Supplementary Table 1. Subject Characteristics

	NMO	MS	HC
Age - years (SD)	47.9 (13.9)	54 (11.5)	53 (15.9)
Disease duration - years (SD)	3.7 (3.2)	15.3 (8.6)	–
Gender - number (%)			
Women	12 (75.0)	8 (50.0)	7 (43.8)
Men	4 (25.0)	8 (50.0)	9 (56.2)
Demographics - number (%)			
White / Caucasian	3 (18.8)	13 (81.3)	11 (68.8)
Black / African-American	3 (18.8)	0 (0)	2 (12.5)
Asian / Pacific Islander	5 (31.3)	1 (6.3)	2 (12.5)
Other / Not Reported	5 (31.3)	2 (12.5)	1 (6.3)
Disease Course - number (%)			
NMO			
Monophasic	0 (0)	–	–
Polyphasic	16 (100)	–	–
MS			
RRMS	–	9 (56.3)	–
SPMS	–	4 (25.0)	–
PPMS	–	3 (18.8)	–

RRMS=relapsing MS, SPMS=secondary progressive MS, PPMS=primary progressive MS. Of the NMO subjects, 8 were actively treated with rituximab, 6 with mycophenolate mofetil, and 1 with azathioprine. Of the MS subjects, 5 were actively treated with rituximab and 1 subject had remote prior exposure to rituximab with B cell reconstitution at the time of sample acquisition.

Supplementary Table 2. Comparison of Age, Weight, Height, BMI and Nutritional Intake Between NMO, MS and HC.

	NMO		MS		HC		
	Mean	SD	Mean	SD	Mean	SD	Prob > F
Age (years)	48.13	14.44	54.27	11.82	54.13	15.77	0.404
Weight (pounds)	157.33	32.81	152.60	17.96	155.73	29.01	0.377
Height (inches)	65.40	3.89	68.27	4.54	67.73	4.89	nd
Body Mass Index (BMI)	26.04	6.28	23.25	3.59	23.83	4.10	0.234
Food energy (kcals)	1277.76	770.01	1477.91	769.96	1439.73	876.90	0.772
Protein (g)	51.86	39.56	56.93	30.02	57.24	35.35	0.896
Fat (g)	54.21	28.42	57.98	23.93	60.06	34.37	0.858
Carbohydrate (g)	142.93	98.10	180.86	122.22	157.69	111.00	0.643
Calcium (mg)	593.41	374.20	628.81	311.82	699.01	456.00	0.748
Phosphorus (mg)	875.89	620.63	990.97	528.91	997.54	612.37	0.818
Iron (mg)	9.24	7.26	13.18	8.58	12.51	8.26	0.365
Sodium (mg)	2066.69	1295.37	2590.91	1482.46	2440.54	1532.65	0.594
Potassium (mg)	1836.98	1307.26	2769.56	1529.76	2188.23	1147.57	0.168
Glutathione, total (mg)	27.40	22.96	39.21	18.18	32.57	18.01	0.275
Glutathione, reduced (mg)	18.26	16.25	24.77	11.59	21.83	12.88	0.435
Thiamine (Vitamin B1)(mg)	1.11	1.11	1.42	1.05	1.32	1.04	0.719
Riboflavin (Vitamin B2)(mg)	1.42	1.07	1.74	0.96	1.86	1.23	0.536
Niacin (mg)	15.73	17.16	18.00	10.64	18.82	15.56	0.838
Vitamin C (mg)	90.55	89.50	144.09	89.42	94.41	66.83	0.154
Saturated fat (g)	16.16	8.13	15.39	6.97	19.02	12.54	0.549
Monounsaturated fatty acids (g)	22.08	11.94	22.68	8.24	23.23	12.04	0.959
Polyunsaturated fatty acids (g)	12.14	7.16	15.33	7.78	13.25	7.92	0.512
Cholesterol (mg)	172.81	96.09	155.60	81.35	193.96	107.08	0.549
Dietary fiber (g)	12.69	13.06	21.97	18.42	14.50	8.63	0.168
Dietary soluble fiber (g)	3.97	3.81	6.67	6.04	4.61	3.14	0.240
Food folate (mcg)	232.62	247.41	375.84	224.22	266.63	141.85	0.160
Alpha-tocopherol (Vitamin E)(mg)	6.40	4.56	8.81	3.55	7.27	4.45	0.294
Zinc, total (mg)	7.07	4.98	8.84	4.50	9.68	6.08	0.387
Zinc, animal sources only (mg)	3.29	1.91	3.17	1.80	4.40	2.33	0.195
Vitamin B6 (mg)	1.46	1.80	1.81	1.04	1.68	1.39	0.792
Magnesium (mg)	251.02	251.95	331.96	200.04	268.60	160.74	0.537
Vitamin A, RAE (mcg)	716.68	612.13	1060.01	616.84	694.18	372.07	0.133
Retinol (mcg)	386.86	359.49	302.86	189.98	286.56	154.48	0.508
Alpha-carotene (mcg)	284.86	232.46	942.88	856.77	457.90	429.55	0.008
Beta-carotene (mcg)	3779.69	4153.71	8645.11	5544.01	4661.54	2810.62	0.008

(continued)	NMO		MS		HC		
	Mean	SD	Mean	SD	Mean	SD	Prob > F
Cryptoxanthin (mcg)	116.24	140.61	205.49	167.74	112.15	100.85	0.129
Lutein-Zeaxanthin (mcg)	2791.78	2972.67	8008.93	5984.31	4220.07	2649.45	0.004
Lycopene (mcg)	2679.46	2102.53	4764.37	4696.59	4470.66	4237.80	0.286
Folic acid (mcg)	97.42	80.05	123.17	126.16	158.30	183.68	0.479
Vitamin B12 (mcg)	4.26	4.00	3.63	2.63	4.41	3.39	0.803
Vitamin D (IU)	119.53	122.72	104.03	99.04	84.03	58.41	0.608
Phylloquinone (Vitamin K_1) (mcg)	158.80	157.07	427.28	307.52	245.53	148.36	0.005
Copper (mg)	1.18	1.20	1.51	1.00	1.19	0.74	0.594
Selenium (mcg)	64.86	44.47	73.65	35.79	77.73	43.61	0.688
Sugars, total (g)	64.29	46.87	77.48	42.86	65.37	42.07	0.663
Trans fats, total (g)	1.45	0.94	1.15	0.69	1.58	1.11	0.431
Isoflavones, total (mg)	4.09	10.75	7.06	22.23	2.84	3.21	0.713
Quercetin (mg)	6.59	5.50	7.64	5.01	6.12	7.84	0.793
Cysteine, S-containing (mg)	0.64	0.45	0.70	0.38	0.74	0.44	0.834
Methionine, S-containing (mg)	1.00	0.58	1.08	0.50	1.12	0.63	0.853
Cystine, S-containing (mg)	0.61	0.40	0.68	0.40	0.62	0.35	0.886
Average daily dietary folate equivalents (mcg)	398.23	364.85	585.23	366.64	535.75	420.19	0.394
Glycemic index (glucose), average daily	48.83	2.86	46.03	4.28	48.64	4.37	0.101
Glycemic load (glucose), average daily	63.45	41.56	72.34	45.31	70.73	54.65	0.862
Dietary arginine (mg)	2382.49	1617.03	3056.05	1704.93	2703.32	1443.06	0.516
Dietary PUFA (~N-6) 18:2, (g)	9.49	5.51	12.21	6.20	10.76	6.46	0.478
Dietary PUFA (~N-3) 18:3, (g)	1.06	0.64	1.36	0.77	1.17	0.85	0.533
Dietary PUFA (~N-4) 18:4, (g)	0.00	0.01	0.00	0.00	0.00	0.00	0.769
Dietary PUFA (~N-6) 20:4, (g)	0.07	0.05	0.07	0.04	0.08	0.05	0.792
Dietary N-3 PUFA 20:5 (EPA)(g)	0.04	0.07	0.03	0.03	0.02	0.02	0.787
Dietary N-3 PUFA 22:5 (DPA)(g)	0.01	0.02	0.01	0.01	0.01	0.01	0.832
Dietary N-3 PUFA 22:6 (DHA)(g)	0.05	0.08	0.04	0.04	0.05	0.03	0.915
Average daily omega-6 FA (g)	9.57	5.55	12.28	6.21	10.85	6.48	0.482
Average daily omega-3 FA (g)	1.16	0.74	1.45	0.79	1.25	0.89	0.597
Fructose (g)	17.76	17.75	23.49	20.31	15.62	8.66	0.404
Lactose (g)	6.74	6.86	4.31	3.37	5.99	5.79	0.474
Maltose (g)	1.76	1.79	1.85	1.51	1.90	1.83	0.973
Galactose (g)	0.12	0.10	0.18	0.12	0.17	0.13	0.374
Sucrose (g)	17.18	15.71	20.25	8.53	20.11	19.10	0.822
Glucose (g)	16.95	17.23	18.13	12.96	14.75	8.10	0.781
Total choline (mg)	214.46	125.36	260.70	129.90	249.24	123.60	0.584
Free choline (mg)	55.53	38.55	83.59	59.04	69.07	36.44	0.256
Phosphocholine (mg)	8.27	4.97	15.57	12.43	9.85	5.77	0.054

(continued)	NMO		MS		HC		
	Mean	SD	Mean	SD	Mean	SD	Prob > F
Glycerophosphocholine (GPC)(mg)	30.27	17.44	31.77	14.10	34.94	19.58	0.751
Phosphatidylcholine (PTD)(mg)	108.61	64.89	119.38	54.57	121.23	65.97	0.835
Betaine (mg)	115.75	106.13	216.81	141.98	146.50	103.60	0.068
Sphingomyelin (SM)(mg)	11.23	6.82	10.03	5.65	13.28	9.34	0.485

Study subjects completed a dietary questionnaire (Block Dietary Data Systems, nutrionquest.com). The following diet variables were derived from the questionnaire: 'Food energy, kcals', 'Protein, gms', 'Fat, gms', 'Carbohydrate, gms', 'Calcium, mg', 'Phosphorous, mg', Iron, mg', Sodium, mg', Potassium, mg', 'Glutathione, total, mg', 'Glutathione, reduced, mg', 'Thiamine (Vitamin B1), mg', Riboflavin (Vitamin B2), mg', 'Niacin, mg', 'Vitamin C, mg', 'Saturated fat, gms', 'Monounsaturated fatty acids, gms', 'Cholesterol, mg', 'Dietary fiber, gms', 'Dietary soluble fiber, gms', 'Food folate mcg', 'alpha-tocopherol (Vitamin E), mg', 'Zinc, total mg', 'Zinc, animal sources only, mg', 'Vitamin B6, mg', Magnesium, mg', 'Vitamin A, RAE (mcg)', 'Retinol, mcg', 'Alpha-carotene, mcg', 'Beta-carotene, mcg', Cryptoxanthin, mcg', Lutein-Zeaxanthin, mcg', Lycopene, mcg', Folic-acid, mcg', 'Vitamin D, IU', 'Phylloquinone (Vitamin K), mcg', 'Copper, mg', 'Selenium, mcg', 'Sugars, total, gms', 'Trans fats, total, gms', 'Isoflavones, total, mg', Quercetin, mg', 'Cysteine (S-containing), mg', Methionine (S-containing), mg', Cystine (S-containing), mg', 'Average daily dietary folate equivalents, mcg', 'Glycemic index (glucose), average daily', 'Glycemic load (glucose), average daily', 'Dietary arginine, mg', 'Dietary PUFA (~N6) 18:2, gms','Dietary PUFA (~N3) 18:3, gms', 'Dietary PUFA (~N3) 18:4, gms', 'Dietary PUFA (~N6) 20:4, gms', 'Dietary N-3 PUFA 20:5 (EPA), gms', 'Dietary N-3 PUFA 22:5 (DPA), gms', 'Dietary N-3 PUFA 20:6 (DPA), gms', 'Average daily omega-G fatty acids, gms', 'Average daily omega-G fatty acids, gms', 'Fructose, gms', 'Lactose, gms', 'Maltose, gms', 'Galactose, gms', 'Sucrose, gms', Glucose, gms', 'Total choline, mg', 'Free choline, mg', 'Phosphocholine, mg', 'Glycerophosphocholine (GCP), mg', 'Phosphatidylcholine (PTD), mg', 'Betaine, mg', 'Sphingomyelin, mg'. ANOVA was used to compare the mean values of each of these dietary factors across the three groups (HC, NMO and MS). In addition to the listed dietary variables, age, weight and BMI were also compared across the 3 groups. Differences were considered significant if the F-test yielded a p-value of <0.05. The following dietary variables differed between the groups: alpha-carotene, beta-carotene, lutein-zeaxanthin, and phylloquinone (vitamin K_1). There were no other significant differences observed between these groups for other any other dietary factor or for the variables: age, weight and BMI.

Comparison of daily nutritional intake between HC, NMO and MS. ANOVA was used to compare the means of each nutrient between the three groups and post-hoc tests (Sidak, Bonferroni or Scheffe) were used to assess pair-wise comparisons for nutrients with F-test *p*-values < 0.05. P-values for nutrients that significantly differed in at least one group are highlighted in grey. No adjustments to the p-values for multiple hypotheses were made. For alpha-carotene, MS differed from both HC and NMO whereas NMO did not differ from HC. For beta-carotene MS differed from both HC and NMO whereas NMO did not differ from HC. For lutein-zeaxanthin, MS differed from both HC and NMO whereas NMO did not differ from HC. For phylloquinone (vitamin K_1) MS differed from NMO whereas NMO did not differ from HC and MS did not differ from HC.

Supplementary Table 3. OTUs that differentiate NMO from HC[a]

Phylum	Class	Order	Family	Genus	Species	Relative abundance in NMO	p-value
Fibrobacteres	unclassified	unclassified	unclassified	unclassified	unclassified	1.20	2.63×10^{-8}
Firmicutes	Clostridia	*Clostridiales*	*Clostridiaceae*	*Clostridium*	*perfringens*	1.12	5.24×10^{-8}
Tenericutes	*Mollicutes*	*Acholeplasmatales*	*Acholeplasmataceae*	*Acholeplasma*	unclassified	1.17	9.21×10^{-8}
Firmicutes	*Clostridia*	*Clostridiales*	*unclassified*	unclassified	unclassified	1.13	2.21×10^{-7}
Firmicutes	*Clostridia*	*Clostridiales*	*Lachnospiraceae*	*Coprococcus*	unclassified	1.34	2.24×10^{-7}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*unclassified*	unclassified	unclassified	1.14	2.68×10^{-7}
Firmicutes	*Clostridia*	*Clostridiales*	*Lachnospiraceae*	*Blautia*	*producta*	1.25	3.95×10^{-7}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Prevotellaceae*	*Prevotella*	97otu18529	0.26	4.71×10^{-7}
Firmicutes	*Clostridia*	*Clostridiales*	unclassified	unclassified	unclassified	1.06	6.31×10^{-7}
Proteobacteria	*Alphaproteobacteria*	unclassified	unclassified	unclassified	unclassified	1.36	6.75×10^{-7}
Firmicutes	*Clostridia*	*Clostridiales*	*Lachnospiraceae*	unclassified	unclassified	1.53	7.33×10^{-7}
Elusimicrobia	*Elusimicrobia*	FAC88	91otu12128	94otu9638	97otu81717	1.26	7.61×10^{-7}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Porphyromonadaceae*	unclassified	unclassified	1.22	1.34×10^{-6}
Proteobacteria	*Gammaproteobacteria*	unclassified	unclassified	unclassified	unclassified	1.38	1.44×10^{-6}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Bacteroidaceae*	*Bacteroides*	unclassified	1.40	1.45×10^{-6}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Prevotellaceae*	*Prevotella*	*melaninogenica*	1.27	1.52×10^{-6}
Firmicutes	*Clostridia*	*Clostridiales*	*Ruminococcaceae*	unclassified	unclassified	1.26	2.16×10^{-6}
Bacteroidetes	*Flavobacteriia*	*Flavobacteriales*	*Flavobacteriaceae*	*Flavobacterium*	97otu13948	1.05	2.19×10^{-6}
Firmicutes	*Clostridia*	*Clostridiales*	*Lachnospiraceae*	*Coprococcus*	unclassified	1.24	2.53×10^{-6}
KSB3	79otu904	85otu2233	91otu6419	94otu17237	97otu28635	1.43	2.68×10^{-6}
Proteobacteria	*Gammaproteobacteria*	*Chromatiales*	*Chromatiaceae*	94otu11281	97otu50557	1.27	2.76×10^{-6}
Proteobacteria	*Gammaproteobacteria*	*Legionellales*	*Coxiellaceae*	94otu3394	97otu55659	0.15	3.96×10^{-6}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Prevotellaceae*	*Prevotella*	97otu35422	0.32	4.35×10^{-6}

(continued)

Phylum	Class	Order	Family	Genus	Species	Relative abundance in NMO	p-value
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Prevotellaceae*	*Prevotella*	*copri*	0.11	4.64×10^{-6}
Gemmatimonadetes	*Gemm-1*	85otu2854	91otu10683	94otu20578	97otu45170	1.27	5.86×10^{-6}
Verrucomicrobia	*[Spartobacteria]*	*[Chthoniobacterales]*	*[Chthoniobacteraceae]*	DA101	97otu17249	0.18	6.09×10^{-6}
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriales*	*Enterobacteriaceae*	unclassified	unclassified	4.08	6.30×10^{-6}
Firmicutes	*Clostridia*	*Clostridiales*	91otu15265	94otu30131	97otu33231	0.14	8.27×10^{-6}
Firmicutes	*Clostridia*	*Clostridiales*	*Lachnospiraceae*	*Blautia*	97otu10785	1.34	8.81×10^{-6}
Firmicutes	*Clostridia*	*Clostridiales*	unclassified	unclassified	unclassified	0.92	9.79×10^{-6}
Actinobacteria	*Actinobacteria*	*Actinomycetales*	*Corynebacteriaceae*	*Corynebacterium*	unclassified	1.26	1.01×10^{-5}
Firmicutes	*Clostridia*	*Clostridiales*	*Ruminococcaceae*	*Ruminococcus*	unclassified	1.19	1.03×10^{-5}
Bacteroidetes	*Bacteroidia*	*Bacteroidales*	*Prevotellaceae*	*Prevotella*	*melaninogenica*	1.15	1.07×10^{-5}
Spirochaetes	*Spirochaetes*	*Spirochaetales*	*Spirochaetaceae*	*Treponema*	*socranskii*	1.19	1.13×10^{-5}
Acidobacteria	*Acidobacteria-6*	iii1-15	91otu412	94otu11629	97otu29451	1.37	1.23×10^{-5}
Firmicutes	*Clostridia*	*Clostridiales*	unclassified	unclassified	unclassified	1.20	1.30×10^{-5}
KSB3	unclassified	unclassified	unclassified	unclassified	unclassified	1.23	1.30×10^{-5}
Planctomycetes	*Phycisphaerae*	unclassified	unclassified	unclassified	unclassified	1.21	1.31×10^{-5}
Proteobacteria	*Gammaproteobacteria*	unclassified	unclassified	unclassified	unclassified	2.05	1.50×10^{-5}
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriales*	*Enterobacteriaceae*	unclassified	unclassified	1.87	1.56×10^{-5}
Tenericutes	*Mollicutes*	unclassified	unclassified	unclassified	unclassified	1.28	1.69×10^{-5}
Tenericutes	*Mollicutes*	*Acholeplasmatales*	*Acholeplasmataceae*	*Candidatus Phytoplasma*	unclassified	0.99	1.82×10^{-5}

[a]OTUs that significantly differed in abundance between NMO and HC after adjusting for multiple comparisons ($p<1.91 \times 10^{-5}$), ranked in order of decreasing statistical significance. The relative abundance is the average HybScore in NMO divided by the average HybScore of HC. Thus, values that are >1 are more abundant in NMO and values that are <1 are more abundant in HC. Although *C. perfringens* was the single specific bacterial species with the most significant association with NMO, an unclassified species of *Fibrobacteres* had a more significant *p*-value whereas other species with less significant associations, e.g., *Prevotella copri* or *Enterobacteriaceae* of an unknown species, had greater effect sizes.