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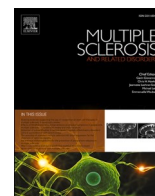
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Original article

Sociodemographic and clinical characteristics of diet adherence and relationship with diet quality in an international cohort of people with multiple sclerosis

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ABSTRACT

Background: Diet has been associated with the onset and progression of multiple sclerosis (MS). Multiple diets, varying in recommendations, have been proposed as beneficial to people with MS. The characteristics of those who follow specific diet-programs and the relationships of these diet-programs with diet quality is under-explored.

Methods: Data from the HOLISM study were analysed. Adherence to selected MS-specific diets (Ashton Embry Best Bet, McDougall, Overcoming MS (OMS), Palaeolithic, Swank, and Wahls Elimination) were each queried on 5-point Likert scales, and moderate ($\geq 3/5$) and rigorous ($\geq 4/5$) adherence defined. Sociodemographic and clinical characteristics of adherence were evaluated by log-binomial regression. Relationships of diet-program adherence with diet quality as measured by Diet Habits Questionnaire were assessed by linear and log-binomial regression, as appropriate, adjusted for age, sex, socioeconomic status (SES), education, and clinically significant fatigue.

Results: Forty-nine percent of participants reported at least 12-month adherence to a diet-program for their MS. Of these, 31.3% rigorously adhered to OMS, 4.9% to Swank, 1.7% to Wahls, and <1.5% to other diet-programs. Only adherence to any diet-program, OMS, Wahls, and Swank, were quantitatively assessed. Females, and participants of lower-than-average SES and longer disease duration were less adherent to any diet-program for MS, as well as those with higher disability, more clinically significant fatigue, greater depression risk, and more comorbidities. Those with higher-than-average SES were more adherent, as were those with higher physical and mental quality of life. Similar relationships were seen for OMS diet-program adherence. Adherence to Wahls diet-program was higher among those with progressive MS types and longer disease duration. No associations were found for adherence to Swank diet-program. Overall diet quality was higher among participants following any diet-program, particularly OMS and Swank, but not Wahls.

Conclusion: Greater adherence to MS specific diets was associated with higher SES, and higher quality of life. Following any diet program was associated with higher overall diet quality, with those adhering to the OMS diet having the highest diet quality. These results may inform health professionals in providing guidance to patients regarding diet in MS.

1. Introduction

Growing evidence shows that modifiable lifestyle behaviours, including diet, may play a role in symptom management and slowing disease progression (Sand, 2018), and might be associated with improving quality of life (QoL) in people with multiple sclerosis (MS) (Hadgkiss et al., 2015). However, the evidence for recommending a

single diet-program for people with MS is lacking (Evans et al., 2019). There is an increasing diversity of studies suggesting that better diet quality is associated with improved clinical outcomes, including relapse (Simpson-Yap et al., 2020), disability (Fitzgerald et al., 2018a), and QoL (Evers et al., 2021). Consequently, there has been a strong motivation among people with MS to use diet to help their MS, leading some investigators to apply these results to develop diet-programs that might

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benefit clinical progression in MS.

The Swank diet-program, developed in the 1950s, minimises intake of saturated fats, fatty meats, and processed food (Swank, 1953). In a longitudinal study of people following this diet spanning several decades, participants maintaining 20 g/day or less intake of saturated fat had lower mortality rate and lower disability progression compared to less adherent participants (Swank, 1970; Swank and Dugan, 1990). The Overcoming MS (OMS) diet-program minimises saturated fats and recommends a plant-based whole-food diet plus seafood (Jelinek, 2016). Adherence to a healthy multimodal lifestyle program, of which the OMS diet-program is a part, has been positively associated with improved physical and mental quality of life, and reduced symptoms of fatigue and depression in people with MS (Hadgkiss et al., 2015a). The McDougall diet-program also recommends a plant-based diet but without seafood (McDougall and McDougall, 2016), and has been shown to improve fatigue in a randomised clinical trial (RCT) (Yadav et al., 2016). The Wahls Elimination diet-program is a modified Palaeolithic diet recommending avoidance of processed foods, grains, soy, dairy, eggs, and legumes, while embracing fruits, vegetables, grass-fed meat, fish, and healthy fats (Wahls and Adamson, 2014). This diet-program has been associated with improvements in QoL and fatigue (Bisht et al., 2014; Irish et al., 2017). The Best Bet diet-program (Embry; Embry, 2018) aims to reduce the effects of leaky gut syndrome by avoiding proteins that trigger immune responses; however, no studies have examined its effects in people with MS. Specific characteristics of each diet are shown in Table 1.

Little is known about the sociodemographic and clinical characteristics of people with MS who adhere to specific MS-diets. The North American Research Committee on MS (NARCOMS) registry assessed adherence to various diet-programs in a survey of 6990 people with MS (Fitzgerald et al., 2018b), 45% of whom reported a history of following a specific diet-program. The Swank and Wahls diet-programs were the only MS-specific diets queried, which had 85 (1.2%) and 104 (1.5%) current followers, respectively. More recently, diet adherence was assessed in the Australian MS Longitudinal Study (AMSLS), finding that 21.2% of 1490 participants reported following a particular diet and roughly 7.7% followed an MS-specific diet, including 6.3% following the

OMS, 0.9% Wahls, and 0.5% the Swank diet-programs (Marck et al., 2021). The characteristics of persons adhering to individual diets were not systematically assessed in either study, however.

There is also interest in the nutritional characteristics of these diets and whether the exclusions of specified foods in the diet-programs impact on diet quality. The nutritional characteristics of the Swank diet-program has been compared with general US dietary recommendations, finding no deficits (Chenard et al., 2019b). However, the Wahls diet-program was found to be lacking in some nutrients and to have excessive saturated fat and sodium (Chenard et al., 2019a). Work in the NARCOMS cohort assessing dietary quality of the Swank and Wahls diet-programs generally found them to have higher diet quality compared to persons not following any diet (Fitzgerald et al., 2018b). However, a robust assessment of the diet quality of people following MS-specific diet-programs and individual diet-programs in a broad international sample is yet lacking.

Accordingly, we conducted a study of the frequency and characteristics of following several MS-specific diet-programs, and their relationships with diet quality, in a large international cohort of people with MS.

2. Methods

2.1. Study design and participants

Data were analysed from the international Health Outcomes and Lifestyle In a Sample of people with Multiple sclerosis (HOLISM) study, approved by the Health Sciences Human Research Ethics Committee at The University of Melbourne (ID=1545102). Participants ($n = 2466$) were recruited online to complete a self-reported survey capturing sociodemographic, clinical, and lifestyle data, and at 2.5-year intervals thereafter (Hadgkiss et al., 2013; Weiland et al., 2018). Adherence to MS-specific diet-programs was queried at 5-year follow-up; therefore analysis for this study was restricted to survey responses at this time-point, among participants aged ≥ 18 years with a self-reported clinician-confirmed MS diagnosis.

2.2. Diet-program adherence

Participants were asked, "Do you currently follow a particular MS diet?". A 'no' response was classified as non-adherent. If "yes", participants were then asked to specify duration and level of adherence on a 5-point Likert scale, 5 being maximum adherence, for one or more of these diets: Ashton Embry Best Bet, McDougall, OMS, Palaeolithic, Swank, and Wahls. Adherence to a diet-program was constrained to those who reported following the diet-program for at least 12 months.

To maximize the sensitivity and specificity, three definitions were used: non-adherent was defined as a Likert score of 1–2, moderate adherence as a Likert score of 3–5/5, and rigorous as a score of 4–5/5. Only adherence to OMS, Swank, and Wahls diet-programs were analysed individually, as other diet-program options had too few participants adhering.

2.3. Other measures

Sociodemographics: Sex (male/female) and birthdate were queried at baseline, and from the latter age was calculated. Perceived relative socioeconomic status (SES) was queried on a 9-point Likert scale (Howe et al., 2011), then consolidated to ≤ 4 =lower-than-average, 5=same (reference), and ≥ 6 =higher-than-average. Highest level of education completed was queried, then consolidated to 'secondary school or lower', 'vocational education' and 'bachelor/postgraduate'.

Clinical: MS type: non-progressive (benign/RRMS), progressive (SPMS/PPMS/PRMS), and 'unsure/other'; number of doctor-diagnosed relapses in the preceding year: 0, ≥ 1 ; duration since MS onset: quartile years; immunomodulatory medication use (yes/no); disability

Table 1
Permitted and not permitted food groups for each MS-specific diet-program.

MS-Diet	Nutritional Guideline
Swank Diet (Wahls et al., 2018)	Permitted: Restrict animal protein to skinless poultry and saturated animal fat intake limit to 15 g/day. Seafood, eggs yolks, dairy, fruits and vegetables, cereals and grains, Not Permitted: Butter, margarine and coconut oil.
OMS Diet (Jelinek, 2016)	Permitted: Seafood, fruits and vegetables (avocado/nuts/seeds in moderation), cereals and grains. Not Permitted: Meat, poultry, eggs, dairy, margarine, coconut oil, palm oil, and vegetable oil.
Wahls Elimination Diet (Wahls et al., 2018)	Permitted: Meat, poultry, seafood, olives, coconuts, ghee, avocado, flax, hemp, walnut, sesame, sunflower oil, tahini, rendered animal fat/ bacon grease. Not Permitted: Eggs, dairy, legumes, nightshades, white fruits or vegetables, cereals, grains and vegetable oil.
McDougall Diet (McDougall and McDougall, 2016)	Permitted: Fruits and vegetables (avocado/nuts/seeds in moderation), non-starchy vegetables/soy based products in moderation, cereals and grains. Not Permitted: Meat, poultry, seafood, eggs, dairy, vegetable oil, margarine.
Best Bet Diet (Embry, 2018)	Permitted: Meat (red meat in moderation), poultry, seafood, eggs (in moderation), fruits and vegetables. Both salad oil, and margarine in moderation. Not Permitted: Eggs, legumes, cereals, grains.

measured by Patient-derived MS Severity Score (P-MSSS (Kister et al., 2013)): 0–3='normal/mild', >3 to <6='moderate', >6='severe'; quality of life by the MSQoL-54 (Vickrey et al., 1995), estimating physical and emotional QoL composite scores; fatigue measured by Fatigue Severity Scale: mean FSS \geq 5 defined clinically significant fatigue (Krupp et al., 1989); depression risk, measured by Patient Health Questionnaire-9 (PHQ-9)(Kroenke et al., 2001), a score>9 indicating depression risk; and treated comorbidity number at baseline assessed by the Self-Administered Comorbidity Questionnaire (SCQ)(Sangha et al., 2003).

Diet quality: Diet quality was assessed by a modified Diet Habits Questionnaire (DHQ) (McKellar et al., 2008), as described previously (Hadgkiss et al., 2013). The DHQ was originally designed for assessing diet quality and diet education requirements among cardiac rehabilitation patients, but has since been applied in the HOLISM study (Hadgkiss et al., 2015; Jelinek et al., 2016) and other MS studies (Marck et al., 2021). The modifications made in the HOLISM context was to omit three questions about salt consumption and one on alcohol intake, this latter element redundant with questions about alcohol consumption elsewhere in the survey. In addition, DHQ questions about whether participants opt for low-fat versus full-fat dairy products, and whether they trim the fat/skin from meat and how often they consume processed meats were modified to include responses of "I do not consume dairy" and "I do not consume meat", respectively. The DHQ estimates an overall diet quality score, ranging 20–100%, higher score indicating better diet quality. It also estimates several subscores, including fruit/vegetable, cereals, and takeaway intake, as well as for their fat, fiber, and omega-3 content, each ranging 1–5 but scaled out of 100%, a higher score indicating healthier diet for that domain. The excluded alcohol and sodium-related questions did not impact on the scoring of other subdomains. For the overall diet quality score and the subscores, a higher score indicates healthier diet.

2.4. Statistical analysis

Characteristics of diet-program adherence were assessed by log-binomial regression, estimating prevalence ratios (PR). Relationships of diet-program adherence with total DHQ score were assessed by linear regression. Total DHQ score and DHQ subdomains were dichotomised at the median of each, and these then evaluated by log-binomial regression. All multivariable analyses were adjusted for sex, age, SES, education, and clinically significant fatigue.

Analyses were conducted using STATA/SE 16.0 (StataCorp, College Park, TX, USA).

3. Results

3.1. Participant characteristics

The study cohort comprised 952 participants (Table 2): of these, 82.9% were female, of mean age 50.9 years, 54.2% reported higher-than-average perceived relative SES, and 69.5% had completed university. MS type was predominantly benign/RRMS (70.2%), and 44.1% reported using immunomodulatory medication. 65.8% of participants were of normal/mild disability, 56.3% had clinically significant fatigue, 20.7% had depression risk, and 39.9% had at least one comorbidity. The median DHQ score was 77/100, and was similarly high across the subdomains.

3.2. Diet-program adherence

Overall, 465 (48.8%) participants reported following an MS-specific diet-program for at least 12 months (Table 3). Proportions of participant adherence for moderate and rigorous diet-program adherence, respectively, were highest for OMS (38.1%, 29.9%), followed by Swank (6.3%, 4.7%), Wahls (3.1%, 1.7%), then Palaeolithic (2.0%, 1.5%), Ashton

Table 2

Participant sociodemographic and clinical characteristics at 5-year review.

	n (%)
Sex	
Male	163 (17.1%)
Female	789 (82.9%)
Age, years	50.9 (10.4) [†]
Perceived relative SES	
Lower-than-average	176 (18.5%)
Same	251 (26.4%)
Higher-than-average	516 (54.2%)
Missing	9 (0.9%)
Highest level of education completed	
Secondary school or lower	148/952(15.6%)
Vocational training	134/952 (14.1%)
University	662/952 (69.5%)
Missing	8 (0.8%)
MS type	
Benign/RRMS	668 (70.2%)
SPMS/PPMS/PRMS	164 (17.2%)
Unsure/other	111 (11.7%)
Missing	9 (0.9%)
MS immunomodulatory medications	
None	532 (55.9%)
IFN	63 (6.6%)
Other	357 (37.5%)
Disability (PMSSS)	
Normal/mild	626 (65.8%)
Moderate	222 (23.3%)
Severe	101 (10.6%)
Missing	3 (0.3%)
Clinically significant fatigue (FSS)	
No	382 (40.1%)
Yes	536 (56.3%)
Missing	34 (3.6%)
Depression risk (PHQ-9)	
No	723 (75.9%)
Yes	197 (20.7%)
Missing	32 (3.4%)
Baseline number of treated comorbidities (SCQ)	
0	572 (60.1%)
\geq 1	380 (39.9%) [†]
DHQ score, total	77 (68–86) [‡]
DHQ cereal subscore	73.3 (60–86.7) [‡]
DHQ fruit/vegetable subscore	76 (64–88) [‡]
DHQ takeaway subscore	66.7 (53.3–80) [‡]
DHQ fat subscore	83.5 (72.3–92.3) [‡]
DHQ fiber subscore	75 (65–87.5) [‡]
DHQ omega subscore	80 (40–100) [‡]
MS duration, years	16.5 (24.6 – 10.5) [†]
Physical QoL (MSQOL-54)	67.3 (84.2– 47.4) [‡]
Emotional QoL (MSQOL-54)	78.4 (87.8–59.6) [‡]

Results presented as n/N (%) unless otherwise denoted.

Abbreviations: DHQ=Diet Habits Questionnaire; FSS=Fatigue Severity Scale; IQR= Interquartile range; MSQOL=Multiple Sclerosis Quality of Life; MS=Multiple Sclerosis; PHQ-9=Patient Health Questionnaire-9; P-MSSS=Patient-derived MS Severity Scores; QoL=Quality of Life; SCQ=Self-Administered Comorbidity Questionnaire; SD=Standard deviation; SES=Socioeconomic status.

[†] Mean (SD; minimum-maximum).

[‡] Median (Interquartile range).

Embry Best Bet (0.7%, 0.5%), and McDougall (0.5%, 0.4%).

3.3. Characteristics of participants adhering to any diet-program for their MS

Sociodemographic and clinical characteristics of participants adhering to any diet-program for their MS (Table 4) showed females had 23% less frequent adherence than males. Compared to participants of same SES, diet-program adherence was 29% less frequent in participants of lower-than-average SES, and 21% more frequent in participants of higher-than-average SES. Diet-program adherence was less frequent in participants with longer MS duration, and more frequent in those with

Table 3
Distribution of participants following any MS diet and individual diets, and adherence rigor, constrained to those following a diet for at least 12 months.

	Total	Moderate adherence	Rigorous adherence
Follow any diet?			
No	487/952 (51.2%)		
Yes	465/952 (48.8%)		
Follow OMS diet?			
Not rigorous at all	580/952 (60.9%)	589/952 (61.9%)	667/952 (70.1%)
2	9/952 (1.0%)	363/952 (38.1%)	285/952 (29.9%)
3	78/952 (8.2%)		
4	146/952 (15.3%)		
Very rigorously	139/952 (14.6%)		
Follow Wahls diet?			
Not rigorous at all	918/952 (96.4%)	923/952 (97.0%)	936/952 (98.3%)
2	5/952 (0.5%)	29/952 (3.1%)	16/952 (1.7%)
3	13/952 (1.4%)		
4	11/952 (1.2%)		
Very rigorously	5/952 (0.5%)		
Follow Swank diet?			
Not rigorous at all	889/952 (93.4%)	892/952 (93.7%)	907/952 (95.3%)
2	3/952 (0.3%)	60/952 (6.3%)	45/952 (4.7%)
3	15/952 (1.6%)		
4	28/952 (2.9%)		
Very rigorously	17/952 (1.8%)		
Follow McDougal diet?			
Not rigorous at all	945/952 (99.3%)	947/952 (99.5%)	948/952 (99.6%)
2	2/952 (0.2%)	5/952 (0.5%)	4/952 (0.4%)
3	1/952 (0.1%)		
4	1/952 (0.1%)		
Very rigorously	3/952 (0.3%)		
Follow Palaeolithic diet?			
Not rigorous at all	930/952 (97.7%)	933/952 (98.0%)	938/952 (98.5%)
2	3/952 (0.3%)	19/952 (2.0%)	14/952 (1.5%)
3	5/952 (0.5%)		
4	10/952 (1.1%)		
Very rigorously	4/952 (0.4%)		
Follow Ashton-Embry diet?			
Not rigorous at all	945/952 (99.3%)	945/952 (99.3%)	947/952 (99.5%)
2	0	7/952 (0.7%)	5/952 (0.5%)
3	2/952 (0.2%)		
4	4/952 (0.4%)		
Very rigorously	1/952 (0.1%)		

Abbreviations: OMS=Overcoming Multiple Sclerosis.

better physical and emotional QoL. Compared to those with normal/mild disability, adherence was 27% less frequent in participants with severe disability, and 30% less frequent in those with clinically significant fatigue, 27% less frequent in those with depression risk, and 24% less frequent in those with comorbidities. Age, education, MS type, number of relapses in the past 12 months, and immunomodulatory medication use were not associated with diet-program adherence.

3.4. Characteristics of participants adhering to OMS, Wahls, and Swank diet-programs

Adherence to the OMS diet-program was positively associated with SES, physical and mental QoL (Fig. 1), and male sex, and inversely associated with MS duration, disability, clinically significant fatigue and depression risk (Fig. 2), and with comorbidity number (Supplementary Table 1). Generally, these associations persisted or enhanced in

Table 4
Sociodemographic and clinical characteristics of participants reporting adherence any diet-program for their MS.

	n/N (%)	PR (95% CI)	aPR (95% CI)
Sex			
Male	100/163 (61.4%)	1.00 [Reference]	1.00 [Reference]
Female	365/789 (46.3%)	0.75 (0.65, 0.87)	0.77 (0.67, 0.89)
		<i>p</i> < 0.001	<i>p</i> < 0.001
Age, years			
23.8–42.9	122/238 (51.3%)	1.00 [Reference]	1.00 [Reference]
43–50.8	127/238 (53.4%)	1.04 (0.88, 1.24)	1.11 (0.94, 1.32)
50.9–58.2	111/238 (46.6%)	0.91 (0.76, 1.09)	1.03 (0.86, 1.25)
58.13–84.1	105/238 (44.1%)	0.86 (0.71, 1.04)	1.03 (0.86, 1.24)
Trend:		<i>p</i> = 0.052	<i>p</i> = 0.81
SES			
Lower	54/176 (30.7%)	0.69 (0.53, 0.90)	0.71 (0.54, 0.92)
Same	111/251 (44.2%)	1.00 [Reference]	1.00 [Reference]
Higher	296/516 (57.4%)	1.30 (1.11, 1.52)	1.21 (1.04, 1.42)
Trend:		<i>p</i> < 0.001	<i>p</i> < 0.001
Education			
Secondary or lower	55/126 (43.7%)	1.00 [Reference]	1.00 [Reference]
Vocational	52/146 (35.6%)	0.82 (0.61, 1.10)	0.79 (0.59, 1.05)
University	355/672 (52.8%)	1.21 (0.98, 1.49)	1.00 (0.82, 1.24)
Trend:		<i>p</i> = 0.006	<i>p</i> = 0.49
MS type			
Benign/RRMS	333/668 (49.9%)	1.00 [Reference]	1.00 [Reference]
Progressive	70/164 (42.7%)	0.86 (0.71, 1.04)	1.11 (0.89, 1.38)
Unsure/other	58/111 (52.3%)	1.05 (0.86, 1.27)	1.08 (0.89, 1.31)
MS duration, years			
4.46–11.41	142/2652 (56.4%)	1.00 [Reference]	1.00 [Reference]
>11.41–17.42	133/246 (54.1%)	0.96 (0.82, 1.12)	0.97 (0.83, 1.14)
>17.42–25.59	109/233 (46.8%)	0.83 (0.70, 0.99)	0.87 (0.73, 1.05)
>25.59–50.17	81/218 (37.2%)	0.66 (0.54, 0.81)	0.72 (0.58, 0.90)
Trend:		<i>p</i> < 0.001	<i>p</i> = 0.004
Relapses in the previous 12 months			
0–1	438/884 (49.6%)	1.00 [Reference]	1.00 [Reference]
2	11/25 (44.0%)	0.89 (0.57, 1.39)	1.04 (0.65, 1.67)
>2	3/11 (27.3%)	0.55 (0.21, 1.45)	0.66 (0.24, 1.81)
Trend:		<i>p</i> = 0.18	<i>p</i> = 0.55
Disability (PMSSS)			
Normal/mild	342/626 (54.6%)	1.00 [Reference]	1.00 [Reference]
Moderate	95/222 (42.8%)	0.78 (0.66, 0.93)	0.92 (0.77, 1.09)
Severe	28/101 (27.7%)	0.51 (0.37, 0.70)	0.63 (0.45, 0.87)
Trend:		<i>p</i> < 0.001	<i>p</i> = 0.003
Clinically significant fatigue (FSS)			
No	238/382 (62.3%)	1.00 [Reference]	1.00 [Reference]
Yes	213/536 (39.7%)	0.64 (0.56, 0.73)	0.70 (0.61, 0.81)
		<i>p</i> < 0.001	<i>p</i> < 0.001

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Table 4 (continued)

	n/N (%)	PR (95% CI)	aPR (95% CI)
Physical QoL (MSQOL-54)			
6.66–47.39	55/196	1.00	1.00
>47.39–67.38	(28.1%)	[Reference]	[Reference]
>67.38–84.21	82/197	1.48 (1.12, 1.96)	1.36 (1.02, 1.83)
>84.21–100	(41.6%)	2.07 (1.61, 2.67)	1.71 (1.27, 2.31)
Trend:	114/196 (58.2%)	2.51 (1.97, 3.20)	2.05 (1.47, 2.86)
	139/197 (70.6%)	p<0.001	p<0.001
Emotional QoL (MSQOL-54)			
5.50–59.55	80/233	1.00	1.00
>59.55–78.41	(34.3%)	[Reference]	[Reference]
>78.41–87.75	95/233	1.19 (0.94, 1.50)	1.08 (0.85, 1.37)
>87.75–100	(40.8%)	1.56 (1.26, 1.94)	1.28 (1.02, 1.60)
Trend:	125/233 (53.7%)	1.93 (1.58, 2.36)	1.45 (1.15, 1.83)
	155/234 (66.2%)	p<0.001	p<0.001
Depression risk (PHQ-9)			
No	398/723	1.00	1.00
Yes	(55.1%)	[Reference]	[Reference]
	55/197	0.51 (0.40, 0.64)	0.63 (0.50, 0.81)
	(27.9%)	p<0.001	p<0.001
Number of Comorbidities (SCQ)			
0	323/572	1.00	1.00
1 or more	(56.5%)	[Reference]	[Reference]
	142/380	0.66 (0.57, 0.77)	0.76 (0.65, 0.88)
	(37.4%)	p<0.001	p<0.001

Determinants of adherence to any MS diet. All results estimated using log-binomial regression estimating prevalence ratio [95% confidence interval]. Results in boldface indicate significance ($P<0.05$). Abbreviations: FSS=Fatigue Severity Scale; IQR= Interquartile range; MSQOL=Multiple Sclerosis Quality of Life; MS=Multiple Sclerosis; PHQ-9=Patient Health Questionnaire-9; P-MSSS=Patient-derived MS Severity Scores; QoL=Quality of Life; SCQ=Self-Administered Comorbidity Questionnaire; SES=Socioeconomic status. *=Adjusted model for sex, age, SES, highest education, and clinically significant fatigue.

Note: age, MS duration, and QoL were summarised as quartile categorical terms.

magnitude on increasing from moderate to rigorous specificity. Age, MS type, relapse number, and education were not robustly associated with OMS diet-program adherence.

Wahls diet-program adherence was more common among those of progressive MS types and longer MS duration, both increasing in magnitude on increasing from moderate to rigorous specificity. No other characteristics were associated with Wahls diet-program adherence (Supplementary Table 2).

No characteristics were independently or consistently associated with Swank diet-program adherence (Supplementary Table 3).

3.5. Diet-program adherence associations with diet quality

Participants who were following a diet-program for their MS had 12.2% higher DHQ score and were 2.9-times more likely to have DHQ score greater than the median, both persisting on adjustment (Table 5). These associations were strongest for the OMS diet-program, having roughly 15% higher DHQ score and 3.5-times greater risk of having DHQ score>median, persisting on adjustment and being similar for both moderate and rigorous adherence. A weaker but still appreciable positive association with DHQ score was seen for Swank diet-program adherents, having 12–13% higher DHQ scores and roughly 3-times more likely to have DHQ>median, and of similar nature for moderate and rigorous adherence. Wahls diet-program adherence were not associated with statistically different DHQ scores.

Examining DHQ subdomains, those following an MS-specific diet program had higher frequencies of scores above the median for cereal (+59%), fruit/vegetable (+231%), takeaway (+69%), fat (+348%), fiber (+211%), and omega-3 (+311%) subdomains (Supplemental Table 4). These associations were replicated with similar or slightly higher magnitudes for participants following the OMS diet-program. Swank diet-program adherents had higher scores for all subdomains but of reduced magnitude compared to OMS. Wahls diet-program adherents had higher fruit/vegetable, takeaway, fat, and omega subdomain scores but no difference in fiber and were significantly less likely to have higher cereal subdomain scores.

4. Discussion

We have described the frequency and characteristics of adherence to a selection of the most commonly followed diet-programs proposed to

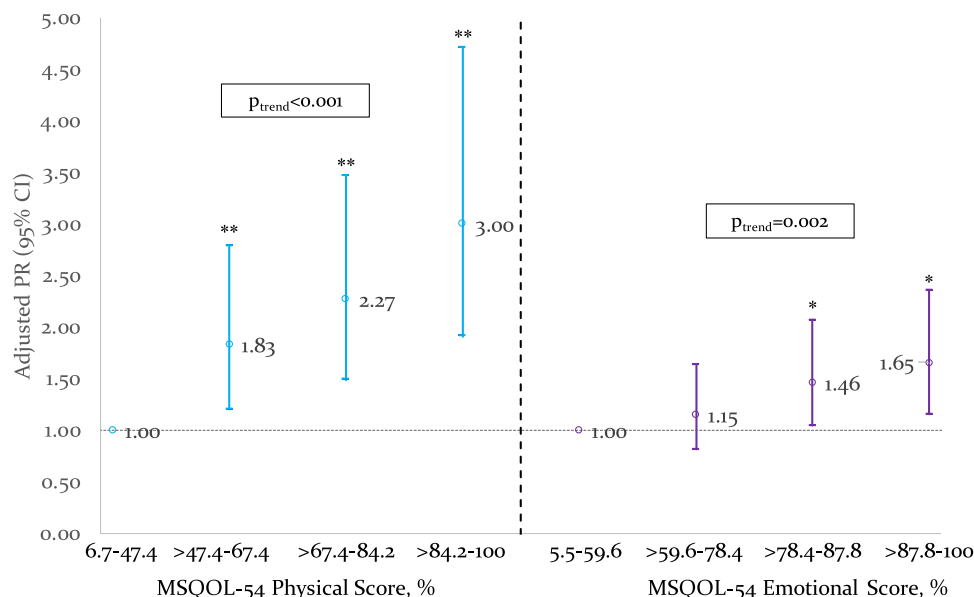


Fig. 1. Adjusted PRs of OMS diet-program adherence vs physical and emotional QoL measures according for rigorous definition. *= $p<0.05$; **= $p<0.001$.

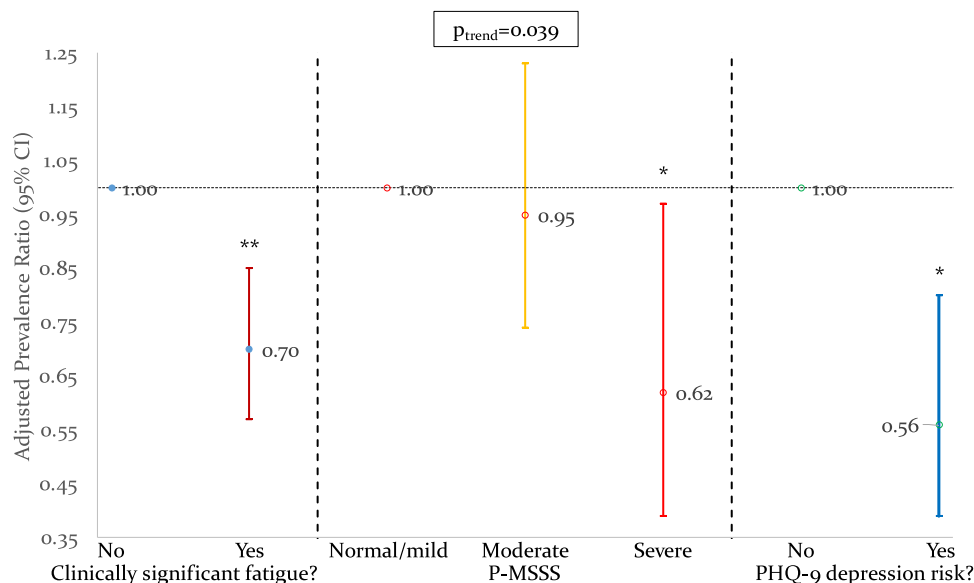


Fig. 2. Adjusted prevalence ratios of OMS diet-program adherence vs clinically significant fatigue, disability, and depression risk for rigorous definition. *= $p < 0.05$; **= $p < 0.001$.

Table 5
Diet quality by adherence to specified diet-programs vs no diet adherence.

	β (95% CI)	a β (95% CI) ^a	PR (95% CI) ^b	aPR (95% CI) ^{a,b}
Any MS-specific diet-program adherence?	12.19 (10.60, 13.78)	11.37 (9.65, 13.10)	2.88 (2.40, 3.47)	2.66 (2.18, 3.23)
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
OMS diet adherence – Moderate	15.32 (13.67, 16.96)	14.60 (12.83, 16.37)	3.54 (2.94, 4.26)	3.30 (2.71, 4.03)
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
OMS diet adherence – rigorous	15.88 (14.03, 17.72)	15.05 (13.10, 17.01)	3.54 (2.96, 4.23)	3.25 (2.68, 3.93)
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Swank diet adherence – Moderate	12.81 (9.38, 16.23)	11.85 (8.37, 15.34)	3.06 (2.44, 3.84)	2.75 (2.14, 3.52)
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Swank diet adherence – rigorous	13.94 (10.19, 17.70)	12.85 (9.02, 16.68)	3.22 (2.58, 4.02)	2.88 (2.27, 3.67)
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p < 0.001$
Wahls diet adherence – Moderate	4.40 (–0.46, 9.26)	4.48 (–0.94, 9.90)	1.43 (0.75, 2.73)	1.44 (0.69, 3.01)
	$p = 0.076$	$p = 0.11$	$p = 0.27$	$p = 0.33$
Wahls diet adherence – rigorous	1.27 (–5.79, 8.33)	–1.54 (–9.86, 6.79)	1.52 (0.64, 3.65)	1.16 (0.36, 3.70)
	$p = 0.72$	$p = 0.72$	$p = 0.34$	$p = 0.80$

Results in boldface denote statistical significance ($p < 0.05$).

^a Models adjusted for age, sex, clinically significant fatigue, disability, and relative perceived socioeconomic status.

^b Models evaluate proportions above the median DHQ score, 77%, estimating a prevalence ratio and 95% CI.

benefit people with MS, finding nearly half of this international cohort of people with MS follow an MS-specific diet-program, the most frequent being the OMS, Wahls, and Swank diet-programs. People who followed a diet-program for their MS in this cohort were more frequently of higher SES and to have higher physical or mental QoL, but less likely to have disability, fatigue, or depression. Those people who adhered to OMS diet-program had less clinical severity, higher QoL, and higher SES. Those adhering to the Wahls diet-program, on the other hand, were

more likely to have progressive MS and longer disease duration. The Swank diet-program showed no associations with any demographic or clinical characteristics, nor any trends in agreement with the OMS diet-program. Diet quality was markedly greater among persons following any diet-program for their MS, particularly the OMS and Swank diet-programs, but no association of Wahls diet-program adherence with overall diet quality was seen.

There is an increasing interest in diet as a potential point of intervention in MS. Diet represents a potentially manageable lifestyle modification for people with MS who are keenly interested in taking some measure of control over their MS. In reaction to this, several diet-programs have been proposed which assert to benefit progression and QoL in this population. These diet-programs are highly variable in nature, however, and have mixed evidence in support of their impact on MS clinical progression (Hadgkiss et al., 2015a; Irish et al., 2017; Swank and Dugan, 1990; Yadav et al., 2016). These studies are of varied quality, however, featuring small sample sizes and cross-sectional study designs, and though some are RCTs, their follow-up is too short and samples too small to draw strong conclusions (Beckett et al., 2019). Moreover, some of the diets (Hadgkiss et al., 2015a; Irish et al., 2017) are one part of a program of various lifestyle modifications, making assessment of the independent effect of diet difficult. Accordingly, some neurologists are hesitant to recommend these diet-programs to their patients (Russell et al., 2020), and may be awaiting demonstration of clinical efficacy through RCTs and other high-level evidence.

In this cohort, we found 48.8% of participants were following an MS-specific diet-program, the largest proportion – 38.1% – following the OMS diet-program, followed by 6.3% following Swank and 3.1% Wahls, and smaller proportions (<1.5%) following other diet-programs. The proportion following any diet-program for their MS is close to that seen in the NARCOMS study, where 45% of 6990 participants reported having ever followed a diet for their MS (Fitzgerald et al., 2018b), and to a web-based survey of diet among 337 people with MS, of whom 42.0% reported having had attempted a diet-program for people with MS or followed dietary recommendations, though in that sample the greatest proportion, 29.7%, followed a Mediterranean-type diet (Riemann-Lorenz et al., 2016). However, these proportions are much higher than that seen in the AMSLS study where only 7.7% reported following a diet-program for their MS (Marck et al., 2021).

Following any diet-program and the OMS diet-program in particular were directly associated with lower disability, clinically significant

fatigue, depression risk, and lower number of treated comorbidities, while adherence was greater among those of higher education and SES. We show a clustering of demographic and clinical characteristics for those following the OMS or Wahls diet-programs, with people adhering to the OMS diet-program less likely to have clinically active disease and more likely to have higher QoL, while the those following the Wahls diet were more likely to be of progressive MS type and have longer disease duration. In comparison with the Fitzgerald study of NARCOMS participants our study evaluated more participant and dietary characteristics. The NARCOMS study found that participants with PPMS were less likely than RRMS and SPMS to have followed one of the specified diets, while those who didn't follow any particular diet were more likely to be male, were current smokers, less physically active, and had less income (Fitzgerald et al., 2018b).

Our finding that participants following a MS-specific diet-program had higher diet quality is in keeping with the results from the NARCOMS study, which found that participants following no diet had the lowest diet quality scores (Fitzgerald et al., 2018b). Similarly, the AMSLS study found that participants following any diet had 8.8% higher DHQ score than those following no diet, though they did not report the difference in DHQ for MS-specific diet programs (Marck et al., 2021). However, whereas we found that those following the OMS and Swank but not the Wahls diet-programs had higher diet quality scores, the Fitzgerald study found adherence to both Swank (+14.6/20) and Wahls (+12.9/20) were associated with higher diet quality, on par with the Mediterranean diet (+14.6/20). Also, in the NARCOMS study, both Swank and Wahls diet-program adherents had similar fruit/vegetable intake, but those following the Swank diet-program had higher intake of whole grains and less red meat consumption, whereas those following the Wahls diet-program consumed less dairy. These results differ from ours, since we found Swank adherents did not have higher cereal intake scores. The differences in diet quality for these two diet-programs from the Fitzgerald study may reflect differences in diet quality measures – the DHQ was used here while they used the NHANES Diet Screener Questionnaire – and the comparative infrequency of participants following these diets in their cohort compared to the HOLISM cohort. This has particular bearing since, while the Swank diet's nutritional profile has been found to not materially differ from a standard healthy diet (Chenard et al., 2019b), the Wahls diet was lacking in calcium and vitamin D and had excessive saturated fat and sodium (Chenard et al., 2019a). The differences in DHQ seen among those following any diet program – 11.4% on adjustment – are potentially very significant as we have previously demonstrated that a 10% higher DHQ was associated with 30% lower frequency of having more severe disability and 5–6% increase in quality of life scores (Hadgkiss et al., 2015), while those with DHQ > 80 had health state utility values 4–5% higher than those of lower DHQ (Campbell et al., 2020). These were cross-sectional analyses and may reflect reverse causality but should these results be substantiated in prospective studies, this may reflect a benefit for MS beyond just improved health and wellbeing. Further examination of these relationships, ideally including a greater array of MS-specific diet-programs, would be worthwhile.

Our study is among the largest investigating the distribution and characteristics of adherence to selected MS-specific diet-programs, and the first to examine in detail the demographic and clinical characteristics of adherence to these programs. That said, it is not without its limitations. Firstly, this analysis is cross-sectional and thus causal directionality cannot be inferred. Indeed, there is potential for reverse causality from characteristics like progressive MS type, higher disability, fatigue, depression, and comorbidity number limiting the capacity or inclination of participants to engage in and maintain a healthy diet, particularly those of the nature described here. Thus, prospective analyses of these relationships are needed to ascertain the causal directionality. Second, the HOLISM cohort has had appreciable attrition since the baseline survey, as described previously (Weiland et al., 2018), the resultant cohort being enriched for healthier participants and

potentially those apt to follow a healthier lifestyle, including the specified diet-programs. Indeed, this is particularly the case for the OMS diet, as the nature of the recruitment may have made people already following the OMS program more likely to participate in the study, this reflected in medium and high engagement with the OMS program comprising three-quarters of the cohort (Lin et al., 2020). This would thus explain the high numbers of participants reporting following the OMS diet-program compared to the other diets, these latter proportions more like that seen elsewhere (Fitzgerald et al., 2018b; Marck et al., 2021; Riemann-Lorenz et al., 2016). Nonetheless, the study is strengthened by a robust and comprehensive data collection of a diversity of factors with wide exposure gradients, allowing the direct assessment of a range of demographic and clinical characteristics of diet adherence, as well as appropriate adjustment for relevant confounders. A potential limitation with regard to our assessment of diet adherence is that it is necessarily self-reported, and there is no set metric of scoring diet intake from the DHQ instrument to assess the extent to which self-reported adherence is valid. Instead, we have utilised a gradation of adherence by two dichotomous terms of moderate and rigorous adherence, since associations persisting on increasing specificity as defined by the moderate vs rigorous adherence definitions should indicate a true association. We also restricted adherence to being at least 12 months, this to better differentiate participants truly following the diet-programs as compared to those only attempting them briefly. Also, there is the potential for people to select more than one of the offered diet programs and so while we did condition on their following diets with some rigor and we would presume there would be one diet participants were following most avidly, this is a limitation. Another issue lies in the fact that the OMS and Wahls diet-programs are one part of multimodal lifestyle modification programs, including physical activity, supplement use, and other behaviours. We did not, however, query whether persons were following the whole program for each. Finally, it is important to acknowledge that what drives people to start and maintain a specialised diet program are complex, being idiosyncratic to the individual and their circumstances. We have explored this to some extent in a qualitative study of what facilitated people maintaining adherence to a multimodal lifestyle modification program, including diet (Barnard et al., 2018), but a broader qualitative study of what helps and harms diet adherence would help better understand this.

Conclusions

For the first time, we have comprehensively examined demographic and clinical associations with adherence to several MS-specific diet-programs, finding that nearly half follow a diet-program, the most common in this sample being the OMS, Swank, and Wahls diet-programs. Adherence to diet-programs is not consistently greater among those of higher clinical severity, education or SES, but rather there were particular characteristics of persons following the individual diet-programs. Greater adherence to MS specific diets was associated with higher SES, and higher quality of life. Following any diet program was associated with higher overall diet quality, with those adhering to the OMS diet in particular having the highest diet quality. Should these results be replicated in other cohorts, it would inform health professionals seeking to advise their patients on the potential benefits to diet quality of following such diet-programs.

CRedit authorship contribution statement

Steve Simpson-Yap: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision. **Nupur Nag:** Conceptualization, Resources, Writing – review & editing, Supervision, Project administration. **Mohamed Jakaria:** Formal analysis, Investigation, Writing – review & editing, Visualization. **George A Jelinek:** Conceptualization, Writing – review & editing, Project administration,

Funding acquisition. **Sandra Neate**: Resources, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

GAJ is the author of “Overcoming Multiple Sclerosis”, founder of the OMS Charity and the data custodian for the HOLISM study. GJ and SN have been previously remunerated for facilitation of residential lifestyle modification workshops.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.msard.2021.103307](https://doi.org/10.1016/j.msard.2021.103307).

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