Effective treatments

for CFS / ME

A systematic review of interventions used to treat, manage and rehabilitate people with CFS/ME

- **Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) affects many people and their families and carers in the UK. It is estimated that a general practice with 10,000 patients is likely to have 30-40 patients with CFS/ME.**
- **This update of a previous systematic review was commissioned by the National Institute for Health and Clinical Excellence (NICE) to inform the development of their guidelines for the diagnosis and management of CFS/ME in adults and children.**
- **A variety of interventions have been used in the treatment and management of CFS/ME. Interventions demonstrating beneficial effects are cognitive behavioural therapy and graded exercise therapy.**
- **In many of the trials, limited information was given about the level of baseline functioning of many of those people included or about the severity of illness experienced by those excluded. Therefore it is difficult to know how the findings apply to other people with CFS/ME.**

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Background

Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) comprises a range of symptoms including fatigue, which can be triggered by minimal activity, malaise, headaches, sleep disturbances, difficulties with concentration and muscle pain. In extreme cases, CFS/ME can cause profound, prolonged illness and disability, and can have a substantial impact on patients and their families.

It has been estimated that a typical general practice of 10,000 patients is likely to have at least 30-40 patients with CFS/ME, and that about half of these would require specialist services.[1]

CFS/ME, like other chronic illnesses with no certain disease process, poses real problems for healthcare professionals. Uncertainties about diagnosis and management, and lack of clinical guidance for health professionals, exacerbate this impact.

Nature of the evidence

This short report is based on an update of a previous systematic review on interventions for the management/treatment/rehabilitation of people with CFS/ME.[2-4] The original review was commissioned by the Department of Health to inform deliberations by an Independent Working Group convened by the Chief Medical Officer. The Working Group examined how the NHS might improve health and social care for people who suffer from CFS/ME.

The Independent Working Group report[1] identified three therapeutic strategies as potentially beneficial: cognitive behavioural therapy, graded exercise therapy (a form of structured and supervised activity management that aims for gradual increases in aerobic activity), and pacing (a programme which encourages people to achieve an appropriate balance between rest and activity).

This update was commissioned by the National Institute for Health and Clinical Excellence (NICE) to inform the development of their guidelines for the diagnosis and management of CFS/ME in adults and children. The full versions of both the original review and this update are available via the CRD website (www.york.ac.uk/inst/crd).

Interpreting the findings

Included studies were classified as having an overall effect (positive or negative) if they showed a statistically significant effect of the intervention for more than one clinical (i.e. not a physiological/ laboratory) outcome or, if only one clinical outcome was measured, it was found to show a statistically significant effect. Where no statistically significant differences occurred, this was classified as showing no effect.

Studies were judged to show some effect of treatment (positive or negative) if any of the outcomes measured showed a statistically significant difference between the intervention and control groups. However, some studies investigated a large number of outcomes, making it possible that any differences could have arisen by chance. The results of those studies evaluating multiple outcomes should therefore be treated with caution.

Finally, in many of the trials very limited information was given about the level of baseline functioning of those people who were included, or about the severity of illness experienced by those who were excluded (e.g. those not well enough to attend an out-patient clinic). Therefore it is difficult to know how the findings apply to other people with CFS/ME.

Findings

Seventy trials are included in this update. The results of each trial, ranked according to methodological quality (validity score), are presented in the Table below.

Overall, the interventions assessed demonstrated mixed results in terms of beneficial effects. The interventions for which there is evidence of effectiveness from good quality randomised controlled trials are cognitive behavioural therapy and graded exercise therapy.

Immunological and anti-viral treatments may have beneficial effects but are associated with harmful side-effects. Most drug treatments have not shown beneficial effects

No rigorous evaluations of pacing were identified. However, a large trial known as PACE (Pacing, Activity and Cognitive behaviour therapy: a randomised Evaluation) involving patients attending specialist CFS/ME clinics across the UK, is underway and is due for completion in 2009.

References:

1. *A report of the CFS/ME Working Group: report to the Chief Medical Officer of an Independent Working Group*. London: Department of Health, 2002.
2. NHS Centre for Reviews and Dissemination. *A systematic review of interventions for the treatment and management of chronic fatigue syndrome and/or myalgic encephalomyelitis*. CRD Report 22. University of York, 2002.
3. Interventions for the treatment and management of CFS/ME. *Effective Health Care* 2002; 7(4).
4. Centre for Reviews and Dissemination. *The treatment and management of chronic fatigue syndrome (CFS) / myalgic encephalomyelitis (ME) in adults and children*. Update of CRD Report 22. University of York, 2006.

Summary of study results

Treatment	Study (Year)	Number of patients	Outcomes investigated	Any effect	Overall effect	Validity score (Maximum 20)
BEHAVIOURAL						
CBT	Deale (1997)	60	PH; PS; QOL	+	+	18
GET & Fluoxetine	Wearden (1998)	136	PH; PS; QOL	+	=	17
GET	Fulcher (1997)	66	PH; PS; LAB; QOL	+	+	17
GET	Powell (2004, 2001)	148	PH; PS; QOL	+	+	17
CBT	Prins (2001)	270	PH; PS; QOL	+	+	16
CBT	Sharpe (1996)	60	PH; PS; QOL	+	+	15
CBT	Stulemeijer (2005)	69	PH; QOL	+	+	16
CBT + DLE	Lloyd (1993)	90	PH; PS; LAB; QOL	+	=	13
GET	Moss-Morris (2005)	49	PH	+	+	9
GET	Wallman(2004)	61	PS; PH: LAB	+	+	9
Rehab	Taylor (2004)	47	PH; QOL	+	+	9
CBT/ rehab	Cox (1999)	130	PH; PS; QOL	+	+	8
CBT/ rehab	Cox (2002)	97	PH; PS; QOL	+	=	7
CBT	De Sanctis (2002)	65	PH; PS;QOL	=	=	3
CBT	Viner (2004)	56	PH; QOL	+	=	2
CBT	Friedberg (1994)	44	PH; PS; QOL	=	=	1
IMMUNOLOGICAL						
Immunoglobulin	Rowe (1997)	71	PH	+	+	16
Immunoglobulin	Peterson (1990)	30	PH; LAB; QOL	=	=	15
Acyclovir	Straus (1988)	27	PH; PS; LAB; QOL	-	=	15
Staphylococcus toxoid	Zachrisson (2002)	98	PH	+	+	14
Immunoglobulin	Lloyd 1990	49	PS; QOL	+	=	13
Immunoglobulin	Vollmer-Conna (1997)	99	PH; PS; LAB; QOL	=	=	13
Ampligen	Strayer (1994)	92	RU; PH; PS	+	+	12
Terfenadine	Steinberg (1996)	30	PH; QOL	=	=	12
Alpha interferon	See (1996)	30	LAB; QOL	+	=	11
Staphylococcus toxoid	Andersson (1998)	28	PS; QOL	+	=	9
Inosine pranobex	Diaz-Mitoma (2003)	16	PH; LAB; QOL	+	=	6
Interferon	Brook (1993)	20	PH	=	=	6
Gancyclovir	Lerner (2001)	11	PH	=	=	1
COMPLEMENTARY/ ALTERNATIVE						
Homeopathy	Weatherley-Jones (2004)	103	PH	+	=	17
Massage therapy	Berneman (1992)	20	PH; PS; LAB	+	+	9
Any homeopathic remedy	Awdry (1996)	64	QOL	=	=	6
Osteopathy	Perrin (1998)	58	PH; PS; QOL	=	=	0
OTHER						
Combination	Teitelbaum (2001)	72	**PH**	+	+	19
Low sugar low yeast diet	Hobday (in press)	57	PH; PS	=	=	11
Buddy/ mentor	Schlaes (1996)	12	**PH**; PS; QOL	+	=	4
Combination	Marlin (1998)	71	QOL	=	=	3
Combination	Goudsmit (1996)	52	PS; **QOL**	+	=	2
Group therapy	Soderberg (2001)	14	PH; QOL	=	=	1

+ positive effect of treatment; - negative effect of treatment; = no effect of treatment. *Essential fatty acids (both studies) = 36mg gamma-linoleic acid (GLA), 17mg eicosapentanoic acid (EPA), 11mg docosahexanoic acid (DHA), 255mg linoleic acid (LA), plus 10 IU vitamin E. Outcome codes: RU = resource use; PH = physical; PS = psychological; LAB = laboratory and physiological; QOL = quality of life and general health. Outcomes which showed a significant difference between intervention and control groups are highlighted in bold. Controlled studies are shaded in the table, all other studies are RCTs. Further details on included studies are available in the full report.[4]

Summary of study results continued

Treatment	Study (Year)	Number of patients	Outcomes investigated	Any effect	Overall effect	Validity score (Maximum 20)
PHARMACOLOGICAL						
Moclobemide	Hickie (2000)	90	PH; PS; LAB; QOL	=	=	19
Hydrocortisone	Cleare (1999)	32	**PH**; QOL	+	=	18
Fludrocortisone	Rowe (2001)	100	PH; PS; LAB; QOL	=	=	18
Fludrocortisone	Peterson (1998)	25	PH; PS; QOL	=	=	16
Galantamine hydrobromide	Blacker (2004)	434	PH; PS	=	=	15
Hydrocortisone and fludrocortisone	Blockmans (2003)	80	PH; PS; LAB; QOL	=	=	14
Hydrocortisone	McKenzie (1998)	70	PH; PS; QOL	=	=	14
Clonidine[70]	Morriss (2002)	10	PS	=	=	12
Oral NADH	Forsyth (1999)	26	**QOL**	+	+	12
Fluoxetine	Vercoulem (1996)	107	PH; PS; QOL	=	=	12
Selegiline	Natelson (1998)	25	PH; **PS**; QOL	+	=	11
Phenelzine	Natelson (1996)	24	PH; PS; QOL	=	=	10
Sulbutiamine	Tiev (1999)	326	PH; QOL	=	=	10
Galanthamine hydrobromide	Snorrason (1996)	49	PH; PS; QOL	=	=	9
Dexamphetamine	Olson (2003)	20	**PH**; QOL	+	=	8
Growth hormone	Moorkens (1998)	20	PH	=	=	5
Melatonin	Williams (2002)	30	**PH**; **PS**	+	+	5
Topical nasal corticosteroids	Kakumanu (2003)	28	PH	=	=	3
Oral NADH	Santaella (2004)	20	PH	=	=	3
Hydrocortisone	Cleare (2002)	120	**PH**; LAB	+	=	2
SUPPLEMENTS						
Essential fatty acids	Behan (1990)	63	**LAB**; **QOL**	+	+	17
Essential fatty acids	Warren (1999)	50	PS; QOL	=	=	16
Magnesium	Cox (1991)	34	**PH**; **PS**; LAB; **QOL**	+	+	15
Liver extract	Kaslow (1989)	15	PH; PS; QOL	=	=	10
Acetyl-L-carnitine and propionyl-L-carnitine	Vermeulen (2004)	90	**PH**; **PS**	+	+	10
General supplements	Brouwers (2002)	53	PH	=	=	10
General supplements	Martin (1994)	42	PH; QOL	=	=	10
Pollen extract	Ockerman (2000)	22	PH; PS; QOL; LAB	=	=	9
General supplements	Stewart (1987)	12	PH	=	=	6
Acclydine and amino acids	De Becker (2001)	90	PH; **LAB**	+	=	3
Medicinal mushrooms	Walker (2002)	70	PH	=	=	3

+ positive effect of treatment; - negative effect of treatment; = no effect of treatment. *Essential fatty acids (both studies) = 36mg gamma-linoleic acid (GLA), 17mg eicosapentanoic acid (EPA), 11mg docosahexanoic acid (DHA), 255mg linoleic acid (LA), plus 10 IU vitamin E. Outcome codes: RU = resource use; PH = physical; PS = psychological; LAB = laboratory and physiological; QOL = quality of life and general health. Outcomes which showed a significant difference between intervention and control groups are highlighted in bold. Controlled studies are shaded in the table, all other studies are RCTs. Further details on included studies are available in the full report.[4]

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The full version of the original review and this update can be downloaded free of charge from the CRD website (www.york.ac.uk/inst/crd). For information about how to obtain paper copies of both of these reports, contact the CRD publications office at: crd-pub@york.ac.uk.

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