7)	6	(25)	1	(7.7)	3	(25)	1	(50)	1	(12.5)
MS severity												

Table 5. Characteristics of participants who used CAM for MS in the past 12 months, frequency by CAM category (continued)

	Alternative medical systems		**Biologically based therapies**		**Manipulative and body based therapies**		**Mind body therapies**		**Energy healing therapies**		**Non-users of CAM**	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
None/minimal	0	(0)	2	(8.3)	0	(0)	1	(8.3)	0	(0)	3	(37.5)
Mild	1	(33.3)	8	(33.3)	4	(30.8)	3	(25)	0	(0)	2	(25)
Moderate	0	(0)	5	(20.8)	4	(30.8)	3	(25)	0	(0)	1	(12.5)
Some support needed for walking	0	(0)	6	(25)	3	(23.1)	3	(25)	0	(0)	2	(25)
Walker/two-handed crutch	2	(66.7)	3	(12.5)	2	(15.4)	2	(16.7)	2	(100)	0	(0)
Unable to walk	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)

Table 6. Total nutrient intake (diet and supplements) of all participants (n=33)

	Mean (sd)	Median	25th	75th	%EAR	%RDA/AI	<EAR (%)	>UL (%)
Energy (kcal)	1859 (646)	1790	1473	2221	--	--	--	--
Protein (g)	84 (30)	84	64	98	--	--	--	--
% kcal from protein	18.5 (4.5)	17.7	15.5	21.9	--	--	--	--
Carbohydrates (g)	208 (74)	210	156	273	--	--	--	--
% kcal from CHO	45.1 (8.5)	45.9	39.1	50.8	--	--	--	--
Dietary fiber (g)	21.5 (11.6)	19.5	12.1	25.6	--	--	--	--
Total Fat (g)	79 (36)	75	49	92	--	--	--	--
% kcal from fat	37.2 (7.8)	36.8	32.0	43.0	--	--	--	--
Saturated (g)	26.5 (19)	21.3	14.8	30.8	--	--	--	--
Cholesterol (mg)	282 (178)	244	149	366	--	--	--	--
Vitamins								
Vitamin C (mg)	203 (293)	120	53	179	335	268	27.3	0.0
Thiamin (mg)	8.2 (15.1)	2.0	1.2	4.6	887	729	9.1	--
Riboflavin (mg)	7.5 (12.9)	2.8	1.7	4.6	797	657	3.0	--
Niacin (mg)	39.1 (23.7)	30.7	23.4	51.3	352	275	3.0	42.4
Vitamin B6 (mg)	9.2 (14.9)	2.9	1.9	7.9	763	674	6.1	0.0
Folate (mcg)	596 (337)	523	359	684	186	149	18.2	12.1
Vitamin B12 (mcg)	204.4 (425.9)	11.1	5.4	156	10,222[a]	8518	3.0	--
Vitamin A (RAE)	1485 (1370)	1247	506	1957	294	210	24.2	6.1
Vitamin E (mg)	32.0 (59.0)	9.8	5.8	32.9	267	213	51.5	0.0
Vitamin D (mcg)	72.0 (215.2)	15.8	8.4	57.2	720	479	27.3	12.1
Minerals								
Calcium (mg)	1429 (723)	1353	847	1841	162	132	21.2	15.2
Iron (mg)	23.1 (19.5)	16.2	13.6	23.5	363	203	6.1	12.1
Magnesium (mg)	434 (237)	349	294	534	161	133	21.2	48.5
Phosphorus (mg)	1391 (450)	1358	1151	1635	238	199	3.0	0.0
Potassium (mg)	3288 (1543)	3048	2282	4039	--	70	--	--
Sodium (mg)	3409 (1439)	3092	2490	3904	--	244	--	81.8
Zinc (mg)	16.8 (11.3)	13.3	8.2	20.8	240	204	12.1	6.1

Table 6. Total nutrient intake (diet and supplements) of all participants (n=33) (continued)

	Mean (sd)	Median	25th	75th	%EAR	%RDA/AI	<EAR (%)	>UL (%)
Copper (mg)	2.0 (1.2)	1.6	1.2	2.6	287	223	6.1	0
Selenium (mcg)	123 (63)	109	85	145	273	223	6.1	0
Vegetables (cup-eq/d)	2.4 (1.8)	1.9	1.1	3.6	--	--	--	--
Fruit (cup-eq/d)	0.9 (1.1)	0.7	0.01	1.2	--	--	--	--

[a] includes supplement users; -- no data available

Table 7. Total nutrient intake of participants, non-supplement users only (n=1)

	Mean	%EAR	%RDA/AI	<EAR (%)	>UL (%)
Energy (kcal)	3015	--	--	--	--
Protein (g)	116	--	--	--	--
% kcal from protein	15.4	--	--	--	--
Carbohydrates (g)	309	--	--	--	--
% kcal from CHO	41	--	--	--	--
Dietary fiber (g)	10.0	--	--	--	--
Total Fat (g)	145	--	--	--	--
% kcal from fat	43.4	--	--	--	--
Saturated (g)	62	--	--	--	--
Cholesterol (mg)	381	--	--	--	--
Vitamins					
Vitamin C (mg)	10.9	18	14.5	100	0
Thiamin (mg)	2.3	257	210	0	--
Riboflavin (mg)	4.4	487	399	0	--
Niacin (mg)	40.5	368	289	0	100
Vitamin B6 (mg)	1.8	163	138	0	0
Folate (mcg)	451	141	113	0	0
Vitamin B12 (mcg)	3.4	167	139	0	--
Vitamin A (RAE)	744	149	106	0	0
Vitamin E (mg)	5.9	49	39.6	100	0
Vitamin D (mcg)	2.8	27	18.3	100	0
Minerals					
Calcium (mg)	1539	192	154	0	0
Iron (mg)	13.8	170	76.5	0	0
Magnesium (mg)	323	122	101	0	0
Phosphorus (mg)	2016	345	288	0	0
Potassium (mg)	3505	--	74.6	--	--
Sodium (mg)	7627	--	509	--	100
Zinc (mg)	10.5	154	131	0	0
Copper (mg)	1.3	182	141	0	0
Selenium (mcg)	132	294	241	0	0
Vegetables (cup-eq/d)	1.1	--	--	--	--
Fruit (cup-eq/d)	0.0	--	--	--	--

-- no data available

Table 8. Total nutrient intake (diet and supplements) of participants, supplement users only (n=32)

	Mean (sd)	Median	25th	75th	%EAR	%RDA/AI	<EAR (%)	>UL (%)
Energy (kcal)	1823 (621)	1781	1464	2215	--	--	--	--
Protein (g)	83 (30)	82	63	96	--	--	--	--
% kcal from protein	18.6 (4.6)	18.0	15.5	22.1	--	--	--	--
Carbohydrates (g)	205 (73)	208	155	268	--	--	--	--
% kcal from CHO	45.2 (8.6)	45.9	38.9	50.9	--	--	--	--
Dietary fiber (g)	21.9 (11.6)	19.9	12.8	25.8	--	--	--	--
Total Fat (g)	76 (34)	74	48	89	--	--	--	--
% kcal from fat	37.0 (7.8)	36.6	31.7	42.4	--	--	--	--
Saturated (g)	25.4 (18.1)	20.6	14.5	29.9	--	--	--	--
Cholesterol (mg)	279 (180)	243	146	350	--	--	--	--
Vitamins								
Vitamin C (mg)	209 (295)	122	56	180	345	276	25.0	0
Thiamin (mg)	8.3 (15.2)	2.0	1.2	5.0	907	745	9.4	--
Riboflavin (mg)	7.6 (13.1)	2.8	1.7	4.6	807	665	3.1	--
Niacin (mg)	39.0 (24.1)	30.2	23.2	51.3	351	275	3.1	40.6
Vitamin B6 (mg)	9.4 (15.1)	3.0	2.0	8.7	782	691	6.3	0
Folate (mcg)	600 (341)	526	341	689	188	150	18.8	12.5
Vitamin B12 (mcg)	211 (431)	19	6	205	10,536[a]	8780	3.1	--
Vitamin A (RAE)	1509 (1386)	1274	498	2020	299	213	25.0	6.3
Vitamin E (mg)	32.8 (59.8)	11.6	6.1	37.1	273	219	50.0	0
Vitamin D (mcg)	74.1 (218.3)	17.0	9.6	60.0	741	494	25.0	12.5
Minerals								
Calcium (mg)	1426 (734)	1349	838	1849	161	131	21.9	15.6
Iron (mg)	23.4 (19.7)	17.2	13.6	24.2	369	207	6.3	12.5
Magnesium (mg)	438 (240)	382	293	535	162	134	21.9	50.0
Phosphorus (mg)	1372 (443)	1338	1140	1605	235	196	3.1	0
Potassium (mg)	3282 (1567)	3010	2212	4060	--	69.8	--	--
Sodium (mg)	3277 (1243)	3088	2472	3842	--	235	--	81.3
Zinc (mg)	16.9 (11.4)	14.7	8.1	21.0	242	206	12.5	6.3
Copper (mg)	2.0 (1.2)	1.7	1.1	2.7	290	225	6.3	0
Selenium (mcg)	122 (64)	108	82	148	272	222	6.3	0
Vegetables (cup-eq/d)	2.5 (1.8)	2.0	1.1	3.6	--	--	--	--
Fruit (cup-eq/d)	0.9 (1.1)	0.7	0.0	1.2	--	--	--	--

[a] includes supplement users; -- no data available

Table 9. Total nutrient intake (diet and supplements) of participants who used CAM and did not use CAM for MS and in the past 12 months (n=33)

	CAM Users (n=25)			Non-Users (n=8)			
	Median	Mean	(sd)	Median	Mean	(sd)	*p*-value
Energy (kcal)	1773	1753	(568)	2021	2192	(795)	0.27
Protein (g)	84	82	(27)	77	89	(37)	0.76
% kcal from protein	18.9	19.1	(4.8)	16.0	16.4	(2.6)	0.20
Carbohydrates (g)	204	193	(69)	285	256	(72)	0.036
% kcal from CHO	45.8	44.1	(8.1)	48.1	48.3	(9.5)	0.45
Dietary fiber (g)	20.6	21.7	(10.9)	17.5	20.8	(14.4)	0.42
Total Fat (g)	75.0	73	(28)	76.9	96	(51)	0.58
% kcal from fat	36.8	37.1	(7.4)	39.2	37.6	(9.3)	0.70
Saturated (g)	18.3	21.3	(10.7)	29.3	42.5	(29.4)	0.074
% kcal from sat fat	10.8	10.8	(3.4)	15.2	16.0	(6.3)	0.049
Cholesterol (mg)	244	287	(179)	231	267	(184)	0.79
Vitamins							
Vitamin C (mg)	107	226	(332)	141	130	(69)	0.76
Thiamin (mg)	1.7	9.3	(17.1)	3.2	4.7	(4.0)	0.15
Riboflavin (mg)	2.7	7.9	(14.6)	4.2	6.2	(5.8)	0.08
Niacin (mg)	29.7	35.8	(20.3)	37.3	49.3	(31.6)	0.29
Vitamin B6 (mg)	2.9	10.3	(16.9)	3.1	5.7	(5.2)	0.76
Folate (mcg)	481	538	(287)	646	774	(433)	0.15
Vitamin B12 (mcg)	7.6	164	(302)	19.2	331	(702)	0.82
Vitamin A (RAE)	1247	1542	(1516)	1226	1308	(812)	0.95
Vitamin E (mg)	9.8	34.1	(66.8)	16.1	25.5	(23.4)	0.79
Vitamin D (mcg)	15.8	81.2	(246)	19.3	43.2	(49.4)	0.82
Minerals							
Calcium (mg)	1328	1285	(626)	1645	1881	(858)	0.09
Iron (mg)	15.8	19.6	(14.7)	25.1	34.3	(28.3)	0.12
Magnesium (mg)	416	425	(242)	333	462	(234)	0.85
Phosphorus (mg)	1319	1313	(421)	1530	1635	(476)	0.16
Potassium (mg)	2874	3020	(1166)	3518	4126	(2272)	0.22
Sodium (mg)	3084	3147	(1217)	3684	4226	(1837)	0.13
Zinc (mg)	12.8	13.8	(7.5)	21.9	26.1	(16.0)	0.025
Copper (mg)	1.6	1.9	(1.1)	1.9	2.5	(1.6)	0.33
Selenium (mcg)	108	119	(67.2)	122	133	(48)	0.40
Vegetables (cup-eq/d)	1.9	2.5	(1.9)	2.1	2.3	(1.6)	0.92
Fruit (cup-eq/d)	0.8	1.0	(1.2)	0.5	0.5	(0.4)	0.37

Table 10. Energy-adjusted total nutrient intake (diet and supplements) of participants who used CAM and did not use CAM for MS and in the past 12 months (n=33)

	CAM Users (n=25)		Non-users (n=8)		
	Mean	(SEM)	Mean	(SEM)	*p*-value
Energy (kcal)	1753	(568)	2192	(795)	0.27
Protein (g)	86	(3.7)	77	(6.8)	0.249
% kcal from protein	18.9	(0.9)	17.0	(1.6)	0.302
Carbohydrates (g)	203	(7.6)	225	(13.7)	0.175
% kcal from CHO	43.8	(1.7)	49.1	(3.1)	0.154
Dietary fiber (g)	22.3	(2.3)	19.0	(3.2)	0.508
Total Fat (g)	78	(3.0)	79	(5.4)	0.980
% kcal from fat	37.5	(1.6)	36.3	(2.8)	0.725
Saturated (g)	23.6	(2.0)	35.3	(3.7)	0.011
% kcal from sat fat	11.1	(0.1)	15.2	(1.5)	0.023
Cholesterol (mg)	303	(31)	216	(57)	0.195
Vitamins					
Vitamin C (mg)	225	(60)	134	(109)	0.481
Thiamin (mg)	9.3	(3.1)	4.6	(5.7)	0.483
Riboflavin (mg)	7.8	(2.7)	6.6	(4.9)	0.830
Niacin (mg)	36.8	(4.7)	46.4	(8.4)	0.335
Vitamin B6 (mg)	10.4	(3.1)	5.5	(5.6)	0.453
Folate (mcg)	537	(67)	777	(121)	0.099
Vitamin B12 (mcg)	184	(84.2)	267	(152)	0.642
Vitamin A (RAE)	1578	(282)	1195	(511)	0.523
Vitamin E (mg)	32.9	(12.2)	29.1	(22.1)	0.884
Vitamin D (mcg)	72.8	(43.7)	69.3	(79.1)	0.970
Minerals					
Calcium (mg)	1300	(140)	1832	(253)	0.080
Iron (mg)	20.2	(3.8)	32.2	(6.8)	0.140
Magnesium (mg)	432	(48.8)	442	(88.4)	0.921
Phosphorus (mg)	1374	(51.8)	1446	(93.7)	0.509
Potassium (mg)	3140	(297)	3751	(488)	0.290
Sodium (mg)	3342	(158)	3615	(287)	0.418
Zinc (mg)	14.2	(2.0)	24.7	(3.6)	0.019
Copper (mg)	1.9	(0.243)	2.3	(0.4)	0.409
Selenium (mcg)	124	(11.8)	119	(21.4)	0.844
Vegetables (cup-eq/d)	2.5	(0.4)	2.2	(0.7)	0.728
Fruit (cup-eq/d)	1.0	(0.2)	0.5	(0.4)	0.271

Table 11. Total nutrient intake (diet and supplements) of participants who used CAM for MS in the past 12 months, by CAM category

	Alternative medical systems n=3		**Biologically based therapies n=22**		**Manipulative and body based therapies n=11**		**Mind-body therapies n=11**		**Energy healing therapy n=2**		**Non-users of CAM for MS n=8**	
	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)	Mean	(sd)
Energy (kcal)	1720	(427)	1760	(564)	1819	(340)	1724	(817)	1834	(535)	2192	(795)
Protein (g)	85	(19)	84	(27)	83	(24)	85	(35)	93	(19)	89	(37)
% kcal from protein	20.8	(7.6)	19.7	(4.8)	18.5	(5.4)	20.6	(5.3)	21.7	(10.5)	16.4	(2.6)
Carbohydrates (g)	179	(115)	193	(68.7)	190	(62)	181	(85)	192	(160)	256	(72)
% kcal from CHO	39.4	(16.8)	43.9	(8.7)	41.4	(9.8)	42.7	(9.0)	38.4	(23.7)	48.3	(9.5)
Dietary fiber (g)	27.3	(17.8)	22.3	(11.4)	23.6	(10.7)	19.7	(9.8)	31.1	(23.3)	20.8	(14.4)
Total Fat (g)	78	(8.3)	73	(27)	80	(17)	72	(41)	83	(1.2)	96	(51)
% kcal from fat	42.2	(8.4)	37.2	(7.7)	40.3	(8.9)	36.1	(7.4)	42.6	(11.8)	37.6	(9.3)
Saturated (g)	16.4	(3.2)	21.1	(10.6)	22.9	(8.6)	21.5	(14.0)	14.6	(1.2)	42.5	(29.4)
Cholesterol (mg)	514	(312)	302	(182)	348	(223)	298	(183)	693	(33)	267	(184)
Vitamins												
Vitamin C (mg)	141	(97)	222	(340)	241	(314)	342	(460)	189	(65)	130	(69)
Thiamin (mg)	1.5	(0.6)	8.0	(15.7)	6.4	(15.4)	13.0	(20.6)	1.8	(0.4)	4.7	(4.0)
Riboflavin (mg)	2.1	(1.1)	6.4	(12.2)	7.2	(15.3)	13.7	(20.6)	2.8	(0.1)	6.2	(5.8)
Niacin (mg)	28.3	(13.4)	34.6	(20.8)	35.1	(19.8)	40.5	(21.7)	34.1	(12.6)	49.3	(31.6)
Vitamin B6 (mg)	2.9	(0.9)	9.1	(15.5)	8.0	(15.4)	13.8	(20.6)	3.4	(0.3)	5.7	(5.2)
Folate (mcg)	656	(544)	522	(301)	600	(347)	517	(236)	917	(427)	774	(433)
Vitamin B12 (mcg)	5.9	(0.6)	182	(318)	148	(320)	155	(317)	6.2	(0.3)	331	(702)
Vitamin A (RAE)	3994	(3362)	1626	(1591)	2164	(2047)	1408	(1648)	5934	(99)	1308	(812)
Vitamin E (mg)	15.5	(9.4)	36.2	(70.8)	41.3	(81.3)	31.1	(62.5)	20.4	(5.6)	25.5	(23.4)
Vitamin D (mcg)	18.4	(14.8)	33.2	(34.6)	32.2	(35.2)	149.3	(367.6)	22.4	(18.5)	43.2	(49.4)
Minerals												
Calcium (mg)	945	(237)	1250	(618)	1342	(671)	1444	(797)	882	(297)	1881	(858)
Iron (mg)	15.4	(4.2)	20.4	(15.5)	19.2	(16.0)	18.8	(16.3)	17.7	(2.2)	34.3	(28.3)
Magnesium (mg)	379	(72)	434	(253)	460	(274)	459	(310)	405	(79)	462	(234)

Table 11. Total nutrient intake (diet and supplements) of participants who used CAM for MS in the past 12 months, by CAM category (continued)

	Alternative medical systems n=3		Biologically based therapies n=22		Manipulative and body based therapies n=11		Mind-body therapies n=11		Energy healing therapy n=2		Non-users of CAM for MS n=8	
Phosphorus (mg)	1309	(268)	1327	(436)	1313	(386)	1367	(553)	1442	(193)	1635	(476)
Potassium (mg)	3453	(1937)	3100	(1208)	3431	(1219)	2893	(1107)	4109	(2218)	4126	(2272)
Sodium (mg)	3217	(1301)	3275	(1211)	3234	(726)	3087	(1590)	3933	(554)	4226	(1837)
Zinc (mg)	12.8	(3.3)	13.4	(7.0)	13.4	(7.0)	14.5	(9.0)	11.1	(2.3)	26.1	(16.0)
Copper (mg)	2.1	(0.7)	1.8	(0.9)	1.9	(1.0)	2.0	(1.3)	2.5	(0.3)	2.5	(1.6)
Selenium (mcg)	106	(51)	114	(54)	102	(39)	119	(75)	134	(26)	133	(48)
Vegetables (cup-eq/d)	4.9	(3.7)	2.7	(1.9)	3.2	(2.3)	1.9	(1.4)	6.3	(3.9)	2.3	(1.6)
Fruit (cup-eq/d)	1.4	(2.4)	0.9	(1.2)	1.2	(1.3)	0.6	(0.8)	2.2	(2.9)	0.5	(0.4)

Table 12. Total nutrient intake (diet and supplements) by specific diet for MS (n=33)

	Swank (n=2)		Paleo (n=2)		Combination (n=3)[a]		Not on diet for MS (n=26)[a]	
	Mean (sd)	%EAR	Mean (sd)	%EAR	Mean (sd)	%EAR	Mean (sd)	%EAR
Energy (kcal)	1449 (60)	--	1723 (71)	--	1857 (380)	--	1902 (710)	--
Protein (g)	77 (10)	--	80 (20)	--	98 (17)	--	83 (32)	--
% kcal from protein	21.4 (3.5)	--	18.5 (4.0)	--	22.2 (7.5)	--	17.8 (4.2)	--
Carbohydrates (g)	167 (17)	--	192 (29)	--	202 (114)	--	213 (75)	--
% kcal from CHO	46.1 (6.7)	--	44.8 (8.5)	--	41.2 (17.4)	--	45.5 (7.9)	--
Dietary fiber (g)	15.7 (5.3)	--	27.8 (8.2)	--	29.6 (16.7)	--	20.5 (11.4)	--
Total Fat (g)	54 (21)	--	76 (8)	--	79 (8)	--	81 (39)	--
% kcal from fat	33.1 (11.9)	--	40.0 (2.7)	--	39.3 (10.1)	--	37.1 (7.8)	--
Saturated (g)	17.9 (2.9)	--	32.2 (6.4)	--	15.3 (1.5)	--	28.0 (20.8)	--
Cholesterol (mg)	204 (71)	--	255 (16)	--	645 (87)	--	248 (148)	--
Vitamins								
Vitamin C (mg)	28.5 (18.3)	48	127.7 (10.7)	213	185.3 (46.5)	289	224 (326)	372
Thiamin (mg)	1.2 (0.5)	128	1.8 (0.1)	197	2.4 (1.2)	256	9.9 (16.6)	1072
Riboflavin (mg)	1.3 (0.6)	147	2.8 (0.4)	316	3.7 (1.6)	370	8.8 (14.4)	933
Niacin (mg)	23.3 (9.1)	212	21.7 (6.1)	197	36.0 (9.6)	319	42.0 (25.6)	378
Vitamin B6 (mg)	1.5 (0.5)	115	2.8 (0.4)	235	5.4 (3.5)	417	10.7 (16.5)	893
Folate (mcg)	229 (133)	71	576 (140)	180	1023 (353)	320	576 (317)	180
Vitamin B12 (mcg)	253 (351)	12,660[b]	5 (1)	250	13.5 (12.6)	675	238 (467)	11,903
Vitamin A (RAE)	366 (357)	73	2528 (414)	506	4523 (2445)	882	1141 (703)	227
Vitamin E (mg)	4.8 (1.2)	40	10.8 (5.0)	90	34.5 (97.4)	287	35.4 (65.6)	295
Vitamin D (mcg)	30.5 (28.3)	305	1.8 (1.1)	18	20.2 (13.6)	202	86.5 (241.2)	865
Minerals								
Calcium (mg)	1746 (953)	175	1352 (34)	152	1036 (339)	120	1456 (772)	167
Iron (mg)	10.2 (0.9)	205	20.1 (2.5)	318	16.8 (2.2)	278	25.1 (21.5)	389
Magnesium (mg)	774 (633)	292	487 (78)	184	415 (59)	143	406 (212)	151
Phosphorus (mg)	963 (113)	165	1359 (97)	232	1517 (188)	260	1412 (488)	242
Potassium (mg)	2026 (164)	--	3795 (1450)	--	4193 (1575)	--	3242 (1586)	--

Table 12. Total nutrient intake (diet and supplements) by specific diet for MS (n=33) (continued)

	Swank (n=2)		**Paleo (n=2)**		**Combination (n=3)**[a]		**Not on diet for MS (n=26)**[a]	
	Mean (sd)	%EAR	Mean (sd)	%EAR	Mean (sd)	%EAR	Mean (sd)	%EAR
Sodium (mg)	2434 (919)	--	2684 (226)	--	4029 (426)	--	3468 (1559)	--
Zinc (mg)	11.6 (6.4)	170	14.5 (7.5)	214	16.9 (10.1)	210	17.3 (12.2)	250
Copper (mg)	1.1 (0.3)	159	1.8 (0.4)	252	3.1 (10.1)	439	2.0 (1.3)	281
Selenium (mcg)	80.2 (41.0)	178	84.3 (33.2)	187	148.4 (31.2)	330	125.9 (66.9)	280
Vegetables (cup-eq/d)	1.5 (0.7)	--	3.0 (2.0)	--	5.5 (3.1)	--	2.1 (1.4)	--
Fruit (cup-eq/d)	0.0 (0.0)	--	1.9 (0.7)	--	2.0 (2.1)	--	0.7 (0.9)	--

[a] excludes one subject with incomplete dietary recall
[b] includes supplement users
-- data not available

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Appendix A

IRB HUMAN SUBJECTS APPROVAL

RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
Ph: 302/831-2136
Fax: 302/831-2828

DATE: August 14, 2012

TO: Laura Masullo, BS
FROM: University of Delaware IRB

STUDY TITLE: [367018-1] Health Practices and Dietary Intake Among Individuals with Multiple Sclerosis

SUBMISSION TYPE: New Project

ACTION: DETERMINATION OF EXEMPT STATUS
DECISION DATE: August 14, 2012

REVIEW CATEGORY: Exemption category # 2

Thank you for your submission of New Project materials for this research study. The University of Delaware IRB has determined this project is EXEMPT FROM IRB REVIEW according to federal regulations.

We will put a copy of this correspondence on file in our office. Please remember to notify us if you make any substantial changes to the project.

If you have any questions, please contact Jody-Lynn Berg at (302) 831-1119 or jlberg@udel.edu. Please include your study title and reference number in all correspondence with this office.

UNIVERSITY OF DELAWARE

RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
Ph: 302/831-2136
Fax: 302/831-2828

DATE: October 10, 2012

TO: Laura Masullo, BS
FROM: University of Delaware IRB

STUDY TITLE: [367018-2] Health Practices and Dietary Intake Among Individuals with Multiple Sclerosis

SUBMISSION TYPE: Amendment/Modification

ACTION: DETERMINATION OF EXEMPT STATUS
DECISION DATE: October 10, 2012

REVIEW CATEGORY: Exemption category # 2

Thank you for your submission of Amendment/Modification materials for this research study. The University of Delaware IRB has determined this project remains EXEMPT FROM IRB REVIEW according to federal regulations.

We will put a copy of this correspondence on file in our office. Please remember to notify us if you make any substantial changes to the project.

If you have any questions, please contact Jody-Lynn Berg at (302) 831-1119 or jlberg@udel.edu. Please include your study title and reference number in all correspondence with this office.

Appendix B

INFORMED CONSENT

Informed Consent

Study Title: The Health Practices and Dietary Intake Among Individuals with Multiple Sclerosis

VERBAL CONSENT SCRIPT

Hi, my name is Laura Masullo and I am involved in a research study at the University of Delaware.

1. **PURPOSE / DESCRIPTION OF THE RESEARCH**
   We are asking you to take part in a research study because we are trying to learn more about the health practices and dietary intake among people with multiple sclerosis, or MS.

2. **WHAT YOU WILL DO**
   If you decide to participate in this study, you will be asked to complete a telephone interview. A member of the research team will administer a survey to you over the phone and record your answers in a computer using Qualtrics Survey Software. In addition, you will fill out a 24-hour dietary recall, for which you will report everything you ate and drank during the previous day. In order to report your food and beverage intake, you will be asked to visit a website from your home computer that will record everything you report. This online tool, called ASA24, will guide you through the reporting process. A member of the research team will remain on the phone to provide assistance. The entire process will take approximately 1-2 hours.

3. **CONDITIONS OF SUBJECT PARTICIPATION**
   To participate in this study, you must be at least 18 years of age and have been diagnosed with multiple sclerosis for at least one year prior to enrollment. Subjects must be home dwelling and have access to a telephone and high speed internet, which are both required for data collection. You must not have had an illness that affects usual intake of food, beverage, or supplements during the three days prior to data collection. We are looking to enroll up to 100 participants.

   All records related to your participation in this study will be stored in password protected electronic files and or locked file cabinets that only research personnel have access to. Study data will be kept for seven years. Your identity on these study records will be indicated by a number rather than by name. After seven years, the information will be destroyed.

The information gathered in this study will be kept confidential. The information will be aggregated for research purposes and no individuals will be identified.

Your participation in this study is completely voluntary. Without loss or penalty of any kind you can: choose not to take part in this study, choose not to answer a question on the questionnaire, or withdraw from the study at any time.

4. RISK AND BENEFITS

There are no known risks associated with participating in this study. You are being asked to complete a survey and dietary recall. All submitted surveys and diet recalls will be anonymous; your name will not be recorded on the survey. There are no known benefits with participating in this study.

Your participation in this study is voluntary; you may drop out of this study at any time if necessary.

Do you have any questions?

5. CONTACTS

If you have any questions or concerns about the research, please feel free to contact Laura Masullo, the Principal Investigator, or Co-Advisor, Jillian Trabulsi, by telephone or email:

Name: Laura Masullo, RD
Phone: 856-571-2342
Email: lmasullo@udel.edu

Name: Jillian Trabulsi, PhD RD
Phone: 302-831-4991
Email: trabulsi@udel.edu

If you have any concerns or complaints about the manner or conduct of the project, you may contact the Chairperson of the Human Subjects Review Board at 109 Hullihen Hall, University of Delaware, Newark, DE, 19716 or by telephone at 302-831-2137.

6. CONSENT

Do I have your consent to participate in this research study?

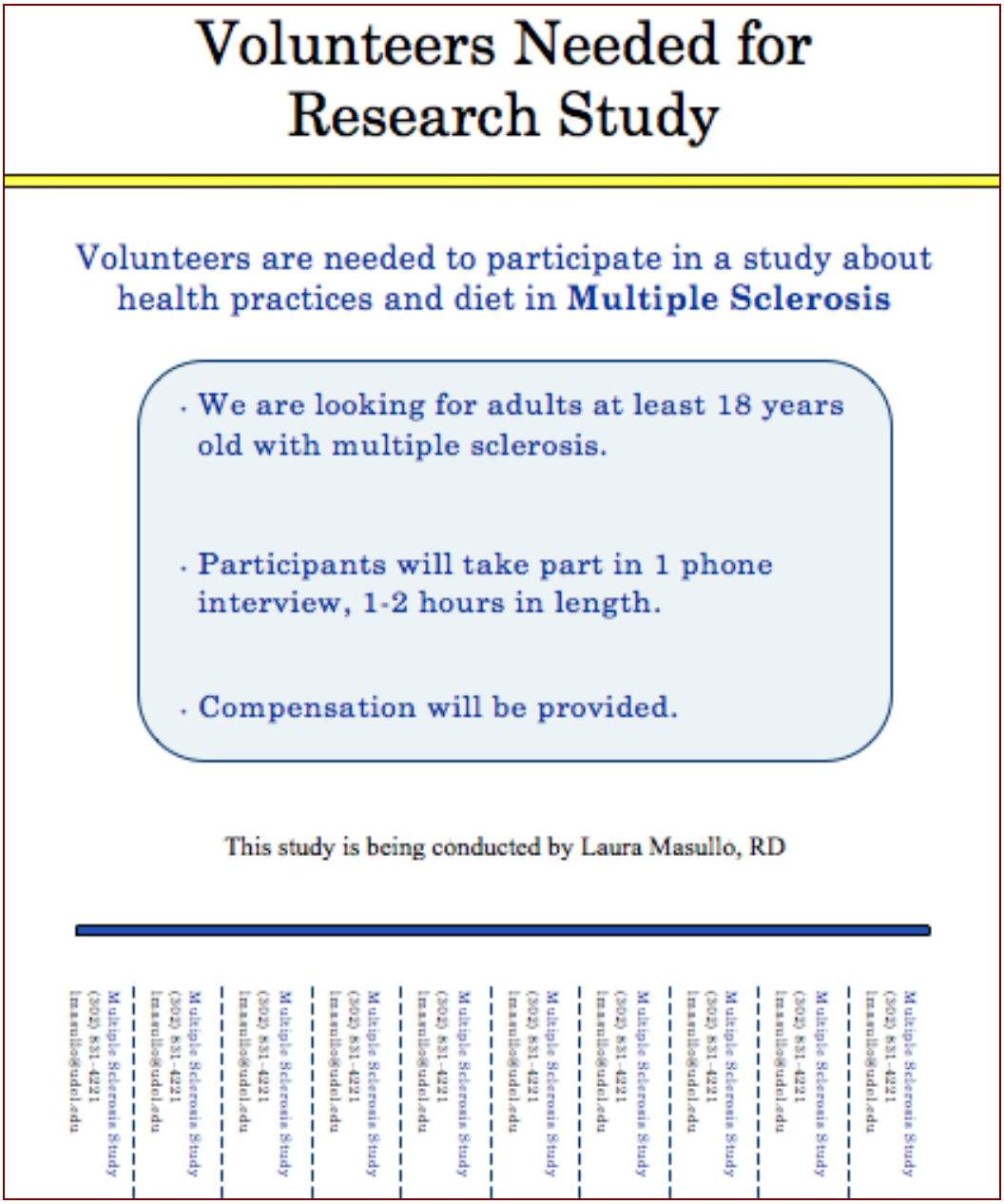
☐ **YES** ☐ **NO**

_____ _____

Subject Name Date

Appendix C

RECRUITMENT ADVERTISEMENTS



Do You Have Multiple Sclerosis?

If so, you may be eligible to participate in a research study. The purpose of the study is to learn more about the health practices and dietary intake of individuals with multiple sclerosis. The study consists of one telephone interview, 1-2 hours in length.

If you qualify to participate, a member of the study team will schedule an appointment with you. A survey will be administered to you over the phone, and you will visit a website on your home computer to complete a diet questionnaire. After you have completed both parts, a $25 gift card will be mailed to you as compensation. To participate, you must be at least 18 years old, have been diagnosed with multiple sclerosis at least one year prior to enrollment, and have access to a phone and high-speed internet. If you are interested in participating or would like to learn more about the study, please contact Laura Masullo at lmasullo@udel.edu or 302-831-2241.

Appendix D

PARTICIPANT HANDOUTS

Page 1: Medical History

Has a health care provider ever told you that you had any of these conditions? Select all that apply.

- High blood pressure
- Heart disease
- Irregular heart beat
- Pacemaker
- Stroke/TIA
- Kidney failure
- Kidney stones
- Seasonal allergies
- Hyperthyroid
- Hypothyroid
- Diabetes
- Liver disease
- Reflux
- Cancer
- irritable bowel syndrome
- Phlebitis/clots
- Asthma
- Glaucoma
- Multiple sclerosis
- Arthritis
- Fibromyalgia
- Hemophilia
- Chronic obstructive pulmonary disease
- Other
- None

Page 2: Health Problems or Conditions:

For what health problems or conditions did you use _____?

- acid reflux or heartburn
- angina
- anxiety
- asthmas
- arthritis
- attention deficit disorder/hyperactivity
- autism
- benign tumors, cysts
- bipolar disorder
- birth defect
- cancer
- cholesterol
- chronic bronchitis
- circulation problems (other than in legs)
- constipation (severe)
- coronary heart disease
- dementia, Alzheimer's Disease
- dental pain
- depression
- diabetes
- emphysema
- excessive sleepiness during the day
- excessive use of alcohol or tobacco
- fibromyalgia
- fracture, bone/joint injury
- gout
- gum disease
- gynecologic problem
- hay fever
- hearing problem
- heart attack
- other heart condition or disease
- hernia
- hypertension
- inflammatory bowel disease
- influenza or pneumonia
- insomnia or trouble sleeping
- irritable bowel
- jaw pain
- joint pain or stiffness/other joint condition
- knee problems (not arthritis, not joint injury)
- liver problem
- lung/breathing problem (not already listed)
- lupus
- mania or psychosis
- memory loss or loss of other cognitive function
- menopause
- menstrual problems
- mental retardation
- missing limbs (fingers, toes), amputee
- multiple sclerosis
- osteoporosis
- tendinitis
- other developmental problem
- other injury
- other nerve damage, including carpal tunnel syndrome
- phobia or fears
- polio (myelitis), paralysis, para/quadriplegia
- poor circulation in legs
- prostrate trouble or impotence
- regular headaches
- rheumatoid arthritis
- schizophrenia
- seizures
- senility
- sinusitis
- skin problems
- sprain or strain
- stroke
- substance abuse, other than alcohol or tobacco
- ulcer
- urinary problem
- varicose veins
- hemorrhoids
- vision problems
- weak or failing kidneys
- weight problem
- back pain or problem
- severe headache or migraine
- stomach or intestinal illness
- I don't know

Page 3: Herbals and Supplements

- ☐ combination herb pill
- ☐ androstenedione
- ☐ black cohosh
- ☐ carnitine
- ☐ chasteberry
- ☐ condroitin
- ☐ coenzyme Q-10
- ☐ comfrey
- ☐ conjugated linolenic acid (CLA)
- ☐ cranberry (pills, gelcaps)
- ☐ creatine
- ☐ DHEA
- ☐ echinacea
- ☐ ephedra
- ☐ evening primrose
- ☐ feverfew
- ☐ fiber or psyllium (pills or powder)
- ☐ fish oil or omega 3 or DHA fatty acid supplements
- ☐ flaxseed oils or pills
- ☐ garlic supplements (pills, gelcaps)
- ☐ ginger pills or gelcaps
- ☐ ginkgo biloba
- ☐ ginseng
- ☐ glucosamine
- ☐ goldenseal
- ☐ guarana
- ☐ grape seed extract
- ☐ green tea pills (not brewed tea)
- ☐ EGCG (pills)
- ☐ hawthorn
- ☐ horny goat weed
- ☐ kava kava
- ☐ lecithin
- ☐ lutein
- ☐ lycopene
- ☐ melatonin
- ☐ MSM (methylsulfonylmethane)
- ☐ milk thistle
- ☐ prebiotics or probiotics
- ☐ SAME-e
- ☐ saw palmetto
- ☐ senna
- ☐ soy supplements or soy isoflavones
- ☐ St. John's wort
- ☐ valerian
- ☐ other :_____
- ☐ I don't know

Page 4: Reasons for Use

For what reason(s) did you use _____?

- For general health or wellness
- Prescription or over-the-counter drugs are too expensive
- To treat or cure a specific disease or health problem
- To prevent a specific disease or health problem
- To improve physical performance
- To improve sports performance
- To improve immune system function
- To improve sexual performance
- To improve mental ability or memory
- Because medical treatments did not help
- Because medical treatments were too expensive
- It was recommended by a health care provider
- It was recommended by family, friends, or co-workers
- Other: _____
- I don’t know

Page 5: Reasons for NOT Using

Please state the reason(s) why you have never used _____. Select all that apply.

- Never heard of it, don't know much about it
- Never thought about it
- No reason
- Don't need it
- Don't believe in it, it doesn't work
- It costs too much
- It is not safe to use
- A health care provider told me not to use it
- Medical science has not shown that it works
- Other: _____
- I don't know

Page 6: Vitamins and Minerals

- Multivitamin and/or mineral combination
- Calcium
- Chromium
- Coral calcium
- Folic acid/folate
- Iron
- Magnesium
- Niacin
- Potassium
- Selenium
- Vitamin A
- Vitamin B complex
- Vitamin B12
- Vitamin C
- Vitamin D
- Vitamin E
- Vitamin K
- Zinc
- Vitamin packet
- None
- I don’t know

Page 7: MS Severity Rating Scale

From the choices below, please indicate the level of MS severity that best fits your condition.

1. **None/Minimal**
   I have no or minimal MS-related symptoms, no limitations in walking, and no limitations on daily activities.

2. **Mild**
   I have noticeable MS-related symptoms but no limitations in walking ability and no limitations on daily activities.

3. **Moderate**
   I have many MS-related symptoms that affect my daily activities but can walk at least 1 block without support.

4. **Some support needed for walking**
   I have significant MS-related symptoms that limit physically demanding activities. I need support (e.g., cane, touching a wall, leaning on someone's arm) to walk ½-1 block.

5. **Walker/two-handed crutch**
   I have significant MS-related symptoms that limit daily activities. I can walk only short distances with a walker or two-handed crutches.

6. **Unable to walk**
   I have many severe MS-related symptoms and am restricted to a wheelchair or bed.