National Institute for Health and Clinical Excellence
CFS/ME consultation draft
29 September – 24 November 2006
Comments on chapter 6

Status	SH organisation	Order no.	Document	Page No.	Line no.	Comments	Responses
SH	25% ME Group	163	FULL	137	16	'Pacing' as CMO Report recommended	Pacing has been defined in the glossary.
SH	25% ME Group	164	FULL	137–255		"Management" The issue of CBT/GET has been addressed above, but four points need to be considered: • on page 188 (in the box), the statement recommending planned increases in duration of physical exercise, especially aerobic exercise, is not accepted by international experts such as Professor Paul Cheney who, in 1999, emphasised that: *"The most important thing about exercise is not to have them do aerobic exercise. I believe that even progressive aerobic exercise, especially in phase one and possibly in other phases, is counter-productive. If you have a defect in the mitochondrial function and you push the mitochondria by exercise, you kill the DNA"* (Cheney lecture, International Congress, Orlando, Florida, 5th – 7th February 1999) • on page 199 (in the box), the	Issue 1 – Aerobic Exercise. The evidence reviewed does not answer this question specifically, and evidence on the biochemical responses of people with CFS/ME is outside the scope of this guideline. However, the evidence reviewed does support that use of GET can improve symptoms, but we recommend that the preferences, needs, and physical functioning of the individual should be considered paramount when agreeing interventions. Issue 2 – The list of strategies is intended as a list of possible options. Regarding the team, this guideline is intended to drive changes in the care of people with CFS/ME. The issues you raise are implementation issues and we will bring these to the attention of the implementation team. Issue 3 – Thyroid. The GDG did not find any published clinical trials the benefits of thyroxine supplementation in ME/CFS. In the absence of clear evidence, the potentially harmful effects of thyroxine supplementation in biochemically euthyroid patientsmust be considered..

						recommendation that when experiencing a set-back, the patient should "*talk to supporters / family / friends*" is both unrealistic (there is virtually no professional support network for those with ME/CFS throughout the UK) and insensitive (countless numbers of severely affected exist in extreme isolation); equally, to refer (on page 200) to "*guidance from the CFS/ME support team*" is ludicrous when most of the country has no such thing. Many people with severe ME/CFS require 24 hour care, but have to endure endless battles with and abysmal minimal input from Social Services • on page 229 the statement "*Thyroxine should not be prescribed when the adult or child is biochemically euthyroid"* is open to question in patients with ME/CFS because it has long been known by experienced physicians that ME/CFS patients are often clinically hypothyroid, especially at tissue level, even if biochemically euthyroid. There may be conversion problems or receptor resistance problems not detectable on routine tests. If there is a receptor blockage, there could in fact be an excess of T3, which is then converted to Reverse T3	Issue 4 – Complementary therapies. No evidence for the use of complementary therapies to treat CFS/ME as a whole was identified. However, we have recommended that individuals may choose to use such therapies for symptom control.

						(which is useless to cells). As reported by Professor Kenny De Meirleir from Belgium, it is known that ME/CFS patients have a much higher level of a protein that is 98% identical to T3. Because this “foreign” protein can bind to T3 receptors, T3 cannot bind to its own receptors and is therefore ineffective in its role of activating cellular metabolism. Thus the bioavailability of T3 needs to be investigated. In ME/CFS, T3 levels are often low, or at the low end of the normal range, so selenium levels need to be investigated in patients with ME/CFS who have reduced T3 levels: this is because selenium (as selenocysteine) is an integral component of two important enzymes, glutathione peroxidase and iodothryonine deiodinase; it is expressed in the liver and it regulates the conversion of thyroxine (T4) to the active and more potent T3. Individuals who have a deficiency of 5’ deiodinase cannot produce T3 from T4, thus it is necessary to establish baseline levels of selenium in ME/CFS patients whose T3 levels are low. TSH levels may vary from week to week. Ultrasound often shows shrinkage of the thyroid. NeuroSPECT scans tend to be grossly abnormal. It is essential to do thyroid antibody tests. Thyroid pathology is but part of a Generalized autoimmune	

						dysfunction (The Complexities of Diagnosis. Byron Hyde. In: Handbook of Chronic Fatigue Syndrome. Leonard Jason et al. John Wiley & Sons, 2003) • on page 253 (in the box), it states: "*There are no complementary therapies that treat CFS/ME and their use is not recommended".* This is a sweeping and unsubstantiated assertion; moreover, many patients with ME/CFS have found real benefit from complementary interventions and the Draft Guideline itself acknowledges that such interventions "*may be helpful for individuals as part of their own management"* (see also patients' surveys referred to in the Draft Guideline)	
SH	25% ME Group	165	FULL	138	1	As in the tragic case of [X] (AND MANY OTHERS), even to think of imposing CBT and GET on house-bound severely affected patients makes such patients objects of derision and shows a disturbing lack of understanding of their situation. Those who are bed-bound are nowhere near "activity management" level (page 138, line 1). Many of those with severe ME/CFS may have between 10% - 20% functional ability, and [X] himself concedes that at least 80% functional ability is needed in order to engage in activity management. The proposed 90 minute sessions (a considerable percentage of which 18 will be via the telephone for those with severe	We have recommended that the needs, preferences (including the mode of delivery of any intervention), and abilities of the individual should be taken into account throughout the process.

						ME/CFS) are not feasible. Many people with even moderate ME/CFS are not able to use the telephone for as much as 10 minutes at a time. How much therapeutic intervention can be delivered by telephone, especially for those who are isolated?	
SH	25% ME Group	168	FULL	138	1 Section 6.3	In the document I can find CBT, then GET – but the next section seems to be about setbacks. Where has pacing (or Activity Management) gone?	Please see section 6.3.1.3 (in original doc – numbering may change for final version).
SH	25% ME Group	169	FULL	139	10 + 16	Why such a specific 'ultimate goal'? Line 5 states that increases are 'individually tailored'. Reading this doesn't give an idea of how variable and serious the illness is. Most patients who fulfil the criteria for CFS/M.E. would be unable to do a 30 minute brisk walk 5 times per week, in fact it would be dangerous for them to attempt this. Risk of relapse from exertion should be included here.	This is the goal used in the clinical trials which have been shown to produce benefits. However, we have stressed the need for individual goals to be agreed, which may be different.
SH	25% ME Group	170	FULL	140	2	What is this 'specific formula'?	Noted and clarified.
SH	25% ME Group	171	FULL	140	13	'as described in this guideline' – where? Page reference.	Noted and revised.
SH	25% ME Group	172	FULL	140	13	'this population' shouldn't include children and severely affected people, but sounds as if it does.	Noted and revised.
SH	25% ME Group	173	FULL	140	24–28	Denies the responsibility that professionals hold in the misuse of inappropriate GET for people with severe ME, blaming seemingly people themselves as undertaking it '*independently*' or '*at the gym'*!!, when it has been unhelpful/ bad , as if it were simply down to not doing it properly without '*adequate professional supervision*'. This is surely inaccurate.	Noted and revised. We have recommended that GET should only be delivered by professionals with appropriate training.

						The 25% Severe ME Group Gibson Inquiry Document shows clearly that people have been advocated GET by Psychiatrists and in Psychiatric units with devastating consequences. http://www.25megroup.org/Campaigning/Gibson%20Parliamentry%20Inquiry/25%25%20submission/25%20final%20sub%20to%20Gibson%20(2).doc	
SH	25% ME Group	175	FULL	141	19	Sleep disturbance in CFS/M.E. can be devastating and sleep hygiene may not help at all. Post-encephalitic sleep disorders are common in ME (not chronic fatigue conditions), and in other neurological conditions affecting the brain stem.	Noted, and we have stressed the need for healthcare professionals to use 'specific intervention if there is a concurrent primary sleep disorder.'
SH	25% ME Group	176	FULL	142	1 + General	Why are 'setbacks' part of 'recovery' and why is there a 'normal course'? Each patient is very different, and it doesn't help clinicians to be led to expect a certain course of illness. Why is the word '**relapse'** not used in this section? It seems that 'setbacks' are to be managed and it is possible to prevent 'relapses' – but this is not my experience. (See page 183 section 6.3.6.7 and page 186 last bullet point)	The section on setbacks has been revised, and the GDG considered the term to be appropriate.
SH	25% ME Group	177	FULL	142	10	'advisable to maintain an exercise programme …' – not borne out by experience. This would be disastrous for an ME sufferer; fine if you have a chronic fatigue condition though. So many ME patients have been told this and been made worse.	This section has been revised.
SH	25% ME Group	178	FULL	143	26	ALL exercise should be stopped at this stage to allow the body to rest and improve.	This section and the recommendations have been revised.
SH	25% ME	179	FULL	143	27	This is not a good description to	This section and the

	Group					communicate patients' experience of a 'severe setback', especially those who are severely affected. Relapses can be devastating and last for months or years.	recommendations have been revised.
SH	25% ME Group	180	FULL	144	21 – 23	Equipment is useful to help with energy management and to improve well-being and quality of life. They are a useful tool, and should be available for as long as they are useful. The 'risks associated with prolonged use' of a car for a healthy person are greater.	Noted, and we have recommended that the use of equipment should be considered as appropriate.
SH	25% ME Group	181	FULL	145	6.3.2.6	QALY = Quality Adjusted Life Year	Noted and added to the Glossary.
SH	25% ME Group	182	FULL	147	11	**Problem: The ignoring of patients' own evidence** "Evidence-based medicine" (EBM) is often quoted as the gold standard by which all interventions are to be judged. Contrary to sound-bytes emanating from the psychiatric lobby, EBM does not consist solely of random controlled trials (RCTs) but must include all three sources of evidence (1) RCTs (2) patient experience and (3) clinician experience. In the case of ME/CFS where -- due to prevailing policy -- there is a paucity of good quality evidence about non-psychiatric interventions such as dietary modification and other forms of complementary medicine, it is irrational to rely on just five RCTs that appear to support GET as the intervention of choice (page 147, line 11) whilst ignoring the other two components, especially given that the RCT study participants may not have had authentic ME in the first place and	Noted and we have recommended the use of a multi-component programme tailored to the needs of the individual.

						that the RCTs excluded those with severe ME/CFS.	
SH	25% ME Group	183	FULL	147	12	Moreover, the sample sizes in the five RCTs ranged from just 49 to a maximum of only 148 (page 147, line 12). How relevant the health status of these few patients is to the large number of severely affected ME/CFS patients in the UK is impossible to say. It is worth recalling that Wessely himself has dismissed other researchers' biomedical studies on the grounds that there were too few participants to be meaningful, yet the NICEDraft Guideline is promoting a national policy on what is by any standards a small and unrepresentative sample.	Noted.
SH	25% ME Group	184	FULL	147	10 – 15	But the sample sizes are to small to be representative and patient surveys, which included 1000s of patients, found a different result and many patients reported a worsening of illness with GET.	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET.
SH	25% ME Group	185	FULL	147	11–12	"Evidence-based medicine" (EBM) is often quoted as the gold standard by which all interventions are to be judged. Contrary to sound-bytes emanating from the psychiatric lobby, EBM does not consist solely of random controlled trials (RCTs) but must include all three sources of evidence (1) RCTs (2) patient experience and (3) clinician experience. In the case of ME/CFS	Noted and we have recommended the use of a multi-component programme tailored to the needs of the individual. We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and

						where -- due to prevailing policy -- there is a paucity of good quality evidence about non-psychiatric interventions such as dietary modification and other forms of complementary medicine, it is irrational to rely on just five RCTs that appear to support GET as the intervention of choice (page 147, line 11) whilst ignoring the other two components, especially given that the RCT study participants may not have had authentic ME in the first place and that the RCTs excluded those with severe ME/CFS. Moreover, the sample sizes in the five RCTs ranged from just 49 to a maximum of only 148 (page 147, line 12). How relevant the health status of these few patients is to the large number of severely affected ME/CFS patients in the UK is impossible to say. It is worth recalling that [X] himself has dismissed other researchers' biomedical studies on the grounds that there were too few participants to be meaningful, yet the NICEDraft Guideline is promoting a national policy on what is by any standards a small and unrepresentative sample.	preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET. We have also made specific recommendations that GET may not be appropriate in people who are severely affected, but that elements may be useful if agreed with the individual after informed, shared decision making.
SH	25% ME Group	187	FULL	159	3(a)	This question produced a very interesting response: When asked about the appropriateness of increasing aerobic exercise GDG round 2 agreed with this treatment in 4 out of 6 patient categories (66%), and disagreed or was uncertain about the other 2 (33%). The wider group disagreed with this treatment in 2 out of 2 patient categories (100%). This	Noted, however, the simple use of percentages here does not indicate the strength of agreement, but simply the number of responses. Details of the strength of consensus can be seen in Appendix 3.

						indicates strong disagreement with this treatment amongst the wider group and it would have been helpful to have measured the strength of this disagreement by including the other four patient categories. Given the 100% disagreement about the appropriateness of this treatment in the wider group, it is un-scientific to recommend increasing aerobic exercise elsewhere in the report. e.g. page 195, 6.3.6.25 page 203 line 26	
SH	25% ME Group	188	FULL	166	3(h)	The wider group also seemed to have more definite views about the envelope theory, and to disagree with the GDG. This seems important and we feel should be mentioned in the report.	Noted and these results should be used in conjunction with the 'Evidence to Recommendations' sections to clarify the intent of the GDG and the derivation of the recommendations.
SH	25% ME Group	189	FULL	169	3(k)	None of the questions about 'normalising sleep patterns' went to the wider group.	Please see the Methods section for details of which questions went to the Wider Group.
SH	25% ME Group	190	FULL	170–171	3(l)	None of the questions about complete rest went to the wider group. I would disagree with the GDG about adults and children with severe symptoms.	Please see the Methods section for details of which questions went to the Wider Group.
SH	25% ME Group	191	FULL	172	3(p)	In contrast, the GDG were more certain about individual CBT than the wider group.	Please see the Methods section for details of which questions went to the Wider Group.
SH	25% ME Group	192	FULL	174	Section 3	'Term (**pacing**) is not clearly defined': there are good definitions available (e.g. Ellen Goudsmit). I think that CBT and GET are also not clearly defined, and pacing is unfairly sidelined when many patients consider it to be the best management approach.	These were questions used in the first round, and cannot therefore be changed.
SH	25% ME Group	193	FULL	175	Sections4 + 5	Why are adults and children with severe symptoms more likely to be offered GET and Graded Aerobics	These were questions used in the first round, and cannot therefore be changed.

						Therapy than those with moderate or mild symptoms? At least by members of the GDG. Will this section be in the final guidelines? Most of the research excludes severely ill patients, and many severely ill people have been made worse by GET.	
SH	25% ME Group	194	FULL	177	Section 11	The phrase ‘CBT techniques’ is used. Are these defined? And could ‘pacing techniques’ be added to other therapies too?	These were questions used in the first round, and cannot therefore be changed.
SH	25% ME Group	195	FULL	181	6.3.6.2	‘..component **of** the programme …’	Noted and revised.
SH	25% ME Group	196	FULL	181	6.3.6.3	Everyone’s dream is to return to normal activities – it is not a ‘goal’ because it cannot be achieved by effort but only if recovery occurs.	Noted and revised.
SH	25% ME Group	197	FULL	183& 184	6.3.6.10	This section is unfair and does not highlight the reality of patient and other ME Organisations reporting. This sort of statement is only said by psychiatrists who want to promote their own ideology i.e. CBT and GET. PACING was accepting as one of the most used and successful management strategies by all the patient organisations in the CMO's Report.	Noted and this section of recommendations has been revised.
SH	25% ME Group	198	FULL	184		Final bullet point – ‘those’ implies that there are ‘strategies’ which encourage complete rest.	The view of the GDG was that this was a strategy that was sometimes used.
SH	25% ME Group	199	FULL	184		Think the word ‘relapse’ would be more appropriate than ‘set-back’ at the end of this section.	Setback is the agreed term in this guideline.
SH	25% ME Group	200	FULL	186	6th bullet point	‘unhelpful beliefs about sleep’ – who is to decide what ‘beliefs’ are realistic?	Any interventions are to be undertaken in partnership, with shared decision making throughout the process.
SH	25% ME Group	201	FULL	187	3–4	How can anyone ‘normalise fluctuations’ in their symptoms?	This has been revised.

SH	25% ME Group	202	FULL	188	6.3.6.14	I have a friend who had mild ME, and was an active mother of [x] young children. A course of Graded Exercise (TRAINED THERAPISTS; also see Personal Experience relating to Page 258. 7.3.1.4 below), has reduced her to a bedbound invalid, requiring nursing care around the clock. Her husband has been forced to give up a good job in order to nurse her. Another friend with moderate ME tried GET, as prescribed by a doctor at one of the ME centres of excellence. Her condition deteriorated, she became severely affected and she is now a long-term hospital inpatient, because her body cells are breaking down.	…
SH	25% ME Group	203	FULL	188	6.3.6.15	Everyone I know with severe ME has had to give up work and many have tried to return, but major relapses have meant they reluctantly ended their careers. I no of no one well enough to work again, as relapses and fluctuations in symptoms render it virtually impossible to hold down jobs long term. I am attempting to work from home, within Permitted Work rights…but I can only achieve a low number of hours per week and that is being very realistic. I know only too well, the consequences of attempting more.	Noted and we have recommended that an individualised approach should be taken when the individual is fit and ready.
SH	25% ME Group	204	FULL	191	Last line	'would like' should be replaced by 'is able to'. Any patient would *like* to progress, but they cannot make themselves able to.	We have noted that this should be done 'if appropriate'.
SH	25% ME Group	205	FULL	194	2	For people who are severely affected 'rest' needs to be as total as possible,	The recommendation is headed 'may include' and would be tailored

						so there is no such thing as a 'rest activity' – even a relaxation tape is a big activity for someone who's very ill and can cause collapse.	to the individual.
SH	25% ME Group	206	FULL	194	5	'stretching' sounds like muscle stretches. Joint mobility is more important for people who are severely affected.	The recommendation is headed 'may include' and would be tailored to the individual.
SH	25% ME Group	207	FULL	194	Last bullet point	There is no guarantee that someone will be able to return to any previous level. Relapses can be serious and long-term.	Noted and revised section on relapses.
SH	25% ME Group	208	FULL	195	6.3.6.25	The GDG disagreed with using GET in adults with severe M.E. (see pages 159 and 161**). It should therefore not be recommended here.** IT SHOULD BE REMEMBERED THAT THERE IS NO 'EVIDENCE BASED MEDICINE', TO RECOMMEND ANY FORM OF GET FOR THE SEVERELY AFFECTED OR CHILDREN	Noted and revised.
SH	25% ME Group	209	FULL	196	6.3.6.29	It is not mentioned that some people with severe CFS/M.E. (especially children) sleep for nearly 24 hours per day, and cannot be kept awake. Most experienced specialists think that the best approach is to let them sleep.	We have made recommendations on the risk of prolonged bed rest, but the needs of the individual should be taken into account when tailoring interventions.
SH	25% ME Group	211	FULL	198	6.3.6. 32	Sleep Management The comment '*if management strategies do not result in improvement the possibility of underlying sleep disorder or dysfunction should be considered*' seems bizarre , when people with severe ME, myself included , do not have good sleep patterns despite trying all sorts of techniques because they actually have True ME not just Chronic fatigue! Sleep dysfunction is part of ME, so one	Noted and we have recognised the impact of this on people with CFS/ME.

						would expect this to be apparent and I do not know anyone who has 'managed' sleep pattern with severe ME. Is this guidance actually for CFS as opposed to ME?	
SH	25% ME Group	212	FULL	198	6.3.6. 34	Certainly the relaxation techniques advocated particularly '*progressive muscle relaxation*' would be absolutely disastrous for people with the true muscle dysfunction found in severe ME, such as myself. Yet no warning is provided. I feel it simply should not be advocated for this group of people in this form as it could easily lead to worsening of symptoms and overuse of muscles.	This section has been revised based on stakeholder comments.
SH	25% ME Group	213	FULL	198	6.3.6.35	The early stages and relapses should be approached particularly carefully: rest, recuperation, and compassionate support are the most important components of improvements when people are first ill and when the relapse	This section has been revised based on stakeholder comments.
SH	25% ME Group	214	FULL	199	6.3.6.36	The healthcare professional should, **with the patient, try to** ascertain the cause of the setback.	Noted and revised.
SH	25% ME Group	215	FULL	200	4th bullet point	In a severe setback, reduction of activities is inevitable – how is a setback defined?	Noted and revised.
SH	25% ME Group	216	FULL	202	14	'needed' should be replaced with **need.**	Noted and revised.
SH	25% ME Group	217	FULL	202	17	'patients' should be replaced with **patients'**.	Noted and revised.
SH	25% ME Group	218	FULL	202	18	'clear' should be replaced with **clearly**.	Noted and revised.
SH	25% ME Group	219	FULL	203	26	Does the evidence support 'gradual increases in aerobic exercise'? See comment for page 159 3(a) The 'evidence' is also very weak for advocating such approaches	Please see the detailed evidence review for protocols on increased aerobic exercise used in the trial evidence.

SH	25% ME Group	220	FULL	204	3– 6	This assumes that any poor outcomes are due to the therapist not the treatment, which is unproven. For the individual patient, benefits may not outweigh the harmful effects, and we do not know that poor experiences 'should be avoidable'. How can patients tell the difference between inflexible programmes and more suitable ones?	The 'Understanding NICE Guidance' based on the clinical recommendations will be available to patients for information on the recommended programmes.
SH	25% ME Group	221	FULL	229	6.4.5.4.	Some research should be done on the thyroid function. Levels of T3 andT4 and thyroid stimulating hormone should be measured at times in all patients and the readings scrutinized to see if many are at the bottom end of the normal range. (There is also evidence to suggest that there may also be some 'peripheral resistance' to thyroid hormone in ME/CFS patients.) This is a very complex but crucial issue that requires detailed research. Also it would be useful to compare readings when very ill with reading taken if symptoms improve. Likewise with B12.	When making treatment recommendations, NICE cannot rely solely on the results of laboratory research. The GDG is not aware of any published clinical trials of thyroxine supplementation in ME/CFS. The GDG has recommended that investigations and diagnosis are regularly reviewed in CFS/ME, and that investigations are repeated if there is no improvement, particularly in the severely affected.
SH	25% ME Group	222	FULL	230	6.4.5.7 and 6.4.5.8	I am very concerned that 2 of the drug treatments have been advocated are *Amytryptyline* , and *Melatonin.(for children)* I have tried both these drugs and both of them resulted in horrendous impact in on my symptoms even at much reduced doses. Amytryptiline made me bed bound and caused me to be very severely affected ever after. Melatonin even 32x lower than the original dose prescribed by an ME consultant made me so ill I could not use my muscles and made me so dizzy	Noted and we have recommended the need to review the efficacy and side effects.

						and sick and increased my pain that I was in bed weeks recovering. Yet neither of these have been acknowledged as possibly risky to use especially with the severely affected, even at significantly reduced doses. The deterioration I experienced was unacceptable and frankly there should be a warning about the risk of making people worse and the need for proper detailed monitoring. I would be very concerned about anybody else having to go through such a severe reaction. I am not sure the drugs should be recommended at all, personally. It is not just about reduced dosage. It is about sensitivity to drugs and risk of worsening an already complex range of severe symptoms.	
SH	25% ME Group	223	FULL	230	5	'skeptical' – spelling - **sceptical.**	This has been changed.
SH	25% ME Group	224	FULL	235	13 -17	There is enormous concern amongst patients about **who** is doing the training and **what exactly they are being taught.**	In accordance with the methodology for clinical scenarios, the assumptions that form the basis for answering the questions must be explicit so that respondents have a common understanding of the factors that influence the appropriateness of treatment. These statements were agreed as assumptions for the questionnaire. They are not guideline recommendations. A fuller explanation is now in the methodology chapter.
SH	25% ME Group	225	FULL	253	6.6.5.1	Delete 'and their use is not recommended'. This is unnecessary for symptom relief as it is accepted that PWME find them useful.	This has been revised. The GDG considered the evidence to be insufficient to recommend any of these therapies to be available on

							the NHS, but that people do find them helpful.
SH	25% ME Group	226	FULL	253	6.6.5.3	Delete 'therefore they are not Generally recommended for the treatment of the symptoms of CFS/ME. Again it is accepted that PWME have found supplements helpful, and the implications of NICE guidelines being adhered to by health professionals, particularly GP's, would mean that PWME would be further restricted in working cooperatively in the self management of their illness. Again biomedical research is desperately needed to identify which supplements may be of help. Most of the supplements that PWME take are Generally accepted as 'safe'. E.g. B12, magnesium. Those specific supplements that NICE have concerns about PWME taking, if any, should instead be specified	This has been revised. The GDG considered the evidence to be insufficient to recommend any of these therapies to be available on the NHS, but that people do find them helpful.
SH	Action for M.E.	39	FULL 6.Mgtmt	137		Many aspects of this are welcomed. These include: an integrated and tailored approach to care; regular contact between the health professional and the patient; and the stated need for an appropriate level of training for health professionals. Concerns have been raised regarding what is considered 'appropriate levels' of training and some clarification of this description is required.	Noted with thanks. Defining 'levels of training' is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	Action for M.E.	40	FULL	138	6.3.1.1	A more straightforward explanation of CBT within the current research context is required. Ambiguity in language such as referring to CBT as a treatment, while placing it under a section entitled 'Management', creates confusion and	We have noted all these issues, particularly those around symptom control, and revised both this section and the relevant recommendations to address these and other comments.

						exacerbates concerns. Similarly, the view that it is not curative should be elucidated. We believe it to be a useful management strategy for some people and should be seen as part of a whole management package. There are few examples of longitudinal studies to determine the long-term benefits of CBT, therefore the statement "CBT is well understood and well researched." is not accurate. The use of CBT has been hotly debated among constituents and, while we consider that it can be useful for some individuals if appropriately applied by experienced practitioners, we must note the concerns of our members and those of the wider M.E. community. CBT must not be 'oversold'. A number of respondents have found it helpful but others are worried that it might be used to replace treatment for more immediate problems, such as the proper management of pain, which is often a significant symptom of M.E.	
SH	Action for M.E.	41	FULL	139	6.3.1.2	GET remains a controversial treatment. NICE have clearly striven to provide a clear definition of this management process. However, further and emphasised acknowledgement of the fear and damage this procedure has created in a considerable number of people with M.E./CFS is required. We noted the recognition that this technique has sometimes been implemented with significant adverse responses and that it is essential that agreement and negotiation be at the very centre of a GET programme. This	These are key concerns and the recommendations have been clarified and expanded to address these and other concerns.

						detailed comment is not reproduced in the nicer guidelines, thereby omitting its FULL context. The limitations of the research on GET – small studies with ill-defined levels of severity of participants – causes concern, particularly when aspects of it are being recommended in the guidelines for the severely affected. Many people with M.E./CFS strenuously rejected the use of aerobic exercise, even for people with initially moderate M.E./CFS. A considerable number of our constituents believe the balance of advice of activity and rest must be reconsidered, and that the guidelines should err on the side of safety. This view needs to be addressed. Clearly delineated criteria for the evaluation of the level of professional expertise is required, and it has been suggested that an appropriately qualified practitioner should be a compulsory member of the multi-disciplinary teams. Practitioners in primary care should always seek expert advice before recommending any aspect of a GET programme.	
SH	Action for M.E.	42	FULL	139	7– 8	The explanation of GET given here is much clearer than that outlined in the NICE guidelines and, presumably, provides a better understanding to health professionals. We suggest it be included in the NICE guidelines.	The recommendations on GET have been expanded and clarified to address such issues.
SH	Action for M.E.	43	FULL	141	6.3.1.3	Activity Management seems to link strongly to Pacing in all but name. Pacing is the favoured method of management shown by patient	Noted and revised.

						evidence.	
SH	Action for M.E.	44	FULL	141	6.3.1.6	There needs to be delineation between a 'setback' and a 'relapse', with 'setback' referring to a very brief period of time with limited symptom impact. Many of our constituents consider that the uniform use of the term 'relapse' fails to acknowledge the duration and severity of symptoms which can occur. In our survey, 91.9% compared to 8.1% considered the term relapse to be more accurate than setback.	The section on setbacks has been revised, and the GDG considered the term to be appropriate.
SH	Action for M.E.	45	FULL	142	7–9	While some delineation of the cause of 'setbacks' is given in the FULL guidelines, they do not appear in the NICEer version, and many of our constituents have commented on this omission.	This section and the recommendations have been revised.
SH	Action for M.E.	46	FULL	142 – 143		A considerable number of constituents noted how they felt obliged to undertake activity which increased the severity of their relapse. Consequently, it would be appropriate to emphasise that the degree of severity in the setback must be defined by the patient and respected by the health professional. Even for 'mild' setbacks some respondents argue that cessation of activity may be required for a short period. The crux of this is listening to the individual patient.	Noted and we have stressed the need throughout for healthcare professionals to acknowledge the impact of symptoms in individuals.
SH	Action for M.E.	47	FULL	145	6.3.2.1	This is a questionable statement and does not aid transparency of communication.	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Action for M.E.	48	FULL	146	6.3.2.8	Research undertaken this year by Dr Hazel O'Dowd indicates that group CBT is less effective than a one-to-one approach.	This recent evidence on clinical effectiveness has been added, but their planned economic analysis was not possible. Please also see the revised

							recommendation.
SH	Action for M.E.	49	FULL	146	6.3.2.10	Computerised CBT would reduce the person-centred approach that is required, particularly with an illness such as M.E./CFS, where personally validating human interaction is often limited.	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Action for M.E.	50	FULL	146		It was noted that the sample sizes were small. In the interests of transparency and building good will and understanding, reiteration of the limitations of the research available would be helpful. Understanding would be improved if this were placed in the context of 'currently available research'.	These are evidence statements agreed by the GDG, based on the evidence reviewed. Details of the trial limitations and strengths are noted in both the grading of the statements (see the Methods section and the NICE Guidelines Manual for details) and the detailed evidence review (Appendix 1).
SH	Action for M.E.	51	FULL	147	7–9	This illustrates one of the problems of offering CBT as a 'one size fits all' approach. Management of this illness requires a portfolio of symptom management and treatments.	Noted and we have recommended the use of a multi-component programme tailored to the needs of the individual.
SH	Action for M.E.	52	FULL	147		The sample sizes in support of GET are very small. The patient voice is overwhelmingly against what they perceive as GET.	Noted and patient concerns are noted in the guideline and in the recommendations.
SH	Action for M.E.	53	FULL	156	6.3.4.6	The importance of patient input is not made clear in lines 17-19.	Noted, thank you for your comment. This sentence has been revised.
SH	Action for M.E.	54	FULL	158	1– 3	These are assumptions about resources which could be stated earlier to ensure that a realistic assessment of the current context for the treatment of M.E./CFS is fully appreciated. Such transparency would be welcomed.	These statements were used to guide respondents when completing the questionnaire.
SH	Action for M.E.	55	FULL	181	6.3.6.2	We welcome this statement and would recommend that this be implemented across Government Departments.	Noted with thanks.
SH	Action for M.E.	56	FULL	181	6.3.6.3	Many constituents found the line 'main goal is to return to normal activities' an	Noted and revised

						unacceptable expression implying that they may not want to get better.	
SH	Action for M.E.	57	FULL	181	6.3.6.4	The evidence is limited to the current research context and needs to be specified. Pain is a significant symptom for a significant number of people with M.E. and needs to be listed here.	Noted and it is anticipated that the research evidence will be re-reviewed in two years. Recommendations on pain management have been added.
SH	Action for M.E.	58	FULL	184		A significant number of our constituents – particularly those with the more severe forms of M.E. – have found the second bullet point in this section (i.e. that there is no evidence for the benefits of complete rest) untrue. Indeed, many found the implicit tone of this section to imply that the patient voice should be disbelieved. In response to our survey question “During a setback, activity management should be maintained but NOT include prolonged rest….” 46.3% strongly disagreed and 27.8% disagreed.	The GDG recognises the need for rest and a section on Rest Periods has been added. However, there is no evidence, as defined above, for the use of complete rest. The GDG were aware of the risks of complete bedrest, including DVT, deconditioning, etc.
SH	Action for M.E.	59	FULL	185	6.3.6.13	“Challenging cognitions which may adversely affect rehabilitation and/or symptom management….fear of activity and perfectionist beliefs”. Significant comment has been received regarding this statement. Constituents have argued that this reinforces an underlying psychological analysis which directs management approaches and a fundamental understanding of the illness. This passage needs to be rewritten to clarify its implicit and explicit meanings.	These are accepted components of any CBT programme.
SH	Action for M.E.	60	FULL	185		“Decreasing somatic attributions and addressing over-vigilance…” See	See response above.

						comments made above (P185 6.3.13).	
SH	Action for M.E.	61	FULL	192	6.3.6.20	Comments regarding the use of the word ‘relapse’ rather than ‘setback’ and issues relating to cessation of activity have already been commented on.	We have used setback/relapse.
SH	Action for M.E.	62	FULL	195	6.3.6.25	Many severely affected people were disturbed by this suggestion – its inclusion needs to be accompanied by a reiteration of the fact that the patient needs to be in charge of their goals.	Noted and revised.
SH	Action for M.E.	63	FULL	195	6.3.628	Regular and frequent reviews are welcome	Noted with thanks.
SH	Action for M.E.	64	FULL	199	6.3.6.36	This should precede recommendations for the management of setbacks/relapses, to ensure the proper context is provided.	Noted and revised.
SH	Action for M.E.	65	FULL	202		A clearer definition of what constitutes a ‘suitably trained CBT therapist’ needs to be provided. We recently investigated a university-linked course for certificates and diplomas in CBT. We were informed that, following a course lasting a few days, we would be able to promote ourselves as a CBT therapist. Some assurance of quality control is necessary.	Defining standards is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	Action for M.E.	66	FULL	202	6.3.6.39	Again ‘appropriately trained’ needs further detail.	Defining standards is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	Action for M.E.	67	FULL	202	6.3.7	Does this mean the guidelines recommend 13-16 CBT sessions? There are linked issues here regarding number and availability of services A number of constituents have expressed the view that the	This is a discussion of the evidence, not recommendations.

						effectiveness of therapy depends primarily on the personal effectiveness of the therapist, rather than the specific therapeutic technique.	
SH	Action for M.E.	68	FULL	202 – 203	15 – 11	This statement is welcome and we would like to see it more prominently located within the guidelines and in any information dissemination regarding them. It should be noted, however, that this statement is omitted from the NICE guidelines and needs to be included. However, there are some ambiguities elsewhere (e.g. p 185 'fear of activity and perfectionist beliefs').	We have revised the description of CBT.
SH	Action for M.E.	69	FULL	203	17	The evidence is questionable. A more appropriate comment would be to state that it is regarded as showing the most significant evidence - according to NICE- in the context of current research.	Clarified, but the GDG considered the evidence to be convincing. And the context of current research is implicit throughout the guideline – please see the NICE version for the Update process.
SH	Action for M.E.	70	FULL	203	20–22	This recognition is very welcome but needs to be highlighted in both the long and the NICE versions of the guidelines.	The recommendations make this explicit.
SH	Action for M.E.	71	FULL	203	27–29	It is significant that patients did not support gradual increases in aerobic exercise. In our survey, 58% of those with mild to moderate M.E.; 76% of those with moderate M.E.; and 82% of those with severe M.E. strongly agreed that aerobic exercise could be damaging. A further 20% (mild), 15% (moderate), and 11% (severe), agreed. Again, there is need for greater understanding in this area. The lines referring to Healthcare professionals are confusing and should be made clear in the directions for	The recommendations have been revised to clarify the use of CBT/GET. Also the need for individualised programmes based on the needs and preferences of patient, with appropriate monitoring and review, is stressed throughout.

						implementing this management technique.	
SH	Action for M.E.	72	FULL	204	1–10	Patient control of goal-setting and pace of progress as a core feature of GET needs to be highlighted in all relevant sections, to establish the proper context and confront patient fears.	Noted and clarified.
SH	Action for M.E.	73	FULL	204	11–14	We received extensive General comment from constituents stating that GET was entirely inappropriate for people with severe M.E./CFS. In addition, in our survey we asked people to respond to the question: 'Aerobic exercise can be damaging for people with M.E./CFS'. For those with mild M.E./CFS 58% strongly agreed and 20% agreed with the statement. In relation to the moderately affected, 76% strongly agreed and 15% agreed. And in relation to how this might impact on the severely affected, 82% strongly agreed and 11% agreed.	We have not recommended GET for people with CFS/ME, but that elements may be appropriate, after a full discussion of the benefits and risks.
SH	Action for M.E.	74	FULL	204	15–23	The concern of the GDG is understandable and supported by the accepted research evidence. However, this issue relates to the integration of the patient voice and underlines the fact that a 'one size fits all' approach to M.E./CFS is ineffective. Again, emphasising the tailoring of management programmes for the individual would be helpful.	We have recommended the need for individualised programmes.
SH	Action for M.E.	75	FULL	205	6.4	Recommendations for pharmacological interventions are limited. Given the range of symptoms occurring with M.E./CFS a menu of treatment approaches is required.	The guideline does not address the management of individual symptoms. Please refer to the scope and methodology chapter. The evidence search was confined to that directly related to CFS/ME.

SH	Action for M.E.	76	FULL	207	4–8	The extremely limited research re. the severely affected has been noted by our constituents.	The GDG agrees.
SH	Action for M.E.	77	FULL	233	9–11	There are inconsistencies between the FULL and NICE guidelines. The FULL guidelines say that melatonin might be considered. In the NICE guidelines this is limited to children. We have had feedback from patients that melatonin is useful in the treatment of sleep disorders.	The view of the GDG was that there were other licensed medications available for adults. This was not the case for children.
SH	Action for M.E.	78	FULL	248	6.5.5.3	Many constituents find a tailored diet extremely helpful, so the input of a dietician as part of a multidisciplinary approach would be welcomed. In our survey, 42.7% strongly agreed and 41.2% agreed that diet and nutrition are important in the management of M.E./CFS.	Noted with thanks.
SH	Association for Psychoanalytic Psychotherapy in the NHS (APP)	14	FULL	181	6.3.6.3	there is no evidence that CBT is better than counselling - this is misleading as a recommendation - why?	Noted and revised.
SH	Association for Psychoanalytic Psychotherapy in the NHS (APP)	16	FULL	202	table 6.3.6.38 + lines 7–17	CBT - add "and / or counselling or psychotherapy should only be delivered by a suitably trained therapist" - the rest of this sentence has no evidence base to support it - that is, there is no evidence to support close adherence to a treatment manual over a more flexible approach adopted by an experienced and suitably trained therapist; nor is there any evidence that CBT has better outcomes for CFS than other psychological therapies, so the GDG are unjustified in supporting CBT alone,	This recommendation relates to the delivery of CBT alone.

						rather than supporting a range of psychological interventions, primarily according to patient preference, which appears to be a key factor for CFS patients, in the absence of any better understanding, or any good relative efficacy evidence	
SH	Association for Psychoanalytic Psychotherapy in the NHS (APP)	17	FULL	138	6.3.1.1	the treatment approach which should be considered first, on grounds of outcome and cost, as acknowledged elsewhere (p. 152) is counselling - why is this not defined here?	Thank you for your comment. This section has now been subject to revision to clarify that conclusions on the cost effectiveness of counselling cannot be derived from this study due to population differences.
SH	Association for Psychoanalytic Psychotherapy in the NHS (APP)	19	FULL	152	3–19	the main findings of this study are reported - that counselling is more cost effective than CBT, and that counselling has better outcomes than CBT - followed by tortuous, vague and perverse reasons given for why this guideline then chooses to ignore these studies - nor is any explanation offered why they do not appear in the list of RCTs reviewed (in the appendices) - this seems to be a result of bias in the GDG, what is the reason for ignoring the findings of this study in the recommendations?	This study was in a population of chronic fatigue patients, and only a subsection was a CFS/ME population. The GDG agreed that no conclusions for the guideline population could be derived. This section has been revised in order to make this clearer.
SH	Association of British Acknowledged – insufficient evidence	34	FULL	205	6.4	There has been no review of levocarnitine (L-carnitine) as a pharmacological therapy in fatigue	The guideline does not address the management of individual symptoms. Please refer to the scope and methodology chapter. The evidence search was confined to that directly related to CFS/ME. No evidence was found for this intervention directly relating to patients with CFS/ME.
SH	Association of British	20	FULL	145	6.3.2	The evidence statements are incorrect because selection criteria for most	These are evidence statements agreed by the GDG, based on the

	Neurologists					studies that showed efficacy of CBT and GET were based on broader Oxford criteria.	evidence reviewed.
SH	Association of British Neurologists	21	FULL	138		Accordingly, there is insufficient evidence that CBT and GET are effective interventions in adult patients diagnosed by the international (modified CDC) criteria	The trials used different diagnostic criteria, but this does not allow the differentiation between subgroups using the different definitions.
SH	Association of British Neurologists	24	FULL	156	9–19 6.3.4.6	There is limited data regarding (a) ideal duration of CBT and (b) long-term outcome of functional recovery from CFS/ME after CBT and GET. In the absence of such information, benefit from wider use of CBT and GET is unpredictable	Acknowledged.
SH	Association of British Neurologists	25	FULL	156	22 –25	The extrapolation of computerised CBT data from patients with anxiety and depression to those with CFS/ME is unscientific. Such extrapolation is only permissible if computerised CBT was recommended for the associated symptoms of anxiety and depression in patients with CFS/ME and the caveat must be clearly acknowledged.	No extrapolation was attempted.
SH	Association of British Neurologists	26	FULL	181	6.3.6.3	This statement, for reasons already stated above, is both unsubstantiated and unjustified as a General recommendation.	These statements represented the consensus views of the GDG.
SH	Association of British Neurologists	27	FULL	181	6.3.6.3	Due to the lack of adequate information in children (already acknowledged in this guideline), stating CBT or GET is a “child’s ..goal” is not appropriate	The statement represents the consensus view of the GDG.
SH	Association of British Neurologists	28	FULL	181		CBT and GET as a goal may be appropriate in selected adult cases (i.e., those who meet the Oxford criteria) rather than for all adults	The choice of treatment should be based on the individual’s needs and preferences, and be tailored to these.
SH	Association of British Neurologists	29	FULL	185	6.3.6.11	There is little evidence to recommend group CBT as an effective intervention in CFS/ME	Noted and revised.

SH	Association of British Neurologists	30	FULL	191	Bullet point	From where did the GDG discover the evidence to recommend that "when the duration of low-intervention has reached 30 minutes…the intensity of exercise should be doubled" Why not 20 or 40 minutes (as an argument)?	This has been revised.
SH	Association of British Neurologists	31	FULL	191		When the intensity of the exercise should be doubled is a matter of decision between the patient and the physician/therapist and no specific cut-off time should be proposed for incremental exercise	The GDG was concerned that GET is misunderstood and not used correctly. Therefore detailed guidance was given. It acknowledges, however, that programmes are individualised and that mutually agreed goals are part of the programme.
SH	Association of British Neurologists	32	FULL	193	Bullet Point (last but one)	Where is the research evidence for suggesting a maximum of 20 minutes rest at a given time? How has the GDG derived this specific time cut-off for "maximum permissible rest"?	Noted and revised – see also section on rest periods.
SH	Association of British Neurologists	35	FULL	202 onwards		There has been no review of modafinil for excessive daytime sleepiness in somnolent CFS/ME patients	Noted, and please see Appendix 1 for details of which interventions were reviewed and why.
SH	Association of British Neurologists	37	FULL	202 onwards		There is no recommendation on the specific use of pregabalin and duloxetine for myalgia given that both these drugs have been found to effective for muscle pain	We searched on CFS/ME exclusively, not for evidence on the management of myalgia.
SH	Association of British Neurologists	38	FULL	234	6.5	A poorly written section on dietary intervention with no advice on caffeine and alcohol both of which are known to worsen fatigue (many CFS/ME patients develop alcohol-intolerance). Avoidance of caffeinated beverages is particularly important for children with CFS/ME in whom headache is also a prominent symptom Advice on dietary modification in patients with irritable bowel is lacking (despite a rather elaborate discussion	No evidence was found. The guideline now cross refers to the NICE IBS guideline in development.

						on the overlap of CFS/ME and irritable bowel in an earlier section)	
SH	Association of Young People with ME	4	FULL	138	5&6	Inconsistencies: '…GDG considered that patients should take the lead on any behavioral approaches to manage their CFS/ME' is excellent … but Page 21 line 20 (above) as it stands, contradicts this statement.	Thank you. We have amended the recommendations on this to clarify and make consistent.
SH	Association of Young People with ME	9	FULL	139	9–18	<u>Goals</u> One cannot be prescriptive in CFS/ME. The Goal in Line 11: '30 mins of moderate aerobic exercise, 5 days out of 7 (for example a brisk walk) is of no practical value. After all - how many healthy people take a brisk 30 mins walk 5 days out of 7? This is only a realistic long-term or 'ultimate' goal for a mildly affected person with ME and then only if it was achievable prior to the onset of the illness. AYME believes that clarification is needed between the 'Ultimate Goals', allowing NICE-, medium- and long-term goals' to be placed in between. This would ensure a more gentle and carefully graded approach, particularly for the very severely affected. Percentages are less prescriptive and more patient-centred All people with CFS/ME, but particularly those who are severely and very severely affected, need to be taught that their activity management must start from a realistic baseline in order to achieve success. A more Generalised statement is needed on page 139, with specific examples, but using percentage ratings rather than specific	We have revised the recommendations to clarify and expand the goals and progression. Also throughout the guideline, we stress the need for patient preference to be taken into account. Regarding the 20% – this is maximum.

						time goals. AYME suggests that somewhere on Page 139 it should be pointed out that: All goals must be achievable. Clinical trials of GET have been based on an ultimate goal of achieving and maintaining 30 minutes of aerobic exercise. However, this stated goal may be completely inappropriate for many patients, especially those severely or very severely affected, who may be bed-bound, unable to weight bear. A sustainable baseline should be built up gradually by increases of 10%-15% for each activity using short-term goals (eg for the very severely affected - Step 1: propped upright for 60 seconds three times a day for one week; Step 2: propped upright for 70 seconds three times a day for one week, and so on).	
SH	Association of Young People with ME	15	FULL	141 Pg 197	19–21 6.3.6.30	Sleep This section is too brief and needs a reference to the excellent document on sleep found at cfspod.net/Document%20files/Bristol/Sleep.doc Please add that ‘one should move waking times back slowly, by 15/30 mins a week as part of a sleep hygiene plan’.	This section has been revised with more detail.
SH	Association of Young People with ME	16	FULL	142	4	Please add ‘…important for the patient to have an agreed written plan’	This section has been revised.
SH	Association of Young People with ME	17	FULL	190	6.3.6.18	Please add ‘… should be reviewed with their clinician and reduced …..’	This has been revised based on stakeholder comments.
SH	Association	18	FULL	188	6.3.6.14	Please add:	This is made clear in the detailed

	of Young People with ME					…gradual increases.	recommendations on how to plan the increases.
SH	Association of Young People with ME	19	FULL	199	6.3.6.37	Following the diagnosis of a viral illness as a set-back it should be recognised that rest is needed whilst the virus is active. The CFS/ME management plan should be returned to, once the virus has cleared.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	126	FULL	137	16	Is 'activity management' to be adopted as NICE's term for 'pacing'? If so will it have the same definition as that for pacing in the CMO Report?	Pacing has been defined in the glossary.
SH	BRAME (Blue Ribbon for the Awareness of ME)	128	FULL	138	23–28	6.3.1.1 CBT is not found to be an appropriate 'treatment' for ME/CFS by the majority of patients with this illness. The word 'treatment' also infers curative abilities, which is not true. Some patients, as with any other chronic illness, may find it of help with coping strategies, however the CBT advocated in this guideline is not about coping strategies, but takes the view of the Wessely and White school of thought that ME/CFS is a somatoform disorder and is about maladaptive illness beliefs. As already explained at 6.3.1 it is only the UK which continues to take this psychological/behavioural approach of CBT and GET to manage/treat ME/CFS. CBT, along with GET, do not manage the underlying core illness that are always present, they are not cures, nor do they promote recovery. As is shown clearly in the patient surveys over the years, the majority have found person-centred counselling	We have revised the wording in this section. Noted, but the evidence supports the effectiveness of CBT in improving both coping AND functioning in some patients. However, it is not clear from the evidence which subgroups will benefit most from the different interventions. Therefore the GDG considered that the needs and preferences of patients are paramount and should be taken into account when making shared decisions on the appropriate management plan.

						far more helpful and effective in enabling them to cope with living with a complex, chronic and debilitating illness. One of our respondents states *"With regard to the use of CBT in the treatment of ME I believe that NICE have started with the hypothesis that CBT works and then attempted to support the hypothesis."* She went on to say that "*NICE should have wiped the slate clean from treating ME as a 'mental health illness', recognised the correct (neurological) classification and started again.*"	
SH	BRAME (Blue Ribbon for the Awareness of ME)	130	FULL	139–140	General	Dr Paul Cheney (USA) who has seen over 5,000 patients with ME/CFS, since his involvement with the Lake Tahoe outbreak in the early 1980s, has been doing further studies/research following on from Peckerman's work. Dr Cheney recently highlighted in his September 2006 Seminar that Patent Foramen Ovale (PFO) is 'tightly associated' with ME/CFS to the order of at least 80% or more of patients. PFO is the persistence (or the acquired re-opening) of the normal foetal opening between the right and left atria of the heart. The assumed PFO is the same as in the foetus, to protect the body from oxygen. In ME/CFS patients are shifted left to right, not because they have an immature way of dealing with oxygen, as in the foetus, but because they have a defective way of handling oxygen . Half of patients exhibit atrial cavitation, and when those patients stood up, in 80% the filling volume	We have noted the need for the potential risks and benefits to be discussed before any intervention is agreed upon.

						collapsed. He found Magnesium helped restore 12% energy. Magnesium affects the intracellular energetics, proving that patients have a tremendous energy problem that is very sensitive to magnesium. Magnesium is needed for ATP to be converted to ADP to produce energy (see also Dr Myhill's interpretation of Peckermans research). This right to left shunt through the PFO means that unoxygenated blood FULL of carbon dioxide as well as products of liver metabolism is literally draining into the right side of the heart and that blood is going straight to the brain. 70% of patients show elevated lactate levels in the ventricular system which indicates a defect in energy in the brain, and correlated significantly with fatigue. 10% have evidence of neuronal destruction and elevated choline peaks – this also links in with the research currently being done by Prof Basant Puri in London, where he has also found raised choline levels in the brain with the ratio of choline to creatinine in the occipital cortex was statistically significant as it would occur by chance only 8 times in a thousand. Cheney said MRI scans showed 78% have punctate lesions which are consistent with small strokes. Mixed venous blood gas picture: PvO2 is 25 (it should be 40) – PvCO2 is 55 (it should be 45). Only 2 diseases he says shows this differential hypoxia with hypercarbia – pulmonary hypertension and ME/CFS. Instead of the oxygen being carried to	

						the mitochondria it is either being pooled in extra-cellular fluid, particularly, abdomen and legs, but is more likely being consumed by the oxidative pathway to create superoxide in massive amounts. Superoxide being the progenitor of all free radicals resulting in increased intra-cellular oxidative stress. He continues attempts to push beyond energy limits will cause injury. Prolonged energy deficits can cause semi-permanent DNA phenotype adaptations and complications can occur, especially with energy-sensitive systems such as the heart, the brain and the muscles. The most likely cause (not trigger) of ME/CFS is a disruption in handling the toxic by-products of oxygen utilisation. In ME/CFS catalase, the most protective enzyme in the body against the ravages of superoxide, is deficient in the heart, lungs and liver, and also that electromagnetic fields 'screw up' superoxide dismutase (SOD), which is a major anti-oxidant scavenger. 20% of deaths are due to heart failure in ME/CFS (Jason et al). This Cheney says in ME/CFS is due to diastolic heart failure (which is not a failure to eject but a failure to fill properly) where primary relaxation deficit gives rise to decreased cellular energy. Cheney says it is increasingly clear that in ME/CFS, a diminished threshold for oxygen toxicity exists, and that each patient will have a unique threshold. These findings have a significant	

						negative effect in hospital situations and operating theatres in using oxygen during surgery – a patient with ME/CFS could be given too much oxygen and be killed. BRAME feels this research shows that obviously reinforces the need for caution to be taken re exercise/activity, but also should be red flagged to doctors/hospitals to observe any adverse reactions particularly oxygen.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	131	FULL	139–140	General	Research showing other bio-medical indicators are: Durval Costa (UK) and his SPECT scans showing reduced blood flow in the brain. Bell and Streeten (USA) on low blood volume and postural hypotension. Dr Stephen Sinatra (USA) on heart muscle disease due to mitochondrail failure. A significant (8%) global reduction in grey matter in the brain compared to controls (Floris P de Lange et al Netherlands 2004)	Noted.
SH	BRAME (Blue Ribbon for the Awareness of ME)	132	FULL	139	2–8	Whilst we do not agree with, or advocate, GET for the ME/CFS population, we hope that any therapist will fully inform patients of all the scientific evidence and risks they are putting on their health by undertaking a course of GET. It is wrong to talk of recovery, as this implies that you can cure people. It is well documented, including throughout the CMO Report (2002), that there is no cure for ME/CFS. Patients may, over a long period of time, make a substantial improvement, or go into remission, but	Noted and we have recommended that the benefits and risks of any treatment should be part of the discussion between the healthcare professional and the patient.

						they are always at risk of having a relapse/set back. Advocates of CBT/GET say that you should be positive for patients, but patients have to live with reality, and for therapists to give false hope can have a very negative effect and impact on patients when a relapse occurs.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	133	FULL	139	9–16	Goals -To expect ME/CFS patients, as they have in the clinical trials, to have the ultimate goal to achieve and maintain 30 minutes of moderate aerobic exercise 5 days out of 7, is quite a challenge for most individuals in the General population, but for those who are ill with ME/CFS is totally incomprehensible. ME/CFS patients would have to be very mildly affected to achieve, and more importantly sustain, such a level, day after day without any adverse affects. Given that GET is only shown to be effective for those who can achieve and sustain this ultimate goal, and that for the majority of the ME population this will never be achievable, this means that GET is not a successful, or appropriate, intervention for the patient population.	Noted and the recommendations on GET have been expanded and clarified to address such issues, including that of patient preference and ability.
SH	BRAME (Blue Ribbon for the Awareness of ME)	134	FULL	139	15–18	To state that the severely affected should aim for this ‘ultimate goal’ of exercise 5 days out of 7, is completely misunderstanding, and underestimating, the level of severity of their illness. Of course they hang on to the hope that one day biomedical research will give answers to their illness, and they all hope and dream to have a normal life. For many the reality	We have stressed the need for different goals to be agreed for people who are severely affected in this section and the recommendations.

						may be improving sufficiently to being able to leave the house in a wheelchair, even better if they have an electric wheelchair and can do it on their own, or to be able to walk around the house using an aid, or even better independently, and being able to wash and dress themselves.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	135	FULL	139	20–26	If GET is used, if anything on mildly affected ambulatory out-patients, then it is important that the patient is in control and they can choose to stop at any point without discrimination against them.	Noted, and this is highlighted as a key principle when deciding upon the appropriate management interventions in the recommendations.
SH	BRAME (Blue Ribbon for the Awareness of ME)	136	FULL	140	2	What is meant by, or what is the ‘specific formula’?	Noted and clarified.
SH	BRAME (Blue Ribbon for the Awareness of ME)	137	FULL	140	17–19	GET is in no way or form appropriate for the severely affected, both adult and children, and that it is used in clinical practice on these groups just shows the amount of people being harmed by this ‘treatment’.	We have noted in the recommendations that elements of GET may be appropriate for people with severe symptoms, but this needs to be undertaken only when the individual’s need, preferences, and ability have been considered. Also, individuals can refuse any component of a care plan without detriment to the provision of other aspects of care.
SH	BRAME (Blue Ribbon for the Awareness of ME)	138	FULL	140	19–22	Of course patients are concerned about being forced to push their bodies beyond their abilities through GET programmes. Patient experience shows that it is harmful, and this is backed up by a wealth of research evidence, showing that the bodies of people with ME and ME/CFS react differently to control groups – there is	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both

						altered muscle excitability, altered breathing, altered heart rates etc. The altered heart rate is particularly important as it shows that aerobic exercise causes physiological distress and harm – so of course there are concerns, valid and research corroborated concerns.	the potential risks and benefits of properly applied GET.
SH	BRAME (Blue Ribbon for the Awareness of ME)	139	FULL	140	22–28	The suggestion that all adverse patient experiences are down to 'General exercise programmes' is erroneous. This may apply to some patients, who are wrongly told by their doctors to exercise, and go to the gym, but the vast majority are down to GET programmes. Do you honestly believe that the severely affected put through GET had got out of their beds, where they often have trouble even sitting up, and toddled along in their wheelchairs to the local gym!! Research evidence and patient experience and testimonies show that it is GET programmes as described within this document that are causing the harm – this is not an appropriate treatment and must stop now – medical practitioners must stop saying, "Oh they must be doing it wrong" and take some responsibility.	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET. We have also made specific recommendations on the use of elements of GET for people with severe symptoms.
SH	BRAME (Blue Ribbon for the Awareness of ME)	140	FULL	140	28–30	Symptom control and energy management are the most appropriate management strategies for the severely affected. Severely affected would even find activity management difficult to achieve.	We have noted only that activity management may be an appropriate choice, alongside symptom control.
SH	BRAME (Blue Ribbon for the Awareness of	141	FULL	141	3–5	GET is not appropriate for the severely affected!!	Noted, but some of the approaches of GET may be helpful for some patients, after a full discussion of the potential benefits and risks.

	ME)						
SH	BRAME (Blue Ribbon for the Awareness of ME)	142	FULL	141	7–17	See comments on Activity Management, FULL, P	Noted and revised
SH	BRAME (Blue Ribbon for the Awareness of ME)	143	FULL	141	19–21	6.3.1.4: This section shows a total non-understanding of sleep dysfunction in ME/CFS. It is not something to be changed using 'behavioural approaches' – this is totally inappropriate. ME/CFS sufferers have difficulty sleeping because of the way the brain works during sleep for this group of people – it does not allow restorative sleep and maintains REM sleep, this is a physiological problem. This type of sleep dysfunction is common in neurological conditions.	Noted, and we have stressed the need for healthcare professionals to use 'specific intervention if there is a concurrent primary sleep disorder.'
SH	BRAME (Blue Ribbon for the Awareness of ME)	144	FULL	141–144	6.3.1.6	Setbacks is not the correct use of language here as there is a real difference between a setback, which may only last some days, weeks or months and is only a minor increase in symptoms – that is 'transient increases in fatigue and other symptoms', and a relapse. A relapse is something completely different, not a setback, it is a significant increase in symptoms, often causing a person to move categories eg mild to moderate to severe to very severe, it is not transient, and can often last months or years – this section should deal with relapses. For relapses, the recommendations here, are not appropriate, and are potentially harmful. Relapses can occur at any stage of the illness, sometimes there is a trigger eg over-	The section on setbacks has been considerably revised in light of this and other comments.

						exertion, infection etc or sometimes they can happen for no apparent reason whatsoever. As the Canadian Guidelines say "*Relapses can occur several years after remission*". One of our respondents says this: "*Referring to relapses as 'setbacks' trivialises them. I have still not recovered from the so called 'setback' after which I became severely affected in 1997 and I have been unable to sit up in a wheelchair for longer than 2 minutes without further relapse since*." Another of our respondents said: *"(The early stages and) relapses should be approached particularly carefully; rest, recuperation, and compassionate support are the most important components of improvement when people are first ill and when they relapse*."	
SH	BRAME (Blue Ribbon for the Awareness of ME)	145	FULL	142	4–6	I hope that this includes, benefits advice, nursing and care packages, GP/consultant domicillary visits, meals on wheels etc are put in preparedness, so that people are not facing increased hardship and battles when they suddenly have a relapse.	This section has been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	146	FULL	142	7–8	There is no mention here to vaccinations, anaesthesia etc or that a relapse may happen for no apparent reason.	This section has been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	147	FULL	142	10–11	DANGER – This is not advisable!! To encourage that patients continue to maintain an exercise programme – no matter what the cause of the relapse is, is very dangerous. This can cause an even more severe relapse, or for the	This section has been revised.

						relapse to continue for a much longer period of time.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	148	FULL	142–143	General	There is a real difference between a mild setback, and a moderate setback, and these should not be put together as the advice should be different.	This section and recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	149	FULL	143	24–25	Patients do not tend to panic as it is part of their illness pattern to have setbacks and relapses. However some of the more severe symptoms which appear during a relapse would cause anyone to have severe concerns eg paralysis, loss of the ability to swallow, blackouts, convulsions etc. This is especially if you are trying to cope on your own, and/or your GP/consultant has little understanding of the complexity and severity of the illness. There is also concern when these severe symptoms, and those such as heart palpitations, may not in fact be part of the illness but the development of a co-morbid condition, which may be treatable or may be fatal.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	150	FULL	143	1–4, 9–10	DANGER – YOU RISK CAUSING REAL DAMAGE TO PATIENTS. To encourage the continuation of activity and exercise during a relapse/setback is playing Russian Roulette with the health of patients. Given the compromised bodies' of patients during a relapse, the physical body of the ME/CFS sufferer may not cope with it. One of our respondents said: "*Most people are so physically drained during a relapse there is no way any activity level could be maintained, anyone who lived the illness will tell you*	Noted, and the needs of the individuals should be paramount when agreeing appropriate intervention.

						that.”	
SH	BRAME (Blue Ribbon for the Awareness of ME)	151	FULL	143	7–8	Stop with the CBT psychobabble! This is not about distressing thoughts – ME/CFS patients have a reality that their illness will consist of setbacks and relapses as this is part of the illness.	This section has been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	152	FULL	143	13–14	It may take weeks or months, or even years, to achieve previous levels prior to the setback/relapse.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	153	FULL	143	15–16	You are living in dreamland if you think that relapses, even mild ones, will mean that just two days later the patient will be able to start building up activities again – particularly if it is a moderate relapse. The same is true for the rest periods as this may take quite a while before reduction of these are possible. When an attempt is made to try and increase the activity levels, whether that is walking to the bathroom, or other low level activities, this must be done with great caution and awareness of the possibility of further relapse. One of respondents said: “*If someone could gradually build up activities after a couple of days they haven't got ME/CFS*”	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	154	FULL	143	22–23	At least put etc. at the end to indicate that there are many possible causes for a relapse.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	155	FULL	143	26	**Do not review the activity/exercise programme – STOP IT. Continuation could cause damage to the body possibly sending it into a downward spiral which may take years to**	This section and the recommendations have been revised.

						recover from, if at all. Please refer back to comments previously made on 'FULL p139/140 GET' regarding biomedical evidence of physiological changes in the body of ME/CFS patients:- oxidative stress can cause cellular injury; mitochondria which is already dysfunctional if pushed further can kill the DNA; cardiovascular dysfunction could lead to organ failure; there is also danger that the patients' hearts may be functioning at sub-optimal levels, and there may also be autonomic disturbances.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	156	FULL	143	27–28	The patient will have no choice but to reduce all activities as it highly likely that they will be bed-bound and probably unable to even lift their head off the pillow, let alone continue any activity. It may be quite a while before symptoms are stabilised and a baseline can be achieved.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	157	FULL	144	1–2	Again the patient will not be able to do activity for quite a while and will only be able to rest – they will have no choice.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	158	FULL	144	3–5	The rest periods will probably be continuous as the patient will need time for their body to try and heal from the relapse – pushing them will only mean that the relapse continues for longer, or they become even more severely affected.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	159	FULL	144	6	The body should be able to achieve a sustainable baseline of activity for quite a period, before thought of trying to attempt activity again – this may be just being able to lift your head off the	This section and the recommendations have been revised.

						pillow, or sit up for a longer period of time. Any activity attempted after a relapse must be done carefully, as there is a real risk of further relapses.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	160	FULL	144	8–16	See comments above which are all relevant to this section, in particular that of achieving a sustainable baseline. This section needs to be done at the right time and with the correct advice. All of this needs to be done in consultation, and agreement with, the patient, so that they are in control of both the time frame, and the pace, within which this takes place.	This section and the recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	161	FULL	144	19–23	6.3.1.7 Rehabilitation: For the severely affected, especially the long-term, equipment is not temporary, it is a necessity. Many patients try to cope without aids for as long as possible before requesting help, and then face a battle trying acquire them eg wheelchairs can take two years. This section will create great fear in patients, as the thought that having fought to get equipment, they will be taken away and people will be forced to try to live without them, causing major relapses, because of your so called fears of 'risks'. Patients do want these aids, they NEED these aids, to help them exist with their very basic of needs. How many patients are going have their equipment removed by practitioners trying to force them into activities beyond their abilities?	Noted, and we have recommended that the use of equipment should be considered as appropriate.
SH	BRAME (Blue Ribbon for the Awareness of	162	FULL	145–147	General	6.3.2.1 – 6.3.2.5. Evidence Statements 6.3.3.1: We, and all of our respondents, do not agree that GET and CBT are effective in adults and	These are evidence statements agreed by the GDG, based on the evidence reviewed.

	ME)					children with ME/CFS for reducing symptoms and fatigue, improving function and improving quality of life. Please refer back to our General comments on CBT and GET covering pages 138-141: 145-147; 181-192 which all highlight the reasons why the research is flawed, and why these are not appropriate management plans for people with ME/CFS.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	163	FULL	145–146	General	6.3.2.6 – 6.3.2.10 CBT Cost Effectiveness: There is not enough evidence to suggest CBT is cost effective, in fact there is now much research to show that CBT is not cost effective, and its effect is only temporary. CBT is particularly not cost effective as far as ME/CFS is concerned given that 93% of patients found it unhelpful.	In accordance with NICE methodology, these statements are strictly based on cost effectiveness evidence.
SH	BRAME (Blue Ribbon for the Awareness of ME)	164	FULL	147–148	21–27 & 1–2	Some of our respondents have said that there are problems with the suitability of the Expert Patient Programme, expressing that it may only be suitable for some mildly affected patients, but that it certainly was not suitable for the severely affected and the majority of the moderately affected.	Noted.
SH	BRAME (Blue Ribbon for the Awareness of ME)	165	FULL	148	4–11 17–19	Chronic fatigue is not ME or ME/CFS and therefore any research pertaining to chronic fatigue should not even be considered as any conclusions cannot be extrapolated for ME patients.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	166	FULL	148	12 –16	Considering research into counselling was seen by the York review, why is no mention made to counselling, and its usefulness in ME and ME/CFS within the guidelines, particularly within the management section.	The paper reviewed (Ridsdale 2001) on counselling included participants with chronic fatigue, of whom 28% had CFS/ME (CDC 1994). This was therefore excluded from the review of clinical

							effectiveness in people with CFS/ME.
SH	BRAME (Blue Ribbon for the Awareness of ME)	167	FULL	148	19–27	All the research here managed to demonstrate was that GET had no effect on improving symptoms – in particular cognitive dysfunction and prove the real problems that patients have with cognitive dysfunction.	The agreed evidence statement for GET was ‘Five trials investigating incremental physical exercise programmes showed improvements in adults in various health outcomes including mental and physical fatigue, global improvement, disability, sleep, mood and cognition.’
SH	BRAME (Blue Ribbon for the Awareness of ME)	168	FULL	149	6–12	6.3.4.1: We would disagree that the ‘clinical benefits of interventions for CFS/ME have been shown in a number of papers”. As we have said before, most of these papers are flawed because they use the Oxford criteria, therefore making the results invalid, and the results are not suitable for extrapolation on the ME/CFS community. This statement also ignores the wealth of patient evidence which shows that there are not clinical benefits, but rather, clinical risks, to the use of CBT and GET.	Please refer to the clinical effectiveness evidence detailed in Appendix 1, and agreed by the GDG.
SH	BRAME (Blue Ribbon for the Awareness of ME)	169	FULL	149	18–21	This percentage would be even lower if the Canadian diagnostic criteria were used, meaning that the proportion of the chronic fatigue community with ME or ME/CFS is minimal.	Noted.
SH	BRAME (Blue Ribbon for the Awareness of ME)	170	FULL	149–157	6.3.4	This section just shows how expensive CBT is, and that it is not a cost-effective tool, especially given the patient evidence to show it’s ineffectiveness. Person-centred counselling concentrating on teaching coping strategies would be more cost-effective and a better use of money.	This section reviews the available health economic evidence and provides information on this evidence base.
SH	BRAME	171	FULL	181	6.3.6.2	At the end of this paragraph, it should	Benefits and insurance claims are

	(Blue Ribbon for the Awareness of ME)					be changed to "…at any time, without fear of recrimination or discrimination for further care, benefit allowance and insurance claims."	outside the remit of a clinical guideline.
SH	BRAME (Blue Ribbon for the Awareness of ME)	172	FULL	181	6.3.6.3	Again, it is the goal of all those with ME/CFS to be able to return to normal activities – to say otherwise is insulting and prejudiced. The therapies of first choice should not be, in any instance, GET and CBT as these are harmful/unhelpful to the patient population. There is not good evidence of benefit for these two management techniques, in fact the evidence is either flawed, after using the Oxford Criteria, or has been discredited by further trials and research papers. There is however good evidence of it causing harm/being unhelpful from the patient population – but as is evident throughout the guidelines, the views of the patient population have been ignored.	Noted and revised. Patient evidence can be seen in Chapter 3. Also, the recommendations stress the need to take into account the preferences of the individual.
SH	BRAME (Blue Ribbon for the Awareness of ME)	173	FULL	181	6.3.6.4	Again, as with the above section, although the illusion of choice is being given to the patient/doctor – CBT and GET are promoted as the only two suitable management plans so much, that all patients will be offered is CBT and GET. These are not appropriate for the vast majority of the patient population. The language within this guideline gives the illusion of choice whilst at the same time taking it away.	Noted and these recommendations have been revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	174	FULL	182	6.3.6.5	There is no mention here, as there is not throughout the guideline about the different stages of illness ie. Acute, chronic and recovery. These stages have a direct impact on how patients	Noted and revised.

						should be managed, and what is appropriate at the different stages. These different stages are vital, and should be acknowledged, and advice given, on how to manage people in these different stages.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	175	FULL	183	6.3.6.6	"the individualised" - 'the' gives the impression that you are referring to one particular programme eg CBT/GET, should be 'an' – therefore allowing for energy management.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	176	FULL	183	6.3.6.8	Do not feel that this section is strong enough and will lead to many more people who vitally need support aids still being denied them – these people need this equipment, it is not a choice, and many people will try to avoid using them for as long as possible, getting to the point of sheer desperation and collapse before acknowledging that they need help. When, finally, they do ask, they should be given what they need.	The intent of this recommendation is to enable access to equipment and adaptations if appropriate.
SH	BRAME (Blue Ribbon for the Awareness of ME)	179	FULL	185	6.3.6.12	Bullet 3 - This just explains the authors' view of CBT, in that, on one hand you say it is stated that CBT is used in the same way as for other chronic conditions and, on the other hand here, "the CBT model for CFS/ME" – acknowledging that you are describing and prescribing a different form of CBT for ME/CFS than would be used for other chronic conditions ie dealing with illness beliefs instead of offering coping strategies. If this could be read as something else, all qualms are lost by the next section as you then go on to explain that you will be using the illness beliefs model of CBT. This whole bullet	These are accepted components of any CBT programme.

						point needs to be removed.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	180	FULL	185	6.3.6.12	Bullet 4 – As with bullet 3, the language used here is totally inappropriate.	These are accepted components of any CBT programme.
SH	BRAME (Blue Ribbon for the Awareness of ME)	181	FULL	185	6.3.6.13	Bullet points 1 & 2: Again the language and recommendations here, bear no resemblance to ME/CFS – patients do not need their thoughts and beliefs changed, just because they think and believe that their illness is physical – they have a wealth of research evidence backing them up.	These are accepted components of any CBT programme.
SH	BRAME (Blue Ribbon for the Awareness of ME)	182	FULL	185 186	6.3.6.13	Bullet point 4: People with ME and ME/CFS do not have 'fear of activity' – they have a realistic knowledge of their body's abilities, if identifying causes of relapse is important, it should be recognised that exercise/activity, particularly if excessive, is one of the main causes. People do not avoid exercise/activity, what they do is live within their available energy limits.	These are accepted components of any CBT programme, with examples of how these may be applied for people with CFS/ME.
SH	BRAME (Blue Ribbon for the Awareness of ME)	183	FULL	188–192	General	When reading our following comments about GET recommendations, please go back and refer to our comments and research evidence about GET made above on FULL, pages 139 & 140 (6.3.1.2 GET). The prescription of graded exercise for recovery is a very dangerous premise which causes great harm to patients. It is not only the severely affected who have found GET has made them worse, many people have become severely/very severely affected when previously they had been only mildly or moderately affected through being put	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET.

						through clinic led GET (I am not talking about General exercise, but GET as described in this document).	
SH	BRAME (Blue Ribbon for the Awareness of ME)	184	FULL	188–192	General	Patients, when attempting activity management/GET often do so at the cost of the previous normal activities. This can be due to two reasons, the pressure that the patient puts on themselves, by wanting to get back to normal life as soon as possible, and believing the doctors who tell them that they can do this through these interventions. Or this can be due to patients wishing to please the therapist, by saying that they have fulfilled their tasks, but then do not mention that it had caused them to spend the rest of the day in bed, unable to achieve anything else.	Noted and we have noted throughout the need for a process of shared decision making and open communication.
SH	BRAME (Blue Ribbon for the Awareness of ME)	185	FULL	188–195	General	There is no mention throughout these two sections to the cumulative effect usually experienced by the ME population – this is extremely important. A person may be able to do a task once, maybe even twice, but then the delayed reaction would kick in, and the accumulation of the effects of these activities leads to a relapse. This cumulative effect is vitally important for management therapists to understand.	We have stressed throughout the need for appropriate monitoring and review.
SH	BRAME (Blue Ribbon for the Awareness of ME)	186	FULL	188	6.3.6.15	Bullet 3: There are not benefits from exercise for ME/CFS sufferers. The symptoms and benefits of exercise in eg. healthy people or people with depression are not valid here, because the physiology of ME/CFS patients means that exercise is not a benefit – but a risk, causing harm. Information	We have noted that any intervention should only be initiated after a full discussion of potential benefits and risks.

						must be given on the risks to the patient, and the negative physiological changes experienced by MECFS patients to exercise.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	187	FULL	190	6.3.6.17	We do not agree with, nor advocate, GET for the ME/CFS patient population. For the few mildly affected ambulant patients who may wish to try it, of their own choice, with FULL knowledge to the risks they may be causing their health, the following recommendations are not suitable. A proper baseline of sustainable activity must be achieved first, this will probably mean a decrease in activity, until the boom and bust cycle is stopped and a sustainable functioning is achieved, then, if this can be sustained, and the patient wishes, a gradual increase in activity may be started – with awareness that this may cause minor setbacks or major relapses. If the patient wishes to stop this at any time, that is there prerogative, and should not lead to the patient being denied further care, benefits and insurance claims, nor being classed as having a 'fear of activity',	We have noted throughout the need for full discussion of the benefits and risks, and the right of the individual to withdraw at any time without detriment to care.
SH	BRAME (Blue Ribbon for the Awareness of ME)	188	FULL	190	6.3.6.17	The healthy population would find undertaking a baseline of exercise for 5 days out of 7 difficult, so how do you expect the ME patient population to achieve this!! This whole section shows a complete misunderstanding of the nature and physiology of ME.	The amount of added activity is tailored to the individual. It is suggesting that it may be sitting up in bed for longer or walking to another room. It is not suggesting a vigorous exercise programme.
SH	BRAME (Blue Ribbon for the Awareness of	189	FULL	190	6.3.6.18	This is likely to cause a large increase in symptoms, possibly causing a setback or relapse. If a person is still having symptoms after a few days, or	We have stressed throughout the need for appropriate monitoring and review.

	ME)					they are severe/distressing, there is no reviewing/stopping of activity/exercise 'if necessary' it is extremely necessary, and all activities should be stopped at once. Not stopping activities/exercise, during setbacks and relapses, is why so many people have severe adverse reactions to GET, and it causes so many relapses. This is a complete disregard for the patient's health and experience.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	190	FULL	190–191	6.3.6.19	Again to be able to maintain and sustain an activity/exercise 5 days out of 7, is virtually impossible for the ME/CFS population. Most patients that we speak to who have gone through GET, do not have a reduction in 'perceived exertion', but rather a worsening of symptoms, and are now in a state of relapse.	The amount of added activity is tailored to the individual. It is suggesting that it may be sitting up in bed for longer or walking to another room. It is not suggesting a vigorous exercise programme.
SH	BRAME (Blue Ribbon for the Awareness of ME)	191	FULL	190–191	6.3.6.19	The ultimate goal of 30 minutes of exercise just shows a complete lack of understanding of the illness, and is completely unachievable for any but the very mildest affected in the recovery stage of their illness – and I believe even they would have trouble achieving that without severe repercussions, particularly if they had to try and sustain it – in fact I doubt many in the healthy population could even achieve this once a week, let alone the 5 times a week you expect the seriously ill, compromised bodies of the ME/CFS population to achieve. Given that in the RCTs GET is only supposed to be successful if the patient is able to achieve 30 minutes of exercise 5 times a week, just goes to	The amount of added activity is tailored to the individual. It is suggesting that it may be sitting up in bed for longer or walking to another room. It is not suggesting a vigorous exercise programme.

						prove that this is completely inappropriate for the ME/CFS population, as it is not achievable by 98% of the ME/CFS population and therefore it is not successful for 98% of the population – so why are you putting seriously ill people through so dangerous a therapy.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	194	FULL	192	6.3.6.20	Please refer also to our comments on the Setbacks section for more comprehensive feedback; FULL, Pages 141-144. DANGER – It is extremely dangerous to the patient to continue exercise/activity during a relapse. This is likely to cause a worsening of their condition, and a lengthening of the relapse, as well as putting great strain on their already compromised bodies. These people need rest and relaxation, not exercise, and particularly at this vulnerable time.	This section has been revised based on stakeholder comments.
SH	BRAME (Blue Ribbon for the Awareness of ME)	195	FULL	192	6.3.6.21	The language used here eg. 'reinforce', is inappropriate and almost intimidating, giving the impression that patients will be forced to continue GET beyond the programme end – taking away their free choice. This section reads as GET is being done to the patient, rather than with the patient.	This section has been revised based on stakeholder comments.
SH	BRAME (Blue Ribbon for the Awareness of ME)	196	FULL	192–195	General	Activity Management: Many of our respondents expressed concerns that Activity Management was just another form of GET. Many of the elements suggested here are the same as pacing, breaking down the elements of activity and spreading them over period of time to manage your energy, however not enough is made of energy management within	We have tried to clarify the distinctions.

						this section, or on the technique of 'switching'. With the emphasis on activity, which could be classed as a subtle form of exercise – and misinterpreted as such by some medical professionals – the fear is, that therapists could use this as a form of GET in disguise. The severely affected were particularly fearful that this would be interpreted this way, and they would be forced into a programme not suitable for their needs, and that it would be used as a gateway into forcing them into CBT and GET programmes. Activity Management should start on a new page, by having it continue within the same page as GET then you are linking the two together.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	197	FULL	193	6.3.6.23	Bullet 7: Exercise should not be mentioned in a section concentrating on activity.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	198	FULL	193	6.3.6.23	Bullet 8: Rest is likely to be needed for longer periods than 20 minutes – the length of time needed in order to rest is based on a multitude of factors eg severity and stage of illness, the activity undertaken, symptom severity on the day and other factors.	Noted and revised – see also section on rest periods.
SH	BRAME (Blue Ribbon for the Awareness of ME)	199	FULL	194	6.3.6.23	Bullet 11: Again as stated previously, maintaining activity and goals during a relapse is extremely dangerous, as is avoiding increased rest. This advice is likely to seriously damage the health of ME/CFS sufferers, and is irresponsible advice.	Noted and revised.
SH	BRAME (Blue Ribbon	200	FULL	194	6.3.6.23	Bullet 12: Again great caution must be undertaken following a relapse, see	Noted and revised.

	for the Awareness of ME)					previous comments on relapses.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	201	FULL	195	6.3.6.24	Bullet 1: Prolonged rest is absolutely necessary for many patients, and trying to avoid this can cause a relapse.	Point of prolonged bedrest dealt with previously.
SH	BRAME (Blue Ribbon for the Awareness of ME)	202	FULL	195	6.3.6.25	NO, NO, NO and NO!! GET is not an appropriate addition, even elements of it, for the severely affected, introducing this will cause great damage. It is not suitable, and there is no research evidence backing its use. There is however patient evidence showing that this is extremely harmful to patients, in particular the severely affected, and GET should be avoided at all costs.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of ME)	203	FULL	195	6.3.6.27	NO, NO, NO and NO!! CBT is not an appropriate addition, even elements of it, for the severely affected. Patients have a hard enough time trying to concentrate and hold a conversation for a few minutes, let alone the 45 minutes needed for CBT. It does not help the patient to be told constantly that if they wanted to get better they should stop believing they have a physical illness, this does more damage than good.	Noted and revised to clarify the intention.
SH	BRAME (Blue Ribbon for the Awareness of ME)	204	FULL	195	General	The title at the bottom of the page needs to go at the top of the next page above sleep dysfunction. However we do not like this statement anyway as we would not class relaxation as part of CBT or GET.	Noted and revised.
SH	BRAME (Blue Ribbon for the Awareness of	205	FULL	196	6.3.6.29	There is a complete lack of understanding within this section as to the nature of sleep dysfunction for ME/CCFS sufferers.	We have recommended strategies to aid sleep problems, and also recommended that there is 'specific intervention if there is a concurrent

	ME)					It is important that sleep dysfunction is investigated in case of a co-morbid sleep ailment such as sleep apnoea, however sleep dysfunction is part of the illness, as it is with many other neurological conditions. ME/CFS sufferers who have been sent for sleep analysis have come back with the diagnosis “Alpha wave predominance due to ME/CFS”. Apart from sleep problems due to increased pain and other symptoms. This core symptom, which produces prolonged dreaming and increased REM sleep, is acknowledged as being a core part of the illness and due to the actual physical illness. The increased REM sleep means that after several hours, when the sufferer finally does enter a deep sleep, they then try to sleep longer to make up for the hours of unrefreshing sleep, hence the perceived over-sleeping. Preventing the sufferer from the ‘extra sleep’ is actually depriving them of the very period of quality sleep which the body needs in order to survive. In some sufferers, especially those with insomnia or sleep reversal, the sleep dysfunction is so bad, that even the strongest medication fails to help, nor does relaxation – and this must be acknowledged. This is why ‘excessive’ sleep, daytime sleep/napping is so vitally important. It is also physiologically extremely difficult to try and turn the sleep reversal pattern around. Therefore, this section is giving an	primary sleep disorder’. Regarding the impact on the family and carer – this is highlighted in the introduction (see the short form of the NICE guidance).

						unrealistic, and belittling, view of this core symptom – as well as being completely inappropriate for the bed-bound severely affected sufferer. It must also be identified within this section of the impact that sleep dysfunction has on the rest of the family, but in particular the primary carer, who is up caring for the person; getting meals, toileting, changing beds, medication – this disruption to their sleep pattern has a serious effect on their health.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	206	FULL	196 + 198	6.3.6.30 6.3.6.31	Bullets 1: as with above, there is a real physical and medical reason why daytime naps are necessary. It has nothing to with affecting night-time sleep, it is the sleep dysfunction and core sleep symptoms that are part of ME/CFS that causes these problems.	This has been revised based on stakeholder comments.
SH	BRAME (Blue Ribbon for the Awareness of ME)	207	FULL	196	6.3.6.30	Bullets 2.1, 2.2, 2.3: Again it is extremely difficult to try and introduce a sleep routine, as it is dependent on so many factors; such as the severity of symptoms, particularly pain, and whether they have had a particularly restless night and not been able to get any sleep. It is near impossible for those who suffer sleep reversal, and disrupted sleep pattern, to have a sustainable sleep routine, the body will just not accept it, most people cannot sustain it for more than a week, before it gradually creeps back to what the body considers its natural sleep pattern.	Noted.
SH	BRAME (Blue Ribbon for the Awareness of	208	FULL	197	6.3.6.30	Bullet 2.4: This is not appropriate for the severely affected, who are bed-bound, and for whom all of the suggestions would create extreme	These are simply examples, and approaches should be tailored to individual circumstances.

	ME)					difficulty; Warm bath – even if they were physically able to even get in or out of the bath, they would have extreme difficulty sitting up and coping with the temperature of the water. Reading – is near impossible for all ME/CFS sufferers, not just the severely affected. Listening to music – many sufferers would find this difficult to tolerate with their hyperacuity. Gentle Stretching – this is likely to cause an exacerbation of symptoms, and pain, therefore is not useful when trying to get to sleep.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	209	FULL	197	6.3.6.30	Bullet 3 – how if you are severely affected and bed-bound are you supposed to keep the bed and bedroom for sleep?	These are simply examples, and approaches should be tailored to individual circumstances.
SH	BRAME (Blue Ribbon for the Awareness of ME)	210	FULL	197	6.3.6.30	Bullet 4 – If you are severely affected you are unable to get up in the night -– and this is not suitable for those sufferers who are insomniacs, they will be up and down like yo-yos and still be unable to sleep.	These are simply examples, and approaches should be tailored to individual circumstances.
SH	BRAME (Blue Ribbon for the Awareness of ME)	211	FULL	197	6.3.6.30	Bullet 7: Our comments on this are best left to one of our respondents, although a number of our respondents made the same comments: "*"Excessive alcohol"?! This gives real cause for concern – are we talking about the same illness here? Most people with ME/CFS can't tolerate alcohol AT ALL. Ref paper by Woolley, Allen & Wessely (2003)*".	Noted.
SH	BRAME (Blue Ribbon	212	FULL	198–201	6.3.6.35–6.3.6.37	This section and its language are completely inappropriate for use with	These recommendations have been revised in light of this and other

	for the Awareness of ME)					people with ME/CFS. Please refer to my comprehensive comments on FULL, 141-144.	comments.
SH	BRAME (Blue Ribbon for the Awareness of ME)	213	FULL	202	6.3.6.38 + 6.3.6.39	We have serious concerns about the competency of training for 'therapists' on interventions for ME/CFS sufferers. Given the psychiatric leaning of CBT and GET, and the apparent lack of good training, based on bio-medical evidence, for the entire medical profession, on the neurological organic illness that ME/CFS is – how are we supposed to have faith in this training? One of our respondents had this to say: "*As yet nobody has 'trained' any 'professionals' in the application of GET to ME. What sort of professionals would they be? With no recognised or appropriate 'training programme' one wonders how one will be devised and who will be responsible. If they subscribe to the psychosocial model of ME, they will cause more harm than good and should not be allowed to treat people with ME. Unless the experiences of patients with ME are taken into account, the effect on patients will be disastrous*." Another respondent said: "*There is enormous concern amongst patients about who is doing the training and what exactly they are being taught*."	Defining standards is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	BRAME (Blue Ribbon for the Awareness of ME)	214	Full	202	3–6	If you are aware of the many inconsistencies and absences in the treatment protocols, then how are we supposed to accept that the descriptions of CBT and GET in this document are those that the flawed	Details of the interventions reviewed can be seen in Appendix 1.

						research papers show as being ‘effective’?	
SH	BRAME (Blue Ribbon for the Awareness of ME)	215	FULL	202	7–14	6.3.7: With regards to research on CBT please refer back to our previous comments and evidence on ‘FULL p138-139 and p185-187. In addition to these one of our respondents has referred to two other papers which have relevance: “*The GDG should also take note of recent research evidence on CBT which found that CBT did not offer any significant overall benefit when compared to education and support and standard medical care (ref: cognitive behaviour therapy in CFS: a RCT of an outpatient group programme. Health Technology Assessment. 2006 Oct;10:37). Another very recent study (Quarmby et al 2006) also found that the efficacy of CBT in a clinical setting compared unfavourably with results in RCTs*.”	O’Dowd has been added to the evidence base. Regarding Quarmby 2006, the authors note many reasons for this possible difference in results. In addition, ‘the majority of patients in both conditions described themselves as better or much better than before treatment, as satisfied or very satisfied with the treatment outcome and as believing the treatment to be useful or very useful’.
SH	BRAME (Blue Ribbon for the Awareness of ME)	216	FULL	202	15–18	If the GDG believed that CBT is not about “unhelpful advice or dictation of illness beliefs” then how could it make the recommendations that are within these guidelines, which read as being exactly that - unhelpful advice and dictation of illness beliefs!! If you had seriously wanted to give a description of coping strategies, then the language and description in these recommendations is totally unacceptable, and bears no relation to your ‘supposed intended views’.	We have revised the structure and the description of these therapies to clarify their use.
SH	BRAME	217	FULL	203	1–4	“The GDG did not regard CBT or other	The recommendations have been

	(Blue Ribbon for the Awareness of ME)					behavioural treatments as curative or directed at the underlying disease process which remains unknown. Rather, such treatments can help some patients cope with the condition and consequently experience an improved quality of life”. This is such an important statement, the meaning of which is completely lost throughout this document. The impression is given, and stated, throughout, that CBT and GET promote ‘recovery’, which in the population’s mind is the equivalent of a cure. **Also you admit here that these ‘treatments’ are only suitable for SOME patients, and yet advocate and prescribe them for the majority of the ME/CFS population, in particular as ‘treatments of first choice’.** Why is this statement not repeatedly used throughout the document, but in particular on pages 138-147 and 181-192 of the FULL document? Why is there no mention of this statement anywhere in the NICE version? Surely this is of paramount importance, and the omission of which could be seen as an attempt to provide a biased viewpoint of these therapies. This statement should be in every single type of guideline on ME/CFS that the NICE produces.	revised to clarify the use of CBT/GET. Also the need for individualised programmes based on the needs and preferences of patient is stressed throughout.
SH	BRAME (Blue Ribbon for the Awareness of ME)	218	FULL	203	13–29	This section just proves that the GDG ignored the viewpoint of the wider questionnaire, and the patient respondents in particular. To give such little thought to the views of the patient	The results of the wider questionnaire were not ignored and were discussed. The reasons given by the GDG are detailed in the guideline.

						group you are supposed to be helping is insulting, insensitive and unhelpful. If you had no intention of undertaking the viewpoints of the wider questionnaire if they did not agree with the 'GDG's Consensus' then why did you ask their opinion in the first place? Especially as so many extremely ill people struggled to complete the questionnaire under the impression that their views would be heard.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	219	FULL	204	1–10	NO, NO, NO and NO!!! There is more evidence stating that exercise is harmful to patients, not just patient evidence where they were describing GET, not exercise therapies as mentioned here, but there is also research evidence showing that the body's of ME/CFS sufferers react differently to exercise, and that it is harmful to them. To ignore this evidence and say that the benefits outweigh the risks, based on flawed research – will lead to the damage of thousands of patients. Given that GET and CBT are not subject to the stringent regulations, and pre-patient testing, that prescription drugs go through to check for their efficacy and safety on the intended patient population, one of our respondents said: "*Will patients be able to sue for compensation should health professionals give inappropriate advice? Doctors and healthcare professionals must prescribe exercise with the same degree of care as with a prescription drug.*"	We have recommended that the benefits and risks of any intervention should be discussed before its initiation. In addition, appropriate monitoring and review is stressed throughout. See also previous comments.

						You have already had the evidence of the death of [X], but this is just one case. To give another example, there was a young man who was seriously damaged by GET, and when he had a severe relapse due to the GET, instead of helping him, they decided to forcibly remove him from his home, and locked him in a paediatric psychiatric ward, for several months, until his parents managed to get him released through the courts. There he was strapped to a metal gurney, made to do more GET, and only allowed one visit from his parents once a week. When through the GET, and stress that was put on his body through this experience, caused him to lose his speech, he started writing with a pencil – then they took that away from him!! This is how ME patients are treated. This is why it is so dangerous for the NICE guidelines to recommend GET and to promote illness beliefs. The young man described above also highlights, as one of our respondents put it, “the worrying trend in diagnosing Munchasuen’s by Proxy.” Please also refer back to our comments on GET on pages 138-147 and 188-192.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	220	FULL	204	11–14	There is a great deal of evidence to show that GET is harmful to the severely affected.	We have not recommended GET for people with CFS/ME, but that elements may be appropriate, after a full discussion of the benefits and risks.
SH	BRAME (Blue Ribbon for the	221	FULL	204	15–23	There is evidence to support the ‘envelope theory,’ which could also be described as the ‘glass ceiling effect.’	No RCT evidence was identified on the use of the ‘envelope theory’ However, we have noted that there

	Awareness of ME)					Both of these theories recognise that the ME/CFS sufferer has a finite amount of energy, and that it can't be exceeded, creating an "activity limit". You are not only ignoring the wealth of patient evidence which states that these are effective but also research papers which support this eg. Jason et al (1999) and Black & McCully (2005). This is yet again another example of patient and bio-medical evidence being ignored. Living within your abilities and your energy levels is one of the most effective forms of management for ME/CFS sufferers, and for many can lead to an improvement in symptoms/level of functioning.	are some approaches without RCT evidence, but with considerable patient support.
SH	BRAME (Blue Ribbon for the Awareness of ME)	222	FULL	205–209 229–233	General	Pharmacological interventions: There is very little on symptom control and pain management. The GDG saying that they can't make those decisions, and give information on this in the guideline, referring doctors to their own 'toolkits', is not helpful. The Canadian Guidelines manages to give a detailed account of pharmacological symptom control, detailing which drugs are most likely to help, and those which are most likely to cause the worst side-effects. If that guideline can do this, then why can't this one? Given that symptom control/pain management, along with energy management and pacing, is the most effective way of managing these patients with ME, why is this given virtually no comment and usable	The guideline does not address the management of individual symptoms. Please refer to the scope and methodology chapter. The evidence search was confined to that directly related to CFS/ME. Within the time and the NICE methodology it would be impossible to address symptom management.

						advice/information? There is a brief mention that any pharmacological intervention must be done carefully, but not enough is highlighted on the sensitivity to medication, the adverse side-effects, and that drugs should be introduced one by one, at a lower dose than expected, and gradually increased in strength. It must always be remembered, and noted, that whilst some treatments/medications may be very helpful for some patients, for others they may cause serious adverse side-effects, even on a very small initial dosage eg many severely affected sufferers have adverse reactions to Zopiclone. Other sufferers have had a severe reaction to amitriptyline, while others have found it helpful in reducing pain and helping sleep. Every one of our respondents commented on the lack of appropriate advice for pharmacological symptom control, in particular pain management. Below are just three of the many comments received from our respondents: "*Symptoms can only be managed conventionally if GPs are advised which drug treatment to prescribe. At the moment many GPs do not prescribe medication for people with ME/CFS as they have not received the appropriate recommendations*." "*There seems to be no detailed suggestions about pain management. Since pain is one of the main problems with the condition, this would be a major oversight. There should be*	

						advice on the pros and cons of various pain medications, muscle relaxants, and sleep medication. There should also be a duty for the healthcare provider to direct the patient to an appropriate pain clinic where necessary." "*There is little or no information on pain management, something that for many people with CFS/ME is a more disabling symptom than fatigue*."	
SH	BRAME (Blue Ribbon for the Awareness of ME)	223	FULL	207–208	General	6.4.3 Given the cost per year per patient for the drugs listed here, surely symptom/pain management is extremely cost-effective – particularly in comparison to GET and CBT, and is far more effective for the patient population.	The GDG is recommending symptom management in addition to non-pharmacological approaches.
SH	BRAME (Blue Ribbon for the Awareness of ME)	224	FULL	209	8–17	This was the wrong choice. The change from 'appropriate' to 'inappropriate' caused great confusion.	This table documents the questions and responses to the questionnaire for transparency. They cannot be changed now.
SH	BRAME (Blue Ribbon for the Awareness of ME)	225	FULL	229 230	6.4.5.4 6.4.5.9	Thyroxine. A few of our respondents highlighted that they felt thyroxine could be a useful treatment, and that people often appear to have normal thyroid levels when in actuality there is an anomaly. One of our respondents said. "*Thyroid hormone may occur, thus causing the patient to appear eurthyroid or hypothyroid on lab date, when clinically hypothyroid due to tissue sensitivity*." Another respondent said: "*Some research should be done on the thyroid function. Levels of T3, and T4 and TSH should be regularly monitored*	Noted and this recommendation has been revised. However, there is no research evidence on the use of thyroxine as a treatment for CFS/ME.

						and the results analysed. If the results are at the lower end of the normal range, they may still need further investigation to eliminate a thyroid problem.”	
SH	BRAME (Blue Ribbon for the Awareness of ME)	226	FULL	230	6.4.5.7	Melatonin: Many doctors use melatonin in the adult population, so why has it not been recommended here for adults? There is no research for its use in children and yet you have recommended its use. Why if the specialist feels that it may be helpful for a patient is it not allowed to be prescribed for adults? There is usually more caution in using drugs in children than in adults.	The view of the GDG was that there were other licensed medications available for adults. This was not the case for children.
SH	BRAME (Blue Ribbon for the Awareness of ME)	227	FULL	232	24-–27	It needs to be added here that the dosage requirement of tricyclics for an anti-depressant effect, will cause severe side-effects in people with ME - as acknowledged in the Canadian Guidelines. It should also be acknowledged that tricyclics should not be used at the same time as SSRIs.	There is no evidence to support the first statement, although there is a general qualification about side effects already in the guidelines. The second point has already been covered (above).
SH	BRAME (Blue Ribbon for the Awareness of ME)	228	FULL	234–235 248–249	General	6.5 Dietary Interventions: All of our respondents felt that this section was completely inadequate and did not provide the advice and information they felt was urgently needed. The Canadian Guidelines say: “*The biochemistry and needs of each patient is unique. Chronically ill patients require nutritional support for healing. If practical a vitamin and mineral profile can assist in assuring that the patient is receiving adequate nutrients and indicate specific deficiencies*.”	The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful. We have also made recommendations on the use of dietary interventions.

						Here are just some of the respondents comments: “*The advice on diet is woefully inadequate. All 3 patient testimonies included in the FULL guidelines referred to issues of diet/food intolerances. With so many people with CFS/ME experiencing food intolerances/allergies/digestive problems, sometimes acute, it is hard to believe that this is all the guidelines are going to say about diet/nutrition.”* “*The effort to buy food and prepare nutritious meals can mean that people with CFS/ME find it difficult to maintain a healthy diet – and yet there is no mention how people can be supported*.” “*Many have found an exclusion diet to be an important part of their treatment protocol. There appears to be no mention of the importance of good fluid intake. Also no mention of appropriate symptom control for nausea, treating IBS or helping to stabilise blood sugar levels*.” “*Maybe a better use of ME/CFS patients time and limited energy would be to have nutrition training – including menus which will meet individual dietary requirements regarding allergies, personal preferences, cost (Another big factor if someone is too ill to work and having to rely on a very limited income from benefits), personal circumstances and energy levels (a crucial one here).* *There needs to be more information about the nutrient deficiencies and the inhibited uptake of nutrients and*	

						vitamins. There is also very little mention of the need by some patients to be tube fed, this is often due to the loss of the ability to swallow. There needs to be more advice about the bio-chemistry of food.”	
SH	BRAME (Blue Ribbon for the Awareness of ME)	229	FULL	234–235 248–249	General	6.5 Supplements: Many respondents were extremely concerned about the lack of support for supplements: “*A number of people with ME/CFS are reporting improvements on EPA/Omega-3 supplements. There is also some evidence to suggest that B12 and magnesium may also have a role to play in some patients*.” “*It says ‘no evidence’ for use of supplements – this is because research has not been funded. I have benefited from taking Vegepa, and Dr Sarah Myhill’s protocol involving B12, magnesium, Co-Q10 etc and have made the most substantial improvement for years*.” There is a great deal of patient support for the use of supplements. However there needs to be the caveat that this should be done, wherever possible, in conjunction with an understanding doctor/dietician, who can monitor blood levels to make sure that any deficiencies are recognised and corrected, and also to make that levels do not go so high as to become dangerous.	The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful.
SH	BRAME (Blue Ribbon for the Awareness of ME)	230	FULL	234–235 248–249	General	There is no mention within this section as to the work of Professor Basant Puri and his work on Essential Fatty Acids, something already studied by Professor Behan.	Please see the evidence review where these studies are reported in detail.

						Professor Puri has shown that there is "*a problem in respect of the turnover of Omega-3 and Omega-6 fatty acids in the membranes of the cells in the occipital cortex*." This was due to a statistically significant higher ratio of choline to creatine found in the ME/CFS patients than in the controls (CFS: A Natural Way To Treat ME) .This research also correlates with the work of Dr Jonathan Kerr on gene expression, where he showed activation of T-Cells and changes in the function of nerve cells and mitochondria. One of the up-regulated genes was EIF4G1 which helps form proteins in mitochondria, this upregulation is consistent with sub-clinical persistent viral infection. Professor Puri found that taking Essential Fatty Acid supplements, which don't contain DHA, to be helpful in managing ME/CFS. This research should have been included in this section.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	231	FULL	248	6.5.5.1	More needs to be mentioned about nausea, and its effects on the sufferer, and what can be done to help. There is also no mention to the loss of appetite experienced by many sufferers, or those for whom even the smell of food makes them feel sick.	We have noted that nausea is only one potential complication.
SH	BRAME (Blue Ribbon for the Awareness of ME)	232	FULL	248	6.5.5.2	Tube feeding is not always down to severe weight loss, but due to loss of the ability to swallow – something that happens with many severely affected sufferers of all ages. There is no mention made here to those sufferers who, despite being	We have removed the recommendation on tube feeding, but note the need to be aware of many possible complications that may occur.

						unable to tolerate food, and have no appetite, put on weight.	
SH	BRAME (Blue Ribbon for the Awareness of ME)	233	FULL	249 + 253	General	6.6 Complementary: Many respondents felt that the guideline was dismissive of complementary therapies, and that many people had found them helpful with symptom control. There needs to be awareness that people should go to properly trained and registered professionals. Here are the comments of some of our respondents: "*It is wrong to dismiss complementary therapies out of hand – some are helpful, like acupuncture and massage*." "*The section on complementary and alternative therapies is not adequate – many people with ME/CFS are obtaining benefit for some of their symptoms, especially pain*." "*There appears to be plenty of evidence that complementary therapies may help with treating symptoms of ME/CFS*."	We have revised the recommendation to note that people do find such therapies helpful.
SH	BRAME (Blue Ribbon for the Awareness of ME)	234	FULL	254–255	General	6.7 Review and Ongoing Management: More needs to be made of the urgent need for on-going monitoring of patients, their blood levels in particular. It is only by constant monitoring that co-morbid conditions or deficiencies can be picked up, and patients referred to the relevant understanding specialists eg cardiologist, gynaecologist etc. Several respondents said that the maximum time in between reviews should be no longer than one year, and many preferred every six months, however if severely affected it should be more regularly.	We have revised these recommendations and made specific reference to the need to be aware of any co-morbidities. We have also recommended that timings of reviews should be as needed, based on the needs of the individual.
SH	British	5	FULL	212		SSRI's in children – these should only	The GDG agree that SSRIs should

	Paediatric Mental Health Group of the Royal College of Paediatrics and Child Health					be prescribed to children and adolescents by specialists (i.e. child psychiatrists)	be prescribed by child psychiatrists.
SH	Chronic Fatigue Research Unit at King's College London	4	FULL	140–141		Whilst we do not take issue with the description of how exercise/activity management might be used (page 140/141) we do not feel that it reflects the totality of the evidence, and nor does it reflect the indisputable effect of the opposite – lack of exercise/activity on patients with severe disability. 6.3.6.9 for example, warning against unstructured/excessive exercise regimes (not GET) is perfectly reasonable, but should surely be linked to an equivalent statement on the clear dangers, physical and psychological, of bed rest. There is a vast and contested literature as to the deleterious effects of lack of exercise on virtually all bodily systems, not to mention psychological functioning.	Noted and this is in the recommendations.
SH	Chronic Fatigue Research Unit at King's College London	6	FULL	185	Group CBT	The O Dowd trial of group CBT has now been published by the HTA. The results showed benefits for CBT on fatigue, quality of life and walking speed, but not overall physical functioning. The finding that CBT was superior to group education/.support echoes the Prins et al Dutch trial. In individual patients The overall improvements were less than in individual CBT, which is a reflection of the fact that group CBT is usually a	Noted and this recommendation has been revised.

						weaker intervention to individual CBT, and is preferred purely on economic grounds, and should of course be considered in the context of the other Dutch group CBT trial already mentioned in the Guidelines. We think that overall the evidence now suggests that group CBT is inferior to individual CBT for CFS, but is an option if resources are stretched.	
SH	Chronic Fatigue Research Unit at King's College London	9	FULL	234 6.5.2.1.		Magnesium. It is of course important to report the only RCT of magnesium supplementation. However, it seems strange not to draw attention to a series of studies that followed showing that Mg levels were normal in CFS, and hence there is no need for supplementation. It is our experience that this is a treatment that has dropped out of fashion since then. Ex Clague J, Edwards R, Jackson M. Intravenous magnesium loading in chronic fatigue syndrome. Lancet 1991;337:757-760. Hinds G, Bell N, McMaster D, McCluskey D. Normal red blood cell magnesium concentrations and magnesium loading tests in patients with chronic fatigue syndrome. Ann Clin Biochemistry 1994;31:459-461. Mawle A, Nisenbaum R, Dobbins J, et al. Immune responses associated with chronic fatigue syndrome: a case-control study. J Infectious Diseases 1997;175:136-141. Swanink C, Vercoulen J, Bleijenberg G, Fennis J, Galama J, Van Der Meer J. Chronic fatigue syndrome: a clinical and laboratory study with a well matched control group. J Internal Medicine	Noted and we did only search for RCTs. Magnesium is not recommended as a treatment, this is a report of the evidence.

						1995;237:499-506.	
SH	Chronic Fatigue Research Unit at King's College London	13	FULL	248	6.5.5.2	My apologies, but we only just noticed this line, which we missed on first reading. We strongly disagree with the comment "Adults or children who experience severe weight loss should be referred to a dietitian for assessment, advice and nutritional support, which in extreme cases may include tube feeding." In our experience weight loss is a serious symptom rarely if ever part of the CFS spectrum – its presence indicates another disorder, sometimes severe eating disorder, sometimes other medical disorders. We feel anyone would be ill advised to follow this advice unless a proper diagnosis had been made, and the appropriate management instituted.	Noted and this has been removed.
SH	College of Occupational Therapists	37	FULL	181	6.3.6.5	*The choice of components of strategies* (where CBT and GET is not appropriate) *should be based on…* Should this also include, recommendations that are made through the clinician's clinical judgement and availability of appropriately skilled staff to administer?	Clinical judgement is accepted as being needed throughout the care pathway. Also the aim of the guideline is to facilitate the setting up and provision of appropriate services, if not currently available.
SH	College of Occupational Therapists	52	FULL	138	Section 6.3	It is not clear where the separate headings/sections are here. For example, some headings such as 'goals' are in bold, but the overall heading, such as 'GET', is harder to pick out. This may be confusing as to which therapy is being discussed. **Suggestion:** Review style/presentation to make clear the sections on each relevant management approach.	Section headings are numbered for ease of navigation, with lower level headings being in bold. This section has been revised in light of this and other comments.

						It is also confusing that nearly 3 pages are used to describe the management of setbacks, but only a paragraph given to important therapeutic approaches such as CBT and activity management. Also General principles which apply across all the therapies, such as use of goal setting, being person centred, etc are only discussed in the context of GET, implying these are not components of the other therapy approaches, which they are.	
SH	College of Occupational Therapists	53	FULL	138	9	'the ordering of access to interventions and being an iterative process, this sentence is not clear in its meaning.	Noted and revised.
SH	College of Occupational Therapists	54	FULL	139	2	Although a self-management process GET should be supervised at least initially by a therapist who understands CFS/ME.	Noted and revised.
SH	College of Occupational Therapists	55	FULL	139	12	x2 "developed"; **Suggestion:** delete first developed.	Revised.
SH	College of Occupational Therapists	56	FULL	139	19	The usual term is 'person centred therapy' not 'patient centre'.	Thank you – revised.
SH	College of Occupational Therapists	57	FULL	140	8–12	This continues to be confusing GET and graded activity, functional tasks involving personal care would be part of an activity programme. **Suggestion:** Is this meaning to refer to the fact that initially a graded activity approach may be used to look at activities such as dressing, which can then be later developed into an exercise programme.	This section has been significantly revised to address this and other concerns.
SH	College of Occupational Therapists	58	FULL	141	7	Although a self-management process, activity management should be supervised at least initially by a therapist who understands CFS/ME.	Noted and revised.

SH	College of Occupational Therapists	59	FULL	141	12	Activity Management / Grading activity is used across all categories of the condition, including the mild.	Noted.
SH	College of Occupational Therapists	60	FULL	141	15	**Suggestion**: Separate out occupational therapists, physiotherapists.	Noted and revised.
SH	College of Occupational Therapists	61	FULL	141	6.3.1.3	There is no mention of providing activity management in groups.	No evidence was found and the GDG did not take a view.
SH	College of Occupational Therapists	62	FULL	142	7	Why bracket things? Use items instead.	This section has been revised.
SH	College of Occupational Therapists	63	FULL	144	9	There appears to be a word missing, for example structured 'way'.	This section and the recommendations have been revised.
SH	College of Occupational Therapists	64	FULL	144	19	Prescription of what ?equipment.	Noted and clarified.
SH	College of Occupational Therapists	65	FULL	144	20	Rehab in FULL – rehabilitation.	Noted and revised.
SH	College of Occupational Therapists	66	FULL	144	23	Prolonged use of ? – missing "of equipment"	Noted and revised.
SH	College of Occupational Therapists	67	FULL	145 181 202 (145)	6.3.2.1 6.3.6.4 6.3.6.38 (6.3.2.6)	Is this referring to **formal CBT or to a CBT based approach?** Few professionals in CFS/ME teams are formal CBT therapists, but many will have sound knowledge, understanding and experience of this approach and the ability to use it safely and effectively to a given level. Many professionals can provide a basic approach suitable for CFS/ME (as described later in 6.3.6.11-13), and the descriptions given in the research studies on CBT in CFS/ME appear to be operating the therapy at a basic 'rehabilitative' level. However referral for more formal CBT	These are evidence statements agreed by the GDG, based on the evidence reviewed. We have also revised the recommendations to clarify areas of potential confusion.

						will also be necessary in people where intervention on underlying schema is required, should this not also be defined, as there are significant resource and professional implications depending on how this is interpreted. Compounding the potential confusion, this section refers to **components** of CBT sometimes being appropriate to utilise, whereas: This section states that CBT must be given by a suitably trained CBT therapist, which is different to a professional with basic CBT skills. This would also greatly effect the costings of therapy, as a psychologist is considerably more expensive than another professional, such as OT, nurse, with CBT skills. **Suggestion:** Perhaps there needs to be clearer differentiation between a CBT based approach and formal CBT, both of which have their place in this setting.	
SH	College of Occupational Therapists	68	FULL	147	20–25	What are the recommendations in relation to the role of Expert Patient Programme in CFS/ME? EPPs do contain elements of rehabilitation, but how does this relate to the recommendation of a review with a rehabilitation professional (pg144, line 20) and where is the duty of care?	See recommendation 1.1.1.1 in draft version. Self-management is a recognised strategy for long term conditions, and such issues are not specific to CFS/ME.
SH	College of Occupational Therapists	69	FULL	151	14	Occupational therapists have skills in both CBT and making graded increases in physical capacity and will combine both approaches in practice. The guidelines imply that these have to be delivered as separate elements, whereas in clinical practice (as opposed	This section reviews the available health economic evidence and provides information on this evidence base.

						to research settings) may therapies are provided on a more eclectic basis.	
SH	College of Occupational Therapists	70	FULL	185	Section on CBT	Many of the statements given are **not exclusive** to CBT, such as assertion, sleep hygiene etc. Moreover, some such as using activity as a therapeutic tool and exploring mastery of tasks, are not listed as core skills of CBT in other settings, and are specifically the core professional skills of occupational therapy. Activity analysis and adaptation is not a key component of CBT training but has been adopted into CBT models for CFS/ME. As occupational therapists receive degree level training in the use of activity as a therapeutic tool we would be concerned that any professional using activity within therapy has the appropriate qualifications and training to do so. Other models also incorporate thoughts and beliefs into their understanding of the human being (such as the Model of Human Occupation, Keilhofner 2002). CBT is the most researched approach in this setting but does not mean that similar models, based on the same principles are not effective as well. It is therefore derisory to other professional groups to state that only a trained CBT Therapist can deliver the elements that have been listed under CBT.	We have revised these recommendations in light of these and other comments. In addition, we recommend that any of the interventions should be delivered by an appropriately trained professional.
SH	College of Occupational Therapists	71	FULL	188	Section on GET	Once again the elements listed are not exclusive to an 'exercise programme'. Points 1 and 2 from 6.3.6.15 could be taken as key approaches of occupational therapy in relation to the meaningful use of activity in relation to	Noted and there are components of each that are similar.

						work, rest and play, but seem to have been adopted as part of an 'exercise' rather than activity approach.	
SH	College of Occupational Therapists	73	FULL	190	6.3.6.19	Some of the examples given seem too vague to be defined as graded, e.g. walk **more frequently** to another room. Also, it is common practice to use a 10% not a 20% increase ratio.	This is based on that quoted in the trials and is quoted as a maximum.
SH	College of Occupational Therapists	74	FULL	192	Box 2	*"…working with the patient should together continue…"* – doesn't make sense; delete "should together continue" and insert collaboratively.	Noted and revised.
SH	College of Occupational Therapists	75	FULL	192	6.3.6.22	Activity Management is also person centred.	Noted and revised.
SH	College of Occupational Therapists	76	FULL	202	18	Sentence unclear.	Noted and revised.
SH	College of Occupational Therapists	77	FULL	204	15–23	A misrepresentation of what the envelope theory is – it's not about reducing or doing substantially less, but increasing as able to and balancing rest and activity within an energy management approach; which is not the same as consistently maintaining levels at lower than capacity.	The GDG considered this to be an appropriate description.
SH	College of Occupational Therapists	78	FULL	232	27	Should this read additionally "in adults and children with mild/ moderate CFS/ ME".	Please see the recommendation on the use of tricyclics.
SH	Department of Health, Peninsula Medical School	36	FULL	138 139	23 2	The initial generic statements about evidence-based treatment for CFS/ME must be qualified in that this evidence is restricted to patients with mild or mild-to-moderate disability. Many moderately and severely disabled patients seen in clinical practice would not have been eligible to enter the studies because they would not have been able to attend the treatment	Noted and additional detail on the patient groups has been added to the chapter.

						programme (frequency, location, duration). This fact is quite evident in careful reading of the papers, but is inadequately reflected when summarised. Whilst the NICEguideline refers to mild-to-moderate in making the later recommendation, it would be helpful and more factually correct to state the qualifier at this juncture, as well as at later detailed points in the text as appropriate. I have not necessarily identified all these places, but this simple factual aspect is central to a proper understanding of the issue, and indeed some of the legitimate concerns of patients and patient advocates about inappropriate extrapolation of the data to more disabled patients. The opening statement should reflect the narrower applicability of the data to only a subset of patients with CFS/ME.	
SH	Department of Health, Peninsula Medical School	37	FULL	139	10–18	This section is helpful but still implies that the extrapolation from clinical trial data to more severely affected patients is an evidence-based assumption at the same level of evidence. This is especially as it is located immediately after a paragraph emphasising the evidence-based nature of the treatment. There should be an explanation of where the extrapolation starts, with the necessary caveats about the assumptions implicit in such extrapolation, especially given patient feedback referred to elsewhere, and in the paragraph following.	Noted and revised.
SH	Department of Health,	38	FULL	140	14	“…. to most ambulant (or mild-moderately disabled) patients ...” This	Noted and revised.

	Peninsula Medical School					qualifier is essential here. After all the studies showed an effect on a proportion of this subgroup. It is moot as to whether this is most CFS/ME patients attending healthcare settings.	
SH	Department of Health, Peninsula Medical School	39	FULL	145	1	6.3.2.1 ambulant adults 6.3.2.3 ambulant adults 6.3.2.4 ambulant adults	Noted and revised.
SH	Department of Health, Peninsula Medical School	40	FULL	146 147 148 148 148 148	6 12 8 9 17 22	Ambulant or mild-moderate CFS Ambulant or mild-moderate CFS Ambulant or mild-moderate CFS Ambulant or mild-moderate CFS Ambulant or mild-moderate CFS Ambulant or mild-moderate CFS	Details of the study participants can be seen in the detailed evidence review, and are reflected in the wording of the questionnaire wording and the recommendations.
SH	Department of Health, Peninsula Medical School	41	FULL	183–4 204	6.3.6.10 15–23	There is a potential for confusion here, and rephrasing would be important. Although the literal text is correct in commenting on “substantially less than FULL capacity” as lacking evidence, the concept of keeping a little energy in reserve to enable healing (and to cope with unexpected activities) is a helpful part of the discourse about setting levels in any activity management/GET/GAT programme. It is important to make it more clear that it is the major extent of under-activity that is being commented on, not the idea of keeping a small reserve, so as not to undermine, through the negative statement here, the use of this valuable concept in discussions with patients. This later statement is similarly problematic, though less so. The key distinction about substantially applies here. It could resolve the disparity of patient evidence. There should be a	The recommendation does state at ‘substantially less than full capacity’ and should be read in conjunction with the recommendations on what strategies are recommended..

						clarification that a small reserve may be appropriate as part of activity management.	
SH	Department of Health, Peninsula Medical School	42	FULL	192	6.3.6.20	This is potentially hazardous, and I can see no evidence to support this recommendation. Indeed this statement is at odds with the more balanced recommendations on pp142-4, and in section 6.3.6.35 I am not clear that there is a justification for separate guidance in these two settings, and it produces confusion. If it is felt necessary to include different setback strategies in relation to GET and activity management, this should be made much more explicit and obvious. It is usual practice to encourage patients to reduce activity during setbacks, and then gradually to build up. Clinical experience repeatedly shows that patients who fail to do so have longer setbacks. There is no evidence that a brief and usually modest reduction in activity is detrimental, nor that it interferes with the regaining of the prior trajectory of improvement. On the other hand, patients who maintain their pre-setback levels have longer setbacks, and take longer to recover, increasing the risk of any deconditioning more.	This section has been revised based on stakeholder comments.
SH	Department of Health, Peninsula Medical School	43	FULL	192 204	6.3.6.25 13–14	This statement suggesting possible benefit of introducing GET to severely affected patients is extraordinary. There are no data to support it, and patient and clinician experience regularly reaffirm the inappropriateness and inapplicability of GET as such to patients with this level of disability. I would suggest that this is either deleted	Noted and revised.

						or rephrased. Perhaps “careful incremental activity adjustment informed by the principles of graded exercise/activity programmes may be possible, but the increments and rate of change would be considerably lower in these patients, and expectations more modest.” Similarly in this later section, “elements of GET” is too strong to be supported by evidence. A similar qualifier about management being “informed by the principles of GET” might be acceptable.	
SH	Department of Health, Peninsula Medical School	44	FULL	206	9	In view of widespread but erroneous views amongst General practitioners and some others, I would suggest that comment is made on the notable evidence of lack of benefit from a range of antidepressants, in numerous trials of patients with CFS/ME who are not depressed or anxious. This is important negative evidence that undermines this view that CFS/ME is primarily a manifestation of a mood disorder. A comment to that effect would be apposite here.	The guideline states clearly that there is inadequate evidence of benefit for CFS/ME in using tricyclic antidepressants, SSRIs, or monoamine oxidase inhibitor antidepressants.
SH	Department of Health, Peninsula Medical School	45	FULL	210–212 229	2a, 2b 6.4.5.4	The normal screening test for hypothyroidism is the TSH not thyroxine. TSH is established as the normal test, which can be supplemented by free thyroxine (FT4) where TSH is abnormal. Surely the question is misleading in the context of normal clinical practice? Similarly the recommendation in 6.4.5.4 should be rephrased. The first section could use the term biochemically hypothyroid, or raised TSH and low thyroxine.	Acknowledged. The recommendation has been changed accordingly.
SH	Department	46	FULL	213	2c	I am puzzled why venlafaxine is	Venlafaxine is a very effective

	of Health, Peninsula Medical School					discussed in the context of pain and not just mood. This is potentially misleading and this agent is not a treatment for pain..	treatment of mood. It is not licensed for pain, although some evidence exists for it being useful where pain is also a factor in depression. Consequently, it may be a rational treatment for depression with pain albeit not specifically licensed for this. Thus the GDG considered it but agreed not to make a recommendation.
SH	Department of Health, Peninsula Medical School	47	FULL	216	2f	It is bizarre that the GDG has expressed uncertainty about the use of gabapentin in the treatment of pain, which is licensed for the treatment of neuropathic pain, and which has proved very helpful where such pain is a major feature of CFS/ME. This leads to an unhelpful lack of comment about this important aspect of symptom management.	The view of the GDG was that while gabapentin may be useful in individual cases, the risks of side-effects of this drug precluded recommending it in a national guideline.
SH	Department of Health, Peninsula Medical School	48	FULL	222	2i	The interpretation of this is potentially ambiguous. If someone “has had” herpes simplex or zoster infection, and has a current recurrence, treatment is appropriate. This issue should be narrowed, in its interpretation, to patients who do not have active herpes simplex or zoster virus infection. See below re p230.	We acknowledge that the question could have been worded more clearly. The GDG agreed that anti-herpes agents were inappropriate in this situation.
SH	Department of Health, Peninsula Medical School	49	FULL	230	6.4.5.8.	Why is the qualifier “unless they are already taking SSRIs” added? Tricyclics have a particular effect on sleep, which is not shared by SSRIs, and indeed more activating SSRIs such as fluoxetine and paroxetine may exacerbate sleep disturbance. Tricyclics in low dosage can be useful in addition to SSRIs. There is no clear evidence to justify the qualifier, and the	The combination of SSRIs and tricyclics is potentially dangerous. SSRIs can increase levels of tricyclics from 20% to 10 fold, and the combination of these two drugs is a well-documented cause of serotonin syndrome. Combinations like this, although used, are best done under specialist care and, as these guidelines are aimed at a

						simplest would be to remove this last phrase.	wider group of doctors, the advice should stand. We also note that co-morbid depression should be managed as in the NICE guidelines on depression.
SH	Department of Health, Peninsula Medical School	50	FULL	230	6.4.5.9.	Last bullet: Add “unless active herpes simplex or zoster infection.” See above re p222.	We have noted that these are not recommended for the treatment of CFS/ME.
SH	Department of Health, Peninsula Medical School	51	FULL	231	17–22	Why were not adult cooptees, with experience of pharmacotherapy in symptom control, used to explore gabapentin and other treatments?	The GDG approached co-optees as they considered appropriate.
SH	Department of Health, Peninsula Medical School	52	FULL	232	15–19	It is disappointing that there is no mention of the widespread experience that less activating SSRIs (citalopram, escitalopram and sertraline) are better tolerated in most CFS/ME patients than fluoxetine and paroxetine. This would be a useful steer and avoid problems where activation enhances the risk of boom and bust behaviour, and of sleep disturbance.	The GDG are not aware of any evidence to support the statement that certain SSRI antidepressants are better tolerated in this group of patients. Some patients indeed may benefit from more activating SSRIs. Clinicians should be able to take decisions based on individual circumstances.
SH	Department of Health, Peninsula Medical School	53	FULL	232	15–27	Why is mirtazapine not mentioned? This is in a class of its own, with some tricyclic-like properties for sleep but with good anti-depressant effect and tolerability in CFS/ME.	The recommendations do not mention each of the individual antidepressants, rather the major classes of antidepressants. There is not evidence of specific advantage of mirtazapine for depression in this condition, and indeed the hypnotic effects wear off after a short period of time.
SH	Department of Health, Peninsula Medical School	54	FULL	232	24–27	It is worth adding Trazodone specifically, as it is tricyclic-like in biological effect, but is not actually a tricyclic molecule.	The recommendations do not mention each of the individual antidepressants, rather the major classes of antidepressants. There is not evidence of specific advantage

							of trazodone for depression in this condition.
SH	Department of Health, Peninsula Medical School	55	FULL	233	1–6	This statement is unjustifiably negative. The agent is actually rather well tolerated in CFS/ME and transforms the lives of many patients with neuropathic pain. The agnostic position is unnecessarily inhibitory to their utilisation for such an intrusive symptom. Pregabalin is a useful option if tolerability is an issue.	Noted, and we have recommended that people should be referred for specialist pain management if appropriate.
SH	Department of Health, Peninsula Medical School	56	FULL	233	9–11	If this refers to both adults and children, then this should be explicit, as currently melatonin is both unlicensed for adults as well as discouraged (for no very clear reason). Some patients have found it modestly helpful for initiating sleep.	The view of the GDG was that there were other licensed medications available for adults. This was not the case for children.
SH	Department of Health, Peninsula Medical School	57	FULL	251	4 (l) 6.6.5.1.	Surely there should be a comment on the use of acupuncture for pain control, for which it is widely used and for which there is evidence of efficacy in a General sense. Some comment that refers this specific exception in the General recommendations would be helpful.	We have noted that some people find this helpful, but no evidence on the use of acupuncture in people with CFS/ME was identified.
SH	Invest in ME	143	FULL	137	*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.	We have recommended that the patient should be in control of their goals', and that any programme should be tailored to the individual.

						IiME Comment: This is to be welcomed and needs to be emphasised elsewhere in these guidelines instead of the inconsistency that exists.	
SH	Invest in ME	144	FULL	138	*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*	Noted and revised.

						ME is a somatoform illness.	
SH	Invest in ME	145	FULL	138	*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!*	Noted and clarified.
SH	Invest in ME	146	FULL	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*	Noted, and the recommendations have been revised in light of this and other comments, but we have stressed throughout the need for patient preferences to be taken into account. Regarding the aetiology, this is an issue noted by the GDG. The varying opinions in this area whilst very strong are still inconclusive without a definitive case definition or diagnostic test. The evidence review therefore purely summarises the evidence from the GET/CBT trials and does not comment on any association with possible underlying disease processes.

						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'?	
SH	Invest in ME	147	FULL	139	*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.*	Noted and the recommendations on GET have been expanded and clarified to address such issues.
SH	Invest in ME	148	FULL	139	*28*	"GET is a carefully mutually developed programme, undertaken with the patient	Issue 1: Details of the patients included in the trials can be found in

						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).*	the full evidence review (Appendix 1) Issue 2: Noted.
SH	Invest in ME	149	FULL	140	*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.	We have revised this to 'be of benefit to some patients.' We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the

						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.	needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET.
SH	Invest in ME	150	FULL	141	*6 onwards*	- 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*	Please see the Introduction and Chapter 5 for discussions on diagnosis and possible aetiology.

						unknown.	
SH	Invest in ME	151	FULL	141	*26*	“ 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?*	This section has been revised.
SH	Invest in ME	152	FULL	142	*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	This section has been revised.

						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.	
SH	Invest in ME	153	FULL	143	*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'*.	Noted, and the needs of the individuals should be paramount when agreeing appropriate intervention.
SH	Invest in ME	154	FULL	143	*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.*	Noted, and the needs of the individuals should be paramount when agreeing appropriate intervention.
SH	Invest in ME	155	FULL	143	*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	This section and the recommendations have been revised.

						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.	
SH	Invest in ME	156	FULL	143	*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.	This section and the recommendations have been revised.

						• 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.*	
SH	Invest in ME	157	FULL	144	*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*.	Noted and revised.
SH	Invest in ME	158	FULL	145	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 [X] says that CBT experts themselves have stated that improvement is not sustainable.	These are evidence statements agreed by the GDG, based on the evidence reviewed.

SH	Invest in ME	159	FULL	147	*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?*	We have recommended the use of a multi-component programme tailored to the needs of the individual.
SH	Invest in ME	160	FULL	147	*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	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET.

						show that GET is most harmful to pwme.	
SH	Invest in ME	161	FULL	147	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.*	People should be given information so that they can access such programmes as they consider necessary and in a way that is appropriate to them.
SH	Invest in ME	162	FULL	148	*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.*	Noted and revised.

SH	Invest in ME	163	FULL	154	*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?*	CBT and other strategies have been discussed and defined by the GDG. The underlying evidence base has been identified and appraised. We have revised the descriptions used.
SH	Invest in ME	164	FULL	155	*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,	The use of coping strategies does not negate the fact that CFS/ME is a real illness.

						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*.	
SH	Invest in ME	165	FULL	*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?*	As stated in this section, this paper did not publish sufficient subgroup analytic figures to draw valid conclusions on the CFS/ME population. The quoted statement alone does not allow any conclusion on the cost effectiveness of treatment for CFS/ME patients, as the populations are likely to be different in more characteristics than merely clinical outcome at baseline.
SH	Invest in ME	166	FULL	158	*1*	4. Treatment is provided by the NHS in the context of availability of adequate numbers of competent, appropriately	These statements were used to guide respondents when completing the questionnaire, and cannot be

						trained health care professionals *IiME Comment: it is not defined what is “appropriately trained”.*	changed.
SH	Invest in ME	167	FULL	*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	6.3.6.1 Noted and we have recommended that the patient should be in charge of the goals etc. 6.3.6.2 Noted and that is the intent of the recommendation. Regarding rationale – this refers to the aim of the intervention. 6.3.6.3 Noted and revised. The choice of treatment should be based on the individual’s needs and preferences, and be tailored to these.

						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.	
SH	Invest in ME	167	FULL	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.	6.3.6.6 No research evidence for cures for CFS/ME was found. The guideline could therefore not make recommendations regarding cure. The guideline presents the evidence available for management of the condition. 6.3.6.7 Noted as an overall aim, but the specific aims of the individual may be different at different stages of the condition. 6.3.6.10 We are simply stating the current lack of evidence for these approaches.

						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.)	

SH	Invest in ME	168	FULL	*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*	6.3.6.4 Noted 6.3.6.6 It is recognised that people may have cognitive difficulties that should be taken into account when agreeing a programme of intervention.

						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.	
SH	Invest in ME	169	FULL	*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 1: 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,	Please note that this recommendation starts with the caveat that the <u>programme may include components as appropriate for the patient</u>. Not as the standard programme. Issue 1: CBT is recommended as part of an overall programme, tailored to the needs and preferences of the individual. Other components may include pharmacological management. Issue 2: Any intervention should be made after shared decision making that respects the needs and preferences of the individual. Issue 3: This has been revised based on stakeholder comments.. Issue 4: This has been revised based on stakeholder comments. Issue 5: People with chronic illnesses may have these feelings. Issue 6: Noted but again this is part of an individualised programme.

						and behaviours • establishing a stable and maintainable level of functioning, followed by a gradual, and mutually agreed, increase/decrease in activity *IiME Comment 2: “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 3: 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 4: this is ridiculous and belittling and shows the basic myths behind ME which NICE keep on peddling out in this document.*	Issue 7: Noted but again this is part of an individualised programme. Please see text, there is research evidence that CBT improved function in people with CFS/ME.

						• 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 5: 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 6: 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 7: 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.	
SH	Invest in ME	171	FULL	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*	*6.3.6.20 Managing Setbacks* Activity programmes are used in many illnesses of a physical nature to improve functioning. (Please see also the guideline on management after a heart attack – NICE Post MI available at www.nice.org.uk). *Activity management* The guideline details the risks of prolonged bedrest.

						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.*	
SH	Invest in ME	172	FULL	*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*	This section has been revised based on stakeholder comments.

						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!*	
SH	Invest in ME	173	FULL	*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.*	We have revised the structure and the description of these therapies (including the appropriate use of rest) to clarify their use.
SH	Invest in ME	174	FULL	*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*	We have revised the structure and the description of these therapies to clarify their use.

						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.	
SH	Invest in ME	175	FULL	203	*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?*	This recommendation has been revised.
SH	Invest in ME	176	FULL	203	*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.*	The recommendations make this explicit.
SH	Invest in ME	177	FULL	*203*	*26*	Both the evidence and the GDG consensus support gradual increases in aerobic exercise in people with <u>mild, moderate </u>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	The recommendations have been revised to clarify the use of CBT/GET. Also the need for individualised programmes based on the needs and preferences of patient is stressed throughout.

						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.	
SH	Invest in ME	178	FULL	*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?*	We have recommended that the benefits and risks of any intervention should be discussed before its initiation. The recommendations give explicit guidance on the programme content, application and the need for delivery by appropriately trained healthcare professionals.
SH	Invest in ME	179	FULL	204	*15*	There is no evidence to support the 'Envelope Theory' of maintaining levels as substantially less that capacity in order to have a reserve.	The 'envelope theory' as described recommends levels at <u>substantially</u> less than capacity on which there is no evidence and differing views.

						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.*	This is as opposed to Pacing, which is described. It is not possible to comment on the methodology of trials currently in progress.
SH	Invest in ME	180	FULL	204	*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?*	Thanks for your comment.
SH	Invest in ME	181	FULL	204	*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*	These are not recommendations, but a summary of the discussions of the GDG when drafting recommendations.

						FULL of contradictions and the lack of precision is astounding.	
SH	Invest in ME	182	FULL	208	*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!*	This is a statement within the health economic section and has been clarified.
SH	Invest in ME	183	FULL	229		*6.4.5 Recommendations* 6.4.5.1 [*There is no known pharmacological treatment* …] *IIME COMMENT: 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* …] *IIME COMMENT: 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 making treatment recommendations, NICE cannot rely solely on the results of laboratory research. 6.4.5.1 This to greater intolerance not reduced effects. The GDG is not aware of any published clinical trials of thyroxine supplementation in ME/CFS. These recommendations have been revised.

						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.	
SH	Invest in ME	184	FULL	*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*	**Issue 1 –** Melatonin was reviewed in the York review. Also the use of melatonin in children was supported in the wider survey. **Issue 2 –** Please see the York review for details of the

						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?	antidepressants reviewed. **Issue 3 –** .We have changed this recommendation to make it clear that antiviral agents should be used where there is an indicative history.

SH	Invest in ME	185	FULL	231	*3*	"In addition, particularly with immunoglobin 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 immunoglobin 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 immunoglobin, 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.	The GDG have noted that there was not convincing evidence for the use of these drugs and no evidence statements were made.
SH	Invest in ME	186	FULL	231	*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	This statement refers to inclusion criteria for the questionnaire.

						research is needed in this area. *IIME COMMENT: Side effects were reported for GET too but accepted.*	
SH	Invest in ME	187	FULL	233	*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.	We have made a recommendation on when serological testing and therefore appropriate treatment should be undertaken.
SH	Invest in ME	188	FULL	234	*l2*	*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	The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful.

						thoroughly as CBT or GET as many patients find benefits from high quality supplements.	
SH	Invest in ME	189	FULL	234	*l4*	*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.*	This is guidance for NHS practice. The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful.
SH	Invest in ME	190	FULL	235	*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?*	This is beyond the scope of the guideline, which is guidance for NHS practice.
SH	Invest in ME	192	FULL	249	*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.*	We have noted that although the evidence does not support prescription of supplements, people may find them helpful as an OTC supplement.

						Fish oils score as highly or better than CBT so why does NICEnot recommend this as a therapy/treatment?	
SH	Invest in ME	193	FULL	249	*19*	*6.6.2.2* Additional Clinical Evidence No new evidence found. *IIME COMMENT: isn't this where one listens to patients for evidence?*	This refers to the update searches carried out as part of NICE methodology.
SH	Invest in ME	194	FULL	253	*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.	The GDG considered the evidence to be insufficient to recommend any of these therapies to be available on the 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).	
SH	LocalME	81	FULL	140	22–28	The biomedical research evidence suggests it cannot be safely assumed that negative effects reported by patients following exercise are attributable to inappropriate application of what we are told is an intrinsically helpful approach. However, as is common practice sales techniques the ‘customer’ is led gently into a corner by a set of very clever designed questions aimed at achieving mutual agreement on everything the salesman offers. One system is known as the Hierarchy-of-Effects Model and is a marketing behavioural response model consisting of stages through which a buyer is presumed to go, including: awareness, knowledge, liking, preference, intention to buy and purchase whatever is on offer.	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET. Any treatment needs to be undertaken only with informed consent and shared decision making.

						As highlighted previously it is highly probable that participation in 'GET' programmes under professional supervision with mutually negotiated meaningful goal setting and education, evokes a similar behavioral response from patients thereby discouraging disagreement with most statements made by the professional with the result that the feel cornered and 'nodding' at all the appropriate times in agreement with the professional.	
SH	LocalME	82	FULL	192	6.3.6.21	It is essential that this issue of deconditioning and exercise/rest is resolved since the advice given to maintain exercise even when there is an increase in symptoms is potentially harmful and dangerous and the supposed negative effects of deconditioning would be negligible in comparison. It is very clear that these guidelines should err on the side of safety and caution.	This section has been revised based on stakeholder comments.
SH	LocalME	83	FULL	229	6.4.5.4.	Some research should be done on the thyroid function. Levels of T3 andT4 and thyroid stimulating hormone should be measured at times in all patients and the readings scrutinized to see if many are at the bottom end of the normal range. (There is also evidence to suggest that there may also be some 'peripheral resistance' to thyroid hormone in CFS/ME patients.) Also it would be useful to compare readings when very ill with reading taken if symptoms improve. Likewise with B12.	See response to 25% ME Group comment number 221.
SH	LocalME	84	FULL	234	10–19	Supplements	We have revised the recommendation to reflect the

			NICE	33	1.3.6.3	Again there is inconsistency between the clinical evidence summary in the FULL and the statement in the NICE, "There is no evidence for the use of supplements …". Whereas the FULL details that there is some evidence for Essential Fatty Acids and Magnesium. It is also known that there has been a further small study with EFAs at Hammersmith Hospital and a much larger study is about to start there. The statement in the NICE is misleading and potentially prevents many patients deriving benefit from certain supplements. It also makes no mention of the common sense advice that prevails in much of the ME/CFS literature to take a good quality multi-vitamin/mineral supplement. Another failing of the strictly evidence-based approach.	evidence – the evidence is insufficient (the GDG considered 1 RCT to be of limited use – see the Methods Chapter for details) and prescribing of these is not recommended. However, patients report finding them helpful, so again this is reflected in the recommendation.
SH	LocalME	85	FULL	235	13 -17	There is enormous concern amongst patients about who is doing the training and what exactly they are being taught.	In accordance with the methodology for clinical scenarios, the assumptions that form the basis for answering the questions must be explicit so that respondents have a common understanding of the factors that influence the appropriateness of treatment. These statements were agreed as assumptions for the questionnaire. They are not guideline recommendations. A fuller explanation is now in the methodology chapter.
SH	LocalME	86	FULL NICE	245 32	1.3.5.3	Diet This is another example of the GDG ignoring the consensus of the wider group. The wider group actually agreed	We have recommended the use of such diets where there are bowel symptoms, and that this should be done under the supervision of a

						that a clinically supervised exclusion diet followed by food challenges is appropriate, where there are bowel symptoms, however, the NICE is worded such as to discourage this and takes no account of the practical experiences of large numbers of people with ME/CFS who often derive benefit from excluding certain foods.	dietician.
SH	ME Research UK (formerly MERGE)	26	FULL	141	26	Management of Setbacks.. People with CFS/ME have variations in the severity of their symptoms and will experience setbacks or transient increases in fatigue and other symptoms.. The usual term used in the ME/CFS literature is “crash” (e.g., Carruthers 2003) or “relapse” (e.g., CDC, “CFS Toolkit for Health Care Professionals: Managing Activity” 2006). Relapses are reported to occur frequently in people with ME/CFS, and can be long-lasting and affect all areas of life, and be much more than transient. THE WORD RELAPSE SHOULD BE REINSTATED AND ROLE OF RELAPSES EXAMINED	The section on setbacks has been revised, and the GDG considered the term to be appropriate.
SH	NHS Fife		FULL	140	22–28	The biomedical research evidence suggests it cannot be safely assumed that negative effects reported by patients following exercise are attributable to inappropriate application of what we are told is an intrinsically helpful approach. However, as is common practice sales techniques the ‘customer’ is led gently into a corner by a set of very clever designed questions aimed at achieving mutual agreement on everything the salesman offers. One system is known as the Hierarchy-of-	We have noted the concerns of patients regarding the safety of GET, but research evidence reviewed for this guideline supports the use of GET. We have recommended that the needs and preferences of the individual need to be taken into account, and this recognises the need to explain both the potential risks and benefits of properly applied GET. Any treatment needs to undertaken only with informed consent and

						Effects Model and is a marketing behavioural response model consisting of stages through which a buyer is presumed to go, including: awareness, knowledge, liking, preference, intention to buy and purchase whatever is on offer. As highlighted previously it is highly probable that participation in 'GET' programmes under professional supervision with *mutually negotiated meaningful goal setting and education,* evokes a similar behavioral response from patients thereby discouraging disagreement with most statements made by the professional with the result that the feel cornered and 'nodding' at all the appropriate times in agreement with the professional.	shared decision making.
SH	NHS Plus	1	FULL	192	6.3.6.21	It is essential that this issue of deconditioning and exercise/rest is resolved since the advice given to maintain exercise even when there is an increase in symptoms is potentially harmful and dangerous and the supposed negative effects of deconditioning would be negligible in comparison. It is very clear that these guidelines should err on the side of safety and caution.	This section has been revised based on stakeholder comments.
SH	NHS Plus	2	FULL	229	6.4.5.4.	Some research should be done on the thyroid function. Levels of T3 andT4 and thyroid stimulating hormone should be measured at times in all patients and the readings scrutinized to see if many are at the bottom end of the normal range. (There is also evidence to suggest that there may also be some 'peripheral resistance' to thyroid	We have noted that thyroxine is not appropriate for the treatment of CFS/ME but is obviously useful if there are thyroid function problems.

						hormone in CFS/ME patients.) Also it would be useful to compare readings when very ill with reading taken if symptoms improve. Likewise with B12.	
SH	NHS Quality Improvement Scotland		FULL NICE	234 33	10–19 1.3.6.3	***Supplements*** Again there is inconsistency between the clinical evidence summary in the FULL and the statement in the NICE, "There is no evidence for the use of supplements …". Whereas the FULL details that there is some evidence for Essential Fatty Acids and Magnesium. It is also known that there has been a further small study with EFAs at Hammersmith Hospital and a much larger study is about to start there. The statement in the NICE is misleading and potentially prevents many patients deriving benefit from certain supplements. It also makes no mention of the common sense advice that prevails in much of the ME/CFS literature to take a good quality multi-vitamin/mineral supplement. Another failing of the strictly evidence-based approach.	We have revised the recommendation to reflect the evidence – the evidence is insufficient (the GDG considered 1 RCT to be of limited use – see the Methods Chapter for details) and prescribing of these is not recommended. However, patients report finding them helpful, so again this is reflected in the recommendation.
SH	North Bristol NHS Trust		FULL	235	13 –17	There is enormous concern amongst patients about who is doing the training and what exactly they are being taught.	In accordance with the methodology for clinical scenarios, the assumptions that form the basis for answering the questions must be explicit so that respondents have a common understanding of the factors that influence the appropriateness of treatment. These statements were agreed as assumptions for the questionnaire. They are not guideline recommendations. A fuller

							explanation is now in the methodology chapter.
SH	North Eastern Derbyshire PCT		FULL NICE	245 32	 1.3.5.3	**Diet** This is another example of the GDG ignoring the consensus of the wider group. The wider group actually agreed that a clinically supervised exclusion diet followed by food challenges is appropriate, where there are bowel symptoms, however, the NICE is worded such as to discourage this and takes no account of the practical experiences of large numbers of people with ME/CFS who often derive benefit from excluding certain foods.	We have recommended the use of such diets where there are bowel symptoms, and that this should be done under the supervision of a dietician.
SH	North Glamorgan NHS Trust - Merthyr Tydfil		FULL	257	1– 6	How can the severely affected possibly receive the same care? Invariably they cannot access the 'services'!	This recommendation was intended to make clear that services should be made available in the homes of people who are severely affected if they could not travel. It has been revised to make this clearer.
SH	Royal College of Nursing	34	FULL	163	11	There is no evidence for a 'cumulative effect' – a management plan would initially stabilise symptoms (whilst the baseline of activity is being established) then small goals will be negotiated and agreed.	It is not clear to what this refers to.
SH	Royal College of Nursing	35	FULL	195	6.3.6.26	E-mail may also be used and helpful.	Noted and revised.
SH	Royal College of Nursing	36	FULL	229	6.4.5.2	There is not enough evidence to make a statement that those with CFS/ME experience increased sensitivity to drugs.	Noted but this was a significant patient concern.
SH	Royal College of Nursing	37	FULL	249	7	Our use of complementary therapy is primarily to support our holistic approach to care where young people are afforded a pleasant and supportive experience.	Noted with thanks.

						In one service, they have the advantage that the Complementary Therapist is a qualified Paediatric Nurse with several years experience within both acute care and the CFS ME Team.	
SH	Royal College of Nursing	38	FULL	253	9	Although there is no evidence for the use of complementary therapies for CFS/ME, as with drug management, patients often turn to complementary therapies for symptoms control. This is already seen and recognised within the cancer services and there is good evidence for the use of complementary therapies for symptoms such as pain, sleep, fatigue, mood etc. Patients currently spend vast amounts of money on complementary therapies – more guidance on this point would have been helpful for health professionals.	This is guidance for NHS practice. The GDG found insufficient evidence to recommend that complementary therapies should be routinely available. It is acknowledged, however, that some individuals may find them helpful.
SH	Royal College of Paediatrics and Child Health	42	FULL	206		In the FULL document it states that immunoglobulin therapy of children is not of overall benefit but there is nothing in the NICE about this. When developing our guideline the RCPCH went further than this and recommended it not to be used for children because of the concerns over safety of blood products and limited evidence of effectiveness.	Noted and the GDG did not make a recommendation on this.
SH	Royal College of Paediatrics and Child Health	43	FULL	212		SSRI's in children – these should only be prescribed to children and adolescents by specialists (i.e. child psychiatrists)	The GDG agree that SSRIs should be prescribed by child psychiatrists.
SH	Royal Liverpool Children's NHS Trust	11	FULL	138	23	I think this paragraph is invaluable and well written. The comment that it is not something 'made up' is necessary and will be helpful for those readers with CFS/ME reading these guidelines.	Noted with thanks.

SH	Royal Liverpool Children's NHS Trust	12	FULL	180		Recommendations set out well and very readable (esp CBT). Clear.	Noted with thanks.
SH	Sheffield South West Primary Care Trust	4	FULL	139	3	The term appropriate physical examination needs clarifying. What does this mean?	Noted and revised in the recommendations.
SH	Sheffield South West Primary Care Trust	5	FULL	139	11	Maintaining 30 minutes of moderate aerobic exercise for 5 out of 7 days may not be a realistic goal for some clients. Encouraging or promoting this a s goal that clients should aspire to may in some cases be detrimental to the therapeutic relationship. Clients should be allowed to identify their own exercise related goals and these may well vary between individuals. Not everyone wishes to aim for 30 minutes of aerobic exercise 5 out of every 7 days.	This is the goal used in the clinical trials which have been shown to produce benefits. However, we have stressed the need for individual goals to be agreed, which may be different.
SH	Sheffield South West Primary Care Trust	6	FULL	145		(6.3.2.6) I do not understand what is meant by a QUALY; please provide a clear explanation of what a QUALY is. This is repeated on page 150	We have added reference to a glossary of terms not specific to CFS/ME.
SH	Sheffield South West Primary Care Trust	7	FULL	151		I find the discussion regarding cost effectiveness difficult to understand. Research jargon is used, such as incremental cost at baseline and cost effectiveness acceptability curves. Please provide a clear explanation of these terms.	The health economic section contains technical information and uses some specialist terms. The NICE glossary is currently being developed to help with those terms and can be found at: http://www.nice.org.uk/glossary/
SH	Sheffield South West Primary Care Trust	8	FULL	190		(6.3.6.17) Clients should be able to make an informed choice about how often to exercise and not prescribed exercise 5 out of 7 days	The guideline stresses the patient's role and informed choice throughout. This recommendation is advising on the programme in general; as advised, all programmes are individualised.
SH	Sheffield	9	FULL	190		(6.3.6.19)	As advised, all programmes are

	South West Primary Care Trust					For some clients a progression of 20% from baseline can exacerbate symptoms and they will need to progress by a smaller percentage	individualised.
SH	Sheffield South West Primary Care Trust	10	FULL	191		(6.3.6.19) Clients should be able to make an informed choice about having a goal of 30 minutes of exercise and whether or not to progress to a higher aerobic heart rate zone. A client may decide that the activity/ exercise that they are practising does not need to produce a higher aerobic heart rate or be done for 30 minutes to be satisfying or worth while.	Noted and this has been reflected in the revised recommendations.
SH	Sheffield South West Primary Care Trust	11	FULL	202		(6.3.6.39) Need to clarify what is meant by an appropriately trained professional with experience of GET with CFS/ME.	Defining standards is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	St Bartholomew's Hospital Chronic Fatigue Services	48	FULL	138	1 +	Separate headings are required for these main treatment approaches, since CBT and GET are not self-management approaches.	This has been changed.
SH	St Bartholomew's Hospital Chronic Fatigue Services	50	FULL	138	6	It is useful to highlight the importance of a guided approach to self management approach to treatment, and that the patient should be willing to take part. Do they really take the lead, or does successful therapy occur through an alliance between therapist and patient?	This section has been revised to make this clearer.
SH	St Bartholomew's Hospital Chronic Fatigue	51	FULL	138	27–8	It is useful to highlight the scope of evidence for CBT in “medical” as well as “mental health” conditions.	Noted and revised.

	Services						
SH	St Bartholomew's Hospital Chronic Fatigue Services	52	FULL	139	24–6	It is useful to highlight the importance of patient control and involvement in GET	Noted and we have revised the recommendations to emphasise this.
SH	St Bartholomew's Hospital Chronic Fatigue Services	53	FULL	139	2	GET is not designed to be a self-management approach and is currently delivered as a professional mediated programme.	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	54	FULL	139	4	It involves setting a mutually negotiated baseline and then an increase in exercise.	This section has been revised in light of this and other comments.
SH	St Bartholomew's Hospital Chronic Fatigue Services	55	FULL	139	10	The ultimate goal of GET is to evoke a behaviour change and increase activity levels by using the medium of exercise to facilitate this (rather than being amount based).	This is the goal used in the clinical trials which have been shown to produce benefits. However, we have stressed the need for individual goals to be agreed, which may be different.
SH	St Bartholomew's Hospital Chronic Fatigue Services	56	FULL	139	10	The idea of aiming towards 30 mins 5 x a week also comes from government guidelines for activity to provide a health enhancing benefit ~(DOH - At least five a week).	Noted.
SH	St Bartholomew's Hospital Chronic Fatigue Services	57	FULL	139	10	There is also a definition of the intensity that should be embarked upon being 50-70% HR max. Of relevance to this, we suggest the guideline mentions the utility of heart rate monitors as a way of the patient knowing they are within their target aerobic activity and are not risking over-doing exercise.	Noted and added to the recommendations.

SH	St Bartholomew's Hospital Chronic Fatigue Services	58	FULL	139	15	Severely affected – We think it may be worth thinking about one of the main aims of GET not being a particular amount of exercise, but more of a behaviour change – therefore for anyone at any level, GET aims to increase what they are doing by changing the way that they currently do things and then adding in something new.	This section has been revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	59	FULL	139	28	The rate of progression in GET is reviewed regularly and mutually negotiated rather than being solely controlled by the patient	Noted and revised, but we have stressed that the patient should be in charge.
SH	St Bartholomew's Hospital Chronic Fatigue Services	60	FULL	140	12	GET programmes usually start with muscle stretches to ensure that there is adequate muscle length for the patients to move comfortably and functionally. There is mixed evidence regarding the physiological benefits of static stretching, but they have been used over the years by many athletes as a preparation exercise before embarking on something more strenuous. Functional tasks would form the aerobic component rather than the introductory stretch part of the programme	GET research describes stretches, but gentle functional activity can also be used. Aerobic tasks would not be used until later in the programme.
SH	St Bartholomew's Hospital Chronic Fatigue Services	61	FULL	140	8	A GET programme is begun after activity analysis has occurred to ensure that the patient is not in an under- and over-activity cycle before they increase the time spent in exercise.	Noted and revised.
SH	St Bartholomew's Hospital Chronic	62	FULL	140	14	A General exercise programme is evidence based in that there have been many studies indicating the benefits of exercise to maintain and improve	Noted and revised.

	Fatigue Services					health. We suggest you clarify that you refer to CFS/ME, while also mentioning the General benefits of exercise. The main differences between the two are mode of delivery, planning and liaison with a trained physiotherapist, activity analysis beforehand and mutual agreement of starting point as well as the specific rate of increments used in this population.	
SH	St Bartholomew's Hospital Chronic Fatigue Services	63	FULL	141	6	Section Headings unclear eg GET/CBT/Activity Mgt	Noted and revised
SH	St Bartholomew's Hospital Chronic Fatigue Services	64	FULL	141	6 +	There is a mention of activity management, but no mention of graded activity programmes or therapy - are we to presume this is the same thing?	Please see the Glossary and the recommendations for details of what we mean by activity management.
SH	St Bartholomew's Hospital Chronic Fatigue Services	65	FULL	142	21 +	Setback principles should be the same whether mild. Moderate, or severe. We are not aware of any evidence to the contrary, and we suggest it is important not to separate degree of severity in this section.	This section has been revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	66	FULL	144	21	Equipment should be a separate section – not part of rehab section	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue	67	FULL	159		Severity of symptoms is not a contra-indication for GET, if prescribed appropriately. For a severely disabled patient, almost any physical activity would raise their pulse rate, and thus	These are the results of the questionnaire and consensus work used to the draft the recommendations, not the recommendations themselves.

	Services					be classified by you as "aerobic".	
SH	St Bartholomew's Hospital Chronic Fatigue Services	68	FULL	181	6.3.6.4 & 6.3.6.33	We are not aware of any evidence to support the use of *relaxation therapies* by themselves in CFS/ME. In fact this technique has often been used as the main component of ineffective comparison treatment arms in several RCTs (see: Fulcher KY & White PD. Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome. *BMJ* 1997;314:1647-52. And: Deale A et al. Cognitive behavior therapy for chronic fatigue syndrome: a randomized controlled trial. *Am J Psychiatry* 1997;154:408-414.) Why, therefore, is an ineffective therapy included? We suggest this is omitted, unless it is clearly qualified by its indication as an aid to sleep, anxiolysis, et cetera, as is done well in 6.3.6.33.	6.3.6.4 cross refers to 6.3.6.33.
SH	St Bartholomew's Hospital Chronic Fatigue Services	69	FULL	183	6.3.6.8	"…equipment and adaptations (for example, a wheelchair, blue badge or stairlift)…" We disagree with this recommendation. Why should someone who is only moderately disabled require any such equipment? Where is the warning about dependence being encouraged and expectation of recovery being damaged by the message that is given in this intervention? We are in no doubt that it is a powerful message for a therapist of any sort to provide such aids. Our view is that such aids should only be considered by a multi-disciplinary therapeutic team as a whole, and usually in the context of providing a temporary means for a patient to	We have recommended such equipment only if appropriate, and as part of an overall management plan and as an aid to independence.

						increase their activity levels. An example would be providing a wheel-chair for a bed-bound patient as part of their active rehabilitation programme. In our opinion, such aids should never be seen as a permanent solution to disability in this illness.	
SH	St Bartholomew's Hospital Chronic Fatigue Services	70	FULL	183	6.3.6.9	You need to balance this advice by equally prominent advice to avoid complete rest. Although you mention this in the next section, there is a world of difference between “not recommended” and “no evidence”. M.E. patient charities warn about the dangers of complete and prolonged rest.	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	71	FULL	185	6.3.6.12	This section is a really good explanation of what well done CBT should look like, although our warning about the weaker evidence of a group delivered CBT should lead to a different level of support by the guideline for a group approach. There is a wealth of evidence for the efficacy of CBT in a range of health conditions such as heart disease, chronic pain, oncology, and diabetes, as well as CFS/ME, fibromyalgia and irritable bowel syndrome. The CBT outlined here is similar in principle to that used with people with these other chronic conditions. In all these conditions looking at thoughts and feelings acknowledges the impact which a chronic condition often has, due the strain people are placed under by suffering from illness and symptoms which last for a long period of time.	Noted with thanks.
SH	St	72	FULL	185	6.3.6.12	Many of the items included under the	Noted, but the GDG considered the

	Bartholomew's Hospital Chronic Fatigue Services					heading, 'a programme of CBT **may** also include:' would normally be referred to as essential elements of any CBT programme for people with chronic health conditions. In the research literature patients with CFS/ME report that: 1) having an understanding of the range of factors which may have caused and/or maintained their symptoms and disability; and 2) developing self-efficacy with experimenting with different ways of doing things, were key ingredients of CBT-based therapy programmes that they participated in (Norris, G. (2004). A qualitative study of mindfulness based cognitive therapy for chronic fatigue syndrome. Unpublished dissertation. University of Oxford Doctorate in Clinical Psychology; Royle, G.H. & Pimm, J. Exploring the process of change in a group CFS/ME management programme. Presentation given at the CFS Network conference, Manchester, October 2006).	wording of the recommendations to be appropriate.
SH	St Bartholomew's Hospital Chronic Fatigue Services	73	FULL	185	6.3.6.12	We would argue that many of the items included under the heading, 'a programme of CBT *may* also include:' are central tenets of any CBT programme and should be labelled as such. Most importantly we regard formulation as an essential start to successful therapy. That is a shared understanding of all factors that led to the onset and maintenance of CFS/ME in the particular individual (which may be why group approaches are perhaps less effective). There is increasing	Noted, but the GDG considered the wording of the recommendations to be appropriate.

						acknowledgement that formulation in psychological therapies is key to driving the intervention (Dallos, R & Johnstone, L (2006) Formulation in Psychology and Psychotherapy. Taylor & Francis Pub., ISBN: 1583917004).	
SH	St Bartholomew's Hospital Chronic Fatigue Services	74	FULL	188	6.3.6.14	"Adults with mild or moderate CFS/ME should be offered a programme that includes planned increases in duration of physical activity/exercise followed by increases in intensity leading to aerobic exercise (that is, exercise which increases the pulse rate) such as GET." We have already mentioned the omission of severely affected from this recommendation. We suggest a clarification, by adding "and, once achieved," between the words "exercise" and "followed". This will make sure that intensity is not increased until adequate duration is accomplished. The published RCTs suggest that it is the exposure to physical exercise that is the essence of efficacy, rather than a training effect, which would follow an increase in the intensity of GET. Incidentally we could not find a definition of exercise in the guidelines, which would help to demystify it. Exercise is defined as "activity requiring physical effort" (Oxford Dictionary of English. 2nd edition, A Soanes, A Stevenson (eds), 2003. Oxford University Press, ISBN 0-19-8613474).	We have made substantive changes to these recommendations. Noted and added. We have made the use of the term exercise clearer.
SH	St Bartholomew's Hospital	75	FULL	188	6.3.6.16	These goals should include recovery, not just exercise and activity goals. If it takes "years" to achieve goals, then	The statistics indicate that total recovery is relatively rare and the GDG felt that to include recovery as

	Chronic Fatigue Services					either the goals are wrong or the therapy is wrong. What other treatment in medicine would take years to work? We suggest “or even years” is deleted. If a therapy is not helping within a few months, either the therapy or the diagnosis or both should be reviewed and changes considered. We suggest that this advice is pertinent to all treatment approaches, not just for GET.	a goal may lead to disappointment. As the goals are patient derived they may be long term. Interim goals would be developed.
SH	St Bartholomew's Hospital Chronic Fatigue Services	76	FULL	190	6.3.6.17	You have left out an important step, which is to establish a baseline of physical activity that can be achieved even on a bad day. This stops the “boom and bust” behaviours, which need to be corrected before additional activities are negotiated. Only when a patient has established a stable baseline, based around current capacity, should any increments be considered.	This has been added to the recommendation.
SH	St Bartholomew's Hospital Chronic Fatigue Services	77	FULL	190	6.3.6.18	It is most important that the physiotherapist explain the physiological basis for the expected small increase in symptoms as the duration or intensity of exercise increases (Delayed onset muscle soreness, deconditioning of muscles and heart, et cetera) so that the patient does not worry about symptoms. Otherwise the patient may stop GET prematurely. It is also important to prescribe strategies to reduce symptoms, such as warming up and down before and after exercise, using muscle stretches. The use of temporary physical rest after (not before) exercise should also be discussed by the physiotherapist.	Noted and added.

SH	St Bartholomew's Hospital Chronic Fatigue Services	78	FULL	196	6.3.6.26	The section on sleep management is excellent and we commend it.	Noted with thanks.
SH	St Bartholomew's Hospital Chronic Fatigue Services	79	FULL	199	6.3.6.37	Patients are unlikely to panic in a set-back, whereas they may more likely be worried and sometimes overly concerned. We suggest substituting the word "panic" with "be overly concerned" with consequent revision of this paragraph.	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	80	FULL	200	6.3.6.37	We do not know any evidence that would support different strategies for severely disabled patients, and believe that singling out this group implies that the illness may behave differently in these patients, which is not the case to our knowledge.	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	81	FULL	202	6.3.6.39	"A GET programme should be delivered by an appropriately trained professional with experience of GET with CFS/ME." We suggest that it may be unwise to differentiate the competencies required for GET in contrast to CBT in this way. GET therapists also need appropriate clinical supervision and training by someone who is experienced in the evidence based approach to GET for patients with CFS/ME.	Noted and revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	82	FULL	203	1– 2	"The GDG did not regard CBT or other behavioural treatments as curative or directed at the underlying disease process, which remains unknown." Treatments in medicine can cure or aid recovery in the absence of knowing the underlying disease process. The five year study by Deale and colleagues, to	Noted. This reflects the discussions and considerations of the GDG during the process. However, there was much ongoing discussion of this point, and we have revised the descriptions and recommendations on these therapies.

						which you refer in this section showed that a quarter of patients regarded themselves as recovered five years after a course of individual CBT. With Dutch colleagues, we have just finished a follow up study of individual CBT, which has corroborated these findings (Knoop H, Bleijenberg G, Gielissen MFM, van der Meer JWM, White PD. Is a FULL recovery possible after cognitive behavioural therapy for chronic fatigue syndrome? Psychotherapeutics and Psychosomatics (in press). Paper available in confidence if required) In this open study we found that 23% of patients referred for individual CBT met conservative criteria for recovery soon after completing therapy. The figure was even higher in the absence of a medial comorbid condition, such as compensated hypothyroidism. When these data are added to the likely heterogeneity of CFS/ME …… (See these four papers: Vollmer-Conna U, Aslakson E, White PD. An empirical delineation of the heterogeneity of chronic unexplained fatigue. Pharmacogenomics 2006;7(3):355-364. Aslakson E, Vollmer-Conna U, White PD. The validity of an empirical delineation of heterogeneity in chronic unexplained fatigue. Pharmacogenomics 2006;7(3):365-373. Carmel L, Efroni S, White PD, Aslakson E, Vollmer-Conna U, Rajeevan MS. Gene expression profile of empirically delineated classes of unexplained	

						chronic fatigue. Pharmacogenomics 2006;7(3):375-386. Smith AK, White PD, Aslakson E, Vollmer-Conna U, Rajeevan MS. Polymorphisms in genes regulating HPA axis associated with empirically delineated classes of unexplained chronic fatigue. Pharmacogenomics 2006;7(3):387-394.), …. which you briefly mention at the beginning, then a more optimistic note seems appropriate, since we believe it more likely that some patients do recover with both CBT and GET. The Deale and Knoop studies merely reflect our clinical experience. This is important information to share with patients and their carers, since the influence of expectation on treatment outcome is well established within medicine as a whole.	
SH	St Bartholomew's Hospital Chronic Fatigue Services	83	FULL	210, 229	6.4.5.4	A low level of thyroid hormone by definition excludes a diagnosis of CFS/ME, so long as it is supported by a high TSH level (the exception being with pituitary disease). It needs investigation as the cause - primary or secondary and if appropriate referral to an endocrinologist. We suggest you add “abnormally” or “pathologically” before the phrase “low thyroxine levels” to avoid misunderstandings, and also explicitly state that the diagnosis of CFS/ME is thus excluded and hypothyroidism is being treated. We agree with the comments in cases of normal thyroid function.	The original question was framed in a misleading way. The GDG agree that both hyperthyroidism and hypothyroidism need to be excluded before a diagnosis of CFS/ME can be made.
SH	St Bartholomew'	84	FULL	229	6.4.5.2	We are not aware of any reliable and replicated evidence to support the	Noted but this was a significant patient concern. The

	s Hospital Chronic Fatigue Services					statement that patients with CFS/ME are more intolerant or have more severe adverse effects; and "more intolerant" than whom? We do not agree that drug treatment should be initiated at *lower dose* than in usual clinical practice. This possible myth is repeated within the guideline at various points, and is important since it may make doctors more likely to prescribe sub-therapeutic doses. If you are going to keep this included, you should make sure that the anecdotal level of evidence for this is explicitly stated. We would suggest changing to "..drug treatment at lower doses *may* be considered…."	recommendation has also been revised.
SH	St Bartholomew's Hospital Chronic Fatigue Services	85	FULL	229	6.4.5.5	"..gut anti-spasmodics.." are not treatments of CFS/ME since bowel symptoms are not part of CFS/ME. You should make it explicit that this treatment might be indicated for the treatment of IBS, if present comorbidly. Alternatively, and perhaps more wisely, you could suggest that IBS, if present, should be treated in the light of the best available evidence, and refer readers to appropriate guidance, which may or may not include considering antispasmodics as the treatment of choice for "bloating", although we would doubt it. You do mention IBS on page 233, line 12.	We have revised this recommendation and referred to the NICE IBS guideline – currently in development.
SH	St Bartholomew's Hospital Chronic Fatigue Services	86	FULL	229	6.4.5.6	We are not aware of any evidence to support the use of potent *anti-spasmodics*, benzodiazepines and baclofen in patients with CFS/ME. They are not indicated for muscle pain, cramps or twitching but are used for	This recommendation has been removed.

						severe muscle spasms, or in the case of baclofen, centrally mediated spasticity. Baclofen is sedating and reduces muscle tone which may impair musculoskeletal rehabilitation. Benzodiazepines have the potential for tolerance and dependence, reduce the proportion of healing slow wave sleep, and can cause sedation and motor dysfunction.	
SH	St Bartholomew's Hospital Chronic Fatigue Services	87	FULL	233	1	The GDG noted the survey support of the use of gabapentin in CFS/ME. However this drug is licensed for *neuropathic pain*. There is no evidence that patients with CFS/ME have a neuropathy and we would not recommend the use of this drug, particularly as one of its significant side effects is sedation, without empirical evidence for its support, which is currently lacking. It would be surprising if NICE gave guidance based on anecdotal evidence, an inaccurate indication, for a drug, which has significant adverse effects.	Noted and we have recommended that people should be referred for specialist pain management if appropriate.
SH	St Bartholomew's Hospital Chronic Fatigue Services	88	FULL	248	6.5.5.2	“Adults or children who experience severe weight loss should be referred to a dietitian for assessment, advice and nutritional support, which in extreme cases may include tube feeding.” This is alarming and arguably negligent advice, which we strongly condemn. Any patient who experiences severe weight loss should be referred for appropriate assessment, not by a dietician alone, but by an appropriate specialist doctor (gastro-enterologist or psychiatrist) so a diagnosis can be	This recommendation has been removed.

						made. We do not know of any reliable or replicated evidence that severe weight loss, in deed any weight loss at all, is a part of CFS/ME. Whereas we are aware of patients referred to our service with a diagnostic label of CFS/ME who on assessment have an alternative diagnosis, most commonly anorexia nervosa (sometimes presenting atypically without a body image disorder, which is well described in the anorexia nervosa literature), but, on occasion, malabsorption.	
SH	St Bartholomew's Hospital Chronic Fatigue Services	89	FULL	255	6.7.1.3–5	Why only re-investigation? We suggest the diagnosis should be reconsidered in such a patient, whether child or adult, by retaking the history, and re-examination (most importantly including the mental state examination), as well as laboratory investigations.	We have recommended the need for healthcare professionals to reconsider a diagnosis at key stages in the care pathway.
SH	Stockport PCT	17	FULL	137	14	Commend the appointment of one clinician as Care Manager.	Thank you – this has been noted.
SH	Stockport PCT	18	FULL	139	2–6	Re GET refers to mutually negotiated meaningful goal setting and on line 1 “self managed”. Some patients may see this as an opt out and maintain limiting goals.	Noted and revised.
SH	Stockport PCT	19	FULL	141	26 – 28	Use of word set back is possibly anxiety provoking. Some patients are terrified of being made worse. Could there be very explicit explanation of what constitutes setback versus deterioration.	This section has been revised.
SH	Stockport PCT	20	FULL	183	6.3.6.8	With reference to provision of aids and equipment. How is this provision going to be achieved – as a matter of right or on prescription?	The intent of his recommendation is to enable access to equipment and adaptations if appropriate.
SH	Stockport PCT	21	FULL	190	6.3.6.19	Appropriately trained professional needs to be defined.	Defining standards is outside the scope of NICE clinical guidelines,

							and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	Stockport PCT	23	FULL	202	6.3.6.39	With reference to provision of CBT GET ‘appropriately trained professionals’, it would be helpful to have more explicit comments on level of training and / or professional background and experience.	Defining standards is outside the scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	Stockport PCT	24	FULL	209	1 – 2	All treatments are offered allowing the patient to refuse without jeopardising therapeutic relationship – what happens when all options are refused by the patient and their position is maintained?	In any situation and with any condition, patients may refuse treatment. People with CFS/ME are no exception.
SH	Stockport PCT	25	FULL	229	6.4.5.2	Drug treatment should be started at lower dose – what is the position if therapeutic dose is not tolerated by patient should the drug be continued?	We have revised this recommendation. But doctors should be aware of usual clinical practice when drugs are not tolerated at any dose.
SH	Stockport PCT	26	FULL	255	6.7.1.2	Refer to specialised care could be seen as inflammatory in view of current financial controls.	The guideline is setting standards for care. How care is delivered should be reviewed locally The issues you raise are implementation issues and we will bring these to the attention of the implementation team.
SH	SWAME (South West Alliance for ME)	5	FULL NICE NICE	202 203 20/21 20 21	15–18 1–4 1.3.1.12 bullet 3 1.3.1.13 bullet 4 1.3.1.13 bullet 7	CBT There is inconsistency between the description of CBT in the NICE p20/21 and the very helpful defining paragraph in the FULL, p202, lines 15-18 and page 203 lines 1-4. This paragraph from the FULL must be included prominently in the NICE, otherwise the NICE risks misinterpretation. The FULL on pages 202/3 makes clear that CBT is not directed at illness beliefs or the	We have made consistent the definition and the description used in the guidelines (NICE and FULL). Some of the terms used are accepted CBT terminology and have specific meaning. In addition this recommendation has been revised.

						underlying disease process and is not regarded as curative. We must assume from this paragraph that the GDG therefore take this view that is more clearly expressed still in the Canadian Guidelines Overview page 10, when defining "Self Help Strategies". This document is available at http://www.mefmaction.net/Portals/0/docs//Canadian_ME_Overview_A4.pdf and sufficient hard copies for each member of the GDG and of the Guidance Review Panel are available from us (see above). Pages 20/21 of the NICE however within several aspects of the description, as well as in the overall tone of the document, suggest otherwise. To give but a few examples, a) "the CBT model for CFS/ME" is widely accepted to be about challenging maladaptive illness beliefs. b) Psychiatrists in earlier times put forward "fear of activity" and "perfectionism" within the ill-conceived hypothesis that CFS/ME were 'all in the mind'. Research has since shown these not to be factors, yet they continue to be mentioned and, in the process, offend patients. c) In the same vein follow "somatic attributions, symptom over-vigilance and/or checking behaviours". Another example of this is in the use of language such as the very obvious replacement of the accepted term "relapse" with the term "setback". This suggests an underlying assumption on the part of GDG that it is about use of	Re setbacks, the GDG considered the term setback/relapse to be appropriate.

						language and the way people think – if you give a more positive name to something nasty it won't be so bad. This philosophy denies patients recognition and understanding of the severity that can be experienced in a "relapse". Patients still get over relapses without it being necessary to call them "setbacks". It is very clear from the many reactions of people who have read the NICE draft that the use of CBT is being misinterpreted. It therefore must be revised and a clear definition such as in the FULL p202/3 included, or better still become as specific as with the SHS of the Canadian Overview document.	
SH	SWAME (South West Alliance for ME)	9	FULL NICE	234 33	10–19 1.3.6.3	Supplements There is inconsistency between the clinical evidence summary in the FULL and the statement in the NICE, "There is no evidence for the use of supplements …". Whereas the FULL details that there is some evidence for Essential Fatty Acids and Magnesium. It is also known that there has been a further small study with EFAs at Hammersmith Hospital and a much larger study is about to start there. The statement in the NICE is misleading and potentially prevents many patients deriving benefit from certain supplements. It also makes no mention of the common sense advice that prevails in much of the CFS/ME literature to take a good quality multi-vitamin/mineral supplement. Another failing of the strictly evidence-based approach.	Please see the evidence review where these studies are reported in detail. The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful.

SH	SWAME (South West Alliance for ME)	11	FULL NICE	245 32	n/a 1.3.5.3	Diet Another example of ignoring the consensus of the wider group. The wider group agreed that a clinically supervised exclusion diet followed by food challenges is appropriate where there are bowel symptoms, however the NICE is worded such as to discourage this and takes no account of the practical experiences of large numbers of people with CFS/ME who indeed experience benefit from excluding certain foods. It would also be helpful to have references to glycaemic indexes for those sub-groups who experience bouts of low blood sugar.	We have recommended the use of such diets where there are bowel symptoms, and that this should be done under the supervision of a dietitian. We have noted the need for dietetic guidance if needed. However, it is not possible to cover all relevant information here.
SH	The Association for Family Therapy	6	FULL	138	21–22	It is important, when CBT is offered to children/adolescents, to also offer supportive interventions for parents/families e.g. psycho-education and systemic family therapy	This is a general point of good practice not specific to patients with CFS/ME.
SH	The Association for Family Therapy	7	FULL	181	6.3.6.3.	It may be important to involve parents/carers in the exploration of the child/adolescent's goals, in order to effectively co-ordinate ideas about change	Noted and carers should be involved as appropriate (see rec 1.1.1.4 in the draft NICE version).
SH	The Association for Family Therapy	8	FULL	202	6.3.6.38	It is important that CBT therapists be specifically trained to work with children and young people where appropriate	Noted and we have stated that 'Healthcare professionals who are responsible for the care of an adult or child with CFS/ME should have appropriate skills and expertise in the condition'. This would include age appropriate expertise.
SH	The British Psychological Society	43	FULL	138	26	The problem with this sentence is that it's not persuasive. The literature on CBT for CFS is quite clear. The CBT	Noted, but the evidence supports the effectiveness of CBT in improving both coping AND

						programmes being offered to most patients are based on the theory that the symptoms of CFS persist/are made worse because of psychological factors, not because of a medical disorder. Patients know this, from their doctors, from their magazines and from the internet. The claim in the draft will just add to the widely-held belief that doctors see the illness as psychological but are trying to hoodwink them. The discussion of CBT in this document supports the notion that the illness is being approached from a purely psycho-social perspective. Advice is given to challenge somatic attributions. This is seemingly being advocated for all patients, rather than a subgroup (e.g. those with a clear history of stress and colds, who attribute their whole illness to a virus). There is also an emphasis on increasing activity levels, obviously based on the assumption of mass deconditioning, despite evidence from several sources that deconditioning does not explain the range and severity of symptoms (e.g. Bazelmans et al 2001, Song and Jason 2005). Patients ask how CBT and GET will normalise the apoptosis and signs of immune activation, and how it will cure their intolerance to alcohol but the literature on CBT has nothing to offer. CBT for CFS just does not recognise any aspect of this syndrome which cannot be explained in terms of faulty beliefs and inactivity. It's something we need to acknowledge and address.	functioning in some patients. However, it is not clear from the evidence which subgroups will benefit most from the different interventions. Therefore the GDG considered that the needs and preferences of patients are paramount and should be taken into account when making shared decisions on the appropriate management plan.
SH	The British	44	FULL	138	27	The suggestion that CBT is used with	Noted and clarified.

	Psychological Society					cardiac and cancer patients is a little misleading. It is not used to treat the underlying disease. Psychologists cannot treat the pathophysiological aspects of cancer etc and make no claims in this regard. CBT is used to help some patients cope more effectively with their illness. The patients in cardiac and oncology departments who are referred for CBT will not have responded to interventions such as counselling, or may have specific and severe psychological problems which may be alleviated using CBT. It is a psychiatric intervention used to deal with (or prevent) psycho-social complications of diseases like cancer. Well-informed patients know this and the sentence as it stands will lead to distrust and may undermine the authority of this document. We suggest that CBT is described as one technique aimed at helping patients to cope more effectively with their illness.	
SH	The British Psychological Society	46	FULL	141	20	Section on management of setbacks is instructive rather than discursive or indicating good practice. Either needs to be placed in context, e.g. “After good clinical assessment of reasons for setbacks and the impact they have, a therapist could recommend various personalised setback management strategies, aimed at varying degrees of setback, such as . . .”	Noted and revised.
SH	The British Psychological Society	47	FULL	145	6.3.2.1	The evidence shows that CBT helps to reduce fatigue, emotional distress and those are the only symptoms which have been assessed in the UK and Dutch trials. This sentence goes well	These are evidence statements agreed by the GDG, based on the evidence reviewed. Ridsdale 2001 included participants

						beyond the evidence. As for effectiveness, it depends on how you define that. If 'effective' means that patients are no longer ill, one cannot substantiate the claim. Often, MOS-SF scores remain below normal (e.g. Prins et al 2001, Stulemeijer et al 2005). Fatigue improves, patients feel 'better' or 'much better' and a minority are well enough to return to work. Some of the benefits appear to be transient. It's worth noting the research by Akagi et al 2001 and Quarmby et al 2006. Moreover, Sharpe revealed at a conference that 4 and a half years after the 1996 trial (cited in the review), "virtually all the group differences between the CBT group and the non-CBT group had faded" (AACFS Conference, Boston, October 10-11, 1998). The results of Deale et al may not reflect the experience elsewhere. Missing from the list is a statement recognising that CBT is no more effective than counselling (Ridsdale et al 2001, cited p 152, line 14). In the original CRD review, this study received a validity score of 18. The other study comparing the two interventions (Chalder et al 2003) also supports the use of counselling. Why is there no reference to counselling as a helpful and cost effective alternative to CBT?	with chronic fatigue, of whom 28% had CFS/ME (CDC 1994). No evidence on the use of counselling in CFS/ME was identified that met the agreed inclusion criteria.
SH	The British Psychological Society	48	FULL	181	6.3.6.4	Why are untested activity management strategies being recommended here? Yet pacing, for which there is some evidence, is not included. Also missing is counselling. Surely an oversight.	The evidence to support activity management can be found in Appendix 1. Pacing – details on pacing have been added to the full guideline.

							No evidence on the use of counselling in people with CFS/ME was identified.
SH	The British Psychological Society	49	FULL	183 and 202	6.3.6.9 6.3.6.38/39	CFS/ME is a complex and difficult condition to treat. In order to successfully treat CFS/ME, therapists need to have good familiarity with the condition as well as being skilled in the particular treatment approach they are using. We therefore agree with the recommendation that management programmes should not be delivered by practitioners with no experience of the condition.	Noted with thanks.
SH	The British Psychological Society	50	FULL	192	6.3.6.22	The strategy looks perfectly sensible, but there's no published evidence e.g. in the CRD review, which supports its inclusion in this draft at this time. It may be part of CBT programmes, but so is GET. So is emotional support, the helpful advice etc. This is important. Patients writing in their magazines have referred to the advice on dealing with specific symptoms as useful but at the same time, have noted that the graded activity element was difficult or led to problems. This suggests that we need to be cautious and not make decisions based on assumptions or Generalisations. Psychologists have been evaluating a number of self-management interventions and similar programmes, yet these have been omitted (e.g. Barlow et al). The restriction of advice to cognitive-behavioural approaches may leave a significant subgroup without appropriate help and advice.	Details of the evidence supporting this approach can be found in Appendix 1. We have stressed the need throughout for an individualised approach to be taken.
SH	The British	51	FULL	Pg 202	6.3.6.38	"Suitably trained" is insufficient, as	Defining standards is outside the

	Psychological Society					there is significant misunderstanding of the requirements for suitable qualification in cognitive-behavioural therapy as opposed to cognitive-behavioural technique utilisation. Suggest that refer here to “suitable CBT qualification (e.g. meeting BABCP or BPS criteria).”	scope of NICE clinical guidelines, and it is anticipated that the relevant professional bodies will define appropriate levels of training and competencies.
SH	The British Psychological Society	52	FULL	204	4	The argument that adverse effects from GET can be attributed solely to unstructured or inflexible programmes is difficult to justify. Some reports have come from participants in the high scoring trials used to support the recommendations re GET and GA, e.g. Prins et al. Those comments are consistent with information provided by researchers at conferences. The recommendation to let the patient keep control comes close to advice on pacing. However, the trials on which the recommendation is based did not give patients significant control. Schedules were pre-determined and patients were encouraged to stick to the regimes and not to reduce activity levels, even if extremely fatigued. One of the few published trials to encourage an increase in activity levels but to avoid over-exertion is Wallman et al (2004). It’s a combination of GET and pacing, but listed under GET. In the appendix, the CRD recognised the element of pacing. This section is not a fair response to the criticisms from patients.	Noted, and we have revised the recommendations to address the issue of pacing and also the need to ensure that the patient control of the aims of the intervention is maintained. Also the need for individualised programmes based on the needs and preferences the of patient, with appropriate monitoring and review, is stressed throughout.
SH	The British Psychological Society	53	FULL	Ending pg 204	Section 6.3	There is a great deal of advertising, numerous web sites and advocating of a therapy termed “Reverse Therapy” or	We have recommended that only those interventions supported by evidence are used.

						“Mickel Reverse Therapy” which claims to have an increasing “evidence-base” for efficacy in treating CFS/ME and Fibromyalgia. Although there are many “Reverse Therapists” being trained, the approach has questionable methodology and spurious conclusions drawn from unscientific evidence. However, it is increasingly reported on CFS web sites (official and unofficial), and may need to be mentioned, and cautioned against, in this document.	
SH	The British Psychological Society	54	FULL	204	15	There is one paper supporting the envelope theory (Jason et al 1999). We agree, however, that this is inadequate and that the envelope theory should be rejected at this stage.	Noted.
SH	The British Psychological Society	55	FULL	204	22	Maintaining levels of activity does lead to a reduction in certain symptoms, including fatigue, somatic symptoms and anxiety (de Ridder et al 2004, Goudsmit 2006, Ray et al and others).	We have simply noted that this was a concern raised.
SH	The British Psychological Society	56	FULL	229	6.4.5.6	Diazepam may help vertigo linked to a disturbance in the vestibular nuclei (dose 2 mg b.d.). The latter comes from articles in neurology journals and a consultant neurologist. See also CNS Drugs 17(2):85-100, 2003.	This recommendation has been removed.
SH	The Chartered Society of Physiotherapy	9	FULL	139	2– 8	Do not agree that evidence base is strong enough for GET. This definition describes a combination of activity management, GET and Pacing therefore should not be labelled as GET	This describes GET as evaluated in the included trials.
SH	The Chartered Society of Physiotherapy	10	FULL	147	11–15	Are 5 reviews enough to describe a strong evidence base? Was the GET definition / criteria the same in all 5 studies?	Details of the study interventions can be found in Appendix 1.
SH	The	11	FULL	181	63, 63	GET is dangerous without activity	This section has been revised to

	Chartered Society of Physiotherapy					management first and without pacing included to take symptom management into account with any increased physical or mental activity	detail the setting of a baseline.
SH	The Chartered Society of Physiotherapy	12	FULL	188	636.14	Implies GET involves physical activity only no reference to mental activity. Does not take individual reactions into account enough	We have stressed throughout the need for appropriate monitoring and review.
SH	The Chartered Society of Physiotherapy	13	FULL	192	636.22	Activity management must be in place **BEFORE** commencing any form of GET	We are uncertain of the reason why you say this.
SH	The Chartered Society of Physiotherapy	14	FULL	202	3–6	Agree re lack of consistency but same mistake is made throughout this document. Must make definitions clearer or consider re-wording.	We have made revisions and clarifications throughout to address this and other comments.
SH	University of Manchester	5	FULL	183 and 202	6.3.6.9 6.3.6.38/39	CFS/ME is a complex and difficult condition to treat. In order to successfully treat CFS/ME, therapists need to have good familiarity with the condition as well as being skilled in the particular treatment approach they are using. We therefore agree with the recommendation that management programmes should not be delivered by practitioners with no experience of the condition. In particular, treatments involving graded exercise and graded activity programmes should be administered by competent, trained therapists, because poorly conducted programmes starting at too high a level or increasing too quickly can be ineffective or harmful.	Noted with thanks.
SH	Welsh Association	87	FULL	138	4– 13	What is the evidence base for CBT in CFS/ME? CBT has not been trialled on	The evidence reviewed supports the use of CBT in some patient groups

	of ME & CFS Support					all patient groups and in those it has they have been very small. CBT is therefore not an evidence based treatment for this condition.	(see review for details), but does not allow distinctions between subgroups. We have recommended that the needs and preferences of the individual should be taken into account.
SH	Welsh Association of ME & CFS Support	88	FULL	138	23 – 28	28 This statement is misleading because it implies that the same form of CBT is used in illnesses like diabetes and cancer, as is described here. CBT is not used as the first therapy of choice in those instances and is not based on the assumption that beliefs can be 'perpetuating factors' (p185).	Noted and revised.
SH	Welsh Association of ME & CFS Support	89	FULL	139	7	Replace the word ‘setbacks’ with relapses	The GDG have used the term they consider to be most appropriate.
SH	Welsh Association of ME & CFS Support	90	FULL	139	2– 8	GET is not an evidence based treatment as it has not been trialled on some patient groups.	We have noted which patient groups were included in the trials and reflected this in the recommendations. We also stressed the need for patient preference to be taken into account.
SH	Welsh Association of ME & CFS Support	91	FULL	139	15 – 18	What is the evidence base used to recommend GET for the severely affected? There have been no trials conducted with this patient group and therefore this is not evidence based.	Noted and revised.
SH	Welsh Association of ME & CFS Support	92	FULL	139	25 – 26	It should be noted here that some patients will not improve regardless of the intervention.	This is true of many interventions, not just GET.
SH	Welsh Association of ME & CFS Support	93	FULL	140	12 – 14	Children and the severely affected have not taken part in GET programmes therefore it cannot be said that GET is beneficial to most patients	Noted and revised.
SH	Welsh Association	94	FULL	140	17	Confusion with lines 13 – 15 above	Noted and revised.

	of ME & CFS Support						
SH	Welsh Association of ME & CFS Support	95	FULL	140	26	It is very unlikely that a severely affected patient nor a child on their own would attend a gym therefore these comments seem unrealistic	Noted and revised.
SH	Welsh Association of ME & CFS Support	96	FULL	141	2	Activity management as described in the glossary is similar to GET and therefore inapporopriate for the severely affected. Pacing is the recommended management tool of choice and this is different from Activity management	The recommendations have been revised to clarify the different interventions and when/how they should be used in the different patient groups.
SH	Welsh Association of ME & CFS Support	97	FULL	141	8	All treatments recommended seem to be goal orientated or Specific Measurable Attainable Realistic and Timed. This is not appropriate for all patients.	Noted and we have stressed the need to tailor programmes to the individual’s needs, preferences and ability.
SH	Welsh Association of ME & CFS Support	98	FULL	141	11 – 13	What is the evidence base used for activity management in the severe and moderate categories?	Please see the evidence review for details of the participants.
SH	Welsh Association of ME & CFS Support	99	FULL	141	19	What is the evidence for sleep hygiene in CFS/ME?	This was supported by GDG consensus, and although not supported by research evidence in people with CFS/ME, as with other symptom management strategies this is general advice which is an accepted intervention for sleep problems.
SH	Welsh Association of ME & CFS Support	100	FULL	141	22 – 25	What is the evidence base for relaxation in CFS/ME?	This was supported by GDG consensus, and although not supported by research evidence in people with CFS/ME, as with other symptom management strategies this is general advice which is an accepted intervention for problems with relaxation.
SH	Welsh	101	FULL	141	26	Use the word relapses as it is in	The GDG considered the term to be

	Association of ME & CFS Support					common use, is readily understood and better expresses the severity and length of decline in ability to function.	appropriate.
SH	Welsh Association of ME & CFS Support	102	FULL	142	7	Relapse is the preferred word and should be changed throughout this section. In the experience of many patients it is not always possible to determine what has caused a relapse, they can happen even when good management principles are in operation and no infection is obvious. What is the evidence to suggest that one type of stress (psychological or physical) requires a different management approach to another (viral)? A relapse is a relapse and patient experience suggests that it is wiser to err on the side of caution and reduce all types of activity until symptoms decrease and they can be carefully increased again.	The section on setbacks has been revised, and the GDG considered the term to be appropriate.
SH	Welsh Association of ME & CFS Support	103	FULL	142	9	missing word after sleep.	Cannot find this – sorry.
SH	Welsh Association of ME & CFS Support	104	FULL	142	9	What is the evidence that relapses due primarily to lack of sleep or low mood should require a continuance of activity? For many patients it is impossible to determine that there are not other factors involved as every day characterised by struggle	Noted, and the needs of the individuals should be paramount when agreeing appropriate intervention.
SH	Welsh Association of ME & CFS Support	105	FULL	142	21	Use the word relapses instead of setbacks	The GDG considered the term to be appropriate.
SH	Welsh Association of ME & CFS	106	FULL	142	25	Use the word relapses instead of setbacks	The GDG considered the term to be appropriate.

	Support						
SH	Welsh Association of ME & CFS Support	107	FULL	143	1– 2	In relapses it is advisable to rest.	This section has been revised.
SH	Welsh Association of ME & CFS Support	108	FULL	143	27 – 28	Patient experience suggests that it is vital to reduce all types of activity when severe relapses occur, in order not to delay improvement in function.	This section and the recommendations have been revised.
SH	Welsh Association of ME & CFS Support	109	FULL	144	19 – 23	This statement implies people with CFS/ME do not want to get better and is offensive.	It is not clear to which statement this refers.
SH	Welsh Association of ME & CFS Support	110	FULL	145		6.3.2.1. What is the evidence base to show that CBT is effective for all adults with CFS/ME?	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Welsh Association of ME & CFS Support	111	FULL	145		6.3.2.2. 145 What is the evidence base to show that CBT is effective for all children with CFS/ME?	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Welsh Association of ME & CFS Support	112	FULL	145		6.3.2.3. What is the evidence base to show that incremental physical exercise programmes are suitable for all adults with CFS/ME?	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Welsh Association of ME & CFS Support	113	FULL	145		6.3.2.4. What is the evidence base to show that incremental activity programmes are suitable for all adults with CFS/ME?	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Welsh Association of ME & CFS Support	114	FULL	145		6.3.2.5. This trial has not finished and therefore the results are not appropriate for these guidelines as they are not evidence based	These are evidence statements agreed by the GDG, based on the evidence reviewed.
SH	Welsh Association of ME & CFS Support	115	FULL	148	6	Standardisation of terminology	Noted and revised.
SH	Welsh Association	116	FULL	152	8	This shows that CBT is more expensive than counselling yet CBT is the first line	This study was in a population of chronic fatigue patients, and only a

	of ME & CFS Support					of treatment.	subsection was a CFS/ME population. The GDG agreed that no conclusions for the guideline population could be derived. This section has been revised to make this clearer.
SH	Welsh Association of ME & CFS Support	117	FULL	152	12	Standardisation of terminology	Noted and appropriate changes have been made.
SH	Welsh Association of ME & CFS Support	118	FULL	152	18 – 19	Confusion of terms and patient groups	Noted and appropriate changes have been made.
SH	Welsh Association of ME & CFS Support	119	FULL	152	22	Transfer benefits from one patient group to another is not helpful as benefits from treatment may not be the same.	Noted.
SH	Welsh Association of ME & CFS Support	120	FULL	155	3	Where is the evidence base to say that this type of CBT is beneficial to people with CFS/ME? It is not an evidence based treatment for all as it has not been trialled with some groups of patients, namely the severely affected.	Noted. The health economics sections review the available published health economic evidence and provide information on this evidence base.
SH	Welsh Association of ME & CFS Support	121	FULL	181		6.3.6.2. The acknowledgement that patients must be able to reject suggested treatment approaches is welcome, but the implication in this document that they would be rejecting the best chance for them to recover, is unsubstantiated due to the paucity of evidence.	Noted, but the evidence does support the use of specific interventions. And the needs and preferences of the individual should be taken into account.
SH	Welsh Association of ME & CFS Support	122	FULL	181		6.3.6.3. This statement suggests that adults and children with ME are poorly motivated and is huighly offensive The studies into CBT and GET themselves have many problems relating to the broad diagnostic criteria, the small samples, high drop out rates	Noted and revised. Details of the study limitations and strengths are reflected in the grading of the statements and the evidence review (Appendix 1). Patient concerns have been reflected in the recommendations.

						in some, and the lack of long term monitoring of subjects in some. Thus the applicability of the results to all sub-groups of patients and all categories of severity is highly suspect. Patient surveys show that many have not benefited and some have been made more ill by these approaches. While this doesn't qualify in NICE's terms as 'evidence', the NHS belief in 'expert patients' (some of whom are health practitioners) should at least encourage NICE to view these experiences as 'red flags', which point to limited efficacy and potential side effects. This should be made clear in the recommendations and practitioners should be encouraged to be honest with patients. To say that people's problems in the past with CBT and GET are due to inflexible programmes and untrained practitioners and that patient participation and control will solve the problem (204:1-8), is oversimplifying the matter and doesn't take into account the fact that the basic goals of CBT and GET remain the same i.e. to keep increasing activity / exercise.	
SH	Welsh Association of ME & CFS Support	123	FULL	181		6.3.6.5. Although the major characteristic of the fatigue in CFS/ME has been given as 'post exertional', (5.2.8) there appears to be no willingness, in the description of CBT and GET, to recognise the potentially serious effects that increasing exercise/activity levels can have. Instead the major belief seems to be that activity / exercise is good and must be gradually increased and that a	We have noted throughout the need to consider individual's needs, preferences, and abilities. We have also revised the recommendations on the stage of illness. Any interventions should only be initiated after a full discussion of the benefits and risks.

						significant amount of rest or relaxation leads to muscle deconditioning, although there is no 'evidence' to support this in CFS/ME. There is no acknowledgement that different management approaches could be needed during the different illness phases (early acute onset, severe relapse etc) or that there is no 'evidence' for their belief that activity should continue during relapse and daytime rests should be avoided. These principles have been adopted from sleep management techniques used with otherwise normal/healthy people. There is also no acknowledgement of the potential of on-going dysfunction in patients' bodies which researchers are constantly finding clues to,or that this could affect patients' ability to keep increasing their activity levels. The emphasis is on constant improvement and rehabilitation (the dictionary definition of which is to 'make fit' or 'bring back into good condition'). However these statements do not acknowledge that the CDC reports that many improve but most do not recover ( ). The GDG also feels that 'CBT or other behavioural treatments are not curative but aim to achieve improvements within the patients abilities'. 202(15-17) The fact that there will be a limit to the improvement that many patients can reach must be acknowledged clearly in the recommendations (not just in the commentary) and both practitioners and	

						patients need to be made aware of this. Not to do so would be to mislead. Accepting limits should not be a deterrent to devising a management plan in order to maximise functioning, but patients will need to accept the reality that at some point they might have to learn to live within their limits and acknowledge the likelihood of ongoing dysfunction in the body, until medical science uncovers more answers.	
SH	Welsh Association of ME & CFS Support	124	FULL	183		6.3.6.9. Things have gone wrong when management plans have been negotiated with and supervised by experienced practititioners. There seems little safeguard for this not happening again.	We have noted the need for continued review and monitoring, and the need for the impact of intervention and symptoms to be recognised.
SH	Welsh Association of ME & CFS Support	125	FULL	183		6.3.6.10 The wording here could be taken as a denigration of these management approaches that patients have found helpful. There is no 'evidence' that they are not helpful but the wording sounds like a warning to health practitioners to avoid them, where other approaches that are also not backed by 'evidence' are recommended (e.g. group CBT, continuing activity during relapses) We suggest alternative wording eg The following strategies practised by patients have yet to be the subject of research.	That is not the intention and no value judgment is explicit in the recommendation.
SH	Welsh Association of ME & CFS Support	126	FULL	184		6.3.6.10 The theories being tested are not the same as the theory being practised by people with CFS/ME	The view of the GDG was that this was a strategy that was sometimes used.
SH	Welsh Association	127	FULL	184		6.3.6.10 There is no evidence to say the opposite either	We have simply noted that there is no evidence, without any value

	of ME & CFS Support						judgement.
SH	Welsh Association of ME & CFS Support	128	FULL	184		6.3.6.10 Use the word relapse instead of setback.	Setback is the agreed term in this guideline.
SH	Welsh Association of ME & CFS Support	129	FULL	185		6.3.6.11 It should be mentioned that the evidence for the effectiveness of Group CBT was not proven.	Noted and revised.
SH	Welsh Association of ME & CFS Support	130	FULL	185		6.3.6.12 This is not as the model of CBT described in the glossary.	The terminology has been clarified.
SH	Welsh Association of ME & CFS Support	131	FULL	185		6.3.6.13 This is goal setting and in theory is GET and CBT	The GDG is aware that there is an overlap amongst approaches.
SH	Welsh Association of ME & CFS Support	132	FULL	186		6.3.6.13 This indicates that the patient is to blame and is holding back their own recovery.	These are accepted components of any CBT programme.
SH	Welsh Association of ME & CFS Support	133	FULL	186		Depression is normally a secondary condition to ME. NICE appear to be trying to address Gulf War Syndrome amongst these guidelines	We have recognised that depression is a common comorbid condition in people with CFS/ME. We have not made recommendations for people with Gulf War Syndrome.
SH	Welsh Association of ME & CFS Support	134	FULL	188		6.3.6.14 The potential here is that people who are mild/moderate sufferers become severe sufferers by following these programmes.	We have stressed throughout the need for appropriate monitoring and review.
SH	Welsh Association of ME & CFS Support	135	FULL	188		6.3.6.16 This document claims that there is no evidence for the effectiveness of GET in severe CFS/ME so the suggested application to severe patients in this section is unwarranted and ill-advised	We have recommended only that elements of GET may be appropriate for some people with severe CFS/ME, and only after a full discussion of the potential benefits and risks.
SH	Welsh	136	FULL	190		6.3.6.19 number Setting goals can be	The guideline stresses realistic

	Association of ME & CFS Support					unrealistic and can result in relapses which people never come out of or they take years to recover from.	goals and slow progress.
SH	Welsh Association of ME & CFS Support	137	FULL	191		6.3.6.19 This whole section is unrealistic and potentially harmful to people with CFS/ME	This has been substantially revised.
SH	Welsh Association of ME & CFS Support	138	FULL	195		6.3.6.24 Where is the evidence that resting during an increase of symptoms is bad? Patient experience does not support this and practitioners need to be aware of the possibility of legal action if such a prescription is pursued	Noted and revised to say 'slight' increase. There are the general risks and deleterious effects of bedrest such as DVT, chest infections, muscle wastage, etc.
SH	Welsh Association of ME & CFS Support	139	FULL	196		6.3.6.29 There is no evidence that excessive sleep and naps don't help CFS/ME? In the ill phases of the illness patients have little option but to sleep and there is a danger that they are made to feel guilty because they feel so ill and exhausted	This has been revised based on stakeholder comments.
SH	Welsh Association of ME & CFS Support	140	FULL	198		6.3.6.32 The implication that sleep management strategies will automatically lead to improvement in sleep unless there is a more serious sleep disorder is unfounded. Other disorders can be investigated if the patient can cope, but patient experience indicates that dysfunctional sleep is a symptom of CFS/ME and can persist for years before it alters or improves.	Noted and we have recognised the impact of this on people with CFS/ME.
SH	Welsh Association of ME & CFS Support	141	FULL	198		6.3.6.5 The term setback is inadequate to describe the experience of worsening of symptoms that patients call relapse.	This is the term considered appropriate by the GDG.
SH	Welsh Association of ME & CFS Support	142	FULL	199		6.3.6.36 there is a need to acknowledge that the cause of a relapse is not always possible to determine and that there are many	This section has been revised based on stakeholder comments.

						other possible causes. The lack of evidence to support the theory that usual activity levels should be maintained during any kind of relapse or setback should be noted.	
SH	Welsh Association of ME & CFS Support	143	FULL	200		6.3.6.37 The danger of not reducing activity during severe relapses or setbacks should be acknowledged	Noted and revised.
SH	Welsh Association of ME & CFS Support	144	FULL	202		Where are all these practitioners going to come from!?	We have passed these concerns on to the NICE implementation team.
SH	Welsh Association of ME & CFS Support	145	FULL	202		Where are these therapists going to come from and who is going to pay for them!?	We have passed these concerns on to the NICE implementation team.
SH	Welsh Association of ME & CFS Support	146	FULL	202	14	So now any old person can give CBT	We have recommended that the healthcare professional delivering any intervention should be appropriately trained.
SH	Welsh Association of ME & CFS Support	147	FULL	202	15 – 17	These statements are at odds with the recommendations given earlier	This has been clarified in the recommendation.
SH	Welsh Association of ME & CFS Support	148	FULL	203	4	Not what you say earlier when you talk about rehabilitation and return to normal	Not clear to what this refers.
SH	Welsh Association of ME & CFS Support	149	FULL	203	20	Are you sure on this? You say earlier about using the mental capacity bill coming in in 2008	This is made clear in the introduction to the NICE guideline.
SH	Welsh Association of ME & CFS Support	150	FULL	203	22	How good of you to blame faulty illness beliefs then	Not clear to what this refers.
SH	Welsh Association	151	FULL	203	26	Is this appropriate across the board without proper investigation of the	This section discusses the results of the questionnaire.

	of ME & CFS Support					underlying cause of the illness.	
SH	Welsh Association of ME & CFS Support	152	FULL	204	3– 6	To say that people's problems in the past with CBT and GET are due to inflexible programmes and untrained practitioners and that patient participation and control will solve the problem, is oversimplifying the matter and doesn't take into account the fact that the basic goals of CBT and GET remain the same i.e. to keep increasing activity / exercise	The recommendations give explicit guidance on the programme content, application and the need for delivery by appropriately trained healthcare professionals.
SH	Welsh Association of ME & CFS Support	153	FULL	204	1– 8	The benefits have not outweighed the harmful effects for many individuals and bearing in mind the cognitive difficulties and low energy levels that many patients have, it is naive to assume that they will always be able to make objective judgements and argue the toss with the 'expert' who wishes them to continue increasing activity levels. Information about the potential dangers of overdoing activity and exercise should be made clear from the start.	We have recommended that the benefits and risks of any intervention should be discussed before its initiation.
SH	Welsh Association of ME & CFS Support	154	FULL	204	10	So NICE are saying GET is appropriate for all.	Please see the revised recommendations.
SH	Welsh Association of ME & CFS Support	155	FULL	204	14	Elements of, which elements?	Please see the revised recommendations.
SH	Welsh Association of ME & CFS Support	156	FULL	204	17	Not the same theory	Revised.
SH	Welsh Association of ME & CFS	157	FULL	204	21 – 23	There was however concern that consistently maintaining activity levels at lower than capacity would not lead to	Not clear what is intended by this comment.

	Support					an improvement symptoms and/or level of functioning.	
SH	Welsh Association of ME & CFS Support	158	FULL	205		6.4 The section on pharmacological interventions is totally inadequate. Many people rely on these for symptom relief and the ability to function	The guideline does not address the management of individual symptoms. Please refer to the scope and methodology chapter. The evidence search was confined to that directly related to CFS/ME. Within the time and the NICE methodology it would be impossible to address symptom management.
SH	Welsh Association of ME & CFS Support	159	FULL	229		6.4.5.2. The General principle that patients may be more sensitive to drugs is helpful but doesn't go far enough. The paucity of trials that fit the NICE requirements is given for the lack of recommendations, but this is no excuse for not giving any information about the range of treatments that are being used and/or trialled. How can doctors be made aware of what is happening if the main guidelines don't include this information?	We have revised this recommendation. Healthcare professionals should be aware of new developments and it is not possible to list all these in the guidelines.
SH	Welsh Association of ME & CFS Support	160	FULL	234		6.5.1.1. This section should include a list of supplements which are being used by patients, for information.	This is guidance for NHS practice. The GDG found insufficient evidence to recommend nutritional supplements routinely. It is acknowledged, however, that some individuals may find them helpful.
SH	Welsh Association of ME & CFS Support	161	FULL	248		6.5.5 These guidelines are inadequate - referring to another document is not helpful to practitioners. There is no mention of the dietary approaches patients are currently trying out. or the role that food allergies or intolerances might play.	This recommendation has been removed. We stress the need for expert dietician input if appropriate, including in the use of exclusion diets.
SH	Welsh Association of ME & CFS	162	FULL	253		6.6.5 These guidelines are inadequate. A detailed list of the therapies used by patients should be	This is guidance for NHS practice. The GDG found insufficient evidence to recommend that

	Support					listed with any potential dangers or promising indications. Why are complementary therapies not recommended? Is there evidence to back their unsuitability If no trials have been done, then that should be stated and leave it at that.	complementary therapies should be routinely available. It is acknowledged, however, that some individuals may find them helpful.
SH	Welsh Association of ME & CFS Support	163	FULL	255		With no services who is going to do this?	The guideline is setting standards for care. Local teams will review their services to deliver the care defined as part of implementation. People with CFS/ME may also want to refer to 'Understanding NICE Guidance' in their consultations with healthcare professionals. The issues you raise are implementation issues and we will bring these to the attention of the implementation team.
SH	Welsh Association of ME & CFS Support	164	FULL	255		If no specialists, who?	The guideline is setting standards for care. Local teams will review their services to deliver the care defined as part of implementation. People with CFS/ME may also want to refer to 'Understanding NICE Guidance' in their consultations with healthcare professionals. The issues you raise are implementation issues and we will bring these to the attention of the implementation team.
SH	Welsh Association of ME & CFS Support	165	FULL	256	3	The Welsh equivalent needs to be placed here.	Noted and revised.
SH	West Midlands Consortium	75	FULL	229	6.4.5.4.	Some research should be done on the thyroid function. Levels of T3 andT4 and thyroid stimulating hormone should	We have noted that thyroxine is not appropriate for the treatment of CFS/ME but is obviously useful if

						be measured at times in all patients and the readings scrutinized to see if many are at the bottom end of the normal range. (There is also evidence to suggest that there may also be some 'peripheral resistance' to thyroid hormone in CFS/ME patients.) Also it would be useful to compare readings when very ill with reading taken if symptoms improve. Likewise with B12.	there are thyroid function problems.
SH	West Midlands Consortium	76	FULL	235	13 -17	There is enormous concern amongst patients about who is doing the training and what exactly they are being taught.	In accordance with the methodology for clinical scenarios, the assumptions that form the basis for answering the questions must be explicit so that respondents have a common understanding of the factors that influence the appropriateness of treatment. These statements were agreed as assumptions for the questionnaire. They are not guideline recommendations. A fuller explanation is now in the methodology chapter.
SH	West Midlands Consortium	77	FULL	257	1–6	How can the severely affected possibly receive the same care? Invariably they cannot access the 'services'!	This recommendation was intended to make clear that services should be made available in the homes of people who are severely affected if they could not travel. It has been revised to make this clearer.