

Supporting Information for Patient-Reported Treatment Outcomes in ME/CFS and Long COVID

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Other supporting materials for this manuscript include the following:

Datasets S1
Datasets S2
Datasets S3

Fig. S1. Rates of Comorbidities in ME/CFS and Long COVID Patients

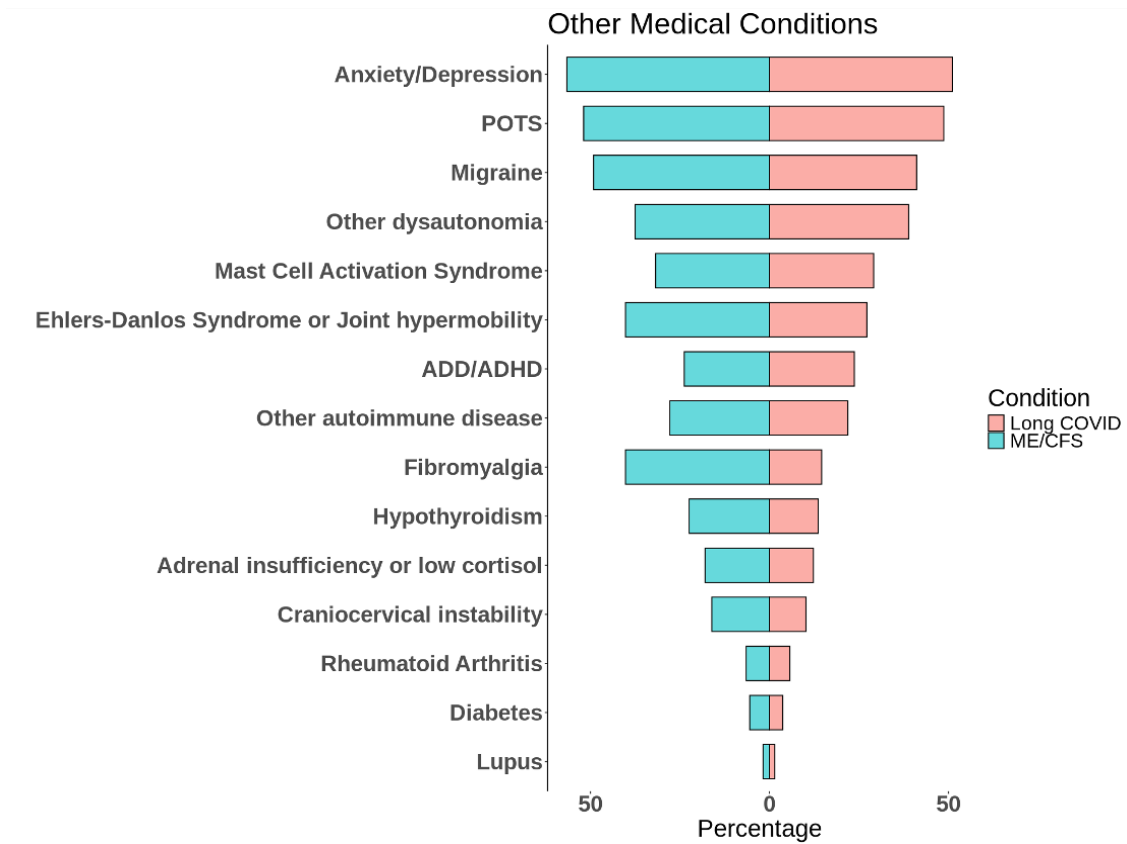
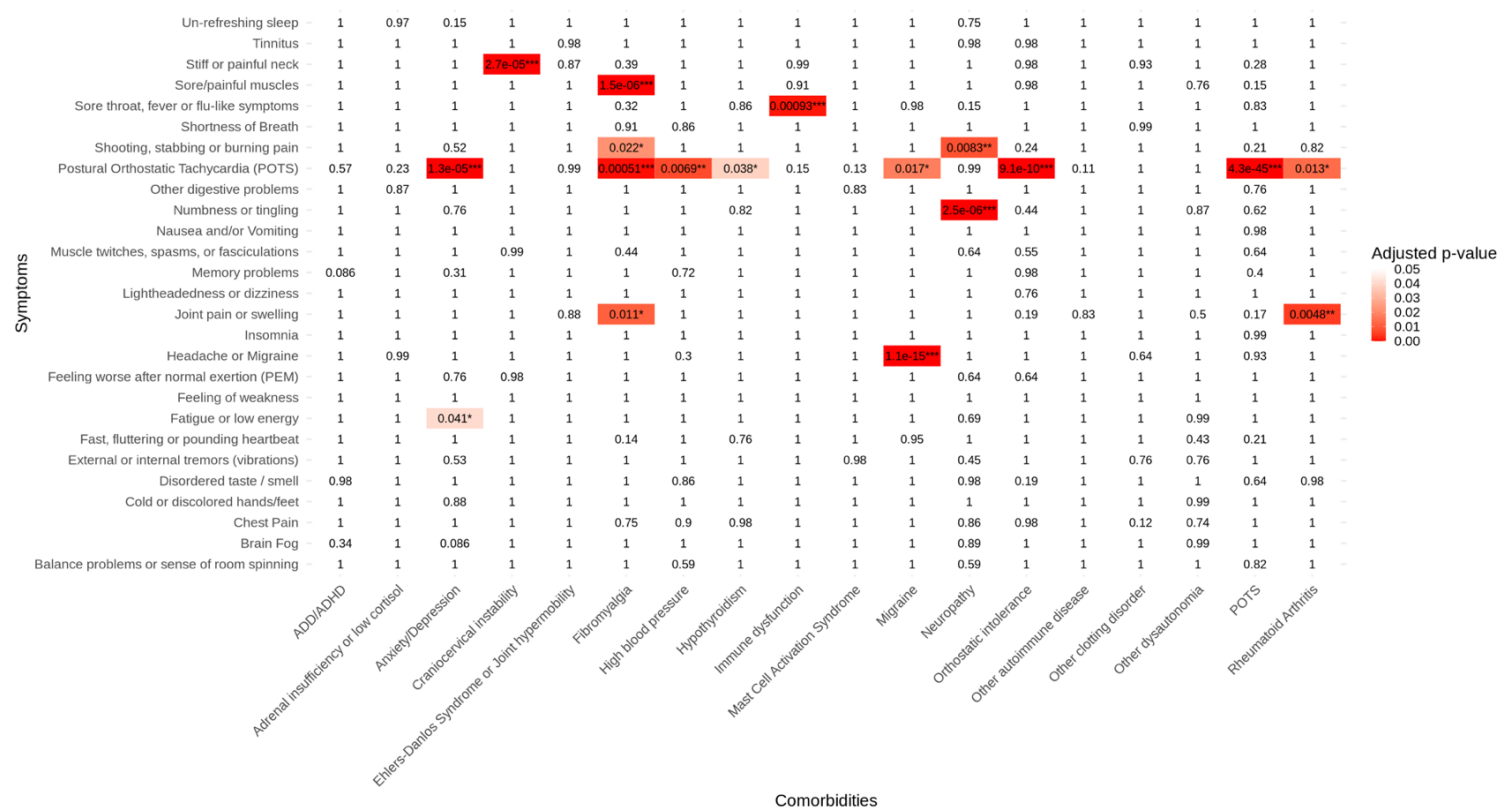


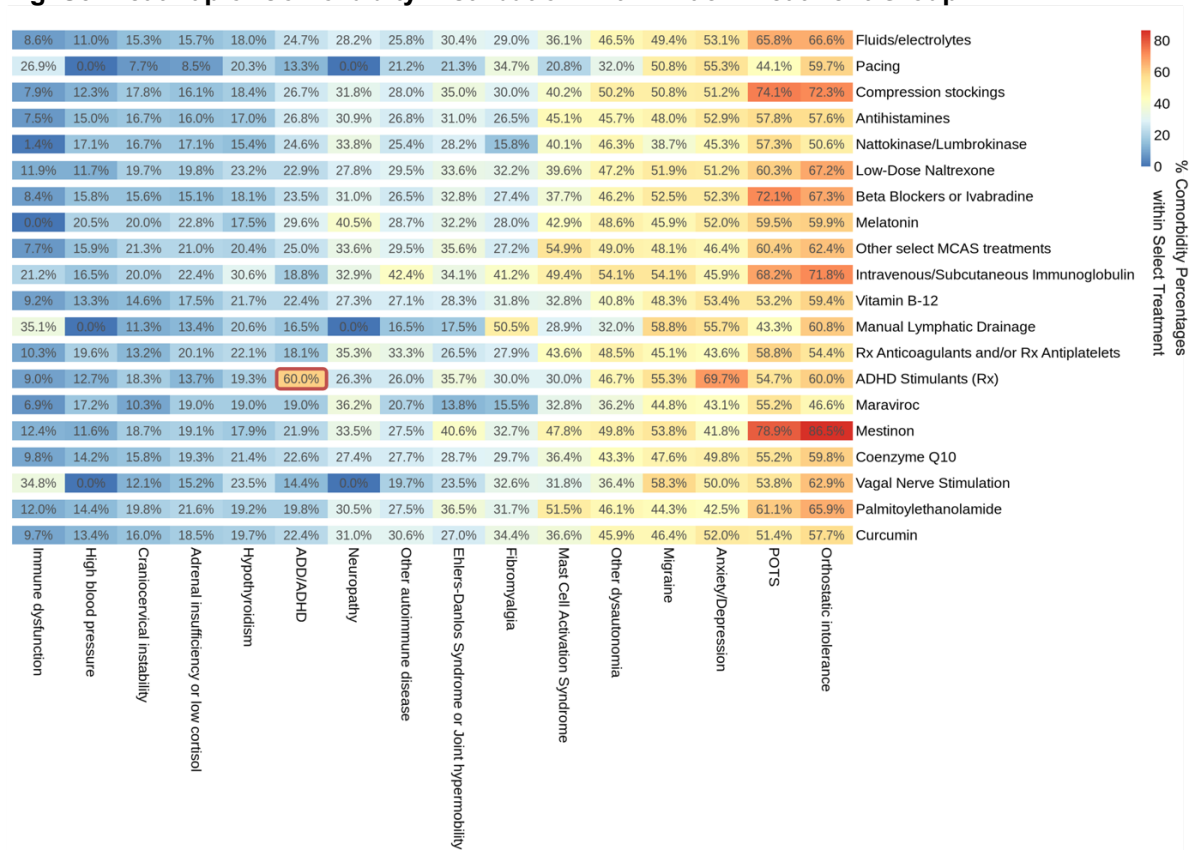
Fig. S2 Symptom-Comorbidity Association Heatmap Based on Adjusted p-values (Chi-square Test)



To assess the association between symptoms and comorbidities, we performed a Chi-square test of independence based on the reported counts of patients with each symptom-comorbidity pair.

The color scale represents multiple test adjusted p-values, with red indicating stronger statistical significance and white representing non-significant associations ($p > 0.05$). Each cell is annotated with its adjusted p-value and corresponding significance level (** for $p \leq 0.01$, * for $p \leq 0.05$).

Fig. S3. Heatmap of Comorbidity Distribution Within Each Treatment Group



This heatmap presents the top twenty leading treatments that contributed to improving patients' overall conditions. It displays the percentage of patients who reported using each treatment and having a specific comorbidity. Each row represents a treatment, and each cell value indicates the percentage of patients with a given comorbidity (column) among those who took that treatment. For example, the highlighted 60.0% in the row "ADHD Stimulants (Rx)" means that 60% of patients who took ADHD Stimulants (Rx) also reported having ADD/ADHD. Note that: Comorbidities with fewer than 100 reports across all treatments were excluded to ensure reliable data. Since patients can report multiple comorbidities, the percentages in each row do not sum to 100%.

Fig. S4. Relative Influence of Variables on Treatment Response (NAS)

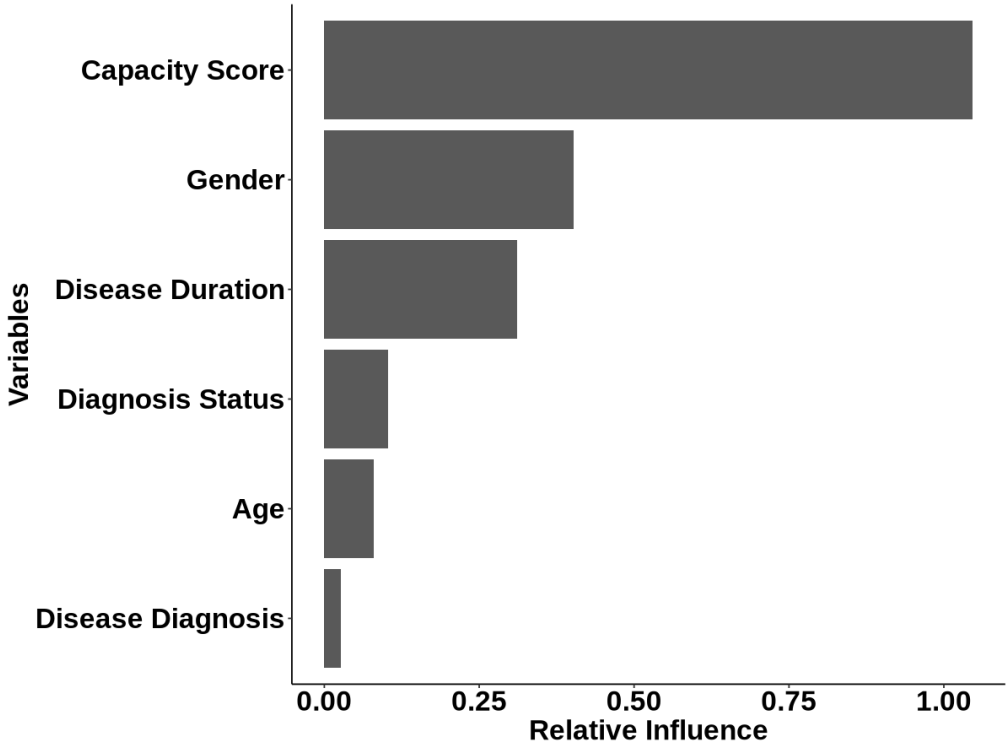


Fig. S5. Capacity levels of patients in each cluster

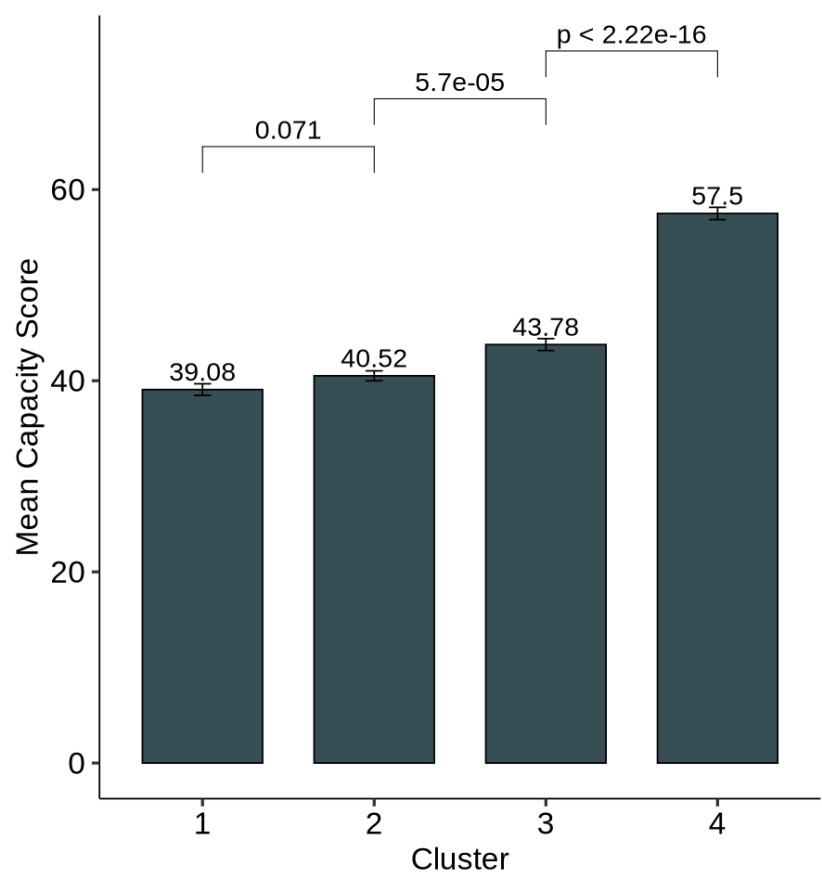


Fig. S6. Patient Subclustering and Symptom Distribution within ME/CFS and Long COVID

ME/CFS					Long COVID				
	98	90	98	78		99	94	99	90
Fatigue or low energy	96	86	91	62	Fatigue or low energy	98	90	95	71
Feeling worse after normal exertion (PEM)	93	68	94	57	Feeling worse after normal exertion (PEM)	94	74	91	59
Brain fog	92	50	80	31	Brain fog	97	61	88	49
Un-refreshing sleep	85	39	82	32	Un-refreshing sleep	88	44	65	24
Memory problems	85	35	69	20	Feeling of weakness	90	32	66	25
Feeling of weakness	85	50	37	34	Sore/painful muscles	81	38	69	22
Fast, fluttering or pounding heartbeat	77	34	56	22	Memory problems	75	36	53	21
Insomnia	83	37	46	21	Insomnia	78	35	44	24
Headache or migraine	85	36	44	17	Headache or migraine	76	29	46	22
Lightheadedness or dizziness	76	33	43	29	Other digestive problems	82	36	34	12
Shortness of breath	81	19	52	18	Lightheadedness or dizziness	77	22	39	12
Sore/painful muscles	66	82	4	5	Stiff or painful neck	74	33	25	16
Postural orthostatic tachycardia (POTS)	67	25	40	15	Fast, fluttering or pounding heartbeat	71	69	4	2
Chest pain	65	29	21	22	Postural orthostatic tachycardia (POTS)	61	16	38	16
Other digestive problems	65	23	31	16	Sore throat, fever or flu-like symptoms	65	15	31	15
Numbness or tingling	72	17	31	12	Joint pain or swelling	63	19	26	13
Joint pain or swelling	66	11	35	13	Shortness of breath	55	21	26	9
Stiff or painful neck	68	15	25	10	Cold or discolored hands/feet	53	15	28	12
Balance problems or sense of room spinning	65	16	22	8	Tinnitus	62	13	24	7
Cold or discolored hands/feet	54	21	26	8	Muscle twitches, spasms, or fasciculations	65	11	20	5
Muscle twitches, spasms, or fasciculations	61	10	24	9	Balance problems or sense of room spinning	57	16	18	8
External or internal tremors (vibrations)	59	13	18	10	Nausea and/or vomiting	62	12	18	7
Shooting, stabbing or burning pain	64	7	16	11	Numbness or tingling	60	12	18	6
Nausea and/or vomiting	53	13	20	10	Shooting, stabbing or burning pain	51	11	14	2
Sore throat, fever or flu-like symptoms	54	12	20	9	External or internal tremors (vibrations)	42	10	9	6
Disordered taste / smell	46	6	18	9	Chest pain	21	4	7	3
Anxiety/depression	64	44	62	59	Disordered taste / smell	64	53	59	60
Postural orthostatic tachycardia (POTS)	67	97	9	17	Anxiety/depression	68	48	49	35
Migraine	64	42	48	33	Migraine	73	94	9	14
Other dysautonomia	64	53	25	25	Postural orthostatic tachycardia (POTS)	59	32	47	27
Mast cell activation syndrome	45	41	17	20	Fibromyalgia	54	48	21	24
Attention-deficit/hyperactivity disorder	34	24	19	26	Other dysautonomia	47	44	14	17
Other autoimmune disease	34	22	25	19	Mast cell activation syndrome	42	38	22	17
Ehlers-danlos syndrome or joint hypermobility	32	28	15	14	Ehlers-danlos syndrome or joint hypermobility	39	27	22	26
Fibromyalgia	31	11	20	10	Other autoimmune disease	32	24	18	24
Hypothyroidism	17	14	18	12	Attention-deficit/hyperactivity disorder	28	21	24	21
Adrenal insufficiency or low cortisol	19	13	13	10	Hypothyroidism	25	17	16	16
Cranio-cervical instability	19	12	8	7	Adrenal insufficiency or low cortisol	28	20	7	8
Rheumatoid arthritis	10	4	8	5	Cranio-cervical instability	8	5	7	8
Diabetes	5	3	5	4	Rheumatoid arthritis	7	4	8	4
Lupus	2	2	2	1	Diabetes	3	1	2	1
	1	2	3	4	Lupus	1	2	3	4

Symptoms

Comorbidities

Symptoms

Comorbidities

Table S1. Question of Patient Capacity Level

How would you describe the CURRENT severity of your ME/CFS? Adapted & condensed from Living with M.E. by Dr Charles Shepherd (ME/CFS Disability Scale, pp. 116-7)

- **FIT & WELL FOR $\geq$ 1 MONTH (100% capacity):**
No symptoms. Capable of full-time employment.
- **GENERALLY WELL (~90% capacity):**
Mild symptoms may sometimes follow activity. Mostly fit & well.
- **MILD (70-90% capacity):**
Occasional restriction of capabilities and/or limited ability to perform some tasks requiring exertion. May be able to work full-time.
- **MILD TO MODERATE (50%-70% capacity):**
Variable limited ability to carry out tasks. Able to work part-time and/or perform lighter duties provided adequate rest periods.
- **MODERATE (40-50% capacity):**
Occasionally homebound. Unable to carry out any strenuous duties, but able to perform light tasks for several hours most days.
- **MODERATE TO SEVERE (25-40% capacity):** Often homebound. Able to perform light tasks 1-2 hrs some days. May require wheelchair assistance at times.
- **SEVERE (15-25% capacity):**
Bedbound and housebound for much of the time. Considerable difficulties with personal care. Require practical support.
- **VERY SEVERE (<15% capacity):**
Bedridden and incapable of living independently. Require a great deal of practical support.
- **Other (please specify)**

Table S2. Most Troubling Symptoms of Patients

Most Troubling Symptoms	ME/CFS	Long COVID
Fatigue or low energy	95.62%	88.28%
Feeling worse after normal exertion (PEM)	89.74%	79.39%
Brain Fog	80.05%	72.33%
Un-refreshing sleep	74.45%	55.28%
Memory problems	54.07%	50.83%
Fast, fluttering or pounding heartbeat	38.49%	47.11%
Feeling of weakness	57.27%	43.61%
Shortness of Breath	31.48%	40.44%
Insomnia	47.29%	40.17%
Headache or Migraine	45.32%	40.06%
Postural Orthostatic Tachycardia (POTS)	41.04%	40.00%
Lightheadedness or dizziness	42.64%	38.50%
Sore/painful muscles	53.69%	34.11%
Chest Pain	17.27%	31.39%
Tinnitus	27.67%	31.11%
Other digestive problems	44.00%	29.06%
Numbness or tingling	25.36%	26.39%
Joint pain or swelling	31.62%	24.44%
Stiff or painful neck	38.45%	24.17%
Cold or discolored hands/feet	28.89%	23.11%
Balance problems or sense of room spinning	26.16%	22.56%
Muscle twitches, spasms, or fasciculations	27.25%	20.39%
External or internal tremors (\vibrations\)	20.71%	20.17%
Nausea and/or Vomiting	25.55%	19.89%
Sore throat, fever or flu-like symptoms	32.94%	19.72%
Shooting, stabbing or burning pain	24.56%	19.06%
Disordered taste / smell	9.04%	15.61%

Table S3. Patients' Responses on Treatments (More details in Datasets S1 and S2)

Category	Treatment Group (when applicable)	Treatment	Net Assessment Score (NAS), Bold: >40 %	NAS+ (%Positive Response), Bold > 50%	NAS++ (%Moderately and Much Better). Bold >30%	NAS- (%Negative Response)	Total Number of Patients	Adjusted p-value (Cyan: p>0.05 and with >100 responses)	Adjusted p-value of a Treatment vs the Rest in the Same Treatment Group
Amino Acids	Amino acid complex	Amino acid complex	41.54%	44.62%	16.92%	-3.08%	65	0.0027	NA
Amino Acids	Branched Chain Amino Acids	Branched Chain Amino Acids	32.73%	39.09%	12.73%	-6.36%	110	0.0562	NA
Amino Acids	Creatine	Creatine	29.79%	34.04%	8.51%	-4.26%	141	0.1388	NA
Amino Acids	L-glutamine	L-glutamine	25.00%	32.78%	3.33%	-7.78%	180	0.5918	NA
Amino Acids	L-tryptophan	L-tryptophan	10.20%	26.53%	7.14%	-16.33%	98	1.0000	NA
Amino Acids	5-HTP	5-HTP	20.11%	33.33%	8.99%	-13.23%	189	1.0000	NA
Amino Acids	L-Lysine	L-lysine	33.92%	37.43%	9.36%	-3.51%	171	0.0083	NA
Amino Acids	L-theanine	L-theanine	28.95%	31.58%	5.26%	-2.63%	38	0.3891	1.0000
Amino Acids	L-theanine	Glycine	31.82%	36.36%	0.00%	-4.55%	22	0.3317	0.8881
Amino Acids	(Acetyl)-L-carnitine	(Acetyl)-L-carnitine <500 mg daily	27.69%	32.31%	10.77%	-4.62%	65	0.3997	1.0000
Amino Acids	(Acetyl)-L-carnitine	(Acetyl)-L-carnitine ≥500 mg daily	41.58%	44.74%	11.05%	-3.16%	190	0.0000	0.0000
Amino Acids	(Acetyl)-L-carnitine	(Acetyl)-L-carnitine (dose unknown)	20.09%	26.20%	5.68%	-6.11%	229	1.0000	1.0000
Anticoagulants & Antiplatelets	Rx Anticoagulants and/or Rx Antiplatelets *	Enoxaparin or Unfractionated Heparin	50.85%	59.32%	40.68%	-8.47%	59	0.0000	0.2685
Anticoagulants & Antiplatelets	Rx Anticoagulants and/or Rx Antiplatelets *	Oral Anticoagulants (apixaban, rivaroxaban, et al)	37.93%	45.98%	21.84%	-8.05%	87	0.0065	1.0000

Anticoagulants & Antiplatelets	Rx Anticoagulants and/or Rx Antiplatelets *	Plavix/Brilinta +/- Aspirin	39.24%	50.63%	24.05%	-11.39%	79	0.0043	1.0000
Anticoagulants & Antiplatelets	Aspirin	Aspirin only	32.55%	35.85%	10.69%	-3.30%	636	0.0001	NA
Anticoagulants & Antiplatelets	Triple Therapy	Triple Therapy	53.33%	62.22%	33.33%	-8.89%	45	0.0000	NA
Antimicrobials I	Antibiotics	Penicillins	21.76%	35.65%	17.13%	-13.89%	216	0.9444	1.0000
Antimicrobials I	Antibiotics	Cephalosporins	7.81%	29.69%	14.06%	-21.88%	64	1.0000	1.0000
Antimicrobials I	Antibiotics	Macrolides	31.88%	41.25%	25.00%	-9.38%	160	0.0413	0.0056
Antimicrobials I	Antibiotics	Doxycycline ≥100 mg	33.02%	46.23%	19.81%	-13.21%	106	0.0517	0.0224
Antimicrobials I	Antibiotics	Doxycycline ≤50 mg	31.82%	45.45%	27.27%	-13.64%	22	0.3289	0.4818
Antimicrobials I	Antibiotics	Doxycycline (unknown dose)	18.75%	33.33%	17.71%	-14.58%	96	1.0000	1.0000
Antimicrobials I	Antibiotics	Minocycline	4.35%	21.74%	13.04%	-17.39%	23	1.0000	1.0000
Antimicrobials I	Antibiotics	Sulfamethoxazole/trimethoprim	0.00%	25.49%	7.84%	-25.49%	51	1.0000	1.0000
Antimicrobials I	Herpes antiviral	Acyclovir	30.10%	33.98%	21.36%	-3.88%	103	0.1708	1.0000
Antimicrobials I	Herpes antiviral	Famciclovir	36.99%	47.95%	21.92%	-10.96%	73	0.0193	0.7507
Antimicrobials I	Herpes antiviral	Valacyclovir	38.27%	44.39%	25.51%	-6.12%	196	0.0000	0.2685
Antimicrobials I	Herpes antiviral	Valganciclovir	25.93%	33.33%	22.22%	-7.41%	54	0.5623	1.0000
Antimicrobials II	Hydroxychloroquine	Hydroxychloroquine	27.27%	37.66%	22.08%	-10.39%	77	0.4076	NA

Antimicrobials II	Ivermectin	Ivermectin	38.03%	45.77%	26.76%	-7.75%	142	0.0005	NA
Antimicrobials II	Azole antifungals	Azole antifungals	33.64%	40.91%	20.91%	-7.27%	110	0.0351	NA
Antimicrobials II	Amantadine	Amantadine	10.71%	25.00%	14.29%	-14.29%	28	1.0000	NA
Antioxidants	Vitamin C (oral, NOT liposomal)	reference Vitamin C (oral, NOT liposomal)	24.07%	26.82%	5.78%	-2.75%	1454	0.7337	NA
Antioxidants	Alpha or R-lipoic acid (oral)	Alpha or R-lipoic acid (oral)	18.72%	24.60%	5.35%	-5.88%	187	1.0000	NA
Antioxidants	Grape seed extract	Grape seed extract	18.29%	25.00%	6.10%	-6.71%	164	1.0000	NA
Antioxidants	Licorice/Glycyrrhizin	Licorice/Glycyrrhizin	30.37%	41.12%	14.95%	-10.75%	214	0.0600	NA
Antioxidants	Vitamin C (oral, liposomal)	Vitamin C (oral, liposomal)	28.79%	32.73%	7.88%	-3.94%	330	0.0844	NA
Antioxidants	Vitamin C (intravenous)	Vitamin C (intravenous)	32.34%	41.92%	18.56%	-9.58%	167	0.0291	NA
Antioxidants II	Glutathione	Glutathione (oral, liposomal formulation)	30.53%	35.79%	10.88%	-5.26%	285	0.0316	0.9411
Antioxidants II	Glutathione	Glutathione (oral, NOT liposomal)	22.22%	25.56%	8.89%	-3.33%	180	0.9070	1.0000
Antioxidants II	Glutathione	Glutathione (injection)	41.74%	51.30%	23.48%	-9.57%	115	0.0001	0.0075
Antioxidants II	NAC	NAC ≤600 mg/day	24.20%	32.56%	9.61%	-8.36%	562	0.7140	1.0000
Antioxidants II	NAC	NAC >600 mg/day	46.02%	49.43%	20.45%	-3.41%	352	0.0000	0.0000
B Vitamins	Vitamin B-12	* B-12 (injection)	47.08%	49.50%	19.52%	-2.41%	497	0.0000	0.0000
B Vitamins	Vitamin B-12	* B-12 (oral)	30.13%	32.76%	6.84%	-2.63%	760	0.0038	1.0000
B Vitamins	Vitamin B-12	* Methylated B-12 (oral)	31.85%	37.50%	13.71%	-5.65%	248	0.0147	1.0000
B Vitamins	B complex	B complex	29.76%	33.40%	8.32%	-3.64%	961	0.0035	0.8090
B Vitamins	B complex	Methylated B complex	28.34%	39.04%	12.83%	-10.70%	187	0.1988	1.0000
B Vitamins	Thiamine & derivatives	Thiamine < 100 mg daily	34.78%	39.13%	10.87%	-4.35%	46	0.1052	0.6005
B Vitamins	Thiamine & derivatives	Thiamine ≥ 100 mg daily	35.35%	40.40%	19.19%	-5.05%	99	0.0190	0.2685
B Vitamins	Thiamine & derivatives	Thiamine (dose unknown)	23.89%	27.43%	5.31%	-3.54%	113	0.7293	1.0000
B Vitamins	Thiamine & derivatives	Benfotiamine or TTFD	28.97%	40.69%	18.62%	-11.72%	145	0.1897	1.0000
B Vitamins	Niacin or derivatives	Nicotinamide riboside	39.67%	46.28%	15.70%	-6.61%	121	0.0003	0.0625

B Vitamins	Niacin or derivatives	Niacin (immediate release)	24.07%	37.04%	11.57%	-12.96%	216	0.7337	1.0000
B Vitamins	Niacin or derivatives	Niacin SR or flush-free	18.28%	25.81%	4.30%	-7.53%	93	1.0000	1.0000
B Vitamins	Niacin or derivatives	Niacinamide	27.78%	33.33%	6.67%	-5.56%	90	0.3504	0.8882
B Vitamins	Niacin or derivatives	NAD+ or NADH	27.93%	32.88%	10.36%	-4.95%	222	0.2077	0.8626
B Vitamins	Niacin or derivatives	NMN	30.95%	33.33%	16.67%	-2.38%	42	0.2760	0.7182
Gastrointestinal & Immune Supplements	Colostrum	Colostrum	19.77%	24.42%	3.49%	-4.65%	86	0.9771	NA
Gastrointestinal & Immune Supplements	Lactoferrin	Lactoferrin (liposomal or acid resistant)	27.66%	40.43%	17.02%	-12.77%	47	0.4400	0.9808
Gastrointestinal & Immune Supplements	Lactoferrin	Lactoferrin (unknown formulation)	27.37%	33.68%	7.37%	-6.32%	95	0.3777	1.0000
Gastrointestinal & Immune Supplements	Probiotics	YourGut+Plus	40.57%	46.23%	16.04%	-5.66%	106	0.0003	0.2264
Gastrointestinal & Immune Supplements	Probiotics	Lactobacillus + inulin	36.56%	43.01%	17.20%	-6.45%	93	0.0116	0.7182
Gastrointestinal & Immune Supplements	Probiotics	L. plantarum 299v	26.32%	40.35%	12.28%	-14.04%	57	0.5267	1.0000
Gastrointestinal & Immune Supplements	Probiotics	Butyrate-producing probiotic	22.22%	25.93%	7.41%	-3.70%	27	0.7965	1.0000
Gastrointestinal & Immune Supplements	Probiotics	Other probiotic(s)	33.04%	36.09%	11.74%	-3.04%	230	0.0065	1.0000
Glucocorticoids & Hormone Replacement Therapy	Corticosteroids	Corticosteroids	39.77%	55.56%	37.43%	-15.79%	171	0.0000	NA

Glucocorticoids & Hormone Replacement Therapy	Testosterone	Testosterone	40.00%	48.00%	16.00%	-8.00%	25	0.0793	NA
Glucocorticoids & Hormone Replacement Therapy	Estrogen and/or Progesterone	Combined estrogen + progesterone	20.51%	38.46%	12.82%	-17.95%	39	0.8944	1.0000
Glucocorticoids & Hormone Replacement Therapy	Estrogen and/or Progesterone	Estradiol or conjugated estrogens	38.00%	46.00%	26.00%	-8.00%	50	0.0344	0.6096
Glucocorticoids & Hormone Replacement Therapy	Estrogen and/or Progesterone	Progesterone	38.71%	48.39%	19.35%	-9.68%	62	0.0145	0.4818
Green or Black Tea	Black tea	Black tea	11.72%	22.27%	4.69%	-10.55%	256	1.0000	NA
Green or Black Tea	Green tea/Matcha/EGCG	Green Tea	14.85%	24.12%	4.33%	-9.28%	485	1.0000	1.0000
Green or Black Tea	Green tea/Matcha/EGCG	Matcha	22.60%	31.51%	9.59%	-8.90%	146	0.9020	0.4690
Green or Black Tea	Green tea/Matcha/EGCG	EGCG ≤ 400 mg	30.14%	36.99%	6.85%	-6.85%	73	0.2265	0.0407
Green or Black Tea	Green tea/Matcha/EGCG	EGCG > 400 mg	44.44%	44.44%	19.44%	0.00%	36	0.0086	0.0005
MCAS Treatments	Antihistamines	H1RA (1st generation)	53.73%	61.94%	22.01%	-8.21%	268	0.0000	0.8090
MCAS Treatments	Antihistamines	H1RA (2nd/3rd generation)	51.22%	56.65%	22.05%	-5.43%	1474	0.0000	0.7182
MCAS Treatments	Antihistamines	H1RA + H2RA (combo)	63.35%	68.18%	37.78%	-4.83%	352	0.0000	0.0001

MCAS Treatments	Antihistamines	*	H2RA (Famotidine)	48.28%	55.54%	21.05%	-7.26%	551	0.0000	1.0000
MCAS Treatments	Antihistamines	*	H2RA (Cimetidine, ranitidine)	40.00%	43.75%	16.25%	-3.75%	80	0.0026	1.0000
MCAS Treatments	Antihistamines	*	Ketotifen (oral)	43.80%	56.93%	28.47%	-13.14%	137	0.0000	1.0000
MCAS Treatments	Antihistamines	*	Ketotifen + H2RA	54.17%	64.58%	39.58%	-10.42%	48	0.0000	0.8881
MCAS Treatments	Antihistamines	*	Hydroxyzine	47.22%	61.11%	25.00%	-13.89%	72	0.0000	1.0000
MCAS Treatments	Other select MCAS treatments	*	Cromolyn (intranasal)	44.74%	51.32%	15.79%	-6.58%	76	0.0001	0.4818
MCAS Treatments	Other select MCAS treatments	*	Cromolyn (oral)	38.78%	53.06%	27.21%	-14.29%	147	0.0002	1.0000
MCAS Treatments	Other select MCAS treatments	*	Luteolin (Algonot formulations)	53.33%	53.33%	23.33%	0.00%	30	0.0005	0.3983
MCAS Treatments	Other select MCAS treatments	*	Luteolin (unknown formulation)	43.75%	45.31%	7.81%	-1.56%	64	0.0007	0.6096
MCAS Treatments	Other select MCAS treatments	*	Montelukast	38.65%	49.80%	27.89%	-11.16%	251	0.0000	1.0000
MCAS Treatments	Other select MCAS treatments	*	Quercetin (unknown formulation)	34.36%	38.63%	13.03%	-4.27%	422	0.0001	1.0000
MCAS Treatments	Other select MCAS treatments	*	Quercetin (enhanced bioavailability)	48.39%	51.61%	18.55%	-3.23%	124	0.0000	0.0684
Melatonin	Melatonin	*	Melatonin <1 mg	33.64%	47.27%	11.82%	-13.64%	110	0.0351	1.0000
Melatonin	Melatonin	*	Melatonin 1-3 mg	45.95%	54.30%	16.22%	-8.35%	407	0.0000	0.2938
Melatonin	Melatonin	*	Melatonin >3-5 mg	37.90%	48.40%	13.70%	-10.50%	219	0.0000	1.0000
Melatonin	Melatonin	*	Melatonin >5-10 mg	49.75%	54.77%	15.58%	-5.03%	199	0.0000	0.0968
Melatonin	Melatonin	*	Melatonin >10 mg	40.38%	57.69%	23.08%	-17.31%	52	0.0119	1.0000
Mitochondrial Enhancers	Coenzyme Q10	*	CoQ10 ≤50 mg/day	17.44%	23.84%	8.14%	-6.40%	172	1.0000	1.0000
Mitochondrial Enhancers	Coenzyme Q10	*	CoQ10 50-100 mg/day	26.70%	30.37%	8.12%	-3.66%	382	0.2667	1.0000
Mitochondrial Enhancers	Coenzyme Q10	*	CoQ10 100 to 200 mg/day	40.99%	42.40%	6.18%	-1.41%	566	0.0000	0.0000

Mitochondrial Enhancers	Coenzyme Q10	*	CoQ10 >200 mg/day	50.66%	51.46%	13.79%	-0.80%	377	0.0000	0.0000
Mitochondrial Enhancers	Coenzyme Q10	*	CoQ10 (dose unknown)	11.35%	16.31%	3.55%	-4.96%	282	1.0000	1.0000
Mitochondrial Enhancers	Mitoquinol		Mitoquinol (any dose)	28.57%	34.69%	22.45%	-6.12%	49	0.3734	NA
Mitochondrial Enhancers	Oxaloacetate		Oxaloacetate	42.86%	49.35%	18.18%	-6.49%	77	0.0004	NA
Mushroom-based supplements	Mushroom-based supplements		Cordyceps militaris	31.63%	40.82%	10.20%	-9.18%	98	0.1001	1.0000
Mushroom-based supplements	Mushroom-based supplements		Lion's mane	29.76%	36.31%	13.69%	-6.55%	168	0.1112	1.0000
Mushroom-based supplements	Mushroom-based supplements		Reishi	26.61%	34.68%	10.48%	-8.06%	124	0.4143	1.0000
Mushroom-based supplements	Mushroom-based supplements		Other mushroom-based supplement	40.51%	45.57%	17.72%	-5.06%	158	0.0000	0.0257
Neuropsychiatric Medications	ADHD Stimulants (Rx)	*	ADHD Stimulants (Vyvanse, Adderall, Ritalin, Focalin, Dexedrine, others)	41.59%	62.69%	34.56%	-21.10%	327	0.0000	NA
Neuropsychiatric Medications	Rx Antidepressants		SNRI	19.90%	45.45%	21.38%	-25.55%	407	1.0000	0.1010
Neuropsychiatric Medications	Rx Antidepressants		SSRI (minus fluvoxamine)	13.00%	40.22%	16.55%	-27.22%	731	1.0000	1.0000
Neuropsychiatric Medications	Rx Antidepressants		Fluvoxamine	5.97%	29.85%	16.42%	-23.88%	67	1.0000	1.0000
Neuropsychiatric Medications	Rx Antidepressants		Bupropion	28.49%	49.42%	30.23%	-20.93%	172	0.1994	0.0001

Neuropsychiatric Medications	Rx Antidepressants	Mirtazapine	27.37%	51.58%	10.53%	-24.21%	95	0.3777	0.0153
Neuropsychiatric Medications	Rx Antidepressants	Trazodone or nefazodone	23.42%	50.45%	18.02%	-27.03%	111	0.8038	0.1039
Neuropsychiatric Medications	Rx Antidepressants	Amitriptyline & other TCAs	13.23%	42.16%	14.93%	-28.92%	529	1.0000	1.0000
Neuropsychiatric Medications	Guanfacine	Guanfacine without NAC	-8.77%	26.32%	12.28%	-35.09%	57	1.0000	1.0000
Neuropsychiatric Medications	Guanfacine	Guanfacine + NAC	52.27%	65.91%	38.64%	-13.64%	44	0.0001	0.0000
Neuropsychiatric Medications	(Ar)modafinil	Modafinil or Armodafinil	16.93%	46.03%	26.98%	-29.10%	189	1.0000	NA
Neuropsychiatric Medications	Gabapentinoids	Pregabalin	27.03%	51.80%	26.13%	-24.77%	222	0.3008	1.0000
Neuropsychiatric Medications	Gabapentinoids	Gabapentin	29.80%	52.98%	26.49%	-23.18%	151	0.1272	0.7182
Neuropsychiatric Medications	Ketamine	Ketamine	56.67%	66.67%	43.33%	-10.00%	30	0.0001	NA
Neuropsychiatric Medications	Abilify ≤ 2 mg (Low-Dose)	Abilify ≤ 2 mg (Low-Dose)	30.15%	54.41%	31.62%	-24.26%	136	0.1234	0.0001
Neuropsychiatric Medications	Abilify > 2 mg	Abilify > 2 mg	-6.06%	27.27%	9.09%	-33.33%	33	1.0000	1.0000
NO-Mediated Vasodilators	Beet juice or supplement	Beet juice or supplement	27.44%	34.76%	10.98%	-7.32%	164	0.3055	NA

NO-Mediated Vasodilators	L-arginine and/or citrulline		L-arginine < 1 g daily	14.86%	27.03%	10.81%	-12.16%	74	1.0000	1.0000
NO-Mediated Vasodilators	L-arginine and/or citrulline		L-arginine 1-2 g daily	26.92%	30.77%	13.46%	-3.85%	52	0.4838	0.4818
NO-Mediated Vasodilators	L-arginine and/or citrulline		L-arginine > 2 g daily	34.48%	41.38%	13.79%	-6.90%	29	0.1946	0.1672
NO-Mediated Vasodilators	L-arginine and/or citrulline		L-arginine (unknown dose)	12.50%	17.50%	0.00%	-5.00%	40	1.0000	1.0000
NO-Mediated Vasodilators	L-arginine and/or citrulline		L-citrulline	25.42%	35.59%	11.86%	-10.17%	59	0.5939	0.6096
NO-Mediated Vasodilators	Sildenafil or Tadalafil		Sildenafil or Tadalafil (sporadic dosing)	13.64%	18.18%	9.09%	-4.55%	22	1.0000	1.0000
NO-Mediated Vasodilators	Sildenafil or Tadalafil		Sildenafil or Tadalafil (daily dosing)	25.00%	37.50%	15.63%	-12.50%	32	0.6567	0.7301
Non-Pharmacological Approaches	Pacing	*	Pacing	75.22%	78.70%	37.36%	-3.49%	803	0.0000	NA
Non-Pharmacological Approaches	Compression Stockings	*	Compression Stockings	61.97%	66.28%	23.74%	-4.31%	952	0.0000	NA
Non-Pharmacological Approaches	Vagal Nerve Stimulation	*	Vagal Nerve Stimulation	45.45%	52.27%	13.64%	-6.82%	132	0.0000	NA
Non-Pharmacological Approaches	Manual Lymphatic Drainage	*	Manual Lymphatic Drainage	55.67%	59.79%	23.71%	-4.12%	97	0.0000	NA
Non-Pharmacological Approaches	Graded Exercise Therapy		Graded Exercise Therapy	-72.24%	10.03%	4.35%	-82.27%	299	1.0000	NA

Non-Pharmacological Approaches	Hyperbaric Oxygen Therapy (HBOT)	Hyperbaric Oxygen Therapy (HBOT)	40.54%	45.95%	29.73%	-5.41%	37	0.0312	NA
Non-Pharmacological Approaches	Cognitive Behavioral Therapy (CBT)	Cognitive Behavioral Therapy (CBT)	2.10%	26.92%	10.14%	-24.83%	286	1.0000	NA
Omega fatty acids	DHA	DHA	20.00%	22.86%	2.86%	-2.86%	35	0.8944	NA
Omega fatty acids	EPA or icosapent ethyl	EPA or icosapent ethyl	44.36%	46.62%	16.17%	-2.26%	266	0.0000	NA
Omega fatty acids	Omega-3 complex (DHA + EPA)	Omega-3 complex (DHA + EPA)	28.36%	30.32%	7.58%	-1.96%	818	0.0351	NA
Omega fatty acids	Omega-3-6 or Omega 3-6-9 supplement	Omega-3-6 or Omega 3-6-9 supplement	23.69%	27.53%	6.27%	-3.83%	574	0.7827	NA
Other Select Supplements & OTC Drugs	Palmitoylethanolamide *	PEA (enhanced bioavailability)	57.78%	60.00%	20.00%	-2.22%	45	0.0000	0.0407
Other Select Supplements & OTC Drugs	Palmitoylethanolamide *	PEA (unknown formulation)	35.71%	40.48%	11.90%	-4.76%	126	0.0067	1.0000
Other Select Supplements & OTC Drugs	Berberine	Berberine	33.33%	36.67%	10.00%	-3.33%	30	0.2253	NA
Other Select Supplements & OTC Drugs	Dextromethorphan	Dextromethorphan	31.91%	42.55%	14.89%	-10.64%	47	0.2112	NA
Other Select Supplements & OTC Drugs	Monolaurin	Monolaurin	15.91%	23.86%	5.68%	-7.95%	88	1.0000	NA
Other Select Supplements & OTC Drugs	Nicotine (patches)	Nicotine (patches)	40.00%	48.00%	24.00%	-8.00%	25	0.0803	NA

Other Select Supplements & OTC Drugs	St John's Wort		St John's Wort	0.00%	21.28%	2.13%	-21.28%	47	1.0000	NA
Phytochemicals	Curcumin	*	Curcumin (enhanced bioavailability)	30.00%	36.92%	7.69%	-6.92%	130	0.1377	1.0000
Phytochemicals	Curcumin	*	Curcumin (unknown formulation)	35.63%	39.38%	10.63%	-3.75%	480	0.0000	0.6005
Phytochemicals	Sulforaphane		Sulforaphane	33.33%	38.10%	14.29%	-4.76%	21	0.2897	NA
Phytochemicals	Pycnogenol (any dose)		Pycnogenol (any dose)	29.03%	30.65%	12.90%	-1.61%	62	0.3280	NA
Phytochemicals	Resveratrol		Resveratrol <500 mg	12.66%	20.25%	2.53%	-7.59%	79	1.0000	1.0000
Phytochemicals	Resveratrol		Resveratrol ≥500 mg	29.58%	33.80%	5.63%	-4.23%	71	0.2670	0.0347
Proteolytic Enzymes	Nattokinase/Lumbrokinase	*	Nattokinase (NK) or Lumbrokinase (LK)	48.42%	55.37%	27.16%	-6.95%	475	0.0000	1.0000
Proteolytic Enzymes	Nattokinase/Lumbrokinase	*	[NK and/or LK] + serrapeptase	51.63%	61.16%	30.47%	-9.53%	430	0.0000	0.6005
Proteolytic Enzymes	Serrapeptase (SP)		Serrapeptase (SP) only	28.85%	37.50%	10.58%	-8.65%	104	0.2550	NA
Select Cardiovascular Medications	Beta Blockers or Ivabradine	*	Cardioselective beta blocker	46.94%	65.50%	37.77%	-18.56%	458	0.0000	0.8626
Select Cardiovascular Medications	Beta Blockers or Ivabradine	*	Non-cardioselective beta blocker (Propranolol)	37.30%	59.10%	30.56%	-21.80%	445	0.0000	1.0000
Select Cardiovascular Medications	Beta Blockers or Ivabradine	*	Ivabradine	66.81%	76.55%	43.81%	-9.73%	226	0.0000	0.0000

Select Cardiovascular Medications	Angiotensin Receptor Blockers (ARBs)		ARBs (losartan, olmesartan, et al)	17.33%	36.00%	14.67%	-18.67%	75	1.0000	NA
Select Cardiovascular Medications	Calcium Channel Blockers		Dihydropyridines	12.61%	33.61%	10.92%	-21.01%	119	1.0000	0.0247
Select Cardiovascular Medications	Calcium Channel Blockers		Non-dihydropyridines	1.54%	35.38%	16.92%	-33.85%	65	1.0000	1.0000
Select Cardiovascular Medications	Statins		Atorvastatin	4.82%	22.89%	10.84%	-18.07%	83	1.0000	1.0000
Select Cardiovascular Medications	Statins		Pravastatin	13.04%	30.43%	19.57%	-17.39%	46	1.0000	0.0795
Select Cardiovascular Medications	Statins		Other statin	3.23%	20.97%	4.84%	-17.74%	62	1.0000	1.0000
Select POTS / Orthostatic Intolerance Treatments	Fluids/electrolytes	*	Oral fluids/electrolytes	68.46%	70.70%	25.73%	-2.24%	2860	0.0000	1.0000
Select POTS / Orthostatic Intolerance Treatments	Fluids/electrolytes	*	IV Saline	69.95%	75.65%	52.33%	-5.70%	193	0.0000	0.6781
Select POTS / Orthostatic Intolerance Treatments	Mestinon	*	Mestinon	41.04%	58.57%	31.87%	-17.53%	251	0.0000	NA

Select POTS / Orthostatic Intolerance Treatments	Fludrocortisone	Fludrocortisone	23.04%	47.93%	25.35%	-24.88%	217	0.8795	NA
Select POTS / Orthostatic Intolerance Treatments	Midodrine	Midodrine	29.89%	55.75%	25.86%	-25.86%	174	0.1001	NA
Select Treatments Used in (Long) COVID	Maraviroc	* Maraviroc ≥15 days	56.90%	62.07%	41.38%	-5.17%	58	0.0000	NA
Select Treatments Used in (Long) COVID	Paxlovid	Paxlovid <10 days	36.23%	45.89%	25.60%	-9.66%	207	0.0004	1.0000
Select Treatments Used in (Long) COVID	Paxlovid	Paxlovid ≥10 days	37.14%	42.86%	28.57%	-5.71%	35	0.0858	0.9411
Select Treatments Used in (Long) COVID	Tollovid	Tollovid < 15 days	18.18%	27.27%	15.15%	-9.09%	33	0.9565	1.0000
Select Treatments Used in (Long) COVID	Tollovid	Tollovid ≥15 days	52.54%	54.24%	35.59%	-1.69%	59	0.0000	0.0061

Select Treatments Used in (Long) COVID	Truvada		Truvada ≥15 days	36.36%	45.45%	22.73%	-9.09%	22	0.1842	NA
Select Treatments Used in (Long) COVID	Vedicinals		Vedicinals (any duration)	37.93%	56.90%	31.03%	-18.97%	58	0.0244	NA
Select Treatments Used in (Long) COVID	Metformin		Metformin	28.57%	37.86%	13.57%	-9.29%	140	0.2245	NA
Select Treatments Used in ME/CFS	Low-Dose Naltrexone	*	Low-Dose Naltrexone	49.42%	60.04%	28.29%	-10.62%	951	0.0000	NA
Select Treatments Used in ME/CFS	Intravenous/Subcutaneous Immunoglobulin	*	Intravenous/Subcutaneous Immunoglobulin	58.24%	64.84%	43.96%	-6.59%	91	0.0000	NA
Select Treatments Used in ME/CFS	D-Ribose		D-Ribose	32.12%	39.23%	10.04%	-7.12%	548	0.0005	NA

Table S4. Effects of Top 20 Treatment Groups on Five Core Symptoms

Treatment Group	Fatigue or low energy	Feeling worse after normal exertion (PEM)	Postural Orthostatic Tachycardia (POTS)	Brain refreshing Fog	Un- refreshing sleep
ADHD Stimulants (Rx)	71.7%	NS	NS	77.1%	NS
Antihistamines	17.9%	NS	NS	NS	18.7%
Beta Blockers or Ivabradine	NS	16.8%	66.0%	NS	NS
Coenzyme Q10	32.3%	15.8%	NS	21.8%	NS
Compression stockings	28.6%	26.4%	63.7%	22.0%	NS
Curcumin	22.9%	17.6%	NS	21.2%	NS
Fluids/electrolytes	43.2%	33.1%	71.7%	36.5%	NS
Graded Exercise Therapy	NS	NS	NS	NS	NS
Intravenous/Subcutaneous Immunoglobulin	55.4%	46.7%	55.8%	50.8%	NS
Low-Dose Naltrexone	41.5%	33.2%	NS	42.3%	NS
Manual Lymphatic Drainage	44.8%	NS	25.9%	40.7%	33.3%
Maraviroc	NA	NA	NA	NA	NA
Melatonin	20.4%	NS	NS	NS	43.0%
Mestinon	37.4%	36.2%	56.9%	23.4%	NS
Nattokinase/Lumbrokinase	49.7%	38.2%	20.3%	49.5%	NS
Other select MCAS treatments	28.2%	NS	NS	27.1%	NS
Pacing	82.7%	62.6%	45.5%	71.2%	23.6%
Palmitoylethanolamide	40.0%	NS	NA	34.6%	NS
Rx Anticoagulants and/or Rx Antiplatelets	40.0%	33.9%	29.7%	34.7%	NS
Vagal Nerve Stimulation	28.0%	25.6%	26.7%	30.3%	33.8%
Vitamin B-12	44.5%	19.6%	NS	33.3%	NS
Vitamin C (oral, NOT liposomal)	21.3%	NS	NS	NS	NS

*NA: NOT Applicable due to limited patient feedbacks (<20); NS: NOT Significant

Table S5. Comparison of treatment effects between MECFS vs Long-COVID

Treatment	ME/CFS NAS	Long COVID NAS	log2(Fold Change)	Adjusted p-value
Oral fluids/electrolytes	63.45%	75.71%	0.2547	0.00000
Ivabradine	61.11%	74.00%	0.2761	0.06053
Vagal Nerve Stimulation	40.00%	72.73%	0.8625	0.01324
Pacing	75.73%	72.27%	-0.0675	0.29963
IV Saline	70.83%	67.35%	-0.0728	0.35871
Compression stockings	59.77%	64.65%	0.1133	0.13065
Glutathione (injection)	31.17%	63.16%	1.0189	0.00416
H1RA + H2RA	65.19%	61.86%	-0.0757	0.32660
Cardioselective beta blockers	36.50%	61.03%	0.7414	0.00000
Mestinon	35.38%	60.71%	0.7789	0.00296
Melatonin 1-3 mg	32.65%	58.29%	0.8361	0.00000
Quercetin (enhanced bioavailability)	40.00%	56.25%	0.4919	0.08897
Ketotifen (oral)	36.78%	56.00%	0.6064	0.04606
Low-Dose Naltrexone	46.69%	55.75%	0.2559	0.02230
[NK and/or LK] + serrapeptase	43.75%	54.40%	0.3144	0.07244
Midodrine	20.80%	53.06%	1.3511	0.00025
B-12 (injection)	45.59%	53.00%	0.2172	0.16908
Gabapentin	22.61%	52.78%	1.2231	0.00257
H1RA (2nd/3rd generation)	49.65%	52.70%	0.0860	0.20938
Azole antifungals	28.24%	52.00%	0.8810	0.04396
H1RA (1st generation)	55.19%	51.75%	-0.0929	0.34380
Cromolyn (oral)	35.09%	51.52%	0.5540	0.10410
Melatonin >5-10 mg	48.39%	50.94%	0.0743	0.38909
Nattokinase (NK) or Lumbrokinase (LK)	42.54%	50.73%	0.2542	0.11868
Corticosteroids	37.76%	50.00%	0.4050	0.19877
Montelukast	31.61%	50.00%	0.6614	0.01059
NAC >600 mg/day	43.78%	49.01%	0.1627	0.25866
Benfotiamine or TTFD	19.39%	48.94%	1.3358	0.00167
H2RA (Famotidine)	47.81%	48.67%	0.0257	0.43040
Melatonin <1 mg	25.71%	47.50%	0.8854	0.03611
CoQ10 >200 mg/day	52.97%	47.47%	-0.1582	0.24021
EPA	42.25%	46.77%	0.1466	0.31412
Non-cardioselective beta blocker (Propranolol)	31.52%	46.75%	0.5685	0.00458
Methylated B complex (oral)	22.92%	46.51%	1.0212	0.00841
PEA (unknown formulation)	30.00%	45.65%	0.6057	0.09329
L-Lysine	28.07%	45.61%	0.7004	0.03823
(Acetyl)-L-carnitine ≥ 500 mg daily	39.68%	45.31%	0.1914	0.31412
Nicotinamide riboside	36.23%	44.23%	0.2878	0.28041
Vitamin C (intravenous)	25.93%	44.07%	0.7653	0.03171
Other mushroom-based supplement	38.46%	43.28%	0.1704	0.32909
ADHD Stimulants (Rx)	40.99%	42.86%	0.0642	0.39593
Doxycycline ≥100 mg	30.00%	42.31%	0.4960	0.21068
Melatonin >3-5 mg	32.63%	41.94%	0.3619	0.14817
Creatine	25.49%	41.03%	0.6866	0.08897

Curcumin (enhanced bioavailability)	23.08%	40.38%	0.8074	0.05274
Beet juice or supplement	18.56%	40.30%	1.1188	0.00739
BCAA	29.87%	39.39%	0.3993	0.25866
Lion's mane	21.35%	39.24%	0.8782	0.02306
CoQ10 >100 to 200 mg/day	42.18%	39.21%	-0.1055	0.32197
Fludrocortisone	18.71%	39.13%	1.0642	0.01059
Valacyclovir	38.10%	38.78%	0.0255	0.46619
Paxlovid <10 days	32.50%	38.58%	0.2475	0.28041
Curcumin (unknown formulation)	33.92%	38.07%	0.1665	0.27120
Methylated B-12 (oral)	29.95%	37.70%	0.3324	0.21843
Glutathione (oral, liposomal formulation)	26.88%	37.37%	0.4754	0.08757
Quercetin (unknown formulation)	31.18%	36.86%	0.2415	0.19803
SNRI	15.85%	36.71%	1.2113	0.00025
Aspirin only	25.88%	36.27%	0.4873	0.01753
L-glutamine	20.77%	36.00%	0.7935	0.05274
Reishi	20.27%	36.00%	0.8286	0.07244
(Ar)modafinil	12.00%	35.90%	1.5808	0.00213
Ivermectin	43.18%	35.71%	-0.2739	0.28967
Pregabalin	23.03%	35.71%	0.6332	0.06925
5-HTP	16.77%	35.29%	1.0732	0.02893
Macrolides	30.19%	35.19%	0.2210	0.32660
Bupropion	26.40%	34.04%	0.3668	0.25866
D-Ribose	31.60%	33.87%	0.1000	0.35546
B-12 (oral)	28.27%	33.33%	0.2375	0.14289
DHA + EPA	24.68%	33.15%	0.4258	0.01789
NADH or NAD+ (oral)	25.81%	32.84%	0.3475	0.23658
NAC ≤600 mg/day	16.83%	32.82%	0.9633	0.00011
Penicillins	17.53%	32.26%	0.8796	0.03278
Licorice/Glycyrrhizin	29.88%	32.00%	0.0990	0.40634
Metformin	27.27%	31.71%	0.2174	0.34655
B complex (oral)	28.96%	30.86%	0.0920	0.32660
Vitamin C (oral)	27.42%	30.56%	0.1562	0.32660
Other probiotic(s)	33.67%	29.41%	-0.1952	0.35546
Other probiotic(s)	33.67%	29.41%	-0.1952	0.35546
Acyclovir	30.49%	28.57%	-0.0937	0.43893
Matcha	17.95%	27.94%	0.6385	0.14673
SSRI (minus fluvoxamine)	7.22%	27.80%	1.9444	0.00000
CoQ10 >50-100 mg/day	26.27%	27.40%	0.0606	0.42067
Omega-3-6 or Omega 3-6-9 complex	22.64%	26.16%	0.2088	0.27740
Glutathione (oral, NOT liposomal)	20.18%	25.76%	0.3524	0.28463
Niacin (immediate release)	21.52%	25.55%	0.2476	0.32660
Dihydropyridines	6.33%	25.00%	1.9819	0.01059
Grape seed extract	15.32%	24.53%	0.6795	0.14673
Alpha or R-lipoic acid (oral)	17.90%	24.00%	0.4230	0.31607
Vitamin C (oral, NOT liposomal)	24.69%	23.28%	-0.0849	0.32660
(Acetyl)-L-carnitine (dose unknown)	19.70%	23.08%	0.2279	0.37784
CoQ10 (dose unknown)	6.97%	22.22%	1.6738	0.00167
Green Tea	10.33%	22.16%	1.1008	0.00213
Thiamine (unknown dose)	24.71%	21.43%	-0.2053	0.38909

Serrapeptase (SP) only	35.00%	20.45%	-0.7749	0.11851
Amitriptyline & other TCAs	10.86%	20.30%	0.9027	0.01393
Trazodone or nefazodone	25.35%	20.00%	-0.3421	0.32660
CoQ10 ,≤50 mg/day	16.38%	19.64%	0.2621	0.34655
Black tea	12.28%	10.59%	-0.2139	0.37784
Graded Exercise Therapy	-75.29%	-50.00%	-0.5904	0.00000