www.margaretwilliams.me

NICE Judicial Review: FACT MANAGEMENT

Margaret Williams **25th November 2008**

1. The political manipulation of the Guideline on "CFS/ME" (CG53) from the outset

The Scope was prepared by the National Collaborating Centre for Primary Care (NCC-PC) in conjunction with the guidelines commissioning and technical team at NICE (Prof Littlejohns' WS, para 20). The final version of the scope was signed off by the Director of Clinical Practice (in the case of CG53, by Dr Mercia Page, who has now left NICE).

The Scope states: "*specific interventions will include graded exercise therapy and psychological therapies (including cognitive behavioural therapy)".* This seems to prove that the decision to recommend CBT/GET was taken by the NCC-PC and NICE before the Guideline Development Group (GDG) had met (ie. before the disorder in question had been identified or defined and before the GDG had considered the suitability of such interventions).

This can only be construed as the intentional construction of "policy-based evidence" instead of the customary evidence-based policy.

2. The bias of the GDG members, including their competing financial interests

In the case of CG53, the required protocol concerning competing interests of GDG members was not observed.

Only those who could be relied upon to support the recommendation of CBT/GET were accepted as GDG members; there was no disease-specific expert and no representative from the oldest-established patient charity (The ME Association), nor indeed from any ME charity. This did not happen with other NICE Guidelines.

In particular, Dr William Hamilton, Dr Fred Nye and Ms Jessica Bavinton (physiotherapist) had significant financial interests in recommending CBT/GET (detailed in previous submissions).

GDG members' competing interests were not declared in the final Guideline as required by the Guideline Development Manual, which was a breach of procedure.

3. Failure to identify and define the disorder in question

This is the heart of the matter.

Although ME/CFS has been officially classified by the WHO as a neurological disorder in the ICD since 1969, ME/CFS is recorded as being deliberately omitted from the process of producing CG53 on "CFS/ME" and – in the absence of credible counter-evidence -- the GDG rejected the ICD classification of ME/CFS as a neurological disorder. This was perverse and irrational.

As a result, ME/CFS patients are actually being prevented by the NICE Guideline from getting better (because the Guideline recommends only psychotherapy to address the single symptom of "fatigue", whilst allowing the disease process to continue unabated and un-investigated).

By its refusal to consider the totality of the evidence-base about ME/CFS, the disease from which these patients suffer was not validated by NICE, so patients are still treated with contempt.

Perversely, the GDG rejected the use of the 2003 Canadian clinical case definition of ME/CFS that has been widely adopted and which clearly distinguishes between chronic "fatigue" and ME/CFS.

Instead, and without consultation, NICE created its own case definition of "CFS/ME" (which consists of "fatigue" plus one other symptom). This obfuscates the cardinal issue of correct identification of the disorder allegedly under discussion.

Fatigue as generally understood is not the central feature of ME/CFS, which is a combination of chronic, relapsing neurological, cardiovascular, immunological, neuroendocrine and musculo-skeletal abnormalities for which there are measurable and reproducible abnormalities. Its pathognomonic feature is post-exertional incapacitating exhaustion and the inability to sustain muscle power, accompanied by malaise, which bears no relationship to tiredness or "fatigue".

From the evidence of GDG member Dr Fred Nye, it is clear that NICE intentionally attempted to blur the distinction between chronic fatigue (CF) and ME/CFS by referring to both disorders as "CFS/ME" (based on the inclusion of patients with a large number of "somatic" – i.e. psychiatric -- symptoms), which means that people with the distinct disorder ME/CFS (ICD-10:G93.3) are likely to attract the psychiatric label (ICD-10:F48) because they have been subsumed within the heterogeneous label "CFS/ME".

This would be to the advantage of the medical insurance industry, since most medical insurance policies exclude psychiatric disorders from benefit eligibility. The medical insurance industry was represented on the GDG by Dr William Hamilton and Ms Jessica Bavinton, and possibly by psychiatrist Dr Alastair Santhouse who, with Professor Simon

Wessely, is one of the two psychiatrists in the Chronic Fatigue *(sic)* Research and Treatment Unit at King's College Hospital London, and Wessely is deeply involved with the medical insurance industry (as are many members of the Wessely School, including those who advised NICE about the desired outcome of CG53 "behind the scenes").

ME/CFS is a serious multi-system organic disorder; it can be fatal, and numerous Coroners have recorded it as the cause of death. The loss of function and extreme suffering experienced by patients is often described by experts in the disorder as "devastating" and ME/CFS has been compared with late-stage HIV AIDS, terminal cancer and heart failure. Many sufferers are house or bed-bound. The Chief Medical Officer's Working Group Report of January 2002 stated that there is no cure for ME/CFS.

In CG53, NICE attempted to marry together two opposing models of the disorder by using the constructed term "CFS/ME" but has failed to do so, because (i) it is impossible to combine two different disorders and impose the same management strategy for both disorders (ii) the GDG was specifically directed not to consider the totality of the existing evidence-base about the nosological entity ME/CFS but to focus on "an inclusive approach" that captured people who are merely "tired", which has placed people with ME/CFS at a significant disadvantage.

The biomedical model of ME/CFS is evidence-based and is predicated on the significant number (over 4,000) of peer-reviewed papers describing the biomedical anomalies that have been demonstrated in ME/CFS; this evidence was intentionally ignored by the GDG.

The psychosocial model of "CFS/ME" is based upon the unproven beliefs of Wessely School psychiatrists and others who work for the medical insurance industry that "CFS/ME" is an "aberrant illness belief" that is perpetuated by deconditioning and "over-vigilance to normal bodily sensations" and that it can be greatly improved or even "cured" by mind-altering behavioural interventions and aerobic exercise. Their "evidence" consists of five random controlled trials (RCTs) of cognitive behaviour therapy (CBT) and five RCTs of graded exercise therapy (GET) undertaken on a heterogeneous population. This "evidence" was accepted by NICE, even though some of those trials use the Wessely School psychiatrists' own Oxford criteria which, by definition, exclude those with ME/CFS but expressly include those with psychiatric disorders in which "fatigue" is a dominant feature.

The wealth of scientific biomarkers that distinguish ME/CFS from "chronic fatigue" (CFS/ME) include the following:

- abnormal brain scans (SPECT & PET scans) and MRI scans that are consistent with organic brain syndrome, showing focal demyelination and/or oedema in the sub-cortical area
- dysregulated HPA axis
- dysregulated antiviral pathway
- cardiac abnormalities

- abnormal capillary flow
- low circulating blood volume
- abnormal ergometry test (indicating immediate anaerobic threshold)
- haemodynamic instability
- abnormal immune profile
- gene profiling (in one US study ["Transcriptional Control of Complement Activation in an Exercise Model of (ME)CFS"; Sorensen et al], expression of several complement genes remained at a higher level in ME/CFS subjects before and post-exercise; this indicates the lack of a necessary response [acute phase transcriptional response] by these genes, which may lead to uncontrollable inflammation-mediated tissue damage. In the UK, Kerr has demonstrated differential expression in 88 genes, 85 of which were up-regulated and 3 were down-regulated; highly represented functions were haematological disease and function; immunological disease and function; cancer, cell death, and immune response and infection: J Infect Dis 2008:197(8):1171-1184).

Referenced evidence of higher rates of cancer in ME/CFS has already been provided.

All the above investigations are effectively proscribed in CG53.

At para 69 of NICE's Detailed Grounds of Resistance, Charles Bear QC states: "*Page 36 of the Guideline contains guidance as to certain diagnostic tests which should not be routinely used, and as the GDG concluded that patients were unlikely to benefit from such intervention the recommendation is entirely rational"*. How can it be "entirely rational" to deprive patients of diagnostic tests that are able to prove if the patient has nosological ME/CFS (which could mean that GET would be contra-indicated, so it would therefore be in patients' best interests not to undergo NICE's recommended intervention that is known to make such patients considerably worse)? Furthermore, there was not a single disease-specific expert on the GDG, so no-one on the GDG was clinically competent to make such a decision.

In relation to drugs that in other countries have been shown to be helpful in ME/CFS, Professor Richard Baker (Chairman of the GDG) states at para 87 of his WS: "*I would hope that the recommendation against their use will dissuade practitioners from using them",* and at para 93 he states: "*It appears to me that the Claimants want the Guideline to recommend anti-viral treatment for CFS/ME because this fits in with their preferred theory that CFS/ME is a 'biomedical' condition"*. This demonstrates Professor Baker's lamentable lack of knowledge of the topic.

Patients who wish to try interventions that NICE has effectively proscribed are simply abandoned: see the ME Association's magazine "ME Essential", November 2008, issue 108, pp 36-37: "*Patients are routinely denied access to these drugs because they are unable to find a doctor willing to prescribe them. This is outrageous, and one of the main reasons why ME patients are so angry and alienated from the medical profession".*

On the issue of proscription, Professor Peter Littlejohns (Clinical and Public Health Director of NICE since its inception in 1999) states at para 58 of his WS: "*The NHS is expected to take into account all the NICE recommendations by permission rather than by proscription".*

For NICE to claim in its Defence that nothing was proscribed in CG53 and that clinicians retain clinical autonomy is to mislead the Court. In his Detailed Grounds of Resistance, Charles Bear QC states at para 22: "*Guidelines do not override clinical judgment"* but this needs to be compared with what Professor Peter Littlejohns stated on the record at the APPGME held on 22nd February 2007. The following transcript is taken from an audiotape recording of the proceedings: ***"(CG53) will form part of the National Clinical Standards. It will form part of every clinician's assessment of whether they are performing to best practice, and (they) will be held to account to that through the normal processes, including the Health Commission assessing whether local communities and professionals have actually taken NICE fully into account in making their decisions".***

(For the avoidance of doubt, there is no problem about the use of this audiotape, because at the beginning of the session, the Chairman, Dr Des Turner MP, asked that, if proceedings were being recorded, those recording them should place their tape recorders in view, so audiotaping was known about and was permitted).

It would take a brave clinician to stand up to -- and defy -- the powers of the State; the reality is that NHS clinicians dare not do so, which effectively means that NICE operates dictatorial control over state medicine in the UK.

By effectively proscribing appropriate testing for ME/CFS patients, NICE has compounded the existing confusion for doctors, patients and paramedical staff throughout the NHS.

CG53 is ineffective in providing assistance to clinicians about diagnosing ME/CFS, because it does not address the clear diagnostic criteria for ME/CFS. ME/CFS should have been recognised for what it is – a complex neuroendocrine immuno-vascular disorder affecting all bodily systems that is a classified neurological disorder (WHO ICD-10: G93.3).

On 6th October 2004, the Director of the US Centres for Disease Control (CDC), Dr Julie Gerberding, is on record as confirming: "*A component of ME that continues to elude efforts to consider it as the same illness as CFS is the presence of measurable neurological findings in individuals with classical ME. A careful reading of the second edition of Dr Ramsay's treatise entitled 'Myalgic Encephalomyelitis and Post-Viral Fatigue States'* (Gower Medical Publishing, 1988) *also identifies a number of other unique characteristics that differentiate CFS from ME".*

Dr Gerberding has confirmed that this is still the case today (Co-Cure NOT, ACT: 20 November 2008).

Dr Gerberding specifically stated: "*Unfortunately, the illness is not a 'one size fits all' situation"*, an observation that NICE expressly disregarded in that CG53 recommends blanket CBT/GET for everyone with "CFS/ME" in the UK.

NICE also disregarded the recommendation of the WHO on this same issue. In May 2006, the WHO published a report on NICE ("The Clinical Guideline Programme of NICE: A Review by the WHO"; pp 67. It stated: "*The report contains a series of recommendations on how NICE could further develop the guideline development process"*). It contained a number of key recommendations. The first was: "*NICE should develop several types of clinical guidelines, rather than continue to use the current 'one size fits all' approach"* and that guidelines should be *"more focused".* In its response of January 2007 to the WHO report's recommendations ("National Institute for Health & Clinical Excellence: Special Health Authority: The Clinical Guideline Programme: A Review by the World Health Organisation (WHO): Response to Recommendations"), NICE stated: "*We broadly agree with the recommendation".* Despite this, in CG53 that was published in August 2007, NICE advocates a 'one size fits all' approach by recommending CBT/GET for every person, child and adult, with "CFS/ME" in the UK (even for the severely affected, who are to undergo "elements" of CBT and GET).

For the record, the WHO key recommendation 4 warns NICE of the need to review all disclosure statements on competing interests prior to the commencement of GDG meetings, but NICE's response states that it would not be feasible to do this and moreover states: "*Nor do we consider it necessary"*.

The WHO key recommendation 5 states that NICE should ensure – throughout the preparation of the document – *"the involvement of clinicians familiar with the topic"*. NICE's response is: " *We will ensure appropriate GDG involvement"*. This did not happen with CG53.

The WHO key recommendation 8 sets out the need for transparency; NICE's response is: "*We agree that the relationship between the evidence and the recommendation should be transparent",* but this did not happen with CG53 (see below).

The WHO key recommendation 12 emphasises the need for NICE to strengthen its collaboration with national and international groups; NICE's response is: "*NICE already has strong collaborative links with national professional organisations and research groups"*. It also states that it has established links with other guidelines organisations in North America but then goes on to state: *"These links need to be balanced with the Institute's primary responsibility to prepare and disseminate guidance".* Despite the WHO's recommendation that NICE should strengthen its collaboration with international groups, NICE declined to engage with the Canadian Guidelines group.

Many published papers point to the need to distinguish between ME/CFS and "CFS/ME", in other words, the need to differentiate a biomedical disorder from psychiatric illness (for example, Jason et al; JCFS 2004:12:1:37-52); all were disregarded by NICE.

It is not just in the UK that CG53 has been rejected as unfit for purpose: an Australian group based at the Centre for Neurological Support in Nedlands, WA, (founded in 1997 and whose members have extensive knowledge and understanding of ME/CFS) comments as follows:

"The following CFS guidelines drew widespread criticism upon publication from both those affected by the disease as well as a significant number of health professionals. Foremost amongst many inadequacies they contain are:

- *use of vague and inaccurate descriptions of the disease*
- *use of inappropriate and potentially harmful treatment recommendations*
- *a failure to clearly differentiate between ME/CFS and the ubiquitous symptom of 'chronic fatigue'*
- *poor understanding of the crucial issue of 'severity' and the potential for ME/CFS to devastate the lives of those it affects"*

see: http://www.mecfswa.org.au/Patient_Resources/Unhelpful_Guidelines

Despite the repeated claims in CG53 that the patient is in charge of the clinician/patient relationship and that the doctor does have clinical autonomy, there is extensive evidence on ME/CFS message boards and websites that such is not the case.

Indeed, Professor Peter Littlejohns himself is on record at the APPGME meeting on 22nd February 2007 as confirming that **compliance with NICE recommendations will be imposed on clinicians.**

It is worth repeating what Professor Littlejohns actually stated (and that there is an audiotape recording of this): "*(A) report that comes out even from the CMO (*Chief Medical Officer*) doesn't have the standing within the medical profession and managerial performance structures within the NHS that NICE guidance does, because this guidance will form part of the National Clinical Standards. It will form part of every clinician's assessment of whether they are performing to best practice, and (they) will be held to account to that through the normal processes, including the Health Commission assessing whether local communities and professionals have actually taken NICE fully into account in making their decisions".*

In their Witness Statements, Professors Richard Baker and Peter Littlejohns make much of the fact that the Guideline emphasises that patients are in control over whether or not to undergo CBT and GET. Not only is the medical profession usually averse to a "working partnership" with patients (especially with those deemed to suffer from an alleged behavioural disorder such as "CFS/ME"), but a NICE publication gives the lie to such a possibility: "*NICE in the British system can provide clear direction and (can) **expect that this will be implemented**"* ("Why is the US interested in NICE?". Andrea Sutcliffe, Chief Executive, Appointment Commission, Former Deputy Chief Executive, NICE; 6th November 2007).

Without addressing the core issues, the efforts of the GDG to provide diagnostic and management advice are ineffectual and may indeed constitute actual misguidance.

This means that extremely sick people who cannot afford to seek private medical care will continue to be coerced into an inappropriate and potentially damaging management regime or else they will be abandoned by the State.

4. Adverse reaction notification

ME/CFS patients are concerned about the facilities for reporting adverse reactions to non-drug interventions such as GET; they want to know what are the contra-indications, what are the special precautions, and what are the interactions, and if adverse reactions to GET are collated nationally (since the yellow card reporting system does not apply to non-drug interventions).

It is claimed by NICE that if GET is delivered by a "specialist", it is relatively safe, but major surveys carried out by the ME charities have shown that 30 –50% of participants have been made worse by GET. If that were a drug, it is almost certain that the drug would have been withdrawn with such a high percentage of adverse reactions, yet NICE advocates GET for everyone with "CFS/ME" in the UK and has chosen to ignore the charities' evidence.

"The Guideline Development Process: an overview for stakeholders, the public and the NHS" (2007) states that in the production of a Guideline (unlike a Technology Appraisal): "*There is no appeal stage in the Guideline development process"* (page 24). The 2004 version (ie. the one in use at the start of the CG53 process) said exactly the same.

Many people with ME/CFS and their carers wrote to NICE expressing their concern, sometimes by Recorded Delivery, but letters were unacknowledged and were apparently ignored.

5. Patients' dissatisfaction with the "CFS" clinics that are delivering NICE's recommendations

Throughout the production of CG53 (for example, in the 1,000 pages of submissions of concern about the draft guideline, at the Implementation Planning Meeting held on 5th October 2006 and at the APPGME on 22nd February 2007), NICE officials were warned time and time again that CBT and GET were not only unsuitable, ineffective and potentially harmful, but also were not cost-effective. The Medical Adviser to the ME Association (Dr Charles Shepherd) informed NICE that the likely cost of implementing their intended regime was in the region of £180 million. All such warnings and concerns were repeatedly and studiously ignored by NICE.

Consequently, people with ME/CFS are now compelled to attend the "CFS" Centres (run by a "Clinical Champion") and undergo CBT/GET if they are to keep their State benefits. If they do not attend, they are deemed not to want to get better and return to work, so their benefits are stopped.

On 10th November 2008, a posting on an ME/CFS list said: "*Any patient representative who challenged this service for CFS/ME was quickly and ruthlessly squashed, as evidenced by the experience of others on this list".*

On 13th November 2006, another posting on the same list said: "*The position of Manchester Clinical Champion was never advertised and a psychiatrist came from no-where and got the job. The large local ME clinic, run for ten years by specialists who think ME is a biological illness, has now been closed. The reason given was that it was not needed anymore as the psychiatrist is now providing services. Virtually all of the Clinical Networking Co-ordinating Centres are headed by those who think ME is a mental / psychological illness".*

When ME/CFS patients wonder about interventions such as immunoglobulin that is used in other countries and ask "*on what basis was it decided that immunoglobulin was not suitable for ME/CFS patients?"*, the answer is the same: Local Multi-Disciplinary Team (LMDT) leaders repeat, mantra-like: "*We can only follow the NICE CFS/ME Guideline".*

6. <u>Misrepresentation in the media as a result of the NICE Guideline CG53</u>

Following an article in Liverpool Daily Post on 12th May 2008, Dr John Greensmith, himself an ME/CFS sufferer, sent the following response:

"Journalists are all led to believe that there is a network of Co-ordinated Clinical Centres to which ME patients are referred by GPs and that, although not fully recovered, tens of thousands have been helped by the recommended treatments CBT and GET. In practice, these Centres are not co-ordinated at all but operate autonomously under a so-called 'Clinical Champion', most often a psychiatrist, working with clinical psychologists, in the psychiatric department of a hospital. Statistical analysis (is) distorted by having people with ME bundled indiscriminately with all patients having the symptom of chronic fatigue. Claims that tens of thousands of ME sufferers have been 'helped' are not supported by any way in which this 'help' is observable or measurable. The statistics are seriously flawed. There is a massive drop-out rate often greater than 50%, which is simply discounted from any analysis, instead of properly being seen as contributing to the failure rate of the treatment. Nor are there adequate follow-ups to (ascertain) how many have relapsed after treatment. We know, from hard experience, that some become irrecoverably worse, in a wheelchair or bed-bound, from which they do not regain even their previous levels (of functioning). We appeal for an end to this propaganda, which is misleading journalists and their readers".

7. More failures of procedure

In addition to the failures of procedure already submitted, there is the important issue of the change of procedure during the production of CG53.

NICE is permitted to make minor changes during the production of any particular Guideline, but if it wishes to make major changes to the protocol, it is obliged to contact all stakeholders and inform them of the change.

At the start of the production of CG53 in 2004, the official timeline on the NICE website listed two consultation processes.

Although for two years (from 2004 to 2006) it was scheduled that there would be two consultations for CG53 (one on the first draft of the Guideline and another on the final draft of the Guideline), in April 2006 NICE decided to drop one of the two consultation processes. These major changes should be recorded, but in this case there seems to be no audit trail. If there is a Guideline in process, NICE is required formally to inform all stakeholders that there has been a change in procedure. Importantly, at this same time (early 2006) there was a secondary consultation in process concerning proposed changes to the Guideline Development Manual, in particular about whether or not NICE would be permitted to drop the second consultation on draft Guidelines. Before the outcome of that secondary consultation was known, the references to two consultations on draft Guidelines were removed from the NICE website. It was not until the end of the secondary consultation period (May 2006) that CG53 stakeholders discovered that they were to be denied a second consultation on CG53.

The rules (set out in The Guideline Development Process: An Overview for Stakeholders, the Public and the NHS, February 2004: 1.1.1. Interim Updates) are clear:

"In some situations, it may be necessary to make small changes to the process. For small changes to be put in place without stakeholder consultation, they must fulfil all the following criteria:

- *a fundamental stage in the process is neither added nor removed*
- *one or more of the stakeholders will not obviously be disadvantaged*
- *the efficiency, clarity or fairness of the process will be improved.*

Stakeholders in guidance under development at the time of change will be notified if they are affected by the change".

This significant change of procedure was recommended by Dr Mercia Page on 20th October 2005. Although a "public consultation" period is listed as being from December 2005 to January 2006 (which is during the Christmas and New Year recess when many

stakeholders would have been away), it seems that NICE did not contact the stakeholders, for example, key ME charities have no record of being contacted by NICE about this major change of protocol. Those key charities include The ME Association, TYMES Trust; The 25% ME Group for the Severely Affected and ME Research UK. The Medical Adviser to the ME Association has provided written confirmation that the ME Association was not notified of this major change in protocol, as has the Chairman and Director of the 25% ME Group for the Severely Affected.

As stated by Charles Bear QC in his Detailed Grounds of Resistance at para 19.25, there was a very considerable response from stakeholders to the first consultation for CG53. GDG member Dr Fred Nye is on record about this: "*When the draft Guideline was sent for consultation, it provoked an unprecedented response. There was more than double the usual volume of replies"* (J Inf 2007:55:6:569-571).

It is therefore remarkable that NICE decided to drop the scheduled second consultation for CG53, especially given that when there has been a larger than usual response to a draft guideline (as was the case with CG53), NICE actually launched a second consultation, as in the document "2007/015: NICE launches second consultation on draft recommendations relating to birth settings" (22nd March 2007). Andrea Sutcliffe, then Deputy Chief Executive at NICE, went on record about the need for a second consultation when there had been a large volume of feedback to the first consultation: "*The sheer volume of feedback we received on the first draft of this guideline shows how vital it is that we get the recommendations right. We look forward to receiving the comments from our stakeholders and will consider them carefully when developing the final guideline".*

Once again, it seems that NICE displays double standards in that it decided to debar the ME/CFS community from the right to a second consultation but it actually offered that right to stakeholders in another Guideline. This is notable, since the "Guideline Development Process – an overview for Stakeholders, the Public and the NHS" 2007 is clear: "*Some Guidelines that were at a late stage of development in April 2006 are being produced by the process described in the 2004 edition"* (and CG53 had then been in production for two years, with an estimated one year to go, so it should have continued under the two consultation procedure).

The issue of NICE's decision to omit the second consultation for CG53 was discussed at the APPGME on 22nd February 2007, when Professor Littlejohns made this important change of procedure look "squeaky clean" when such seems not to have been the case.

Much concern was expressed at the removal of the second consultation process, and the Medical Adviser to the ME Association (Dr Charles Shepherd) asked Professor Peter Littlejohns: *"Would you foresee that this (will be) a take it or leave it situation as far as we're all concerned?"*, to which Professor Littlejohns replied: *"It's one consultation, so you'll see the document in August. Originally we started our programme with two consultations. This (Guideline) is going through the process where you have one (consultation)".* The Medical Adviser responded: *"(So) we're not going to see it until you*

actually put it out for publication?", to which Professor Littlejohns replied: *"Yep".* The Medical Adviser then asked Professor Littlejohns: *"Would you consider doing a second consultation?"* and a member of the public said: "*You wanted everything to be transparent and open, and particularly you said you wanted the issues arising in the consultation to be answered (but) that's not going to happen unless you have a second consultation"*. Professor Littlejohns replied: "*Well, we started with second consultations, and the NICE Board decided that if there was sufficient consultation (on) one occasion, then issues around timelines and getting the Guideline out to be useful to professionals and patients was what was important, and that was a NICE Board decision".* The Chairman of the APPGME, Dr Des Turner MP, then asked Professor Littlejohns: "*But would you perhaps take back the view (to NICE) that it's so very important to have these guidelines correct, and that we don't have a set of guidelines that could end up doing more harm than good, and that we address some of the actual hazards that we've heard so graphically about?".* The Medical Adviser to the ME Association then said that there was a *"unique situation here – you've got a guideline which from what I understand has never had so much public comment (directed) at it: is that right?"*, to which Professor Littlejohns replied: *"We certainly get a lot of public comment on a lot of our guidance (but) I think in terms of volume……"*, whereupon the Medical Adviser to the ME Association interrupted: *"Volume? And probably in terms of concern"*. Professor Littlejohns continued: "*The reason why we're doing today* (ie appearing before the APPGME) *is to address these concerns"*. At this point, the Chairman, Dr Des Turner, said: *"There are clearly some core issues which cannot…..you know, though, what they are; (you) heard what they are, so I don't need to spell them out, but particularly the recommendations concerning CBT and GET need to be very carefully, very very carefully, gone over, it seems to me, and it would be worth the process taking another couple of months. If it's got approximately right, if you can at least try and satisfy 95% of the population that you're addressing, it would be a great achievement and worth waiting for".* Professor Littlejohns responded: "*I take what you're saying, Chairman, but obviously you don't expect me to make a decision, because it is the Guideline executive NICE Board that makes the decision"*. Dr Turner rejoined: "*We're giving you a message to take back"*, to which Professor Littlejohns replied: "*I'll take back the message that you would prefer a delay in guidance"*. Dr Turner then said: "*Yes, and (we need) sight of what you imagine will be the final report before it is finally finalised"*, to which Professor Littlejohns replied: *"No. We either need to formally consult or not. (Anything) in between I think would cause difficulties".* At this point, the Medical Adviser to the ME Association asked Professor Littlejohns: *"Would it not be helpful to NICE to get some sort of feeling as to what the patient community (needs) on this before you just publish it regardless of the patient community? This is not the spirit of the patient-led NHS"*, to which Professor Littlejohns replied: "*I agree".*

Notwithstanding Professor Littlejohn's expressed agreement, it is the case that stakeholders' comments and concerns were suppressed by NICE until after the publication of the Guideline and that no second consultation process took place.

It is the case that in the same month that NICE decided to drop the second consultation process (April 2006), the Questionnaire was sent out to CG53 stakeholders, and that there

were serious issues of incompetence concerning the Questionnaire (including "misprints" relating to questions 29 – 61, making a nonsense of responses to over one third of the questions, but respondents were given only two days to correct their responses, and NICE's insistence that all responses had not only to be online, but on their own proforma, which was impossible for many sick people) so a full, fair and transparent consultation process did not take place in the single consultation as required by the Guideline Development Manual (for details, see documents previously submitted). In his Detailed Grounds of Resistance at para 14, Charles Bear QC misleads the Court when he asserts: "*The GDG is expected to follow standard procedures set out in NICE's Guideline Development Manual and did so in respect of the impugned Guideline".*

Another issue which was addressed by Professor Littlejohns at the same APPGME was the matter of random controlled trial evidence (RCTs). What Professor Littlejohns is recorded as saying on 22nd February 2007 differs substantially from what he says in his Witness Statement on behalf of NICE.

In his WS at para 26, justifying the over-reliance by NICE on just one level of evidence, Professor Littlejohns states: "*RCTs are the internationally recognised gold standard of evidence"*. However, he is on record (with audiotape evidence) as expressing a different view to Members of Parliament on 22nd February 2007, when he said: "*All our guidance is produced under the principles of being based on the best available evidence. That evidence is not Randomised Controlled Trials – it's the best evidence to answer specific clinical questions that are relevant to patients, service users, and professionals. I took a paper to the NICE Public Board meeting not a long time ago* ***in which we all accepted and recommended to all its Guidance Development Bodies that no longer could you adopt a hierarchy of evidence automatically. That is now not NICE policy. What NICE policy is about is information. It's identifying the relevant key clinical questions and then taking into account ALL the relevant evidence.*** *Now obviously, RCTs have got to be taken into account, but* ***professional experience*** (and) ***patients' experience is all included****".* At this point, Tony Wright MP said: "*We have to be very careful that Guidelines themselves aren't used to give the medical profession the protection against mistakes that will be made if they go through under the current conditions. I really think they need to take on board all of the comments that have been made – and I'm sure that they have been made very well – during the consultation process. I'd be interested to know when they finally come up with the report what elements of the consultation process documents were accepted and those that were rejected (and) the reasons why they were rejected".* Professor Littlejohns replied: "*All the comments will be presented and those that have been agreed, and changes in the guidance, will be documented. (For) those that aren't incorporated, the reason will be there*".

Once again, promises that were made by NICE were broken, because GDG member Richard Eddleston, a patient representative (this is a misnomer, because "patient representatives" were not there to represent the views of anyone apart from themselves) is on record as saying that he believes the submissions that were handwritten (ie. not online) did get "lost": on 15th April 2008 he confirmed this on an ME messageboard: "***I think there were areas where the patient voice was not listened to and that there were***

deficiencies with the process. As for those who submitted comments on the draft Guidelines as individuals, I suspect that their comments did get lost. It was near enough an impossibility reading all the stakeholder comments, let alone the comments from individuals as well*".*

This is a matter for concern, because the Guideline Development Manual is clear: the rules are that Guideline developers are obliged to address every submitted concern and to answer each and every one *"as fully and factually as possible"* and developers must "*acknowledge that each point has been seen and has been understood"* (Guideline Development Manual 2006:14.1.2, p 81).

Even with online submissions, NICE failed to do so. For example, SWAME (South West Alliance for ME) asked a direct question: referring to a paragraph in the draft Guideline, they wrote: "*This paragraph is unhelpful and displays a disingenuous way of using one statement to point to another. What is not mentioned is the fragile nature of any evidence for any strategies at all, including those recommended. As it says in the draft Guideline that research is currently being undertaken to evaluate the evidence for the (recommended) approach, does this refer to the PACE trial?".* (The PACE trial is the on-going MRC trial of CBT and GET for "CFS/ME" run by the Wessely School psychiatrists). The GDG did not answer the question; the comment offered to SWAME (and to nearly all other the enquiries on this topic) consisted of: "*The guideline has been revised"*. Not to answer specific questions is in breach of procedure.

References to the MRC trial that appeared in the draft Guideline were omitted from the final Guideline, for example: "*Research is currently being undertaken to evaluate the effectiveness of this approach"* and *"Pacing is the subject of a current research trial which aims to see if pacing is a useful approach"* do not appear in the final version. No-one could challenge NICE on this because the opportunity to do so (by way of the usual second consultation) was removed by the NICE Board.

This leads to a very important consideration: it seems that NICE was trying to avoid mention of the current MRC trials on "CFS/ME" in the final Guideline. This may well be because the MRC trial investigators hold views about the RCTs upon which NICE relied for its "evidence-base" that cast doubt on the wisdom of relying on those RCTs.

For example the MRC investigators are on record as noting that the RCTs were *"criticised for being too small, too selective and for using different outcome measures"*. The MRC investigators also note that patients have been harmed by CBT and GET: *"patient organisations' surveys have reported adverse effects"*.

Furthermore, the Guideline makes no mention of the conflicts of interest of GDG member Jessica Bavinton as a PACE trial "*treatment leader"*, nor of psychologist Hazel O'Dowd as a "CFS Centre leader", nor of Professor Anthony Pinching's involvement with Simon Wessely (Pinching advised Wessely about "*design and execution").* Both O'Dowd and Pinching are singled out in the Guideline for special thanks for their input into CG53, but no declaration of their competing interests is recorded.

There are interesting references to on-going trials on the NICE website (for example on organ preservation, on carmustine implants), all indicating that appraisals / guidelines committees should await the outcome of on-going trials before producing guidance. In the case of CG53, numerous stakeholders urged NICE to await the outcome of the MRC trials (for example: Action Against Allergy said: "*How far has (the MRC trial) progressed and with what result? This could surely have a bearing on the considerations for drawing up the Guidelines"* and Action for ME said: "*It does seem sensible that the NICE Guidelines should be integrated with other programmes such as the MRC)".*

The MRC PACE trial started in Autumn 2004 and is due to be completed in 2009. For reasons that have not been explained, in the case of CG53, NICE chose not to abide by its own policy of awaiting the outcome of MRC trials on the disorder that was the subject of its Guideline.

Importantly, NICE's own guidance (for both appraisals and guidelines) is that if MRC trials on the topic under review are still on-going, then NICE must await the outcome of those MRC trials before producing guidance on that topic. The Minutes of the NICE Committee in question were placed in the public domain and, whilst they relate to an Appraisal rather than to a Guideline, the precedent exists.

The relevant guideline development manual points to a discussion paper from the Department of Health on the timing and selection of topics (March 2002) for both appraisals and guidelines, which says: *"Proposed criteria: is the evidence base sufficient to develop robust guidance across all the interventions to be covered by the proposed guidance?"*. When there is insufficient evidence for definitive guidance, NICE's own guidance methodology affords NICE the "Only in Research" option. Even though NICE revisited this issue in January 2007, in the case of CG53, this was disregarded by the GDG and the Guideline was published in August 2007 in advance of the outcome of the MRC trials.

8. <u>The issue of "transparency"</u>

Both Professors Baker and Littlejohns emphasise in their respective Witness Statements that the process of the production of CG53 was "transparent". Neither mentions the requirement for GDG members to sign a confidentiality agreement (The Guideline Development Process: An Overview for Stakeholders, the Public and the NHS, April 2006): "*NICE has developed a code of conduct for GDG members and external members. This includes a confidentiality agreement form*". Specifically, GDG members are not permitted to comment on any discussion or documents relating to a Guideline. The requirement of NICE for GDG members to be gagged is not in accordance with the concept of "transparency".

9. The issue of "controversy"

In its Defence, NICE refers to the "controversy" surrounding "CFS/ME" and attempts to rely on the fact that the Court cannot debate the "biomedical" versus the "psychosocial" models of "CFS/ME", and also argues that the aetiology of the disorder was not within NICE's remit.

This expedient introduction by NICE of the "controversy" issue seems to be a ploy to deflect attention away from the key issue, namely that NICE failed to consider the totality of the evidence-base about the disorder in question (in order to prevent the Court from considering whether or not this was a blatant failure of procedure).

Given that both Professors Baker (WS para 43) and Littlejohns (WS para 15) have already introduced the "controversy" issue, surely the Judge is entitled to know to what they are referring.

The only "controversy" in this Judicial Review is the challenge to the refusal of NICE to accept the international evidence that ME/CFS is a classified neurological disorder, and NICE's determination to turn it into a completely different disorder, which is a clear breach of procedure.

However, GDG member Dr Fred Nye describes "CFS/ME" as "*the most controversial illness ever"* (J Inf 2007:55:6:569-571).

GDG members Drs Crawley and Nye state: "*The aetiology of CFS/ME is controversial"* (Behind the medical headlines, April 2007).

GDG member Dr William Hamilton refers to *"this controversial condition"* and states: "*The subject of CFS/ME is controversial"* (http://www.eguidelines.co.uk/links/gip/vol_10/dec_07/hamilton_cfs_dec07.php)

NHS Plus states: "*The nature, pathology and aetiology are controversial"* ("Occupational aspects of the management of CFS: a national guideline"; 4th October 2006)
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4139436

It is not the Claimants who have introduced the "controversy" issue, but the Defence itself.

Conclusion

On 24th November 2008, The Daily Telegraph carried an article by its Medical Editor, Rebecca Smith, ("Victory for arthritis patients as NICE to review restrictions on drugs") which drew attention to NICE's Internal Appeal Panel's decision to review NICE's guidance that drugs for patients with rheumatoid arthritis should be restricted. Ailsa Bosworth, Chief Executive of the National Rheumatoid Arthritis Society, said: *"We are delighted that NICE have listened to patients and clinicians and agreed to re-look at the evidence".* Responding to this decision, a spokesman for NICE said this Internal Appeal process "*ensured that NICE produces guidance in a fair and reasonable way".*

There is significant evidence that the NICE Guideline on "CFS/ME" was not produced in a *"fair and reasonable way"* and that NICE did not listen to patients and clinicians. Not to do so is in breach of procedure.

The NICE Guideline on "CFS/ME" is ill-founded and has failed both the ME/CFS community and the medical profession.

That NICE has been shown to be compromised is evidenced by decision after decision that has over-turned its guidance: NICE cannot be defended on a number of issues on which it has ruled, including its Guideline on ME/CFS.

NICE is clearly an instrument for the implementation of Government policy, which is not serving the needs of sick people or of the NHS which was created for that purpose.