

Chronic Fatigue Syndrome / Myalgic Encephalomyelitis

Version 1 Final

Document control

Version history

Version	Date	Comments
1 final	12 January 2010	Comments from MSCMT incorporated
1e draft	23 October 2009	Formatting
1d draft	08/07/09	Final Q.A.
1c draft	10/03/09	Incorporation of external Q.A. comments
1b draft	08/10/08	Incorporation of Internal Q.A.
1a draft	09/09/08	Initial Draft

Changes since last version

Introduction

“a long-standing, severe, disabling fatigue usually without demonstrable muscle weakness”

Historically Chronic Fatigue Syndrome (CFS) was used interchangeably with Myalgic Encephalomyelitis (ME) although some patient groups would vehemently insist on their distinction. However the Chief Medical Officer for England in 1998 called for a consensus to be reached on terminology and definition, and while awaiting this, suggested that the composite term CFS/ME is used and that it is considered as one condition or a spectrum of disease. [1]

The chronic fatigue syndrome is a clinically defined condition characterized by severe disabling fatigue and a combination of symptoms that prominently features self-reported impairments in concentration and short-term memory, sleep disturbances, and musculoskeletal pain. Diagnosis of the chronic fatigue syndrome can be made only after alternate medical and psychiatric causes of chronic fatiguing illness have been excluded. [2]

Description

The term CFS/ME is used to describe an illness that is characterised by physical and mental fatigue and fatigability, not substantially alleviated by rest which results in substantial reduction of previous levels of occupational, educational, social, or personal activities.

Other related complaints may be impaired short-term memory or concentration, recurrent sore throat, tender lymph nodes (neck or armpits), muscle pain, pains in a number of joints (without arthritis), new headache or un-refreshing sleep. [3]

The fatigue element as described by CFS reflects that in the majority of cases, the main symptom is chronic fatigue and there is little evidence that inflammation of the brain and spinal cord occurs.

ME is often the preferred term of people who have CFS/ME. This is due to the fact that they feel fatigue is too general and does not reflect the severity, and different types of fatigue. Also, it is felt that even though fatigue may occur in most cases, it is not the main, or only, symptom some people experience. [4]

Prevalence

It is widely agreed that prevalence is impossible to state precisely. Prevalence may vary because of differences in diagnostic evaluation, physician-patient attitudes, social acceptability, risk of exposure to an infectious or toxic agent, or definition and case finding.

Atos Healthcare

While the Merck Manual of 2005 states that the prevalence may be as low as 7 per 100,000 of population a study in Georgia in 2007 concluded it could be as high as 2540 per 100,000. [5] However certain features of this study have been criticised.

ME Research U.K. supports the findings of the Witicha, Kansas study of 2003 [6] stating “the overall estimate (235 per 100,000) obtained is broadly in accord with previous estimates from informed sources: 200–400 per 100,000 (CMO report, UK) and 422 per 100,000 (Jason et al, Arch Intern Med 1999; 159: 2129–37)”.

Department for Work and Pensions – Corporate Medical Group have published on their web site that 500 per 100,000 (1 in 200 persons) may be estimated to have CFS/ME. [3]

There is general agreement that it is more common in women than in men. Also that It usually develops in the early twenties to mid-forties. Children can, however, be affected and this is most commonly between the ages of 13 and 15 years.

The female : male ratio is unclear with even the accepted studies above citing ranges which vary from 3 : 2 to 9 : 2.

Aetiology

Aetiology is controversial with some definitions positively excluding infections such as Borreliosis, HIV and Hepatitis B & C. The precise cause(s) and pathogenic mechanism(s) are yet to be fully defined. A central defect in the brain remains a strong possibility, though immunological abnormalities are increasingly being elucidated. These are not mutually exclusive. The multiplicity of proposed causes such as an infectious disease (e.g. infectious mononucleosis), altered stress hormone response, altered immune response, altered gene expression, sleep problems, alterations of mood, coping strategies, and toxin/chemical exposure give further weight to the argument that the composite term CFS/ME best describes this condition and that it is a spectrum of disease.

A recent paper [7] concluded that 'prolonged fatigue states after infections are common and disabling' and that chronic fatigue syndrome was predicted 'largely by the severity of the acute illness, rather than by demographic, psychological, or microbiological factors'.

Infective agents which have been implicated include

- acute viral infections, such as infectious mononucleosis
- latent infections, such as toxoplasmosis, Epstein-Barr virus or cytomegalovirus
- chronic bacterial infections, such as borreliosis
- chronic viral infections, such as HIV or hepatitis B or C

However, it has proved difficult to establish a link between CFS/ME and serology indicating past viral infection.

Environmental factors, abnormal physiological pathways and genetic pre-disposition are all likely to contribute to symptom production and response to illness in CFS/ME.

There is good evidence of altered physiology in CFS/ME, particularly affecting neuroendocrine and hypothalamic-pituitary-adrenal (HPA) axis function.

Classic twin studies have demonstrated a strong heritable component to CFS/ME and other conditions of abnormal fatigue.

New genetic information describes associations between patients with fatigue and CFS/ME and genes involved in neuroendocrine and sympathetic nervous system function.

One model that may explain this is provided by evidence that vagal nerve activity may modulate the release of fatigue-inducing cytokines. [8]

Other stressful life events or difficulties may precede development of CFS/ME, particularly if the stress is ongoing. Other factors may contribute to prolonging the illness, for example, poor sleep, poor nutritional uptake, or a concurrent mood disorder. [3]

An understanding of CFS/ME is best served by taking all the likely aetiological factors into account. The new genetic information helps us to move away from the conflict between medical models of CFS/ME and a bio-psychosocial view of the illness. [8]

Diagnosis

Although to a certain extent a diagnosis of “exclusion” CFS/ME may be recognised on clinical grounds with a careful and structured history.

Signs and symptoms that can be caused by other serious conditions should not be attributed to CFS/ME without consideration of alternative diagnoses or co-morbidities. These would be:

- localising/focal neurological signs
- signs and symptoms of inflammatory arthritis or connective tissue disease
- signs and symptoms of cardiorespiratory disease
- significant weight loss
- sleep apnoea
- clinically significant lymphadenopathy.

Once serious conditions have been discounted, CSF/ME should be considered if there is:

FATIGUE with all of the following features:

- new or had a specific onset (that is, it is not lifelong fatigue)
- persistent and/or recurrent pattern
- unexplained by other conditions
- has resulted in an average daily activity level to below 50% of patient's premorbid activity level.
- characterised by post-exertional malaise and/or fatigue after normal activity (typically for at least 24 hours, with slow recovery over several days)

AND

one or more of the following symptoms:

- difficulty with sleeping, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pain that is multi-site and without evidence of inflammation
- headaches
- painful lymph nodes without pathological enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding, planning/organising thoughts and information processing
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness and/or nausea
- palpitations in the absence of identified cardiac pathology. [1]

Where symptoms suggest CFS/ME, the following tests should usually be done:

- urinalysis for protein, blood and glucose
 - full blood count
 - urea and electrolytes
 - liver function
 - thyroid function
 - erythrocyte sedimentation rate or plasma viscosity
 - C-reactive protein
 - random blood glucose
 - serum creatinine
 - screening blood tests for gluten sensitivity
 - serum calcium
 - creatine kinase
 - assessment of serum ferritin levels (children and young people only).
- Tests for serum ferritin in adults should not be carried out unless a full blood count and other haematological indices suggest iron deficiency.

Serological testing should not be carried out unless the history is suggestive of an infection.

Clinical judgement should be used when deciding on additional investigations to exclude other diagnoses.

GRADING

The degree to which CFS/ME affects a person's functioning and daily life has been the basis for grading CFS/ME as mild, moderate or severe. [9]

MILD

People with mild CFS/ME are mobile, can care for themselves and can do light domestic tasks albeit with occasional difficulty. Most are still working or in education, but to do this they have probably stopped all leisure and social pursuits. They often take days off, or use the weekend to cope with the rest of the week.

MODERATE

People with moderate CFS/ME have reduced mobility and are restricted in all activities of daily living, although they may have peaks and troughs in their level of symptoms and ability to do activities. They have usually stopped work, school or college and need rest periods, often sleeping in the afternoon for 1 or 2 hours. Their sleep at night is generally poor quality and disturbed.

SEVERE

People with severe CFS/ME are unable to do any activity for themselves, or can carry out minimal daily tasks only (such as face washing or cleaning teeth). They have severe cognitive difficulties and depend on a wheelchair for mobility. They are often unable to leave the house, or have a severe and prolonged after-effect if they do so. They may also spend most of their time in bed, and are often extremely sensitive to light and noise.

Treatment

There is no specific treatment for CFS. Diagnosis and advice about how to deal with the condition can help. CFS tends to last for months, if not years, but most people do recover to some extent, if not completely, or adjust their lifestyle to improve their symptoms.

There is no cure for CFS, so treatment tends to focus on rehabilitation, avoidance of precipitating factors and easing the symptoms. Early diagnosis, balancing rest with activity, medication to control certain symptoms, and self-help measures can all help to varying degrees.

In CFS/ME management may be a more appropriate term than treatment. [10]

Cognitive behavioural therapy (CBT), graded exercise therapy (GET), activity management, pacing, sleep management and relaxation have all been advocated as useful therapies. Other treatment modalities include pharmacological interventions, dietary interventions and supplements and complementary therapies.

It has been recognised that it is important to the outcome that the objectives of any programme must be agreed with the patient. They should understand the aims and objectives, and be willing to take part. The suitability, preference, ordering and timing of interventions should be discussed and this may be an iterative process.

The NICE guideline development group have given specific definitions of a number of therapeutic interventions and their wording and advice is included below and their full glossary is reproduced as Appendix [A].

Cognitive Behavioural Therapy is a specific psychological therapy, based on underlying theoretical principles, with a broad evidence base across a variety of conditions. CBT is a collaborative approach that aims to reduce the levels of symptoms, disability and distress associated with CFS/ME. CBT or psychological approaches to CFS/ME do not imply that symptoms are psychological, 'made up' or in the patient's head. CBT is used as part of the overall management for many conditions, including cardiac rehabilitation, diabetes and chronic pain. [11]

Graded Exercise Therapy is a professionally mediated approach to CFS/ME involving appropriate physical assessment, mutually negotiated and meaningful goal-setting and education. An achievable baseline of physical activity is agreed, followed by individually tailored and planned increases in the duration of exercise. This is followed in turn by an increase in intensity as the patient is able, taking into account their preferences and objectives, current activity patterns, sleep, setbacks/relapses and other factors, with the objective of improving symptoms and functioning. [12]

Atos Healthcare

GET is a structured, mutually developed and monitored programme that plans gradual increments of exercise or physical activity, using a specific method shown to be successful for patients with CFS/ME.

This is in contrast to a general exercise programme involving simply 'going to the gym' or 'just getting walking a bit more', or perhaps 'swimming a few lengths every day'.

What makes GET different from a general exercise programme is the delivery by and liaison with a trained professional (such as a physiotherapist), activity analysis before starting the programme, and mutually agreed starting points and progression.

A GET programme is delivered in partnership with the patient, and after a thorough assessment of current daily activity. It would not be appropriate, for example, for a patient to undertake a GET programme involving swimming if they cannot get up and get dressed every day. The start to their programme is likely to involve a physical functional task involving personal care, for example, or gentle stretches.

A general exercise programme has not been shown to be of benefit for this patient population and it is currently considered that it can do patients more harm than good.

Unsuccessful general exercise programmes, perhaps undertaken independently by the patient, or under brief advice from professionals not adequately trained in the use of GET, are often begun at a high, unachievable level, with an inappropriately rapid rate of progression, or without adequate professional supervision or support. An unstructured and poorly monitored or progressed exercise programme can cause significant symptom exacerbation, and can arguably make CFS/ME worse.

GET programmes have generally been studied on ambulant people with mild or moderate symptoms of CFS/ME and have been shown to be of benefit. In clinical practice, elements of GET such as a gradual increase in gentle walking, or gentle stretches are commonly used successfully in the severe group. However, some patients report that they have significant reservations about exercise (aerobic exercise in particular) and that exercise will significantly adversely affect their symptoms and function.

It is unlikely that patients with severe CFS/ME will be undertaking aerobic exercise, although they may be able to start the non- aerobic component of the GET programme (such as gentle stretches). If they reach the stage at which aerobic exercise can be added to a GET programme, it is likely that they will now be re-classified as having moderate or mild CFS/ME.

Before commencing a GET programme appropriate assessment will include the patient's history, activity patterns, symptom patterns, functional capacity, sleep patterns, medication and current physical capacity, and other factors as appropriate.

Atos Healthcare

Physical capacity can be determined by a simple, global measure such as a walking test or sit-to-stand test, alongside measures of heart rate and perceived exertion.

To avoid triggering post-exertional symptoms, a detailed, strenuous or lengthy physical assessment of range of movement, aerobic fitness or strength is avoided.

The goal of GET is to achieve and maintain 30 minutes of moderate aerobic exercise 5 days out of 7 (which may be by a brisk walk). In clinical practice, patient-centred goals should be developed (which may be less or more than those reported in clinical trials).

Through discussion, it should be agreed how this could be achieved in everyday life, according to the patient's individual circumstances and physical ability: for example, a 2 x 15 minutes daily brisk walk to the shop, or a return to some previous active hobby, such as cycling or gardening.

It is important to note that while this is the ultimate (long-term) goal of the GET programme, the patient will not start their programme at this level. The first short-term goal may be gentle stretching or a small, slow walk which (for those that are able) is gradually increased to 30 minutes.

Activity Management is a person-centred, collaborative approach to managing symptoms. It is goal directed and promotes the skills of activity grading and analysis to enable patients to improve and/or maintain their function and sense of well-being in self-care, work and leisure roles. Examples include spreading activities over the week, breaking tasks down into small manageable parts, interspersing activity with rest and setting appropriate, realistic goals for increasing activity.

Activity management is the approach that many therapists adopt for those with severe or moderate CFS/ME, and indeed it teaches skills for life to those moving towards a return to work and higher levels of productivity.

Patients should have ongoing access to and contact with therapists who use this (and any of the other approaches), such as community rehabilitation teams, occupational therapists, physiotherapists and rehabilitation care assistants. Ideally, patients should be able to refer themselves for 'top-up' sessions should life demands make it necessary.

Pacing is defined as energy management, with the aim of maximising cognitive and physical activity, while avoiding setbacks or relapses due to overexertion. The keys to pacing are knowing when to stop and rest by listening to and understanding one's own body, taking a flexible approach and staying within one's limits. Different people use different techniques to do this.

In practice, the term pacing is used differently by different groups of people. One understanding of its meaning is as adaptive pacing therapy, which is facilitated by healthcare professionals, in which people with CFS/ME use an energy management strategy to monitor and plan their activity, with the aim of balancing rest and activity to

Atos Healthcare

avoid exacerbations of fatigue and other symptoms.

Another understanding is that pacing is a self-management strategy, without specific intervention from a healthcare professional.

People with CFS/ME generally support this approach.

Sleep Management includes techniques such as sleep hygiene, which uses behavioural approaches, and changes in environmental conditions which can be introduced to improve the quality of sleep.

Relaxation is described as a state characterised by a reduction in physical and mental arousal, leading to feelings of peace, and release from tension and anxiety. Achieving it often requires practice but it can be a helpful strategy for people with CFS/ME.

Relaxation training and memory aids such as organisers and written resource manuals may also be helpful for addressing cognitive problems.

Pharmacological interventions have been assessed with studies on anticholinergic agents, antidepressants (tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOIs), NADH (reduced β -nicotinamide adenine dinucleotide), dexamphetamine, antihypertensive agents and steroids. Sample sizes were generally small.

Very few randomised controlled trials evaluating pharmacological interventions suggested a beneficial effect.

In particular, no benefit was found in patients with CFS/ME from treatment with anticholinergic agents, antidepressants, antihypertensives or growth hormone.

Results were mixed in trials of oral NADH (reduced β -nicotinamide adenine dinucleotide) and melatonin as well as in the studies of steroid therapy and MAOIs.

A trial of dexamphetamine found significant improvements in fatigue in the treated patients but reduced food consumption was a side effect.

Treatment with immunological agents have to date been inconclusive. There have been few published studies and participant numbers have been small. The results have been contradictory with some showing physical improvement and others not. Improvement in cognition but not depression has been claimed. There is as yet no good evidence to recommend this class of drug far less a specific member of the class.

Antiviral drugs have also been tried with no evidence of benefit.

Atos Healthcare

NICE conclusions on pharmacological interventions currently are:-

The following drugs should not be used for the treatment of CFS/ME:

- monoamine oxidase inhibitors (such as meclizolam)
- glucocorticoids (such as hydrocortisone)
- mineralocorticoids (such as fludrocortisone)
- dexamfetamine (used in ADHD)
- methylphenidate (used in ADHD)
- thyroxine
- antiviral agents.

If chronic pain is a predominant feature, referral to a pain management clinic is appropriate.

Prescribing of low-dose tricyclic antidepressants, specifically amitriptyline, should be considered for people with CFS/ME who have poor sleep or pain.

Tricyclic antidepressants should not be offered to people who are already taking selective serotonin reuptake inhibitors (SSRIs) because of the potential for serious adverse interactions.

Melatonin may be considered for children and young people with CFS/ME who have sleep difficulties, but only under specialist supervision because it is not licensed in the UK.

Dietary interventions including general supplements, pollen extract, medicinal mushrooms, acetylcholine (an alkaloid which stimulates the pituitary release of growth hormone), amino acids, essential fatty acid supplements and magnesium supplements have been considered.

A group with postviral syndrome did report an overall beneficial effect with essential fatty acid supplements with improvements in symptom measures.

Magnesium supplements had an overall positive effect of improvements in measures of energy and pain, emotional reactions, general health and laboratory measures, but not in sleep, physical mobility or social isolation.

Prognosis

The prognosis is highly variable in this unpredictable condition, which may be worsened or perpetuated by mismanagement or exposure to further triggering factors.

People with mild illness may recover spontaneously, or with some general advice or a limited treatment programme over a six month period. These people are likely to be treated in a general practice setting and recover before specialist referral is required.

People with established CFS/ME of moderate severity lasting one to two years or more are likely to need a more extensive management programme, lasting 6 to 12 months or more. Most will have been referred for specialist assessment and those who are able to attend hospital for treatment are likely to make a significant improvement with appropriate management.

Some people will recover fully, but others will not achieve their previous level of functioning. Some may not improve.

Recovery rates for CFS/ME are unclear as studies have tended to be on those attending specialist units and thus being in the moderate or severe categories. It appears that in this group full recovery occurs in 5 – 10%. Recovery rates appear to be highest in the first two years of the disease suggesting an extension of the group who recover before referral would be indicated. On the positive side a median of 40% (in some studies 65%) who do not report full recovery do show improvement.

Indicators of a good prognosis are:

- Male sex,
- A definite history of an acute viral illness like glandular fever at the onset,
- Mild disability and few symptoms,
- Clinical features showing a pattern of evolution towards functional recovery,
- Early diagnosis aimed at eliminating associated physical disorders and/or identifying psychiatric illness along with other complicating psychological or social factors,
- A management approach which may encompass physical, psychological and social elements that allows a stepwise approach to functional improvement using rehabilitation.

While indicators of a poorer prognosis include:

- Older age group
- Female and overweight
- Onset of symptoms without any clear precipitating factor,

Atos Healthcare

- Clinical course characterised by severe and unremitting symptoms,
- Severe and persistent disability,
- A management approach that over-emphasises the importance of either complete rest or which advocates a rapid return to pre-illness levels of physical activity,
- Co-associated conditions such as fibromyalgia, fluid retention syndrome or irritable bowel syndrome
- Those with co-morbid significant medical conditions or mood disorders,
- A complex background of adverse psychological and social factors (including illness beliefs, search for legitimacy and pervasive inactivity).

In many patients, disability and quality of life can be improved, sometimes to a significant extent. Those who recover may be at risk of recurrence. Those who improve are at risk of relapse.

People with CFS/ME have variations in the severity of their symptoms and will experience setbacks/relapses or transient increases in fatigue and other symptoms. These setbacks/relapses can vary significantly in their duration and severity, being anything from a slight reduction in function through to severe symptoms resulting in significant disability.

Setbacks/relapses are to be expected as part of the normal course of CFS/ME. With effective management interventions, the frequency, severity and duration of setbacks/relapses should be reduced.

Setbacks/relapses appear to be caused by different things; triggers can include, for example, sleep disturbance, overactivity, stress or an active infection (such as a common cold). However, it may not always be possible to identify a cause.

Management of setbacks/relapses may vary according to the cause. For example, it may be appropriate to maintain an exercise programme if stress has been a causative factor, but not if there is an active infection.

Difficulty may arise in distinguishing symptoms caused by CFS/ME from those of an active infection, as such symptoms are often similar (for example, increased fatigue, myalgia, headache, sore throat).

Severe cases are less likely to recover completely or benefit substantially from a management programme.

Atos Healthcare

All-cause mortality was not increased according to a Centre for Disease Control study on 1200 fatigued patients followed up to 14 years and a study published in 2006 found that in 166 deceased CFS patients the 3 most prevalent causes of death were heart failure, suicide, and cancer, accounting for 59.6% of all deaths. [14]

Debate continues as to what extent, if any, CFS/ME contributes to the development of heart failure and cancer and the mechanisms involved.

Main Disabling Effects

The disabling effects of CFS/ME in individuals are variable. Both physical and cognitive problems may be seen. The extent of problems is related to the severity grading for each individual but not all problems occur in every individual.

In mild cases the ability to walk long distances may be reduced, but the person is likely to be able to walk short distances on an unrestricted basis most of the time.

Cognition such as judgment, thought processes and communication are not affected. Self care is not affected and the person would normally be able to wash, dress, bathe, use the toilet and get up and downstairs without difficulty. Fatigue may be coped with by avoiding leisure and social pursuits and requiring occasional days absence from work to rest.

Those with moderate CFS/ME do experience more marked limitations in activities of daily living. Mobility is likely to be restricted with difficulty walking more than 100 metres consistently but severe restriction of walking is unlikely. Judgment, thought processes and means of communicating are not affected to the extent that they would be unable to find their way around in familiar and unfamiliar places.

They may have stopped work or education finding a need for regular rest periods with often afternoon sleep for 1 to 2 hours.

Tasks may take longer than normal and may need to be followed by a period of rest. The ability to maintain personal hygiene and nutrition is likely to be unimpaired. Sleep at night is generally of poor quality and disturbed.

75% of those with CFS/ME are in the mild or moderate category. The remainder are considered to have severe functional restrictions.

They will exhibit problems with mobility, cognition, particularly tasks requiring concentration and self care, and they may only manage minimal tasks such as face washing or cleaning teeth.

They may be severely restricted in their ability to walk. There may be a requirement for supervision either at home or out of doors as a result of significant cognitive impairment, but it would be uncommon.

At the most extreme end of the spectrum those with a severe level of functional restriction, who spend most of the day in bed or are otherwise immobile and depend on a wheelchair may have clinically evident muscle wasting. They may well need help with personal care and preparing food. In addition they are often extremely sensitive to light and noise.

References

- [1] Turnbull N, Shaw EJ, Baker R, Dunsdon S, Costin N, Britton G, Kuntze S and Norman R (2007). Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children.
London: Royal College of General Practitioners. August 2007
- [2] The Chronic Fatigue Syndrome: A Comprehensive Approach to its Definition and Study, Fukuda et al,
Annals of Internal Medicine, Vol. 121, December 15, 1994, pp. 953-959
- [3] DWP _ Corporate Medical Group Chronic Fatigue Syndrome
<http://www.dwp.gov.uk/publications/specialist-guides/medical-conditions/a-z-of-medical-conditions/chronic-fatigue-syndrome/prevalence-cfs.shtml>
- [4] NHS Direct Health Encyclopaedia
<http://www.nhsdirect.nhs.uk/articles/article.aspx?articleId=102§ionId=4>
- [5] Reeves WC, Jones JF, Maloney E, Heim C, Hoaglin DC, Boneva RS, Morrissey M, Devlin R.
Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia.
Population Health Metrics 2007, 5:5
- [6] Reyes M, Nisenbaum R, Hoaglin DC, Unger ER, Emmons C, Randall B, Stewart JA, Abbey S, Jones JF, Gantz N, Minden S, Reeves WC
Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas
Arch Intern Med 2003 Jul 14; 163(13): 1530–6.
- [7] Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD et al.
Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study.
BMJ 2006; 333(7568):575.
- [8] Nye F, Crawley E. Chronic fatigue syndrome: altered physiology and genetic influences. R.C.Phsy. Ed.
- [9] Carruthers BM, Jain AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM et al.
Myalgic encephalomyelitis/chronic fatigue syndrome: clinical working case definition, diagnostic and treatment protocols. *Journal of Chronic Fatigue Syndrome* 2003; 11(1):7- 115.

- [10] Centre for Reviews and Dissemination. Interventions for the management of CFS/ME.
Effective Health Care 2002; 7(4):1-12.
- [11] Prins JB, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL et al. Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. Lancet 2001; 357(9259):841-847.
- [12] Ridsdale L, Darbishire L, Seed PT. Is graded exercise better than cognitive behavioural therapy for fatigue? A UK randomized trial in primary care. Psychol Med 2004; 34(1):37- 49.
- [13] Royal Australian College of Physicians. Chronic fatigue syndrome. Clinical practice guidelines--2002. Med J Aust 2002; 176(Suppl):S23-S56.
- [14] Jason LA, Corradi K, Gress S, Williams S, Torres-Harding S. Causes of Death Among Patients with Chronic Fatigue Syndrome. Health Care for Women International, 27:615 – 626, 2006

APPENDIX A

Glossary of interventions

Activity	Any task or series of tasks that a person performs. A task may have physical, emotional, cognitive and social components.
Activity analysis	A process of breaking down activities into their component parts and specific sequences to identify the skills and abilities required to complete them.
Activity cycling	See 'Boom and bust' cycle.
Activity management	A person-centred approach to managing a person's symptoms by using activity. It is goal-directed and uses activity analysis and graded activity to enable people to improve, evaluate, restore and/or maintain their function and well-being in self-care, work and leisure.
Age	<ul style="list-style-type: none"> • Adult: aged 18 years and older. • Young person: aged between 12 and 17 years. • Child: aged between 5 and 11 years. <p>The age at which care is transferred between child and adult health services varies between 16 and 19 years, depending on the young person and their family's preferences and local circumstances.</p>
Baseline	A sustainable and stable range of functioning that can be maintained without significant symptom exacerbation.
'Boom and bust' cycle	Cycles of fluctuating activity levels and symptoms, which are a common feature of CFS/ME. Boom and bust cycles can happen when a person with CFS/ME is overactive when they are feeling better, which may lead to an increase in symptoms and a decrease in function.
Breathing techniques	Used to reduce respiratory rate, promoting parasympathetic activity and therefore stimulating relaxation. A number of techniques may be used, such as diaphragmatic breathing (using the diaphragm to breathe rather than the rib-cage) and 7/11 breathing (inhaling to a count of 7 and exhaling to a count of 11).
Cognitive behavioural therapy (CBT)	An evidence-based psychological therapy that is used in many health settings, including cardiac rehabilitation and diabetes management. It is a collaborative treatment approach. When it is used for CFS/ME, the aim is to reduce the levels of symptoms, disability and distress associated with the condition. A course of CBT is usually 12-16 sessions. The use of CBT does not assume or imply that symptoms are psychological or 'made up'.
Deconditioning	Loss of physical fitness as the general physiological response to, for example, a prolonged period of inactivity.

Atos Healthcare

Exercise	Any form of physical activity that uses the major muscle groups of the body. Activities of daily living (for example, brushing hair or getting dressed), sitting up in bed and walking about are all exercise in the context of this guideline.
Goal-setting	A collaborative process in which the patient and healthcare professional set reasonable short-term and long-term goals, including discussing the components of the goals and methods to reach them. Goals should be specific, achievable and measurable (that is, describe the patient's behaviour when the goal is reached), set within a definite timeframe and recorded clearly for reference by patient and healthcare professionals in review sessions.
Graded activity	Activities that have been selected, adapted and graded for therapeutic purposes to promote health and well-being.
Graded exercise therapy (GET)	An evidence-based approach to CFS/ME that involves physical assessment, mutually negotiated goal-setting and education. The first step is to set a sustainable baseline of physical activity, then the duration of the activity is gradually increased in a planned way that is tailored to the person. This is followed by an increase in intensity, when the person is able, taking into account their preferences and objectives, current activity and sleep patterns, setbacks/relapses and emotional factors. The objective is to improve the person's CFS/ME symptoms and functioning, aiming towards recovery.
Over–under activity	See 'Boom and bust' cycle.
Pacing	<p>The report of the Chief Medical Officer's working group defined the principles of pacing, and these are supported by people with CFS/ME and patient groups. Many of the principles are included in this guideline's recommendations on CBT, GET and activity management. Examples include spreading activities over the week, breaking tasks down into small manageable parts, interspersing activity with rest and setting appropriate, realistic goals for increasing activity.</p> <p>In this guideline, pacing is defined as energy management, with the aim of maximising cognitive and physical activity, while avoiding setbacks/relapses due to overexertion. The keys to pacing are knowing when to stop and rest by listening to and understanding one's own body, taking a flexible approach and staying within one's limits; different people use different techniques to do this.</p> <p>However, in practice, the term pacing is used differently by different groups of people. One understanding of its meaning is as adaptive pacing therapy, which is facilitated by healthcare professionals, in which people with CFS/ME use an energy management strategy to monitor and plan their activity, with the aim of balancing rest and activity to avoid exacerbations of fatigue and other symptoms.</p> <p>Another understanding is that pacing is a self-management strategy, without specific intervention from a healthcare professional. People with CFS/ME generally support this approach.</p>
Persistent fatigue	Fatigue that lasts for at least 3 or 4 months and substantially outlives its precipitating cause.
Relaxation	A state of reduced physical and mental arousal, characterised by feelings of peace, and release from tension and anxiety. Achieving such a state often requires practice.

Atos Healthcare

Rest periods	Short periods when a person is neither sleeping nor engaged in physical or mental activity. Rest periods are a core component of all management approaches for CFS/ME.
Setback/relapse	An increase in symptoms above the usual daily fluctuations, which may result in a reduction in function for a time.
Severity*	<p>The degree to which CFS/ME affects a person's functioning and daily life .</p> <ul style="list-style-type: none"> • People with mild CFS/ME are mobile, can care for themselves and can do light domestic tasks with difficulty. Most are still working or in education, but to do this they have probably stopped all leisure and social pursuits. They often take days off, or use the weekend to cope with the rest of the week. • People with moderate CFS/ME have reduced mobility and are restricted in all activities of daily living, although they may have peaks and troughs in their level of symptoms and ability to do activities. They have usually stopped work, school or college and need rest periods, often sleeping in the afternoon for 1 or 2 hours. Their sleep at night is generally poor quality and disturbed. • People with severe CFS/ME are unable to do any activity for themselves, or can carry out minimal daily tasks only (such as face washing, cleaning teeth). They have severe cognitive difficulties and depend on a wheelchair for mobility. They are often unable to leave the house, or have a severe and prolonged after-effect if they do so. They may also spend most of their time in bed, and are often extremely sensitive to light and noise.
Sleep hygiene	Behavioural strategies and environmental adaptations to improve sleep quality.
Specialist	A healthcare professional who has expert knowledge of and skills in a particular clinical area.
Specialist CFS/ME care	A service providing expertise in assessing, diagnosing and advising on the clinical management of CFS/ME, including symptom control and specific interventions. Ideally this is provided by a multidisciplinary team, which may include GPs with a special interest in the condition, neurologists, immunologists, specialists in infectious disease, paediatricians, nurses, clinical psychologists, liaison psychiatrists, dietitians, physiotherapists and occupational therapists.
Stage	There are different stages in the natural course of CFS/ME: acute illness, maintenance or stabilisation, and recovery.

These definitions are based on the RCPCH guidelines¹, the CMO's report², citing Cox and Findley.³