

Webinar Series



Diet in MS: Clinical Research & Practical Meal Planning

March 12, 2019

Presented by:

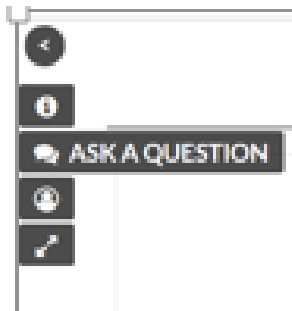


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- Type in your question in the “Ask A Question” Box
- Expand the second box in your control panel on the left side of your screen



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Overview

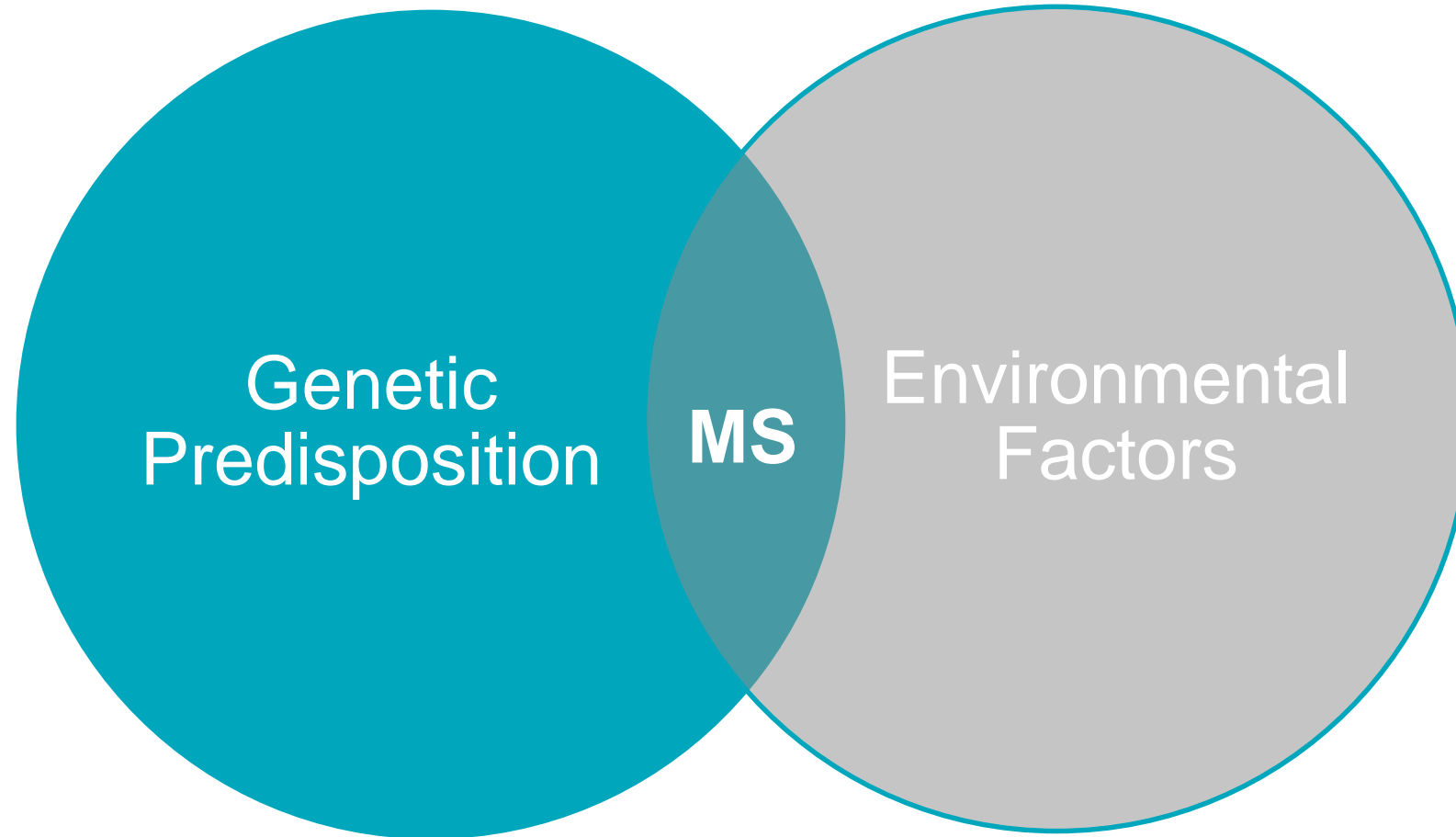
1. Rationale for interest in the role of diet in MS
2. Potential contributory mechanisms for dietary influence in MS including gut microbiota
3. Current evidence for dietary components in MS
4. Current evidence for dietary patterns in MS
5. Barriers to studying diet in MS
6. Preliminary results of a pilot clinical trial of a dietary intervention for MS

Why are we interested in diet?

- People living with MS have demonstrated an interest in diet
 - Something people living with MS can do to take an active role in their own health
 - “Natural” approach
- There is increasing scientific rationale
 - There is a strong environmental component to MS; search for modifiable factors that may impact disease course
 - Research demonstrating obesity in childhood/adolescence as a risk factor
 - Basic science research elucidating potential mechanistic links including through the gut microbiota



Multiple Sclerosis Etiology



- HLA-DR2 (DRB1*15:01) (antigen presentation)
- IL-2Ra (regulatory T-cells)
- IL-7Ra (memory T-cells)

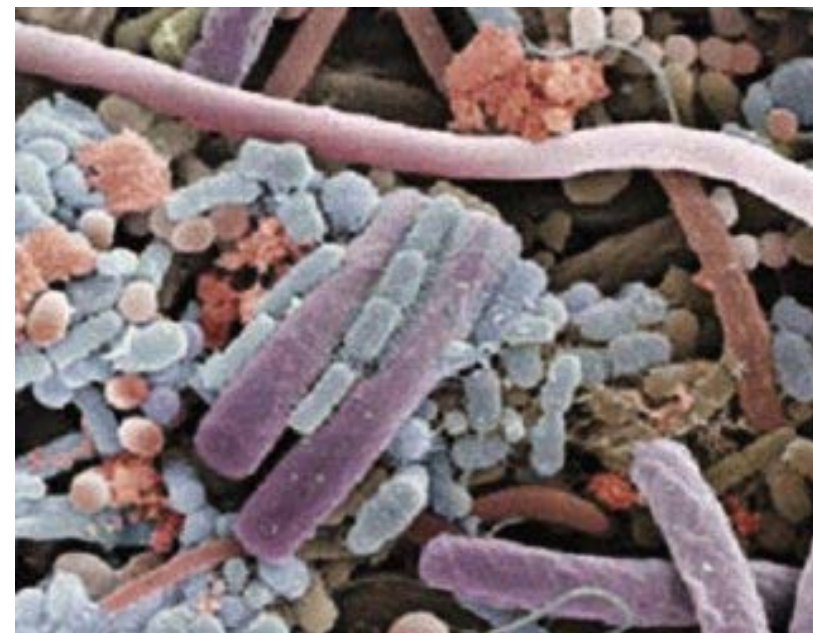
- Smoking
- Vitamin D
- Viral exposures (EBV, HHV6)
- Obesity

Diet may affect MS outcomes through:

- Immune system actions: favoring immune regulation rather than overactivity
- Neuroprotection
 - Protection against demyelination
 - Protection against nerve damage
- Repair
 - Encouragement of remyelination

Potential mechanisms for dietary effects

- Indirect effects mediated by comorbidities associated with worse outcomes
 - Obesity
 - Cholesterol levels
 - Other vascular risk factors
- Effects of dietary components
 - Direct effects of dietary metabolites
 - Effects mediated through the gut microbiota
 - Effects on microbial composition
 - Induction of metabolite production by gut microbiota



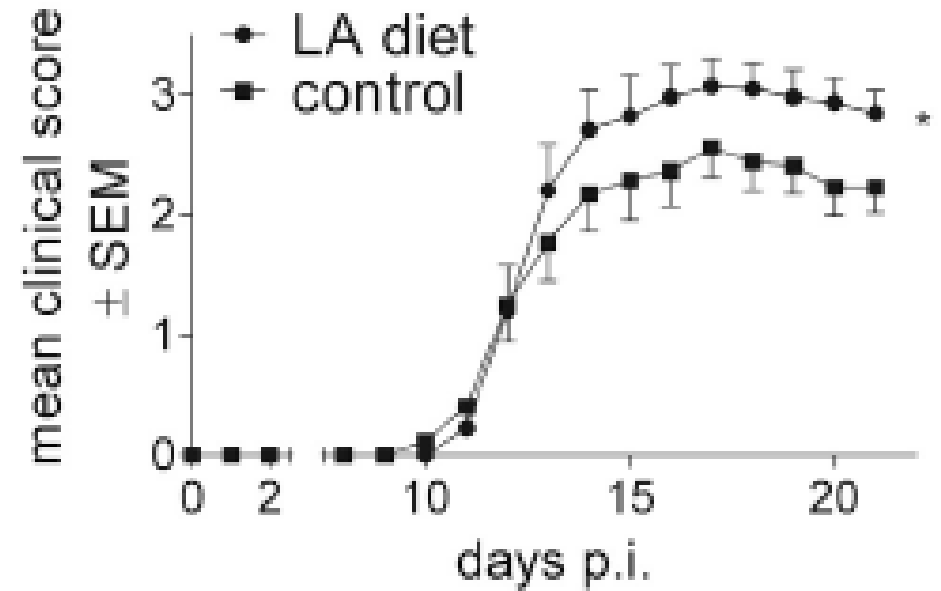
Evidence for particular dietary components in MS

Fatty Acids

- Saturated fats: meat, dairy
- Polyunsaturated fats: walnuts, flax seeds, fish
 - Of particular interest: omega-3 fatty acids (fish, plant-based)
- Monounsaturated fats: avocado, olive oil, peanuts

Saturated Fats

- Raise LDL (“bad”) cholesterol which is associated with poor outcomes in MS
- Ability to activate pro-inflammatory pathways
- Long-chain fatty acids typical in processed “Western” diets can worsen animal model of MS



	Good dieters	Poor dieters
Minimum disability (grade 1)		
Number (M:F)	23 (14:9)	6 (3:3)
Mean (SD) age (yr)	31.0 (8.4)	30.8 (7.5)
Mean (SD) duration of MS	31.0 (5.8)	25.9 (7.1)
Before trial	2.4 (2.1)	3.5 (2.4)
Diet period	28.6 (5.0)	23.8 (5.9)
Mean (SD) final neurological grade [change]	1.9 (2.2) [0.9]	5.3 (1.6) [4.3]
Deaths		
All causes	5 (21%)	5 (83%)
MS only	1 (5%)	4 (80%)
Mean lipid intake		
Fats	17.1 (2.4)	35.7 (11.5)
Oils	16.3 (4.3)	11.0 (2.2)
Moderate disability (grade 2)		
Number (M:F)	25 (9:16)	33 (16:17)
Mean (SD) age (yr)	31.8 (9.3)	34.4 (8.2)
Mean (SD) duration of MS (yr)	32.0 (7.2)	28.0 (9.0)
Before trial	4.9 (5.2)	5.3 (4.6)
Diet period	27.1 (6.8)	22.7 (8.0)
Mean (SD) final neurological grade [change]	3.6 (2.4) [1.6]	5.3 (1.3) [3.4]
Deaths		
All causes	10 (40%)	25 (76%)
MS only	8 (34%)	16 (66%)
Lipid intake		
Fats	15.4 (3.4)	46.1 (17.0)
Oils	18.2 (3.5)	10.2 (4.1)
Severe disability (grades 3-5, mean 3.21 [0.4])		
Number (M:F)	24 (7:17)	33 (17:16)
Mean (SD) age (yr)	34.2 (10.2)	37.1 (7.5)
Mean (SD) duration of MS (yr)	33.8 (9.5)	29.9 (10.7)
Before trial	6.2 (7.10)	10.4 (7.8)
Diet period	27.6 (8.5)	19.5 (9.6)
Mean (SD) final neurological grade [change]	4.0 (1.8) [0.8]	5.6 (1.0) [2.4]
Deaths		
All causes	8 (33%)	28 (85%)
MS only	5 (21%)	25 (83%)
Lipid intake		
Fats	15.8 (2.6)	36.5 (10.5)
Oils	18.1 (7.9)	10.5 (6.9)

Clinical studies of saturated fat intake in MS

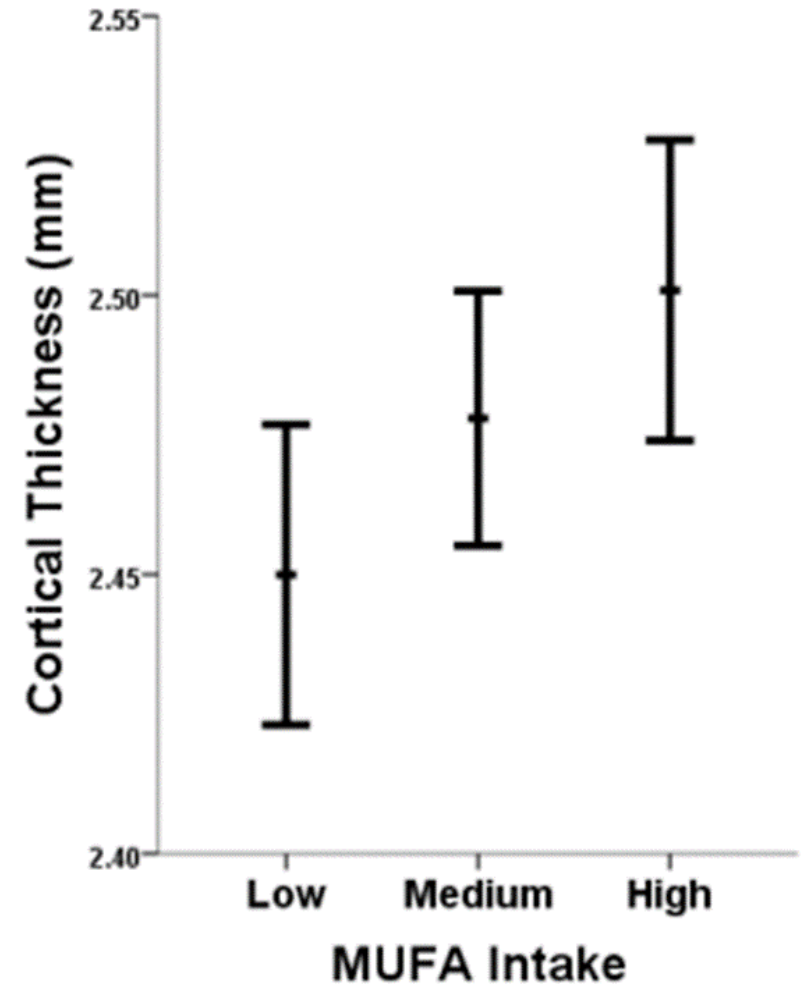
- Swank studies
 - Observational studies regarding MS incidence
 - Interventional study of low saturated fat diet (Swank, Lancet 1990)
- Prospective pediatric MS study
 - 219 children followed for an average of nearly 2 years
 - For every 10% increase in energy intake from saturated fat, the risk of relapse was increased 3.37 times

Polyunsaturated Fats

- Found in fish, walnuts, flax seeds
- Animal model effects on:
 - Immunomodulation
 - Neuroprotection
 - Remyelination and repair
- Epidemiologic studies in MS with conflicting results
 - Nurses Health studies suggest link between MS incidence and intake of alpha linolenic acid (ALA)
 - Several other studies demonstrate link between intake of fish and omega-3 fatty acids, but not clearly ALA
- Clinical trials of PUFA supplements with mixed results

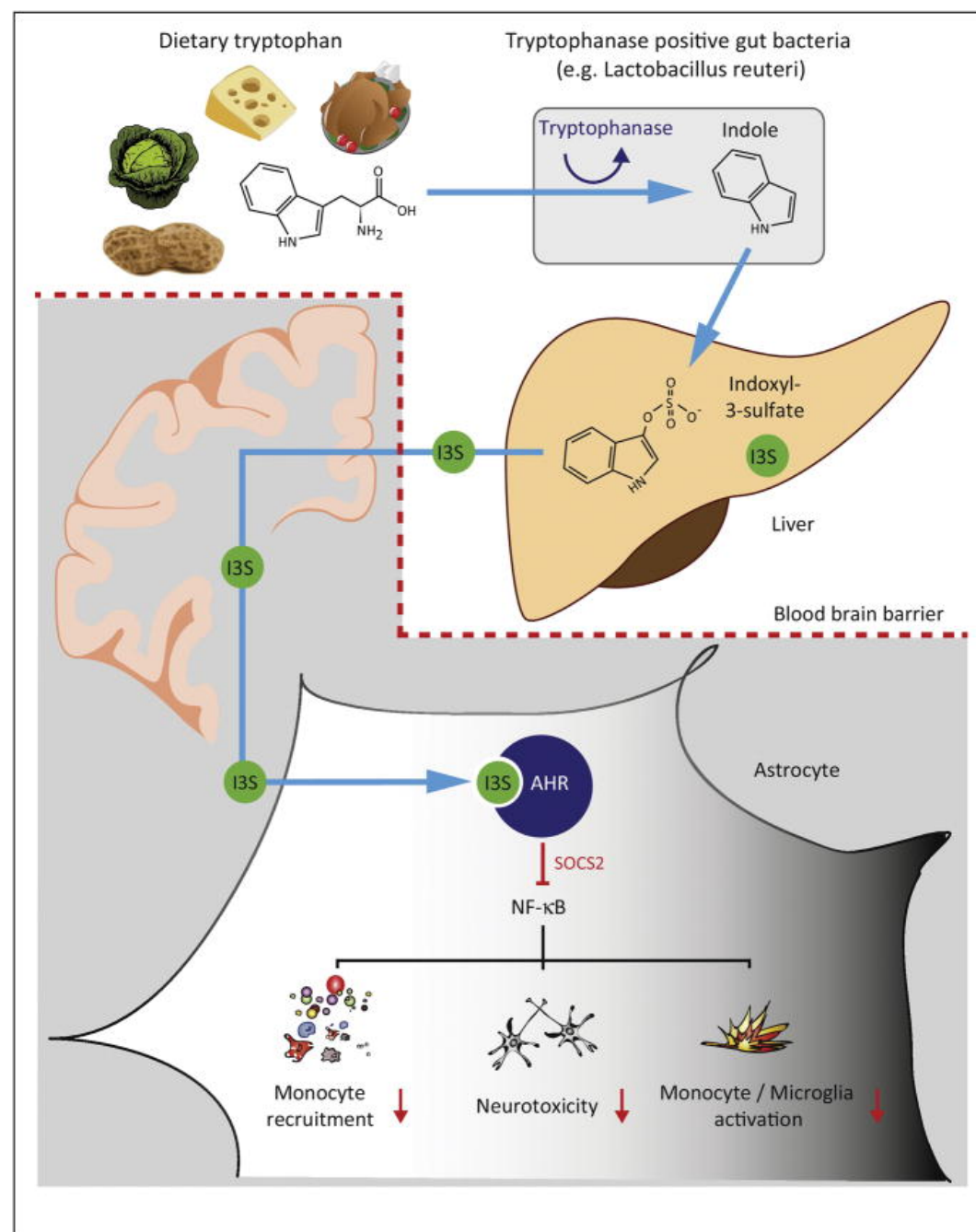
Monounsaturated Fats

- Found in olive oil, avocados
- Evidence in the aging literature, suggested as potential driving factor behind benefits of Mediterranean diet
- In our cohort of patients with early MS (<5 years from diagnosis), we note an association between intake of MUFA and cortical thickness (measure of brain atrophy)



Fruits & Vegetables

- Fiber intake: induction of production of short chain fatty acids by gut microbiota
- Flavonoids (brightly colored) effects on:
 - Immunomodulation
 - Neuroprotection/Repair
- Example: **tryptophan derived from the diet can cross the blood brain barrier** and have important effects inside the brain



Fruits & Vegetables (continued)

- Pediatric MS study: a one-cup equivalent increase in vegetable intake decreased the risk of relapse by 50% (HR 0.50, $p=0.024$)¹
- Registry-based study found link between higher intake of fruits and vegetables and patient-reported disability and disease activity²

¹Azary et al. *JNNP* 2017

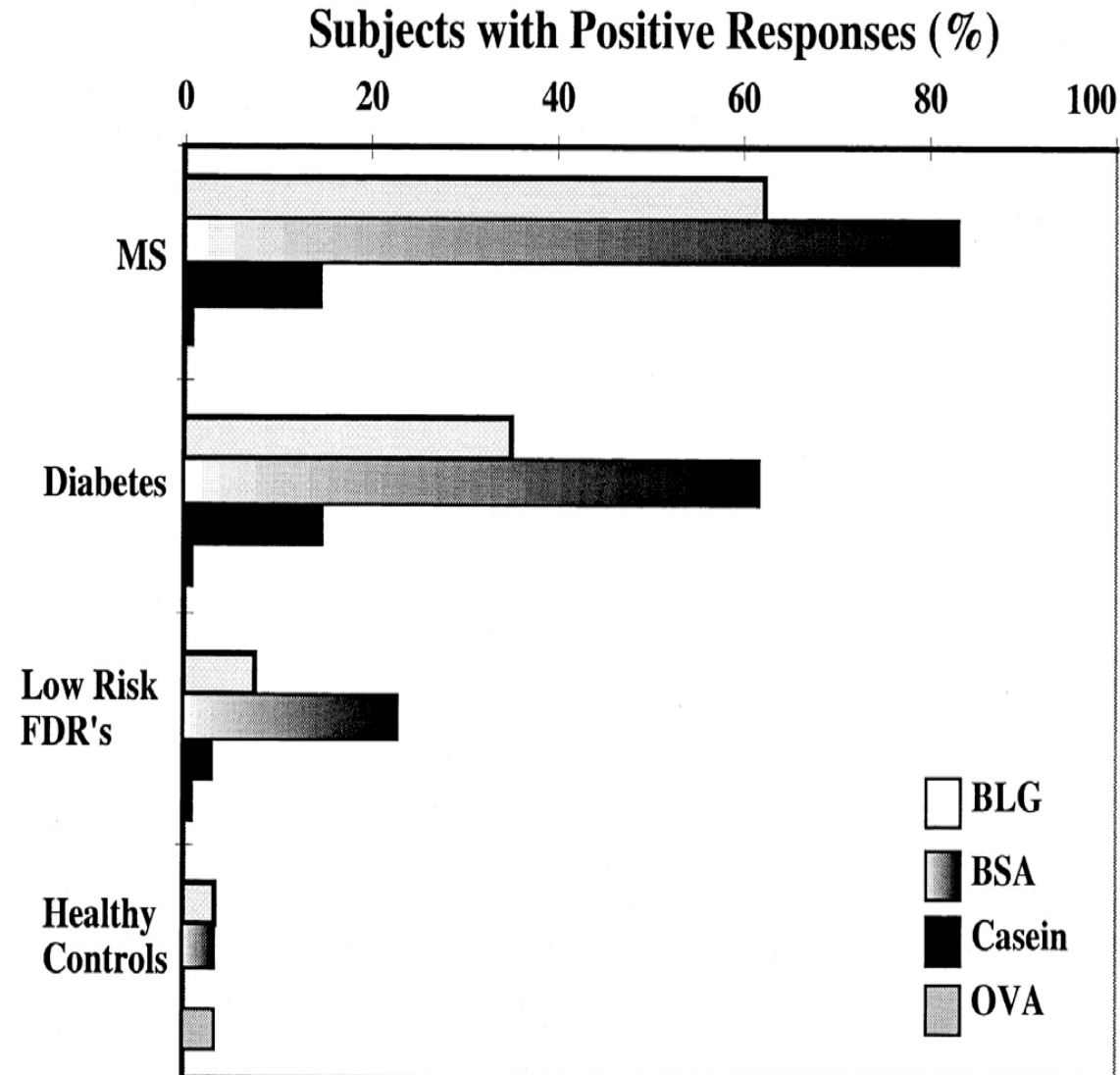
²Hadgkiss *Nutritional Neuroscience* 2014

Whole Grains

- Little work has been done exploring grains
- NARCOMS study found an association between higher intake of whole grains and lower level of MS-related disability
- High fiber content may be of benefit, possibly related to production of short chain fatty acids

Dairy

- A study of immune cell reactivities in MS patients showed abnormally heightened responses to multiple components of milk
- The milk protein butyrophilin has been implicated due to similarity to myelin components
- Increased inflammation may also be mediated through the intestinal microbiome
- Registry studies with mixed results



Salt

- High salt intake encourages the development of higher number of pro-inflammatory immune cells
- Pro-inflammatory immune cells that develop in a high salt environment are more aggressive and mice fed a high salt diet exhibit worsened course of “mouse MS”¹
- Observational study: 70 MS patients stratified by sodium intake
 - Medium and high intake with higher relapse rates over 2 years
 - Also with increased number of MRI lesions

¹ Kleinewietfeld et al. *Nature* 2013

RESEARCH PAPER

Sodium intake is associated with increased disease activity in multiple sclerosis

Mauricio F Farez,¹ Marcela P Fiol,¹ María I Gaitán,¹ Francisco J Quintana,² Jorge Correale¹

Table 2 Association between sodium intake and exacerbation rate in a regression analysis

	IRR	95% CI	p Value
<i>IRR of exacerbation (univariate model)</i>			
Sodium intake (g/day)			
<2	1 (baseline)	–	–
2–4.8	2.56	1.3 to 4.9	0.005
>4.8	3.37	1.5 to 9.55	0.001
<i>IRR of exacerbation (adjusted model)</i>			
Sodium intake (g/day)			
<2	1 (baseline)	–	–
2–4.8	2.75	1.3 to 5.8	0.008
>4.8	3.95	1.4 to 11.2	0.01
Age (1-year increment)	0.992	0.96 to 1.02	0.59
Gender (male)	1.09	0.49 to 2.42	0.82
Disease duration (1-year increment)	0.99	0.98 to 1.01	0.08
Vitamin D (1 ng increase)	1	0.96 to 1.04	0.85
Smoking (smoker)	1.13	0.56 to 2.28	0.73
BMI (1 unit increase)	0.97	0.87 to 1.07	0.58
Treatment (immunosuppressant vs immunomodulators/untreated)	1.46	0.79 to 2.73	0.22

BMI, body mass index; IRR, incidence rate ratio.

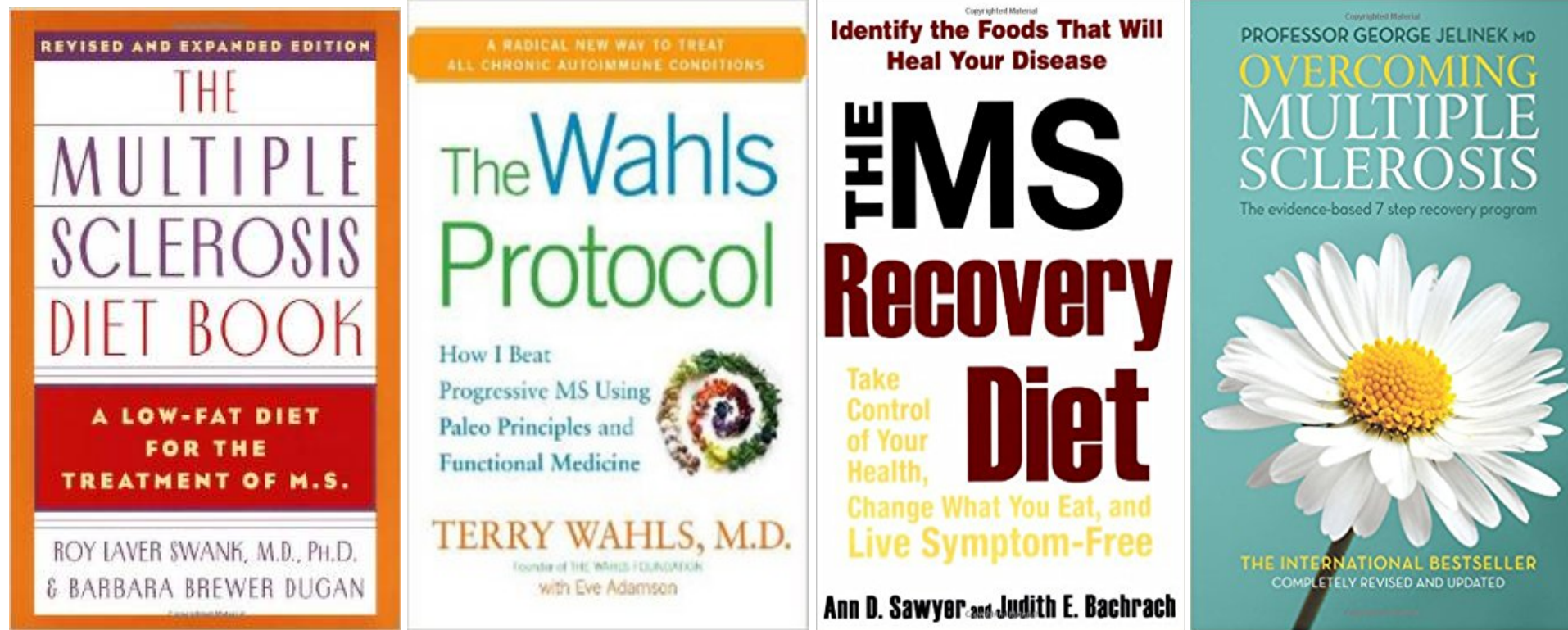
Additional studies have not confirmed these effects



- Pediatric case control study of 170 MS patients and 331 controls using food frequency questionnaire (FFQ) to estimate dietary sodium found no link¹
- Pediatric study of 174 RRMS participants followed for 1.8 years found no link between relapse rates and sodium intake by FFQ²
- BENEFIT trial data³
 - Median of 14 urine samples per participant → estimate dietary sodium
 - Over 400 patients in the trial, followed for 2 years then additional 3 year extension
 - No link between dietary sodium and clinical relapses or MRI lesions

Evidence for dietary patterns in multiple sclerosis

Many popular MS diets to choose from BUT...



- Each recommends something different: which one is “RIGHT?”
- What is the evidence?

Overall Dietary Quality

- Within the HOLISM (Health Outcomes in a Sample of people with MS) study, 2047 participants completed the Diet Habits Questionnaire (DHQ) as part of a comprehensive survey including information on relapse rate, disability status, and quality of life.
 - **10-point increase on the DHQ** (overall score ranging from 0-50, higher scores indicating higher quality diet) was associated with a **30% less likelihood of higher disability level.**
 - Higher DHQ scores were also significantly associated with **better physical and mental health-related quality of life**
- North American Research Committee on MS (NARCOMS) Registry, 6989 participants completed a dietary screener questionnaire (DSQ) in addition to providing information on recent relapses, progression, and disability.
 - Participants with top diet quality scores were at 20% lower odds of higher disability scores compared to those in the bottom range.

Modified Paleolithic (Wahls) Diet

- Paleolithic diets: include meat, fish, certain vegetables and fruits, eliminate dairy and grains
- Multimodal intervention including modified Paleo diet along with exercise regimen, electrical stimulation, meditation was effective at reducing fatigue in a small study of 10 SPMS patients (open-label, 6 completed the study)
- Ongoing studies

McDougall Diet

- Based on intake of starchy plant-based foods, with addition of non-starchy vegetables and fruits
 - 10% of energy intake from fats
 - No animal products or oils (including olive oil)
- One study randomized 61 MS patients to either follow the diet or participate as wait-list control x 1 year
 - Primary endpoint (new lesions on MRI) not satisfied
 - No difference in clinical relapse rate
 - Significant reduction in fatigue, moderated by weight loss
- Current study aims to enroll just over 100 participants, focused on fatigue

Caloric Restriction and Intermittent Fasting

- Chronic caloric restriction of benefit in MS animal model
- “Fasting mimicking diet” with multiple benefits in MS animal model
 - Immunomodulation
 - Oligodendrocyte (cells that make myelin) protection
 - Promotion of oligodendrocyte differentiation and repair
 - In animal model of MS and in model that is independent of inflammation
- Current studies in MS patients of both chronic caloric restriction and intermittent fasting

**Why hasn't there
been more dietary
research in MS?**

Barriers to studying diet in MS

- Is recruitment feasible?
- Will participants be able to follow the diet?
- Will participants be adherent to the diet? How can we best promote adherence?
- Can we effectively measure adherence?
 - Biological markers
 - Biases in self-reported data
- What is an appropriate “control” group?
 - Will controls maintain their group assignment?
 - How do we keep controls engaged?

Barriers to studying diet in MS

- Participants cannot be blinded to group assignment
- What diet should be studied?
 - Popular vs. rational diet
 - Individual dietary components or overall diet
- Should food be prepared by study or by participants?
- What are appropriate study endpoints?
- How large do we need the study to be?
 - Challenges of estimates

Pilot study of a dietary intervention for MS

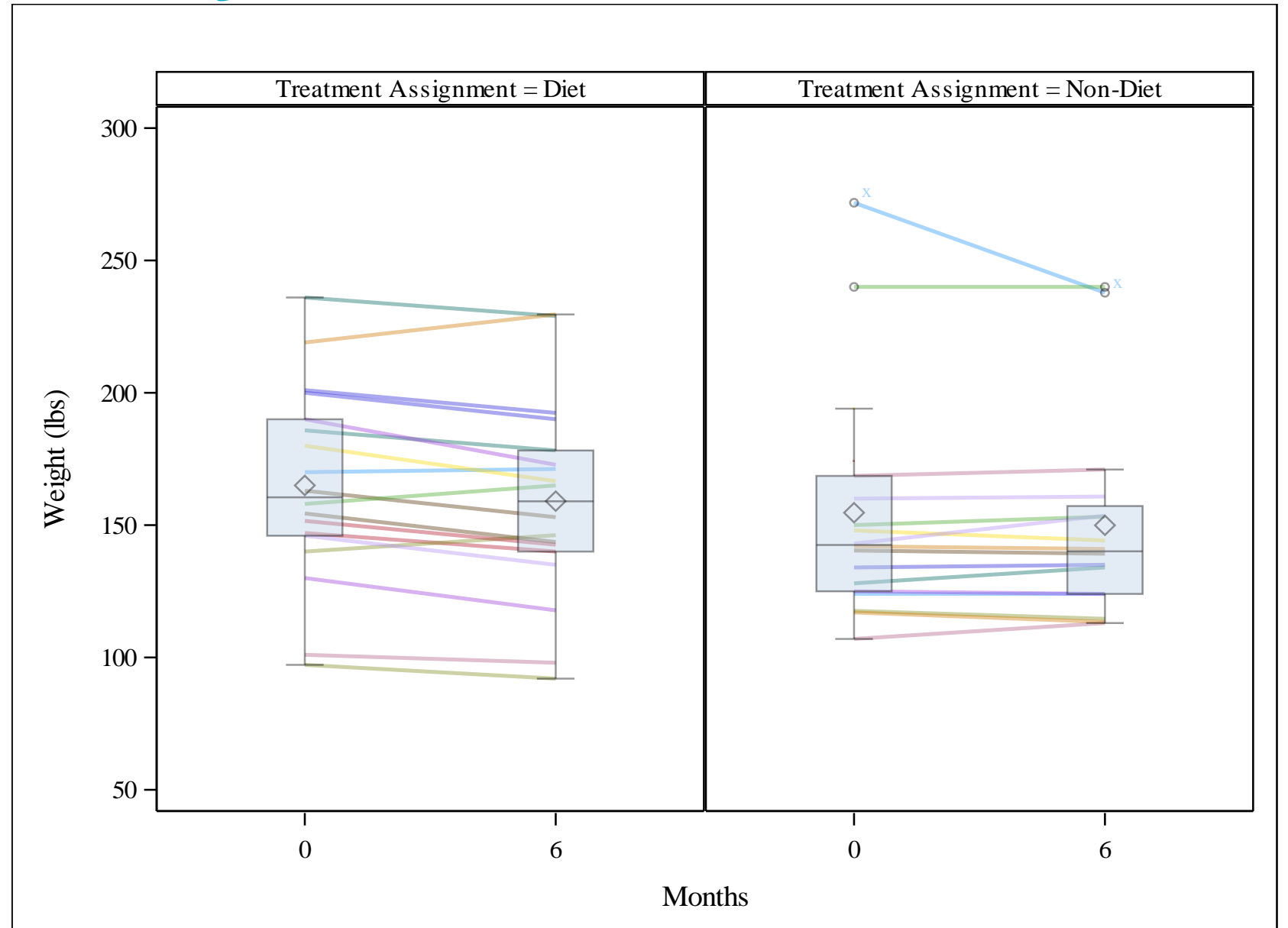
- Women w/ MS randomly assigned to +/- dietary intervention for 6 months
- Dietary intervention: modified Mediterranean diet
 - Encourages foods high in mono and polyunsaturated fatty acids, high fiber (fruits, vegetables, whole grains)
 - No meat, no dairy
 - Limitation on salt → eliminate processed foods
- Intensive training with nutritionist
 - Handouts with menus, recipes, grocery lists
- Monthly group meetings and routine contact between meetings
- Adherence assessments
 - Biological markers: urinary sodium, plasma carotenoids, fatty acid profiles
 - DietDay recalls, FFQ, questionnaires
- Exploratory look at fatigue, QOL, cognition
- Specimen collection for microbiome and metabolomics

Study Enrollment, Completion, and Adherence

- Target enrollment: 30 participants
- 131 potential participants screened over 9 months, 36 eligible and willing to participate (27.5%)
- 18/18 in the dietary intervention group completed the study and 16/18 in the non-intervention group completed the study: overall completion rate 94.4%
- Self-reported level of adherence at 6 months: 90.3%
- Dietary recall, food frequency questionnaire, and biologic data pending

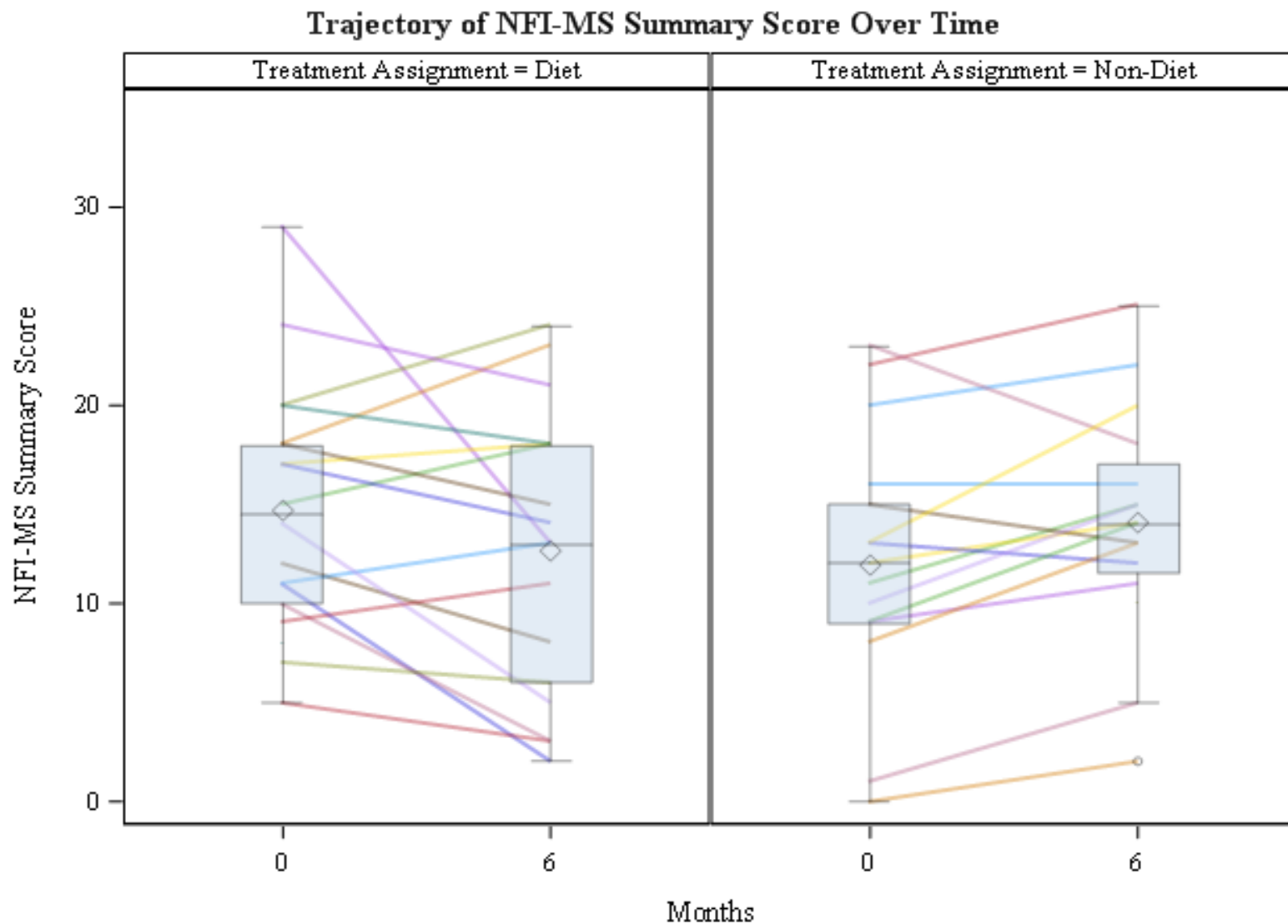
Impact of Dietary Intervention on Weight

	Model 1	Model 2 - excluding outlier(s)
	b (se)	b (se)
	p-value	p-value
Intercept	154.69 (9.22)	147.80 (8.56)
Timepoint		
Baseline	-	-
6 months	-1.19 (2.14)	1.02 (1.60)
Treatment		
Non-Diet	-	-
Diet	10.31 (13.04)	17.20 (11.94)
	0.43	0.16
Treatment*		
Timepoint		
Diet, 6 months	-4.76 (2.94)	-6.96 (2.17)
	0.12	0.003



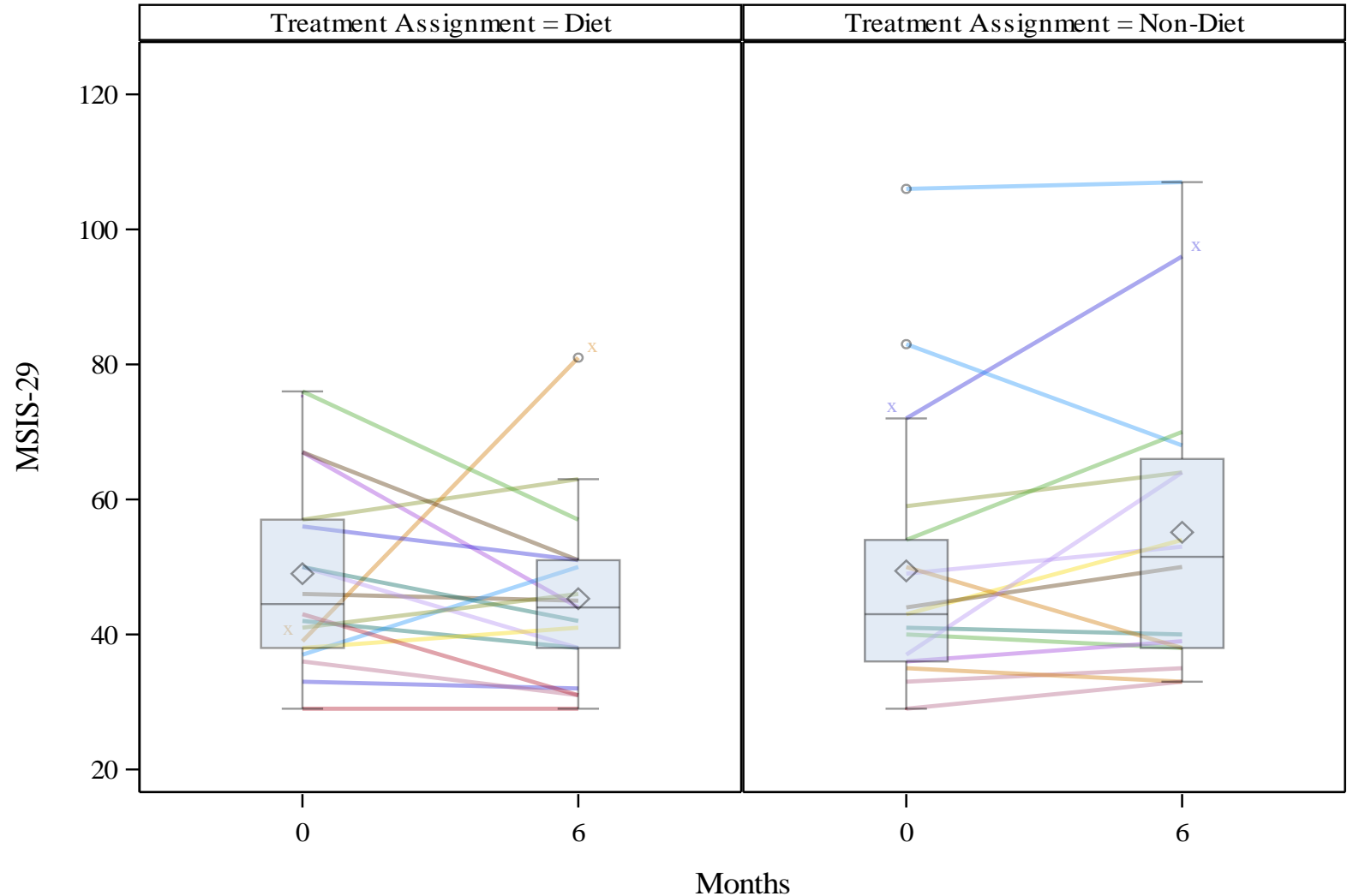
Impact of Dietary Intervention on Fatigue

	Model 1
	b (se) p-value
Intercept	11.77 (1.51) <0.001
Timepoint	
Baseline	-
6 months	2.17 (1.15) 0.07
Treatment	
Non-Diet	-
Diet	2.95 (2.13) 0.17
Treatment* Timepoint	
Diet, 6 months	4.55 (1.58) 0.01



Effects of Dietary Intervention on MS Impact Scale-29 Score

	Model 1	Model 2 - excluding outlier(s)
	b (se) p-value	b (se) p-value
Intercept	49.41 (4.37) <0.001	48.00 (4.22) <0.001
Timepoint		
Baseline	-	-
6 months	4.78 (3.28) 0.16	3.35 (2.56) 0.20
Treatment		
Non-Diet	-	-
Diet	-0.41 (6.10) 0.95	1.59 (5.88) 0.79
Treatment* Timepoint		
Diet, 6 months	-7.36 (4.57) 0.12	-8.57 (3.57) 0.02



Pending Analyses

- Additional adherence data using biologic measurements, dietary recalls and food frequency questionnaires
- Effects on formal cognitive testing
- Effects on plasma fatty acid levels
- Metabolomics
- Gut microbiota analyses

Future research on Mediterranean-style diet in MS

- Larger study specifically designed to evaluate fatigue or other MS symptoms
- Studies evaluating the potential of this dietary intervention as a disease modifier
 - MRI outcomes
 - Clinical outcomes

Conclusions

- There is patient-driven and scientific rationale for interest in the role of diet in MS
- There are multiple potential contributory mechanisms for dietary influence in MS including gut microbiota
- Limited evidence for a role for particular dietary factors and patterns on MS outcomes
- There are several barriers to studying diet in MS which must be overcome in future research
- Preliminarily, a modified Mediterranean dietary intervention seems to reduce fatigue and impact of MS symptoms
- Further research is needed

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Samantha Gallo

UCLA

Lenore Arab

Johns Hopkins

Kate Fitzgerald

Our patients and their families!



Cited Sources

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- Slide 9: <http://triwellnesscenter.com/rainbow-of-wellness>
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- Slide 15: Azary et al *JNNP* 2017
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- Slide 19: ¹Azary et al. *JNNP* 2017; ²Hadgkiss *Nutritional Neuroscience* 2014
- Slide 20: Fitzgerald *Neurology* 2017
- Slide 21: Stefferi *J Immunology* 2000; Guggenmos *J Immunology* 2004
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- Slide 24: ¹McDonald *MSARD*; ²Nourbakhsh *JNNP* 2016; ³Fitzgerald *Annals of Neurology* 2017
- Slide 27: Hadgkiss *Nutritional Neuroscience* 2014; Fitzgerald *Neurology* 2017
- Slide 28: Bisht *J of alternative and complementary medicine* 2014
- Slide 29: Yadav *MSARD* 2016

Webinar Series



Practical Meal Planning Techniques & Strategies

March 12, 2019

Presented by:



Celgene | Genentech | Mallinckrodt Pharmaceuticals

Complete an honest evaluation of your skills/deficits as relate to your MS

Areas that may be impacted by your MS include:

- Fatigue
- Sensation
- Balance
- Cognition
- Fine motor skills
- Strength



Do You Have Issues With Cognition?

Compensatory Strategies may include:

- Use meal planning phone/tablet apps
- Choose meals with fewer ingredients
- Make lists
- Use a slow cooker
- Use the microwave
- Use a kitchen timer



Do You Have Issues with Community Mobility?

Compensatory Strategies may include:

- Use of a motorized cart while shopping
- Use of delivery/pick up services
- Shop at a smaller store
- Use a handicapped placard for parking
- Shop during your “best time of the day”



What's Happening Today?

Day of the week: _____ Date: _____

Daily Schedules

5am
6am
7am
8am
9am
10am
11am
12pm
1pm
2pm
3pm
4pm
5pm
6pm
7pm

To-Do List

What's for dinner?

Notes

Inspiration

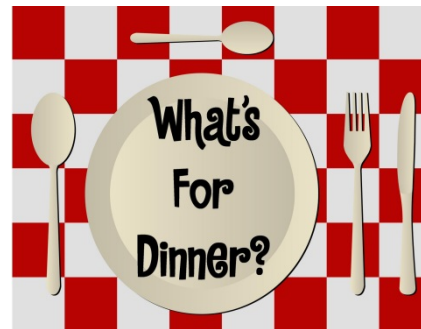


Lambert's Patch 2015

Do You Have Issues With Fatigue?

Compensatory strategies may include:

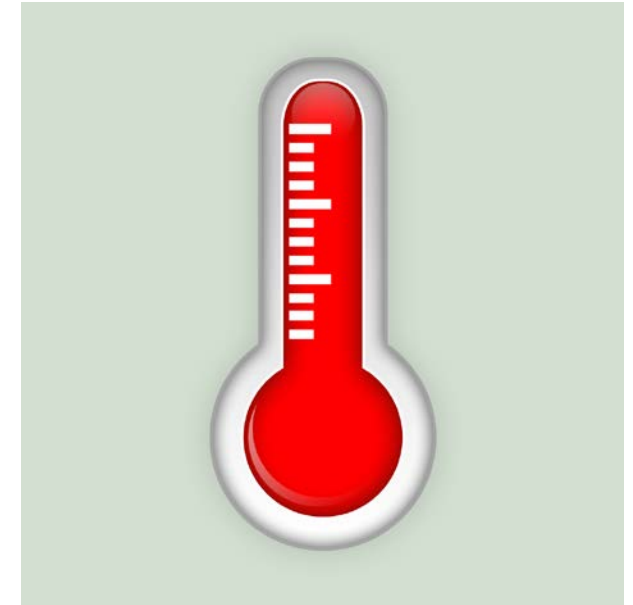
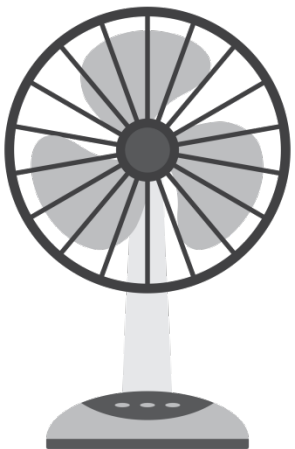
- Sit to complete as much meal prep as possible
- Cook on days that aren't too busy with other activities
- Cook with a friend/family member/caregiver
- Slide heavy objects instead of trying to lift and carry
- Soak pots and pans to eliminate scrubbing



Do You Have Issues With Heat Tolerance?

Compensatory strategies may include:

- Use a fan
- Wear a cooling vest
- Sip on cold water while you are working



Do You Have Issues With Vision?

Compensatory strategies may include:

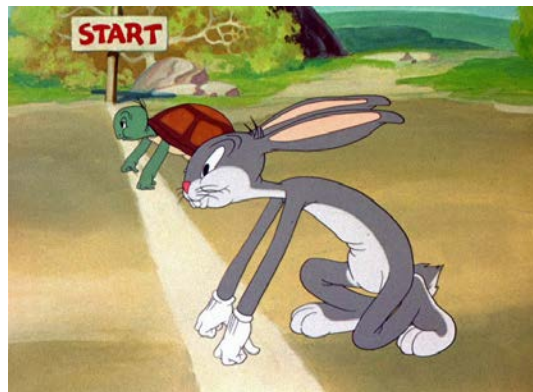
- Put bright colored or raised stickers on the stove/microwave knobs and/or buttons
- Use an angled mirror on the wall behind the stove so that you can see into the pots if you are in a wheelchair
- Use pot stabilizers to keep the pot in place
- Use silicone cooking gloves



Energy Conservation Tips to Remember

Remember and Practice the “4P’s”

- Prioritize- what has to be done today
- Plan – to avoid making extra trips
- Pace – slow and consistent wins the race!
- Position – too much bending and reaching can increase fatigue. Sitting can reduce your energy expenditure.

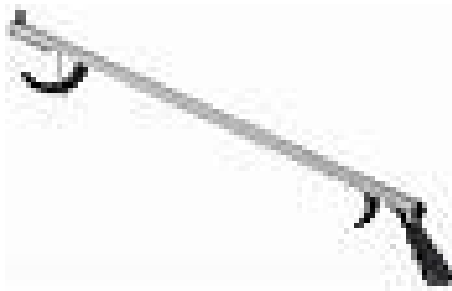


Balance Rest and Activity During Cooking

- Cook when it is your “best time of day”
- Cook when you don’t have a lot of other activities to do that day
- Plan for extra time to complete the meal prep so that you can take rest breaks while you are preparing the food
- Use a timer to remind you about taking a rest break
- Frequent short rest breaks can be better than a long one
- Take a break before you need it



Adaptive Equipment (just a few examples!)



Work Space Considerations



- Make sure your workspace is at the appropriate height
- Create a work flow system in your kitchen
- Use good lighting
- Use good work temperature (not too hot and not too cold)



Community Resources

- Car/curb pick up of groceries
- Grocery delivery services (Insta-cart, local grocery stores, etc.)
- Asking for help from family and friends (your support network)



Availability of Skilled Therapy Services

- All you need is a written referral from your physician
 - Occupational Therapy – can assist you in finding ways to maximize your meal preparation skills through the use of adaptive equipment/adapted techniques, organizational skills, and incorporation of energy conservation techniques
 - Physical Therapy – can help with mobility issues (home and community)
 - Speech Language Pathology – can help with high level cognitive issues that impact your meal preparation skills



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