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## Review Article

# Management of Nutritional Failure in People with Severe ME/CFS: Review of the Case for Supplementing NICE Guideline NG206

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In the United Kingdom, a small but steady stream of people diagnosed with ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) have run into serious problems with nutrition because of difficulties with eating and drinking, and some have not survived. The clinical problem is extremely difficult, with little or no formal evidence on which to base diagnosis-specific recommendations for care, or information about prognosis. In several cases, however, the problem has apparently been compounded by a lack of provision of adequate services, misunderstandings, and conflict between health care professionals over diagnosis and approach to management. The following is a review of the clinical problem, including some suggestions for protocol content that might supplement NICE Guideline NG206. The main conclusion is that there is an urgent need for a consensus amongst professionals that focuses on practice based on reliable evidence rather than theory-laden diagnosis. The author is a physician with no direct involvement in ME/CFS care but with an interest in the clinical and scientific problems the condition poses.

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## Background Review

Recent concern over the care of people in the UK with severe ME/CFS with difficulties in feeding (see Baxter et al., 2021) has prompted calls for a more explicit management protocol in addition to the current NG206 Guideline from the National Institute for Health and Care Excellence (NICE) (<https://www.nice.org.uk/guidance/ng206>). There is no rapid route to writing and agreeing on such a protocol. Moreover, it is unclear exactly what additional guidance

is needed. In this context, what follows is a brief review of the salient background.

### 1. Diagnosis

Where care and trust have broken down in the management of nutritional failure in people with severe ME/CFS, confusion over diagnosis appears to have been a major avoidable factor.

Following an international trend amongst clinicians and scientists, NICE Guideline NG206 (2021) adopted the diagnostic category of ME/CFS for people with long-term disabling symptoms of as yet unknown cause, with delayed and/or prolonged post-exertional exacerbation. This has the advantage over either

historical name of (i) being a pragmatic clinical category, without assumptions about causation or mechanism in individual cases, whether infective, metabolic, immunological, or psychosocial, while (ii) retaining specific features, including unrefreshing sleep, exertion intolerance with a complex prolonged time course, typified by post-exertional malaise (and related 'crashes'), and intolerance of environmental stimuli such as light and sound. These intolerances are directly relevant to the approach to care and are the main justification for a distinct clinical category.

Patients within the category of ME/CFS show a spectrum of severity; those with severe intolerance of exertion and environmental stimuli may fail to maintain nutrition – mechanisms being unknown. It is possible that these patients differ from less severe ME/CFS in some aspect of causation. However, in the absence of clear evidence of a difference, Guideline NG206 covers the group under 'very severe ME/CFS' with general, if brief, advice on the approach to nutritional support.

Many patients will present having already been given a diagnosis of ME/CFS, or CFS, which NICE refers back to NG206 (see <https://cks.nice.org.uk/topics/tiredness-fatigue-in-adults/diagnosis/diagnosis-of-cfs/>). Lack of medical education on the severe aspects of ME/CFS may mean the diagnosis is missed, but NICE advice is clear. Uncertainty about diagnosis may require investigation to exclude unidentified structural problems, but this does not impact on an immediate need for nutritional support (except perhaps on route).

Some patients have been put into other diagnostic categories by healthcare teams, and this has been a major source of conflict with a negative impact on care. These categories all make some form of assumption about cause or mechanism, usually invoking psychological or behavioural aspects. There is no reliable scientific evidence for these assumptions in the literature, making such categories unjustified and problematic in that they invite care driven by theory rather than evidence. (The same risk applies to speculative diagnoses invoking infective, metabolic, or haemodynamic mechanisms, although these do not usually lead to conflict with patients' and carers' wishes.) Use of the Long Covid/PASC diagnosis may be justified, but as a contextual stratifier rather than an alternative category. At present, therefore, there is no reliable scientific or clinical evidential basis for patients who fall under the remit defined in NG206 to be managed in ways inconsistent with Guideline NG206.

## 2. History and Aetiology

From an outside perspective, a concerning element is potential harm from polarisation of clinical views that leave a patient and their carers with conflicting advice. Historical confusion over diagnosis may have a direct impact on care. ME/CFS is not an understood 'biopsychosocial' process, but nor is it a clearly defined disease of which we understand the physiological mechanism. It is hard not to conclude events in both immune and nervous systems are involved in many cases, but that is about as much as can be said. Patients and carers seek precise explanations, but if conflicting explanations are given, trust is likely to be lost. The hope is that the ME/CFS term, emphasising a pragmatic clinical category of disabling illness, can defuse conflict by focusing on the reliable evidence base for care.

The historic diagnosis of 'ME', linked to an epidemic of acute illness with neurological features at the Royal Free Hospital (RFH), and Acheson's (1959) speculation of 'encephalomyelitis' may not have served us so well. (Neither Acheson's nor McEvedy and Beard's (1970) psychiatric analyses are relevant, being of an acute illness, not ME/CFS.) The long-term disabling condition fits Ramsay's (1984) account of persisting symptoms at RFH but probably has no more relation to the acute illness than it does to Epstein-Barr virus or Covid-19 infection.

ME/CFS has no identified tissue pathology. Whatever the basis of this long-term illness, it is outside our current understanding of systemic pathology. Covid-19 has reminded many of us personally that disabling post-viral fatigue occurs with no plausible relation to psychosocial factors. Claims for psychosocial perpetuation in ME/CFS never had an evidence base. Equally, if ME/CFS was an inflammatory or ischaemic process, at least a few cases should show a consistent pattern of relevant pathology, but they do not. The condition appears to reflect a process that so far we do not have concepts to cover. That should not be unexpected. Clinical patterns of many diseases indicate the presence of causal steps that we do not understand. The hope is that genetic analysis or clues from Covid-19 may soon provide a better understanding.

## 3. General Aspects of Care

There are no controlled study data supporting any specific modality of care for severe ME/CFS. The FINE trial of behavioural approaches to severe ME/CFS (Wearden et al., 2006) failed to show benefit. Current practice recommendations rely on the expertise of a few physicians with experience with such cases. The

number of people requiring parenteral or enteric feeding is small, so clinicians' experience is often limited. The methods available are standard, but in the context of severe environmental intolerances, experience with managing such cases is likely to be valuable, if only in terms of anticipating patients' other needs.

There is a consensus amongst physicians experienced with such cases that ensuring nutrition, through whatever means is required at the time, takes precedence over all other considerations. There have been reports of health professionals refusing to make use of methods of nutritional support on grounds of speculated psychological mechanisms, but no reliable evidence justifies such an approach.

Management of nutritional failure is, nevertheless, inevitably bound up with the more general approach to care of severe ME/CFS, where opinion has divided into two camps. One approach is to avoid challenging patients with stimuli to which they are intolerant and to allow natural recovery, to the extent that this is possible. The other approach is to introduce challenging stimuli, which in this case may include normal feeding, proactively, if gradually. The NG206 Guideline takes the first of these approaches. In essence: 'When the person feels ready to do more, guide and support them in doing so with care,' rather than 'Encourage the person to do more, step by step, even if that may be difficult.'

The policy of the Guideline was informed by a standardised assessment of existing evidence of benefit from controlled studies of treatments such as Graded Exercise Therapy and Cognitive Behavioural Therapy, that encourage active introduction of challenges. The conclusion was that evidence of benefit from treatments involving deliberate challenge was unconvincing and did not justify their use. In view of the major risk of expectation bias in these studies, my own view of the most plausible interpretation of the data (given as expert witness testimony to the NG206 Guideline Committee) is that these treatments are ineffective. (Subjective outcomes were unimpressive even compared with open label data on a treatment now known to be ineffective: rituximab.) Moreover, strong *prima facie* evidence from patient experiences suggests that large numbers of patients experienced adverse outcomes (Kindlon, 2017).

Health care professionals who advocate a policy of gradually increasing challenges with stimuli to which patients are intolerant claim this is justified by their experience in clinical practice. 'We have seen it work.' The difficulty with this claim is that the clearest indicator of the extent of subjective improvement

achievable (there is no objective evidence) comes from the PACE trial (White et al., 2011; Wilshire et al.), which indicates that any real improvement would be too small, over and above improvement with time (let alone artefacts of social interaction such as loyalty to therapists), to be identifiable in individuals in routine care.

In the absence of further reliable evidence, the position taken by NG206 is that the priority is to accommodate patients' intolerances of environmental stimuli as far as is practical within service constraints. Certainly, there appears to be no justification for using a stimulus challenge approach with insistence on normal feeding in the context of nutritional failure. The hospital environment is stressful for anyone and significantly more so for people with severe ME/CFS. Hospital admission is only justified in the context of feeding problems if there are specific procedures that require it. Domiciliary provision must be preferable unless there are safety concerns, or where practical demands placed on a person living alone or on full time carers become prohibitive.

Patients with severe ME/CFS and feeding problems are faced with having an illness that nobody understands, some knowing that not everyone in their situation survives. Most are dependent full-time on family carers, and provision for continued attendance by these carers in hospital may also be important. As for stimulus challenges, there is no available evidence that removal of carers is beneficial and much evidence of major distress.

Equally, it should be noted that there is no reliable evidence base for recommending proactive protection of patients from stimuli on purely, or predominantly, theoretical grounds. Patients report worsening of symptoms and general health status following exposure to stimuli, whether physical, cognitive, or environmental. There is, however, no established evidence for stimuli causing long-term harm through any specific mechanism. For instance, most patients have orthostatic intolerance, but the physiological basis, and associated risks, are not established. It is important that natural fears related to the illness, of both patients and carers, are not compounded by fear of mechanisms that remain speculative. Nonetheless, if concerns about overprotective behaviour do arise, this will be a context in which trust, informed consent, and explanation of the evidence for care policy become even more critical.

Pro-actively protective approaches may have disadvantages. Although there is no evidence that the inability of people with ME/CFS to enjoy normal

working and personal lives has to do with deconditioning, and no evidence for ME/CFS patients benefitting from pro-actively increasing levels of exercise, physiological changes from lying flat may be significant. Risks from being bed bound include plantar flexion contractures and biochemical and haemodynamic changes from recumbency that may worsen orthostatic intolerance. It may be that encouragement to maintain some time sitting, or even upright, is useful, and it may be that specialist units have developed ways of exploiting this approach. However, at present, neither operational nor explanatory studies are available to provide clear advice. What is needed is evidence; there is a strong case for setting up formal studies in a designated clinical academic unit to address this.

In summary, nutritional support for people with severe ME/CFS should follow general guidelines, as for other conditions. Health care professionals with responsibility for resolving these difficult clinical problems need to be able to follow their judgment until we have better evidence. Nevertheless, in the absence of evidence of efficacy of approaches that involve deliberate challenge with stimuli (whether feeding, general environmental factors, or deliberate prevention of attendance of carers), these cannot be justified. Until this is generally understood, staff in non-specialist units are likely to expose patients to unnecessary distress, leading to a breakdown in co-ordinated care. It is crucial that the stimulus challenge approach does not jeopardise basic life support. Making it possible for the patient to tolerate the safest form of feeding support may require attention to reduction in environmental stimuli on a wide front, including sound, light, odours and physical contact.

#### *4. Methods of Nutritional Support*

Recommendations in NG 206 for patients having nutritional difficulties without major weight loss appear adequate and self-explanatory. Difficulty finding dietitians with expertise in ME/CFS is not a major barrier, since advice should follow general principles of nutrition and risk factors like being housebound and immobile.

The patients of more concern are those requiring alternative feeding routes such as a nasogastric tube or other forms of enteral/parenteral feeding. In the absence of reliable evidence for a condition-specific approach, these procedures should be offered according to standard guidelines such as those of the British Association for Parenteral and Enteral Nutrition. Decisions on the optimal route depend on the

envisaged length of time for which support is required. Input from a physician with experience of severe ME/CFS cases is likely to be of great value. Patients with severe ME/CFS may find intubation particularly distressing, especially if replacement is required. However, past case histories suggest that most tolerate tubes well once in position. The possibility of specific gut motility problems or small intestinal bacterial overgrowth may merit gastroenterological advice, but evidence is limited.

A practical issue that has surfaced is the recommended body position for nasogastric feeding. Patients with severe ME/CFS have orthostatic intolerance. The mechanisms are not clear. There are reports of posture-related reduction in cerebral blood flow in research studies but no documented clinical cases of harm from cerebral ischaemia. A head-up position (~40°) is used for periods of NG feeding in some circumstances because of the risk of aspiration of gastric contents. If there is evidence of orthostatic hypotension, it may be important to allow the patient to remain flat most of the time, but an informed decision needs to be made about risks during feeding periods. The relative risks for the individual patient need to be evaluated and explained. The evidence available from systematic review of adverse events is that positioning is not a source of problems for chronically ill children at least (see Page, 2019; Coulthard, 2024).

#### *5. Ethical, Legal and Educational Aspects*

Despite calls for a new protocol, publicly available information suggests that failure of care has had more to do with deviation from the existing guideline. Ensuing conflict has impacted on patients and carers and may have contributed to adverse outcomes. Issues of informed consent and, for younger patients, safeguarding, become critical.

Any provision of care must be consistent with the patient's wishes, unless they lack mental capacity. In recent cases, the problem does not appear to have been a lack of patient consent to receiving nutritional support, but rather to other aspects of care. If patients consent to support procedures (or decline and show full mental capacity), the use of the Deprivation of Liberty should be inappropriate. An essential part of care is trust between patient and carers and the health professional team, as emphasised by the BACME (2024) resource document on the care of severe ME/CFS. Even if there was evidence of benefit from considering psychosocial aspects of the illness, it seems highly unlikely that any will occur in the absence of such trust.

Concern in this area highlights the fact that health professionals may not appreciate that giving advice on care, when reliable evidence for that advice does not exist, is a form of misrepresentation or deceit. In practice, recommendations based on psychological analysis have been most associated with distress through challenge or perceived coercion. These are ethically unjustifiable in the absence of any documented evidence base, especially if they involve going against patients' wishes or any form of coercion.

Legal precedents relating to the need for informed consent to include an explanation of the evidence base for diagnosis or care include *Montgomery v Lanarkshire Health Board* (<https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf>). Patients are entitled to be given the scientific evidence base for a change in diagnosis from ME/CFS if the new diagnosis involves causal attribution, whether psychosocial or biomedical. Patients must be told that there is no reliable evidence for challenge-based/confrontational approaches being effective. Equally, treatments based on immunological, vascular, or metabolic concepts should only be offered with an explanation of the lack of reliable evidence.

Although these cases are uncommon, provision for management is essential for all UK areas, whether locally or via tertiary centres. Education of health care professionals on the clinical scope of ME/CFS has been poor, and it is essential that the complexity is understood by those faced with providing care. It would be useful to have an established panel of experienced physicians to whom professionals could refer.

## 6. Potential Sources of Confusion

My general conclusion from reviewing current guidance on feeding support is that it is adequate, if followed with care and expertise. However, recent documents from professional bodies (Royal College of Physicians, 2021; Nightingale, 2020) suggest a trend towards identification of a 'third' group of patients who have neither structural intestinal failure nor psychiatric illness justifying deprivation of liberty under the Mental Health Act, for whom feeding support may be actively discouraged. Recent events suggest that people with ME/CFS have been seen as falling into this group.

The recent United Kingdom Royal College of Physicians (2021) advice document appears excellent as a whole but there is a section referring to 'functional gastrointestinal problems' that appears confused and misleading. The term 'functional' probably has no place in this field, being deliberately ambiguous – claimed

both to mean simply 'non-structural', and to imply a psychological origin of somatic symptoms. Either way, in the absence of validated psychological treatments, it is merely a marker of our ignorance.

The RCP document claims that 'functional' problems are associated with Ehlers Danlos Syndrome (EDS). Yet EDS is a genetic structural problem (with no known reason for association with psychological issues). The document refers to a 'Toolkit' put out by the Royal College of General Practitioners on 'hypermobile EDS'. Of note, much of this Toolkit is speculative and if 'hEDS' is defined as suggested, over 90% of patient being given an EDS diagnosis will not have a monogenic connective tissue disorder – central to the EDS concept. Moreover, there is no good epidemiological evidence for common polygenic hypermobility being associated with either fatigue or visceral problems. The BSG document (Nightingale et al., 2020) also refers to functional problems and a link to EDS (although separately) and also to mast cell activation – another very doubtful claim. There appears to be a serious muddle.

I see two points as central to this confusion. Firstly, many physicians use 'functional' to imply a role for inappropriate fears or beliefs by the patient about causes of symptoms. Secondly, those inappropriate fears and beliefs ultimately derive from physicians themselves. The irony is that confused beliefs about both psychological mechanisms and unfounded structural/ physiological mechanisms attributed to 'hEDS', or a perhaps a 'gut-brain axis', may stem from the same sources (Voermans et al., 2010). The catastrophe is that patients are starving to death while physicians argue over these beliefs.

Guidance on good practice is available, but in view of the above there appears to be a need for advice on support for feeding difficulties from professional bodies to return to a strictly evidence-based agenda that does not imply that it is legitimate to withhold support and send patients for psychological (or otherwise 'multidisciplinary') intervention in situations where there is no reliable evidence for such intervention being beneficial, or even relevant.

## Content for a Protocol

In the absence of an immediate prospect of a more detailed protocol for care of severe ME/CFS with nutritional failure to supplement NG 206, the question arises as to what might be useful for it to contain if clarification is needed. The following suggestions are based on consultation with health care professionals

with experience in the care of severe ME/CFS. They are in line with both NG206 and the section on nutritional support in the recent BACME Shared Clinical Practice Document on Severe and Very Severe ME/CFS (2024).

Indication: The protocol should apply to any patient if:

1. They have persistent and severe clinical features of ME/CFS as defined by disabling fatigue or exhaustion, exertion intolerance with post-exertional malaise, and more generalised intolerance of environmental stimuli.
2. They are unable to maintain body weight and/or hydration through normal feeding.
3. There is no contraindication to specific feeding procedures (such as intestinal obstruction).

If patients who have been given a diagnosis of ME/CFS are to be given an alternative diagnosis, with implications for treatment outside this protocol, this must be based on reliable scientific evidence, and the patient must be given a full explanation of the evidence, both at a general and an individual level, for such a diagnosis.

Recommendations: An outline of management is given in NICE Guideline NG206, including general recommendations on minimising environmental stimuli in hospital. The latter appears to be absolutely crucial to successful outcome. All reasonable efforts should be made to avoid stimuli to which patients are intolerant, which can include light, sound, physical contact, and odours. Exposure to stimuli has in the past led to a breakdown in trust and care and failure of life support. Further detailed recommendations for the physical care of severe ME/CFS cases are given in *A Physiotherapist's Guide to Understanding and Managing ME/CFS* (Clague-Baker et al., 2023).

The account of care of nutritional problems in BACME (2024) usefully expands on NG206. Eating disorders are raised, but only in terms of differential diagnosis. BACME literature has recently been modified in line with the 2021 NG206 Guideline. Its wider coverage of ME/CFS is still to a degree couched in rehabilitative, goal-setting terms that lack an evidence base, with references to physiological rationales for which evidence is lacking. The resource on nutritional problems, however, appears well-grounded.

Feeding support with nasogastric tube, gastrostomy, PEG, or other methods should be offered in a timely fashion according to standard guidelines based on loss of weight and poor oral intake, in line with recommendations from the British Association for Parenteral and Enteral Nutrition (which uses the

Malnutrition Universal Screening Tool, MUST (see [https://www.bapen.org.uk/pdfs/must/must\\_full.pdf](https://www.bapen.org.uk/pdfs/must/must_full.pdf))).

Home-based services should be made use of wherever possible. Principles of nutritional support are covered by NICE in CG32 (<https://www.nice.org.uk/guidance/cg32> 0). An important rider for ME/CFS is that assessment of whether feeding support is needed, and what type, must include ability to complete an adequate meal rather than simply swallow a mouthful, since the problem is not being able to tolerate adequate intake.

In severe ME/CFS in adults, intolerances of environmental stimuli, of which feeding difficulties appear to be a part, are often a long-term problem with shifts in severity over time, but in many cases, there is no complete resolution. Nutritional support needs to be seen in the context of long-term care. Advice on prognosis from tertiary referral centres with experience with such cases (whether ME/CFS or neuro-gastroenterology and nutrition based) may be useful.

Nasogastric feeding may require modification in the context of orthostatic intolerance without the use of a standard angle of head elevation during feeding periods. The choice of position should be based on an assessment of safety in the individual context, but a flat position is considered safe in at least some contexts (Coulthard, 2024; Page, 2019).

## Conclusions

The above analysis is based on discussion with people with direct involvement with ME/CFS, by an outsider trying to understand what underlies present concerns. The simplest, and I think robust, analysis is that management of patients with stimulus challenge, often in the context of unsubstantiated diagnoses and outside established guidelines, has caused a huge amount of avoidable distress and needs to be abandoned. It has become clear that the challenge approach was *never validated before use*, and subsequent studies have shown no evidence of efficacy. Theories about psychosocial factors have failed to stand up; methods used to corroborate them have been poor, but good enough to show that the theories are flawed. The least one can say is that if psychosocial factors are involved, nobody has shown a useful understanding of them, or of how to manage them.

While there may appear to be a need for clearer guidelines, available guidelines on nutritional support appear to be adequate. They just need to be followed.

Failure of the medical community to come to a consensus on the diagnosis and management of severe

ME/CFS remains a serious problem and a potential source of conflict with a direct impact on patient care. This needs to be addressed urgently. The bottom line must be to stick to reliable clinical evidence. Care must centre on the principle of 'first do no harm' and on truly informed consent and trust.

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