



**Centre for Clinical Effectiveness**

Enhancing patient outcomes through clinical application of the best available evidence

**EVIDENCE CENTRE**  
**CRITICAL APPRAISAL**  
Series 2001: Therapy

# **Chronic fatigue syndrome – exercise and cognitive behaviour therapies**

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## **SUMMARY STATEMENT**

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**Publication of materials** – please use the following format when citing this article:

Bernath, V. (2001). Chronic fatigue syndrome – exercise and cognitive behaviour therapies. [Online]. Available from <http://www.med.monash.edu.au/healthservices/cce/>  
[Access Date...]

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## **REQUEST**

Are exercise or cognitive behaviour therapies effective in reducing symptoms of chronic fatigue syndrome in hospitalised patients or patients visiting outpatient clinics?

## **REQUESTED BY**

**Robyn Hudson**, Physiotherapist, Department of Physiotherapy, Monash Medical Centre, Clayton.

## **METHODOLOGY**

### **Search Strategy**

The Centre for Clinical Effectiveness defines the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to pre-defined National Health and Medical Research Council (NHMRC, 2000) criteria (see Appendix 1).

First, we search for systematic reviews, evidence based clinical practice guidelines, health technology assessments and randomised controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable or have other methodological difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Such studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

### **Details of Evidence Request**

Patients (Subjects): with chronic fatigue syndrome  
Intervention: exercise or cognitive behaviour therapy  
Comparisons: any  
Outcomes: reduction of symptoms

### **Search terms**

(see Appendix 2 for exact search strategy)

Patient (Subject): fatigue syndrome, chronic; chronic fatigue  
Intervention: exercise; exercise therapy; behaviour; behavior; cbt; behavior therapy; cognitive therapy

## **Resources Searched**

We searched the following databases:

Cochrane Library (CD-ROM)- Issue 4, 2001

Medline (OVID)- 1966 to October Week 5 2001

PREMEDLINE (OVID)- December 11, 2001

CINAHL (OVID)- 1982 to November Week 5 2001

Current Contents (OVID)- 1993 Week 26 to 2001 Week 51

PsycINFO (OVID)- 1984 to December Week 1 2001

EBM Reviews - Cochrane Database of Systematic Reviews (OVID) – 4<sup>th</sup> Quarter 2001

EBM Reviews – ACP Journal Club (OVID)- 1991 to September/October 2001

EBM Reviews – Database of Abstracts of Reviews of Effectiveness (OVID)- 4<sup>th</sup> Quarter 2001

EBM Reviews – Cochrane Controlled Trials Register (OVID)- 4<sup>th</sup> Quarter 2001

Australasian Medical Index- December 2001

PubMed- December 13, 2001

## **Refinements, Searching & Reporting Constraints**

As this is an update of a previous report we have searched the literature for material published from 2000 onwards. Two recent highly relevant systematic reviews were identified by the search so we have restricted our report to Level I and Level II records.

We have included items of evidence that were available to us on 14 December 2001. The full reports of the two systematic reviews summarised in the paper by Whiting et al 2001 are not yet publicly available and therefore we were unable to appraise them individually.

## RESULTS

From our sources we identified 6 potentially relevant articles. We obtained the full text of these articles to determine their relevance.

After examination of the articles, the following were excluded as follows:

<b>Reason for exclusion</b>	<b>Number</b>
Narrative Reviews	2
Randomised controlled trial already included in a systematic review	2
<b>Total</b>	<b>4</b>

2 articles then remained for appraisal. These studies are classified as follows:

<b>Study Design</b>	<b>Number included</b>
<b>Systematic reviews or meta-analyses</b>	<b>2</b>
Evidence-based clinical practice guidelines	0
Randomised controlled trials	0
<b>Total</b>	<b>2</b>

Based on our refinements, searching and reporting constraints we are reasonably confident these articles represent the most relevant findings published to date.

The findings of the two systematic reviews were favourable for the use of cognitive behavioural therapy and exercise in patients with chronic fatigue. However there are reservations about the general applicability of the findings to patients other than those visiting outpatient clinics. The conclusions are based on a few small trials of adequate quality.

## EVIDENCE SUMMARIES

### Format

Evidence summaries are presented as spreadsheets attached to this report. Each spreadsheet contains the article citation, details of the study design, patient description, scientific validity of the article, results, and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

## REFERENCES

### ARTICLES CRITICALLY APPRAISED FOR THIS REPORT

Price JR and Couper J (2001). Cognitive behaviour therapy for chronic fatigue syndrome in adults (Cochrane Review). In: The Cochrane Library, Issue 4 2001. Oxford: Update Software.

Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD & Ramirez G (2001). Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. JAMA 286: 1360-1368.

### ARTICLES NOT CRITICALLY APPRAISED

#### Randomised controlled trials included in systematic review

Powell P, Bentall RP, Nye FJ & Edwards RH (2001). Randomised controlled trial of patient education to encourage graded exercise in chronic fatigue syndrome. BMJ 322: 387-390.

Prins JB, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL, van der Wilt GJ, Spinhoven P & van der Meer JW (2001). Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. Lancet 357: 841-847.

#### Narrative reviews

Friedberg F & Jason LA (2001). Chronic fatigue syndrome and fibromyalgia: clinical assessment and treatment. J Clin Psychol 57: 433-455.

Natelson BH (2001). Chronic fatigue syndrome. JAMA 285: 2557-2559.

# APPENDIX 1

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## Levels Of Evidence

Based on "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I		Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II		Evidence obtained from at least one randomised controlled trial.
Level III	-1	Evidence obtained from pseudorandomised controlled trials (alternate allocation or some other method).
	-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV		Evidence obtained from case series, either post-test or pretest/post-test.

## APPENDIX 2

### Search strategy

	<b>Search terms for MEDLINE</b>
1	fatigue syndrome, chronic/
2	chronic fatigue.te
3	1 or 2
4	exercise/
5	exercise therapy/
6	exercise.tw
7	(behaviour\$ or behavior\$ or cbt).tw
8	behavior therapy/ or cognitive therapy/
9	or/5-8
10	3 and 9
11	limit 10 to yr=2000-2002

<p style="text-align: center;"><b>Evidence Summary Systematic Review</b></p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: 80%;"> <p style="text-align: center;">Chronic fatigue – exercise and cognitive behaviour therapies</p> </div>	<p style="text-align: center;"><b>Study 1</b></p> <p style="text-align: center;">Price JR and Couper J (2001). Cognitive behaviour therapy for chronic fatigue syndrome in adults (Cochrane Review). In: The Cochrane Library, Issue 4 2001. Oxford: Update Software.</p>	<p style="text-align: center;"><b>Study 2</b></p> <p style="text-align: center;">Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD &amp; Ramirez G (2001). Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. JAMA 286: 1360-1368.</p>
<p><b>STUDY DESIGN &amp; NHMRC LEVELS OF EVIDENCE</b></p>	<p style="text-align: center;">Level I: Systematic Review</p>	<p style="text-align: center;">Level I: Systematic Review</p>
<p><b>DESCRIPTION:</b></p> <p>Patient (subjects), Interventions, Comparisons, Outcomes, Inclusion &amp; Exclusion Criteria</p>	<p><b>Patients (Subjects):</b> Over 16 years, fulfilling criteria for Chronic fatigue syndrome (CFS)</p> <p><b>Intervention:</b> Trials of experimental interventions meeting following criteria:</p> <p>psychological treatment with both attempted modification of thoughts and beliefs about symptoms and illness, and attempted modification of behavioural responses to symptoms and illness such as rest, sleep, and activity.</p> <p><b>Comparisons:</b> Any other intervention including orthodox medical management.</p> <p><b>Outcomes:</b> Long term improvement in physical functioning and a range of other outcomes including fatigue, quality of life, health care resource use, and compliance.</p> <p><b>Inclusion criteria:</b> All randomised studies in which patients with CFS receiving Cognitive Behavioural Therapy (CBT) were compared with a control group. Trials including several disorders were included if over 90% of patients had CFS. Trials which randomised therapists, rather than patients, to control or intervention groups were included if the specific aim of the study was to examine the effect of the intervention.</p> <p><b>Exclusion criteria:</b> Drug treatment as part of the intervention, self-help treatments without direct therapist contact.</p>	<p><b>Patient (Subjects):</b> Adults and children with CFS</p> <p><b>Intervention:</b> All available interventions</p> <p><b>Comparisons:</b> Any</p> <p><b>Outcomes:</b> Any</p> <p><b>Inclusion criteria:</b> Any intervention used in the treatment of CFS. Randomised controlled trials and controlled trials.</p> <p><b>Exclusion criteria:</b> Studies including patients with fibromyalgia.</p>
<p><b>VALIDITY:</b></p> <p>Methodology, rigour, selection, analysis</p>	<p><b>Focussed question:</b> The systematic review was designed to test the hypothesis that CBT is more effective than other interventions in adults with CFS.</p> <p><b>Search strategy:</b> A comprehensive search strategy is presented, and appropriate sources, including the major relevant databases and grey literature, were searched. Included references and known experts were also followed up. Language was not limited to English.</p>	<p><b>Focussed question:</b> Assessment of the effectiveness of all available interventions that have been evaluated for use in the treatment or management of adults and children with CFS.</p> <p><b>Search strategy:</b> Strategies not stated in this paper. Relevant major databases were searched.</p> <p><b>Assessed validity:</b> Modified checklist used, and a score was assigned to each included study. Validity scores of individual studies not provided.</p>

	<p><b>Assessed validity:</b> Trials were allocated to three quality categories based on meeting stated methodological quality criteria covering allocation, intention-to-treat analysis, valid well defined outcomes, blinding of assessors, adequate follow-up, reporting of important baseline characteristics, identical care programs of trial groups, and definition of inclusion and exclusion criteria.</p> <p><b>Consistent results:</b> Generally the three included studies produced similar results.</p> <p><b>Appropriate analysis of results:</b> The three included studies compared different interventions and have been analysed separately and no meta-analysis was performed. Where possible Odds ratios and Numbers Needed to treat have been provided.</p>	<p>studies not provided.</p> <p><b>Consistent results:</b> Details not provided</p> <p><b>Appropriate analysis of results:</b> Due to significant heterogeneity between studies a qualitative analysis was undertaken.</p>
<p><b>RESULTS:</b> Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>Two of the studies demonstrated a beneficial effect of CBT treatment at final follow-up, one compared with relaxation the other with routine medical care. These studies also found CBT to be more effective in reducing fatigue than the control interventions. The third study did not clearly report its results and conclusions are difficult infer.</p> <p>No significant difference was found between CBT and other treatments on mood or anxiety, or on compliance. About two patients need to be treated with CBT for one adverse physical outcome to be prevented at about 6 months after the end of treatment.</p>	<p><b>RESULTS:</b> Three randomised controlled trials (RCTs) evaluating graded exercise therapy found an overall beneficial effect of the intervention compared with the control groups.</p> <p>Three of the four RCTs comparing CBT to control conditions found a positive overall effect. The fourth study found no benefit of CBT .</p>
<p><b>AUTHORS COMMENTS:</b> Limitations, implications for practice and research</p>	<p>"Trial participants in each of the three included trials were out-patients with CFS. There is, therefore, no satisfactory evidence with which to evaluate the effectiveness of CBT for the milder forms of chronic fatigue seen frequently in primary care, or for more severe cases of CFS, who may be unable to attend out-patient clinics." ... "Despite these issues, this review provides convincing evidence that CBT in adults with CFS improves physical functioning, and other relevant outcomes such as mood, compared to orthodox management." The authors recommend further research conforming to accepted standards of reporting and methodology.</p>	<p><b>AUTHORS COMMENTS:</b> The applicability of the findings may be limited by inclusion criteria specified in some studies, where participants were only eligible if they could physically get to the clinic, which implies a certain level of fitness.</p>
<p><b>OUR COMMENTS:</b> Opportunity for bias, weakness and strength</p>	<p><b>Potential for bias:</b> The methodology of the review is designed to minimise bias.</p> <p><b>Weakness:</b> The review is based on three relatively small trials that cannot be combined for analysis due the use of different controls.</p> <p><b>Strength:</b> This is a well-designed systematic review of the best available evidence.</p>	<p><b>Potential for bias:</b> This paper represents a summary of two independent parallel systematic reviews, for neither of which is the full report currently available. Details of search strategies, validity assessment, results of studies, are not provided in this paper.</p>

## EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

**Level of evidence:** A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.

**Focussed question:** The review should address a clearly focused issue, in terms of the population studies, the intervention given and the outcomes considered.

**Search strategy:** A description of methods used to identify relevant studies from various computer databases and other sources.

**Systematic review:** The process of systematically locating, appraising and synthesising evidence from scientific studies in order to obtain a reliable overview.

**Validity:** The degree to which reviewers assessed the quality of the studies they included

Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.

Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).

**Consistent results:** The similarity of results from the included studies. Often called heterogeneity which refers to the differences in treatment effect between studies contributing to a meta analysis (systematic review). If there is significant heterogeneity, this suggests that the trials are not estimating a single common treatment effect.

**Appropriate analysis of results:** When study results are pooled in a meta-analysis it is important that the results are combined in appropriate manner. The studies should be sufficiently similar in study design, the results of included studies should be clearly displayed and reasons for any variation in results should be discussed.

**Potential for bias:** Bias is a systematic deviation of a measurement from the 'true' value leading to either an over or underestimation of the treatment effect. Bias can originate from many different sources, such as allocation of patients, measurement, interpretation, publication and review of data.