

## Appendix 2: Data Extraction Tables

### 1.1 *Economic Evidence*

Bibliographic reference  Ref ID: 2760	Severens JL, Prins JB, van der Wilt GJ, van der Meer JW, Bleijenberg G, Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome Q J Med 2004;97:153-161
Economic study type and outcomes	CUA / CEA
Population, country & perspective	270 patients, aged 18-60, score of 40 or more on the subscale fatigue severity of the Checkpoint Individual Strength, and a score of 800 or more on the Sickness Impact Profile  Netherlands  2 separate analyses for a societal perspective and a health-care perspective
Intervention  Comparison(s)	Eight months of CBT or guided support groups followed up for six further months  The 'natural course' (no protocol based interventions) This involves GP care but no specialist interventions.
Source of effectiveness data	Economics analysis was run parallel to clinical trial
Method of eliciting health valuations (if applicable)	N/A
Cost components included	GP visits, specialist visits, physical therapist visits, company doctor visits, alternative practitioner visits, prescribed and unprescribed medication, home care (both formal and informal)  The societal perspective also included traveling costs and productivity costs of the condition
Currency and cost year	Euro (1998)
Results – cost per patient per alternative	The medical cost of diagnosis and protocol in CBT, guided support groups and the control were €556, €1 184 and €790 respectively. Once non-medical costs are included, these figures increase to €1 044, €2 173 and €1 504.
Results – effectiveness per patient per alternative	The QALY gains in the populations undertaking CBT, guided support groups and the control were 0.0737, -0.0018 and 0.0458 respectively.
Results –incremental cost-effectiveness	Since guided support group was more expensive and less effective than CBT, the only useful comparison is CBT relative to the natural course approach. The incremental cost-effectiveness ratio for (i) treatment costs, (ii) treatment costs, other medical costs

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	and patient costs and (iii) these costs plus productivity costs were €60 108, €51 642 and €21 375 per QALY respectively.
Results-uncertainty	The authors undertook a non-parametric bootstrap approach. There was considerable uncertainty concerning the baseline result
Time horizon	14 months
Discount rate	No discount used due to short time frame
Source of funding	Public
Comments	Focuses exclusively on CFS/ME patients
Overall study quality (+,-)	+

Bibliographic reference Ref ID: 3	McCrone P, Ridsdale L, Darbishire L, Seed P, Cost-effectiveness of cognitive behavioural therapy, graded exercise and usual care for patients with chronic fatigue in primary care. <i>Psychological Medicine</i> 2004;34:991-999
Economic study type and outcomes	CEA
Population, country & perspective	132 patients in South East England recruited between January 1999 and June 2001. Since the paper is an economic evaluation of the trial of Ridsdale et al. (2004), the population is that of the clinical trial.  The perspective employed was largely societal in that it includes the cost of informal care.
Intervention Comparison(s)	The details of the intervention and the control are given in the clinical trial paper. The economic evaluation reports that "(c)onsenting patients were randomized to six sessions of CBT or GET. Sessions each lasted 45 min. CBT was delivered by trained cognitive behavioural therapists and included an initial assessment, activity planning, homework and establishing a sleep routine. The aim of the CBT was to enable patients to address negative beliefs regarding symptoms, self-expectations and self-esteem. GET was tailored to each patient's physical capacity and aimed for a gradual increase in aerobic activities, especially walking, and was delivered by physiotherapists."  Patients in the control group were subsequently recruited from the general practices and were given a booklet on self-management, and received standard GP treatment.
Source of effectiveness data	Economics analysis was run parallel to clinical trial
Method of eliciting health valuations (if applicable)	N/A
Cost components included	Intervention costs, GP and other HCP contacts (nurse, physiotherapy, counselor,

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	nutritionist, social services, complimentary therapy and informal care.
Currency and cost year	£ (2001)
Results – cost per patient per alternative	The study looked at the costs in the three months prior to baseline and in the three months prior to re-assessment at 8 months. The cost levels in the graded exercise group increased from £1 392 (s.d. = 2 827) to £1 684 (2 584). In the CBT group the baseline figure was £2 225 (3 920) and the follow-up was £1 970 (2 895). However, once the sample differences were controlled for, the incremental cost of CBT relative to GET was £519 at baseline (90% CI -£814 to £1904; p=0.522) and -£193 at follow-up (90% CI -£946 to £458; p=0.62).
Results – effectiveness per patient per alternative	There was no statistically significant difference between outcome in the CBT and GET groups. Details are provided in the clinical extraction.
Results –incremental cost-effectiveness	
Results-uncertainty	If society values a four point improvement on the Chalder fatigue scale at £500, there is an 81.9% probability of therapy (be it CBT or GET) representing a cost-effective option.
Time horizon	8 months
Discount rate	No discount used due to short time frame
Source of funding	Academic
Comments	<p>This paper is dealing with chronic fatigue rather than chronic fatigue syndrome. The relevance of the result depends on the extent to which the costs and benefits of the treatments are comparable in the two patient groups.</p> <p>It is noteworthy that the significant cost driver is informal care. The time of informal carers was valued at the same rate as formal home care workers. This component of costs is not explicitly addressed in cost-effectiveness issues within the Institute. However, the significant magnitude of the cost should entail it is considered.</p> <p>A QALY measure of benefit would be preferable.</p>
Overall study quality (+,-)	+

Bibliographic reference Ref ID: 1097	Chisholm D, Godfrey E, Ridsdale L, Chalder T, King M, Seed P, Wallace P, Wessely S and the Fatigue Trialists' Group. Chronic fatigue in general practice: economic evaluation of counselling versus cognitive behaviour therapy. BJGP 2001;51:15-18
Economic study type and outcomes	<p>Cost consequences</p> <p>Outcomes are the Chalder fatigue score (primary) and Hospital Anxiety and Depression Scale and a social adjustment scale (secondary).</p>

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Population, country & perspective	129 patients from 10 general practices across London and the South Thames region who had experienced symptoms of fatigue for at least 3 months						
	UK						
	NHS and societal presented						
Intervention	Details of the intervention and comparator can be found in the clinical data extraction.						
Comparison(s)							
Source of effectiveness data	RCT						
Method of eliciting health valuations (if applicable)	N/A						
Cost components included	CBT / counselling, inpatient care, outpatient care, GP contacts, community care, alternative therapies, cost of days off work and informal care giving						
Currency and cost year	£ (1998)						
Results – cost per patient per alternative	<p>The cost in the CBT group (mean = £164, s.d. = £67) was higher than in the counselling group (mean = £109, s.d. = £49) (P&lt;0.001). However, the changing cost level from baseline to 6-month assessment “revealed no statistically significant differences between the two groups in terms of aggregate health care costs, patient and family costs or incremental cost-effectiveness”.</p> <p>The paper does not undertake subgroup analysis on cost for those meeting the CDC 1994 criteria.</p>						
Results – effectiveness per patient per alternative	The effectiveness of the two wings are described in the clinical data extraction.						
Results –incremental cost-effectiveness	ICER(cost per unit change in fatigue score)	Counselling		CBT		Difference (counselling minus CBT)	
		Mean	95% CI	Mean	95% CI	Mean	95% CI
	Service costs	7.9	(-2.5, 18.2)	17.5	(4.2, 41)	-9.6	(-33,8.5)
	Patient and family costs	-29.3	(-101, 46)	-16.9	(-157, 90)	-12.3	(-122, 174)
	Total	-21.4	(-98, 48)	0.6	(-134, 117)	-22.0	(-157, 151)
Results-uncertainty	The authors used a non-parametric bootstrapping technique to produce confidence intervals around the effectiveness and cost-effectiveness of CBT, counselling and the						

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	<p>difference between the two.</p> <p>The difference between the two in terms of cost per unit change in fatigue score contained the value 0 within the 95% confidence interval irrespective of the inclusion or exclusion of patient and family-borne costs.</p>
Time horizon	6 months
Discount rate	Due to the short time period, discounting was not undertaken.
Source of funding	Charity (Wellcome trust)
Comments	This paper looks at chronic fatigue rather than chronic fatigue syndrome. Only 28% of the population met CDC 1994 criteria. While the clinical paper undertook subgroup analysis for this reduced population, the cost-effectiveness paper did not. Therefore, the generalisability of the result is questionable.
Overall study quality (+,-)	+

## 1.2 Update searches

Any relevant literature that met the inclusion criteria is presented below. Details have also been added to the appropriate chapter. No additional evidence was found for questions 2, 4, or 5.

### 1.2.1 Question 1

Reference: Reeves 2005
Evidence Level 1-
<p>A. Study Description</p> <ol style="list-style-type: none"><li>1. Aim: to apply the 1994 CFS criteria by standardized reproducible criteria.</li><li>2. Environmental or prognostic factor: Diagnosis of CFS: the International CFS Study Group recommendations for diagnosis (including 1. Medical Outcomes Survey Short Form -36 – SF-36 2. Checklist Individual Strength or Multidimensional Fatigue Inventory to quantify fatigue 3. CDC Symptom Inventory for occurrence, duration and severity of symptoms) were applied and compared to diagnosis by the case definition algorithm used in the surveillance study (based on subjective responses to direct questions re fatigue and whether at least 4 case defining symptoms were present).</li><li>3. Comparison (control): see above</li><li>4. Sample size: Cases: CFS 58; ISF (insufficient symptoms of fatigue) 59; CFS + MD (melancholic depression) 27; ISF + MD 28. Controls: 55</li><li>5. Characteristics of the patient population: matched to CFS on sex, race, age and body mass index.</li><li>6. Length of follow up: NA</li><li>7. Outcome measures: illness classification by surveillance criteria and by International CFS Group recommendations (see above).</li><li>8. Source of funding: CDC</li></ol>
<p>B. Internal validity</p> <ol style="list-style-type: none"><li>1. The study addresses an appropriate and clearly focused question: Yes</li><li>2. Cases and controls taken from comparable populations: Yes</li><li>3. Same exclusion criteria for cases and controls: Yes</li><li>4. Percentage of each group participated: Cases: 83% of CFS;84% of ISF; 66%CSF and MD; 72% ISF and MD. Controls: 55/58</li></ol>

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5. Comparison made between participants and non-participants to establish differences: Yes

6. Cases clearly defined and differentiated from controls: Yes

7. Clearly established that controls are non-cases: Yes

8. Measures taken to prevent knowledge of primary exposure influencing case ascertainment: NA

9. Exposure status measured in a standard, valid, reliable way: NA

10. Main confounders identified and taken into account: Yes

C. External validity (Generalisability – see also other sections for details)

1. Setting: Participants were admitted to a Wichita hospital research unit for two days.

2. Inclusion criteria: All participants participated in the 4 year Wichita CFS Surveillance Study

3. Recruitment: All 70 CFS patients from the Surveillance Study were invited; matched controls were selected from healthy study participants; 70 randomly selected ISF patients were asked; all 41 surveillance participants with depression were asked.

4. Safety issues: none

D. Results/Effect size

Odds ratios not provided (mean standard deviation given). Only 13% of patients who met 1994 surveillance criteria for CFS met those same criteria in this study. 40% fulfilled CFS criteria of the International CFS Study Group using a clinically empirical definition.

Overall, this study aids in the definition and diagnosis of CFS by testing a diagnostic strategy which provides health care providers with objective measures of the disability associated with CFS and which may be less affected by the day to day fluctuation of the illness and, rather reflect the underlying chronic illness process.

E. Quality rating

Study design: Case control

The statistical analysis is not fully described but this study does appear to be of adequate size and careful case control design to represent a relationship between diagnostic category and scores on the empirical measurement tools recommended by the International CFS Study Group

Consistency of results with other studies in the field: Unknown

Directness of comparisons to intervention or patient population of interest in this guideline: Yes

### 1.2.2 Question 3

Reference: Bazelmans 2005
Evidence Level 1-
<p>A. Study Description</p> <ol style="list-style-type: none"><li>1. Aim: To investigate the effect of a maximal exercise test (MET) on fatigue, muscle pain, rest and activity on the days surround the exercise test.</li><li>2. Intervention: A bicycle ergometer test with incremental load was used as an exercise test. The workload was increased every minute in steps of 10% of estimated maximal workload to complete all MET in approximately 10 min. Steps varied from 10 to 30 W/min.</li><li>3. Comparison (control): Controls were recruited by the CFS patient and were neighbors of the same gender and about the same age as the patient</li><li>4. Sample size: 20</li><li>5. Characteristics of the patient population: CFS patients who met The Fukuda criteria and had a Checklist Individual Strength (CIS) fatigue severity score of 40 or more and a total score of the sickness impact profile (SIP)-8 of more than 800 were included.</li><li>6. Length of follow up: Self observation and actometer given for 3 days before and up to 5 days after the MET.</li><li>7. Outcome measures: Time spent on the bicycle ergometer; self observation of fatigue, muscle pain and activity; actometer readings</li><li>8. Source of funding: Unknown</li></ol>
<p>B. Internal validity</p> <ol style="list-style-type: none"><li>1. The study addresses an appropriate and clearly focused question: Yes</li><li>2. The assignment of subjects to treatment groups is randomized: No, this is a controlled trial.</li><li>3. An adequate concealment method is used: NA</li><li>4. Subjects and investigators are kept 'blind' about treatment allocation: NA</li><li>5. The treatment and control groups are similar at the start of the trial: Similar in terms of gender, age and home location</li><li>6. The only difference between groups is the treatment under investigation: Only known difference was in fatigue and functional impairment. Other medical and social conditions not discussed.</li><li>7. All relevant outcomes are measured in a standard, valid and reliable way: Self assessments necessarily subjective; actometer (a piezoelectric sensor that sense activity level) was pretested in previous studies but failing actometers were a problem for 7 participants; time spent on bicycle ergometer was measured.</li><li>8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before</li></ol>



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the study was completed? None

9. All the subjects are analysed in the groups to which they were randomly allocated (ITT): NA

10. Where the study is carried out at more than one site, results are comparable for all sites: NA

## C. External validity (Generalisability)

1. Setting: Hospital exercise laboratory

2. Inclusion criteria: CFS patients who met The Fukuda criteria and had a Checklist Individual Strength (CIS) fatigue severity score of 40 or more and a total score of the sickness impact profile (SIP)-8 of more than 800 were included. Controls: Recruited by the CFS patient and were neighbors of the same gender and about the same age as the patient

3. Recruitment: CFS patients diagnosed at the General Internal Medicine outpatient clinic of the University Medical Center Nijmegen, The Netherlands

4. Intervention (mode and intensity): A bicycle ergometer test with incremental load was used as an exercise test. The workload was increased every minute in steps of 10% of estimated maximal workload to complete all MET in approximately 10 min. Steps varied from 10 to 30 W/min.

5. Duration of active intervention: One ten minute MET test

6. Control (mode and intensity): The workload was increased every minute in steps of 10% of estimated maximal workload to complete all MET in approximately 10 min. Steps varied from 10 to 30 W/min.

7. Delivery of intervention/control (who): Hospital investigators

8. Potential confounders: Hawthorne effect; self assessment

9. Safety (as reported in the trial): NA

## D. Results/Effect size

1. Primary outcome measures:

Time spent on bicycle ergometer: 8.0 +/- 2.3 minutes for CFS and 9.2 +/- 1.9 minutes for controls. The percentage of predicted maximal workload reached was 83% for controls and 70% for CFS.

Self observation of fatigue and muscle pain on a scale from 0-4: For daily observed fatigue, a statistically significant day by group effect was found ( $p=0.011$ ); A significant time by group effect was also found for daily observed rest ( $p=0.033$ ). On daily observed muscle pain, daily observed activity and the actometer, the average profiles of scores after the MET appeared not significantly different for the two groups.

2. Secondary outcome measures (note any variations in internal or external validity for secondary outcomes): NA

## E. Quality rating

Controlled trial

No randomization; controls chosen by patient group; small sample size; actometer failure

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This study is too small and the potential biases are too great to be certain that the effects are reproducible in a larger randomized population.

Consistency of results with other studies in the field: Unknown

Directness of comparisons to intervention or patient population of interest in this guideline: The results are applicable to CFS patients but this topic should be further studied.

Reference: Cho 2005

Evidence Level 1+

### A. Review description

1. Aim: To do a systematic review of placebo response
2. Type of studies included in the review: RCTs and controlled trials
3. Sample size (total  $n$ ) 859
4. Characteristics of the patient population: Among participants with known gender (27/29 trials) 70.3% were female. The mean age was 38.3 years. The mean duration of illness in 26 trials was 61.6 months (frequencies only provided).
5. Outcome measures evaluated: Placebo effect in CFS patients
6. Was meta analysis done? Yes
7. Source of funding: Unknown

### B. Internal validity

1. The study addresses an appropriate and clearly focused question: Yes
2. A description of the methodology used is included: Yes
3. The literature search is sufficiently rigorous to identify all the relevant studies: Yes
4. Study quality is assessed and taken into account: Yes
5. Number of studies in meta analysis: 29
6. If meta analysis was done, there are enough similarities between the studies selected to make combining them reasonable? The major limitation of the review was the heterogeneity of the outcome measurement systems across the trials. Different scales and instruments were used to define and measure the endpoint, clinical improvement. The pooled result from this meta analysis with high heterogeneity was compared with pooled placebo responses from other meta-analyses also with high heterogeneity. This comparison of like with like showed that the summary placebo response in CFS was lower compared with the comparison disorders (statistics not provided).

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D. Results of meta analysis: Pooled placebo response of 19.6% (CI 15.4 to 23.7) and the test for heterogeneity was highly significant ( $p < 0.001$ ).

### E. Quality rating

Study designs included in the review and meta analysis: RCT and controlled trial

Broad search strategy and well designed quality assessment of literature

Consistency of results among studies in the review: Significant heterogeneity

Consistency of results among other reviews in the field: Good

Directness of comparisons to intervention or patient population of interest in this guideline: Yes

Reference: Cook 2005

Evidence Level 1-

### A. Study Description

1. Aim: To determine the effect of submaximal steady-state exercise on cognitive performance in patients with CFS alone, CFS with FM and sedentary healthy controls.
2. Intervention: Cognitive testing using the automated neuropsychological assessment matrices (ANAM) comprising of simple reaction time, running memory, memory recall, math processing and matching to sample were administered at baseline, immediately before and twice following 25 minutes of either cycle ergometry set at 40% of peak oxygen capacity or quiet rest.
3. Comparison (control): Each group was randomly assigned to exercise or quiet rest.
4. Sample size: CFS 20; CFS and FM 19; control 26.
5. Characteristics of the patient population: No significant differences in age, height, weight, education or gender of three groups.
6. Length of follow up: 30 minutes post exercise:
7. Outcome measures: Cognitive performance for each group for each of the five categories simple reaction time, running memory, memory recall, math processing and matching to sample.
8. Source of funding: Unknown

### B. Internal validity

1. The study addresses an appropriate and clearly focused question: Yes
2. The assignment of subjects to treatment groups is randomized: Yes
3. An adequate concealment method is used: Unknown

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4. Subjects and investigators are kept 'blind' about treatment allocation: NA
5. The treatment and control groups are similar at the start of the trial: At baseline the CFS patients displayed deficits in speed of processing, performance variability and task efficiency during several cognitive tests compared with healthy controls. The CFS and FM group was not different to controls. No significant differences in age, height, weight, education or gender of three groups.
6. The only difference between groups is the treatment under investigation: See above
7. All relevant outcomes are measured in a standard, valid and reliable way: The ANAM testing has been validated.
8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? None
9. All the subjects are analysed in the groups to which they were randomly allocated (ITT): NA
10. Where the study is carried out at more than one site, results are comparable for all sites: NA

### C. External validity (Generalisability)

1. Setting: Controlled environmental conditions
2. Inclusion criteria: All CFS patients met the US CDC case definition of CFS; CFS and FM patients met the criteria of FM of the American College of Rheumatology and 'sedentary' was defined as working in an occupation that does not require moderate to intense physical labor and not participating in physical exercise more than one session per week.
3. Recruitment: Recruited from a large patient pool available through the New Jersey CFS Cooperative Research Center.
4. Intervention (mode and intensity): Cognitive testing using the automated neuropsychological assessment matrices (ANAM) comprising of simple reaction time, running memory, memory recall, math processing and matching to sample were administered at baseline, immediately before and twice following 25 minutes of either cycle ergometry set at 40% of peak oxygen capacity or quiet rest.
5. Duration of active intervention: 30 minutes post exercise with cognitive testing at baseline, immediately pre-intervention, immediately post-intervention and 30 minutes post intervention.
6. Control (mode and intensity): Quiet rest with cognitive testing at baseline, immediately pre-intervention, immediately post-intervention and 30 minutes post intervention.
7. Delivery of intervention/control (who): Researchers
8. Potential confounders: Hawthorne effect; small sample size
9. Safety (as reported in the trial): NA

### D. Results/Effect size

#### 1. Primary outcome measures:

There were no group differences in average percentage of peak oxygen consumption during exercise. There were

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no significant effects of acute exercise on cognitive performance for any group. Across all tests CSF but not CFS and FM were significantly less consistent ( $p=0.03$ )\* and less efficient ( $p=0.01$ )\* than controls. \*no confidence intervals provided

2. Secondary outcome measures (note any variations in internal or external validity for secondary outcomes): NA

### E. Quality rating

Study design: RCT

Small sample size; blinding not possible; no description of allocation concealment

This is a very small study with sample sizes of 9-14 in intervention groups. It is therefore, not generalisable.

Consistency of results with other studies in the field: Unknown

Directness of comparisons to intervention or patient population of interest in this guideline: Yes

Reference: Rimes 2005

Evidence Level 1-

### A. Review Description

1. Aim: To review studies evaluating the treatment of chronic fatigue and chronic fatigue syndrome; to describe predictors of response to treatment.
2. Type of studies included in the review: Inclusion and exclusion criteria not described. Treatment trials appear to be RCT's and controlled trials.
3. Sample size (total n): Sample sizes not described
4. Characteristics of the patient population: Populations in each study not described. There are no summary tables of patient populations.
5. Outcome measures evaluated: Outcome measures not described specifically for each study.
6. Was meta analysis done? No
7. Source of funding: Unknown

### B. Internal validity

1. The study addresses an appropriate and clearly focused question: The study aimed to evaluate treatment trials for chronic fatigue and chronic fatigue syndrome.
2. A description of the methodology used is included: Quality assessment criteria not described.
3. The literature search is sufficiently rigorous to identify all the relevant studies: Two databases, Medline and PsychInfo searched along with 'reference lists.'

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4. Study quality is assessed and taken into account: No quality assessment provided.

5. If meta analysis was done, there are enough similarities between the studies selected to make combining them reasonable: NA

D. Results of meta analysis, if included: NA

E. Quality rating

Study designs included in the review and meta analysis: The review appears to include RCTs and controlled trials.

Limited literature search. No description of quality assessment methodology.

Possible incomplete analysis of literature or biased assessment of literature.

Consistency of results among studies in the review: There generally appears to be consistency of results among studies.

Consistency of results among other reviews in the field: Yes

Directness of comparisons to intervention or patient population of interest in this guideline: Distinction not made between studies of CF and CFS. However, it is likely that there is reasonable directness to the population of interest.

Reference: Taylor 2006

Evidence Level 1-

A. Study Description

1. Aim: To evaluate the impact of a consumer driven rehabilitation program on perceptions of loss and gain of interpersonal relationships, energy, material objects, work benefits and opportunities, well being, and experiences of mastery in persons with chronic fatigue syndrome.

2. Intervention: Participation in eight sessions of an illness management group, occurring every other week over a period of 4 months. Following a postgroup assessment during a one month break period program participants then completed 7 months of one on one peer counseling followed by another assessment (23 sessions average during 7 month period). A participatory action design involving participants in an egalitarian partnership with researchers was used.

3. Comparison (control): Controls only completed the assessments during the 12 month period of the study.

4. Sample size: 47 individuals with CFS; 23 assigned to immediate program group (treatment) and 24 were assigned to the delayed program (control) group.

5. Characteristics of the patient population: CFS patients who were diagnosed with CFS based upon a screening procedure which included the Chronic Fatigue Syndrome Screening questionnaire, a semistructured psychiatric interview, The Structured Clinical Interview, past medical records, independent physician review of results to determine whether the participants met CFS Fukuda criteria. Frequencies were provided for sociodemographic characteristics. The sample was predominately middle aged, female, middle socioeconomic status and single. Most

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were Caucasian and were unemployed.

6. Length of follow up: 12 months in each group. The Controls received their program after the treatment group completed their program.

7. Outcome measures: The COR-E is a 74 item inventory that measures the extent of the past month's gain and loss of resources.

8. Source of funding: US Department of Education National Institute on Disability and Rehabilitation Research Grant.

### B. Internal validity

1..The study addresses an appropriate and clearly focused question: Yes

2. The assignment of subjects to treatment groups is randomized: Yes

3. An adequate concealment method is used: Not well described

4. Subjects and investigators are kept 'blind' about treatment allocation: Patients not blinded.

5. The treatment and control groups are similar at the start of the trial: Yes

6. The only difference between groups is the treatment under investigation: Generally similar socioeconomic demographics.

7. All relevant outcomes are measured in a standard, valid and reliable way: COR-E instrument is validated.

8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? None

9. All the subjects are analysed in the groups to which they were randomly allocated (ITT): Yes

10. Where the study is carried out at more than one site, results are comparable for all sites: NA

### C. External validity (Generalisability)

1. Setting: A center for independent living, a community based advocacy organization for individuals with disabilities.

2. Inclusion criteria: CFS patients who were diagnosed with CFS based upon a screening procedure which included the Chronic Fatigue Syndrome Screening questionnaire, a semistructured psychiatric interview, The Structured Clinical Interview, past medical records, independent physician review of results to determine whether the participants met CFS Fukuda criteria.

3. Recruitment: 52 women and men were recruited between Oct. 2000 and December 2000 from a. local CFS self help organizations and Chicago area physicians specializing in the treatment of people with CFS and b. from advertisements posted in CFS newsletters, Chicago area newspapers and on CFS web sites and listservs and on a local cable TV station.

4. Intervention (mode and intensity): Participation in eight sessions of an illness management group, occurring every other week over a period of 4 months. Following a postgroup assessment during a one month break period program

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participants then completed 7 months of one on one peer counseling followed by another assessment (23 sessions average during 7 month period). Controls only completed the assessments during the 12 month period of the study. A participatory action design involving participants in an egalitarian partnership with researchers was used.

5. Duration of active intervention: 12 months in each group.

6. Control (mode and intensity): The Controls received their program after the treatment group completed their program.

7. Delivery of intervention/control (who): Illness management group co-led by peer counsellor and a researcher for first 3 months; then, peer counselling sessions for the last 7 months.

8. Potential confounders: The COR-E instrument is a subjective measurement of loss and gain as well as self esteem, well being mastery, work, material objects, energy, interpersonal relationships and family relations.

9. Safety (as reported in the trial): NA

### D. Results/Effect size

1. Primary outcome measures: There was a significant main effect of the program for overall resource gain ( $p < 0.05$ )

2. Secondary outcome measures (note any variations in internal or external validity for secondary outcomes): Significant for self esteem gain ( $p < 0.01$ ), well being gain ( $p < 0.01$ ), mastery gain ( $p < 0.05$ ), work gain ( $p < 0.05$ ), material gain ( $p < 0.05$ ), energy gain ( $p < 0.05$ ), interpersonal gain ( $p < 0.05$ ).

### E. Quality rating

Study design: RCT

Small sample size, subjective measurement instrument; self selected patients.

The self selected patient population and lack of blinding as well as small sample size casts doubt on study effect.

Consistency of results with other studies in the field: Unknown

Directness of comparisons to intervention or patient population of interest in this guideline: Yes.