

## Important points in relation to the NICE Guideline on “CFS”

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1. The spin throughout the NHS and UK Departments of State (and in Ministers' answers) suggests that the NICE Guideline was produced and is being implemented with the cooperation of patients with ME/CFS. Nothing could be further from the truth. The AGREE Instrument requires that equal weighting be given to users' input (i.e. that undue weight should not be accorded to RCTs but that equal weight must be given to all three categories of evidence --- RCTs, expert evidence and patients' evidence), but there is first hand evidence that this did not happen. A patient representative on the Guideline Development Group, Richard Eddlestone, wrote about this: *“I think there were areas where the patient voice was not listened to and that there were deficiencies in the process. I suspect that (patients') comments did get lost, although to be fair to the staff at NICE, they were excellent at reading everything, so any shortfall would not lie with them (but with the GDG members themselves)”*.
2. Despite the fact that the UK is a signatory to the WHO ICD-10 – in which ME/CFS is coded to the neurology chapter and not to psychology/psychiatry – the Guideline has not recommended referral for neurological investigations but instead emphasises that the primary management must be psychotherapy (cognitive behavioural therapy/CBT and graded exercise therapy/GET). This is illogical, because NICE is funded by and accountable to the Department of Health, which does accept that ME/CFS is a neurological disorder (see below).
3. The refusal of the NICE Guideline's authors to accept that ME/CFS is a neurological disorder is even more illogical given that ME/CFS is included in the UK National Service Framework (NSF) for people with long-term neurological conditions. The NSF was launched on 10<sup>th</sup> March 2005 (i.e. well before the publication of the NICE Guideline on 22<sup>nd</sup> August 2007). That ME/CFS is indeed included in the NSF has been confirmed on numerous occasions, for example: Hansard: 6<sup>th</sup> March 2006 (HC Column 1200 W), where the Under Secretary of State for Health, Liam Byrne MP said: *“NHS organisations are expected to demonstrate that they are making good progress towards achieving the level of service quality described in the NSF for long term conditions. The NSF sets out a clear vision of how health and social care organisations can improve the quality, consistency and responsiveness of their services **and help improve the lives of people with neurological conditions, including CFS/ME**”*. Further confirmation was provided by Ivan Lewis MP, Parliamentary Under Secretary at the

Department of Health: *“Those most severely affected by CFS/ME have access to the full range of health and social services support as outlined in the National Service Framework for long-term conditions”* (Hansard 12<sup>th</sup> May 2006 HC). The most recent confirmation was on 2<sup>nd</sup> June 2008. When asked by The Countess of Mar whether the current NHS review will include consideration of CFS/ME as a long-term neurological condition, the Parliamentary Under Secretary of State, Department of Health, Lord Darzi of Denham, replied: *“The long-term conditions pathway is one of the care pathways that strategic health authorities are examining as part of the NHS next stage review. The review will increase awareness and ensure better care for people with CFS/ME and will help support local delivery of the NSF for long-term neurological conditions. **The Government accept the World Health Organisation’s classification of CFS/ME as a neurological condition. My ministerial colleague Ann Keen reaffirmed that position at the meeting of the All Party Parliamentary Group on ME in January of this year. My Lords, I have acknowledged that CFS/ME is a neurological condition**”* ([http://www.publications.parliament.uk/pa/ld/ldtoday/01.htm#spkr\\_2](http://www.publications.parliament.uk/pa/ld/ldtoday/01.htm#spkr_2)).

4. It is imperative to be aware that despite these assurances from Ministers of State, patients with ME/CFS are denied such access because the NICE Guideline (which, even though it is called a “guideline”, is in practice mandatory) recommends only a psychosocial management regime. The Guideline dresses this up by using the term “multidisciplinary approach”, but throughout the NHS, the term “multidisciplinary” is shorthand for “this is a psychiatric problem, though do not let the patient think so, otherwise they will not comply”.
5. In the Hansard reference of 2<sup>nd</sup> June 2008 (above), The Countess of Mar drew attention to the effects of such a management strategy: *“Does (the Minister) appreciate that, despite the fact that it has been 40 years since the World Health Organisation recognised ME as a neurological disease and 20 years since the Department of Health did so, adults are still sectioned or deemed as lacking in capacity and children whose parents are blamed for their illness are put on the at-risk register or are made wards of court, with people from both these groups forcibly put into mental hospitals? This has been described to me as abuse by professionals”*.
6. As noted by Dr John Greensmith in a letter to the Daily Telegraph on 18<sup>th</sup> March 2008: *“Government advisers, who are dominated by psychiatrists, say they do not believe that ME is ‘all in the mind’ (but) since most patients are treated by psychiatrists, using treatment developed for psychiatric illnesses, most often in psychiatric units of hospitals, it is hard to think how otherwise they would treat them if they did believe it was of psychiatric origin”*.
7. Under the proven influence of the Wessely School psychiatrists and in defiance of the published evidence that ME/CFS is an organic disorder, The Royal College of General Practitioners and The Royal Society of Medicine (as well as the Medical

- Research Council) have colluded to categorise ME/CFS as a mental disorder. The Chief Executive of the RSM (Mr Ian Balmer) wrote on 23<sup>rd</sup> April 2008 about the RSM's position on ME/CFS: *"Our agenda was drawn up to reflect current thinking on its diagnosis and treatment, as outlined in the NICE guidelines"*.
8. Citing the NICE Guideline, the RCGP has confirmed in writing that it categorises ME/CFS as a mental disorder (and will therefore train GPs accordingly). By letter dated 15<sup>th</sup> May 2008, Dr Bill Reith, Chairman, Postgraduate Training Board, RCGP, when asked why the RCGP included people with ME/CFS in its Curriculum Statement 13 'Care of People with Mental Health Problems', wrote that the decision *"was taken largely on the grounds that many specialist services are currently configured and based in, or are linked to, psychology services. In reaching their decision, the group also took into account the NICE guideline for CFS/ME"*.
  9. In the Hansard reference of 2<sup>nd</sup> June 2008 (above), Baroness Howe of Idlicote asked: *"Can the Minister explain to the House why the Royal College of General Practitioners continues to insist on categorising CFS as a mental illness?"*, to which the Minister, Lord Darzi, replied: ***"My Lords, the Government have made it clear that they consider that CFS/ME should be classified as a neurological condition. It is for professional bodies to look at the evidence base and I will encourage the RCGP to look at the WHO classification, which is that it is a neurological rather than a mental condition"***.
  10. Such robust confirmation serves to strengthen how illogical it is for the NICE GDG to single out ME/CFS alone of all the neurological disorders in stipulating that the primary management must be behavioural interventions, as well as how unreasonable NICE has been in refusing to accept the WHO classification of ME/CFS as a neurological disorder.
  11. However, GPs are too scared of censure and of being hauled up before the GMC to speak out against the NICE Guideline (some of those doctors who have openly supported ME/CFS patients with non-psychiatric interventions have been made to appear before the GMC on charges of professional misconduct and their livelihoods have been threatened), but privately many say that they wish the constraints under which they must work could be removed so that they could start to refer ME/CFS patients to appropriate specialists such as neurologists / immunologists / endocrinologists / vascular medicine specialists, and not to psychiatrists.
  12. Professor Leslie Findlay (consultant neurologist in Essex) wrote in the following terms about the NICE Guideline in the Sussex ME Newsletter: *"A basic principle of medicine is that 'First do no harm'. Guidelines were supposed to be evidence-based, however, in the case of chronic fatigue syndrome, the evidence base is just not there, therefore these Guidelines are not truly evidence-based. There are three areas in the Guidelines which I am concerned about. Firstly, I do not think*

*the complexity of CFS/ME really comes out. A second adverse comment would be about the strong and repeated recommendations for CBT. It is extremely difficult to obtain (and) there are no plans to provide therapy for 250,000 plus people with CFS in this country. Finally, the needs of the severe group are poorly covered. These Guidelines satisfy a Government requirement (so) they are going to be quoted to us by officialdom for some time to come”.*

13. In relation to the 250,000 plus people with ME/CFS in this country (for comparison, the Multiple Sclerosis Society says there are 83,000 in the UK with MS), a relevant consideration is that on 8<sup>th</sup> May 2008 Professor Simon Wessely himself stated in The New Statesman (Can talking make you better?): *“To become a skilled CBT therapist takes about the same length of time as it does to become a doctor”*. Since the NICE Guideline stipulates that only skilled therapists should deliver its recommended regime for people with “CFS/ME”, how can it be cost effective to train 3,500 new therapists to deliver NICE’s recommendations to so many ME/CFS patients if it takes so long to train such skilled therapists? The Guideline fails to address this important issue of logistics.
14. The psychotherapy regime recommended by NICE ignores the substantial biomedical evidence (over 4,000 internationally published papers) which include evidence of altered muscle metabolism, brain metabolic abnormalities, vascular (endothelial) dysregulation, biochemical abnormalities, dysregulation of anti-viral pathways, a disrupted immune system, endocrine dysfunction, autonomic dysfunction and gene research, all of which show conclusively that ME/CFS is not a behavioural disorder and therefore people with ME/CFS cannot be expected to respond to inappropriate behavioural therapy (so the NICE management regime is a waste of tax-payers’ money as well as being potentially harmful to all patients with true ME/CFS as distinct from those under the undifferentiated umbrella term of unexplained “chronic fatigue”, which the Wessely School wrongly equates with ME).
15. In the Sunday Telegraph on 11<sup>th</sup> May 2008, Dr James LeFanu commented on the increasing prevalence of a mentality of insidious subversion of good judgment by an unreasonable adherence to the letter of the law: *“The same mentality in the guise of a legalistic adherence to ever-proliferating ‘guidelines’ increasingly affects medicine, to the detriment of the health and wellbeing of those whom its purpose is to serve”*.
16. The ME Association secured an acknowledgement by NHS Plus that GET (recommended in the NICE Guideline as part of CBT -- i.e. as the primary management for “CFS/ME”) can be harmful to people with ME/CFS. The NHS Plus Guidance leaflets (though not the full Guidance) will now say: *“Although some RCTs show evidence of improved functional capacity for work, and reduced fatigue, some patients experience a significant deterioration in symptoms with this intervention”*. The MEA notes: *“This is a significant acknowledgment by the NHS that GET has dangers to people with ME/CFS”*.

17. To coincide with ME Awareness Day on 12<sup>th</sup> May 2008, the charity Action for ME (AfME), together with the charity The Association of Young People with ME (AYME) released the results of their Survey; the Press Release said:

- *“Survey finds recommended treatment makes one in three people worse”*
- *“Results published today show that one third of people surveyed, who said that they had had graded exercise therapy (GET), reported that it made them worse”*
- *“Of the 2,763 people with ME who responded to the charity’s survey, 699 said they had received GET within the past three years. One in three said that it had made them worse”*
- *“The charity is also concerned about the number of GPs who are still unsupportive towards patients who have ME”*
- *“One in three people who responded to our survey said that their GP was either unsupportive or uninformed about the illness, yet GPs are the gatekeepers to diagnosis and treatment”*
- *“It is very disturbing to see figures like these, six years after the Chief Medical Officer called for better treatment, care and understanding of ME”*
- *“At their worst, 36% had been bedbound and a further 52% had been housebound. 41% had been unable to shower, bathe or wash themselves and 15% had been unable to eat unaided”.*

Dr Esther Crawley, a paediatrician and member of the GDG that drew up the NICE Guideline, dismissed the AfME / Ayme report’s findings, saying the survey was unreliable: *“This survey is based on a biased sample of people who have had an issue with treatment and we cannot deduce who had graded exercise therapy delivered by a specialist, as NICE recommends”*. Her dismissal is notable, given that she is Medical Adviser to the charity Ayme.

Astonishingly (or perhaps not, given that AfME receives Government funding to support its policy of managing “CFS/ME” only with CBT/GET), AfME’s response is to call for greater investment in GET and even more therapists.

Most national ME charities have issued a statement voicing some degree of opposition to GET.

18. On 15<sup>th</sup> May 2008 a Joint Statement about the recommended NICE regime of CBT and GET by the ME Association and The Young ME Sufferers’ Trust noted their *“serious concern for the safety of patients given this controversial approach to management. Put simply, the illness worsens as a result of physical and mental effort. Advocating progressive exertion is to show a worrying lack of knowledge about the nature of the illness. Any treatment that causes an adverse reaction in 33% - 50% of those using it cannot be recommended as a blanket form of treatment, as in the Guideline produced by NICE. The MEA and TYMES Trust are therefore jointly calling for an urgent review of the NICE recommendation.*

*We consider this is likely to result in iatrogenic damage to some patients".* The Government's response to the numerous requests for the NICE Guideline to be reviewed is always the same, for example, on 3<sup>rd</sup> December 2007, Dawn Primarolo MP, Minister of State for Public Health, said: *"We have no plans to ask NICE to review that guidance at this time"* (Hansard WA 3<sup>rd</sup> Dec 2007).

19. In its magazine "Vision" 2008 – 1: 18-19, The Young ME Sufferers Trust referred to its Report produced in consultation with Dr Nigel Hunt (a GP and Associate Director of Post Graduate GP Education, Eastern Deanery). A key finding in this Report was that 96% of respondents wanted a choice of which professional co-ordinated their care, yet they were being made to feel that their care must be overseen by a particular doctor (i.e. by a psychiatrist). 92% did not want the automatic involvement of psychologists or psychiatrists. 88% reported that exercise (as recommended in the NICE Guideline) made them worse. Overwhelmingly, people wanted practical help, but there were many negative experiences: many "CFS" clinics do not provide what young people with ME/CFS --- a neurological disease -- need or want because those clinics are following the NICE Guideline on management (which recommends only psychiatric intervention and management and, as noted above, those clinics are dominated by psychiatrists and are housed in psychiatric units and deliver only psychiatric treatment that is based on the psychosocial model of "CFS/ME", in which states of psychiatric fatigue are not differentiated from ME/CFS).
20. On 3<sup>rd</sup> February 2008 Professor Peter Littlejohns, Clinical and Public Health Director at NICE, went on record in the Sunday Telegraph as confirming: *"NICE acknowledges that the advisory bodies which develop the institute's guidance may need to incorporate social values into the advice they give"*. This seems to mean that in addition to the two key elements of clinical effectiveness and cost effectiveness, social values in the form of government policy also are taken into account by NICE (as is apparent in the "CFS/ME" Guideline, since there is no evidence of either clinical or cost effectiveness, yet NICE still recommends the Government-favoured policy of psychosocial management for ME/CFS).
21. Even the authors of the York Systemic Review (upon which NICE relied for supposed evidence of clinical effectiveness) themselves concede the methodological inadequacies of the studies upon which NICE based its management recommendations (Whiting et al; JAMA 2001:286:1360-1368). For example, it is common knowledge and has been much discussed on the internet that:
  - The NICE Guideline (and the York Systematic Review upon which NICE placed so much reliance) relied on very few studies: these were of poor quality with flawed methodology and they lacked scientific rigour

- The studies that were relied upon used different entry criteria and different outcome measures, so were impossible to compare. With no standardisation of outcomes, any meta-analysis is invalid
- The severely affected and children were excluded from study
- No attention was paid to subgroups and there is no evidence of how different subgroups might respond differently to the recommended regime
- Trials that claimed to be randomised were not randomised at all: for example, the much-criticised Prins, Severens et al (Dutch) study (Lancet 2001:357:841-847), which formed the bed-rock of the NICE Guideline's cost-effectiveness recommendations, was not randomised and used a biased cohort to start with
- There were extremely high drop-out rates (20% - 40% in the Prins et al study), indicating a lack of patient acceptability; this makes it possible to over-estimate the alleged benefits, as well as making it impossible to know the results if there had been no drop-outs. No reasons were provided for the high drop-out rate, which means that no adverse effects were noted (which, if there were any, ought to have been reported, not simply ignored). Equally, drop-outs may have contained patients who might not have been harmed by the intervention but who might not have derived any benefit from it, a fact which would also skew the results in favour of the recommended regime
- In the Prins et al study, out of 476 patients diagnosed with "CFS", only 278 were eligible and willing to take part (note that the authors assert: "*Fatigue is not the result of an organic disease*", which would by definition exclude those with ME/CFS)
- The few other studies that claim success with CBT used a very small number of patients
- Although ME/CFS is a long-term disorder, the studies upon which NICE relied were of short duration
- Based on the evidence upon which it claims to rely, it is irrational for NICE to have recommended CBT/GET as clinically effective interventions in ME/CFS
- Even the Wessely School themselves publicly concede that CBT confers no lasting benefit and that there is no evidence of objective, measurable increase in activity levels in ME/CFS patients after a course of CBT. Wessely himself stated in 2001 that CBT is "*not remotely curative*" and that: "*These interventions are not the answer to CFS*" (JAMA 2001:286:11)
- The Medical Research Council's PACE trial of CBT/GET for "CFS/ME" (run by Wessely School psychiatrists and designed to show that CBT/GET is effective was initially granted funding of £2.6 million, which according to one of the Principal Investigators has now risen to over £4 million) is still on-going and the outcome is not yet known, but NICE has pre-empted the outcome by recommending the national use of CBT/GET for "CFS/ME"

- No amount of CBT/GET can correct the many biomedical abnormalities that international research has demonstrated in ME/CFS, and it is therefore illogical and unreasonable of NICE to recommend that the management intervention of choice should be one that is designed to modify patients' rational beliefs about the disorder (patients' beliefs that ME/CFS is an organic disorder are described by Wessely School psychiatrists as 'aberrant beliefs').
22. A key element of NICE's remit is to evaluate the cost-effectiveness of a proposed intervention, so it ought to be imperative that NICE gets its figures right, but according to the composition of the Guideline Development Group supplied by NICE, there was no medical statistician on the GDG.
  23. In numerous instances, NICE did not get its figures right. NICE made significant mathematical errors, and the wrong figures were used, for example: in their Table 2 on page 201 of the full Guideline, the claimed improvement in the CBT group was from 0.4859 to 0.6014, which is a difference of 0.1155, not 0.0737 as reported in Table 4 on page 207.
  24. Further, the assessment of cost per QALY (a QALY is a Quality Adjusted Life Year, which is the product of life expectancy and a measure of the quality of the remaining years) at 14 months between the control group and treated group was clinically and statistically insignificant, producing a cost per QALY of 0.0015 and a difference at the end that was nearly 27 times smaller than at the start.
  25. Another arithmetical error appears in Table 7 on page 209 of the full Guideline: £447 divided by 0.001579 is £283,343.89, not £283.420.81 as shown by NICE.
  26. There is yet another arithmetical error: on page 201 of the full Guideline, the differential cost of CBT versus no protocol is given in the table as being €1,648, when in fact the correct figure is €1,237.
  27. There is also a big question mark attached to the principal figure of 0.02790 being used by NICE as their basis for almost all relevant calculations.
  28. For NICE to make such basic arithmetical errors in a document of such importance is incomprehensible, and it raises the question of how many other errors are lurking in the Guideline. Does such apparent carelessness run through all the calculations in the Guideline? Why has nobody noticed during the reading and editing before publication? As Martin Bland, now Professor of Health Statistics at The University of York but formerly Professor of Medical Statistics at St George's Hospital Medical School, London, wrote in the BMJ: *"Potentially incorrect conclusions, based on faulty analysis, should not be allowed to remain in the literature to be cited uncritically by others"* (BMJ 2000;320:515).



29. From the figures provided by NICE itself, the true cost of CBT in patients with ME/CFS is not £16,036 (page 207 of the full Guideline) but, using NICE's own ICER (incremental cost effectiveness ratio) figures after averaging assumptions for the differences at baseline, the true cost is a staggering £283,420.81 (which should in fact be £283,343.89). **This would mean that there is no cost-effectiveness whatever in the psychotherapy management regime recommended in the NICE Guideline, a fact that would invalidate the entire Guideline.**
30. A further consideration is the undue reliance placed by NICE upon its own ICER. In a paper published in 2002, Professor Cam Donaldson from The School of Population and Health Sciences at the University of Newcastle drew attention to the problems with ICERs in the economic evaluation of healthcare interventions: *"In economic evaluation of healthcare interventions, the dominant practice is to calculate an incremental cost effectiveness ratio (ICER), usually based on the comparison of a new intervention against current practice. The basis of the use of incremental cost effectiveness ratios needs re-examination. In this paper we revisit the basic economic principles. We make the case that lack of adherence to such principles, through current practice of reducing everything to incremental cost effectiveness ratios, leads to contradictions (in which) conclusions could be harmful to patients' health. Misuse of the incremental cost effectiveness ratio may lead to inefficient treatments being adopted. Making adoption of the recommendations of NICE compulsory adds a further threat"* (BMJ 2002;325:891-894).
31. In his 2004 BMJ article, Professor Rawlins from NICE stated that a QALY over £25,000 would need a special reason. Using the figures provided on page 2007 in the full NICE Guideline, the cost of a QALY for the recommended management is £16,036 (which is well below the cost-effectiveness cut-off of £25,000). Rawlins' quote seems to come close to admitting that as long as the costs are low, NICE is happy to recommend clinically ineffective procedures. In the case of ME/CFS, even though there is no evidence whatever of the clinical effectiveness of GET, NICE still recommends it and is willing to pay for it, seemingly simply because the cost is low. This is unreasonable.
32. As far as GET is concerned, there is no evidence at all of cost-effectiveness: the single study which attempted to demonstrate that GET is more (or indeed less) effective than CBT was unable to show any difference between CBT and GET (McCrone P et al: Psychological Medicine 2004;34:991-999). There are, however, at least five surveys of ME/CFS patients (all but one having been carried out by ME/CFS charities) showing evidence of clinical harm.
33. Any interested person who looks at the literature can easily deduce that there are only two studies that have considered the cost effectiveness of CBT. One was a study by Wessely et al (BJGP 2001;51:15-18). It showed no benefit from CBT. The other was the flawed Prins / Severens et al (Dutch) study referred to above. It

is from the flawed Prins study that NICE assigned the cost per QALY at £16,036 (on page 207 of the full Guideline). However, the Guideline itself expresses “*serious concern*” at the base-line differences between subjects and controls in the Prins et al study (i.e. at the difference in quality of life [QOL] between the subjects and the control group at the outset). This difference is significant, because the control group had a higher quality of life than the subjects, so from the outset, the study was not comparing like with like. **This baseline difference has a significant impact upon the cost-effectiveness analysis, a fact noted but inexplicably ignored by the Guideline Development Group (GDG). Given that from the outset, the control group had a higher QOL than the subjects means that uncorrected bias was introduced into the study, resulting in a biased analysis of the outcome. Irrationally, the NICE GDG decided not to let this major statistical aberration deter them from robustly recommending the regime so inappropriately favoured by Prins et al who themselves acknowledged that flaws in their study included self-selection of the participants and high drop-out rates (reasons unrecorded), as well as a base-line bias between subjects and controls.**

34. The reason given by NICE for not checking the trial data is unsustainable – NICE simply said it had no access to the Prins et al trial data. It is the case that anyone should be able to access the original paper and the trial data in order to check the calculations. If Prins et al refused to make their trial data available, NICE ought not to have relied upon this study. Since this study is the single study upon which the GDG relied for the alleged cost effectiveness of its recommended management regime, why did the GDG not insist on seeing the Prins et al trial data? **It is improper for NICE to have made a major decision that affects the welfare of a very large number of very sick people on unverified data from one single study, which even on its own admission, has serious limitations.**
35. Could it be that the GDG knew perfectly well that if they did see the trial data, they could not have relied upon the Prins et al study and they would then have had no evidence to support their claim that CBT is cost-effective (and it is common belief that this was to be the pre-determined outcome)? The Prins et al paper is unreliable and seriously inadequate as the single basis of NICE’s recommendation that CBT is cost-effective. No amount of “miscalculations” on the part of NICE will make this fact go away. NICE has tried to make bricks without straw and has consequently built a house that will not stand up.
36. The conclusion seems inescapable that either NICE “cooked the books” because it had to recommend something (and Government policy has long been to refuse to fund the many submitted sound applications for biomedical – not psychosocial – funding) or else NICE ought to be held accountable.