

## Supplemental Appendix A: Supplement Use Protocol

The program includes review of each participant's pre-existing supplement regimen. Supplementation to replete nutrient deficiencies is recommended if not already being addressed. Supplements identified as triggering symptoms, those taken in excess of recommended daily allowances and those known to interact with prescribed medications or other supplements are flagged; the participant is then advised to review this(ese) supplement(s) with the recommending physician or, if taken independently, advised to consider discontinuation. Anything recommended is conditional, matched against scientific guidelines, and tested within the personalized trial methodology.

### Magnesium

Magnesium supplemented in the following participants:

1. If participant provides lab work showing magnesium deficiency.
2. If participant is having trouble sleeping or is reporting frequent muscle twitches or restless leg syndrome.

Depending on a participant's lifestyle and preferences, magnesium may be taken orally (200mg/day) or used topically via Epsom salt baths (1 daily bath, 2 cups per bath).

### Vitamin D

Vitamin D supplemented in the following participants who are not already on a Vitamin D supplement:

1. If participant provides lab work showing D-vitamin deficiency (25(OH)D <20ng/mL) which was not in the past/currently being repleted.

### Vitamin B12

B12 in methylated form supplemented in the following participants:

1. If participant provides lab work showing B12 deficiency [ $<120$ – $180$  picomol/L ( $<170$ – $250$  pg/mL)] and/or elevated methylmalonic acid levels ( $>0.4$  micromol/L).

### Probiotics

Probiotics supplemented in the following participants:

1. If participant has recently (within last 6 weeks) been on antibiotics and is experiencing digestive issues.

### Digestive Enzymes

Digestive enzymes supplemented in the following participants:

1. If participant has had their gallbladder removed and is experiencing digestive issues.

### Bile Salts

Bile salts supplemented in the following participants:

1. Participants without a gallbladder with symptoms consistent with gallbladder dysfunction.

## Supplemental Appendix B: Demographics and Baseline PROMIS29+MSx of Non-Completers

	Missing Data Points	N	%	Mean
<b>Age (years)</b>	0	110		44.0
17-29		10	9%	
30-39		32	29%	
40-49		35	32%	
50-59		17	15%	
60-69		14	13%	
70+		2	2%	
<b>Sex, female</b>	0	83	77%	
<b>Race/Ethnicity</b>	3			
White, non-Hispanic/Latino/a		66	61%	
White, Hispanic/Latino/a		17	16%	
Black or African American		9	8%	
Asian		2	2%	
Multiracial		1	1%	
Native Hawaiian/Other Pacific Islander		1	1%	
American Indian/Alaska Native		1	1%	
Pakeha New Zealander		1	1%	
Prefer not to state		9	8%	
<b>Annual income</b>	8	102		
Under \$50,000		22	21%	
\$50,000 to \$99,999		13	13%	
\$100,000 or More		37	36%	
Prefer not to state		30	29%	
<b>Education</b>	8	102		
Bachelor's degree		39	38%	
Advanced/Professional Degree		32	31%	
Some college, no degree		15	15%	
Associates degree		9	9%	
Less than a high school diploma		3	3%	
High school or equivalent		2	2%	
Prefer not to state		2	2%	
<b>Employment</b>	8	102		
Employed full-time		47	46%	
Self-employed		18	18%	
Unable to work/on disability		12	12%	
Employed part time		7	7%	

<i>Unemployed</i>		5	5%	
<i>Student</i>		4	4%	
<i>Homemaker</i>		2	2%	
<i>Retired</i>		2	2%	
<i>Prefer not to state</i>		5	5%	
<b>Marital status</b>	8	102		
<i>Married or in domestic partnership</i>		53	52%	
<i>Single</i>		41	40%	
<i>Divorced or separated</i>		4	4%	
<i>Widowed</i>		1	1%	
<i>Prefer not to state</i>		3	3%	

Supplemental Appendix C: List of other autoimmune diagnoses found in  $\leq 6$  participants

Other autoimmune diagnosis	#
Hashimoto's thyroiditis	6
Mixed connective tissue disease	6
Celiac disease	2
Sarcoidosis	2
Susac Syndrome	2
Diabetes Type 1 - Juvenile onset	2
Autoimmune dysautonomia	1
Dupuytren's contracture	1
Erythema nodosum	1
Grave's disease	1
Hidradenitis suppurativa	1
Lichen sclerosus	1
Myasthenia gravis	1
Sjögren's syndrome	1
Spondyloarthropathy - other	1
Undifferentiated connective tissue disease	1

Supplemental Appendix D: Participants without a definitive autoimmune diagnosis had the following syndromes/symptoms (Note: some participants are represented in more than 1 of these categories)

Syndromes/symptoms of participants without a clear autoimmune diagnosis	#
Chronic fatigue syndrome	5
Raynaud's phenomenon	3
Arthralgias/arthritis - chronic	2
Cancer - w/ chronic fatigue and arthralgias	2
Fibromyalgia	2
Irritable bowel syndrome	2
Asthma	1
Chronic recurrent multifocal osteomyelitis	1
Gluten intolerance	1
Keratoconjunctivitis sicca	1

## Supplemental Appendix E: Linear Regression and Kruskal-Wallis Analyses

Linear Regression Analyses											
	Stats	PROMIS Domains									
		SR	ANX	COG	DEP	FATG	MgSx	P INTF	SLEEP	P INTS	PHYS
Weeks in program	B	-0.005	0.064	-0.203	0.037	-0.019	-0.080	0.040	0.101	0.053	-0.013
	SE	0.154	0.152	0.159	0.136	0.201	0.166	0.173	0.156	0.045	0.133
	P value	0.972	0.676	0.204	0.783	0.925	0.629	0.820	0.518	0.244	0.921
	R <sup>2</sup>	<0.001	0.001	0.008	<0.001	<0.001	0.001	<0.000	0.002	0.007	<0.001
	95% CI	[-0.307, 0.296]	[-0.234, 0.361]	[-0.516, 0.109]	[-0.229, 0.304]	[-0.412, 0.374]	[-0.405, 0.244]	[-0.300, 0.379]	[-0.205, 0.408]	[-0.036, 0.142]	[-0.273, 0.247]
Amount tracked		SR	ANX	COG	DEP	FATG	MgSx	P INTF	SLEEP	P INTS	PHYS
	B	0.205	-0.104	0.074	-0.105	-0.160	0.084	-0.195	-0.189	-0.021	-0.025
	SE	0.173	0.171	0.180	0.153	0.226	0.187	0.195	0.176	0.051	0.150
	P value	0.236	0.545	0.684	0.492	0.480	0.653	0.318	0.283	0.686	0.867
	R <sup>2</sup>	0.007	0.002	0.001	0.002	0.003	0.001	0.005	0.006	0.001	<0.001
	95% CI	[-0.133, 0.544]	[-0.439, 0.232]	[-0.280, 0.427]	[-0.405, 0.194]	[-0.603, 0.283]	[-0.282, 0.450]	[-0.577, 0.187]	[-0.534, 0.155]	[-0.121, 0.080]	[-0.318, 0.268]
Weight change		SR	ANX	COG	DEP	FATG	MgSx	P INTF	SLEEP	P INTS	PHYS
	B	-0.148 ±	0.040 ±	-0.088 ±	0.015 ±	0.196 ±	-0.058 ±	-0.025 ±	0.158 ±	0.019 ±	0.038 ±
	SE	0.102	0.107	0.096	0.085	0.141	0.109	0.101	0.103	0.028	0.080
	P value	0.154	0.711	0.362	0.860	0.171	0.601	0.807	0.133	0.507	0.638
	R <sup>2</sup>	0.041	0.003	0.017	<0.001	0.038	0.006	0.001	0.045	0.009	0.005

	<b>95% CI</b>	[-0.352, 0.057]	[-0.176, 0.255]	[-0.281, 0.105]	[-0.160, 0.186]	[-0.088, 0.481]	[-0.278, 0.162]	[-0.227, 0.178]	[-0.050, 0.365]	[-0.038, 0.076]	[-0.123, 0.199]
<b>Sex</b>		<b>SR</b>	<b>ANX</b>	<b>COG</b>	<b>DEP</b>	<b>FATG</b>	<b>MgSx</b>	<b>P INTF</b>	<b>SLEEP</b>	<b>P INTS</b>	<b>PHYS</b>
	<b>B</b>	1.455	-0.394	-1.338	-1.345	-3.235	0.855	-0.042	-1.473	-0.261	1.178
	<b>SE</b>	1.253	1.242	1.304	1.106	1.624	1.352	1.416	1.274	0.372	1.081
	<b>P value</b>	0.247	0.751	0.306	0.225	0.048*	0.528	0.977	0.249	0.484	0.277
	<b>R<sup>2</sup></b>	0.007	0.001	0.005	0.007	0.019	0.002	<0.001	0.007	0.002	0.006
	<b>95% CI</b>	[-1.016, 3.926]	[-2.843, 2.054]	[-3.910, 1.234]	[-3.525, 0.835]	[-6.438, -0.032]	[-1.811, 3.521]	[-2.834, 2.751]	[-3.986, 1.041]	[-0.994, 0.472]	[-0.954, 3.309]
<b>Baseline severity</b>		<b>SR</b>	<b>ANX</b>	<b>COG</b>	<b>DEP</b>	<b>FATG</b>	<b>MgSx</b>	<b>P INTF</b>	<b>SLEEP</b>	<b>P INTS</b>	<b>PHYS</b>
	<b>B</b>	2.515	-2.503	4.978	-2.949	-4.029	2.947	-3.553	-3.459	-0.928	2.324
	<b>SE</b>	0.534	0.532	0.758	0.533	0.583	0.593	0.553	0.616	0.113	0.445
	<b>P value</b>	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
	<b>R<sup>2</sup></b>	0.09974	0.09969	0.1776	0.1325	0.1929	0.1101	0.1712	0.1363	0.2516	0.1199
	<b>95% CI</b>	[1.461, 3.568]	[-3.551, -1.454]	[3.484, 6.472]	[-4.000, -1.897]	[-5.179, -2.880]	[1.779, 4.116]	[-4.643, -2.463]	[-4.673, -2.245]	[-1.151, -0.705]	[1.446, 3.201]

\*p&lt;0.05

Anx = anxiety; Cog = cognitive function; Depr = depression; Fatg = fatigue; MgSx = Ability to manage symptoms; Phys = physical function; P ints = Pain intensity; P intf = Pain interference; SE=standard error; SR = Ability to participate in social roles and activities.

<b>Kruskal-Wallis Analyses</b>											
	<b>Stats</b>	<b>PROMIS Domains</b>									
		<b>SR</b>	<b>ANX</b>	<b>COG</b>	<b>DEP</b>	<b>FATG</b>	<b>MgSx</b>	<b>P INTF</b>	<b>SLEEP</b>	<b>P INTS</b>	<b>PHYS</b>
<b>Edu</b>	<b>H</b>	5.665	7.402	7.352	11.031	4.221	7.202	4.566	6.851	2.270	3.888
	<b>df</b>	7	7	7	7	7	7	7	7	7	7
	<b>p value</b>	0.579	0.388	0.393	0.137	0.754	0.408	0.713	0.445	0.943	0.793

		SR	ANX	COG	DEP	FATG	MgSx	P INTF	SLEEP	P INTS	PHYS
<b>Emp</b>	<b>H</b>	7.538	2.874	11.678	3.039	4.895	9.972	4.804	4.955	6.501	6.323
	<b>df</b>	8	8	8	8	8	8	8	8	8	8
	<b>p value</b>	0.480	0.942	0.166	0.932	0.769	0.267	0.778	0.762	0.591	0.611
<b>Income</b>	<b>H</b>	3.072	1.456	5.391	1.205	0.617	1.453	0.713	0.504	2.833	0.717
	<b>df</b>	3	3	3	3	3	3	3	3	3	3
	<b>p value</b>	0.381	0.693	0.145	0.7512	0.893	0.693	0.870	0.918	0.418	0.869
<b>Marital Status</b>	<b>H</b>	1.092	3.150	1.77	9.377	4.948	3.406	2.695	5.569	2.495	4.556
	<b>df</b>	4	4	4	4	4	4	4	4	4	4
	<b>p value</b>	0.896	0.533	0.778	0.0523	0.293	0.492	0.610	0.234	0.646	0.336
<b>Ethnicity</b>	<b>H</b>	7.644	7.249	6.133	4.632	8.026	6.525	8.065	5.268	12.298	5.900
	<b>df</b>	7	7	7	7	7	7	7	7	7	7
	<b>p value</b>	0.365	0.404	0.524	0.705	0.330	0.480	0.327	0.627	0.0912	0.552
<b>Age</b>	<b>H</b>	3.373	1.867	4.165	5.432	3.693	4.705	0.777	2.373	5.234	3.002
	<b>df</b>	4	4	4	4	4	4	4	4	4	4
	<b>p value</b>	0.498	0.760	0.384	0.246	0.449	0.319	0.942	0.668	0.264	0.558

Anx = anxiety; Cog = cognitive function; Depr = depression;



df = degrees of freedom; Fatg = fatigue; MgSx = Ability to manage symptoms; Phys = physical function; P ints = Pain intensity; P intf = Pain interference; SE=standard error; SR = Ability to participate in social roles and activities.

Supplemental Appendix F: Primary analysis of change in PROMIS29+MSx from BL to EOP in participants with an autoimmune diagnosis (n=189)

	Mean (SD) at BL	Mean (SD) at EOP	Change (SD)	<i>p</i>
<b>Ability to participate in social roles*</b>	46.1 (9.2)	51.9 (9.7)	5.8 (7.4)	<i>p</i> <0.0001
<b>Cognitive function*</b>	49.2 (7.0)	52.3 (7.0)	3.1 (7.4)	<i>p</i> <0.0001
<b>Ability to manage symptoms*</b>	43.2 (8.0)	49.5 (8.7)	6.3 (8.0)	<i>p</i> <0.0001
<b>Physical function*</b>	43.7 (9.3)	47.9 (8.8)	3.2 (6.5)	<i>p</i> <0.0001
<b>Anxiety**</b>	55.6 (8.5)	51.5 (8.9)	-4.1 (7.3)	<i>p</i> <0.0001
<b>Depression**</b>	51.3 (8.8)	48.3 (7.9)	-3.0 (6.6)	<i>p</i> <0.0001
<b>Fatigue**</b>	58.1 (10.6)	50.5 (10.7)	-7.5 (9.7)	<i>p</i> <0.0001
<b>Pain interference**</b>	57.5 (9.4)	51.9 (9.5)	-5.5 (8.4)	<i>p</i> <0.0001
<b>Sleep disturbance**</b>	53.6 (7.9)	47.8 (8.3)	-5.8 (7.7)	<i>p</i> <0.0001
<b>^Pain intensity**</b>	4.1 (2.5)	2.6 (2.8)	-1.4 (2.2)	<i>p</i> <0.0001

\*Higher score indicates improvement

\*\* Lower score indicates improvement.

^ Pain intensity was measured on a 0-10 VAS.

BL = baseline; EOP = end of program.