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Randomized-controlled trial of a modified Mediterranean dietary program for multiple sclerosis: A pilot study

Ilana Katz Sand[a,*], Emma K. T. Benn[b], Michelle Fabian[a], Kathryn C. Fitzgerald[c], Elise Digga[a], Richa Deshpande[b], Aaron Miller[a], Samantha Gallo[d], Lenore Arab[e]

[a] Department of Neurology, Icahn School of Medicine at Mount Sinai, United States
[b] Center for Biostatistics and Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, United States
[c] Department of Neurology, Johns Hopkins, United States
[d] Department of Clinical Nutrition, The Mount Sinai Hospital, United States
[e] Department of Medicine, The David Geffen School of Medicine, University of California Los Angeles, United States

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ABSTRACT

Background: There is a high level of interest in the potential role of diet among the MS community. There is a limited level of evidence for a Mediterranean-style dietary pattern in MS; the feasibility of conducting studies using educational tools to deliver this type of intervention and study its effects is unknown.
Objectives: To establish clinical trial feasibility for future studies utilizing educational delivery of a dietary intervention in MS; to explore the effects of a modified Mediterranean dietary intervention in MS.
Methods: We randomly assigned women with MS to follow/not follow the prescribed modified Mediterranean dietary intervention for 6 months, delivered through educational sessions. The diet encouraged the intake of fish and other foods high in poly- and monounsaturated fats, fresh fruits, vegetables, and whole grains and eliminated meat, dairy, and most processed foods and limited salt intake to < 2 g/day. Primary endpoints related to meeting target enrollment within the specified time frame, adherence, and study completion. Clinical endpoints were evaluated in an exploratory fashion.
Results: We screened 128 potential participants and enrolled 36 within 9 months, surpassing target enrollment of 30 participants at a single center in 1 year. Self-reported adherence was excellent (90.3%), with an overall study completion rate of 94.4%. The intervention group exhibited a statistically significant decline in the trajectory of Neurological Fatigue Index-MS scores ($p = 0.01$), a trend toward reduced Multiple Sclerosis Impact Scale-29 scores that became significant after outlier removal ($p = 0.12$; $p = 0.023$), and a reduction in Expanded Disability Status Scale ($p = 0.01$) over time as compared to the non-intervention group.
Conclusions: It is reasonable to expect a high level of interest and commitment to this type of dietary intervention study in MS, and feasible to deliver it purely through education in a clinical setting with high adherence levels despite restrictive requirements. In this pilot study, a modified Mediterranean dietary intervention reduced fatigue, impact of MS symptoms, and disability. Further work is needed.

1. Introduction

Recent enthusiasm for potential dietary approaches to benefit MS among patients is quite high (Brenton, 2016). Interest by the MS clinical and research community dates back to initial studies conducted by Dr. Roy Swank and colleagues beginning in the 1950s (Swank and Dugan, 1990). However, multiple barriers to conducting dietary intervention studies in MS have limited further progress on this topic until relatively recently. These barriers include outstanding questions about the feasibility of conducting dietary research in MS such as: is it possible to recruit participants to a study that requires a major lifestyle change? Is it possible to randomize participants and will they maintain their group assignment? Will participants adhere to the prescribed dietary regimen and how can adherence be measured? Can the intervention be delivered through education alone or should food be pre-prepared for participants? Further, there is relatively little guidance on the optimal type of diet that should be studied. These issues are in addition to more advanced unanswered questions about appropriate clinical and imaging endpoints to be measured in dietary research in MS.

* Corresponding author at. The Corinne Goldsmith Dickinson Center for MS, 5 East 98th Street, Box 1138, New York, NY 10029, United States
E-mail address: ilana.katzsand@mssm.edu (I. Katz Sand).

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Based on best available evidence in the basic science and epidemiologic literature in MS, evidence in the cognitive aging literature, as well as established general health benefits, we designed a modified Mediterranean dietary intervention for MS. Here we present results of a pilot randomized clinical trial of this intervention, designed to evaluate clinical trial feasibility and explore its impact on select MS symptoms.

2. Methods

2.1. Study participants

Participants were recruited at the Corinne Goldsmith Dickinson Center for Multiple Sclerosis at Mount Sinai in New York City. The study was approved by the Mount Sinai Institutional Review Board and all participants provided written informed consent. The study was posted on clinicaltrials.gov prior to enrollment of the first study participant (NCT02986893). Eligible participants were aged 18–65, female, with a diagnosis of MS (Polman et al., 2011) and currently following a Western-style diet that included at least one of the major exclusions for the study (meat and dairy). Potential participants also had to be willing to be randomized and commit to study participation regardless of the randomization outcome. Dietary supplements other than vitamin D that had been recommended by a health care provider were not permitted. A washout period of 2 weeks was required for non-allowed supplements.

2.2. Study protocol

The study visit schedule is described here in the text and outlined in Table 1. All participants completed screening and the baseline study visit prior to randomization to help reduce potential biases in the baseline assessment related to group assignment. The baseline assessment consisted of completion of a food frequency questionnaire (Block FFQ 2005, nutritionquest.com), completion of 3 online Diet Day 24 h dietary recalls (www.ucladietday.com), measurement of vital signs and weight, collection of demographic and MS history data, Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), Multiple Sclerosis Functional Composite (MSFC) (Polman and Rudick, 2010), The Neurological Fatigue Index-MS (Mills et al., 2010), Multiple Sclerosis Impact Scale-29 (McGuigan and Hutchinson, 2004), Multiple Sclerosis Quality of Life-54 (Vickrey et al., 1995), and MACFIMS cognitive battery (Benedict et al., 2002). Blood and stool samples were also collected and stored for future analyses. All data management was administered through Research Electronic Data Capture (REDCap), a secure, open source web application for building and managing online surveys and databases (Harris, 2009). Participants were then randomized 1:1 in blocks of 10 (except for the final group of 6) and stratified by race (white/non-white) to either the dietary intervention or non-dietary intervention group. We generated our stratified block randomization scheme using the Robust Randomization App (RRApp) (Tu, 2017), which could be directly imported into REDCap.

The dietary protocol encouraged the intake of fresh vegetables and fruits, fish, nuts, legumes, whole grains, avocados, and use of olive oil in cooking. It advised against the intake of meat (including red meat as well as poultry), dairy, “white” grains, and processed foods. Participants were also advised to limit salt intake to 2 g/day and to abstain from eating for at least 12 h per night (recommended 7 p.m. to 7 a.m.). The rationale for these recommendations is further outlined in the Discussion, below. No specific advice was given regarding overall caloric intake or weight loss. Participants in the dietary intervention group met with the study's registered dietician (SG) for an educational session in groups of five as they began the protocol. They were provided with handouts with tips for grocery shopping, a sample menu plan, and guidance regarding reading food labels, eating in restaurants, and travel. They returned for a follow up session after 2 weeks. Throughout the length of the study they returned monthly (or dialed in) to meetings to discuss issues with following the diet and complete a self-assessment questionnaire. The registered dietician, principal investigator, and research coordinator were available between meetings by email and telephone to answer questions and help troubleshoot any issues. Participants also completed approximately monthly DietDay 24 h recalls (dates randomly assigned, notifications send through REDCap) throughout the study.

Participants in the non-dietary intervention group were offered participation in educational (non-interventional) seminars on MS and were offered a group session with the registered dietician and study PI and access to the handouts after study completion.

All participants returned for a follow up visit mimicking the baseline assessment after following the study protocol for 6 months. The dietary intervention group participants also completed a final self-assessment questionnaire, including feedback for future dietary studies in MS.

Table 1
Study schedule.

	Baseline	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Group meetings							
Intervention		x	x	x	x	x	x
Control			x		x		x
Patient questionnaires							
Intervention	x			x			x
Control	x			x			x
Self assessments							
Intervention		x	x	x	x	x	x
Control							
Food frequency questionnaire							
Intervention	x			x			x
Control	x			x			x
Diet day recalls							
Intervention	x	x	x	x	x	x	x
Control	x	x	x	x	x	x	x
EDSS and VS							
Intervention	x						x
Control	x						x
Biospecimen collection							
Intervention	x						x
Control	x						x

EDSS: Expanded Disability Status Scale.
VS: Vital Signs.

Table 2
Baseline characteristics (n = 36).

	Total n = 36	Diet n = 18	Non-Diet n = 18	p-value
Demographics				
Age, yrs	43 (32–51)	44 (37–51)	41 (30–49)	0.33
Ethnicity				0.18
Hispanic/Other	6 (16.7%)	1 (5.6%)	5 (27.8%)	
Non-Hispanic	30 (83.3%)	17 (94.4%)	13 (72.2%)	
Race				0.40
Non-White	7 (19.4%)	2 (11.1%)	5 (27.8%)	
White	29 (80.6%)	16 (88.9%)	13 (72.2%)	
Educational Attainment				1.00
Below College	5 (13.9%)	2 (11.1%)	3 (16.7%)	
College	16 (44.4%)	8 (44.4%)	8 (44.4%)	
Above College	15 (41.7%)	8 (44.4%)	7 (38.9%)	
BMI	25 (23–30)	26 (25–37)	25 (23–30)	0.26
Disease Duration, yrs.	4.8 (2.0–11.2)	5.4 (2.0–10.7)	4.1 (2.1–11.7)	0.76
Disease Type				
CIS	3 (8.6%)	2 (11.1%)	1 (5.9%)	1.00
RRMS	28 (80.0%)	14 (77.8%)	14 (82.3%)	
SPMS	3 (8.6%)	1 (5.6%)	2 (11.8%)	
PPMS	1 (2.9%)	1 (5.6%)	0 (0.0%)	
Total EDSS	2 (0–3.5)	2 (0–3)	2 (0–5)	0.91

2.3. Study aims and outcome measures

The main aim of this study was to establish clinical trial feasibility for future dietary research in MS. Therefore, our primary aims related to the ability to reach target enrollment within the specified time frame (goal of 30 participants at a single center within one year), maintaining engagement and study adherence (goal 80% attendance to sessions and 80% self-reported adherence to the diet), and study completion rates (goal less than 20% attrition). Furthermore, the United States Department of Agriculture (USDA) Dietary Guideline for 2015–2020 includes calorie-specific recommendations for a Healthy-Mediterranean Style eating pattern for Americans that emphasizes intake of fruits, vegetables, whole grains, fish and healthy oils and de-emphasizes intake of refined grains, red meat, and “empty calories” (sweets, candy, excess alcohol). We tested whether the percentage of participants who met recommended intakes for the USDA's Mediterranean-style eating pattern changed over the course of the study. We also calculated a composite adherence to US-style Mediterranean diet score. For fruits, vegetables, fish, oils, whole grains and dairy, individuals who met the USDA's requirement for a given food group (based on calorie levels) were given 1 point; individuals who ate less than the recommended amount of empty calories were also given one point. The final score was calculated as the sum of the individual parts; scores ranged from 0 to 6. Given the study's small sample size, relatively short duration, and lack of prior data to guide expectations of effects on clinical endpoints, these outcomes were considered exploratory.

2.4. Statistical analysis

Data were summarized as mean ± standard deviation or median (interquartile range) for continuous variables and frequency (percentage) for categorical variables. Bivariate assessments of differences in demographic factors between the dietary intervention and non-dietary intervention groups at baseline were conducted using t-tests or Wilcoxon Rank Sum tests for continuous variables, whereas χ^2 or Fisher's Exact Tests were used for categorical variables. We conducted exploratory analyses to examine whether the trajectory differed between the intervention groups over time using mixed effects models with a random intercept for the following outcomes: weight in pounds, the Multiple Sclerosis Impact Scale-29 Total Score, the Neurological Fatigue Index-MS Summary Score, the Expanded Disability Status Scale, and the MSQOL-54 Physical and Mental Health Composite Scores. Our models consisted of terms for intervention group (dietary vs non-dietary), time point (0 vs 6 months), and an interaction between intervention group and time point. If our bivariate assessments revealed significant differences in any demographic factors between the intervention groups at baseline, we additionally adjusted for those potential confounders in our models. Models testing whether change in dietary intake of the specified food groups occurred were fit using mixed effects regression models. Akaike's Information Criterion (AIC) was used to assess model fit. All analyses were conducted using SAS 9.4 and a type I error rate of 0.05.

3. Results

3.1. Enrollment and clinical trial feasibility

3.1.1. Meeting target enrollment

A major outstanding question regarding dietary research of this type in MS was that while expressed interest in dietary approaches is quite high, the level of willingness to volunteer to participate in a study requiring randomization to either a large lifestyle change or to maintain the status quo was unclear. We screened 128 women with MS between December 2016 and September 2017 and enrolled 36 (28.1%), surpassing our target enrollment of 30 participants during this time frame, at a single center. Baseline demographic information for the cohort can be found in Table 2.

3.1.2. Maintaining engagement and adherence

The monthly sessions were designed to keep the dietary intervention group engaged and adherent to the study protocol. Attendance (in person or by phone) was excellent (overall rate 90.6%) despite enrollment of a group with a high level of employment as well as family responsibilities. Mean self-reported adherence at the 6-month time point was 90.3%. Participants were reminded at each visit that self-assessments would be reviewed anonymously and that honesty was extremely important for future study design. Over the 6-month period, participants in the dietary program significantly improved adherence to

Table 3
Change in dietary intake over the 6-month period.

	Control 6-month change (95% CI)	*P*-value	Diet 6-month change (95% CI)	*P*-value	*P*-value for difference in change over time
Overall Mediterranean Diet Score	0.23 (−0.39, 0.86)	0.47	1.91 (1.02, 2.79)	< 0.001	0.02
Fruits (cups-equivalent/day)	−0.02 (−0.42, 0.38)	0.92	0.75 (0.28, 1.22)	0.002	0.05
Vegetables (cups-equivalent/day)	−0.16 (−0.62, 0.30)	0.49	1.09 (0.42, 1.76)	0.001	0.01
Oils (grams)	−1.17 (−4.86, 7.20)	0.70	5.06 (−2.55, 12.67)	0.19	0.13
Whole grains (oz/equivalent/day)	−0.22 (−0.55, 0.12)	0.49	−0.11 (−0.52, 0.31)	0.62	0.47
Dairy (cups-equivalent/day)	−0.20 (−0.55, 0.15)	0.27	−1.01 (−1.41, −0.61)	< 0.001	0.003
Fish (oz-equivalent/week)	−1.05 (−6.57, 4.58)	0.71	11.55 (5.01, 18.09)	0.0005	0.003
"Empty" calories[a] (% of calories)	0.41 (−3.89, 4.22)	0.83	−7.29 (−13.20, −1.37)	0.02	0.03

*a denotes intake of sweets, added sugar and excess alcohol.

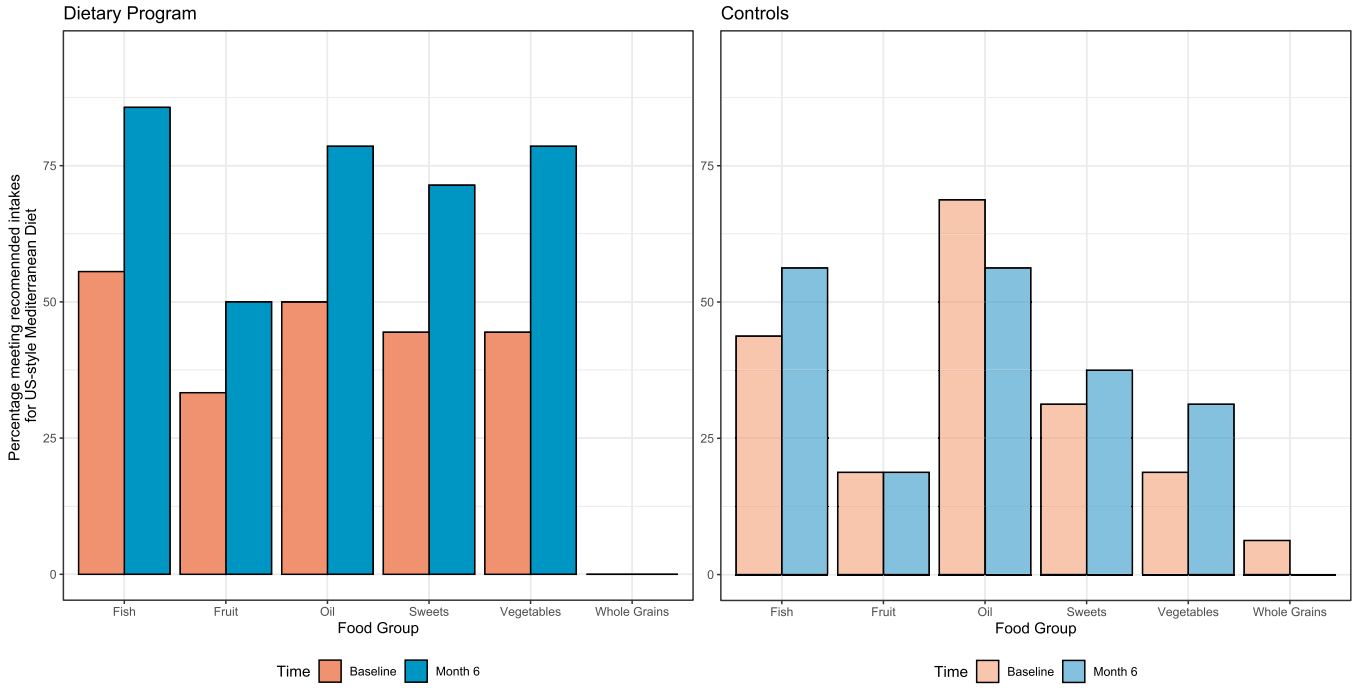

Fig. 1. Percentage meeting recommended intakes for US-style Mediterranean diet at baseline and at 6 month follow up.

a US-style Mediterranean diet; dietary quality scores increased on average by 1.91 points (95% CI: 01.02, 2.79; $p < 0.001$, Table 3, Fig. 1), while dietary scores in the control arm did not significantly change (6-month change: 0.23; 95% CI: −0.39 to 0.86; $p = 0.47$).This change over time was significantly different between study arms ($p = 0.02$). Individually, participants in the dietary program significantly increased consumption of fruits, vegetables and fish and decreased consumption of dairy and empty calories over the six month period (Table 3).

3.1.3. Study completion rate

All 18/18 (100%) participants in the dietary intervention group completed the study. 16/18 (88.9%) participants in the non-intervention group completed the study (one with an ill relative who left the country for a long period of time and one who simply did not return requests to schedule the final assessment visit), giving an overall study completion rate of 94.4%.

3.2. Clinical outcomes

Baseline demographic characteristics are outlined in Table 2 and demonstrate no significant differences between the study arms. Due to the small sample size, relatively short study duration, and lack of prior data to guide expectations of effects on clinical outcomes, these outcomes were considered exploratory.

3.2.1. Weight

The non-intervention group weighed approximately 154.7 lbs. (b_0) on average, with the intervention group weighing 10.3 lbs. (b_1) more at baseline, however this difference was not statistically significant ($p = 0.43$; Table 4). Although the participants were not provided any specific advice regarding weight loss or calorie counting, the non-intervention group had a 1.2 lb. (b_2) decline in weight over the 6-month study period, with the intervention group declining by about 4.8 lbs. (b_3) more than the non-intervention group ($p = 0.12$; Fig. 2). The 1.2 lb decline in the non-intervention group is inclusive of one outlier who lost 34 lbs.

3.2.2. Fatigue

Fatigue was measured using the Neurological Fatigue Index-MS (NFI-MS) (Mills et al., 2010), with higher scores indicating worse fatigue. No specific score was required for study entry. We observed a mean score of 11.8 (b_0) at baseline for the non-intervention group with the intervention group exhibiting a score of about 3.0 points (b_1) higher, on average, at baseline ($p = 0.17$). The non-intervention group increased by about 2.2 points (b_2), on average, over the 6-month study period ($p = 0.07$; Table 4). The dietary intervention group exhibited a statistically significant decline in the 6-month trajectory of NFI-MS scores over time as compared to the trajectory of the non-intervention group (−4.6 (b_3), $p = 0.01$), illustrated in Fig. 3.

3.2.3. Multiple Sclerosis Impact

The impact of MS symptoms on daily life was measured using the Multiple Sclerosis Impact Scale-29 (MSIS-29) (McGuigan and Hutchinson, 2004), with higher scores indicating worse MS symptoms/higher impact on daily life. No specific MSIS-29 score was required for study entry. We observed a mean MSIS-29 score of 49.4 (b_0) for the non-intervention group compared to the intervention group which had a similar score that was negligibly lower by 0.4 points (b_1), on average, at baseline ($p = 0.95$). An increase in the MSIS-29 score of about 4.8 (b_2) ($p = 0.16$), on average, over the 6-month study period was observed for the non-intervention group (Table 4). The intervention group's change in score, however, was approximately 7.4 points (b_3) lower than the trajectory observed among the non-intervention group over the 6-month study period ($p = 0.12$; Fig. 4). This observed trend was statistically significant ($p = 0.023$) when one outlier was removed from each group (both in the same direction).

3.2.4. Disability Status

Physical disability was measured by the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), with higher scores indicating worse disability. No specific EDSS score was required for study entry. We observed a mean EDSS score of 2.6 (b_0) at baseline for the non-intervention group compared to a mean score of 0.3 points (b_1) lower at baseline for the intervention group ($p = 0.7$). A statistically significant increase of 0.6 points (b_2) ($p = 0.03$), on average, was noted for the

Table 4
Mixed effects models (Random Intercept) examining the trajectory of weight (lbs.), NFI-MS, MSIS-29 and EDSS over time.

	Model 1 - Weight	Model 2 - NFI-MS	Model 3 - MSIS-29	Model 4 - EDSS
	b (se) *p*-value	b (se) *p*-value	b (se) *p*-value	b (se) *p*-value
Intercept (b_0)	154.69 (9.22) < 0.001	11.77 (1.51) < 0.001	49.41 (4.37) < 0.001	2.56 (0.62) 0.0002
Treatment (b_1)				
Non-Diet	–	–	–	–
Diet	10.31 (13.04) 0.43	2.95 (2.13) 0.17	−0.41 (6.10) 0.95	−0.33 (0.88) 0.71
Timepoint (b_2)				
Baseline	–	–	–	–
6 months	−1.19 (2.14) 0.58	2.17 (1.15) 0.07	4.78 (3.28) 0.16	0.59 (0.26) 0.03
Treatment*Timepoint (b_3)				
Diet, 6 months	−4.76 (2.94) 0.12	−4.55 (1.58) 0.01	−7.36 (4.57) 0.12	−0.98 (0.36) 0.01
Diet, Baseline	–	–	–	–
Non-Diet, 6 months	–	–	–	–
Non-Diet Baseline	–	–	–	–

NFI-MS: Neurological Fatigue Index- Multiple Sclerosis.
MSIS-29: Multiple Sclerosis Impact Scale-29.
EDSS: Expanded Disability Status Scale.

non-intervention group over the 6-month study period (Table 4). The dietary intervention group displayed a statistically significant decrease in the trajectory of EDSS scores over the 6-month study period as compared to the trajectory of the non-intervention group (−0.98 (b_3), $p = 0.01$), as shown in Fig. 5.

3.2.5. Self-reported benefits regarding general health and MS symptoms

16/18 participants in the dietary intervention group expressed the view that their health was improved overall since beginning the diet and 14/18 reported that there had been specific benefits with regard to their MS.

There was no statistically significant difference between the groups with respect to change in MSFC, MSQOL-54 physical or mental health composite score, or MACFIMS composite score over the 6 month study period.

4. Discussion

In developing the dietary intervention, we had to make several key decisions early on that would impact the future directions of this work. First, we opted to investigate an overall dietary pattern rather than a specific dietary component such as a “low-sodium” or “low-fat”

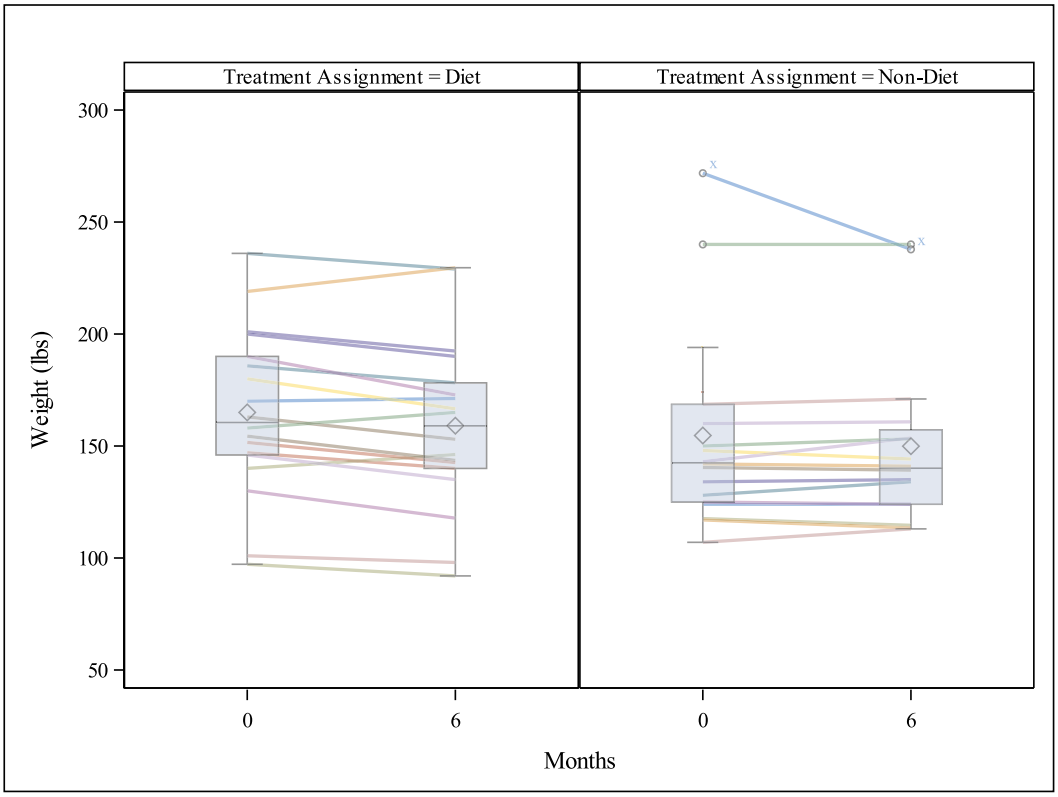

Fig. 2. Trajectory of weight by treatment assignment. Note: an “x” indicates an outlier.

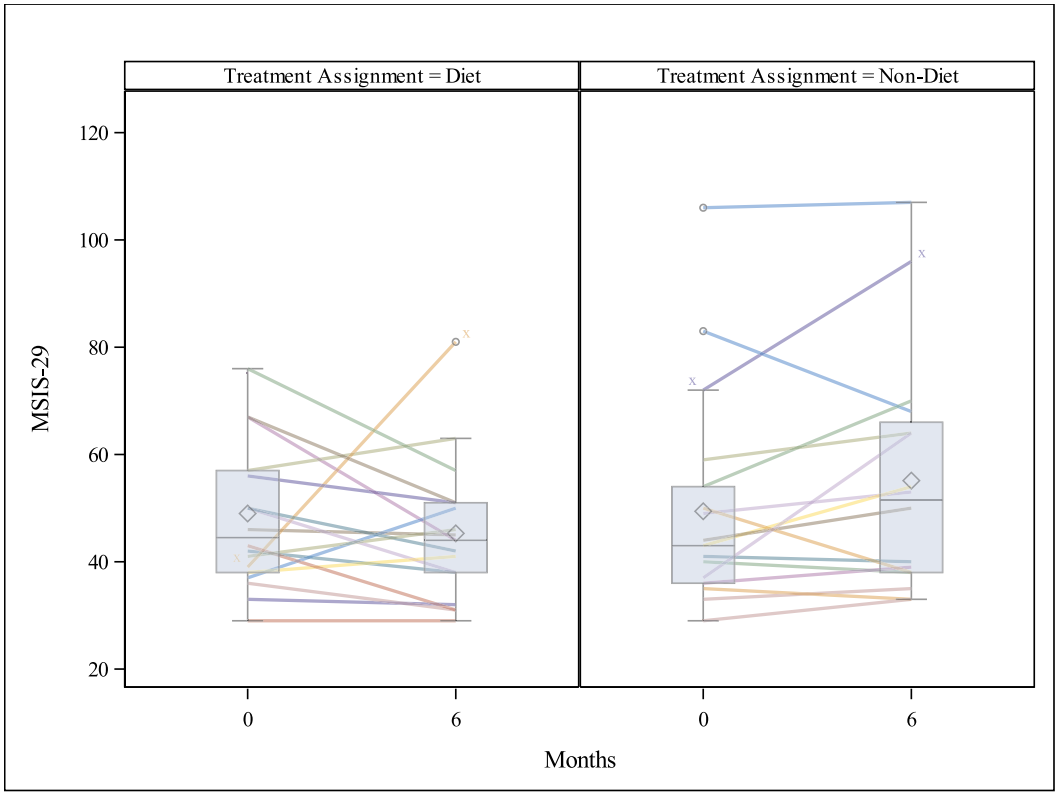

Fig. 3. Trajectory of Neurological Fatigue Index-Multiple Sclerosis by treatment assignment.

regimen because from a practical standpoint people consume an entire diet; the way varying foods interact with each other is likely to be significant. We were also concerned that if we provided specific guidance regarding eliminating or limiting only certain components that these might be replaced with other components that were harmful, similar to "low-fat diet" advice leading to the replacement of fats with

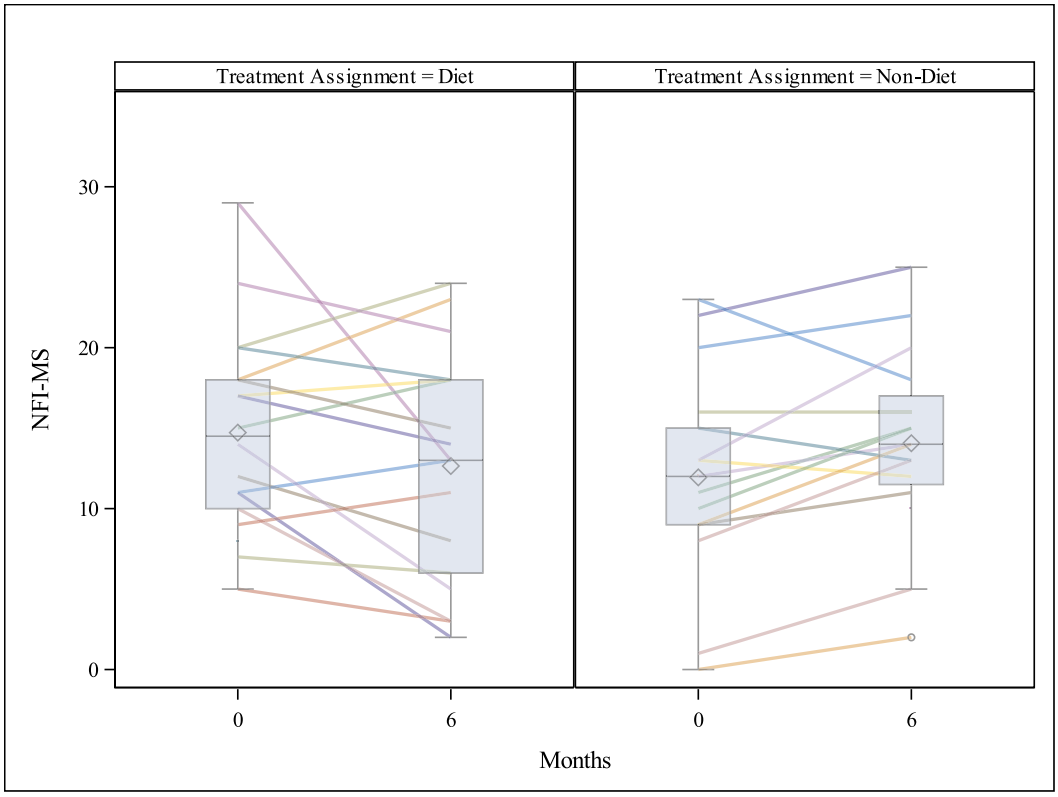

Fig. 4. Trajectory of Multiple Sclerosis Impact Scale-29 score by treatment assignment. Note: an "x" indicates two outliers.

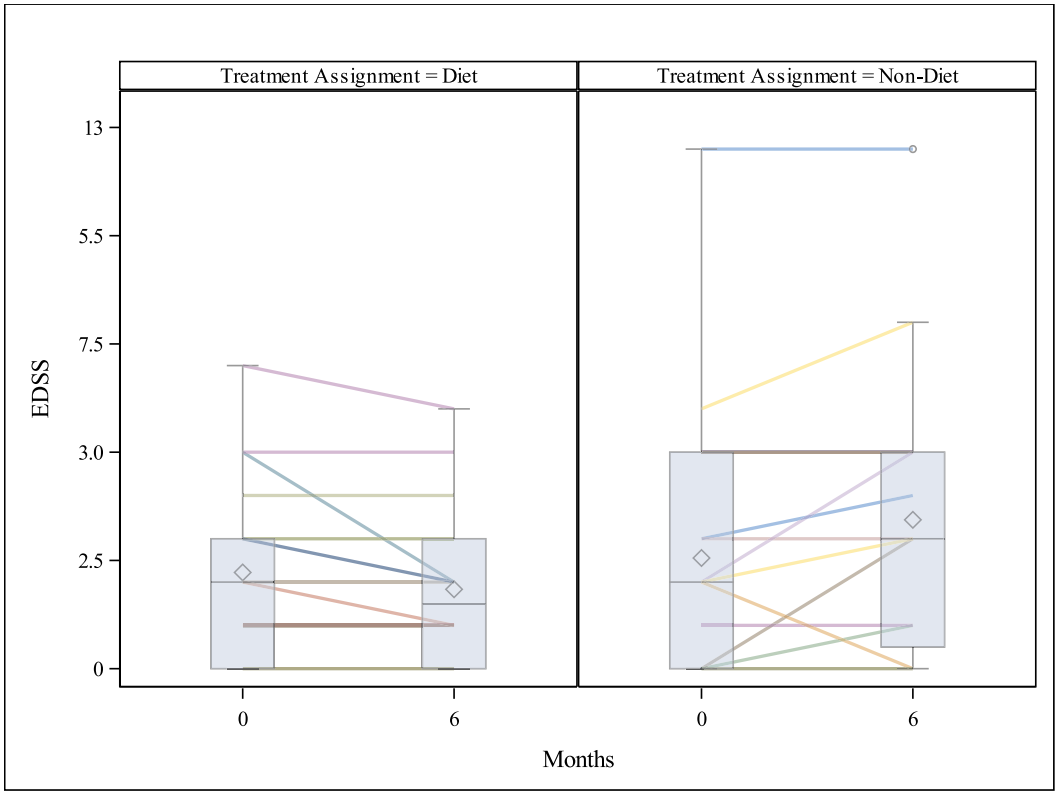

Fig. 5. Trajectory of Expanded Disability Status Scale score by treatment assignment. Note that all participants were included in the analysis but several had overlapping values.

low-quality carbohydrates, contributing to the current epidemic of obesity and the metabolic syndrome (Smith, 2015; Willett, 2011). We therefore provided advice on the entire diet and encouraged participants to view the study as an overall change in their approach to eating rather than as a "diet." We also considered whether to utilize a service to prepare food for participants as opposed to implementing the dietary plan through education. We determined that although provision of food might improve adherence and would almost certainly improve the measurement of adherence, the cost of anything other than a very short study would have been prohibitive. Perhaps more importantly, this would have limited the applicability of our results given that our ultimate long-term goal is to develop a program that can be disseminated through education and is accessible for all persons living with MS.

We considered several factors in developing the specifics of our dietary intervention. First, we evaluated the limited available literature suggesting potential benefit or harm of particular components with respect to MS. We noted potential benefit for foods with high polyunsaturated and monounsaturated fatty acid content (particularly fish) (Bazinet and Laye, 2014; Chen et al., 2014; Hoare et al., 2015; Janssen et al., 2015; Torkildsen et al., 2009; Unoda et al., 2013; Gu et al., 2016; Zhang et al., 2000) and foods with high polyphenol/flavonoid content (Imler and Petro, 2009; Muthian and Bright, 2004; Aktas et al., 2004; Shindler et al., 2010; Fonseca-Kelly et al., 2012; Xin et al., 2012). We noted potentially detrimental effects of foods with high saturated fat content (Timmermans et al., 2014, Azary, 2018) and high sodium content (Farez et al., 2015; Kleinewietfeld et al., 2013). Next we considered the likely impact of our proposed diet on overall health. This was important both because of the established negative impact of obesity and cardiovascular comorbidities on MS prognosis (Uher et al., 2017; Weinstock-Guttman et al., 2011; Tettey, 2014; Tettey et al., 2017; Marrie, 2010) and because our patients do not have MS in isolation; their overall general health is extremely important. We therefore recommended limiting added sugars, easily accomplished given the sodium restriction essentially requiring the elimination of processed foods. We then considered feasibility regarding participant adherence with respect to simplicity of following the "rules" and keeping the plan from becoming overly complicated. For example, we had decided to exclude red meat given the saturated fat content however we were not certain of the impact of poultry. We were concerned that if we did not place a limit on poultry intake that this might decrease the intake of fish and other foods we hypothesized would be more beneficial. We also speculated that the impact of poultry might differ by sourcing/farming techniques leading to large variability in nutritional content. Therefore, we decided to completely eliminate any meat other than fish in this initial study.

As described, we encouraged participants to view this as a lifestyle change with a move towards eating fresh rather than highly processed foods, replacing snacks like chips or granola bars with fresh fruits and vegetables, for example. This dietary pattern has proven overall health benefits (Tosti, 2018), its guiding principles are relatively straightforward to follow, and the pattern is feasibly sustainable in the long-term. It is therefore a pattern that can be adopted not only by persons living with MS but also by their entire families, improving the ease of implementation and adherence, as we saw in many of our study participants.

Given our clinical experience with high levels of patient interest in diet we anticipated a high level of interest in the study, however given the level of commitment required for study participation over a 6-month period as well as the randomization component we were naturally concerned about our ability meet our enrollment target. Demonstrating that MS patients are in fact willing to commit to this type of research, we exceeded our recruitment target, enrolling 36 women with MS in just nine months at a single center. There were also concerns regarding adherence and study follow-through. However, most participants reported an easier time following the protocol than they anticipated. Self-reported adherence was excellent, exceeding

90%. The significant increase demonstrated in Mediterranean diet scores determined through food frequency questionnaires supports this claim. In addition, all 18 participants in the intervention group completed the study and 16/18 in the non-intervention group completed it. These data help confirm that trials of dietary protocols that include randomization, are fairly restrictive, and are implemented entirely through education command high patient interest and are feasible to conduct in MS.

Despite the study not having been specifically powered to detect an impact on MS symptoms, those in the dietary intervention group noted a significant reduction in fatigue, one of the most common and disabling MS symptoms (Krupp, 2006). In addition we noted a trend for a decrease in the impact of MS symptoms measured by MSIS-29 as compared to the non-intervention group which became statistically significant after removal of outliers. We noted an impact on disability as measured by EDSS though we interpret this cautiously given that this was an unexpected finding in a study of such short duration. Additional studies will be needed to confirm these potential benefits however the signal present in a small sample size over only six months is highly encouraging.

Although no specific advice was given regarding caloric intake, participants in the intervention group lost weight at a healthy pace of approximately one pound per month. Over time this would be expected to result in a reduction in the incidence of vascular comorbidities that could otherwise develop and worsen MS prognosis and overall health. A longer study would be required to determine whether weight loss would be sustained and the precise impact on general health.

This study has several limitations. The sample size is relatively small and in the context of MS disease duration the study duration is relatively short. The nature of the study does not permit blinding to treatment assignment. To maintain homogeneity only women were enrolled; an additional study including men would be required to determine whether adherence and effects on symptoms would be similar. We would also aim to increase racial and ethnic diversity in a future study. The relatively short study duration and lack of available neuroimaging data precludes an assessment of whether this type of diet may act as a disease-modifier regarding inflammatory activity or progression in MS. However, this study lays the groundwork for evaluation of these important questions going forward.

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Declaration of Competing Interest

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