A Review of BMJ Best Practice Document on Chronic Fatigue Syndrome by Professor James Baraniuk

Malcolm Hooper **24th June 2018**

NOTE: *I was asked by the BMJ Section Editor (BMJ Best Practice and BMJ Learning) to provide a peer review of Professor James Baraniuk's document on "CFS", to which I agreed. My comments below relate to the version sent to me. In my opinion, it indicated how dangerous the medical education programme about ME/CFS is in the UK. This was borne out by my face-to-face discussion with Professor Baraniuk himself on 1st June 2018 in London: he confirmed to me that his original report had already been sent by the BMJ to other referees and that he had received 156 comments which he was instructed had to be incorporated in his report. It was plainly obvious that those comments had been included in the version sent to me. Professor Baraniuk assured me that I should go ahead and respond as I wished, so it seems he knew his report was not as he intended it to be. In telephone discussions with the BMJ Section Editor, it was stressed to me that the BMJ had to have (quote) "equality".*

Current BMJ Best Practice for CFS/ME (October 2018):
https://bestpractice.bmj.com/topics/en-gb/277/

My Review

My response to reading this long document of 102 pages is such that I am unable to carry out the review by simple annotations or minor additions to it.

I am grateful for the invitation to respond by means of a single document that sets out my major concerns which I hope the editor(s) will find helpful.

1. Introduction

The document is far too long if it is intended to be a BMJ Best Practice reference tool help GPs and others to **quickly diagnose and support** their patients presenting with ME/CFS.

As it stands, it is not fit for purpose. The document is badly presented: it needs to be clear and factually accurate.

It lacks focus and any critical awareness of the issues under consideration.

It shows little understanding of the latest research, or the social and political considerations (eg. access to social security payments) that patients and informed clinicians feel so strongly about.

The confusion and complexity of the Best Practice document is far from satisfactory and in need of a thorough overhaul.

It is a wasted opportunity to clarify a situation that has evaded medical education for the last three decades.

2. **The Title**

The report is entitled "Chronic Fatigue Syndrome" but throughout the text the term "CFS/ME" is used, yet the name myalgic encephalomyelitis does not even feature in the title.

Myalgic Encephalomyelitis (ME) has been classified as a neurological disorder by the World Health Organisation (WHO) in its International Classification of Diseases (ICD) since 1969, but there is no mention of this anywhere in the document.

Throughout the document there is confusion about terminology (ME, CFS/ME, fatigue) but it is essential to be aware that the terms are not clinically interchangeable.

On pages 11, 19, 22, 23, 28, 30, 51 and 102, Baraniuk refers to "CSF/ME", which appear to be typographical errors, since cerebrospinal fluid (CSF) is not being discussed.

3. **Historical perspective**

The term myalgic encephalomyelitis was coined in 1955 (Lancet 1955:394-395) and in 1969 it was formally classified by the WHO as a neurological disorder; it was accepted by The Royal Society of Medicine as a distinct disease in 1978; in 1987 the term "chronic fatigue syndrome" was introduced at a meeting of CDC scientists for political, not medical reasons, at which it was decided to change the name from ME to CFS and "CFS" appeared in publications from 1988 onwards.

In 1992 the term "CFS" was included in ICD-10 as a synonym for ME (referable only to ME at G93.3), but in the UK, a group of psychiatrists intended to eradicate the neurological disease ME and introduced the term "CFS/ME" (in that order, as distinct from "ME/CFS") with their stated intention of dropping "ME" from "CFS/ME" when expedient and then reclassifying "CFS" as a behavioural disorder (BMJ 2003:326:595-597).

In the UK, recruitment for the PACE Trial began in 2004 and the Patient Clinic Leaflet stated: "*Chronic fatigue syndrome"* is *"also known as postviral fatigue syndrome, myalgic encephalomyelitis (ME) or myalgic encephalomyelopathy….Medical authorities are not certain that CFS is exactly the same illness as ME but until scientific evidence shows that they are different they have decided to treat CFS and ME as if they are one illness".*

To complicate things even further, despite his having received ethical approval and funding to include ME in the clinical trial, following publication in 2011 of selective PACE

Trial results in The Lancet, the Chief Principal investigator, psychiatrist Professor Peter White, wrote to Richard Horton, editor-in chief of The Lancet, denying outright that the PACE Trial had been studying patients with ME: *"The PACE trial paper refers to chronic fatigue syndrome (CFS) which is operationally defined; it does not purport to be studying CFS/ME*".

CFS came to be applied to many different things and considerably broaden the meaning of CFS/ME making it virtually meaningless. Hence, it allowed consideration of other chronic infections, EBV and other herpes viruses, lyme, chlamydia, rickettsia, some vaccines, eg Hep B and latterly HPV and other intracellular organisms eg brucellosis, chemical and environmental toxins, organophosphates, Gulf War Syndrome, Aerotoxic Syndrome, some metals etc. This is 'confusion worse confounded.'

Clinically, ME is a separate disorder from what is now termed CFS or "CFS/ME": ME is a recognisable post-enteroviral disease with specific features; it may also follow vaccinations (for which significant evidence already exists and more evidence is emerging). However, there are a number of states of chronic fatigue which now fall under the "CFS/ME" umbrella and the resultant confusion is responsible for the heterogeneity of the patient population and hence the diverse research findings.

Unless the report author provides the contextual background, he affords a disservice not only to the physicians he is endeavouring to educate but – more importantly -- to those patients who depend on those clinicians.

4. <u>The way forwards</u>

The term "CFS/ME" now has come to mean a behavioural disorder and this report repeatedly portrays CFS as deconditioning which can be effectively treated by cognitive behavioural therapy (CBT) and graded exercise therapy (GET), but there is no evidence whatsoever of deconditioning in patients with ME/CFS. If this whole document is not based on ME/CFS as a neurological/neuroimmune disorder, then it is falsely grounded.

The report does mention biomedical research, but it appears to look on it sceptically, and the take-home message is clear: *"Patients should be educated on how secondary physical deconditioning can emerge due to increased resting and activity restriction"* (page 76). This is misleading and it perpetuates the widely-disproven psychosocial dogma that "CFS/ME" is a mental disorder.

It is essential to gain the immediate attention of the reader seeking up-to-date information, so it would be better to start off with a high impact paragraph such as:

> "Studies suggest that there is a risk of earlier mortality in ME/CFS and UK Coroners have recorded ME as the cause of death. ME is a serious, disabling, chronic neuroinflammatory disorder: as long ago as August 2004 the US CDC added it to its top priority list of emerging infectious diseases. It is not a behavioural disorder; it is not a form of chronic fatigue (which is not the same as chronic fatigue <u>syndrome</u> as

listed in ICD-10 at G93.3), nor is it a form of depression and most patients have no psychiatric disorder. There is a state of chronic, low-grade immune activation, with abnormal T-helper/T-suppressor cells and extremely low NK cell numbers/function; brain abnormalities have been proven, as have neuroendocrine abnormalities. ANS dysfunction is integral to the diagnosis, as is disordered gene expression (important in energy metabolism – metabolomics have convincingly demonstrated defects in pathways converting sugars, lipids and amino acids into energy https://www.youtube.com/watch?v=VprqU9knS4Y). There is evidence of biochemical dysregulation in the 2-5A synthetase/RNASE L pathway (ie. an abnormally elevated anti-viral response). Cardiovascular abnormalities are seminal (including altered brain perfusion, reduced cardiac mass and low circulating blood volume), as is an abnormal response to exercise, with muscle weakness (enteroviral sequences being found in muscle), as well as evidence of impaired oxygen delivery to muscles, with recovery rates for oxygen saturation being 60% lower than in normal controls (Kevin K McCully et al. Clinical Science 1999:97:603-608). Since 2000, patients with ME have been advised to consider taking legal action against health professionals when inappropriate exercise is prescribed. (ME Association). Inability to tolerate medication is well-documented as being virtually pathognomonic (Professor Charles Poser, Department of Neurology, Harvard Medical School, Dublin International Meeting on ME/CFS, 18th-20th May 1994, World Federation of Neurology). There is high occurrence of allergies and hypersensitivities. 25% of patients with ME are severely affected and are bed/house-bound. 80% of patients do not get better: published CDC statistics show only 4% in remission (not recovery) at 24 months (US CDC CFS Programme Update, 29th August 2001)".

Physicians need to be presented right from the beginning of the document with a clear list of key physical symptoms, but as it stands, the document fails to do so and the author focuses on cognitive problems. He does not mention immune, cardiovascular, neuroendocrine or gastro-intestinal symptoms until much later in the document, whereas from the outset there needs to be a prominent box listing the cardinal symptoms; these include:

post-exertional malaise (PEM); exhaustion; muscle pain and weakness; abdominal pain; diarrhoea; balance disturbance/dizziness; shortness of breath; palpitations; joint pain; easy bruising; allergies/hypersensitivities to foods previously tolerated; chemical sensitivities (including to therapeutic drugs); frequency of micturition including nocturia; visual problems; flushing (not the same as hot flushes); emotional lability; lack of restful sleep and cognitive problems. Pain may be intractable but it may sometimes be absent; hair loss may be total or partial.

5. The challenge

a. ME is basically a **clinical diagnosis** - this should be a **positive diagnosis** based on the classical constellation of symptoms, **NOT** a diagnosis of exclusion. Time should be allowed

for a very thorough history; this would be time well spent as it makes the patient feel validated and believed.

b. The ability to diagnose ME should be **part of the clinical competence of ALL physicians, GPs and paediatricians, however specialised.**

c. Standard laboratory investigations are normal, but the patients may be extremely sick (see Appendix for necessary investigations).

d. There is currently **no curative treatment.**

e. Despite this, patients should not be abandoned, but deserve the support afforded to those with other neurological diseases (such as state benefits, education, wheelchairs and other disability aids, all of which are usually denied to those with ME/CFS) and symptomatic treatment, as with other chronic organic diseases. In the case of children, they (and their parents also) need **protection** from misguided diagnoses of Factitious and Induced Illness (in April 1999, Dr Nigel Speight, Consultant Paediatrician at the University Hospital of North Durham and an acknowledged expert on ME/CFS, reported that the frequency of psychiatrists diagnosing Munchausen's Syndrome by Proxy in parents of children with ME/CFS amounted to an epidemic, and this was reported by the ME Association in the Autumn 1999 issue of Perspectives).

f. Doctors need to carry out a basic checklist on a patient presenting with possible ME/CFS: this should include asking questions about the onset of non-life-long exhaustion, weakness of muscles, lack of energy, walking distance, cardiac and vasomotor episodes (including chest pain), alterations in sleeping pattern, cognitive difficulties, disturbances in vision, symptoms of dysautonomia (especially thermodysregulation, a labile blood pressure and frequency of micturition), and a neurological examination which should include testing for nystagmus, a positive Romberg, quadriceps jitter, cogwheeling, tandem gait and supinator/pronator imbalance, all of which are commonly seen in ME/CFS.

g. Patients **do not need referral to psychiatrists** unless there are positive indications of additional psychiatric disorder, but secondary depression may follow due to the hopelessness of the situation in which so many patients with ME/CFS find themselves.

What is needed is recognition and acceptance by those opposed to the concept of ME/CFS as a biomedical disorder of the already vast but ever-increasing evidence of biomedical pathophysiology that underpins ME. Previous attempts to do so have always foundered on the fixed ideological views of the illness held by those who maintain that CFS/ME is a behavioural disorder and, despite the evidence that they are wrong, continue to cling tenaciously to their own disproven beliefs. This stalemate situation not only hinders the advancement of medical science but it actively harms patients.

Evidence from the largest trial (the PACE trial) to test the efficacy of behavioural interventions (i.e. CBT and GET which are predicated on the belief that CFS/ME is perpetuated by "unhelpful illness beliefs" and physical deconditioning), showed that, with respect to objective measures, neither CBT or GET improved a participant's physical

fitness, capacity to work or their reliance on social security payments. Furthermore, at long-term follow up CBT and GET were no more effective than usual medical care alone.

Once the trial was underway, the principal investigators weakened both of the primary outcomes measures such that it was possible for a participant's physical function to deteriorate during the trial and still be classed as recovered at the end. In fact, following the post-hoc changes to the trial's protocol, nearly 13% of participants met recovery criteria for physical function when they entered the trial.

In an egregious departure from clinical trial norms, they abandoned the trial protocol which they had published and registered, and instead used a statistical analysis plan that only published after the main trial results themselves had been published. Notably, the new statistical analysis plan contained no definition of "recovery".

At a Science Media Centre arranged press conference to publicise the trial results, one of the trial P.I.'s, Trudie Chalder, stated that that twice as many people "got back to normal" from CBT and GET as in the other two arms without making clear that her definition of "normal" overlapped with the trial's definition of "abnormal levels of physical function" (Psychol Med. 2013 Oct; 43(10): 2227–2235).

The influential group of psychiatrists continue to propagate the deconditioning / unhelpful illness belief-based model of the disease despite evidence from their own trials which shows that it is incorrect and therapies based on this model do not work. Their intransigence in the face of published evidence means that there can be no realistic chance of a unified approach about the nature and management of CFS/ME. However, in the United States the psychiatric model has been recognised as both wrong and harmful.

On 10th February 2015 The Institute of Medicine (now called The National Academy of Sciences) released a report entitled "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness". The report considered 9,112 published papers on ME/CFS and concluded that it has serious, multi-system pathology and that it is not a behavioural disorder: *"It is clear from the evidence compiled by the committee that ME/CFS is a serious, chronic, complex, and multisystem disease that frequently and dramatically limits the activities of affected patients"* (http://www.cdc.gov/cfs/toolkit/archived.html).

After publication of that report, the US Centres for Disease Control decided to archive its CFS Toolkit that recommended CBT and GET as interventions for ME/CFS because these interventions have been shown to be scientifically invalid.

The US Agency for Health Research Quality ME/CFS Evidence Review (addendum July 2016) concluded that there was insufficient scientific evidence to support the use of CBT/GET on measurable outcomes like function, fatigue, quality of life, employment, and overall symptom improvement. CBT was also found to be inefficient or barely significant (https://www.ncbi.nlm.nih.gov/books/NBK379582/?report=reader).

It is therefore disturbing that throughout this report, Baraniuk focuses on such comprehensively disproven interventions and promotes them despite the published evidence showing they have no validity.
To find them promoted and given so much weight in the report is misconceived, supporting as it does the scientific fraud that has been internationally ascribed to the PACE trial (see http://www.virology.ws/mecfs/).

Concern about the situation for people with ME/CFS is now a major political item, as evidenced by the 3 hour Parliamentary debate on ME held on 21st June 2018 and recorded in Hansard
(https://hansard.parliament.uk/Commons/2018-06-21/debates/A49A6117-B23B-4E35-A83B-49FEF0D6074F/METreatmentAndResearch).

For the BMJ's Best Practice reference tool to recommend CBT and GET, as in this report, flies in the face of published data. It is not evidence-based medicine!

There is a large evidence-base showing that GET is harmful to patients with ME/CFS (http://www.margaretwilliams.me/2010/magical-medicine_hooper_feb2010.pdf).

The BMJ editors have a professional responsibility to ensure that their Best Practice reference tools are factually accurate and do not merely reflect the strongly-held beliefs of a group of influential psychiatrists.

The editors need to take seriously their role as a source of knowledge for doctors who are required by the GMC to keep their knowledge-base up-to-date as is necessary for patients' safety.

Finally, clinicians need to be aware that the long-established bench-mark when deciding if medical negligence has occurred ("a reasonable body of opinion", known as the Bolam principle) has been superceded by the Montgomery case (Supreme Court Judgment, March 2015: https://www.supremecourt.uk/vases/docs/uksc-2013-0136-judgment.pdf). This landmark change in the law means that hiding behind "a reasonable body of opinion" and cherry picking what information is given to patients is no longer admissible: all clinicians now have a duty to fully inform all patients of any material risks with a therapeutic intervention which they would find significant. In other words, the law on informed consent means that UK doctors must now fully inform their patients of all material risks of CBT/GET or risk litigation (https://www.dropbox.com/sh/zw94poey7h6ulqm/AABq2XPLhnFxzOg7JbVxG3cia?dl=0).

This BMJ Best Practice report, as it stands, cannot be remedied by any amount of revision or corrections. It must be rewritten entirely based only on an impartial and up to date review of the published literature.

With a document like that, it is not surprising that ME/CFS is not seen for what it is, especially by members of the medical profession: it is a serious, devastating, potentially life-threatening condition and needs to be managed as such by all clinicians.

Malcolm Hooper PhD, B Pharm, MRIC, C Chem
Emeritus Professor of Medicinal Chemistry
University of Sunderland, UK

23rd June 2018

APPENDIX

Specific comments

-- page 4:

"Diagnostic criteria" are not synonymous with case definitions, of which there are at least nine.

"CFS/ME can be distinguished from other medical and psychiatric conditions" immediately conveys the impression that the topic under discussion is itself a psychiatric condition, which is factually incorrect.

"The chronic but fluctuating disabilities require substantial lifestyle changes" – patients have no choice but to make substantial lifestyle changes: these apply not only to the patient but to their families and carers and this should be acknowledged.

-- page 5:

"The term myalgic encephalomyelitis is also problematic, given the limited evidence for brain inflammation". The term is not problematic: it has been accepted by the World Health Organisation, by The Royal Society of Medicine, by the UK Department of Health and Social Care and by the Department for Work and Pensions; it is accurate, because there is significant evidence of brain inflammation, not least the evidence from numerous post-mortems, not only in the UK but in the USA. There is significant published evidence of whole body chronic, low-grade inflammation.

"Pain was not considered unique to CFS/ME" – many people with ME/CFS are in pain 24 hours a day; the problem of intractable neuropathic pain is well-documented in the ME/CFS literature.

“to stay competent in normal occupational, educational, and social settings”: this disregards the fact that many people with ME/CFS are too ill for any sort of occupation, educational or social life. Walking is not a simple task for people with ME, nor do they have “a few hours per day of productive endeavours”. This is misleading as it entirely ignores the severely ill.

-- page 8:

“Immunisation is not a significant precipitant”: there is substantial evidence that immunisation is definitely a significant precipitant in some patients, particularly Hepatitis B vaccine. The Medical Advisor to the UK ME Association has a substantial data base on this. Others have been made worse by immunisations and people with ME are advised not to take up offers of vaccinations.

“other viruses, including enterovirus, have also been implicated”: enteroviruses (especially Coxsackie B) are the most common trigger of classic ME and this is well-documented in the literature.

-- page 9

“Inflammatory, autoreactive, and metabolomics mechanisms have been proposed, but not verified, to explain the pathophysiology of CFS/ME”: this statement gives the wrong impression; many studies have now demonstrated significant abnormalities in these systems.

“diagnosis will be based entirely on self-reported symptoms”: this is untrue; many abnormalities show up if the correct laboratory investigations are carried out; the problem in the UK is that NICE has actively proscribed such investigations (They also advised against them later in his document).

“Exercise may be beneficial for the recovery of athletes, healthy individuals, cardiac patients, and others who may experience temporary immobility, but it is not clear whether patients with CFS/ME respond in the same way”: this is incorrect; it is well-established that people with ME/CFS respond abnormally to exercise. It has now been shown that calibrated exercise on a bicycle ergometer on two consecutive days indicates clear differences in muscle metabolism between ME/CFS patients and healthy but sedentary, ie deconditioned, controls. In the ME/CFS patients, the anaerobic threshold lowers on the second exercise day, whereas it increases in the controls (Snell et al. Phys Ther 2013 Nov;93(11):1484-92).

-- page 10

“HPA axis dysregulation may occur secondary to behavioural changes”: the cause of HPA axis dysfunction is unknown and it is premature to attribute it to behavioural changes when it may be a central component of the disease process.

-- page 12

“A larger rituximab study is currently under way to confirm these initial findings”: it is now known that this study failed as the results have been reported informally by the researchers.

-- page 13

“The condition is approximately 2 to 3 times more common among women than among men”: all autoimmune disorders are more common amongst women: it has now been shown that this is because of the oestrogen link with autoimmunity. There is emerging evidence that ME/CFS is an autoimmune disorder.

-- page 16

“PEM does not respond to rest and may last several days or longer”: this is much too weak: PEM may last weeks, months or years; people are not simply fatigued -- they feel very ill and struggle to look after themselves (many cannot do so and need full-time 24 hour care). Importantly, following episodes of PEM, the pre-morbid level of functioning is not always achievable, leading to permanent deterioration.

-- page 17

“exclusion of other medical and psychiatric conditions in the differential diagnosis”: ME/CFS is not a psychiatric condition, but this sentence clearly implies otherwise.

The “Diagnostic criteria”: some of the criteria included in this table have been compiled by those who do not accept the WHO classification of ME as a neurological condition, so why are they included in Baraniuk’s document?

-- pages 18 - 24

“A valid criticism (of the Canadian Consensus Criteria) is the inclusion of neurological signs such as ataxia, muscle weakness, and fasciculations, which may be due to neurological diseases”. Where is the clinical acumen in not looking for neurological signs and symptoms in a confirmed neurological disorder?

-- page 25

“There are presently no reliable or specific biological causes, biomarkers, objective findings, or laboratory anomalies that are indicative of CFS/ME”: this statement is egregiously untrue. There are at least three biomarkers indicative of ME/CFS that should always be looked for in a suspected case: (i) immune complexes; (ii) IgG and (iii) atypical lymphocyte count >2%. There are many other well-documented signs and laboratory abnormalities including multiple abnormalities seen on MRI; areas of reduced signal seen on SPECT; immune cell activation (neuroinflammation) seen on PET, and EEG abnormalities including sharp spike waves, a distinctive spectral

coherence pattern and impaired connectivity. There is evidence from metabolomic studies of disrupted energy production (regulated by the availability of NAPDH); ion channel abnormalities have been shown -- 13 polymorphisms are significantly different in ME/CFS cases, most of them in the TRPM3 ion channel, but not seen in healthy controls; abnormalities in muscles show central sensitisation, with hyperalgesia; there is increased reactive oxygen and nitrogen species: eg. ↑ TBARS (products of lipid peroxidation); proven mitochondrial dysfunction with reduced levels of succinate reductase, cytochrome-C oxidase and Co-enzyme Q10, and there is proven bioenergetic dysfunction: ↓ proton efflux after exercise; ↑ intramuscular acidosis with exercise. Furthermore, plasma cytokine levels correlate with severity of symptoms; there are proven changes in cytokine levels after exercise (the molecules that best distinguish ME/CFS from healthy subjects were IL-1β, IF-α, CD40L, CXCL1 and platelet activation inhibitor); there are antibodies to dUTPases in ME/CFS (proteins produced by a virus that activate innate immunity (TLR2 □ NFkB) that are significantly higher in ME/CFS patients than in healthy controls); there is a clear, statistically significant difference in the length of telomeres in ME/CFS patients; changes in gene structure have been demonstrated in people with ME/CFS, with SNPs in genes involved in neurotransmitter regulation, with genes involved in HPA axis regulation and with genes involved in the inflammatory/immune response -- many studies have found abnormal expression of genes involved in immune activation, in energy metabolism and in the brain hormones – neurohormones – that are involved in the stress response in people with ME/CFS; abnormalities in all four of the central mechanisms by which genes are turned on and off have been found in people with ME/CFS (ie. (i) the DNA methylome is different, particularly with regard to glucocorticoid sensitivity genes and in genes important in cellular metabolism; (ii) expression of microRNA is different, particularly in NK cells; (iii) there is a difference in transcription factor levels, with increased levels of NFkB and (iv) there is increased HDAC expression, leading to decreased gene expression); levels of a bacterial toxin called LPS or lipopolysaccharide in the blood stream of ME/CFS patients are significantly higher than in healthy individuals and – importantly – it has been shown by Cornell University that following exercise in patients with ME/CFS, actual live bacteria get into the blood: levels that were not measureable before exercise become measureable following exercise, whereas this is not seen in healthy individuals.

“maladaptive coping skills may predate or co-occur with CFS/ME”: this is another egregiously false statement: there is no credible evidence to support it. Many people with ME/CFS struggle to cope with basic activities of daily living (although some are too ill to do so and require 24 hour care) but that is not the same as having “maladaptive coping skills”.

-- page 26

“A multidisciplinary team may be required, with referral to appropriate specialists”: this is the accepted and established code used by clinicians for the involvement of psychiatrists.

-- page 27

“Major neurological diseases”: in the interests of accuracy, this should state “other major neurological diseases”: once again, there is no acknowledgement that ME/CFS is a classified neurological disease.

-- page 28

“PEM has been described as a group of symptoms following mental or physical exertion, lasting 24 hours or more”: once again, this is too weak and it denies the reality for many ME/CFS patients; many cannot stay in normal occupations or carry out normal activities for days, weeks, months or years.

“Patients may actively avoid this level of activity”: this is demeaning: it may be physically impossible for patients with ME/CFS to engage in any level of activity.

“Fatigue”: the word “fatigue” usually equates with tiredness but it bears no relationship to the overwhelming physiological exhaustion experienced on a daily basis by people with ME/CFS.

-- page 29

“Chronic pain”: earlier in his document, Baraniuk states that pain is excluded as a component of ME/CFS, but then he includes it under “Key Symptoms”.

-- page 30

“There are no typical objective findings from physical examination of a patient with CFS/ME”: again, this is untrue. Well-documented physical objective findings include:

- labile blood pressure (this is a cardinal sign); low systolic BP -- <100 in 50%
- nystagmus and vestibular disturbance (vestibular dysfunction seen in 90%)
- sluggish visual accommodation
- fasciculation
- hand tremor
- neuromuscular incoordination
- cogwheel movement of the leg on testing
- muscular weakness
- marked facial pallor
- postural orthostatic tachycardia syndrome (POTS)
- positive Romberg
- abnormal tandem or augmented tandem stance
- abnormal gait
- evidence of Raynaud’s syndrome and vasculitis (vascular signs cross dermatomes)
- mouth ulcers
- hair loss

- singular reduction in lung function (shortened breath-holding capacity seen in 60%)
- enlarged liver

None of these signs are usually looked for by psychiatrists.

“However, signs of visual dysfunction in CFS/ME are under Investigation”: there is published evidence of latency in accommodation, of reduced range of accommodation and of decreased range of duction (ME patients being down to 60% of the full range of eye mobility); there is evidence of nystagmus; there is evidence of reduced tracking; there is evidence of problems with peripheral vision; there is evidence that the ocular system is very much affected by, and in turn affects, this systemic condition. Most recently, ME patients have been shown to exhibit a restricted spatial window of visibility for encoding stimulus contrast, indicating abnormal visual processing at a level of the retina and in cortical and subcortical visual pathways.

-- page 31

“Romberg testing…(has)not been well documented for CFS/ME diagnosis”: a positive Romberg is well-documented in ME/CFS patients, not only in the published literature (eg. Komaroff et al. Clin Inf Dis 1991: 13 (Suppl 1): S8 – S11) but also in textbooks.

“Extensive laboratory or imaging studies are not indicated”: this statement is contrary to good medical practice; it is such tests that have revealed the significant pathology now known to underpin ME/CFS. Because standard laboratory tests are usually normal, specific tests are vital to confirm the diagnosis, but Baraniuk specifically warns physicians not to order them. Not to investigate seriously sick patients might amount to medical negligence.

-- page 34

“Widespread muscular pain may be compounded by physical deconditioning secondary to excessive resting”: no evidence of deconditioning has been found in patients with ME/CFS. This suggestion is part of the psychosocial school’s unproven dogma that “CFS/ME” is a behavioural disorder due to a patient’s fear of exercise. Hyperalgesia has been shown to be due to central sensitisation, not to deconditioning.

-- page 54

“Counselling therapies and graded exercise therapy have been shown to improve fatigue, function, global improvement....Counselling therapies have also been shown to improve quality of life”: counselling therapies (CBT) and GET have NOT been shown to improve fatigue and function, nor do they improve global function as claimed; quite the reverse is true: CBT makes no difference at all and GET makes people worse (plentiful evidence to support this). As far as ME/CFS patients are

concerned, the CBT used was specially formulated by the Wessely School: it is not standard supportive therapy to help patients cope with devastating illness: it is intended to “challenge unhelpful illness beliefs” and Simon Wessely has publicly stated: “CBT is directive – it is not enough to be kind or supportive” (New Statesman, 1st May 2008).

-- page 55

“Initial treatment plan”: no such plans exist for ME/CFS patients: GPs haven’t got a clue, so any plan would simply follow national guidelines, which are to use CBT and GET.

“Initial treatment begins with counselling and supportive care”: the reference for this (188) is by someone intractably committed to the notion that “CFS/ME” is a behavioural disorder and who ignores the biomedical evidence in over 9,000 published papers (https://hope4mefibro.org/wp-content/uploads/2017/07/Hope-4-ME-Fibro-NI-comments-form-2.pdf and http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2015/MECFS/MECFS_Powerpoint.pdf); the reference quoted is talking about chronic fatigue, which is not ME/CFS. People with ME/CFS do not need counselling as a first line of management (there is no treatment currently available): they need knowledge about the disease, not fictitious beliefs.

-- page 56

“Exercise programmes….will provide patients with CFS/ME with a 'paced' approach to treatment”: this appears to be confusing graded exercise with pacing; the two are completely different. Graded anaerobic exercise is potentially harmful, whereas pacing is keeping within the individual’s personal limits without causing a relapse.

“Exercise-induced symptoms may be reduced by mindfulness”: the psychological process of bringing one's attention to experiences occurring in the present moment cannot correct defective energy metabolism (ie. “mindfulness” cannot convert sugars, lipids and amino acids into the energy necessary to function).

-- page 57

“For patients with milder symptoms of CFS/ME… treatment can begin with interval training with swimming, or pedalling on an exercise bike”: this is enough to tip someone with mild ME/CFS (who is trying to pace themselves sensibly) into a serious and possibly permanent relapse.

“The brain training involved in cognitively preparing and planning exercise may be as beneficial as the exercise itself”: once again, this is predicated on disproven psychosocial dogma that patients with ME/CFS are merely deconditioned through lack of exercise; it is offensive to those with the neuro-immune disease ME/CFS.

-- page 58

“CBT facilitates the patient to identify unhelpful, negative emotion-provoking thoughts, dysfunctional behaviours, and cognitive patterns”: this is pure psychosocial dogma; patients with ME/CFS do not have such beliefs, so not only is it abusive -- it has been comprehensively disproven.

-- page 59

“Body awareness therapy”: this is insulting to people with ME/CFS, especially to those so sick that they are bed-bound. Would “body awareness therapy” be offered to patients with other neurological diseases such as multiple sclerosis or Parkinson’s Disease?

“Studies of CBT in people with CFS/ME report significant improvements in… 6-minute walking”: this is fallacious: the authors of the PACE results themselves refute this: “6-minute walking distances…were not different after CBT compared with APT (adaptive pacing therapy) and SMC (specialist medical care)”.

-- page 60

“CBT should be planned by the practitioner as 'brain retraining sessions' to improve attention, working memory, and organisation of daily routines (e.g., going to social events, shopping, and other outings)”: many people with ME/CFS are not well enough to do any of those things and yet again, this presumes that people with ME/CFS have faulty cognitions, but this presumption has long been disproven by neuroimaging of impairments in information processing speed, memory and attention, not explained by concomitant psychiatric disorders.

“Although referral to a mental health professional with expertise in CBT has been recommended regardless of CFS/ME severity, this is limited by a lack of availability in some settings of a qualified CBT psychologist, social worker, nurse, or other practitioner with CFS/ME training”: again, this is straight from the psychosocial school who continue to dismiss or ignore the ever-mounting evidence that they are wrong about the nature of ME/CFS: they base their dogma on the widely-rejected “Oxford” criteria which intentionally includes people with psychiatric disorders. It is unnecessary for most people with ME/CFS to be referred to a mental health professional. The evidence that CBT does not work in ME/CFS is universal and easily available.

-- page 61

“Non-adherence with prescribed exercise protocols”: “Non-adherence” implies non-compliance, which in turn implies that ME/CFS patients obdurately refuse to cooperate with medical professionals; this in turn has grave implications for people with ME/CFS (who may be physically unable to be compliant with management interventions that harm them) because it means that their State benefits needed for basic survival are withdrawn.

-- page 62

“discomfort will prevent them from travelling”: this is inaccurate; “discomfort” is not an adequate descriptor for the severe pain (previously excluded as part of “CFS”), the total lack of energy, feeling terribly ill, dysautonomia, lack of balance, vertigo, nausea, inflamed joints, visual problems, incontinence of urine and faeces and shortness of breath that prevent people with ME/CFS from travelling.

“Severe CFS/ME represents about 5% to 10% of cases”: it is well-established that 25% , not 5% to 10% of cases are severely affected (see The 25% ME Group website).

-- page 64

“Multidisciplinary rehabilitation treatment: occupational therapists and social workers supervise social reintegration by making plans to return to work or school, and to increase social activities. Advice is provided to help relapse”: this refusal to accept reality is actively harmful for patients with ME/CFS because it implies that people have recovered (“Advice is provided to help relapse” would be better expressed as “Advice is provided to help avoid relapse”). Not only does it ignore the statistics showing that 80% of patients do not get better, it conveys the message that recovery is possible, a claim made by the authors of the UK PACE study but which has been internationally discredited.

-- page 65

“CBT and graduated exercise therapy are cost-effective”: to support this assertion, Baraniuk relies on a paper by Paul McCrone, Michael Sharpe and Trudie Chalder, but CBT and GET are only cost effective under certain highly questionable assumptions about the cost of informal care (ie. care provided by family members). In their paper, McCrone et al said that their findings were robust regardless of how informal care was costed, but he later conceded that he was wrong. Importantly, PLoS have issued an expression of concern about McCrone et al’s paper (under transparency requirements, PLoS should be able to publish the actual figures, but McCrone et al consistently refuse to provide their figures to PLoS).

-- page 72

“Qigong exercise”: claims that this is effective for ME/CFS have been demolished by the charity ME Research UK:

“The key point is that studies like this – where an ‘active’ therapy (delivered face-to-face by a therapist–expert) is compared with an ‘inactive’ control group – tend to have positive results, i.e. for the therapy to be found ‘helpful’ whether or not it is in reality. This well-recognised phenomenon is bound up with various non-specific effects thought to occur in clinical trials in all illnesses. So, we cannot conclude from this study that Qigong is specifically effective for ME/CFS or its symptoms”.

-- page 74

“The National Institute for Health and Care Excellence (NICE) has made the following general recommendations regarding treatment strategies: …. detailed advice should be provided in the form of individualised exercise regimens; exercise and cognitive behavioural therapy should be offered to people with mild or moderate CFS/ME”: NICE have admitted that their existing Guidelines are unfit for purpose and are to be completely reviewed. In a Parliamentary debate on ME/CFS held on 21st June 2018, an MP (Sir Ed Davey) stated that if the existing Guidelines remain in place until 2020, there is potential for patients harmed by its recommendations to take legal action against NICE. This is recorded in Hansard.

-- page 74

“Occupational aspects of the management of chronic fatigue syndrome: a national guideline. NHS Health Service Plus: National Health Service evidence-based guidelines for managing CFS/ME in the workplace. Key findings as follows: cognitive behavioural therapy and managed exercise regimens can facilitate the return to work”: this statement has been shown to be untrue.

-- page 76

“Patients should be educated on how secondary physical deconditioning can emerge due to increased resting and activity restriction. Difficulties and fears associated with attempting to increase levels of physical activity should be normalised”: this is not just offensive – it is factually incorrect. CBT and graded exercise have been demonstrated to be unsafe and inappropriate interventions. It has been shown that people with ME have no higher rates of mental illness than controls. Often patients need to be advised to do less, and it is rarely the case that they need to be encouraged to do more, since they are not depressed and want to engage in activities that they previously enjoyed.

-- page 102

“CFS can last for years. And, although it's not medically dangerous…” ME/CFS can be fatal. As noted above, numerous UK Coroners have recorded ME as the cause of death.