

A mixed-methods systematic review of post-viral fatigue interventions: Are there lessons for long Covid?

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Published version

FOWLER-DAVIS, Sally, PLATTS, Katharine, THELWELL, Michael, WOODWARD, Amie and HARROP, Deborah (2021). A mixed-methods systematic review of post-viral fatigue interventions: Are there lessons for long Covid? PLOS ONE, 16 (11).

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Table 1. Overview of intervention effectiveness using standardised measures, including follow-up assessments.

Author/year	Control/Intervention Groups	Baseline fatigue severity (%)	Post-intervention				Follow-up			
			Change in fatigue from baseline (%)	Mean difference (95% CI)	Sig.	SMD	Change in fatigue from baseline (%)	Mean difference (95% CI)	Sig.	SMD
O'Dowd (2006)	SMC	72.4	-6.4							
	CBT	75.8	-21.5	-11.8 [-20.8, -2.8]	0.027	0.503				
	GET	75.5	-10.6	-1.2 [-9.8, 7.3]	0.957	0.055				
Wiborg (2015)	Waiting list	87.3	-6.9							
	CBT (large group)	90.4	-36.9	-26.9 [-33.1, -20.6]	<0.001	1.126				
	CBT (small group)	88.5	-35.6	-27.5 [-33.7, -21.3]	<0.001	1.170				
Hansen (2013)	Healthy controls	34.8	0.0							
	CBT/GET/Group therapy	76.8	-47.4	-5.4 [-17.7, 6.9] [‡]	0.398 [‡]	0.278 [‡]				
Heald (2019)	Waiting list	78.9	-1.6							
	Group CBT	77.3	-23.7	-23.7 [-29.2, -18.2]	<0.001	2.266				
Kim (2015)	SMC	58.0	-0.2				-3.3			
	Acupuncture + SMC	61.2	-21.5	-18.2 [-23.5, -12.8]	<0.001	0.984	-22.2	-15.7 [-21.5, -9.8]	<0.001	0.773
	Sa-am Acupuncture + SMC	62.5	-19.5	-14.8 [-20.4, -9.2]	<0.001	0.768	-20.7	-12.8 [-18.7, -7.0]	<0.001	0.629
Mist (2018)	Group Education	70.6	-1.2				4.9			
	Group Acupuncture	72.9	-23.9	-20.4			-28.0	-30.6		
Ng (2013)	Sham Acupuncture	85.2	-16.4							
	Acupuncture	91.6	-27.5	-4.6 [-8.3, -0.9]	0.016	0.204				
Shu (2016)	Acupuncture (Healthy Controls)	45.5	-15.0							
	Acupuncture	68.7	-23.9	14.4						
	Moxibustion	66.2	-30.0	5.7						
UÄYürlu (2017)	Sham Acupuncture	89.4	-11.9				-24.4			
	Acupuncture	85.7	-15.1	-7.0 [-13.1, -0.8]	0.077	0.512	-33.4	-9.0 [-17.0, -1.1]	0.088	0.493

Kim (2013)	Sham Moxibustion	60.0	-4.3							
	Moxibustion	59.8	-14.4	-10.3						
Clark (2017)	SMC	78.8	-9.4							
	GET + SMC	79.7	-21.8	-11.5 [-17.6, -5.4]	<0.001	0.524				
Ericsson (2016)	Relaxation	81.8	-5.5							
	Group-based GET	81.4	-8.6	-3.5						
Oka (2014)	Pharma	79.1	-0.9							
	Yoga + Pharma	78.5	-20.3	-20.0 [-34.6, -5.4]	0.012	0.978				
Windhorst (2017)	GET	61.0	-15.3							
	Biofeedback	51.9	-16.6	-10.5 [-38.3, 17.3]	0.077	0.486				
Weatherley-Jones (2004)	Placebo	77.1	-10.2							
	Homeopathic Medication	77.8	-14.5	-3.7 [-4.9, -2.5]	<0.001	0.855				
Dailey (2013)	No TENS	52.0	-2.0							
	Active TENS	50.0	-6.0	-6.0 [-16.9, 4.9]	0.535	0.239				
	Placebo TENS	50.0	5.0	5.0 [-6.5, 16.5]	0.647	-0.189				
Fitzgibbon (2018)	Sham rTMS	68.3	-8.0				-7.3			
	rTMS	73.3	-13.6	-0.6			-28.3	-16.0		
Van Hoof (2003)	No infection (with HBOT)	76.0	-4.1				-3.3			
	Mycoplasma hominis infection (with HBOT)	74.9	-4.4	-1.4 [-3.5, 0.8]	0.215	0.367	-2.1	0.0 [-2.9, 2.9]	1	0
Perrin (2011)	Healthy controls	4.3	-0.9							
	CFS patients (osteopathic treatment)	50.0	-18.2	28.4 [-4.6, 61.4] [¥]	0.0013 [¥]	-1.827 [¥]				
	CFS patients (any treatment)	39.8	5.9	42.3 [33.2, 51.3] [¥]	<0.001 [¥]	-4.313 [¥]				
Keijmel (2017)	Placebo	87.9	-25.8							
	Medication	90.4	-22.1	6.3 [3.7, 8.8]	<0.001	-0.752				
	CBT	86.9	-37.7	-12.9 [-15.1, -10.8]	<0.001	1.784				
Racine (2019)	Control	67.4	1.4							
	Operant Learning	64.1	-5.9	-10.6 [-22.5, 1.3]	0.155	0.520				

	Energy Conservation	68.3	0.5	0.0 [-9.6, 9.6]	-	-				
Ridsdale (2012)	SMC + CBT Booklet	70.9	-24.5				-29.1			
	GET	75.2	-30.9	-2.1 [-10.2, 6.0]	0.855	0.084	-31.2	2.1 [-5.5, 9.7]	0.8583	-0.09
	Counselling	75.2	-26.1	2.7 [-5.1, 10.6]	0.784	-0.111	-29.1	4.2 [-3.5, 12.0]	0.5167	-0.173
White (2011)	SMC	85.8	-13.0				-13.6			
	SMC + APT	86.4	-14.5	-0.9 [-5.5, 3.7]	0.983	0.043	-16.4	-2.1 [-6.8, 2.5]	0.835	0.1
	SMC + CBT	83.9	-18.8	-7.6 [-12.5, -2.7]	0.011	0.339	-22.4	-10.6 [-15.5, -5.7]	<0.001	0.476
	SMC + GET	85.5	-19.7	-7.0 [-11.6, -2.3]	0.024	0.328	-23.0	-9.7 [-14.4, -5.0]	<0.001	0.453
Sharpe (2015)	SMC	85.8	-24.5							
	SMC + APT	86.4	-24.2	0.9 [-5.7, 7.5]	0.993	-0.035				
	SMC + CBT	83.9	-28.2	-5.5 [-12.1, 1.2]	0.362	0.210				
	SMC + GET	85.5	-27.6	-3.3 [-9.7, 3.0]	0.742	0.133				
Vos-Vromans (2016)	CBT	89.7	-31.0				-22.9			
	Multidisciplinary rehabilitation	90.6	-37.6	-5.7 [-13.6, 2.2]	0.158	0.197	-36.7	-12.9 [-20.8, -5.1]	0.001	0.454
Raijmakers (2019)	Placebo	87.9	-27.3							
	Medication	90.4	-21.0	8.7 [6.4, 11.1]	<0.001	-1.120				
	CBT	86.9	-21.3	5.0 [2.7, 7.3]	<0.001	-0.670				
Fernie (2016)	CBT	69.6	-21.5				-25.0			
	GET	68.2	-14.5	5.6 [-2.9, 14.1]	0.199	-0.224	-21.3	2.3 [-5.3, 9.8]	0.568	-0.096
Stubhaug (2008)	Placebo	77.4	-5.6							
	Medication	75.0	-6.2	-3.0 [-6.8, 0.7]	0.349	0.447				
	CBT	74.6	-10.9	-8.2 [-13.2, -3.1]	0.001	0.916				
Lee (2015)	Waiting List	65.0	-6.7							
	Oriental medicine music therapy	60.0	-23.3	-21.7 [-30.4, -12.9]	<0.001	1.237				
El Mokadem (2020)	Waiting List	82.3	-7.7							
	Three Principles	81.0	-45.4	-39.0 [-51.8, -26.2]	<0.001	1.670				
Maddali (2016)	Educational course	32.9	-0.9							

	Tai Ji Quan	39.5	-7.9	-0.4 [-9.6, 8.9]	0.933	0.023				
Jason (2010)	Waiting list	90.7	2.6							
	Social support	93.9	-12.6	-12.0 [-20.7, -3.4]	0.014	0.826				
Wearden (2010)	SMC	31.3	-3.1				-2.6			
	Pragmatic rehab	31.8	-6.4	-2.8 [-5.7, 0.1]	0.112	0.270	-5.4	-2.3 [-5.0, 0.4]	0.2254	0.236
	Supportive listening	31.9	-2.6	1.1 [-1.4, 3.6]	0.703	-0.117	-3.4	-0.3 [-2.8, 2.2]	0.9883	0.03
Marques (2014)	SMC	81.3	0.7							
	Self-regulation based physical activity	79.2	-7.0	-9.9 [-16.3, -3.4]	<0.001	0.513				
Friedburg (2016)	SMC	93.7	-3.3				-3.3			
	Self-management & web diaries	92.0	-6.7	-5.0 [-9.1, -0.9]	0.048	0.434	-8.7	-7.0 [-11.8, -2.2]	0.014	0.514
	Self-management & paper diaries	90.8	-8.8	-8.3 [-12.4, -4.3]	0.000	0.724	-5.8	-5.3 [-10.2, -0.5]	0.0824	0.391
Marques (2017)	SMC	81.3	3.2							
	Self-regulation based physical activity	79.2	-8.4	-13.7 [-20.1, -7.3]	<0.001	0.720				
Tummers (2010)	SMC	87.3	-31.3							
	Self-instruction & CBT	85.6	-29.2	0.4 [-6.2, 7.1] [‡]	0.883 [‡]	-0.015 [‡]				

P < 0.05, SMD = Standardised mean difference (Cohen's d and Hedges' g), ‡ = non-inferiority trial to see if one treatment is no less effective than the other, ¥ = fatigued individuals vs healthy controls, SMC = Standard Medical Care, Cognitive behavioural therapy = CBT, Graded exercise therapy = GET, Adaptive pacing therapy = APT, 95% CI = 95% Confidence intervals.