



Invest in ME

Response to NICE Draft Consultation Document

(Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children

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1. Introduction

Invest in ME (IiME) is a UK charity registered in May 2006, that is run by people with Myalgic Encephalomyelitis (ME) or parents of children with ME on a totally un-paid, voluntary basis.

The sole objectives of IiME in reviewing the NICE Draft Guidelines are to ensure that people with ME and their families receive appropriate treatment; that Myalgic Encephalomyelitis receives whatever public funding is necessary to allow proper diagnosis, treatment based on science evidence and not vested interests, and for a cure for this devastating illness to be developed.

IiME have reviewed the NICE Guidelines (Chronic fatigue syndrome/Myalgic encephalomyelitis: diagnosis of chronic fatigue syndrome/Myalgic encephalomyelitis in adults and children) and wish to record the enclosed comments.

Although NICE has taken two years to formulate these proposed Draft Guidelines, IiME, along with the ME community, have been limited to two months to respond with comments.

Within the constraints of this deadline, while enduring ME and caring for ME sufferers, we have provided this response with as much detail as we are able and we submit this response document to NICE for consideration.

Itemised comments referencing the Draft Guidelines text can be found in Section 5 of this response.

We have submitted the comments in this document to NICE.

2. Summary of IiME Comments on These Guidelines

People with ME (pwme) hope that their illness will be taken seriously by the medical profession as the neurological illness that is ME and that research is publicly funded to provide early diagnosis, treatment, and eventually a cure.

IiME find the NICE draft guidelines document a travesty of the real requirements for people with ME and their carers.

We believe these guidelines provide little to further the treatment of ME and this is, essentially, an opportunity missed by those entrusted with the responsibility for producing these guidelines.

The NICE draft guidelines lack any vision in moving forward the treatment of people with ME (pwme).

Although we agree, and welcome the areas of the guidelines which state that the patient/carer is in control of actions and decisions relating to the illness, the statement that "treatments which are offered allow the person with the CFS/ME to refuse without compromising the further therapeutic relationship" must apply always.

We agree, and welcome, the offer of information about ME support groups. Although we have doubts about the use of the NHS Expert Patient web site as it contains erroneous information.

We cannot accept that these guidelines use as broad a section of fatigue states as possible in describing ME.

Psychiatric paradigms are referred to and recommended as therapies and as treatments for ME despite ME patients and groups stating they are ineffective or harmful.

In fact Graded Exercise Therapy (GET) has been shown to be harmful or useless yet it is wrapped up into a psychiatric paradigm to allow vested interests to perpetuate the same old myths about ME. The Draft Guidelines explicitly state that "There was strong agreement that persistent, debilitating, post exertional fatigue characterised the condition", yet the Draft Guidelines still recommend GET as a therapy/treatment.

Cognitive Behaviour Therapy (CBT) is being recommended as a treatment and the Draft Guidelines disingenuously compare CBT for CFS/ME to the usage by cancer patients and others. Yet CBT is not offered as first line treatments for these illnesses which NICE are recommending here for CFS/ME. Where CBT is offered to cancer patients then it is not the same type of CBT as is being proposed here for CFS/ME.

IiME strongly disagree with the priority recommendation that the therapies of first choice should be Cognitive Behaviour Therapy (CBT) or GET. It is incredible that this should be a recommendation at all, since the Draft

Guidelines document a lack of evidence and yet produce more policy-based evidence making.

Even results from patient group surveys, which show rest made people feel better and GET made them worse, are given a spin which skews the result.

IIME are left wondering why NICE sees fit to create this “spin”, since it benefits nobody in the long run and pwme and the medical profession are at the receiving end of more erroneous information.

The use of other treatments such as supplements and alternate medicines are not recommended even though patient experiences, as evidenced in this document and elsewhere, show them to be useful to some.

The current and previous biomedical research is seemingly ignored.

There is obvious bias in these guidelines – so much that it is impossible to take some of the statements seriously.

Out of interest one can see how skewed is the analysis. In these guidelines –

- 68 pages cover CBT, GET, Activity Management and other self management techniques (pages 138 – 204).
- 28 pages cover pharmacological interventions – (pages 205 – 233).
- 14 pages cover Dietary interventions and supplements (pages 234 – 248)
- 4 pages cover Complementary therapies (pages 249 -253)

Doesn't this say something about these guidelines? Are the objectives and the result already predetermined before the publication?

2.1. Views from the ME Community

Perhaps some of the most illuminating parts of the draft guidelines, and seemingly unused in many of the recommendations, are the three personal testimonies from people with ME.

The testimony from Ute Elliot, for example, shows clearly how dangerous the recommendation to get people active and back to work is.

Such results are only too familiar to the patients with ME. Yet these guidelines want to enforce more graded exercise and force people to be active rather than take adequate rest.

How many patients might have recovered had they followed sound advice to rest until their bodies told them it was possible to be active?

Yet the recommendations for CBT and GET seem to ignore what ME patients themselves are saying. They do not work.

It is a pity that Sophia Mirza could not have given evidence or participated in these studies as we are sure that her experience would also have been compelling.

Unfortunately, Sophia Mirza is dead. The Cause of Death was noted to be ME on the Death Certificate [[Appendix 6 – 16](#)].

IIME believe these Draft Guidelines should state unequivocally that it is unacceptable for patients with ME to be subjected to “sectioning” by psychiatrists, supported by Social Services and the Police, simply because the person has ME.

It is also rather short-sighted to ignore all of the politics which have been going on for years as the vested interests of psychiatrists, including the original Beard analysis back in the eighties, have effectively clouded the issue of ME and allows the myths (which are perpetuated in the draft guidelines) to distort thinking and action and so adversely affect the chance of ME patients to get sensible and proper consideration for the underlying biological illness.

We dispute the frequent statements characterised by this text *‘There is little understanding of the nature of the disease’*. There are over 4000 biomedical research papers on the illness which the NICE searches should have seen and analysed.

Views by ME support groups show that ME must be seen as a distinct and separate illness from CFS so we fail to understand why NICE often use the term CFS alone in these guidelines.

This, we feel, is part of the problem with healthcare staff and others – by broadening the view of what ME is it will inevitably dilute the requirements for diagnosing and treating ME patients.

The fact that these guidelines do not address the stress to pwme caused by being disbelieved by healthcare ‘professionals’ and having to endure the humiliation of applying to DWP for benefits seems only to re-enforce the conviction that these guidelines are pre-determined and will do little to improve the situation.

The guidelines are a quite biased and narrow-looking report which mixes up far too many illnesses and research information simply to prove the original intention of the document – to force pwme to be given psychological therapies and repeat the myths of the past.

It also attempts to subjugate ME into a bag of common illnesses all falling under the term CFS. In this NICE have done a major disservice to people with ME who are needlessly suffering from the perceptions of biased

healthcare professionals who maintain their views with little good scientific evidence.

This questions the impartiality of NICE and the Draft Guidelines.

2.2. Epidemiological Data

The NICE guidelines admit that there is a lack of epidemiological data for the UK. So why is the UK DoH not collecting epidemiological data? How old is this data that states “prevalence of at least 0.2–0.4%”? What is the latest estimate for the UK?

It has been reported by one leading charity study that ME is now the leading cause of long-term absence from school for children. Yet this is not addressed in these NICE Draft Guidelines.

Why does NICE not take the opportunity to join Invest in ME in making ME a notifiable illness in schools to allow epidemiological studies to be augmented? This would help the epidemiological analysis as well as ensuring that schools take this illness seriously. It also would reduce stress on children and their families as it would likely be taken more seriously.

The NICE guidelines do not carry a single reference to vaccinations despite research being present from over ten years ago (see [Appendix 6 – 21](#)). Why?

The recent investigations in Norway (published prior to NICE’s August review of new research information) reveal the extent of ME cases caused by vaccinations (see [Appendix 6 – 22](#) and (see [Appendix 6 – 23](#)).

None of this has been mentioned by NICE. Why?

The NICE guidelines do not carry one reference to epidemics despite strong evidence to support this from numerous references (detailed in [Appendix 2](#)). Why?

The NICE guidelines do not carry any reference to organo-phosphate poisoning despite the evidence indicating it causes ME. Why?

These are all major oversights by NICE. IiME consider that these links are important and should at least be included in any serious review of the bio-medical situation for patients who present with conditions similar to ME.

IiME suggests that research ought to be performed on historical evidence from epidemics and vaccinations that have resulted in similar conditions to ME and the NICE GDG ought to have analysed these topics sufficiently to include comment as the information can directly affect diagnosis and management. Yet again, NICE could have taken the initiative here, but yet again another opportunity to provide leadership has been lost.

2.3. Terminology

The terminology may be crucial in dealing with ME, especially as GPs, paediatricians, other healthcare personnel and the media use different terms.

These guidelines state -

'Appropriate and agreeable terminology and understanding is important when making a diagnosis and establishing a therapeutic relationship.'

IiME totally agree with this statement.

So it is even more surprising that NICE remains committed to perpetuating the terminological mess around ME.

Perhaps the principal problem is that ME/CFS is not a "clean" diagnosis. Indeed, the terms Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) mean different things to different people. None of the professionals in medical schools use the term "ME", they use CFS since the 1994 definition of CFS - flawed though it is - has come to be the dominant catch-all definition.

These guidelines could have moved this issue on by using and recommending the term recognised and used by the WHO – under ICD 10 G93.3. However, NICE has chosen to ignore this international definition.

The Draft Guidelines also refer to research into chronic fatigue. Let us be unequivocal - Chronic Fatigue is a symptom, not a disease or illness. This means that the guidelines and evidence are flawed as we are supposedly dealing with CFS/ME. Indeed the lack of precision in the document allows CFS to be used sometimes and CFS/ME at other times.

It also allows "encephalopathy" to be used, which merely serves certain organisations or individuals who benefit from having as wide a set of paying subscribers/patients as possible.

IiME suggests that **Myalgic Encephalopathy does not exist, save in the fictional arguments between parties with vested interests in maintaining vagueness.**

IiME believe that NICE should have had the courage, and the morals, to demand that the proper terminology is to be used by all healthcare staff. ME/CFS is the name that should be used. Instead, by its own statements and by its recommendations, NICE has allowed itself to be seen as hypocritical in stating the need for consistent terminology yet allowing the current subterfuge to continue.

This alone undermines the draft guidelines and the integrity of NICE.

2.4. Diagnosis

The recommendations regarding diagnosis of ME in the Draft Guidelines are conspicuous by their absence.

To disqualify a check for Lyme Disease is incomprehensible, especially with the latest evidence of misdiagnosis in many patients. We believe that these guidelines should state that there is a need to check for Lyme disease and that the current UK check should be upgraded to ensure that it is as accurate as can be to avoid misdiagnosis.

There are at least ten definitions of Chronic Fatigue Syndrome ([Appendix 6 – 19](#)). In these guidelines a frequently used case definition is the Oxford Criteria which includes patients with no physical signs and selects subgroups of patients with high levels of psychiatric diagnoses ([Appendix 6 – 20](#)).

IiME feels that the use of the Oxford criteria for any discussion/diagnosis or treatment for ME has long since reached its sell-by date and should be terminated forthwith. Most sections of the ME community, who have no desire to retain as wide a selection of subscribers for their own financial gain, now ignore the Oxford guidelines as they believe them to be worthless. The NICE guidelines should not be using research based on these criteria as they are flawed and biased – something which will cause all results based on these criteria to be worthless.

The 2003 Canadian definition states that cardinal symptoms are no longer optional and that patients must have neurological, immune and/or neuroendocrine manifestations.

In section 5.3.2.2 Summary of evidence presented in these guidelines admit that the number of varying diagnostic guidelines is a problem. It is something the ME community has been saying for a long time.

IiME feel that NICE have again lost an opportunity here to bring discipline and consistency to this area by not adopting the latest and most **stringent** (the word used by NICE themselves in these Guidelines) guidelines available – the Canadian Guidelines. This would have led to a substantial shift in the diagnosis and treatment of ME in the UK. NICE have failed in this respect.

On Page 35 lines 24-27 the Draft Guidelines state that ‘several factors have been suggested (as to the cause), including: immunological, genetic, viral, psychological and neuroendocrine.’

If this is accepted as a biological illness then why is the report slanted at psychological paradigms to manage the illness?

From this approach, IiME can only conclude that the basis of these Draft Guidelines is in viewing as broad a section of fatigue states as possible, where high quality biomedical research into ME/CFS has been ignored. Essential research showing the multi-system nature of ME has been ignored and is not considered or discussed, e.g. enteroviruses, orthostatic intolerance and oxidative stress.

There is little in the guidelines that would persuade a GP to conduct a proper and full medical examination before diagnosis. Imaging is mentioned once as regards recommendations. It is never mentioned anywhere else, although

many doctors now believe proper medical examination to exclude other illnesses should include SPECT scans.

2.5. Management

IIME find this section one of the most disappointing – and quite biased. The true agenda for these guidelines seems to be illustrated in this section.

The comments in the management section are often worthless as they seem to be dealing with patients suffering from burn-out rather than from a neurological illness. They also seem to be contradictory with a great deal of print sometimes emphasizing the use of psychological therapies such as GET and CBT and at other times stating that the choices are the patients’.

The complete disparity between the amount of space given to non-psychological treatments/therapies as compared to psychological treatments/therapies shows an obvious and unscientific bias in these Draft Guidelines. The information on CBT and GET in these guidelines often seems to read more like propaganda than a scientific, analytical review of management aids.

The bias shown in favour of psychological therapies undermines the value of these Draft Guidelines.

The Draft Guidelines contain an inordinate number of pages on management using psychological therapies compared to other management aids. Apparently so much time has been spent with cherry-picked research from psychiatrists, most of whom have no credit or respect in the ME community, yet where is the biomedical research analysis. It appears that the biomedical research is dealt with in a limited, dismissive and unscientific manner.

In Appendix A of the draft guidelines the membership of the Guideline Development Group appears to have very little expertise in the clinical definition, analysis and research of neurological ME as defined by WHO ICD-10 G93.3. If there are specific levels of expertise, then these should be included but none of the nationally or internationally recognised bio-medical experts in ME are included.

IIME would like NICE to state whether these experts are to be included in the Guideline Review Panel. Proposals can be made from the ME Research Community and ME Charities involved in research.

The psychological approach has been comprehensively covered in this initial proposal for a NICE Guideline. Any future iteration needs to clearly demonstrate a balanced approach and include the compelling biomedical research that shows the organic nature of ME and which will likely dictate the diagnosis and treatment of ME.

For example, the work of Prof Puri at the Hammersmith Hospital is indicating a “fingerprint” marker using elevated Choline levels in brain chemistry SPECT-scan results. There is also the work by Dr Spence at ME Research UK that shows post-exertional oxidative stress that appears to be unique to neurological ME.

Careful consideration should be given to the inclusion of related NICE guidelines, since there are a number of related psychological and clinical illnesses. The differentiation should clearly distinguish ME from other fatiguing syndromes and illnesses. It should be remembered that ME has been found to have inflammation of the brain and central nervous system and that pathology will provide increasing evidence. Some charities are proposing to support a protocol for pathologists where evidence is collected. NICE should consider this further in the Draft Guidelines.

CBT

CBT is stated to be a treatment for ME. It then is stated that it is a therapy and compares its use with ME to the use with cancer and heart disease etc.. These guidelines infer that CBT is a first line treatment for these illnesses – which it is not.

Here the NICE guidelines and those behind them are shown to be totally disingenuous.

CBT is not used as first line treatment for cancer or diabetes. Yet this is what NICE are proposing for ME. The CBT offered to cancer patients is not the same as that offered to ME patients where patients are asked to change their illness beliefs! (The CBT used for CFS/ME in the guidelines relates to *‘the relationship between thoughts, feelings, behaviours and symptoms, and the distinction between causal and perpetuating factors’* (Page 185)).

The attempt to compare CBT usage with cancer and diabetes is an appalling obfuscation of the true facts and can only be seen as a shameful act by those responsible to misrepresent this information in such a skewed fashion.

We have also included comment from the president of the Norwegian ME Association as they are somewhat ahead of their UK counterparts in discussions with the proposed Norwegian NICE guidelines. It is indicative of that fact that mistakes are being made (or planned) across the world. [See [Appendix 1](#)].

In NICE’s own words these guidelines have stated that –

‘trials (to) look at the effect of CBT performed over only 6 sessions... did find considerably poorer outcomes from 6 sessions of CBT in people with CFS/ME than with general chronic fatigue’.

This has no place in a set of guidelines meant to be used for a neurological illness and certainly has no place being used as a first-line treatment.

GET

A primary recommendation for treatment of ME/CFS in the NICE draft guidelines for those who are "mild to moderately affected" are Cognitive Behavioural Therapy (CBT) and GET. In making this recommendation, the Guideline Development Group seem to be ignoring credible evidence that such treatments are potentially dangerous for those who suffer from this illness, particularly in the case of GET.

Of particular concern is a mounting body of evidence that shows that exercise or over-exertion can worsen the health of ME/CFS sufferers and that, as such, GET has the potential to induce relapse, rather than being an effective recuperative therapy.

GET, as practiced today with ME patients, does not take into account a patient's preferences. How can a recovery be an objective with the use of GET when the causes of ME are unknown? Yet this is what the NICE guidelines propose.

GET cannot be recommended for severely, or even moderately affected ME patients. It is tantamount to inviting diabetics to take more sugar. This is where the NICE agenda for imposing psychological therapies onto ME patients shows the basic irresponsibility behind the policy.

Whilst activity management is essentially a common-sense approach to managing symptoms GET is totally unacceptable. What benefit does GET hold for a tube-fed, incontinent, bed bound patient? The proposition is risible.

It is well known that those who perform GET studies do "cherry-pick" their patients (i.e., choose only those patients well enough to be able to exercise in the first place and thus contribute to the overall 'success' of the trials). **No severely affected ME patients have ever been shown to benefit from the use of GET.**

Every medication has to have a list of side-effects – these need to be stated here also with reference to GET. GET needs to carry a government health warning for ME patients.

If NICE continue to recommend GET then they have to shoulder some of the responsibility for the consequences. In light of the evidence presented, it is possible that use of GET for those with ME/CFS will ultimately be self-defeating. By increasing the risk of relapse and increasing overall health risks rather than reducing them, it is dangerous for patients and risks increasing the burden of illness posed by ME/CFS on society at large.

We are left to wonder about the litigation that will follow if these guidelines ever see the light of day as a standard method for treatment of ME patients.

Will the chair of these NICE guidelines be willing to be held responsible for any damage that will inevitably result from using GET on severely affected patients by healthcare staff who will likely be unconvinced of the biological nature of ME?

Late in the preparation of IiME's response we received an email from a correspondent to IiME (Philip Pierce). We have included this as [Appendix 4](#) as we feel it provides more analysis and information regarding the use of GET for pwme.

Supplements and Alternative Medicines

The NICE guidelines provide an incredibly poor and limited summary on supplements as aids in managing ME.

Supplements are dismissed with little research or attempt to analyse.

Yet they can be a useful part of the diet for pwme who cannot cook always or who cannot eat properly and could benefit from such supplements (fish oils, vitamin C, multi-vitamins etc.) - surely this is a negligent oversight from NICE.

In some places the use of supplements is rejected and is not considered worthy of more investigation (page 234) -

“evidence is insufficient to support a beneficial effect of dietary supplements”

and (Page 249) -

“the GDG agreed that they could not be recommended for the management of CFS/ME”

Yet in other places in these guidelines it is stated that there may be a use for them (Page 263) -

“There may be a need for use of prescribable supplements or where there are severe problems, tube feeding may be required.”

It becomes totally confusing which recommendations are meant to be used. Imagine how GPs must react when reading these guidelines!!

The inconsistency is appalling.

Other Points

NICE recommend against resting after a relapse or during the illness. This shows little understanding of the real world.

During the early onset of ME rest is of paramount importance.

The wording by NICE is easily able to be misconstrued, or misunderstood, by healthcare staff lacking in real knowledge of ME and will severely impact many ME patients if promoted via these guidelines.

The emphasis on exercise at the expense of proper rest is appalling. Guidelines such as these ought to be for the benefit of the patient. These guidelines do not fulfil this objective.

2.6. Human Rights

It is not for sensation that IiME would like to see a lawyer added to the NICE consultation group. The lawyer would be there to represent ME patients as, undoubtedly, there will be litigation against the people making these recommendations for use of GET/CBT when yet another patient dies from putting into practice such guidelines.

It has also been stated that by ignoring the serious issues with regard to CBT and GET, the NICE guidelines, as currently drafted, may violate the right of clinicians and patients to the highest, safest standards of medical practice and care, amounting to a violation of their Human Rights.

Late in the preparation of IiME's response we received an email from a correspondent to IiME asking us to incorporate into our response some information concerning the use of GET and CBT. Rather than incorporate them into the body of our response we have included this documentation in full in [Appendix 3](#) for more legibility.

Apart from major concerns about the efficacy of use of CBT or about the danger in the use of GET the information in Appendix 3 refers to the human rights of patients being subjected to these therapies via a set of guidelines from an organisation such as NICE.

The email points out that there seems to be no regulatory framework governing the development and use of CBT and GET thus leaving ME patients vulnerable to exploitation and abuse at the hands of the vagaries of power, politics and prejudice.

IiME would state that this is already the case, as frequent letters to our information mailbox attest to this fact.

The NICE guidelines will allow such exploitation to continue and even increase.

2.7. Sub-Grouping

The guidelines make no mention of the need for sub-grouping of the current CFS and ME patients. The only reference the NICE guidelines make to sub-grouping is in relation to the use of CBT or GET!

Professor Leonard Jason of DePaul University, Chicago published in 2005 [[Appendix 6 – 15](#)] an excellent review on the need for sub-grouping of the over-broad "diagnostic category" CFS which can catch widely different groups of patients in its net. As he said,

"This review suggests that there is a need for greater diagnostic clarity and that this might be accomplished by subgroups that integrate

multiple variables including genetic, neurological, psychological and biological domains."

To quote Dr. Vance Spence of ME Research UK

"This illness is very big, very complicated and we are not going to solve anything by pushing everyone in to one large group called CFS. At present, what patients are left with is a "devalued" diagnosis consisting of (in one researcher's words) a "...ragbag of common non-specific symptoms with many causes, mistakenly labelled as a syndrome"."

2.8. Implementation

One section which was included in the short version but not present in the full version was implementation.

As for the cost of all of the psychological therapies (posing as treatments) are concerned it is difficult to understand how this will be paid for with an estimated 250,000 people suffering from CFS/ME in the UK, especially considering the low priority and lack of funding given to ME in the past. To have sparse resources squandered on therapies which the ME community do not need or want is an appalling waste.

Perhaps implementation should consider what is the need of the medical community, especially clinicians to assist in the diagnosis of ME and the exclusion of related non-specific fatiguing conditions.

The greatest factor in the UK and the Rest of the World is the lack of a clear diagnostic tool and the mixing of patient cohorts with numerous fatiguing conditions.

The use of the WHO ICD-10 G93.3 for Myalgic Encephalomyelitis and the development of a "fingerprint test" possibly based on the elevated levels of Choline in the brain blood chemistry, which has been the only unique identifier found to-date, could be used and validated.

2.9. Document Structure

We find the full version of the guidelines document poorly structured and cumbersome to read. They are very unwieldy and the shortened version is probably the only version which will be read fully. This would then lead to the fuller guidelines being ignored as regards supporting evidence. But if this evidence is flawed then the whole draft is suspect.

The way the document is composed, with recommendations all over the place, references everywhere, sections which should be broken down into more manageable entries and tables and pagesets of varying formats – the whole document is badly formatted. Even a healthy person would find it difficult to read the full version.

3. Guideline objectives

These were the stated aims of the document as written on Page 21 Executive summary and recommendations Aims of the guideline.

It is appropriate to determine if these objectives were met by this draft document.

The Guideline Development Group developed this guideline with the aims of -

3.1. Increasing the recognition of CFS/ME

It is doubtful if this has been met as it provides nothing new for sufferers and carers.

The few places where the document has requested that healthcare professionals take the illness seriously and that the recognition of this is paramount is good.

Essential research showing the multi-system nature of ME is not discussed – enteroviruses, orthostatic intolerance, oxidative stress – none of these are allowed to be discussed in detail. Yet without a basic understanding or awareness of the pathology of the illness how are healthcare staff supposed to recognise the true nature of ME. Increasing the recognition of ME can only be achieved by increasing the knowledge of the illness itself.

However, the recommendations that once again force non-functional and biased psychiatric therapies as a management technique will lead to more harm and probably contribute to fostering even more antagonism between healthcare staff (especially those who are untrained in ME) and the patient/carer.

Increasing recognition of the illness could also have been assisted by the use of the correct terminology – as detailed by the WHO. ME/CFS is the correct term and myalgic encephalomyelitis is the correct name for the acronym ME. By pandering to organisations and individuals, who have a vested interest in using other terms, NICE does nothing but harm to itself as the consensus amongst patients will be that NICE cannot be trusted.

3.2. Influencing practice in the 'real world'

It is doubtful if this has been met as it provides nothing new for sufferers and carers.

By immediately stating that CBT and GET are the most useful therapies NICE has shown it is not willing to move the issue of ME into an area which offers any real hope of progress.

These guidelines will not influence practice but will lead to already established myths being perpetuated. The lack of a decision on endorsing one set of diagnostic guidelines – the '*more stringent*' Canadian guidelines –

is a travesty. It seems that NICE is intent on using as broad a definition for ME as possible.

This will result in little change in the 'real world'.

The absence of emphasis on the lack of funding for biomedical research into ME will not help to alter the government's position on this subject and therefore gives little to change the current unsatisfactory position where patients are given possible harmful GET. It will not inform healthcare staff of the missing link in research into ME – funding for biomedical research.

It shows little awareness of other biomedical research being carried out or performed in the past. It should include references to new research in this area so that healthcare staff can be aware of the overwhelming evidence of the neurological source of this illness.

The guidelines state that a patient/carer can refuse any therapy without it impacting the relationship with the healthcare practitioner(s). We would like to see this occur but we are afraid that it will not.

In the face of insurance companies and DWP staff forcing an ME patient to undergo potentially harmful or useless GET or CBT then we doubt if these guidelines are forceful enough to avoid this happening.

In such instances recourse to litigation will be the only possibility for ME patients.

It might have been useful for these guidelines to detail what avenues are open for legal aid for ME patients who wish to challenge insurance companies and healthcare staff who insist on ME patients undergoing GET or CBT against their will.

The guidelines make little headway in influencing 'real world' issues such as insurance companies forcing claimants with ME to undergo psychiatric therapies.

The guidelines do little to influence 'real world' issues such as the requirements from the DWP to go through elaborate processes to prove they are ill.

The guidelines do little to influence 'real world' issues such as the need for parents to battle with schools for the rights of their children with ME.

Will NICE state that nobody should be refused insurance and sick benefit if they refuse to take anti-depressants or CBT/GET?

3.3. Improving access to appropriate services, and supporting consistent service provision

It is doubtful if this has been met as it provides nothing new for sufferers and carers. Little is given in support of ME patients in their dealings with DWP staff and no reference is made regarding how ME patients are meant to deal with the harassment and bias of insurance companies who propose psychiatric treatment for ME.

3.4. Emphasising the need for multidisciplinary working

These guidelines patently fail to achieve this due to the concentration on psychological therapies at the expense of real research of published biomedical research papers.

Although there are a few statements stating that multi-disciplinary working is required in dealing with ME patients the bias toward psychological therapies, and the amount of space given to these therapies in these guidelines, means that there is little credit given to non-psychiatric disciplines in treating and managing ME.

3.5. Improving care for patients, and particularly for those severely affected

The guidelines offer little for severely affected. There is no provision for specialist treatment – simply rehashed dogma relating to therapies which are entirely inappropriate for severely (and moderately) affected pwme. There is little here for carers.

3.6. Providing guidance on ‘best practice’ for children with CFS/ME

Here it fails abjectly. The best practice is not psychiatric therapies where the onus is on the patient to attend meetings with psychiatrists. It does little to move the debate on.

3.7. Balancing guidance with the flexibility and tailored management, based on the needs of the patients

By emphasising GET and CBT as primary treatments it is not possible to state that these guidelines help in basing management on the needs of patients. Its predilection for asserting that activity and exercise help ME patients already undermines any confidence that the ME community may have about the impartiality of these guidelines.

3.8. Facilitating communication between practitioners and patients, and their families or carers.

It cannot be said to achieve this as the emphasis on psychological therapies posing as treatments using heavily skewed data will inevitably influence GPs and paediatricians – especially if they have little time available for ME patients. The subject matter is skewed to allow a multitude of fatigue-related patients to be included in this study. If it purports to be for ME then the studies need to use patients with ME – not CFS or other fatigue conditions.

4. Conclusion

NICE had a real opportunity with these guidelines to improve the future for patients with ME. After all, two years and unknown costs were expended in their preparation.

Yet these guidelines fail on a number of levels and give no real help to a GP or paediatrician to make an informed evaluation or provide any useful treatment. They are, in fact, an appalling shambles of perpetuated myths, psychiatric dogma, outdated practices and prejudice.

One walks away from this document wondering whether the National Institute of Clinical Excellence needs to be renamed to the National Institute of Clinical Expediency.

The document shows little new thinking and is clearly lacking in impartial analysis of all areas of research into ME. How can this profess to have consulted patients or used real experience? Who was elected to be part of NICE committee?

The lack of comment on epidemics and vaccinations shows how lacking in vision, scope and thoroughness has been the work carried out by NICE. The lack of analysis of the extensive biomedical research also shows a lack of rigorous control exercised in the formulation of these guidelines.

IIME cannot endorse these guidelines as they will condemn people with ME to a false and perilous future which will again be dominated by psychiatrists and the institutionalised psychiatric dogma which pervades many organisations and healthcare departments.

We urge NICE to withdraw this document and reconvene with representative scientists, researchers, patient groups and others who are in contact with the 'real world' of ME suffering. This will obviously prove embarrassing to the lead of NICE and will unlikely be listened to – despite a chorus of patient complaints with which these guidelines are likely to be met.

Yet what is the purpose of producing a set of guidelines which are unusable and which will be criticised for the bias they contain?

They will serve neither patient or healthcare practitioner.

NICE state in these guidelines that they wish for the patient and medical community to work together. They will achieve the opposite with these guidelines.

By maintaining the intention to authorise these guidelines NICE will not only do an injustice to a new generation of ME sufferers - they will also herald the end of NICE as any form of reliable guidance for ME.

Failing a revision of these guidelines Invest in ME recommends that all ME patient groups, charities and people with ME and their carers walk away from these NICE guidelines. They will do more damage than ever before.

Invest in ME have recommended in this review that a lawyer should be added to the NICE governing group to represent ME patients and their families. IIME will also be seeking advice on whether NICE are liable for damages if some of the recommended psychological therapies are forced on ME patients which then cause degradation in health.

To repeat the comments of one of our correspondents if NICE does not see the depth and breadth of the failures and omissions in the draft guidelines, following the consultation process, then a judicial review must be inevitable.

Should these guidelines be implemented without substantial change or revision then Invest in ME urges all ME support groups to notify their GPs/Paediatrics departments/PCT staff that these are merely guidelines and that individual healthcare staff are able to accept ME support group information to extend necessary tests, as appropriate.

By the date at which NICE have proposed that all submissions regarding the draft guidelines are to be received from stakeholders it will be exactly one year to the day since Sophia Mirza died from ME. It is a sobering thought that in this century in the UK such an event could occur. These NICE guidelines will do nothing to prevent more deaths.

As they stand these NICE guidelines are, to use a topical phrase, not fit for purpose.

As Ellen Piro of the Norwegian ME Association states –

“If the map doesn't match the terrain, it is the map that is wrong and not the terrain.”

These guidelines are unacceptable and Invest in ME will do everything in its power to oppose them as they currently stand.

Invest in ME November 2006

5. Itemised Comments on Guidelines Document

The following chapter includes comments on individual lines in the full version of the guidelines which we feel need to be corrected or reviewed. Due to the format of the document it is not possible to comment on every section. IIME have done their best, though, to constructively review all of the evidence within the constraints of time and energy. The comments relate to the draft guidelines by page and line number, as appropriate.

Page 1 Title:

Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children

IIME Comment: The title is misleading and incorrect. It is not encephalopathy – but myalgic encephalomyelitis. See WHO ICD 10 G93.3

Dr. B. Saraceno of the WHO clarified the classification in writing on October 16, 2001.

“I wish to clarify the situation regarding the classification of neurasthenia, fatigue syndrome, post-viral fatigue syndrome and benign myalgic encephalomyelitis. Let me state clearly that the World Health Organisation (WHO) has not changed its position on these disorders since the publication of the International Classification of Diseases, 10th Edition in 1992 and version of it during later years.”

“Post-viral fatigue syndrome remains under the diseases of nervous system as G93.3. Benign **myalgic encephalomyelitis** is included within this category.”

“Neurasthenia remains under mental and behavioural disorders as F48.0 and fatigue syndrome (note: not THE CHRONIC FATIGUE SYNDROME) is included in this category. However, post-viral fatigue syndrome is explicitly excluded from F48.0.”

Page 8 Glossary of Terms: Definition of Activity and Activity management

IIME Comment: This needs to be revised. For some patients even 5 minutes is long. Some ME patients have remained bed bound for years without sitting up. An increase in activity might be one minute in a week.

“*Activity Management*” is exactly what the title suggests, i.e. a scheme for a patient to proactively manage activity levels. The definition given, which includes “*to enable patients to improve and or maintain their function*” is totally misleading for a patient with severe ME, where it is not possible to perform Activity Management.

Page 8 Glossary of Terms: Boom-bust / activity cycling / over-under-activity

These terms describe fluctuating activity levels and symptoms, as a common feature to CFS/ME. People with CFS/ME may be over-active when they are feeling better, which may lead to an increase in symptoms and a decrease in function.

IIME COMMENT: This is completely without foundation and would be far too generic a labeling in any case.

Page 9 Glossary of Terms: Cognitive Behavioural Therapy (CBT)

CBT is an evidence based treatment for CFS/ME. CBT is a psychological therapy and collaborative treatment approach which 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. It is used in many health settings including cardiac, cancer, diabetes and chronic pain as well as with mood disorders such as anxiety and depression.

IIME Comment: This is not true – CBT is not a treatment for severe ME and it has been proven to be positively dangerous to such patients. Maybe CBT is used in other health settings, however, not where post-exertional oxidative stress can cause more serious problems.

The evidence base for CBT is poor and based on research using the flawed Oxford criteria as they use all states of fatigue. The description of CBT is confusing. Is it treatment or therapy? The CBT offered for ME/CFS patients, differs from the one offered for cardiac, cancer, diabetes or chronic pain patients. There is a big difference between CBT for somatoform illnesses and CBT for physical illnesses such as ME.

How can a therapy also be a treatment? Is NICE stating that CBT cures ME? The glossary definition states that CBT does not imply that symptoms are psychological, 'made up' or in the patient's head. Yet later in the document it refers on page 202 to '..CBT or other behavioural treatments...'. The guidelines are inconsistent.

It is also proven to be ineffective. If this 'therapy' is to be included then Reflexology, Bowen Technique, Acupuncture, and host of other therapies need also to be included – as none of these provide a cure yet all may be used to try to ameliorate some part of ME.

Page 10 Glossary of Terms: Graded Exercise Therapy (GET)

GET is an evidence-based self-management approach to CFS/ME involving appropriate physical assessment, mutually negotiated meaningful goal

setting and education. It involves setting an achievable baseline of physical activity, followed by individually tailored and planned increases in duration of exercise. This is followed by an increase in intensity when able; taking into account a patient's preferences and objectives, current activity patterns, sleep, setbacks, and emotional factors; with the objective of improving CFS/ME symptoms and functioning aiming towards recovery.

IIME COMMENT: Evidence-based? Evidence has shown this is of no help. It is a proposed self-management technique that is not appropriate for patients with severe ME, where post-exertional oxidative stress can cause more serious problems. "Increases in duration of exercise" are very dangerous, as blood pressure can drop and patients can be subject to numerous adverse reactions to any forced exercise. "Aiming towards recovery" implies that recovery is possible with increased exercise, which is unproven and fallacious.

Page 11 Glossary of Terms: Mild CFS/ME

Individuals who are mobile, can care for themselves and can do light domestic tasks with difficulty. The majority will still be working. However, in order to remain in work they will probably have stopped all leisure and social pursuits, often taking days off. Most will use the weekend to cope with the rest of the week.

IIME COMMENT: The definition states that the majority of individuals with mild CFS/ME will still be working. Where is the evidence for this? No epidemiological studies can substantiate this. Studies by ME Research UK show that around 50% are employed but struggling to maintain their lives, with another 40% existing on benefits. This is a different spin on the facts.

Most will not use the weekend to cope with the rest of the week. This is so generic as to be unusable. Many students for example will use the weekend to make up for lost time during the week.

Page 11 Glossary of Terms: Pacing

The term pacing is used differently and understanding of its meaning can range from Adaptive Pacing Therapy, whereby activity is reduced to Incremental pacing, whereby activities are gradually increased.

Many of the principles of pacing as defined in the CMO report and supported by some patient groups are included in the GET and Activity Management section, for example spreading activities over the week, breaking tasks down into small manageable parts, interspersing activity with periods of rest and setting appropriate, realistic goals for increasing activity.

Pacing is aimed at managing activity and rest to achieve a balance. Activity can be physical, emotional and mental. It is essential that the person listens to and understands their own body. People with CFS/ME frequently like this

approach as they feel in control. Pacing is the subject of a current research trial which aims to see if pacing is a useful approach.

IIME COMMENT: Please also add COMMON SENSE. If anybody is ill then they do not run a marathon the day their symptoms improve. Let us include CST – COMMON SENSE THERAPY.

Pacing is not necessarily about adoption of a psychological paradigm with expensive and unnecessary people making their living from this. Pacing is also common sense.

The CMO report has been criticised for their definitions and conclusions by organisations and charities involved with Severe ME sufferers.

Page 13 Glossary of Terms: Severe / very severe CFS/ME

A person whose functioning will only allow them to carry out minimal daily tasks only (e.g. face washing, cleaning teeth) or are unable to mobilise and do any of these for themselves. Have severe cognitive difficulties and be wheelchair dependent for mobility. People with these symptoms are often unable to leave the house except on rare occasions with severe prolonged after-effect from effort. They may also be in bed for the majority of the time and are often unable to tolerate any noise, and are generally extremely sensitive to light.

IIME COMMENT: They may also not be able to do anything (literally) for years. This needs to show the whole range of effects.

Page 13 Glossary of Terms: Specialised care

Provides expertise in the assessment, diagnosis and advice on clinical management of CFS/ME, including symptom control and specific interventions. Ideally this will be provided by a multidisciplinary team and members may include general practitioners with a special interest, neurologists, immunologists, liaison psychiatrists, and specialists in infectious disease, paediatricians, clinical psychologists, dieticians, physiotherapists, occupational therapists and nurses.

IIME Comment: What is the defined specialised care, when there is no agreed definition of ME or treatment protocols?

“Ideally this will be provided by a multidisciplinary team and members may include general practitioners with a special interest” where is the evidence to indicate that a multi-disciplinary team is the correct approach?

If ME is related to elevated levels of chemicals (e.g. choline) in the brain and there are modified gene expressions as noted by Prof Puri and Drs Kerr and Gow, then there is physical evidence of damage to the endocrine system. Therefore, shouldn't an endocrinologist be the first port of call for the medical profession?

Pages 8-14 Glossary of Terms:

We would like to see the following terms added as they need to be used later in the document:

Orthostatic intolerance

Oxidative stress

Why not also include other biomedical terms which have been proven to exist in pwme?

Why the concentration of terms connected to psychiatric paradigms and therapies? Why not others?

Pages 15 Guideline Development Group members

IiME Comment: IiME would like to see a lawyer added to the consultation group. The lawyer would be there to represent ME patients as, undoubtedly, there will be litigation against the people making these recommendations when yet another patient dies from such guidelines

Pages 15 Guideline Development Group members

It should be noted that the make-up of this Guideline Development group was as follows –

- Patient representatives - 4
- Physiotherapists - 1
- Paediatrician - 3
- General practitioner - 2
- Dietitian - 1
- Neurologist - 1
- Clinical psychologist - 1
- Infectious disease consultant physician - 1
- Psychiatrist - 2
- Occupational health physician/therapist - 2
- Nurse - 2
- Immunologist - 1

IiME Comment: For a neurological illness there is one neurologist but 2 psychiatrists?

Pages 21 Executive summary and recommendations Aims of the guideline

🕒 increasing the recognition of CFS/ME

IiME Comment: If this were so, it would then be useful to use the recognized term as per WHO consistently.

Pages 21 line 20 Priority recommendations

- When the adult or child's main goal¹ is to return to normal activities then the therapies of first choice should be CBT or GET² because there is good evidence of benefit for this condition in mild to moderately affected adults and some evidence in mild to moderately affected children.

IiME Comment: Obviously any child's or adult's main goal is to return to normal activities. This needs to be removed as it is insulting.

IiME Comment: There is little unequivocal evidence to show that CBT or GET have good evidence of benefit and much which shows the contrary result. Most of these studies have also used the flawed Oxford criteria for selection of participants in the programme.

At this time there is no evidenced-based proof that these therapies are appropriate which has been accepted as rigorous and independent from the psychosocial approach to ME by some experts.

IiME Comment:

The report on ME from the Chief Medical Officer of 2002 stated that 65% of patients trialled using CBT found that it was of no value. An even more alarming figure of 50% stated that GET had made them worse. Reference was also made to the most recent study on CBT (ref: Cognitive behaviour therapy in chronic fatigue syndrome: a randomised controlled trial of an outpatient group programme. Health Technology Assess. 2006 Oct; 10 (37): 1-140) which had failed to demonstrate any major overall benefit when CBT was compared to either education and support or standard medical care.

CBT and Graded Exercise can worsen ME symptoms

In a survey of 3074 ME/CFS patients conducted between 1998 – 2001,

55% of patients said that CBT had made no difference to their illness, whilst 22% said CBT had made their illness

worse. 16% of patients said that Graded Exercise had made no difference to their illness whilst 48% said it had made their illness worse [[Appendix 6 – 3](#)].

A survey by the 25% ME Group (for severe sufferers) of 437 patients, demonstrated that of the 39% of group members who had used graded exercise, 95% had found this therapy unhelpful, whilst -

82% reported their condition had been made worse by graded exercise. Some patients were not severely ill with ME until after graded exercise.

In the same survey -

93% of those who had undergone Cognitive Behavioural Therapy had found it unhelpful [[Appendix 6 – 4](#)].

There has been much research on muscle and immune cells. Christopher Snell in 2005 reported that the results of exercise capacity and immune function in male and female patients with CFS “implicate abnormal immune activity in the pathology of exercise intolerance in CFS and are consistent with a channelopathy involving oxidative stress and nitric oxide-related toxicity”. This could explain why people with ME/CFS can’t exercise, as there is a limit, beyond which one cannot train.

Lane et al [[Appendix 5 - 1](#)] have found evidence of abnormal muscle physiology in a significant number of ME/CFS patients that could not be explained by physical de-conditioning or muscle disuse. Jammes et al [[Appendix 5 – 2](#)] make a connection between such muscle dysfunction and increases in oxidative stress observed in people with ME/CFS when subjected to incremental increases in exercise activity, a finding corroborated by Nijs et al [[Appendix 5 – 3](#)].

Magnetic Resonance Imaging (MRI) brain scans compared between control patients and patients with ME/CFS indicated areas of reduced blood flow - indeed, myalgic encephalomyelitis might be a good name for such “brain-muscle” anomalies.

Hooper [[Appendix 5 – 4](#)] takes this one step further by making the association between increased oxidative stress and generation of free-radicals. Given the link between free-radicals, aging and cancer this is surely a matter of particular concern for those with ME/CFS. To put things succinctly, excessive exertion has the potential to cause premature aging and increased risk of cancer in those with ME/CFS.

The work of Chia [[Appendix 5 – 5](#)] establishes a link between enterovirus re-activation through over-exertion (exercise is mentioned as a specific

example). This itself further supports the work of Lane [Appendix 5 - 1] who states -

"we have correlated abnormal lactate responses to exercise with the detection and characterisation of enterovirus sequences in muscle."

It is therefore possible to state that over-exertion by those with ME/CFS has the potential to lead to enterovirus re-activation as a result of faulty muscle metabolism.

An additional concern involves measurable cardiac insufficiency in those with the illness. Peckerman et al [[Appendix 5 - 6](#)] have demonstrated a link between symptom severity and cardiac dysfunction. This work is backed up by that of Vanness, Snell et al [[Appendix 5 - 7](#)], who go so far as to state that:

"The blunted heart rate and blood pressure responses in the 'mild' through 'severe' groups are similar to those seen in chronic heart failure."

It is also worth noting that in their study, they accounted for any potential "lack of effort" on the part of their subjects:

"it was felt that the multiple testing protocol employed in this study was sufficient to ensure that the results obtained accurately reflect patients' functional capacities."

With regard to cardiac function and exercise therapy, Carruthers and van de Sande [[Appendix 5 - 8](#)] issue the following warning:

"Externally paced 'Graded Exercise Programs' or programs based on the premise that patients are misperceiving their activity limits or illness must be avoided."

Thus we have several health risks for those with ME/CFS which may be exacerbated by exercise: excessive oxidative stress and resultant generation of free-radicals, enterovirus reactivation, and cardiac dysfunction. All three have the potential to cause serious harm, and arguably have lethal potential. Given this situation, it is surely irresponsible to recommend exercise therapy for this particular patient group.

Pages 22 line 2-4 Priority recommendations

IIME Comment: We welcome line 2-4 on page 22 stating that decision-making lies with the patient/carer.

Pages 22 line 6 Priority recommendations

- provide information about the range of therapies and management strategies as detailed in this guideline

iIME Comment: This guideline needs to include a significant increase in evidence-based assessment and treatments beyond the psychosocial model and CBT/GET treatments before it can be accepted as an independent, expert guideline for the treatment of ME

Pages 22 line 12 Priority recommendations

- consider patient preference, experience and outcome of previous treatment(s)

iIME Comment: This needs to be 'Allow patient preference...'. All the way through the document repeats that the patient should be able to decide. If so then this wording needs to change. See also Page 93 lines from 1 onwards where allows is used.

Pages 22 line 14 Priority recommendations

- offer information about access to self-help groups and support groups for adults and children, families and carers (see www.nhsdirect.nhs.uk, and also the NHS Expert Patient Programme www.expertpatients.nhs.uk/)

iIME Comment: We welcome this but feel that the NHS direct web site contains incorrect and dangerous information and cannot be used as a reference in its current form. A list of local and national support groups, charities should be available.

Pages 22 line 17 Priority recommendations

- be aware that all adults and children with CFS/ME have the right to refuse any component of a care plan without detriment to the provision of other aspects of care.

iIME Comment: It is to be welcomed that patients are in control. Also health insurance needs to be an area to be looked into.. This includes any or all of the therapies used by psychiatrists.

Refusal of (possibly inappropriate) treatment has also been proposed as a means of reducing Incapacity Benefits or Disability Benefits.

Pages 22 line 22 Priority recommendations

sustain or gradually extend, if possible, the person's physical, emotional, cognitive capacity and manage the physical and emotional impact of their symptoms

IIME Comment: Why is the inference always on the emotional state, by having “emotional” and “emotional impact” at the start and end of this statement? Surely, it could be better worded not to cause possible offence by stating “achieve a return to normal health and capabilities for the patient”.

Pages 23 line 1 Priority recommendations

A diagnosis of CFS/ME in an adult should be made after symptoms have persisted for 4 months

IIME Comment: Why are the Canadian Guidelines not adopted for this diagnosis, which are comprehensive, evidence-based and accepted by leading biomedical experts on ME? They also define the critical symptomology in a clear and concise manner that permits objective assessment. The above definition does not define the “symptoms”.

Pages 23 line 3 Priority recommendations

The diagnosis of a child should be made by a general paediatrician after symptoms have persisted for 3 months

IIME Comment: Why should there be a difference in the timescale for children compared to adults? Is there a different symptomology or aetiology?

Pages 23 line 9 Priority recommendations

- When an acute infection is followed by excessive fatigue, the adult or child should receive advice on how to promote recovery. The advice should focus on sleep management, risks of prolonged bed rest (for example, deterioration in muscle function), and a gradual return to a normal daily routine.

IIME Comment: This cannot be allowed. Advice has to be specific to each patient – gradual return to normal daily routine is not advice.

It cannot apply if the condition/infection is still present.

All patients should receive advice on how to promote recovery, irrespective of the starting symptoms or aetiology? If sleep disturbances are experienced, then the nature should be investigated before appropriate advice given, since sleep management may not be appropriate, or possible. Also, severely affected ME patients may not be able to avoid prolonged bed-rest, therefore, dangers should be managed but not be a focus of treatment. Curative treatments are required, but no basis is given in this text apart from possible scare-mongering!

The assumption that an ME patient can always do more is an erroneous one. There are overwhelming international research findings on ME, which support multi-system involvement particularly of the immune, endocrine,

cardiovascular and neurological systems [Appendix 6 – 5]. Also, there is evidence indicating pathology of the central nervous system and immune system [Appendix 6 – 6] and evidence of metabolic dysfunction in the exercising muscle [Appendix 6 – 7]. Also, Dr. Jay Goldstein has demonstrated through SPECT scans the severely decreased brain perfusion of an ME patient 24 hours after physical exercise [Appendix 6 – 8]. The Canadian Criteria (2003) states that *the worsening of symptoms after exertion is a principal symptom of ME* [Appendix 6 – 9]. Raised levels of noxious by-products of abnormal cell membrane metabolism, associated with exercise and correlating with patients' symptoms have been demonstrated [Appendix 6 – 10].

Dr Byron Hyde M.D. of the Nightingale Research Foundation for ME in Canada, who has studied ME since 1984 [Appendix 6 – 13] states that

“Patients who improve after physical exercise programmes do not have ME/CFS.” .

Dr. Hyde stresses that ME is primarily a disease of the Central Nervous System [Appendix 6 – 14].

Pages 23 line 22 Priority recommendations

•Healthcare professionals should be proactive in advising about fitness for work and education, and recommend adjustments or adaptations to work or studies to enable rehabilitation of adults and children with CFS/ME. This includes liaising (with the person's consent) with employers, education providers and support services e.g.:

- occupational health services
- disability services through Jobcentre Plus (<http://www.jobcentreplus.gov.uk/JCP/Customers/Helpfordisabledpeople/index.html>)
- Connexions for schools
- disability advisers in universities and colleges

IIME Comment: Why not also advice/help regarding DWP? One of the biggest stresses on patients with ME is the necessity to prove that they are ill to DWP staff who have little real knowledge of the illness and the aetiology. If the objective is to make it better for the patient then why cannot healthcare staff defend the patient's need for understanding from DWP?

Healthcare professionals should recognise the biological nature of ME (P 22 line 5) and advise disability services departments of the inappropriateness and inability of pwme to be forced into return to activity or work if they are not able to.

Also healthcare staff should be able to advise insurance companies of the above.

Part of stress on parents/carers also relates to education as schools are often apathetic and ignorant toward pwme.

One could also ask why should this be even noted, since it should be within the bounds of normal practice? However, if there is a psychosocial element to be addressed then this should be removed from the treatment of a biomedical physical illness.

Pages 23 line 16 Priority recommendations

Referral to specialised care for adults and children with CFS/ME should be based on the person's needs and symptoms, the duration and severity of symptoms, and the decision should be made in partnership.

iIME Comment: What is the element of "partnership" and does this indicate agreement being necessary by all parties prior to proceeding with treatment? How is this different from normal procedures? If there is agreement by the medical profession on aetiology and treatments for ME, then specialised care could be provided in an agreed manner that includes biomedical treatment rather than psychological interventions.

Pages 23 line 19 Priority recommendations

In the absence of a definite diagnosis and/or while waiting for referral, advice and symptom management should not be delayed until a diagnosis is made.

iIME Comment: This is a most unusual statement, as if there is a missing diagnosis, then the best course of medical treatment cannot be defined. Is the NHS routinely encouraged to prescribe treatments where the diagnosis is not clear?

Pages 23 line 22 Priority recommendations

Healthcare professionals should be proactive in advising about fitness for work and education, and recommend adjustments or adaptations to work or studies to enable rehabilitation of adults and children with CFS/ME.

iIME Comment: Surely, healthcare professionals should be proactive in the diagnosis and application of appropriate treatments to return the patient with ME back to a healthy, normal standard of living? Shouldn't this include the provision of advice on rehabilitation from professional experts on rehabilitation that includes experience of ME at all the grades of severity? Is the medical profession responsible for inputs to JobCentres or the Connexions service independent of requests for input from those services or the patient?

Pages 28 line 14 Research Recommendations

iIME Comment: If this is about research then why aren't more demands being made to fund biomedical research into ME.

Pages 28 line 14 Research Recommendations

Are there more efficient (cost effective without decreasing efficacy) ways of delivering standard methods of care? For example a) group versus individual CBT or GET or b) telephone or computer CBT or GET?

IiME Comment:

What are standard methods? Why is the only standard method CBT or GET – for a neurological illness – what are standard methods? This is not the same CBT offered to cardiac patients. The Canadian guidelines have a chapter on this – why does this document not refer to that?

Why focus on these two methods? why not alternative medicines? This is already skewed and reasserts the old myths that CBT/GET can help (treat) ME.

Pages 28 line 17 Research Recommendations

Randomised controlled trials, with adequate power, should be used to compare different methods of delivering standard methods of care. Sub-group analysis (if appropriate) may clarify which approach is most effective in different groups of patients (for example, people who are severely affected).

IiME Comment: Sub-group analysis needs to be explored. Why are there no research recommendations into sub-grouping?

Pages 28 line 21 Research Recommendations

What is the prevalence and incidence of CFS/ME in different populations?
What is the natural course of the illness?

We recommend that these questions are answered using a mixture of the following methods: a) cross-sectional population studies which ensure that patients from all ethnic groups, social class and disease severity are included, b) longitudinal cohorts of patients with CFS/ME as well as population cohorts to assess the incidence and prognosis of CFS/ME in a previously normal cohort.

We need reliable information on prevalence and incidence of this condition to plan services. This will require well constructed epidemiological studies across different populations to collect longitudinal data needed to predict outcome, and to calculate the economic impact due to loss of work/education.

IiME Comment: What about previous studies showing epidemics, contraction after vaccination etc?

Research ought to be on epidemics and vaccinations.

ME is now the leading cause of long-term absence from school for children. Why not make ME a notifiable illness to allow epidemiological studies to be augmented?

Pages 29 line 2-5 Research Recommendations

IiME Comment: We agree with this. Well constructed epidemiological studies are required.

Pages 29 line 21 Research Recommendations

It is not known how much improvement is important for patients with CFS/ME.

IiME Comment: This is a ludicrous and insulting comment – which patient wants to be ill? It needs to be removed.

Pages 29 line 21 Research Recommendations

Future research studies to investigate cost effectiveness of treatment require functional outcomes such as return to work.

IiME Comment: Again a ludicrous comment – getting health back is the most important thing – everything follows from that. Only biomedical research will provide a cure for ME.

Pages 29 Research Recommendations

IiME Comment: Look at the number of pages made for management techniques as opposed to anything related to biomedical research. The document is skewed.

Why is there not a single recommendation for more biomedical research?

This shows extremely poor quality analysis and indicates a lack of vision from this group.

CBT and GET are reported to be dangerous and hazardous to health for severe ME – has this been examined? If yes, where is the reference material to support the view that CBT and GET are safe? All of the questions noted miss the key questions for research: Aetiology; Diagnostic test; Valid treatments (i.e. successful medical interventions with pharmaceuticals or other treatments); Epidemiology (how the illness is transferred from patient to patient); Demography (are there patient clusters?).

Pages 30 line 5

Encephalopathy needs to be removed as this was not in the 2004 commission statement.

IiME Comment: Was the 2004 NICE guideline for encephalopathy?

Pages 32 line 2 Clinical management

- the appropriate use of laboratory tests, imaging or other tests

IiME Comment: Imaging is mentioned here as regards recommendations. It is never mentioned anywhere else although many doctors now believe proper medical examination to exclude other illnesses should include SPECT scans.

Pages 32 line 10 Clinical management

The guideline also makes recommendations on:

- criteria for referral to appropriate specialist services for children, young people and adults
- the provision of advice by healthcare professionals on home tuition or return to school
- the provision of advice by healthcare professionals on return to work

IiME Comment: Regarding return to work needs to be balanced with advice on dealing with DWP when somebody is being harassed or being intimidated from insurance companies.

Pages 33 line 6

The guideline does not address:

- the management of co-morbidities

IiME Comment: How can these be ruled out? Who knows which came first if diagnosis has taken 3-4 months, or longer? Also ME produces other co-morbidities over time which need to be looked at. This guideline itself recommends other examinations on Page 27. (a review of the diagnosis especially if signs and symptoms change). Therefore this document is already lacking in precision.

🕒 service provision or models of care.

IiME Comment: Is this not impacted by the management techniques being forced on pwme by these guidelines? Surely forcing someone to do GET has a bearing on models of care as the results of GET will affect directly the amount of care which a pwme will require when it causes deterioration in the health of pwme.

Pages 34 line 1

Plans for guideline revision

NICE clinical guidelines are updated as needed, so that recommendations take into account important new information. The emergence of new evidence will be checked 2 to 4 years after publication of the guideline to decide whether all, or part, of the guideline should be updated. If important new evidence is published at other times, a more rapid update of some recommendations may be considered.

IiME Comment: By whom is new information checked? Who decides what is new evidence?

Pages 35 line 2

1 Introduction to Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy)

IiME Comment: Please remove encephalopathy

Pages 35 line 4

CFS/ME is chronic illness that places a substantial burden on patients, carers and families, and hence on society. It comprises a range of symptoms including fatigue, malaise, headaches, sleep disturbances, difficulties with concentration, and muscle pain

IiME Comment: Why not document that this is a multi-system biological illness? See press-release. Also state that this is a multi-system illness.

Why exclude other symptoms? For example the list of symptoms does not include orthostatic intolerance. Yet Dr Peter Rowe found as long ago as 1994 that ME/CFS patients had significant cardiovascular responses to standing upright, manifested by changes in vascular volume/heart rate/blood pressure. An article entitled "Standing Up For ME" in The Biologist in 2004, Professor Julian Stewart and Dr Vance Spence outlined some of the "physical" arguments surrounding this aspect of the illness. The first thing to recognise is that the blood pressure in most ME/CFS patients is maintained by a significant increase in heart rate, at least in the early stages of upright posture.

Professor Stewart of New York has published some interesting data on what happens to ME/CFS patients when they are upright, and it shows that there is a group of patients whose leg blood is low when lying down and it *increases* when upright, a wholly abnormal response and indicative of a shift of vascular volume towards the legs. Images of the leg of an 18 year old

woman suffering from ME were shown when in the supine and upright position to illustrate the increased blood flow (redness of colour).

This whole area of orthostasis is extremely complex. Might there be a problem with peripheral blood vessels in ME/CFS patients? Since 2000, the group at the University of Dundee has been looking at how skin blood vessels respond to the endothelium-dependent vasodilator, acetylcholine. In ME/CFS patients, blood vessels are sensitive to acetylcholine driven through the skin; i.e. the skin blood vessels dilate more than expected, a novel if not unique finding (i.e., most diseases show the opposite response to acetylcholine, which is a blunted or decreased blood flow). A review of this work has been published ([Appendix 6 - 1](#)), and ME Research UK continue to fund research on this aspect of ME/CFS especially given its importance to understanding some of the unusual vascular phenomena which characterise the illness.

Dr Vance Spence has highlighted a finding ([Appendix 6 -2](#)) of increased isoprostanes in the bloodstream of ME/CFS patients, and the fact that these were correlated with symptoms. This was the first investigation to measure isoprostanes in patients, which are now recognised as one of the most reliable approaches to assessing in vivo oxidative stress and which seem to be a biomarker of great potential in the assessment of cardiovascular risk. There are several possible sources for these oxidants, including blood vessel endothelium, inflammatory/immune cells and muscle, and a range of precipitating factors can be involved.

The high degree of correlation of increased isoprostane levels associated with post-exertional myalgia from a sample of 29 patients shows the grades of post-exertional fatigue in patients reporting mild, moderate and severe symptoms after exercise. It may be that the muscle pain experienced by ME/CFS patients after exercise is due to the elevated levels of isoprostane and oxidation in the muscle, but we have work to do to understand the mechanisms. This is not shown in the guidelines.

Pages 35 line 9/10

It raises especially complex issues in severely affected children and adults.

IiME Comment: These issues affect so called 'mildly affected' patients also – being at home for years with little contact can also be classified as severe.

Pages 35 line 14

In 1998, the Chief Medical Officer convened an Independent Working Group which reported in 2002. In the report, the Working Group acknowledged that CFS/ME is a chronic illness and that health and social care professionals should recognise it as such. As a result of the report, the Medical Research Council was commissioned to develop a research strategy, and has made research on CFS/ME a priority.

IiME Comment: It should be stated that the MRC has refused to fund biomedical research and this needs to be mentioned.

Pages 36 line 2-5

1.3 Aetiology

This is the view of aetiology taken by the guideline group and recommended for adoption, pending the findings of current research.

iIME Comment: Current research is defined. Will this include research underway by Dr. Jonathan Kerr, by the projects being sponsored by ME Research UK or by other biomedical research projects?

Page 36 line 6 Diagnosis

The clinical practice guidelines on chronic fatigue syndrome developed by the Royal Australian College of Physicians defined CFS as “a descriptive term used to define a recognisable pattern of symptoms that cannot be attributed to any alternative condition

iIME Comment: Are we discussing CFS or CFS/ME?

Page 36 line 11 Diagnosis

There is also ongoing debate about the most appropriate diagnostic criteria to be applied.

Two frequently used definitions for CFS/ME are the UK (Oxford) criteria and the US Centres for Disease Control and Prevention criteria.

iIME Comment: The Oxford criteria are now discredited as they are based on too broad a range of patients. Why aren't Canadian criteria mentioned?

Page 36 line 25

It is also clear that, at present, there are no physical signs that identify CFS/ME and there are no diagnostic laboratory tests that can confirm a diagnosis of CFS/ME Therefore a diagnosis of CFS/ME is one of exclusion.

iIME Comment: This is contradictory. See Page 35 lines 6-7 – there are physical signs. The Canadian Guidelines list the range of symptoms and NICE should be using that data.

Page 37 line 12 - 16

The approach taken in this guideline is that of managing CFS/ME as a condition. Detailed guidance about the management of every potential

symptom has not been included since the management of symptoms should follow established principles. For example, the principles of pain management should be applied in managing pain in someone with CFS/ME.

IiME Comment: yet the title includes diagnosis – if not every symptom is analysed then why have you included those chosen? How can the title include diagnosis if not all symptoms are to be examined?

Page 38 line 8

However, there is a lack of epidemiological data for the UK, which means that population estimates are based on extrapolations from other countries.

IiME Comment:

Why is the UK DoH not collecting epidemiological data? How old is this data that states “prevalence of at least 0.2–0.4%”? What is the latest estimate for the UK? This lack of data means that the basis for this document is also suspect as are much of the data from trials.

Page 39 line 7

The 2004 - 2006 CFS/ME Service Investment Programme, which was initiated to address major gaps in service provision across England, has led to the phased establishment of 13 Clinical Network Co-ordinating Centres, 36 local teams for adults’ services and 11 specialist teams for Children and Young People. 65% of the population of England is now covered by the new CFS/ME services.

IiME Comment: However, these are based mainly on psychiatric therapies and are not representative of ME support groups or patients. The job application details are mostly for psychiatric-based experience from job applicants.

Page 39 line 11

Within the first two years of the project, 11,040 adult patients were seen and enrolled into treatment programmes. The children and young people teams have seen 669 children and have established multi-agency arrangements for treatment and support.

IiME Comment: There is no indication or evidence of them being successful or useful. These clinics are called fatigue clinics and will include a wide range of fatigue states which are not ME.

Page 40 line 22-27

This guideline was developed by the NCC-PC and supported by the evidence review carried out by the University of York. The NCC-PC Methods team consisted of a project lead, project manager/researcher and health economist. The evidence review was commissioned from the Centre for Reviews and Dissemination at the University of York (see Appendix 1), and was an update review based on a previous systematic review on the diagnosis, treatment and management of CFS/ME in adults and children.⁵

IiME Comment: This review has been criticized by Professor Malcolm Hooper ([Appendix 6 – 17](#)). 'As a summary of evidence-based medicine for the treatment of Chronic Fatigue Syndrome, section 3 of this systematic review from Bagnall et al. is a failure.'

Page 41 line 5-7 The Guideline Development Group

IiME Comment: By being broad enough membership this guideline development group perpetuates the current situation where a wide range of conditions are mis-represented as ME.

Page 41 line 24 - 2.4 Developing key questions

The following questions were addressed:

- ⌚ Question 1: what are the existing case definitions for chronic fatigue syndrome in adults and children and what evidence exists to substantiate or validate these case definitions?
- ⌚ Question 2: are there any substantiated or validated evaluations to support the diagnosis of chronic fatigue syndrome in adults and children? (Subquestion: In people presenting with early suspected CFS/ME (before 6 months) what are the risk factors/ prognostic flags that might be linked with progression to CFS/ME?)
- ⌚ Question 3: does the evidence show that any particular intervention or combination of interventions is effective in treatment, management or rehabilitation of adults and children with a diagnosis of CFS/ME? (Subquestion: In people presenting with early suspected CFS/ME what interventions might be effective in preventing progression to CFS/ME?)

IiME Comment: Here we reiterate the criticism of the precision of the NICE guidelines with respect to terminology. The first question refers to chronic fatigue syndrome. The second and third questions refer to CFS/ME.

Page 43 line 3 - 2.6 Identifying the evidence

The aim of the literature review was to identify the most relevant, published evidence in relation to the key clinical questions in order to produce an evidence review using a systematic and transparent approach.

IiME Comment: who decides what is relevant? What process is in place to decide what is relevant? How is it that much biomedical research is not referenced in these guidelines? The York review is not adequate to use for this purpose ([Appendix 6 -17](#)).

Page 43 line 21

The GDG found this information is helpful in understanding the patient view, it recognised that surveys from self selected respondents are subject to bias and not necessarily representative of the wider population of people with CFS/ME.

IiME Comment: The same applies to published research using different research criteria. To ignore the history of this illness (ME) and the way it has been shamelessly portrayed by psychiatrists as a somatoform illness is to ignore a vital part of why the state of treatment and research into ME in the UK is in such a mess.

Page 40 and 44

IiME Comment: *"best available evidence"* and *"Information for National Collaborating Centres and Guideline Development Groups"* There is some question about the *"best available evidence"* as input from biomedical researchers has been ignored in preference to the psychosocial input and the National Collaborating Centres have been subject to criticism in their approach to people with ME, especially with the Severity level of *"severe"*.

Page 44 – 45 - Review of the clinical evidence

IiME Comment: *"Consensus development methods were also used"*, however, all biomedical research and proposals of physical illness were downgraded or removed in preference to supporting the psychosocial model. Therefore, in ignoring the inputs available from Prof Puri, Drs Myhill, Kerr, Gow, Spence, Dowsett, et al, this Guideline cannot be considered to have included *"consensus"*.

Page 49 line 20-27

All stakeholder organisations registered with NICE in May 2005 were contacted and asked to nominate 5 to 50 people with knowledge or experience of CFS/ME to take part in the questionnaire. In order to ensure a representative sample of healthcare professionals with experience of the condition, nominees from the CFS/ME Clinical Centres were also solicited. In addition, people who had been nominated to join the GDG, but had not been selected were invited to participate. All patients and carers were nominated by a stakeholder organisation, who asked to obtain their agreement before the Methods team contacted them directly.

IIME Comment: Is this already skewing the results as these are not all CFS/ME patients and are bound to include others who do not have neurological ME.

Look at the stakeholders – even a cursory glance shows mental health institutes, pharmaceutical companies, psychotherapy, Royal College of Psychiatrists. If we are blending these illnesses then the results of these guidelines are bound to be inaccurate and unusable.

Page 50 line 3 onwards

Participants had to agree:

- ⌚ to reading the evidence review, including the evidence and evidence statements, and take part on this basis
- ⌚ that the GDG would have final authority on the content of the guideline
- ⌚ to complete the work and return the questionnaire with their ratings within the allotted deadlines.

Participants were first sent the systematic review from York University (see Appendix 1) and the agreed evidence statements so that they understood the evidence base which the GDG had reviewed before completing the questionnaire.

IIME Comment: This then amounts to a group of people selected to participate without knowledge of their diagnosis, selected by people on a committee who are not necessarily representative of ME patients, and provision of results from a study which is not accepted by the ME community!!!

Page 52 line 7

4. "I truly believe that a lot of people without the condition would have a problem getting to grips with the information and questionnaire!!! I, for one will not be able to help you by returning the questionnaire, When I agreed to be sent the questionnaire I assumed it would be a simple task of answering questions, that would go some way to helping the medical profession reach a worthwhile conclusion. I did not think for one minute it would need over 450 pages of accompanying notes!!!"

5. "How I, or anyone else with ME or even recovered could possibly read, digest and understand the NICE document enough to be able to answer the Questionnaire, is beyond my comprehension.

I surely cannot be the only person who has had this problem, or am I the only honest one around?

I would like this letter to go on record as I feel it is very important for Non-Sufferers to know how difficult a task this was for an ME Patient. Just writing this letter has been hard enough!”

iIME Comment: This is surely typical for most people with ME? Most will have the same problems getting to grips with these guidelines.

Page 54 line 14

Finally, the GDG added some general additional recommendations, which were not rated, where they identified gaps in the guideline’s recommendations.

iIME Comment: Which recommendations are these if they are not substantiated even by the participants in the questionnaire?

Page 54 line 21

The guidance has been developed in accordance with the NICE guideline development process, using additional consensus development. This has included allowing registered stakeholders the opportunity to comment on the Scope and the draft guidance. In addition the first draft was reviewed by an independent Guideline Review Panel (GRP) established by NICE.

iIME Comment: Who was sitting on this ‘independent’ panel? These guidelines need to state this. Is this ‘independent’ panel broadly based or is it composed of career psychiatrists?

Page 57 - 3.2.5 Diet

- “A total of 73% of those who had indicated that they had tried some form of dietary therapy said that it had helped them and only 2 said that it had made them worse.” (*Report on Survey of Members of Local ME Groups, Cooper, 2000*)
- 59% found dietary changes helpful; 25% were uncertain and 16% reported feeling worse. n=354 (*Action for ME, Members Survey, 2003*)

iIME Comment: This is interesting as supplements are not in the recommendations.

Page 57 - 3.2.6 Bedrest

- “Complete bed rest did make 10% of respondents worse. Yet 37% said they were helped a lot by doing this. Total bed rest helped a total of 74% of respondents who had done this.” (*Report on Survey of Members of Local ME Groups, Cooper, 2000*)
- Rest, including bed rest, helped 90%.n=354 (*Action for ME, Members Survey, 2003*)

IiME Comment: Strange, then, that the emphasis of these guidelines seems to be to get pwme out of bed and back to work with GET being offered, despite the comments above.

Page 58 lines 3.2.8 General comments:

Even the least successful regime, graded exercise did help 39% of the respondents to some extent.

IiME Comment: How does this statement tally with the table in this section where 26% said it made them worse and 67% say no change! What about 50% of those using GET who were made worse – how much worse? These comments are really skewing the results.

91% said resting made them better – this should be stressed especially as NICE are recommending exercise to aid recovery and stating that rest is not to be used as an aid to recovery.

Page 78 lines from 1 onwards - 4.1 Recommendations

4.1.1.1 Shared decision-making between an adult or child and healthcare professionals should take place during diagnosis and all phases of care. To facilitate shared decision-making the healthcare professional should:

- acknowledge the reality and impact of the condition and the symptoms.
- provide information about the range of therapies and management strategies as detailed in this guideline.
- provide information on the aetiology, nature, course and approaches towards CFS/ME, including the use of any therapy (such as benefits, risks, likely side effects), and returning to work or education.

IiME Comment: This is a laudable aim. However, significant research is required to identify the aetiology, nature and course of ME, let alone any biomedical approaches in the treatment of ME. Therapies have yet to be established that are safe for application with severe ME sufferers, given the evidence of physical neurological damage from SPECT brain scans and post-mortem examinations of inflammation to the dorsal root ganglia.

Shared decision-making needs to be changed to patient empowerment.

- offer information about access to self-help groups and support groups for adults and children, families and carers. (see www.nhsdirect.nhs.uk, and also the NHS Expert Patient Programme www.expertpatients.nhs.uk/)

IiME Comment: As commented before this site cannot be trusted currently. Also a list of ME charities and support groups could be given.

- be aware that all adults and children with CFS/ME have the right to refuse any component of a care plan without detriment to the provision of other aspects of care.

IIME Comment: Also knowledge of current biomedical research which is underway and what biomedical research is being funded by the Medical Research Council

We welcome the statement that patients are in charge of decisions being made about their care.

We welcome the statement that healthcare staff need to acknowledge the reality and impact of the condition and the symptoms. We would like to have seen this emphasised yet again in the overall recommendations

This would be an improvement if evidence-based logic could support the acknowledgement and replace the conventional medical professional training that states that ME is a psychological problem that can be treated with CBT/GET. Also, the medical professionals should be trained that the psychosocial model is not correctly applied for people with ME, since they do not have a psychological illness as the root-cause of ME, accepting that ME can cause long-term depression and sensitivities to external suggestions.

Page 78 4.1.1.2

Healthcare professionals who are responsible for the care of an adult or child with CFS/ME should have the appropriate skills and expertise in the condition.

IIME Comment: What are appropriate skills? This is meaningless unless these skills are described. Psychiatric skills would not be relevant for a responsibility for pwme.

Page 79 4.1.1.4

As part of the transition process, diagnosis and management should be reviewed. Throughout the transition process there should be clarity about who is the lead clinician to ensure that there is continuity of care.

IIME Comment: We welcome the review of diagnosis and management. We feel that clarity about lead clinician should also be affected/decided by the patient/carer.

Page 79 4.2 Information

This section outlines how good communication between healthcare professionals and patients is essential. People with CFS/ME have diverse information needs and they should be able to access accurate information suitable to their needs. The information patients are given should also be culturally appropriate and accessible to people who do not speak or read English. Carers and relatives should also be provided with the information they need.

IIME Comment: We agree. Accurate information is mandatory. Does this extend to the proper basis for defining the illness? Terminology, the name used by the WHO, the policy of the government/MRC on funding for research,

the ratio of funding given to biomedical research compared with non-biomedical research etc.

Page 79 4.2.2 Evidence Statements

4.2.2.2 There is no evidence as to whether this need for information is specific to CFS/ME or on the content and appropriate mode of delivery of the information (3/4).

IiME Comment: There is much evidence that this is specific to ME. The testimonies of ME patients in this document illustrate how poorly informed many healthcare practitioners are about ME. We do not understand this.

4.2.3 Clinical Evidence Summary

Twelve research survey reports considered the information needs of adults with CFS/ME, their carers and healthcare professionals. Two guideline documents were also reviewed. All agreed that there was a need for information but opinions varied as to the source and type of required. There were no studies with a robust research design which evaluated the effectiveness of different types and sources of information.

In terms of children and adolescents, only two studies and one guideline document were identified. The publications agreed that there was a need for more information but the source and type of information needed is less clear.

Page 80 lines from 9 4.2.4 Health Economics Evidence Summary

No studies were found that addressed the clinical question.

IiME Comment: Isn't this significant?

4.2.5 Clinical Scenarios

Page 80 lines from 9

The GDG decided that clinical scenarios would not contribute to decision making.

IiME Comment: Why? We do not understand this.

Page 81 lines from 1 onwards - 4.2.6 Recommendations

4.2.6.1 Consistent and universally understood definitions of treatments and medical terminology should be applied throughout CFS/ME care (such as those in this guideline. See glossary).

IiME Comment: Why not start with the WHO standard definition and name? Definitions of symptoms and treatments are not universally understood or agreed and some differ significantly from those included in this guideline. Moreover, notable biomedical researchers challenge the basis of the diagnosis and treatment included in this proposed guideline.

Page 81 4.2.6.5

Where adults and children with CFS/ME are able to continue at, or return to work or school, the healthcare professional should ensure that, with the patient's informed consent, employers, occupational health or education institutions have information on the condition and the agreed management plan.

IiME Comment: "*agreed management plan*" shouldn't this be the "*agreed treatment plan*"?

Page 82 4.2.6.6

Healthcare professionals should be proactive in advising about fitness for work and education, and recommend adjustments or adaptations to work or studies to enable rehabilitation of adults and children with CFS/ME. This includes liaising (with the person's consent) with employers, education providers and support services for example:

- occupational health services
- disability services through Jobcentre Plus (<http://www.jobcentreplus.gov.uk/JCP/Customers/Helpfordisabledpeople/index.html>)
- Connexions for schools
- disability advisers in universities and colleges.

IiME Comment: Why not also DLA – the government needs to be informed. Insurance companies should also be informed of the real nature of this illness and be advised not to attempt to enforce therapies or 'treatments' which are not in the interests of the patient.

Page 82 lines from 11 - 4.3 Support

People with CFS/ME should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals.

IiME Comment: Does this include whether to be sectioned or not by police/psychiatrists? Will NICE comment that ME patients should not be allowed to be sectioned if they refuse to take CBT/GET?

Page 83 lines from 1

Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the patient's care and treatment.

iIME Comment: Does this include whether to be sectioned or not by police/psychiatrists?

Page 83 lines from 3

If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (available from www.dh.gov.uk).

iIME Comment: Where has this been analysed by stakeholders? Who determines if these guidelines are valid? How does this statement stand with the statement made on Page 82 lines from 11? How does this stand in relation to the code of practice accompanying the Mental Capacity Act 2005 which needs to be followed by healthcare professionals from April 2007 (That individuals must retain the right to make what might be seen as eccentric or unwise decisions)?

Page 83 lines from 9

Loss of employment or education is generally detrimental to health and well-being. Moreover, the longer that a person is off work due to illness or disability, the less likely they are to return to employment. Therefore, it is very important that work and education are addressed early in the care pathway for CFS/ME, and are reviewed regularly as part of the ongoing management programme.

iIME Comment: Not at the risk of impairing the patient's health. The stress inflicted on patients by insurance companies who force a patient to accept unhelpful therapies and the attitude of DLA personnel needs to change. First one should start by making DLA informed of what ME is.

Page 83 lines from 14

In the case of adults, this would include working with the employer, education and social services to provide appropriate support, adaptations (e.g. reduced or flexible working hours, flexible rest breaks, arrangements for home-working and reduced heavy physical work) and/or equipment (e.g. wheelchair) so that the person can continue at, or return to, work or further education.

Occupational health services are best placed to facilitate rehabilitation back to work.

iIME Comment: Only if they understand fully what a neurological illness like ME is.

Page 83 lines from 27

In the case of children and adolescents, there is a need to work with the family and the education provider (school, college, or university) to provide support. There needs to be close liaison between health, social care and education so there is a common understanding of goals and objectives. Therefore, the view of the GDG was that a key worker, responsible for co-ordinating care was needed. There may need to be a flexible approach with home tuition and use of equipment that allows a gradual reintegration into schools. It is important for the child that their peers understand and they are being supported rather than stigmatised.

IIME Comment: What about education of schools? Schools should have access to the research regarding the biological nature of ME.

Page 86 lines from 1 – 4.3.6

4.3.6.1 A documented, individualised management plan should be developed with the adult or child with CFS/ME, and the carer, where appropriate to include:

- relevant symptoms and history
- plans for care
- information and support needs
- education or employment plans
- details of the healthcare professionals involved in care and their contact details.

IIME Comment: "*individualised management plan should be developed*" - shouldn't this be an "individualised treatment and care plan should be developed"? Shouldn't the subsequent text also refer to "treatment and care" rather than "management"?

Information from ME support groups – details of organizations should be included.

4.3.6.2 A designated healthcare professional should be identified who is responsible for coordinating care for each adult or child with CFS/ME.

IIME Comment: Who designates – what type of healthcare professional. It is pointless having a psychiatrist designated as responsible for coordination of care for a patient with a neurological illness such as ME. It must be somebody who knows the biological background to ME

4.3.6.3 Healthcare professionals should aim to establish a supportive and collaborative relationship with the adult or child with CFS/ME, family, and carers to facilitate their effective management.

iIME Comment: Agree – with patient/carer at centre and in charge of decisions about the patient

4.3.6.4 Support that should be considered for any adult or child with, or suspected to have, CFS/ME are:

- information concerning the illness (see information recommendations)
- acceptance and understanding
- assistance negotiating the healthcare, benefits and social services systems
- availability of care regardless of ability to travel to services
- assistance with social activities including work and education.

iIME Comment: Assistance dealing with insurance companies who do not listen to the patient should be added.

“assistance with social activities including work and education” - is this within the normal purview of support provided by the general medical practitioner to patients with biomedical conditions? Could this be a further indication that the NICE Guideline is following the psychosocial model in preference to the biomedical physical illness model?

Page 87 lines from 1 – 4.3.6.5

Adults and children who are severely affected may need to access, at various times, community services such as nursing, physiotherapy, psychology and occupational therapy (ref NSF long term conditions) –The input of various professionals should be coordinated by a named professional and those involved in care need to be trained in the management of CFS/ME.

iIME Comment: Why psychology for a neurological illness? why not a neurologist? Why not continued medical examinations by a qualified physician?.

Page 87 lines from 2

4.3.7 Deriving Recommendations

The view of the GDG was that support should be provided to assist the person in maintaining as much of their normal life as possible. The emphasis should be on self management with goals and objectives important to the individual.

iIME Comment: We feel the document would need to stress here that goals and objectives need to be balanced with the prime objective of avoiding a relapse or deterioration in the state of the patient.

The GDG discussed the very severely affected who were frequently isolated at home away from services and support.

iIME Comment: Even so-called mildly/moderately affected patients can be isolated – it is not just severely-affected who are isolated at home.

The view of the GDG was that all patients should have access to appropriate service and care regardless of their ability to attend hospitals or clinics. Sometimes, there could be follow-up contact by telephone. The point was made that small improvements in quality of life were very important.

Page 88 lines from 1 - Making a diagnosis of CFS/ME

5.1 Introduction

CFS/ME (Chronic Fatigue Syndrome/Myalgic Encephalomyelitis or Myalgic Encephalopathy) is a condition for which causation is uncertain and diagnostic criteria variable.

iIME Comment: It is not encephalopathy – see WHO ICD 10 G93.3.

Page 88 lines from 9

- The range of presenting symptoms is wide, and fatigue and pain are not always the prominent features.

iIME Comment: So why is fatigue so heavily emphasised and used to influence elsewhere in this document?

Page 88 lines from 11

- Patients may have been investigated extensively, but fruitlessly, for varied physical symptoms and may feel frustrated by the lack of help they have received from the medical profession by the time the diagnosis is made.

iIME Comment: The lack of a proper medical examination and lack of funding by MRC for biomedical research needs to be emphasized as a cause also.

Page 88 lines from 18

- CFS/ME cannot be diagnosed by any test currently available.

iIME Comment: But there are markers (see Dr. Byron Hyde [-Appendix 6 - 14](#)).

Page 88 lines from 23

'Red flags' in the history and examination indicate the need for urgent specialised investigation.

IiME Comment: They also indicate the urgent need for biomedical research to find a diagnostic test for ME.

Page 89 lines from 13 - 5.2.2.1

There is insufficient evidence to show that potential diagnostic tests for CFS/ME are useful diagnostically for adults and children.

IiME Comment: Potential diagnostic tests will be useful in allowing a patient to become prepared early with a diagnosis of ME.

Specific diagnostic tests reviewed are:

- the head up tilt test(2/3)
- five laboratory blood tests (fibrinogen, prothrombin fragment 1+2, thrombin-anti-thrombin complexes, soluble fibrin monomer (SFM) and platelet activation (CD62P, ADP)) (3)
- auditory brainstem responses (3)
- electrodermal conductivity (3).

IiME Comment: These tests may, however, identify subgroups of CFS/ME.

Page 90 lines from 1 - 5.2.4 Evidence Statements

5.2.4.1 Clear risk factors for CFS/ME have not been identified. (2-)

5.2.4.2 There is low grade or limited evidence for a wide range of risk factors including:

- sick certification after viral illness,

IiME Comment: What about the viral illness itself?

- presence of fatigue at time of viral illness,

IiME Comment: Is this implying that the fatigue is the causative factor rather than the viral illness?

- lower physical functioning,

IiME Comment: This must be really low grade evidence if it exists?

- higher pain and fatigue scores at baseline, older age (adults and children),

IiME Comment: We fail to see what evidence this can refer to.

- exhaustion,
- being female,
- low educational level,

IiME Comment: Well, this puts the end to the idea of “yuppie flu”!!!! Are NICE really stating that people of lesser education are now the suspects for ME?

- visits to the GP,

IiME Comment: This we find ridiculous! Are NICE stating that people who need to visit their GP are more inclined to get ME? Maybe the frequency of visits might have something to do with being disbelieved? It might have something to do with symptoms persisting despite ‘standard’ treatment? Is NICE attempting to portray ME patients as hypochondriacs?

- longstanding limiting medical condition aged 10 years,
- higher social class in childhood,

IiME Comment: And yet lower educational level earlier!

- psychological distress prior to presentation,

IiME Comment: Where is the evidence for this? It does NICE no credit to list these ‘risk factors’ without supplying evidence.

- presence of infectious mononucleosis,
- positive Monospot tests at time of onset,
- time in bed at onset,
- exercise power,
- mood disorder. (-2)

IiME Comment: We do not believe this is worthy of a document purporting to assist diagnosis or treatment of ME.

It is widely accepted that ME follows viral or bacterial infections, vaccinations, chemical exposure. Yet these risk factors are not mentioned at all.

There is no mention of the pressure on returning to work or school prematurely after infection as a cause for long term ME.

What is low grade is the research funding and epidemiological studies.

5.2.4.3 Clear risk factors for development of CFS/ME in children and young people have not been identified (2-)

IiME Comment: How about pressure to return to school too early?

Page 91 lines from 18-23 - 5.2.5.2 Additional Clinical Evidence

No new evidence was found in the update searches.

However, a recent paper in the BMJ concluded that 'prolonged fatigue states after infections are common and disabling' and that post-infective fatigue syndrome was predicted 'largely by the severity of the acute illness, rather than by demographic, psychological, or microbiological factors'. This strengthened the recommendation regarding post viral management.

IiME Comment: What about Vance Spence and oxidative stress? This is due, perhaps, to the make up of the NICE group which seems to have nobody qualified to analyse this data.

Page 91 lines from 25 - 5.2.6 Health Economics Evidence Summary

The investigations needed to rule out other significant disease before making a positive diagnosis of CFS have a number of components which are of importance from an economic perspective.

IiME Comment: Are we still discussing ME or is it just now CFS? These are very lax standards of precision in this document.

Page 92 lines from 12-17

Any approach which produces the same outcome for less healthcare provider time will improve the cost-effectiveness of the overall process.

IiME Comment: This last sentence is so risky as it will inevitably lead to short-cuts, lack of precision in diagnosis and almost inevitable degradation in treatment.

Page 92 lines from 18

Regarding the role of investigations after a positive diagnosis of CFS has been made, the likelihood of the result of the investigation changing management should be considered, together with the improvement in quality of life that change might bring, and contrasted with the cost of the investigation and the disutility of the investigation to the individual

IiME Comment: Are we still discussing ME or is it just now CFS? These are very lax standards of precision in this document.

Page 93 lines from 1 onwards - 5.2.7 Clinical Scenario Questionnaire to GDG and Wider Group

1. The person with the CFS/ME and health care professionals involved in their care will make decisions in partnership. These are directed by the patient's personal preferences and builds on the existing experience and skills of the professional.

iIME Comment: Elsewhere it is the patient who is in control yet here it is partnership. It should be consistent throughout these guidelines that the patient is always in control. Decisions cannot be based on existing experience of the 'professional' if they are biased or lacking in appropriate knowledge. This very much depends on the healthcare professional associated with the patient.

2. All treatments are offered allowing the person with the CFS/ME to refuse without compromising the further therapeutic relationship.

iIME Comment: Yes – this is extremely important

4. Treatment is provided by the NHS in the context of availability of adequate numbers of competent, appropriately trained health care professionals.

iIME Comment: This is important but who decides 'appropriately trained'?

Page 104 from line 1- 5.2.8 Recommendations

Primary healthcare professionals should be familiar with the presenting features of CFS/ME, and be able to identify these features when adults and children consult.

CFS/ME should be considered if an adult or child has fatigue that is all of the following:

- persistent and/or recurrent, and
- unexplained by other conditions, and
- results in substantial reduction in previous activity level, and
- characterised by post-exertion malaise and/or fatigue (often delayed with slow recovery),

AND one or more of the following symptoms:

- difficulty with sleeping (for example,, insomnia, hypersomnia, unrefreshing sleep, disturbed sleep/wake cycle)

- muscles and/or joint pain(multi-site without evidence of inflammation)
- significant headaches of new type, pattern or severity
- painful lymph nodes without pathological enlargement
- sore throat
- cognitive dysfunction, for example difficulty thinking, inability to concentrate, impairment of short-term memory, word-finding difficulty, difficulty to plan/organise thoughts, difficulty with information processing
- physical or mental exertion making symptoms worse
- recurrent flu-like symptoms
- dizziness, nausea and palpitations.

IiME Comment: This is too broad a definition. The Canadian Guidelines is more specific and should be used.

Many tests exist in aiding a diagnosis for ME. Therefore, using psychological therapies for 'unexplained fatigue' is inappropriate. Although diagnostic tests for ME are still being worked upon with promise, nevertheless many tests and procedures can be administered in aiding a diagnosis of ME. These include the use of SPECT, MRI and PET scans, test for NK cell activity and endocrine abnormalities, Tilt Table Test, viral tests and many more ([Appendix 6 – 13](#)). Although these tests aren't always offered by the NHS for ME, they have nevertheless shown evidence of physical abnormalities.

Head-up tilt test is used in research for examination of ME patients. Serology for chronic bacterial infections e.g. borelliosis – this ought to be present as standard.

It is unbelievable that serology testing for latent infections (toxoplasma, EBV (Epstein Barr virus), CMV (cytomegalovirus)) "in the absence of any indicative history," is not performed.

Where is the test for mycoplasma which is implicated in many ME cases?

Page 105

"similar symptoms and signs as CFS/ME"

IiME Comment: The biomedical community have listed a number of contraindicative conditions that need to be considered in isolating a diagnosis of ME These could be proposed for inclusion here to replace the existing text.

Primary healthcare professionals should listen carefully to parents' and/or carers' concerns and be willing to reassess their initial opinion, or to seek a second opinion from a 'colleague' if a child fails to recover as expected.

IiME Comment: who is 'qualified' and who is a 'colleague'?

This is a very interesting formulation of expression, as this could come from the discredited MSBP diagnosis criteria, and is obviously biased towards the psychosocial model. Biomedical experience of ME professionals confirm that it is quite a common occurrence that patients do not recover in the traditionally anticipated manner. However, this does not indicate psychological intervention, rather a lack of understanding of the aetiology and treatment attempted.

Surely a referral to a paediatrician with expertise in ME should be made to ensure that ME is correctly assessed, rather than a general paediatrician? Shouldn't a referral be made more rapidly than "within 6 weeks"?

As with other potentially chronic conditions, before progressing to a diagnosis of CFS/ME, medical examination and assessment of mental health (both targeted according to the presenting symptoms) should be carried out.

IiME Comment: Why mental health – is this applicable to all other illnesses – such as cancer, MS, IBS? This is quite shocking.

Is it usual to have psychiatric assessments of patients presenting with "*potentially chronic conditions*"? This, again, indicates bias towards the psychosocial model.

Page 106

In the absence of a definite diagnosis and/or while waiting for referral, advice and symptom management should not be delayed until a diagnosis is made.

IiME Comment: This statement again goes in direct contravention of the biomedical model, where treatment requires a specific diagnosis.

When an acute infection is followed by excessive fatigue, the adult or child should receive advice on how to promote recovery. The advice should focus on sleep management, risks of prolonged bed rest (for example, deterioration in muscle function), and a gradual return to a normal daily routine.

IiME Comment: Surely the promotion of adequate rest is more important. The testimonies in this document alone detail the risk of returning to activity too soon. You are not listening to the patients.

How about the risks of GET and CBT and other psychological therapies? The benefits of adequate rest need to be emphasised along with adequate supplies of current, accurate information about ME and the research which is underway.

Investigations should be tailored to the history, and signs and symptoms of the adult or child, taking into account other possible diagnoses.

iIME Comment: What does this mean? It is so loose that it is an irrelevant comment.

Before progressing to a diagnosis of CFS/ME, investigations should be carried out to exclude other diagnoses that would explain the symptoms. Such tests could include the following, but clinical judgment should be used.

- Urinalysis for protein, blood, glucose.
- Full blood count.
- Assessment of blood ferritin levels (children only).
- Urea & electrolytes.
- Liver function tests.
- Thyroid function tests.
- Erythrocyte sedimentation rate / plasma viscosity.
- C-reactive protein.
- Random blood glucose.
- Serum creatinine.
- Screening blood tests for gluten sensitivity.
- Serum calcium.
- Creatinine kinase (children only).

iIME Comment: What is the physical biological/biomedical basis for defining these clinical tests in relation to the aetiology of ME? This list needs to be modified, at a minimum. Prof Puri has identified raised levels of Choline along with other chemicals in the brain blood interface in ME patients, and Drs Kerr and Gow have identified modified gene expressions unique to ME patients. If we look at the gene array we do find some abnormalities, but if patients with ME/CFS, exercise then we find a lot more abnormalities. The standard NHS blood and thyroid function tests have been shown not to address specific expressions in ME patients and, therefore, cannot provide reliable results. There is still debate about specific thyroid function tests being implicated in ME, e.g. maladjustment of T3 and T4 levels that do not provide the expected results.

Page 107

The following tests should not be done routinely.

- Serology testing for chronic bacterial infections (for example, borelliosis) in the absence of any indicative history.

IiME Comment: It is an odd assessment to ignore this with current evidence available. The potential of misdiagnosis is great. This test needs to be considered.

- Serology for general viruses (for example, heterophile antibody tests for infectious mononucleosis) in the absence of any indicative history.
- Serology testing for latent infections: toxoplasma, EBV (Epstein Barr virus), CMV (cytomegalovirus) in the absence of any indicative history.

IiME Comment: Mycoplasmal infections need to be found early as it is implicated in CFS/ME cases and can be treated with antibiotics.

Some of the infectious agents which have been associated with development of CFS/ME and for which an established treatment exists are Enteroviruses, Epstein-Barr virus, Cytomegalovirus, Human herpes virus-6, Parvovirus B 19, Hepatitis C, Chlamydia pneumoniae and Coxiella burnetii ([Appendix 6 - 18](#)) and whether elevated levels of Choline can be used as a "fingerprint test" for ME, as suggested by Prof Puri.

Page 107 lines 3-6

5.2.9 Deriving Recommendations

The GDG decided that certain investigations should be carried out to rule out other diseases and conditions, but it was impossible to recommend a definitive, comprehensive list

IiME Comment: which surely shows a failing in these guidelines. We need to have a list, which can be added to as more research becomes available. These guidelines already rule out necessary testing of known mis-diagnoses.

Page 108 lines 3 onwards

As stated above, viral serology, in the absence of a recent history suggesting viral infection, should not be carried out. In reviewing the results from the wider survey, the GDG decided that it was difficult to establish a link between CFS/ME and serology indicating past viral infection and that serological evidence of past infection would not alter the patient's management

IiME Comment: But it might give earlier diagnosis- what about antimicrobials used early? ([Appendix 6 - 18](#)). See earlier response re Devanur and Kerr.

Page 109 lines - 5.3 Arriving at a Diagnosis

5.3.1.1 Evidence to substantiate existing case definitions of CFS or ME is limited. No studies have established the superiority of one case definition over another

IiME Comment: Why are the Canadian Guidelines Criteria not referenced here, since they are becoming more widely accepted around the world by the biomedical community of ME experts, rather than inventing a further set of criteria that are not agreed outside the psychosocial model practitioners?

5.3.1.2 Community based studies have indicated that patients meeting CDC 1994 criteria form a more heterogeneous group than patients meeting CDC 1988 criteria (2-)

IiME Comment: So shouldn't Canadian guidelines ("even more stringent" according to NICE) now be used ?

Page 110 - 5.3.2 Clinical Evidence Summary

The definition of CFS/ME is based upon its classification as a 'syndrome,' that is, a pathological condition characterized by its symptoms rather than its cause. The systematic review conducted by the Centre for Reviews and Dissemination (CRD) at the University of York forms the primary evidence base for adult-onset CSF/ME in this guideline

IiME Comment: Isn't this then putting the whole guidelines document at risk as that York review was limited and unrepresentative

Page 111 lines 4-8

The Oxford Criteria of CFS/ME, developed in 1991 by British psychiatrists Simon Wessely and Michael Sharpe defined CFS/ME as a "syndrome in which fatigue has been present for at least six months, during which time it has been present more than 50 per cent of the time." Other symptoms may also be present such as myalgia, mood and sleep disturbance. .

IiME Comment: These are psychiatrists and cannot represent a pathological illness. The Oxford criteria are far too broad to be of any use.

Page 111 lines 27

The 2003 Canadian definition is more stringent and was developed by an international CFS clinical team.

iIME Comment: So why not recommend the use of the Canadian Guidelines if they are more stringent.

Page 113 lines 17 onwards Health Economics Evidence Summary

iIME Comment: The economics of diagnosis are of little interest. Accurate diagnosis is the requirement and will likely lead in the long term to economies. We believe it is a false economy to attempt to quantify at the outset which line of diagnosis is to be used based on this ROC curve model.

Page 116 lines 4 onwards

1. The person with the CFS/ME and health care professionals involved in their care will make decisions in partnership. These are directed by the patient's personal preferences and builds on the existing experience and skills of the professional.

iIME Comment: Patient must be in control, not just partnership. Will this model then support a patient who refuses CBT and GET, in the knowledge that these therapies are either unhelpful or harmful, when insurance companies demand that they be used?

2. All treatments are offered allowing the person with the CFS/ME to refuse without compromising the further therapeutic relationship.

iIME Comment: Agreed. We welcome this.

3. There is a good rapport in which the patient and their families/carers feel believed and validated.

iIME Comment: Do NICE apply similar comments to other biological illnesses – cancer, MS, HIV/AIDS? Do these patients have to be 'believed' and 'validated'? Isn't this indicative of the current environment where ME patients are treated as having a somatoform condition?

4. Treatment is provided by the NHS in the context of availability of adequate numbers of competent, appropriately trained health care professionals.

iIME Comment: Who decides which 'professionals' are competently trained. These should be specified.

Page 124 lines 1 - 5.3.5 Recommendations

5.3.5.1 A diagnosis of CFS/ME in an adult should be made after symptoms have persisted for 4 months, and after other likely causes of the symptoms have been ruled out

IiME Comment What are the agreed criteria for diagnosis? Shouldn't the international Canadian Guidelines be used for such a diagnosis, and what is the reason for the proposed 4 months delay? This again flouts accepted international wisdom that early diagnosis and intervention can help prevent the onset of severe ME and provide evidence for refinement of diagnostic tools.

5.3.5.2 The diagnosis of a child should be made by a general paediatrician after symptoms have persisted for 3 months and other likely causes of the symptoms have been ruled out

IiME Comment Again, a paediatrician with expertise in ME would, surely, be more appropriate. Also, why wait 3 months for a diagnosis, as a different time period from an adult? Early diagnosis is even more important for children.

5.3.5.3 When a diagnosis is made, a prognosis of cautious optimism should be conveyed. With appropriate management, most children and adults, but not all, will have some improvement and some will recover fully.

IiME Comment: What is the scientific basis for this statement? Why single out this illness from others. Where is the basis for this statement? 'Some' adults, 'some' children, 'some' will and 'some' won't. Define or quantify 'some'.

Otherwise this is a totally pointless statement. Patients want honesty – even children – so it is better to be realistic and factual rather than woolly and unspecific

Has there ever been any scientific research published in the international community to base such a prosaic statement for cautious optimism. Has there been a scientific or rigorous assessment of the outcomes of ME patients? This paragraph/statement raises a number of major questions that need to be answered before the statement could be accepted, such as: how many patients were involved; what was the patient selection criteria; what were the diagnostic tools used to confirm the cohort was purely suffering ME; were there other medical or clinical influences; over what period of time did the study follow individual patients progress; what happened to the severe ME sufferers; what were the demographics; what were the statistical analysis results; what appropriate management techniques were trialled; what were the statistical samples of age and gender; what definition of "most" was employed, e.g. simple majority of all participants over/under a defined age; what percentage recovered fully; how was "some improvement defined"; who performed the research; was more than one medical research centre involved in the research; was the research approved by the Medical Ethics Committee; what clinical and research qualifications did the researchers possess; where were the study results published; who were the independent academic referees who assessed the academic and scientific rigorousness; and, who funded the study to be conducted? If any of the above questions

can not be answered with adequate academic probity, then the statement must be removed.

Page 124 line 5 - 5.3.6 Deriving Recommendations

Diagnostic Criteria

The GDG reviewed the current diagnostic criteria, but did not find any one of them particularly helpful in managing the condition or in making a definitive diagnosis.

IiME Comment: This cannot be correct. The Canadian guidelines give specific expertise on diagnosis. Other specialists (Dr. Byron Hyde) also have good diagnostic criteria.

Page 124 line 7

The case definitions used in research papers are not necessarily helpful in clinical practice, especially in a condition whose symptoms evolve gradually and where early recognition and treatment is probably beneficial.

IiME Comment: Acute onset ME is not gradual. Most ME cases are acute onset.

Page 124 line 12

The GDG was concerned that the application of narrow diagnostic criteria may make it less likely that advice and treatment is given early in the course of the illness. On the other hand, the GDG were also concerned that if broader criteria were used, people would be falsely diagnosed and other serious conditions missed.

IiME Comment: Exactly - which is why the Oxford criteria are unfit for ME. Why does NICE continue using these criteria and not come out in favour of the Canadian guidelines which are more stringent? There is no point in having generalised and inaccurate criteria – such as the Oxford – if it means including other conditions due to the range allowed. This document is supposed to be for a neurological illness.

Page 125 line 12 - Making a diagnosis

However, the GDG decided that a diagnosis was crucial to the patient and their families in understanding their symptoms and receiving appropriate treatment. It must however, be considered a working diagnosis and regularly reviewed

IiME Comment: Shouldn't it be based on a thorough medical examination? Patients should be treated as individuals and not be the object of labelling.

CFS/ME should not be seen as a dead end diagnosis where all investigations stop and patients are only called in for note taking.

Page 125 line 18

Signs and Symptoms

There was strong agreement that persistent, debilitating, post exertional fatigue characterised the condition

iIME Comment: So why is GET recommended?

Page 132 line 1 - 5.4.5.1

iIME Comment: [*Referral to specialised care ...*] A referral of a patient diagnosed with ME should follow agreed diagnostic criteria that have been developed by gaining an understanding of the aetiology of the illness. Is there a “fingerprint test” that can differentiate Chronic Fatigue states from the neurological condition defined by the WHO ICD-10 93.3 definition? If not referral should be based on “cautious best practice approach”, noting that patients suffering with severe ME may be damaged by the application of GET and that there is no proof that CBT can assist such conditions. In fact, the “drop-out” rate of severe ME patients from the CNNC centres would suggest that CBT provides no positive outcomes. The CNNC should be able to provide statistics for their operation. However, it is noted that without scientifically rigorous statistical analysis this response statement is purely anecdotal, like much of the content of the proposed NICE guidelines.

[*Referral ...*] In addition to previous comments about timescale delays for referrals, what criteria are to be used to select the “moderate” or “severe” ME symptoms to instigate accelerated or immediate referral action? This statement seems to contradict a previously stated (and challenged) need for a diagnosis after 4 months for an adult and 3 months for a child.

Page 132 line 1 - 5.4.5.3

The GDG considered that when seen in the early stages of illness, it is reasonable to observe adult patients for a few weeks before specialist referral as some patients will improve spontaneously. The view of the GDG is that no adult should wait for more than 6 months for a referral.

iIME Comment: In the early stages of illness it is important to identify viral or bacterial causes and treat them early with relevant antimicrobials.

What are the statistics relating to this (wonderful event of) spontaneous improvement? From which clinical study are the published and peer-reviewed results available? The Guideline Development Group and the Independent Guideline Review Panel established with the National

Collaborating Centre should have reported the significant findings to support this statement. Without the scientific basis to support this statement, this statement should be removed or reworded to - "Some patients who are not found to have ME will improve spontaneously".

Page 133 line 7 onwards

Referral to a multi-disciplinary team specialising in CFS/ME

The GDG decided that a referral should be made following a diagnosis. However, this may be a provisional diagnosis rather than a certainty. The view of the GDG was that 3-6 weeks following the onset of symptoms was generally too short a time but that 6 months is too long. The GDG decided that 3-4 months following the onset of symptoms, once exclusion tests were completed and following a provisional diagnosis, was generally the appropriate time to refer patients to a multi-disciplinary team specialising in CFS/ME. However, this needed to be based on the individual, as people with severe symptoms needed to be referred immediately.

IiME Comment: Infectious agents (such as *Mycoplasma pneumoniae*), which are implicated in ME, may not be picked up by the test recommended to be performed by a GP. It is no point in waiting 3-4 months before prescribing antibiotics.

Lyme Disease needs to be treated early so the diagnostic test (preferably the more precise US or Euro version) needs to be made.

It is not only patients with severe symptoms who need to be treated early.

Page 133 line 16 onwards

5.5 A Conceptual Framework

There is little understanding of the nature of the disease and there were differing views on the GDG about this with lengthy discussions. A view held by a few individuals on the GDG was that CFS/ME could not be identified or managed unless a broader view was taken. This perspective is put forward below.

IiME Comment: Views by ME support groups show that ME must be seen as a distinct and separate illness from CFS. This is part of the problem with healthcare staff and others – by broadening the view inevitably the requirements for diagnosing and treating ME patients will be diluted.

Page 133 line 20 onwards

A conceptual framework for patients and health professionals when making a diagnosis of Chronic Fatigue Syndrome

IiME Comment: Are we now talking only of CFS? Complete lack of precision in this terminology !!!

A diagnosis of Chronic Fatigue Syndrome (CFS) is made on clinical grounds alone after the exclusion of conventional disease processes that could account for the wide-ranging symptoms that are usually experienced by patients with CFS. As there are no objective abnormalities to account for the illness experienced and the associated disability suffered in CFS, additional distress for patients, their families and the wider social network commonly occurs. Importantly, the lack of an objective definition of CFS as a discrete disease entity can jeopardise the therapeutic relationship between patient and healthcare professional with a consequent adverse impact on the healing process.

The relationship between the individual with CFS, their families and health professional can be further stressed by disagreements about the origins of CFS.

IiME Comment: Are we now talking only of CFS? Complete lack of precision in this terminology !!! Appalling precision in these guidelines.

Page 134 line 5 onwards

Entrenchment and polarisation of viewpoints about a physical or psychological origin of CFS undermines relationships that support recovery

IiME Comment: so much evidence exists to support the biological viewpoint that this should not be here at all. ME patients are concerned about treatment for ME patients – not CFS

Another consequence of the unclear definition and aetiology of CFS is the difficulty experienced by patients and healthcare professionals in distinguishing CFS from several overlapping conditions such as fibromyalgia and irritable bowel syndrome.

IiME Comment: This is ludicrous – ME has clearly distinct symptoms which proper medical examination will show.

Differing beliefs about definition and cause of CFS can extend from the patient and the doctor to family members and the wider community resulting in dissatisfied, disabled patients and frustrated doctors.

IiME Comment: It also results in bigoted and biased doctors

The patient journey can become an ordeal with unnecessary distress, added costs and waste for the health economy, the patient and their family.

CFS has been described as part of a broader condition that includes a range of related disorders including fibromyalgia, irritable bowel syndrome, chronic pain, pelvic pain, temporomandibular joint dysfunction and atypical facial pain.

IiME Comment: Are we talking about CFS or ME?

ME has also been described as a multi-system order involving immunological, endocrinological, cardiovascular and gastroenterological.....

Page 134 line 25 onwards

Terminology used by doctors such as 'functional syndrome' and 'medically unexplained symptoms' are part of common usage in clinical practice today. The terms have arisen to describe non-conventional diseases and are intended to validate CFS and overlapping conditions to help improve patient care and research into the disorder. Although the term 'functional' has been found to be more acceptable with patients than terms such as 'psychosomatic' or 'medically unexplained', some terminology has become derogatory with use.

IiME Comment: Are we talking about CFS or ME?

This shows the hypocrisy with current healthcare in the UK toward ME. The reason that some terms have become derogatory relates to the lack of guidelines to healthcare staff to see the biomedical evidence behind ME and to obfuscate the issue by insisting on treating ME with psychological therapies.

"The terms have arisen to describe non-conventional diseases and are intended to validate CFS and overlapping conditions to help improve patient care and research into the disorder".

The term ME has been in the WHO ICD category as a neurological illness for a long time.

NICE could have taken the initiative and used the WHO term. Instead it does nothing but perpetuate the myths here.

For some patients and health professionals, the functional concept and all associated terminology are deemed unacceptable. The 'mental or physical' condition debate predominates in the clinical encounter undermining the doctor patient relationship.

IiME Comment: These NICE guidelines are doing little to prevent this from continuing.

Page 135 line 1 onwards

Outcomes are likely to improve if the diagnosis of CFS is communicated more successfully through a collaborative approach between the patient and doctor leading to a therapeutic relationship.

IiME Comment: Are we talking about CFS or ME?

This requires doctors to take an active approach to provide accurate information and to discuss key issues with patients on an ongoing basis to achieve better outcomes.

IiME Comment: It also requires the doctor to be aware of current and past biomedical research.

If an effective therapeutic relationship is to develop, doctors must acknowledge that, despite the current lack of understanding of underlying causes of CFS (**IiME Comment: Are we talking about CFS or ME?**), the symptoms are real and the suffering and associated disability is genuine. The ideas, concerns and expectations of the patient, carers, families and the doctor should be explored for differences and similarities.

Appropriate and agreeable terminology and understanding is important when making a diagnosis and establishing a therapeutic relationship. The definition and concept of CFS (**IiME Comment: Are we talking about CFS or ME?**) through a biopsychosocial model acknowledges the role of both external and internal influences on the development of and recovery from CFS (**IiME Comment: Are we talking about CFS or ME?**). The biopsychosocial model negates the duality of mind or body and a significant cause of conflict between the patient and healthcare professional.

IiME Comment : The failure to explain the biopsychosocial theory on which NICE recommendations for treatment are based;

This is caused by bodies such as NICE perpetuating these myths in the face of evidence and patients' experiences, supported by overwhelming biomedical evidence, proclaiming that Wessely-style theories are nonsense.

What is the science behind biopsychosocial approach.

As with any other chronic disorder the patients attitude to his or her illness experience and disability, the understanding of the nature of the condition and its likely course over time together with the relationship between patient and doctor are likely to have a significant impact on long term outcomes.

IiME Comment: This document purports to discuss CFS/ME – but the number of times CFS alone is mentioned shows poor editing, analysis and devalues the contents. This chapter is named MAKING a DIAGNOSIS of CFS/ME – CFS is mentioned alone many times. CFS is not the same as ME!

Page 135 line 25 - References

IiME Comment: The references below are related to psychiatric papers and should have no place in discussion about neurological ME. Unless there is a separate agenda with the NICE document?

Why not list references from Spence, Hooper, Hyde, Carruthers, Jason, Cheney, Peterson, De Meirleir, Myhill, Kerr, Puri etc.

Page 137 line 1 onwards

6 Management

6.3 CBT, GET, Activity Management and other self management techniques

6.3.1 Introduction

It is recognised that patients would access the expertise of the appropriate health care professional for advice and support, but the GDG considered that patients should take the lead on any behavioural approaches to manage their CFS/ME.

IiME Comment: This is to be welcomed and needs to be emphasised elsewhere in these guidelines instead of the inconsistency that exists.

Page 138 line 21-28 onwards

6.3.1.1 Cognitive behavioural therapy (CBT)

CBT is a well understood and well researched therapy which is described in detail in the recommendations.

CBT is an evidence based treatment for CFS/ME.

IiME Comment: Here, in the same section, NICE state that CBT is a therapy. The next sentence states that it is a treatment. This is appalling precision and contradicts the earlier definition in the glossary. The evidence is based on research using Oxford criteria which are discredited.

CBT is a psychological therapy and collaborative treatment approach which 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

IiME Comment: Unfortunately this isn't true as the number of psychiatrists whom NICE have included as references in this document are all earning livings from recommending psychological therapies and from treating ME with a biopsychosocial model for treatment and by stating that ME is a somatoform illness.

Page 138 line 27

It is used in many health settings including cardiac, cancer, diabetes and chronic pain as well as with mood disorders such as anxiety and depression.

IiME Comment: This infers something which should not be here. It is not first line treatment for cancer, diabetes. This is what NICE are proposing for ME. The CBT offered to cancer patients is not the same as that offered to ME patients where patients are asked to change their illness beliefs!

Page 139 - 6.3.1.2 Graded exercise therapy (GET)

GET is an evidence-based self-management approach to CFS/ME involving appropriate physical assessment, mutually negotiated meaningful goal setting and education. It involves setting an achievable baseline of physical activity, followed by individually tailored and planned increases in duration of exercise. This is followed by an increase in intensity when able; taking into account a patient's preferences and objectives, current activity patterns, sleep, setbacks, and emotional factors; with the objective of improving CFS/ME symptoms and functioning aiming towards recovery.

IiME Comment: GET has a poor record of doing anything useful with ME patients. GET, as practiced, does not take into account a patient's preferences. How can a recovery be an objective with the use of GET when the causes of ME are 'unknown'?

Page 139 – line 9 Goals

In clinical trials the ultimate goal of GET which showed benefit is to achieve and maintain 30 minutes of moderate aerobic exercise, 5 days out of 7 (for example, a brisk walk). Clinically, patient-centred goals developed are developed from this objective by discussing what this means in their everyday life and according to their circumstances: for example, 2 x 15 mins daily brisk walk to the shop, return to previous active hobby, such as cycling or gardening. For the more severely affected, it may be useful to set more achievable goals and progress to this ultimate goal if and when able. This may include such tasks as walking around the room, or sitting up in bed to eat a meal.

IiME Comment: This is nonsense - and not only severely affected people with ME will be at risk. Also moderately affected people with ME can relapse due to this advice. 2 * 15 minute brisk daily walks are impossible for some mildly affected patients. This is more like a treatment for burn-out or over-training syndrome than for an illness where infection may play a part. ME is a neurological illness.

Page 139 – line 28

GET is a carefully mutually developed programme, undertaken with the patient in control of their goals and their rate of progression. It is a structured and monitored programme that plans gradual increments of exercise or physical activity, utilising a specific formula known to be successful for patients with CFS/ME in previous research.

IiME Comment: What criteria are used by indicating ME patients? Again these are probably based on research using the flawed Oxford criteria and are therefore worthless.

This is in vast 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'. An unstructured and poorly monitored or

progressed exercise programme such as this can cause significant symptom exacerbation, and can make people with CFS/ME worse.

IiME Comment: there is no argument amongst ME patients. There is proof from surveys that GET is harmful. Oxidative stress caused by this type of treatment is known, and proven to be harmful (see ME Research UK Research Appendix 6 - [10](#)).

Page 140 line 12

A **GET** programme, as described in this guideline, is evidence- based for this population and has shown to be of benefit to most patients; a **general exercise programme** is not evidence based and can do patients more harm than good.

IiME Comment: Untrue – research has shown it to be harmful. It shows a complete lack of vision to trawl out this same therapy when it is known to be harmful.

NICE also ignore what happened to other patients who did not benefit. Maybe the frequency and propensity for relapse ought to be monitored.

Page 141 - 6.3.1.3 Activity management

Activity management is a person centred and 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.

Activity management is the approach that many therapists adopt for those in the severe and moderate categories and indeed it teaches skills for life for those who are moving towards a return to work and higher levels of productivity. Access to, and contact with therapists who use this (and any of the other approaches), such as community rehabilitation teams, occupational/physio-therapists and rehabilitation care assistants should be ongoing and ideally, patients should be able to refer themselves for "top up" sessions should life demands make it necessary.

IiME Comment: This all reads as an accepted view that activity is required even though the cause of the illness is unknown.

Page 142 - 6.3.1.6 Management of set backs

People with CFS/ME have variations in the severity of their symptoms and will experience setbacks or transient increases in fatigue and other symptoms. Setbacks are to be expected as part of the normal course of recovery and rehabilitation in CFS/ME. With effective management of CFS/ME, the frequency, severity and duration of setbacks should reduce

IiME Comment: where is the evidence of this? What is effective management? Is this common sense applied to the situation? Or is NICE inferring that this is due to psychological therapies?

Page 142 line 7

Setbacks appear to be caused by different (things), commonly sleep disturbance, overactivity, stress, or during an active infection (such as a common cold)

IiME Comment: One could also argue that setbacks are caused by graded exercise, CBT, lack of knowledge of the biological nature of ME by GPs, efforts performed having to argue with DLA officials etc.

The advice given regarding the management of setbacks may vary according to the cause: for example, it is advisable to maintain an exercise programme if stress has been a causative factor, but not if there is an active infection

IiME Comment: this contradicts earlier statements. Dr. Jonathan Kerr's research has shown that active infection is still prevalent in ME patients without other causative factors – i.e. an infection present from the start of the ME which is still ongoing may be the cause of relapse.

Page 143 line 1 onwards

Mild / moderate setbacks

– Maintain usual activity levels or implement a gentle reduction in levels of activity and exercise

IiME Comment: NO – it is imperative that a patient listens to their body and stops activity if necessary. This type of advice is worthless in a document as no one in their right minds would consider it. This is dangerous documentation by NICE especially as the cause of this illness is 'unknown'.

Page 143 line 3

– Continue activity management by alternating activities with breaks and pacing activities

IiME Comment: Wrong! A patient should discontinue until one's body is telling one to restart. This shows how lacking in reality this document is. Temperature can be associated with the symptoms of ME and should not be ruled out as part of an infection.

Page 143 line 13 onwards

- Resume your usual activity and normal living as soon as possible in a structured way with guidance from the CFS/ME team

- A couple of days later gradually build up activities
 - Slowly begin to decrease frequency and length of rest periods
- Ensure that the setback plan is kept somewhere easily accessible

iIME Comment: who needs this sort of advice? The patient must go by their own body signs and feelings – not by an enforced regime of activity. It is totally ridiculous to talk of waiting ‘a couple of days’ before building up activities. It has to be based on an individual’s experience. This is nonsense. It is impossible for patients, even moderately affected, to follow guidelines like this. Again this seems to be advice for burn-out – not for a neurological illness.

Page 143 line 24

During a severe setback

- Follow setback plan – contact support, put strategies into place
- Review activity/exercise programme with CFS/ME team

iIME Comment: The advice needs to be to stop exercise and non-functioning psychological therapies and contact a doctor.

- Reduction of some activities may be necessary initially to re-establish a baseline and stabilise symptoms
- Ensure that a rest/activity programme is in place using good quality rest periods and relaxation techniques.
- Increasing the frequency of rest periods may be required, increasing the duration of rest periods may be appropriate depending on the severity of symptoms – this should be discussed with the CFS/ME team initially
- Activity levels should be increased as CFS/ME symptoms stabilise and improve.

iIME Comment: The advice here is contradictory.

Page 144 line 1 onwards

6.3.1.7 Rehabilitation

iIME Comment: rehabilitation from what. If the cause is ‘unknown’ then how can rehabilitation be discussed?

Prescription and review should always be considered as part of an overall rehabilitation plan, and assessed and reviewed by a rehab professional

IIME Comment: what is a rehab professional? What qualifications does this person have for a neurological illness? There is no definition of such a profession in these guidelines.

Page 145 line 1 onwards

6.3.2.1 Cognitive behavioural therapy is effective in adults and has been shown to reduce symptoms, improve function and improve quality of life. [1+] [Q3/ES1(a)]

IIME Comment: Selective evidence – what about other evidence, Also Professor Malcolm Hooper says that CBT experts themselves have stated that improvement is not sustainable.

Page 147 line 4 onwards

6.3.3 Clinical Evidence Summary

Six studies of other treatment regimes with either mixed methods or behavioural interventions were reviewed. Only one was a high quality RCT and this study of multiple symptom based treatments (including supplements) found significant improvements in favour of the treatment group in symptoms scores. However in such studies it is difficult to determine which interventions were responsible for the observed effects.

IIME Comment: If this was high-quality and found significant improvements then why isn't it made more use of as an alternative to CBT or GET?

Page 147 line 10

Graded Exercise Therapy

Five RCTs were reviewed which assessed the effects of graded exercise therapy (GET) in patients with CFS. Sample sizes ranged from 49 to 148. Validity scores ranged from 9 (2 studies) to 17 (3 studies). Significant improvements in measures of fatigue and physical function were found in all five RCTs. When exercise was combined with fluoxetine there was no additional effect.

IIME Comment: The highest validity scores in your own data was for an alternative therapy.

Research has shown how bad GET is and these tests do not indicate what the patients had as an illness, what severity level the patient had. Patient surveys show that GET is most harmful to pwme.

Page 147 line 21 onwards

Expert Patient Programme

The Expert Patient Programme was introduced into the NHS in 2001. The programme provides an opportunity for patients who have chronic long-term conditions, to develop new skills to manage their condition better on a day-to-day basis and run generic lay-led group workshops. Information is available at <http://www.expertpatients.nhs.uk/index.aspx>

iIME Comment: How on earth are pwme meant to get to such groups, even if they were thought to be useful? This completely ignores the basis of ME.

Page 148 line 3

Update of evidence following the systematic review

An update search of evidence published following the original review for the treatment of CFS/ME produced five new studies which met the inclusion criteria. A systematic review of treatments for chronic fatigue, which searched only PsychInfo and Medline and failed to describe the quality assessment criteria, concluded that CBT generally appeared to be effective

iIME Comment: this is easy to dispute as the basis of patients is questionable. Also this again is a review for chronic fatigue, not CFS/ME.

Page 154 line 21

One issue the group felt would be worthwhile exploring was the possibility of group CBT. A twelve month follow-up study with 153 participants looked at this issue. The study was based in the health psychology department of a general hospital and used group CBT, education and support (EAS) and standard medical care (SMC). The CBT programme was designed to *“attempt to modify thoughts, beliefs and behavioural responses to symptoms and illness with a view to increasing adaptive coping strategies”*.

iIME Comment: How revealing to associate a neurological illness with comments such as ‘attempt to modify thoughts’!!!! This shows the true nature of what these guidelines are aiming for. Is this the type of CBT which is given to cancer and diabetes patients?

Page 155 line 6

The authors give four key areas of therapy.

The key elements of group CBT highlighted by the authors were,

- “Elucidation of core beliefs about their illness and its management

IiME Comment: How insulting is this? The patient knows they are ill yet the therapist attempts to modify their cognitive behaviour toward their illness. Yet earlier in the guidelines the statement was made that clinicians need to treat ME as a real illness.

- Monitoring of activity levels and introduction of appropriate aerobic, strength and stretching exercises designed to increase fitness, balance and confidence in exercise

IiME Comment: What about oxidative stress?

The purpose of the EAS group was to allow for the effect of receiving a therapy per se and the time of the therapist. Both group CBT and EAS were delivered by the same therapists, to cohorts of between 8 and 12 individuals in a series of 8 fortnightly meetings, each lasting two hours.

IiME Comment: How are patients expected to get to these?

The lack of a statistically significant difference in SF36 scores between EAS and group CBT suggests that the effect of CBT is somewhat diluted by the use of larger groups

IiME Comment: Or maybe by the disparate set of patients used.

Page 156

As described previously, Ridsdale did find considerably poorer outcomes from 6 sessions of CBT in people with CFS/ME than with general chronic fatigue

IiME Comment: And as this report is about CFS/ME then surely this proves how CBT does not help ME patients?

Page 158 line 1

4. Treatment is provided by the NHS in the context of availability of adequate numbers of competent, appropriately trained health care professionals

IiME Comment: it is not defined what is appropriately trained.

Page 180

6.3.6.1 An individualised programme should be offered to all adults and children with CFS/ME and agreed with them.

IiME Comment: to be agreed by them – not with them. The patients should always be in control.

6.3.6.2 The programme should be the choice of the adult or child with CFS/ME and mutually developed, after the rationale has been fully explained. During the programme the patient should be in control of their goals, has the right to refuse any component the programme and can withdraw at any time.

IIME Comment: It should be emphasised that the patient can withdraw without consequences, with acceptance by all that the patient has valid reasons for refusing such 'programmes' and is well within their right to refuse.

What is the "rationale" in this particular use? Rationalisation would indicate that some form of treatment has been established based on well understood scientific analysis and clinical aetiology of the illness/infection and then agreed/accepted formulations of treatment regimes by respected clinicians to deal with the physical conditions of the patient. Patient choice should be "informed" rather than subject to the tactics of psychological warfare operations (PsyOps) to gain a desired outcome.

6.3.6.3 When the adult or child's main goal is to return to normal activities then the therapies of first choice should be CBT or GET because there is good evidence of benefit for this condition in mild to moderately affected adults and some evidence in mild to moderately affected children.

IIME Comment: [*When the adult or child's main goal is to return to normal activities ...*] This is a ridiculous statement! Who wishes to be ill? Isn't everyone's goal to get better? GET is a dangerous tool to employ. You already admit that it has been used by untrained people. Now you wish to foist it on to neurologically sick patients.

This is typical of PsyOps, where the subject is deliberately obfuscated, in that only patients with psychological problems could be proposed as not wishing to search for a return to normal activities. Therapies of first choice should always be directed at attacking a known and understood damaging agent. Only when the damaging agent is psychological-based, should the treatment of "first choice" be considered from psychological-based treatments or interventions, such as CBT. No clinician would propose the first course of treatment for a "broken-leg" would be CBT to come to terms with living with such a problem. So why should the ME patient suffering from neurological damage be subject to such an approach?

As stated previously, where is the robust evidence that can support the statement that such treatments have been successful in treating people with ME? It is possible that the successes were related to the patients having other fatigue-related illnesses if the selection process was not sufficiently rigorous to isolate the ICD 10 G93.3 class of neurological ME.

Page 181

6.3.6.4

iIME Comment: [... *not appropriate* ... (treatments) ... (alternatives)] Most ME patients perform activity management just to operate at some level, so Activity Management optimisation could help, but whether it is effective in the treatment of the condition is highly questionable. No activity management will address the illness and the aetiology only the impact of the symptoms on the individual. Similarly Sleep Management and Relaxation techniques may offer some assistance to individual cases but they do not address the clinical aetiology of the illness. In fact, it is known that some patients with ME do not respond well to sleeping tablets and Melatonin, while some do. This really is “A Shot In The Dark” approach that illustrates the lack of understanding of the neurological illness or an appropriate evidence-based approach to clinical and scientific research. When “evidence-based approach” is quoted, it usually indicates the lack of understanding and need for independently peer-reviewed scientific research.

6.3.6.6

iIME Comment: [... *choice ... should be based on:*] Since when has a medical treatment included the “cognitive functioning” of the patient outside of the psychological environment in determining the appropriate treatment? Surely the ability of the patient to undertake a specific treatment protocol is covered under the item relating to their “skills and abilities”? Otherwise, the only conclusion that can be drawn is that this becomes a PsyOps activity.

Page 183

6.3.6.6

iIME Comment: [*objectives of the individualised programme*] Where is the objective to “treat” and “cure” the illness? Without this objective, the guideline becomes psychological intervention/management only. If this is the case, then NICE should clearly define the limitations (and should be ashamed of such a minor ambition and role in the approach to treatment of ME).

6.3.6.7 The choice of programmes or components should take into account the aims of the individual (for example, prevention of relapse, maintenance, treatment of deterioration or improvement of symptoms) and should be reassessed if these aims change.

iIME Comment: the aims of the individual are surely to recover and, at least, not deteriorate.

6.3.6.10 Health professionals should be aware that there is no evidence for the following strategies:

- those which encourage maintenance of activity levels at substantially less than full capacity in order to have reserve energy for the body to heal itself (can be known as the envelope theory) as there currently is no evidence of benefit.

IiME Comment: We disagree entirely. This is entirely erroneous. If patients find this method works for them then they should be allowed to do this. This goes against patient experience.

This statement is made out of ignorance and fear of counter-arguments. Health professionals should be aware that there is no government funded research underway as to the aetiology, testing, clinical treatment or biological medication to counter the neurological illness. There are some limited privately-funded research activities that are now reporting that deliberate physical exercise regimes can be harmful, e.g. oxidative stress and arterial damage. (It is noted that “Envelope Theory” and “Set-Back” are terms from the psychology lexicon rather than the clinical treatment environment.)

Page 184

However, there is considerable patient support for this (particularly for adults and children with severe symptoms of CFS/ME), and research is currently being undertaken to evaluate the effectiveness of this approach

IiME Comment: So why not listen to patients!!

- those which encourage complete rest (cognitive, physical and emotional) during significant increases in symptoms (a ‘set-back’).

IiME Comment: are you really saying that someone with a neurological, multi-system illness should not rest when they have a relapse until feeling able to resume any activity? This has to be removed. Health professionals need to be aware of all of the research – see Dr. Vance Spence/ME Research UK. Patient evidence shows that mildly affected patients with ME can become severely affected if they push too hard. Read your own published testimonies from patients!

Page 185

6.3.6.13 A programme of CBT may also include:

- developing awareness of thoughts or expectations, or beliefs and defining fatigue-related cognitions and behaviour

IiME Comment: this is ridiculous and belittling and shows the basic myths behind ME. Where is the medical treatment by a clinician? Without such, it remains a psychological-based programme only. Therefore, if this is the basis for the NICE Guidelines, then the title should be proposed to become “The Psychological Treatment Programmes Available to assist ME and CFS Patients Manage their Perception and Attitudes to a Fatiguing Illness”.

- self-monitoring to record patterns of activity and rest, and thoughts, feelings, and behaviours
- establishing a stable and maintainable level of functioning, followed by a gradual, and mutually agreed, increase/decrease in activity

IiME Comment: “mutually agreed” We disagree – the decision is the patient’s – not a mutual agreement with another person. And this highlights again the inconsistency in the document.

- challenging cognitions which may adversely affect rehabilitation and/or symptom management, for example, fear of activity and perfectionist beliefs

IiME Comment: this is insulting. Where is the evidence of perfectionist beliefs being something which inhibits recovery. On the contrary, it can be useful to have an ambition/objective as you state elsewhere. This again provides more lines enforcing the view that ME is a psychological illness. This needs to be removed.

- development of a supportive and collaborative therapeutic relationship rehabilitation and/or symptom management, for example, fear of activity and perfectionist beliefs

IiME Comment: this is ridiculous and belittling and shows the basic myths behind ME which NICE keep on peddling out in this document.

- addressing complex adjustment to diagnosis and acceptance of illness limitations, for example, grief, anger and guilt-evoking beliefs and expectations such as ‘I should be able to do more’ or ‘I can’t do what I used to do’

IiME Comment: this is ridiculous and belittling and shows the basic myths behind ME which NICE keep on peddling out in this document

- decreasing somatic attributions and addressing symptom over-vigilance and/or checking behaviours by providing physiological explanations of symptoms and using refocusing/distraction techniques

IiME Comment: surely a patient should always be aware of symptoms – this is a multi-system illness with possible grave consequences if not treated properly.

- problem solving using activity management and homework tasks to test out alternative thoughts or beliefs. For example, activity as a therapeutic tool, pleasure and mastery tasks

IiME Comment: Many patients will not have the energy to do this. Many patients will receive no pleasure from ending up even more tired by this therapy. This is belittling.

There is a fundamental assumption that a patient who addresses the belief system will be able to increase activity. Are there any recorded examples of CBT assisting sustained ability increase in non-psychological illnesses and the eradication of the illness in the individual? Without even one such clear example, the argument for CBT is laid bare, in that it is purely a technique to assist in the management of symptoms with significant psychological impact. Neurological ME may have such impact in certain cases but it is highly questionable that CBT will ever provide a curative disposition in the patient. This supports the need for very careful exclusion of other fatiguing conditions from the definition of ME.

Page 188 - Graded Exercise Therapy (GET)

IIME Comment: The whole GET philosophy for ME patients is wrong. Therefore we have not commented on this section as the findings and recommendations are flawed. There is plentiful evidence of the effects of GET on ME patients – oxidative stress etc.

The example of 2 * 15 minutes daily brisk walks to the shop for an ME patient, either mild, moderate or severely affected is palpably ridiculous – this could be extremely dangerous to a mildly/severely affected pwme. It needs to be removed! Even healthy people might not be able to manage 2*15 minute brisk walks. There is no basis for this. If someone could manage this then one wonders why any intervention is necessary.

The guidelines state that if exercise increases symptoms for more than a few days the level should be reviewed and reduced (section 6.3.6.18). Later (6.3.6.20) it is stated that if a relapse occurs then exercise should be maintained.

All of this is dangerous advice for ME and does not take into account the delayed and cumulative detrimental effect of exercise on ME.

We would like a comment from the head of NICE if he is prepared to be accountable for any fatalities to patients who take this advice.

Reference to 'reinforcing learning and lifestyle changes' again perverts the true nature of neurological ME. The only reinforcing these guidelines are achieving in this section is to reinforce the old myth that ME is a behavioural syndrome.

If ME is a severe fatiguing condition, then performing exercises will exacerbate the fatigue condition. In research published by the University of Dundee, ME patients have shown that severe reactions to exercise can occur. In fact, one researcher, Dr Vance Spence, has expressed concerns that undertaking aerobic exercise could lead to fatal consequences. Is NICE in a position to recommend GET in the face of this evidence? Is NICE willing to face the potential legal consequences of proposing GET should a patient with ME suffer fatal after-effects in following the proposed NICE Guideline? Has NICE taken any legal advice to accept the publishing of this proposed guideline?

Page 192 - 6.3.6.20

[*Managing Setbacks*]

IiME Comment: This statement just emphasises the psychological nature of GET. However, if ME patients were able to perform exercise, then they wouldn't have ME according to this fallacious argument. The failure of ME patients to achieve a return to full health using CBT and GET indicates that ME is not a psychological illness. Patient cohorts that do recover as a result of CBT and GET undoubtedly include patients with other fatiguing states. To not select patients correctly and then claim benefits for exercise strategies and discount failures or withdrawals does not indicate an "evidence-based" approach is being used correctly.

Activity management

IiME Comment: Regarding activity management we believe this is just common sense and requires no paradigm to be designed around it. There seems little point repeating the same comments as were there for GET. There is no one method for managing an illness as people are all individuals and behave differently and cope differently.

The recommendation that activity management should not include prolonged rest or extended periods of day-time rest in response to an increase in symptoms is derisory. It risks long term damage to a patient to recommend this. NICE are not listening to patients.

The advice is so generic as to be unusable.

Page 198

6.3.6.31 Sleep management should not include:

IiME Comment: Even healthy people can benefit from day-time sleeping/naps. Southern European countries embed this in their lifestyle. Why cannot ME patients adopt this if it is of benefit to their recovery? More rest periods are even recommended later under setbacks. In the previous section it was stated that a plan should not be rigidly/inflexibly adhered to. This is what is being stated here. It is just common sense and requires no paradigm. The inconsistency in these guidelines coupled with fallacious arguments used in favour of psychological therapies all undermine the supposed impartiality or credibility of NICE.

The section 6.3.6.30 states that alcohol should be avoided. If NICE had done their homework they would have known that alcohol intolerance is one of the features of ME!

Page 202

6.3.7 Deriving Recommendations

The GDG was, however, clear that CBT was not about unhelpful advice or dictation of illness beliefs, but about changes in lifestyle and learning to achieve improvement within the patients abilities

IiME Comment: And here you perpetuate the myth. This terminology at best needs to change and at worst needs removing. The previous pages clearly state that rest is not an option and that the patient needs to change their illness beliefs.

Page 202

In addition, the objectives of the programme must be agreed with the patient who clear must be willing to take part. The GDG did not regard CBT or other behavioural treatments as curative or directed at the underlying disease process which remains unknown.

IiME Comment: The wording “..CBT or other behavioural treatments” gives the lie to the earlier statement that “CBT was not about unhelpful advice of illness beliefs”. This clearly shows that CBT is at the heart of the somatoform lobby led by psychiatrists. Also, elsewhere CBT is said to be a therapy – here it is stated to be a treatment!

The recognition that CBT (or other behavioural treatments) are not regarded as a curative treatment or directed at the underlying disease process also gives the lie to the proposition that CBT is a treatment of any sort. This needs to be highlighted in many more places and as a high-level bullet point.

Page 203 line 17

Because of the strong evidence of the benefits of CBT, the GDG recommended it as best practice, but did not make a recommendation regarding individual versus group as there was no evidence nor consensus.

IiME Comment: This comment is contentious as there are no strong evidence in the case of ME?

Page 203 line 19

The GDG noted that it was always the patient’s choice whether or not to participate

IiME Comment: This should not be ‘noted’ but it should read EMPHASISED.

Page 203 line 26

Both the evidence and the GDG consensus support gradual increases in aerobic exercise in people with mild, moderate CFS/ME. The patients in the

wider survey did not support this view as indicated by the response to 3a2. Healthcare professionals rated this as 'uncertain' but did not disagree with the statement.

IIME Comment: This is not correct and will cause moderate patients to be severely effected. What about research into oxidative stress from exercise?

Also, if healthcare professionals are uncertain then they should err on the side of caution.

Page 204

The view of the GDG was that all treatments have the potential to cause harm as well as provide benefit. GET is no different, but the overall research evidence is that the benefits outweigh any harmful effects

IIME Comment: Even medication has to have a list of side-effects – this needs to be stated here also. Drugs take years of trials and go through regulation. Where does this exist for GET? If some people become severely affected by GET is it accepted because some people getting better outweigh this.

Some patient surveys have described poor experiences with exercise therapies, though these experiences were usually from unstructured or inflexible exercise programmes often delivered by untrained personnel.

IIME Comment: What makes NICE think this will change in the future?

Page 204 line 15

There is no evidence to support the 'Envelope Theory' of maintaining levels as substantially less than capacity in order to have a reserve.

IIME Comment: there is a lot of patient evidence. Surely this is just common sense.

Trials are currently in progress should answer this question

IIME Comment: the trials in progress are using flawed selection criteria and have a broad base of patients with a range of conditions which are not ME.

Page 204 line 17

The results from the wider group indicated that patients generally support this approach while health professionals do not

IIME Comment: And who knows better – patients living with this illness or health professionals who have not been able to diagnose, treat or understand this illness for many years?

Page 204 line 19

The GDG supported the view that people with CFS/ME need to learn to listen to energy levels of the body in order to manage their daily life and that sudden large increases in activity were not advised, There was however, concern that consistently maintaining activity levels at lower than capacity would not lead to an improvement in symptoms and/or level of functioning

IIME Comment: This is common sense. This cannot be dictated by a set of general guidelines. The above recognition that the patient must listen to their own energy levels of the body totally contradicts the previous section which repeatedly recommends retaining levels of exercise. These guidelines are full of contradictions and the lack of precision is astounding.

Page 208 line 6

Evidence exists regarding infectious triggers for CFS/ME

IIME Comment: This should read there is an abundance of evidence which exists. These guidelines should elaborate more on this. If this were discussing GET or CBT then these guidelines would be detailing this evidence with multiple pages!

Page 229 - 6.4.5 Recommendations

6.4.5.1

[*There is no known pharmacological treatment ...*] So what is the MRC and NICE doing to address this position? There are a number of drugs being studied around the world and the results of studies are available to indicate that some drug treatments may help. Where are these considered or listed?

6.4.5.1

[*... may experience greater intolerance ...*] Where is the documentary evidence and the references to published material that supports this statement? Are there any trials evidence that some drugs have reduced effects in ME patients?

6.4.5.4

Prescribing of thyroxine should only be considered for adults and children who have low thyroxine levels or for children when standard biochemical tests indicate that they are hypothyroid. Thyroxine should not be prescribed when the adult or child is biochemically euthyroid.

IIME COMMENT: [*Thyroxine*] Why is this selected as a named drug? There is some evidence that the standard NHS thyroid testing is inadequate in explaining the role of the T3 and T4 in the operation of the thyroid gland, especially in ME patients, where T1 and t2 levels can appear normal but T3

and T4 levels are modified. Blood tests for thyroid function are still relatively new and can't be trusted yet. So a thorough thyroid examination should be part of a general medical examination always.

6.4.5.5

IIME COMMENT: [*Drugs for Bowel symptoms*] Some ME patients are known to have severe problems with intestines, e.g. Ulcerative Colitis and Irritable Bowel Syndrome (IBS). The research as to the interactions appears to be needed. Advising drug use to alleviate the symptoms without understanding the causal and interactional factors would need to be questioned in the event of any personal injury claim.

Page 230

6.4.5.7

IIME COMMENT: Is the NICE Guideline proposing the use of a "not-licensed" drug in the UK? Melatonin has been studied in other countries and not produced successful outcomes for some ME patients. The details would need to be reviewed to support this statement or otherwise. Has the UK and NICE accessed such research results to support the statement in the Guideline?

6.4.5.8

IIME COMMENT: [*Prescribing of low-dose tricyclic antidepressants*] Has there been any research on such prescriptions for ME patients? What were the results and were there any contra-indications?

6.4.5.9

The following treatments are not generally recommended for the management of CFS/ME.

- The use of anti-viral agents

IIME COMMENT: Dr. Jonathan Kerr's research should be looked at. There has been a number of research activities reported in the press that include anti-viral agents, for example, Dr J Kerr has proposed a trial of beta-Interferon as an anti-viral. Anti-microbials have been found to be helpful where there is evidence of identified infection ([Appendix 6 - 18](#)). This should have been part of the search for research.

What is the basis for this list of "not recommended treatments"? Are there references to research that could be included to support these statements? Has any clinical research been reviewed?

Page 231 line 3

In addition, particularly with immunoglobulin studies, there were large dosage variations in the studies which made any comparison difficult; there is not necessarily a dose response effect and different doses may elicit very different effects. It was agreed that the Staphylococcus toxoid papers should be rejected as patients studied were women with muscle pain/fibromyalgia and thus not representative of a CFS/ME population. The complication and side-effect rates were high also very high in the immunoglobulin studies. The GDG agreed that it did not want to make any evidence statements on immunotherapy.

IIME COMMENT: Yet on Page 35 lines 24-27 the guidelines states that 'several factors have been suggested (as to the cause), including: immunological, genetic, viral, psychological and neuroendocrine.'

Of four studies using immunoglobulin, one had positive impacts and rated a score of 16. The others did not have statistically significant effects, yet somehow rated scores of 15, 13, and 13 respectively.

Page 231 line 11

The GDG was also mindful of the side-effects or adverse effects of many of the treatments reviewed. The GDG felt unable to exclude the use of pharmacological interventions where evidence is lacking to support or reject their use and referred included these in the questionnaire. It is felt that much research is needed in this area.

IIME COMMENT: Side effects were reported for GET too but accepted.

Page 233 line 15

Antivirals and immunoglobins: The consensus was that they do not have benefit in the treatment CFS/ME

IIME COMMENT: Chia's research proves this is beneficial.

Devanur and Kerr (Journal of Virology 2006) state that "there are many infectious agents which are known to trigger and perpetuate CFS(/ME), and which have been or may be targeted with antimicrobial therapy. In some of these instances there has been clear evidence of clinical benefit or cure in infected CFS patients".

These infections include enteroviruses, EBV, Cytomegalovirus (CMV), human herpes virus-6 (HHV-6), parvovirus B-19, hepatitis-C, Chlamydia pneumoniae and Coxiella burnetii.

Page 234 line 2

6.5.1.1 At present, evidence is insufficient to support a beneficial effect of dietary supplements, including essential fatty acids in CFS/ME. [ref. Q3/ES5a]

IIME COMMENT: Is that it? This is quite a poor document when there is much patient evidence showing benefits. See also later comparison with CBT patient evidence. Anti-oxidants to combat oxidation which is a problem in ME/CFS (Kennedy et al 2005). This topic should be discussed as thoroughly as CBT or GET as many patients find benefits from high quality supplements.

Page 234 line 4

6.5.2.1 Summary of evidence presented in Appendix 1

IIME COMMENT: Incredibly poor and limited summary for this important area. Very unprofessional. This is not very detailed compared with the extensive propaganda documented for GET and CBT earlier in the guidelines. See York review tables 1 and 2.

Page 235 line 9

6.5.4 Clinical Scenario Questionnaire to GDG and Wider Group

2. All treatments are offered allowing the person with the CFS/ME to refuse without compromising the further therapeutic relationship.

IIME Comment: Will NICE state that nobody should be refused insurance/sickness benefits if they refuse to take anti-depressants or CBT/GET?

Page 248 line 1

6.5.5.1

IIME Comment: [... *balanced diet ... strategies to minimise complications ...*] Is food purchasing, preparation and eating significantly more important for ME than other illnesses? Is this a standard text inclusion for medical guidelines? If there are specific contra-indications for certain types of food, then these should be defined and alternatives noted.

6.5.5.2

IIME Comment: [... *tube feeding* ...] Along with Item 1.3.2.2 on sleep management, this paragraph appears to give vent to sadistic/psychotic tendencies but not necessarily for the benefit of the patient. The ability of psychologists to take children away from parents, incarcerate adults under Section 5 of the Mental Health Act and inflict “forced activity” or environment needs to be carefully supervised by the medical profession and society at large to prevent intolerant practices from being imposed on the public.

6.5.5.3 Where an adult/child experiences nausea or severe bowel symptoms, these should be managed conventionally. Exclusion diets are not generally recommended for the management of CFS/ME. However where an exclusion diet is undertaken for the investigation and treatment of bowel symptoms, it should be clinically supervised by a dietitian because of the risks of a severely limited diet.

IIME Comment: [Exclusion diet] What is the background and documented evidence to support the inclusion of this paragraph?

In the York review a low-sugar, low-yeast diet had equivocal results yet a score of 11. One remains perplexed at the conclusions drawn. Either there was something wrong with the methodology (the scoring system) - or the conclusions drawn had nothing to do with the study which was conducted.

Page 249 line 3

This view was supported by the questionnaire. While supplements may be useful for general health, the GDG agreed that they could not be recommended for the management of CFS/ME.

IIME COMMENT: They can be a useful part of the diet for pwme who cannot cook always or who cannot eat properly – fish oils, vitamin c, multi-vitamins – surely this is a negligent oversight from NICE.

Fish oils score as highly or better than CBT so why does NICE not recommend this as a therapy/treatment?

Page 249 line 19

6.6.2.2 Additional Clinical Evidence

No new evidence found.

IIME COMMENT: isn't this where one listens to patients for evidence?

Page 253 line 1

6.6.5.1 There are no complementary therapies that treat CFS/ME for adults and children and their use is not recommended. However, people may choose to access some of these therapies for symptom control and find them helpful.

IIME COMMENT: [*Complementary Therapies*] What research has been done in Complementary therapies and documented to support these statements? What assessment work supports the statement that some may be helpful? Without specifics, these statements are not useful. Prof Puri's analysis of long chain fatty acids has resulted in his assessment of EPA products being useful for ME but this is not listed or discussed. This example is not necessarily recommended but included purely as an example that needs to be confirmed by independent assessment.

What about the one high quality study – shouldn't people be given a choice instead of CBT and GET? And it would be easier for ME patients if these therapies were available on NHS.

Isn't this where one listens to patients for evidence?

6.6.5.3 There is no evidence on the use of supplements for adults and children with CFS/ME (for example, vitamin B, vitamin C, co-enzyme Q10, magnesium, NADH, or multivitamins and minerals), and therefore they are not generally recommended for the treatment of the symptoms of CFS/ME. .

IIME Comment: In terms of supplements, two "essential fatty acids" studies had positive results and very high rankings - 16 and 17 respectively. Carnitine, liver extract, and magnesium also scored as high as CBT in terms of therapies (10, 10, and 15).

Page 255

IIME Comment: [*Reviews*] What is an effective review period for different levels of severity of ME? This would be usefully used to indicate the level of support that a service should provide to an individual patient. If the numbers of ME patients with different levels of severity were known, then the NHS could estimate the scale of demand and the potential need for clinics to provide appropriate assessment, treatment and pastoral advice. To this point in the document, no treatments have been specified and only management techniques with (un-detailed) general advice on sleep, diet and use of complementary medicines. The proposed review topics go outside the medical expertise and in to the pastoral and Benefits Agencies regimes. Should NICE Guidelines encompass the pastoral and Benefits Agencies agendas? If so, there are a number of areas of omission. Otherwise, perhaps NICE should consider the political impact of being seen as attempting to manage input to social security and other benefit agendas, unless of course there is a specific remit. In which case, the specific remit should be clearly stated and referenced.

[*Review Interval*] ME is a long-duration illness, where some patients have endured the illness for over 20 years. The concept of reviewing progress and taking action against relatives or friends in addition to the ME patient in the case where improvement is not detected is questionable. This smacks of psycho-babble and the discredited Munchausen's By Proxy Syndrome, where great care should be taken to raise this denounced psychological approach.

Page 256 line 7

7 People who are Severely Affected

It is therefore common for this group of people to experience isolation, loneliness and barriers when accessing all forms of care

IIME COMMENT: This is not only severe pwme. Also moderately affected children can be affected by isolation. Home tuition is often necessary but schools seem unable to handle this and often forget about the child studying from home. They frequently offer no help to involve the child in school activities (via post, email, telephone or visits by colleagues). NICE do nothing to address this.

Page 258 line 1

7.3.1.1 Adults and children who are severely affected should be able to access the same diagnostic and therapeutic options as those who are not severely affected, as appropriate.

IIME COMMENT: The only options given are CBT and GET.

7.3.1.3 Adults and children who are severely affected should be offered an individually tailored programme based on activity management which may be delivered at home (and/or by telephone if appropriate).

IIME COMMENT:

[*Programme ... which may be delivered ... by telephone if appropriate*]
Should any medical intervention programme be delivered by telephone? This is insulting to the severely affected patients.

Some need to be given just care – no management possible. These people may be in an active phase of the illness and need rest.

7.3.1.7 [*Hospital Admission*] What would be the purpose of hospital admission apart from easing the provision of access by the patient to the doctors in the clinic. If the severity of ME is causing access problems, perhaps home visits should be considered more seriously and the provision of training for the District Nursing staff to provide enhanced support?

7.3.1.4 Activity management should be the core therapeutic strategy but elements of CBT and GET may be suitable for some adults and children.

IIME COMMENT: Wrong. Some severely affected can't cope with any management strategies. This is far too generalized and can therefore be misinterpreted by busy GPs or by those with bias toward the condition. This is quite a short-sighted analysis.

7.3.1.6 Adults and children who are severely affected may need to access, at various times, community services such as nursing, physiotherapy, psychology and occupational therapy (ref NSF long term conditions). The input of various professionals should be coordinated by a named professional and those involved in care need to be trained in the management of CFS/ME. (4.3.6.5)

IIME COMMENT: [*Access ... to community services ...*] The list seems to be missing clinicians, medical doctors and treatment facilities such as clinics and hospitals, was this by design? The balance seems to indicate a bias towards the psychological end of the spectrum of possible specialist supporting care. Perhaps this should be considered carefully.

We also feel that ME patients may need access to legal advice to prepare for litigation if/when NICE proposed therapies prove harmful to the health of the patient.

Page 260 line 17

7.4.3 Carers

One of the main difficulties for carers, which may have an impact on their health, is that people with severe CFS/ME find it very difficult to sleep. This means that for the carer, sleep is fragmented and restricted as during the night the carer is often caring for the person with CFS/ME. As a result the primary carer can also feel isolated whilst having given up their job they may experience a loss of their individuality and professional status. Carers may also face difficulties in claiming benefits and access to services whilst the widespread disbelief in the condition can compound the situation.

IIME Comment: perhaps this could also comment on the intransigence of the medical community to accept neurological ME as a real illness, lack of help from schools for children with ME, and the lack of education of medical staff regarding the research which has been made which proves ME as a neurological, multi-system illness.

Page 261 line 1

Family life may also be affected as people with severe CFS/ME are often sensitive to sounds and smell.

IIME Comment: Family life **IS** affected – there is no *may*.

This is not only the case for severe ME – so-called ‘mild’ or ‘moderate’ ME can severely affect a family.

Page 262 line 21

7.6 Additional information related to Chapter 6 - Management

Because of the complexity of the illness, they usually are excluded from recruitment into research trials and consequently there is a poor understanding and a lack of agreement over the management of severely affected people. .

IiME Comment: This doesn't stop cancer patients being included despite that being a complex illness. Perhaps it is easier to get the desired result by excluding severely affected ME patients?

Page 263 line 2

For children, the management plan should also include educational arrangements which recognise individual needs.

IiME Comment: How is this achieved. Schools are not compliant in giving children with ME the correct service and often parents have to battle to get the school to act or be pro-active.

Page 263 line 6

As the group is often excluded from research there is a lack of evidence and agreement over the management of severely affected patients.

IiME Comment: Shouldn't NICE make a recommendation that severely affected ME patients are included in research trials on ME.

Page 263 line 11

7.6.1 Self Management Strategies

People with severe symptoms may be more susceptible to the cumulative effect, with their bodies being able to neither undertake nor sustain .

IiME Comment: Yet GET is advised earlier even for severely affected patients.

Page 263 line 13

In devising a programme the healthcare professional should understand, that to sit up or for some severely affected people to lift their head is an achievement and having a conversation is a good day. As travel may exacerbate symptoms, people with severe CFS/ME may also need support with the rehabilitation or care within the home.

IiME Comment: And yet these guidelines are recommending GET!!!

Page 264 line 21

There may be a need for use of prescribable supplements or where there are severe problems, tube feeding may be required. .

IiME Comment: Yet earlier in these guidelines supplements were not recommended – it becomes totally confusing which recommendation is meant to be used. Imagine how GPs must react!

Page 266

IiME Comment: The references are full of CBT studies. It shows the skewing of these guidelines away from biomedical research and toward psychological therapies as the basis for any form of treatment or service being provided. The bias is incredible.

6. Appendix 1 – President Norwegian ME Association

At the IACFS medical conference in Madison, Wisconsin in October 2004, professor Charles Lapp chaired the clinical session. He started the session by saying that "CBT has become a dustbin word". He could not have said it better.

I am reading your comments and arguments on the IMEGA-e and I am concerned. With respect, I believe that you don't seem to understand that as far as CBT and GET goes, there are now A and B versions of both. The B-versions are coping strategies, and not CBT or GET. This must be made very clear. When CBT is recommended and argued that it has proven helpful in the treatment of cancer or diabetes or whatever other recognised organic disease, it is coping strategies and not the CBT the psychiatric lobby is promoting. They, in contrast, believe that ME-patients are suffering from a 'behavioural problems'.

The usual interpretation by doctors and health personnel of CBT and GET as treatments is that ME-patients suffers from "avoidance behaviour" and "catastrophic thoughts/thinking". At a meeting recently for doctors and health personnel in this country (Norway), ME was the topic and how to treat them. The patients were ridiculed and stigmatised.

"What should we do? They won't take antidepressants. Perhaps the best thing would be to commit them to psychiatric hospitals for their own good".

This is a result of the recent report from the Norwegian "NICE" which stated clearly that all studies on CBT and GET are weak, but to get this message across they would have to read the report which they don't.

Now the psychiatry lobby here is running courses on how to "best treat ME-patients" and taking advantage of GPs uncertainties, confusion and lack of knowledge.

We know for a fact that a lot of GPs are totally confused by all the different messages, even when they take ME seriously.

If you don't agree 100 per cent with the NICE guidelines, please, please make your protests in the strongest possible way! We did – we pulled out in protest although we agreed in parts of the report, and we went to the press. At the same time we released our comments on our website: key point, short version and full version.

It has not been negative as many believed. On the contrary - we have had a lot of support from many sources in the health services and the medical profession. They have read our 'full version' (most read; we see that on the statistical recording) where we argued our points with reference to the medical literature with links to the original articles whenever possible.

If the map doesn't match the terrain, it is the map that is wrong and not the terrain.

Ellen (in Norway)

7. Appendix 2 – References on Epidemics

1	A Review of The Clinical Syndrome Variously Called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthenia by ED Acheson (American Journal of Medicine, 1959) by Dr J Gordon Parish, Patron of ME Research UK
2	Acheson ED. The clinical syndrome variously called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthenia. Am J Med 1959; 26: 569-595.
3	Henderson DA, Shelokov A. Epidemic Neuromyasthenia – Clinical Syndrome. N Engl 1959; 260: 757-764, 814-818.
4	Leading Article A new clinical entity? Lancet 1956; 1: 789-790. Written by ED Acheson, introducing the term Benign Myalgic Encephalomyelitis.
5	Paul L, Wood L, Behan WMH, Maclaren WM. Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome. European J Neurol 1999; 6: 63-69.
6	Pellew RA, Miles JA. Further investigations on a Disease resembling Poliomyelitis seen in Adelaide. Med J Aust 1955; 42: 480-482
7	Ramsay AM. Encephalomyelitis in North West London. An endemic infection simulating poliomyelitis and hysteria. Lancet 1957; 2: 1196-1200. Description of 10 cases illustrating the association of behavioural disorders (neurasthenia) with brain disorders (cranial nerve palsies).
8	Acheson ED. The clinical syndrome variously called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthenia. Am J Med 1959; 26: 569-595.
9	Shelokov A, Habel K, Verder E, Welsh W. Epidemic Neuromyasthenia. An outbreak of poliomyelitis-like illness in student nurses. N Engl J Med 1957; 257: 345-355. The Chestnut Lodge Epidemic, Washington, USA in 1953.
10	Sigurdsson B, Sigurjonsson J, Sigurdsson JHJ, Thorkelsson J, Gudmundsson KR. A disease epidemic in Iceland simulating Poliomyelitis. Am J Hyg 1950; 52: 222-238.
11	Wallis AL. An investigation into an unusual illness seen in Epidemic and Sporadic Form in a General Practice in Cumberland in 1955 and subsequent years.
12	White DN, Burtch RB. Iceland Disease – a new infection simulating Acute Anterior Poliomyelitis. Neurology 1954; 4: 506-516.

8. Appendix 3 – Letter from R. Mitchell and V. Mitchell

(This appendix) outlines concerns with regard to Psychological Therapies designed to 'alter specific brain function' such as CBT. There are important ethical, regulatory and safety considerations to be addressed. We believe this to be a Human Rights concern.

We would be grateful if you would consider the points raised in this paper and reflect them in your response to NICE

26 October 2006

CBT, GET And Human Rights:

The NICE CFS/ME: full guideline DRAFT was published in September 2006 and recommends CBT or GET as the therapies of first choice for CFS/ME ([Appendix 3 - 1](#)). Detailed critiques of the draft are appearing on the internet ([Appendix 3 - 2](#)) and already the guideline has been declared unfit for purpose ([Appendix 3 - 3](#)).

This paper seeks to show that failures and omissions in the draft guidelines highlight a human rights issue with regard to the application of psychological therapies, with implications for society as a whole.

The failures this paper examines are:

- the failure to explain the biopsychosocial theory on which NICE recommendations for treatment are based;
- the failure to address the scientific and medical dispute with regard to the safety and appropriateness of the use of the biopsychosocial theory and the use of CBT and GET in ME/CFS;
- the failure to address the moral, ethical and safety issues arising from its recommended therapies.

By ignoring these serious issues with regard to CBT and GET, we believe that as currently drafted the NICE Guidelines violate the right of clinicians and patients to the highest, safest standards of Medical practice and care, amounting to a violation of their Human Rights.

Turning first to the issues of the failure to explain the biopsychosocial theory and the scientific and medical dispute with regard to the safety and appropriateness of the use of the theory and CBT and GET in CFS/ME:

Carruthers and van de Sand in an Overview of the Canadian Consensus Document on CFS/ME state:

'A hypothesis underlying the use of Cognitive Behaviour Therapy (CBT) for ME/CFS is based on the premise that the patient's impairments are learned due to wrong thinking and "considers the pathophysiology of CFS to be entirely reversible and perpetuated only by the interaction of cognition, behaviour, and emotional processes. The patient merely has to change their thinking and their symptoms will be gone. According to this model, CBT should not only improve the quality of the patient's life, but could be potentially curative".'

‘ Proponents ignore the documented pathophysiology of ME/CFS, disregard the reality of the patients’ symptoms, blame them for their illness, and withhold medical treatment. Their studies have often included patients who have chronic fatigue but excluded more severe cases as well as those who have other symptoms that are part of the clinical criteria of ME/CFS. Further, their studies fail to cure or improve physiological impairments such as OI, sore throat, IBS, etc. Dr. A. Komaroff, a Harvard based world authority, stated that the evidence of biological process “is inconsistent with the hypothesis that (the syndrome) involves symptoms that are only imagined or amplified because of underlying psychiatric distress. It is time to put that hypothesis to rest.” ‘ ([Appendix 3 - 4](#))

Hooper (2006) writing in the August Journal Of Clinical Pathology states:

‘The challenge of these syndromes to modern medicine is in accord with the growing understanding of the neuroendocrineimmune (NEI) paradigm, sometimes referred to as the psychoneuroimmune (PNI) paradigm. This has emerged as a result of the identification of complex biological messenger molecules that serve to communicate between these NEI systems.’

‘This understanding, supported by extensive human and animal studies, provides an extensive intellectual foundation for the biological approach to investigating these complex and challenging syndromes of uncertain origin.’

‘In contrast, the alternative and controversial claims of some psychiatrists that all these syndromes are expressions of somatisation or covered by the biopsychosocial (BPS) theory lack any sound intellectual basis and spell the failure and possible imminent extinction of modern psychiatry.’

‘Undoubtedly the perverse use of chronic fatigue syndrome, to impose a psychiatric definition for ME/CFS by allying it to fatigue syndromes, has delayed research, the discovery of effective treatment(s), and care and support for those suffering from this illness ‘

‘Any activities associated with increased free radical production should not be recommended to sick ME/CFS patients as this will intensify the damage. This is why GET is so damaging for many ME patients since exercising muscle is known to generate increased oxidative stress.’ ([Appendix 3 - 5](#))

Hooper and Reid (2006) published a critique exposing the inadequacy of the evidence base of RCTs relied upon by NICE, which include inter alia the following:

‘There is no objective evidence that CBT & GET are effective, nor that claimed improvements are sustained long term. These treatments are not tolerated by a large minority of patients. Internationally, a number of prominent researchers have strong reservations about GET. ‘([Appendix 3 - 6](#))

In a presentation to the Group on Scientific Research into Myalgic Encephalomyelitis (Gibson Parliamentary Inquiry) ME Research UK Chairman Dr Vance Spence (2006) said:

‘The evidential basis of the CBT model for ME/CFS, consists of 8 discrete RCTs, 3 "negative" for the intervention and 5 "positive". While there are arguments for and against each of these trials, I think we can agree that this constitutes a far-

from-impressive evidence base, particularly when set beside other evidence bases and beside patients' reports and surveys.' ([Appendix 3 - 7](#))

Marshall, Williams, Hooper (2001), give the opinion of an eminent Leading Counsel (a member of the House of Lords) which states:

'On the document you have sent me there is an overwhelming case for the setting up of an immediate independent investigation as to whether the nature, cause and treatment of ME (biopsychosocial theory and the use of CBT and GET) as considered by the Wessely School is acceptable or consistent with good and safe medical practice.

There is substantial doubt as to whether such could be the case in view of the clear division of medical opinion.' ([Appendix 3 - 8](#))

There are therefore serious concerns within the scientific and medical community as to the safety of both CBT and GET with regard to CFS/ME and the theoretical basis on which they are founded. The draft maintains a deafening silence on these issues.

Turning to the moral and ethical issues with regard to the safety and appropriateness of the use of CBT and GET in CFS/ME:

Marshall And Williams (2006) draw attention to studies that show Psychological therapy brings about physical changes in the brain comparable to those brought about by drug therapy. They quote Friedman (2002) who describes three brain imaging studies, one looking at obsessive-compulsive disorder and the other two at depression, all of which showed that when patients improved, the changes in their brain, as shown on PET scans, 'looked the same regardless of whether they had received antidepressants or CBT.'

They also draw attention to "The MRC Neuroethics Report, April 2005: Session 2 ("Altering the brain") in which Psychiatrists explain 'a growing understanding of neurotransmission at a molecular level has allowed the design of interventions to alter specific brain functions, one such intervention being CBT: Psychological therapies such as CBT have now been shown to alter brain function. These developments may alter our view of individuality.'

The MRC Report also asks; 'What are the risks of changing personality? Is cognitive enhancement acceptable to society? Psychological treatments also raise a number of issues about consent and coercion. How much information should patients be given about the possible effects of therapy on their brain?' and concludes that 'further research is needed to determine whether such therapies are reversible, or if there are persistent adverse effects', noting: '**There is already evidence that in certain situations psychotherapy can do harm.**' ([Appendix 3 - 9](#))

There are therefore serious ethical concerns about whether this type of therapy is 'acceptable to Society', as well as outstanding safety issues. Where are the safeguards for this form of treatment? The draft again maintains a deafening silence on these issues.

Drugs undergo exhaustive testing over an extended period of time overseen by an independent body thus ensuring their safety and efficacy. Comprehensive information on the intellectual foundation of the treatment, its effects and counter effects are provided to clinicians and patients. In the US, according to a report by Wierenga and Eaton '*It takes 12 years on average for an experimental drug to travel from lab to medicine chest. Only*

five in 5,000 compounds that enter preclinical testing make it to human testing. One of these five tested in people is approved.' ([Appendix 3 - 10](#)).

Similar rigorous testing processes apply to the UK under European Community regulations. The MHRA UK Regulatory Authority website states:

'Safety, quality and efficacy are the only criteria on which legislation to control human medicines is founded. It is the responsibility of the MHRA and the expert advisory bodies set up by the Medicines Act to ensure that the sometimes difficult balance between safety and effectiveness is achieved. MHRA experts assess all applications for new medicines to ensure they meet the required standards. This is followed up by a system of inspection and testing which continues throughout the lifetime of the medicine. Safety monitoring is also continuous and the MHRA also ensures that doctors and patients receive up-to-date and accurate information about their medicines. This is achieved by ensuring that product labels, leaflets, prescribing information and advertising meets the required standards laid down by the Regulations.' ([Appendix 3 - 11](#)).

Contrast the intellectual and scientific rigour applied in the approval process for the licensing of drugs for clinical use, with the lack of scientific and intellectual rigour applied in the NICE draft with regard to the recommendations for the use of Psychological Therapy in CFS/ME. When compared with the extensive clinical trialling over many years and the independent scrutiny a drug therapy is subjected to, the small and heavily criticised evidence base used to justify the recommendation of CBT and GET for CFS/ME in the NICE draft is seen to be totally inadequate.

In respect of informed consent, it cannot arise. There simply cannot be informed consent since there are important ethical, safety and regulatory questions arising from these treatments, to be addressed.

Ethical and safety questions such as those raised in the MRC Neuroethics Report 2005 should be paramount. It is hard to envisage any Independent authority clearing a drug for Human testing or use without ethical and safety issues, like those surrounding Psychological Therapy, being resolved.

By ignoring these serious issues with regard to Psychological Therapy, we believe that, as drafted, the Guidelines violate the right of clinicians and patients to the highest, safest standards of Medical practice and care, amounting to a violation of their Human Rights.

This is a Human Rights issue. Without an answer to whether this type of therapy is 'acceptable to Society' and if it is, without an effective Regulatory framework governing its development and use, there is the serious risk that sick and vulnerable people everywhere will be vulnerable to exploitation and abuse at the hands of the vagaries of power, politics and prejudice.

Following the consultation process, if NICE does not see the depth and breadth of the failures and omissions in the draft guidelines then a judicial review must be inevitable.

R Mitchell, V Mitchell

References for Appendix 3:

1	NICE CFS/ME: full guideline DRAFT http://www.nice.org.uk/page.aspx?o=368933
2	Responses to NICE CFS/ME Guidelines available at: http://www.theoneclickgroup.co.uk/documents/NICE/Charities/
3	Comprehensive MEA response to NICE Guideline on ME/CFS (draft 2) http://meassocnews.blogspot.com/
4	Carruthers and van de Sand : An Overview of the Canadian Consensus Document http://www.mefmaction.net/Portals/0/docs//Canadian_ME_Overview_A4.pdf
5	Myalgic Encephalomyelitis (ME):a review with emphasis on key findings in biomedical research. Malcolm Hooper University of Sunderland, JCP Online First, published on August 25, 2006 as 10.1136/jcp.2006.042408"
6	Hooper and Reid (2006) (Inadequacy of the York (2005) Systematic Review of the CFS/ME Medical Evidence Base, Comment on Section 3: the Diagnosis, treatment and management of CFS/ME in adults and children: Work to support the NICE Guidelines") available online at www.meactionuk.org.uk/FINAL_on_NICE_for_Gibson.html
7	Dr Vance Spence (2006). A presentation to the Group on Scientific Research into Myalgic Encephalomyelitis (Gibson Parliamentary Inquiry) by ME Research UK Chairman. http://www.meresearch.org.uk/archive/gibsonpres.html
8	Marshall, E.P. Williams, M. Hooper, M. 'What is ME? What is CFS? Information for Clinicians and Lawyers' December 2001
9	Marshall And Williams in their paper CBT IN ME/CFS More Information dated 23 August 2006 http://www.meactionuk.org.uk/CBT_in_ME_More_Information.htm
10	Dale E. Wierenga, Ph.D. and C. Robert Eaton <i>Office of Research and Development Pharmaceutical Manufacturers Association available at</i> http://www.allp.com/drug_dev.htm
11	. MHRA UK Regulatory Authority website available at : http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=27

9. Appendix 4 – Letter from S. Pierce and P.W. Pierce

8/11/06

Sir / Madam,

I am writing to you with regard to your recent release of draft guidelines for the treatment of CFS/ME.

While I have reservations about several of the recommendations made, I feel that the recommendation of Graded Exercise Therapy (GET) as one of your therapies of first choice is the most inappropriate. If included in the final draft of the guidelines, it would represent the very worst medical practise.

Such practise has severe negative implications for the health, well-being and long term prospects for those, like myself, who have the illness. I have enlisted the help of my brother, a biologist (who is thankfully healthy), as principal author of a review of the scientific case for NOT recommending exercise as a form of therapy for those with CFS/ME, a copy of which I have attached to this message.

This paper draws on a variety of references, the majority of which have been published in established, peer-reviewed scientific and medical journals. By setting them within the context of exercise as therapy for CFS/ME, we hope that the persuasiveness of the arguments presented will dissuade NICE from recommending the use of GET, or any form of exercise therapy, in their final draft of the guidelines for the treatment of CFS/ME.

The charity Action for ME have made estimates about the annual cost of CFS/ME to the UK economy. They range from £3.4 to £6.4 billion a year. The use of GET may well add to this cost. It certainly won't decrease it.

Thank you,

Phillip Pierce

The physiology of exercise intolerance in patients with myalgic encephalomyelitis (ME) and the utility of graded exercise therapy

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ABSTRACT – This review discusses the suitability of graded exercise therapy for the treatment of myalgic encephalomyelitis (ME), based on current knowledge of the underlying physiology of the condition and the physiological effects of exertion on ME patients. A large body of peer-reviewed scientific literature supports the hypothesis that with ME an initial over-exertion (a period of metabolic stress) in conjunction with viral infection depletes concentrations of the metabolic regulator glutathione, initiating a cascade of physiological dysfunction. The immune system and muscle metabolism (including the muscles of the cardiovascular system) continually compete for glutathione, inducing a state of constant stress that renders the condition chronic. The impairment of a range of functions means that subtly different suites of symptoms are apparent for different patients. Graded exercise therapy has proven useful for a minority of these, and the exacerbation of symptoms for the majority is not subjective but has a physiological basis. Blanket recommendation of graded exercise therapy is not prudent for such a heterogeneous group of patients, most of which are likely to respond negatively to physical activity.

Following exercise, patients with myalgic encephalomyelitis (ME) uniquely exhibit exacerbated symptoms and a suite of measurable physiological changes indicative of stress (sub-optimal metabolic performance; e.g. reduced respiration and heart rate, increased glycolysis and lactic acid production, and concomitant limitation of activity¹⁻⁵). Although these symptoms may not be universal⁶, a significant subgroup of ME patients are affected in this manner⁷. The issue of exercise is critical for the treatment of the condition as one school of thought recommends “graded exercise therapy” as a general remedy for ME whilst another recognises that exercise intolerance may have an underlying physiological cause that may actually be aggravated by physical exertion. This difference of opinion influences policy: graded exercise therapy is one of the principal recommendations of the current NICE draft guidelines for the treatment of patients “mildly to moderately affected” by ME (p. 21, lines 20 to 23)⁸.

Although recent general reviews of ME exist⁹⁻¹¹, our aim is to specifically review evidence for the mechanisms by which physical activity affects ME

patients, and to investigate how graded exercise therapy may help or hinder recovery.

Although no single randomised controlled study has yet attempted to investigate every aspect of ME, the combined weight of empirical evidence to date indicates that the condition is characterised by a complex series of events involving reserves of metabolic regulators such as glutathione, muscle metabolism and the cardiovascular system. A significant body of literature suggests that these imbalances are associated with a dysfunctional immune system impaired by viral infection. Indeed, a hallmark of ME is a range of symptoms, varying in extent between patients, suggesting that a range of functions are impaired to greater or lesser degrees.

ME typically follows a flu-like illness, with elevated concentrations of viral particles subsequently detectable in blood and muscle tissues¹². Post-viral fatigue is a well established possible consequence of infection by a range of different viruses¹³⁻¹⁷, with enteroviruses specifically implicated in the case of ME – elevated concentrations of viral RNA sequences resembling coxsackie virus B are detectable in muscle tissue¹². Furthermore, the majority of the limited number of ME patients so far treated with antiviral drugs (interferons) were able to return to work following treatment¹⁸, also suggestive of a persistent ‘smoldering infection’¹⁹.

Crucially, post-viral fatigue is not related to the muscle disuse and deconditioning that can result from the initial period of illness¹². Indeed, the mechanism underpinning post-viral fatigue is a multifaceted physiological imbalance. Nijs and co-workers²⁰ found that, for ME patients, graded exercise resulted in faulty regulation of the immune system, specifically increased activity of the enzymes “elastase” and “RNase L”. RNase L is a key component in the cell’s virus detection system and is up-regulated in response to viral infection. However, elastase degrades RNase L and is normally involved in removing it from the cell when concentrations are too high. Why should both be highly expressed in ME patients? Elastase is activated and degrades the RNase L in the absence of metabolic regulators such as glutathione. (Glutathione is an amino acid complex that modifies enzyme activity throughout the body, and ME patients exhibit either lower concentrations or an imbalance between its active and inactive forms²¹⁻²³.) Thus the simultaneous over-activation and mis-regulation of this part of the immune system can be explained by glutathione depletion. A range of factors contribute to glutathione depletion in the general population, including infection, the oxidative stress induced by strenuous or sustained exercise, and the long-term elevation of the stress hormones cortisol and

adrenalin²⁴. Furthermore, glutathione is also involved in sustaining respiration (i.e. the production of chemical energy compounds such as ATP in the mitochondria) thereby providing energy for active tissues such as muscle. Thus muscle tissue effectively competes with the immune system for glutathione²⁵ – sustained physical activity reduces the amount of glutathione available to the immune system, resulting in immune dysfunction. Conversely, an overactive immune system reduces the amount of energy available for muscle tissue, also exacerbating oxidative stress, and can account for both the chronic fatigue and pain (by inducing lactic acid production) that characterise ME. Thus, following an initial period of stress, glutathione concentrations may be too low for the optimal function of both the immune system and muscle tissues, paving the way for both persistent viral infection and fatigue, both of which feedback from each other to render the condition chronic.

This situation is compounded by the fact that glutathione not only has a supporting role in the immune response but also directly inhibits the replication of enteroviruses by blocking the formation of one particular protein (glycoprotein B) shared by all – including coxsackie viruses. Indeed, glutathione concentration is a major factor influencing the expression of other persistent viral infections such as HIV²⁶⁻²⁹. Thus glutathione depletion not only suppresses the immune system, it leaves the body particularly defenceless against enteroviruses. Sustained exercise or stress can deplete glutathione concentrations to the point where viral RNA is no longer prevented from replicating, aiding either an initial infection or the renewed replication of previously blocked viral RNA present in muscle tissue and blood^{27, 29}. Thus glutathione depletion is a strong candidate for 'the trigger for reactivation of endogenous latent viruses' in ME³⁰. A small number of studies demonstrate that foods rich in glutathione or direct glutathione injection help to relieve fatigue in ME patients, and may clear active viral infections^{31, 32}.

Although the above studies have concentrated on skeletal muscle, the heart (and the postural leg muscle involved in pumping blood back to the heart) is not exempt from glutathione depletion. Thus the above mechanism can also account for the range of cardiovascular problems associated with ME, including orthostatic (standing) intolerance (reviewed by Spence and Stewart³³). Patients with orthostatic intolerance 'have continuous disability and commonly have exercise intolerance'³³.

Together, this evidence suggests that chronic fatigue in ME is symptomatic of the following sequence of events: a period of infection or strenuous physical or mental activity results in glutathione depletion; this renders the immune system relatively ineffective, particularly against enterovirus infection; the immune system becomes constantly activated (and inefficiently governed) because it has insufficient resources (glutathione) to completely rid the body of viral particles; the constantly elevated energy demand of the immune system detracts from other metabolic functions (particularly energy-demanding systems such as skeletal muscles and the cardiovascular system); limitation of respiratory and cardiovascular systems further locks the patient into a vicious cycle of inefficient energy production and use;

increased reliance on anaerobic metabolism leads to lactic acid production and associated muscle pain.

Clearly, the performance of energy-demanding activities such as exercise can only aggravate this situation. Indeed, 82 % of ME patients in a recent study stated that graded exercise therapy worsened their condition, and only 5 % found it useful (compared to 70 – 75 % of patients who found either pain management or ‘pacing’ of daily activities useful)³⁴. Furthermore, the Canadian Clinical Treatment Protocol warns that “externally paced ‘Graded Exercise Programs’ or programs based on the premise that patients are misperceiving their activity limits or illness must be avoided”³⁵. If exercise is so detrimental, why is graded exercise therapy often recommended as a treatment for ME? Firstly, many of the studies cited here are recent, and the information and implications have perhaps not yet filtered up to policy makers. Secondly, the reclassification of ME as an ambiguous ‘chronic fatigue syndrome’ (CFS) by members of the psychiatric profession assumes that the symptoms have no physiological basis and are best treated with the traditional psychiatric method of facing and overcoming a problem, rather than direct removal of the problem at source. However, this approach jumps from hypothesis to treatment without investigating the mechanisms involved, perhaps explaining why “no psychiatrist has ever cured an ME patient using psychiatric treatments”¹⁹. Psychiatry, by definition, should not have authority over the treatment of physiological disorders, particularly those that occur chiefly in muscle tissues. Graded exercise therapy is founded on, and perpetuates, the myth that ME patients are simply malingering, while most are frustrated by their incapacity to satisfactorily conduct critical aspects of daily life³⁴.

ME is a heterogeneous disorder that affects different patients to varying degrees and with subtly different suites of symptoms. At best, graded exercise therapy has relieved symptoms for (but not cured) a tiny minority of patients, whilst the weight of empirical evidence indicates that exercise has direct and persistently negative impacts on the physiology and quality of life of a significant subgroup of ME patients. Any universally applied therapy is unlikely to address the heterogeneity of ME, and graded exercise is particularly unsuitable as it may worsen the condition, and should not be generally recommended without a high degree of confidence that it will not be applied to susceptible patients: it is difficult to conceive of a more inappropriate therapy for ME. By increasing the risk of relapse and overall health risks, rather than reducing them, graded exercise therapy also risks increasing the burden of illness on society at large. The present review suggests that an approach based on treatment of the underlying physiological dysfunction will be more fruitful.

Abbreviations

ATP = Adenosine triphosphate, RNase L = 2',5'-oligoadenylate (2-5A) synthetase/Ribonuclease L

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