

Evidence Table 1. Study characteristics

	k	n
Total	53	4,558
Publication Year		
1988 - 1994	11	1,030
1995 - 2001	42	3,528
Accrual Years Reported	13	1,226
Study Location		
USA	28	1,869
Canada	2	73
Western Europe	20	1,807
Australia/New Zealand	2	65
Multicontinental	1	744
Study Design		
Prospective	21	1,800
RCT	10	1,042
nRCT	1	71
Case control	2	321
UCS	8	366
Retrospective	1	94
Case series	1	94
Cross-sectional	31	2,664
Interventional - all	17	1,348
Observational - all	36	3,210
CFS Diagnostic Criteria Used*		
CDC 1988	23	2,267
CDC 1994	20	1,912
Oxford 1991	18	2,173
Australia 1990	1	744

k = number of studies

n = number of patients with CFS

RCT = randomized controlled trial

nRCT = non-randomized controlled trial

UCS = uncontrolled case series

CDC = Centers for Disease Control

* Numbers sum to greater than the total number of studies, as some studies used more than one of these criteria.

Evidence Table 2. Study quality and validity

	k	n
MacMahon Quality Criteria - Longitudinal		
I a	10	1,312
I b	3	140
III a	3	300
III b	6	142
MacMahon Quality Criteria - Cross-sectional		
II a	4	520
II b	14	409
IV a	9	1,639
IV b	4	96
MetaWorks Internal Validity Score (2-6 points)		
2	2	136
3	5	424
4	15	1,779
5	21	950
6	10	1,269
MetaWorks External Validity Score (0-2 points)		
0	35	1,737
1	3	403
2	15	2,418
MetaWorks Total Validity Score (mean) (range 2-8)	5.2	4,558
Jadad Quality Score - RCT only (mean) (range 0-5)	3.3	1,042

k = number of studies

n = number of patients with CFS

Jadad Quality Scores (0-5): Higher numbers = best quality

MacMahon Quality Criteria (Ia - IVb): Lower numbers = best quality

MetaWorks Total Validity Score (2-8): Higher numbers = best validity

Evidence Table 3. Patient demographics, history, and employment status

Demographics	CFS			Healthy Controls		
	% of patients or mean *	k	n	% of patients or mean *	k	n
Total patients (enrolled/randomized)	100	53	4,507	100	22	775
Percent female	76	49	4,378	73	19	605
Mean age (years)	38.4	48	4,372	37.7	19	596
Mean CFS or symptom duration (years)	5.5	40	3,976	NA	--	--
Mean total education, years	14.1	14	1,310	14.4	6	212
Comorbid conditions						
Patients with any current psychiatric diagnosis	39	17	1,830	6	4	200
Patients with any current psychiatric diagnosis	65	12	930	12	4	200
Patients with depression or dysthymia **	45	13	1,718	12	2	65
Employment Status						
Total employed ¹	42	35	2,652	90	9	340
Employed full time	19	16	967	75	2	53
Unemployed ²	54	37	2,720	9	9	340
Disability benefits	51	6	364	4	1	47
Disability or temporary sick leave	55	10	511	1	2	89
Work limitations due to illness	64	20	1,919	0	1	38

* For those studies where the value is known

** All patients with reported history of depression or dysthymia diagnoses.

k = number of studies contributing data

n = number of patients in studies contributing data (less than the total number of patients enrolled at the study level, because some studies did not account for, or present demographic information for all patients)

¹ Employed includes working or in school

² Unemployed includes retired, not working, or unable to continue schooling

Employed + unemployed does not sum to 100% of patients because complete employment data could not be extracted for all patients.

Number of studies reporting number of patients employed does not equal number of studies reporting number of patients unemployed because 2 studies only reported number unemployed, and the remainder of the patients were either employed or unaccounted for.

Evidence Table 4. Employment status and impairment domains

Employment Status	Domain Totals by Work Data Reported *													
	Cognitive		Disease Severity/Symptoms		Exercise Testing		Functional		General Health		Mental (Psych/Affective)		Physical Activity	
	k	n	k	n	k	n	k	n	k	n	k	n	k	n
Employed	6	478	18	1634	6	183	4	455	10	659	20	1572	11	1246
Full time	4	363	6	717	3	35	3	288	3	122	8	632	4	517
Part time	2	310	5	574	3	35	2	169	3	122	6	579	3	398
Unemployed	7	519	19	1675	6	183	4	455	11	700	21	1613	12	1287
Disability benefit	0	0	3	240	1	2	0	0	1	51	2	208	2	208
Disability benefit or temporary sick leave	4	165	4	202	1	2	0	0	4	202	6	336	4	252
Work limitations due to illness	6	181	9	694	3	150	3	264	4	184	12	702	4	237
Other work data														
Work scales	5	449	5	491	0	0	1	32	4	148	7	524	5	474
Mean hours worked per week	1	51	1	270	1	2	1	270	1	270	1	270	1	51

* At baseline/single time point or at outcome, all study designs

k = number of studies contributing data

n = number of patients in studies contributing data

Evidence Table 5. Employment and physical impairments

Author	Year	Validity Score	# CFS patients	% CFS patients employed	# Healthy controls	% Healthy controls employed	Significant differences: CFS vs. healthy controls	No significant differences: CFS vs. healthy controls
Buchwald	1996	7	185	46	99	91	MOS SF-36 - physical function: 40 vs. 96 ($p \leq .001$) MOS SF-36 - general health: 32 vs. 81 ($p \leq .001$)	
Claypoole	2001	5	22	41	22	86		VO2 max: 18.9 vs. 20.5 ml/kg/min
Garcia-Borrequeiro	1998	5	42	27*	41	100	POMS - fatigue: 19.9 vs. 6.3 ($p < .0001$) POMS - vigor/activity: 8.0 vs. 19.0 ($p < .0001$)	
Lloyd	1994	5	12	42	13	100	POMS - fatigue: 18.1 vs. 2.2 ($p < .05$)	MVC (% decline after exercise): 61.8 vs. 63.8
Natelson	1995	6	41	18**	36	100	POMS - vigor: 6 vs. 21 POMS - fatigue: 21 vs. 2	
Ray	1993	5	24	13***	24	71***	PFRS - fatigue: 4.0 vs. 0.7 ($p < .001$) PFRS - somatic symptoms: 2.6 vs. 0.4 ($p < .001$)	
Schmaling	1998	4	15	13	11	91	MOS SF-36 - health perception: 23.3 vs. 95.8 ($p < .001$) MOS SF-36 - physical functioning: 37.0 vs. 95.8 ($p < .001$)	
Vercoulen	1997	7	51	49	53	89	Actometer: 23.3 vs. 35.5 ($p < .05$) SIP - mobility: 26.2 vs. 33.5 ($p < .05$) SIP - walking: 31.6 vs. 40.8 ($p < .05$)	

Measures of dispersion are not included in this table, p values are listed when reported.

MOS SF-36 = Medical Outcomes Study Short-Form General Health Survey

POMS = Profile of Mood States

MVC = Maximal Voluntary Contraction

PFRS = Profile of Fatigue-Related Symptoms

SIP = Sickness Impact Profile

CIS = Checklist Individual Strength

* This study reported the number of patients with vocational disability. It was assumed that the remainder of patients were employed. For controls, vocational disability was reported as N/A, and 100% employment was assumed.

** This study reported the number of patients disabled, and it was assumed that the remainder of patients were employed.

*** This study reported only the number of patients employed full-time.

Evidence Table 6. Neuropsychological tests and work status for CFS patients vs. healthy controls (Key Question 2)

Author	Year	Validity Score	# CFS patients	% CFS patients employed	# Healthy controls	% Healthy controls employed	Significant differences: CFS vs. healthy controls	No significant differences: CFS vs. healthy controls
Buchwald	1996	7	185	46	99	91	MOS SF-36 - mental health: 57 vs. 83 ($p<.001$)	
Claypoole	2001	5	22	52	22	86		Hopkins verbal learning: 26.1 vs. 27.4
Garcia-Borrequero	1998	5	42	27*	41	100	POMS - confusion: 12.0 vs. 5.9 ($p<.0001$) POMS - depression: 9.2 vs. 5.4 ($p<.05$)	POMS - tension/anxiety (scores not reported) POMS - anger/hostility (scores not reported)
Lloyd	1994	5	12	42	13	100	POMS - confusion: 14.8 vs. 2.4 ($p<.1$) POMS - depression: 21.5 vs. 0.6 ($p<.001$)	
Michiels	1996	5	35	26	33	100	WAIS digit span forward: 45.3 vs. 52.6 ($p<.0005$)	
Natelson	1995	6	41	18**	6	100	POMS - depression/dejection: 10 vs. 3 POMS - confusion: 14 vs. 2	
Ray	1993	5	24	13***	24	71***	EAQ: 35.6 vs. 49.3 ($p<.001$) PFRS - emotional distress: 3.5 vs. 1.2 ($p<.001$) PFRS - cognitive difficulty: 3.8 vs. 1.0 ($p<.001$)	
Schmaling	1998	4	15	13	11	91	SCL 90-R - depression: 59.3 vs. 25.8 ($p<.001$) MOS SF-36 - mental health: 69.1 vs. 85.5 ($p<.001$)	
Vercoulen	1997	7	51	49	53	89	SIP - concentration: 35.0 vs. 2.2 ($p=.0001$) CIS - concentration: 5.2 vs. 1.9 ($p=.0001$)	

Measures of dispersion are not included in this table. *p* values are listed when reported.

MOS SF-36 = Medical Outcomes Study Short-Form General Health Survey

POMS = Profile of Mood States

EAQ = Everyday Attention Questionnaire

PFRS = Profile of Fatigue-Related Symptoms

SCL 90-R = Symptom Checklist 90 - Revised

SIP = Sickness Impact Profile

CIS = Checklist Individual Strength

* This study reported the number of patients with vocational disability. It was assumed that the remainder of patients were employed.

For controls, vocational disability was reported as N/A, and 100% employment was assumed.

** This study reported the number of patients disabled, and it was assumed that the remainder of patients were employed.

*** This study reported only the number of patients employed full-time.

Evidence Table 7. Interventions and work or impairment domains (Key Question 3)

	Domain Totals at Follow-up, post-intervention																	
	Total		Work *		Cognitive		Disease (Severity/ Symptoms)		Exercise Testing		Functional		General Health		Mental (Psych/ Affective)		Physical Activity	
Interventions	k	n	k	n	k	n	k	n	k	n	k	n	k	n	k	n	k	n
Behavioral	4	143	2	62	1	32	3	92	1	30	2	62	2	83	3	92	1	30
Psychiatric	2	94	1	30	0	0	2	94	0	0	0	0	0	0	1	30	1	30
Drug Therapy	5	218	0	0	0	0	4	165	1	35	1	18	2	85	4	165	2	85
Physical/Exercise Therapy	2	148	0	0	0	0	2	148	1	34	0	0	0	0	2	148	1	114
Dietary Therapy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Placebo	6	247	0	0	0	0	6	247	2	64	1	30	2	85	6	247	2	85
Mixed	4	92	0	0	1	23	3	90	2	35	1	23	0	0	3	90	1	34
All Interventional Studies	14	907	2	92	2	55	11	741	3	168	4	133	2	94	10	772	4	378

* Includes work function scales reported at follow-up, post intervention.

k = number of studies

n = number of patients

Evidence Table 8. Restoring ability to work in CFS patients (Key Question 3)

Author	Year	Validity Score	Intervention	Time of Followup Assessment (months)	# CFS patients enrolled	% Dropouts	% CFS patients employed at baseline	% CFS patients employed at followup*
Akagi	2001	6	Cognitive behavioral therapy	6	51	0	29	53
Dyck	1996	3	Rehabilitation program	3	2	0	0	50
Fulcher	1997	5	Exercise therapy	15	66	29	39	47
Marlin	1998	2	Individualized programs	6	71	28	0	44
Tiersky	2001	4	None	42	47	26	32	23
Vercoulen	1994	7	None	18	298	17	31	24

* % of patients employed at follow-up = # patients employed at followup/ # patients enrolled

Evidence Table 9. Baseline characteristics for CFS patients Reported as improved (Key Question 4)

Author	Year	Validity Score	Intervention	Time of Outcome Assessment (months)	# CFS patients enrolled in study	# CFS patients evaluated for improvement	% CFS patients improved	Baseline Characteristics of Improved vs. Unimproved patients
Bombardier	1995	4	none	18	226	226	61	Absence of dysthymia ($r = -.15$, $p < .03$)
Butler	1991	5	CBT	1.5	32	27	85	Absence of treatment-resistant affective disorder (BDI: 8.3 vs. 11.7) Same gender, disease severity, disease duration (numbers not reported).
Deale	1997	6	CBT	6	60	27	70	No significant difference on any pretreatment characteristic (numbers not reported).
Kruesi	1989	4	Acyclovir or placebo	6	28	24	88	No significant difference on clinical, chemical, immunologic, or serologic features (numbers not reported).
Lerner	1997	4	Ganciclovir	6	38	18	72	Male gender (3 men in study, all improved), Shorter mean duration of symptoms (1.6 vs. 2.8 yrs)
Peterson	1991	6	none	onset of illness	177	177	12	Female: 61.9% vs 80.1% ($p = .09$) Employed at presentation: 66.7% vs. 49.4% ($p = .06$) Physical functioning scores: 68.5 vs. 58.9 ($p = .01$) Social functioning scores: 3.2 vs. 42.8 ($p = .02$) SCL-90 anxiety scores: 0.43 vs. 0.66 ($p = .01$) SCL-90 Obsessive/compulsive sco
Saltzstein	1998	4	none	24	15	15	12	Perception that physician's prognosis was positive, social support (numbers not reported).
Tiersky	2001	4	none	42	47	35	57	Higher anxiety: median score 38 vs. 27 ($p = .02$), Ability to perform light duty. No significant differences in age, education, illness severity or duration, employment status, gender, level of depression (all $p > .05$).
Vercoulen	1994	7	none	18	298	246	20	Self-reported improvement was related to younger age, shorter disease duration, less symptom severity, less functional impairment, more sense of control over symptoms (numbers not reported). "Demographic variables were not predictive for

Measures of dispersion are not included in this table. p values are listed when reported.

CBT = Cognitive Behavior Therapy

BDI = Beck Depression Inventory

SCL 90 = Symptom Checklist 90

Table 10. Studies reporting work status correlations

Study ID	Author	Year	Validity Score	n	Relationship Investigated	Finding
701825	Bombardier	1995	4	226	Demographic (age, gender, education), clinical (duration of fatigue), and psychiatric (lifetime psychiatric diagnoses) variables at initial evaluation vs. return to work at follow-up (median 1.5 years later).	Among CFS patients, none of the initial demographic, clinical, or psychiatric variables were predictive of return to work.
699067	Jason	1999	5	32	Demographic (age, gender, marital status), clinical (symptom severity, activity level, physical function) and psychiatric (COPE scales) measures by work status, at single time point.	Working patients with CFS were more likely to be male, younger, never married, had less severe muscle and joint pain, higher activity levels, and better physical functioning than non-working patients.
698360	Moss-Morris	2001	5	53	Cognitive-behavioral factors at initial evaluation vs. SIP Work subscale at 6 month follow-up.	Somatic illness identity (extent of symptoms associated with illness) and limiting coping (extent to which patients limited stress, exercise, and activity) were significant predictors of work dysfunction.
698505	Wilson	2001	6	744	Symptom severity self-report and history of major depressive episode vs. ability to work, at single time point.	Severe functional impairment correlated with inability to work. Presence of major depression was not associated with ability to work.

n = number of CFS patients in study

SIP = Sickness Impact Profile