Inadequacy of the York (2005) Systematic Review of the CFS/ME Medical Evidence Base.

Comment on Section 3 of

The diagnosis, treatment and management of chronic fatigue syndrome (CFS)/(ME)

in adults and children

Work to support the NICE Guidelines

carried out by

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October 2005

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Comment.

As a summary of evidence-based medicine for the treatment of Chronic Fatigue Syndrome, Section 3 of this systematic review from Bagnall et al. is a failure.

Evidence-Based Medicine: What it is and what it isn't.

David L Sackett, (BMJ 1996; 312: 71-2).

"Evidence-based medicine is not restricted to randomised trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions."

"And if no randomised trial has been carried out for our patient’s predicament, we follow the trail to the next best external evidence and work from there".

"The practice of evidence-based medicine means:

1. Integrating individual clinical expertise with the best available external clinical evidence from systematic research.

2. The more thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care."

"Evidence-based medicine is not "cook-book" medicine. … it requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient-choice."

This latest Bagnall et al. review is deficient under each of these headings, (although they may have been restricted by their remit). The reviewers have (1) failed to realise the limitations of the RCT (randomised controlled trials) evidence base, (2) failed to integrate the great body of literature on individual clinical expertise, and (3) failed to fully reflect the rights, preferences and choices of the patient community.

Index.

1. Inadequacy of RCT evidence base for CFS/ME.

2. Concerns about existing RCTs for GET (graded exercise therapy) & CBT (cognitive behavioural therapy).

3. The American experience.

4. Experience in Australia, Canada & New Zealand.

5. Publication bias.

6. Imposed top-down therapy initiatives rejected by CFS/ME Patients.

7. Counselling.

8. Treatment choice - the Australian model.

9. Reports of adverse GET events neutered.

10. York Review- The Dog That Did Not Bark.

1. Inadequacy of the RCT evidence base for CFS/ME.

Evidence-based medicine is not restricted to randomised trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions. - David Sackett, "The Father of Evidence Based Medicine".

Bagnall et al. have restricted their choice of evidence to randomised and controlled trials. While this may be normal practice in other areas of medicine, it is an inadequate approach for CFS/ME, where the evidence base is so small.

Senior UK researchers are the first to admit that there is a serious deficiency of good-quality research on CFS/ME.

"The evidence on which to base clinical decisions is slender", reported the editors of a BMJ survey of treatments.[1]

Referring to the "*weakness of the CFS evidence base*", one very senior British researcher remarked that

"*there is little evidence available for review and much of what exists is poor quality, made worse by the chaos surrounding case definitions, nonstandardized outcome measurements, and variations in study duration and follow-up*."[2]

1.2 Deficiency of RCTs cited by the Bagnall et al. .

They are old, ranging from 1992 to 2001. Bagnall reviewed much the same papers in 2001.

They are mostly UK based, "Anglocentric" according to one New Zealand authority.
They are small in number.

They have small sample sizes.

They have questionable methodology.

The sole multicentre trial had excessive drop outs in each treatment arm.

The sole 5-year follow-up trial suffered from corrupt data, and its results may be meaningless. Internationally there is doubt about the validity and generalisability of UK findings. Their results have not been replicated in the USA. One leading American researcher doubts they can be.

1.3 Inadequate foundation for definitive guidelines.

By itself the RCT evidence base is not an adequate foundation for definitive guidelines. If NICE base their deliberations only on the Bagnall systematic review, then they will:

Make binding recommendations for tens of thousands of UK patients,

On a evidence base totalling only 777 patients,[3]

Where there was high drop out from treatments, averaging 18.5%,
Where there was little lasting benefit at 5-year follow-up.

Recognising the limitations of the RCT base, the compilers of the Canadian CFS/ME guidelines conducted a much wider literature search: [4]

"The level of evidence (LE) categories we have used are:

I. Large double blind randomized, control trials (RCT)s, or metaanalyses of smaller RCTs, clinically relevant outcomes;

II. Small RCTs, non-blinded RCTs, RCTs using valid surrogate markers

III. Non-randomized controlled studies, observational (cohort) studies, case-control studies, or cross-sectional studies

IV. Opinion of expert committees or respected authorities

V. Expert opinion."

A working group in New Zealand hopes to implement a similar comprehensive search.[5]

"The ideal guideline for New Zealand would have a simple, clinically useable presentation, supported by well-detailed text,"

"drawn from evidence which would include a systematically searched, inclusive body of research literature,"

" plus clinical expertise from specialists in the field, "

"and input from people with CFS to ensure a consumer focus is maintained."

There must be *"A literature search to check the evidence base is up-to-date, inclusive and non-selective."*

It would be indefensible for NICE to make recommendations solely on the evidence of existing RCTs. The Bagnall review team need to modify their strategy and go back to first principles. If there are insufficient RCTs, then they should follow Sackett's advice: "*follow the trail to the next best external evidence and work from there*". There is an international abundance of *"individual clinical expertise"*, documented in leading medical journals, to inform best practice guidelines.

Key Message: NICE should not rely solely on the deficient UK RCT evidence base.

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2. Concerns about existing RCTs for GET & CBT.

In this 2005 review Bagnall et al. reviewed RCTs by Fulcher, Powell, Wearden, Deale (1 & 2), Sharpe, Prins and Lloyd. In 2001 another Bagnall team jointly complied a systematic review of the same RCTs, which was published in JAMA.
Negative comments on the RCTs, published by Bagnall and American co-authors in 2001, are listed below. For some inexplicable reason, the greater part of this negative comment has disappeared from the 2005 version. Considering that the same RCTs were scrutinised, and that Bagnall was a member of both teams, this is all the more puzzling.

Concerns about RCTs on GET & CBT, published in JAMA 2001.

2.2 Methodological Inadequacy:

"All conclusions about effectiveness should be considered together with the methodological inadequacies of the studies. Interventions which have shown promising results include cognitive behavioral therapy and graded exercise therapy. Further research into these and other treatments is required using standardized outcome measures."

("Methodological inadequacies" changed to "methological quality", 2005).

2.3 Study Withdrawals

"The highest dropout rates were in the behavioral interventions."

(This comment missing from 2005 version).

2.4 Dropout Rates for CBT:

"Cognitive behavioral therapy trials had a dropout rate of 19% (114/589). This high dropout rate was due largely to the high dropout rates in 1 of the RCTs of CBT. This trial had significantly higher dropout rates in the CBT group (40%) than in the support group (32%) or control group (20%; chi 2, 8.27; P = .02). The other RCTs of CBT had lower dropout rates (range, 2%-17%)."

"One RCT showed very high dropout rates in all 3 intervention groups; the rates were highest in the CBT group but reasons for dropouts were not reported."

2.5 Dropout Rates for GET:

"Trials of GET also had a high dropout rate of 18% (68/370)."

(This comment missing from 2005 version).

2.6 Unacceptability of treatments:

"Where dropout rates are higher in the intervention group than in the control group it may be the case that there is something about the intervention that trial participants find unacceptable."

"Although studies of behavioral interventions reported high dropout rates, none of these studies found any adverse effects from the intervention and so the reasons for withdrawing from these studies is not clear."

"When deciding what treatments should be given to patients it is important to take adverse effects, especially those which are so severe as to cause patients to discontinue treatment, into consideration."

(These comments missing from 2005 version).

2.7 Severely affected patients excluded.

"In some studies participants were only eligible if they could physically get to the clinic, which implies a certain level of fitness. … It is not possible to assess whether the interventions investigated would be effective, ineffective, or even hazardous for a more severely disabled group of people."

2.8 Reported improvements might be illusory:

"Outcomes such as "improvement," in which participants were asked to rate themselves as better or worse than they were before the intervention began, were frequently reported."

"However, the person may feel better able to cope with daily activities because they have reduced their expectations of what they should achieve, rather than because they have made any recovery as a result of the intervention."

(These comments missing from 2005 version).

2.9 No objective evidence of improvement:

"Some studies measured employment status at baseline, but this was often not reported at the end of the intervention."

"An objective measure of the effect of any intervention would be whether participants have increased their working hours, returned to work or school, or increased their physical activities."

(Second comment missing from 2005 version).

2.10 Little lasting benefit from CBT.

"At 5-year follow-up, improvements remained for some of the outcomes evaluated (eg, improvement and proportion of participants completely recovered)"

"no differences were reported between the groups for the other outcomes measured (physical functioning, fatigue, general health, symptoms, relapses, or the proportion of participants that no longer met CFS criteria) ." [6]

The Deale 5-year follow-up suffered from its own methodological inadequacies, as its own authors conceded. Over the course of five years, treatment of many patients had deviated from the trial protocol. The distinction between treatment arm and controls had thus become thoroughly blurred.

2.11 Corrupted data:

"Since completing treatment at our facility, 14 (56%) of the patients undergoing cognitive behavior therapy and 16 (57%) of the patients receiving relaxation therapy reported receiving further treatment for their chronic fatigue symptoms."
"Six (21%) of the relaxation therapy patients had received cognitive behavior therapy"

"Other treatments used were antidepressants, counselling, physiotherapy, and complementary medicine. "

(This methodological defect undetected by Bagnall et al. 2001 & 2005).

2.12 Inconclusive in respect of CBT:

"It is difficult to draw firm conclusions about the effect of cognitive behavior therapy, given that many of the patients received further treatment during follow-up." [7]

(This finding not recorded by Bagnall et al. 2001 & 2005).

2.13 Follow-up revealed relapse after CBT:

Sharpe confirmed that patients relapsed after CBT, subsequent both to the Deale et al. 1997 and Sharpe et al. 1996 trials.

"Both the Deale et al. trial and the trial that I conducted have received five-year follow-up assessments. Both long term follow-ups show some persistent benefit."

"However there is a tendency for the difference between those receiving CBT and those receiving the comparison treatment to diminish with time due to a tendency to relapse in the former and improvement in the latter. This finding is not surprising, it is characteristic of many chronic and relapsing conditions such as depression." [8]

Key Message for NICE: There is no objective evidence that CBT & GET are effective, nor that claimed improvements are sustained long term. These treatments are not tolerated by a large minority of patients.

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3. The American Experience.

Evidence-based medicine is not restricted to randomised trials. … It involves tracking down the best external evidence with which to answer our clinical questions. - David Sackett.

If there is a dearth of RCTs on the treatment of CFS/ME, then there is a wealth of treatment regimes described in leading international medical journals, textbooks and patient manuals. Had Bagnall et al. allowed themselves to access this material, instead of restricting themselves to largely British research, they could have benefited from the much larger pool of experience in America.
In the USA there are many more well-funded world-class CFS/ME research teams, covering a wider field of investigation: immunology, genetics, neurology, and psychology. All of the principals (Buchwald, Komaroff, Klimas, Natelson and Jason) accept that CBT is a useful management tool. However a number have a different view of the nature and effectiveness of this therapy. Klimas and Jason have strong reservations about GET. All of them dissent from the Wessely/Sharpe philosophy that CFS/ME is a psychiatric disorder. Some of them have reservations about British clinical practice, and also about the validity of British research findings.

3.2 Philosophy & Treatment Protocols in the USA.

Dr. Dedra Buchwald, University of Washington, Seattle.

"The data thus far suggest that chronic fatigue syndrome and psychiatric disorders (especially major depression) are distinct." [9]

3.3 Dr. Anthony L. Komaroff, Harvard Medical School, Boston, Massachusetts, USA

"There is now considerable evidence of an underlying biological process in most patients who meet the CDC case definition of chronic fatigue syndrome."

"There is an hypothesis that chronic fatigue syndrome involves symptoms that are only imagined or amplified because of underlying psychiatric distress - symptoms that have no biological basis."

"It is time to put that hypothesis to rest and to pursue biological clues, in our quest to find answers for patients suffering from this syndrome."[10]

3.4 Dr. Nancy G. Klimas, University of Miami, et al.

"The complexity of CBT studies, their varied inclusion and exclusion criteria, the very limited portions that can be properly blinded, and the subjective means used for most evaluations, puts in question the validity of their results.

"The question arises whether a formal CBT or GET program adds anything to what is available in the ordinary medical setting. A well informed physician empowers the patient by respecting their experiences, counsels the patients in coping strategies, and helps them achieve optimal exercise and activity levels within their limits in a common sense,

non-ideological manner, which is not tied to deadlines or other hidden agenda."[11] (quoted from Canadian CFS/ME Management Guidelines).

3.5 Dr. Benjamin H. Natelson, Department of Neurosciences, New Jersey Medical School.

"While the results (of CBT trials) support the role of beliefs in maintaining illness in CFS, this does not mean that CFS is necessarily psychological in origin. For instance, CBT can improve the symptoms of patients with other chronic diseases such as rheumatoid arthritis."
"Furthermore, CBT is not always effective in treating CFS and its efficacy may be greater in treating patients who are at a relatively low functional level because of a possible "ceiling effect" for high-functioning patients."
"Thus, while some patients may have cognitive and behavioral factors that impede recovery, this is not necessarily true for every patient with CFS."[12]

3.6 Dr. Leonard Jason, De Paul University Chicago.

Like Drs. Wessely and Sharpe in the UK, Dr. Jason is a mental health professional. He is also their most consistent critic. When they published their landmark thesis, that CFS/ME is a psychiatric disorder a "Functional Somatic Syndrome", Dr. Jason openly rebuked them in the pages of the "Lancet".[13]

Speaking as a psychologist, Dr. Jason's view is that CFS/ME is not a mental disorder.

"The fact remains that a large group of patients do not have any Axis 1 psychiatric disorders; therefore, one can not conclude that this is a psychiatric illness."[14]

In a textbook published by the American Psychological Association in 1998, Jason said that in his own extensive practice with a large number of patients, he was emphatically unable to replicate the findings of British researchers. And until UK findings were confirmed in the US, he would not recommend the use of GET.

"Our reluctance to endorse graded activity arises from our vastly different clinical experience in the United States. A replication of graded activity outcomes in a well-designed U.S. study would be necessary before we would recommend its general use in CFS populations." (He was referring to Deale et al., 1997 & Sharpe et al., 1996).[15]

This was a non-too-subtle indication that, like Klimas, he does not trust the findings of his British counterparts.
Dr. Jason believes that the use of GET and CBT is harmful for some patients:

Our clinical experience suggests that GA/CBT for clients who do not exhibit fear-based avoidance may be counterproductive and trigger symptom flareups.[16]

Of all ME/CFS researchers, Dr. Jason is the one most often cited in the Bagnall et al. 2005 systematic review.

3.7 The American view of CBT.

It is telling that in the US, few researchers have investigated the effects of GET or CBT on CFS/ME.[17] Seemingly the NIH, the world's largest funder of medical research, considers that this is not a promising area of investigation.

American clinicians have their own view on CBT. Over-enthusiastic British researchers have exaggerated the benefits of CBT & GET, to the point where they almost seem to be offering a cure. However in the US, CBT often has a more limited role. Practitioners like Jason and Klimas see it more as a means of reconciling patients to the limitations of an incurable long-term condition.

3.8 Effect of CBT not specific for CFS/ME.

Also, US clinicians do not see CBT as a therapy that benefits CFS/ME uniquely; (i.e. no one can claim to have found a treatment specifically for CFS/ME). It is a non-specific approach which can benefit patients with a variety of physical illnesses.
This point escaped the notice of Bagnall et al. (2001), even when made by their JAMA co-authors in a separate report, thus:

"No effective treatments specific only to CFS have been identified."

"Behavioral interventions that emphasize increasing activity levels may improve quality of life and function in some people with CFS."

"It is unlikely that the beneficial effects of such general treatments are specific or limited only to patients with CFS. In other words, although these therapies may help some people with CFS, their effectiveness does not help establish an underlying etiology or cause of CFS."[18]

Professor Peter White acknowledges that CBT is not effective for veterans with Gulf War Syndrome, but claims it is beneficial for CFS/ME.[19] The authors of a systematic review on CBT compiled by the American AHRQ team, quoted above, would probably not support that view.

3.9 Summary:

A number of leading American researchers have well-founded reservations about the practice and research competence of their British counterparts. None of them endorse the unique British theory that CFS/ME is a psychiatric disorder.
Faced with this challenge, retreat into an intellectual laager is not an adequate response for UK clinicians, nor for guideline compilers at NICE. A defensive parochial outlook will do the NHS no favours in the treatment of CFS/ME.

Key Message: Some American clinicians see CBT as a coping strategy, not as a treatment. Some US researchers strongly doubt the validity of UK research on CBT & GET. NICE must take into account extensive US expert practice, when formulating UK guidelines.

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4. Experience in Australia, Canada & New Zealand.

Australia.

The compilers of the Australian national guidelines emphasised that in CFS/ME the therapeutic alliance between doctor and patient is indispensable. They rejected many of the assumptions underlying standard UK medical practice. They saw much of British psychiatric management as stigmatising, and a source of patient alienation.

4.1.2. Avoid unrealistic goals and false hope.

"Additional elements of good clinical management are the development of a clear and mutual understanding of the nature of the illness; a sensible approach to physical and mental activity; and realistic expectations about long-term outcome possibilities."

4.1.3 Not a Functional Somatic Syndrome.

"Although depression is a common symptom in people with CFS, the disorder as a whole cannot be regarded simply as a "somatised" variant of a depressive illness.

"Psychiatric labelling is generally unhelpful. In most cases, there is little evidence that the disorder is "psychosomatic."

"In everyday clinical practice "somatisation" and "somatoform" are unhelpful diagnostic labels which are best avoided in patients with CFS."

4.1.4 Limitations of GET & CBT, and of their research base.

"There have now been a number of controlled or partially controlled studies of the various components of cognitive behavioural management approaches. Although most have shown significant short-term or longer-term benefit (or both), improvement has not been observed in all patients or in all studies and, when observed, may be modest."

"It is important to note that studies differ substantially in patient selection, intensity and duration of treatment provided, and suitability of the "control" interventions used for comparison. In most studies patients were only included if they were physically well enough to attend clinics for assessment, treatment and follow-up. It is therefore difficult to extrapolate the results to patients with more severe disability."

4.1.5 Limited generalisability.

"Many studies have significant refusal and drop-out rates, which may reflect on the acceptability of the treatment regimens. These factors significantly limit the generalisability of the findings."

4.1.6 Doctor/patient Therapeutic alliance.

"Doctors who display the essential therapeutic characteristics of empathy, acceptance of their patient's suffering, non-judgemental style and a commitment to continued care are more likely to make an appropriate diagnosis and to minimise the adverse effects of the illness experience. Conversely, those who reject the patient's illness experience are likely to promote feelings of alienation and perpetuate ill health. A qualitative study of people with CFS found that lack of perceived medical support and understanding was associated with increased seeking of alternative medicine."

4.1.7 Psychiatric stigma and patient alienation.

"Rejection by family, friends, peers and doctors leads many to experience CFS as a "delegitimising" illness. Dismissing a patient's suffering as non-existent or imaginary is anti-therapeutic."

"Broaching the issue of psychological factors in causation should be done with caution and sensitivity, avoiding stereotypic value judgements. The hypothesised role of "somatisation" is particularly problematic. Outdated and simplistic notions of "psychogenesis", with their implications of "imaginary" illness and "unconscious malingering", leave patients feeling stigmatised, guilty and resentful. Pejorative terms reflecting a false dichotomy between "organic" and "functional" disease are best avoided."

"Unwarranted speculation about psychogenesis, based on the outcome of trials of cognitive behavioural therapy in CFS, should also be avoided. This is only likely to further alienate patients and cause resistance to potentially beneficial management strategies. If an effective therapeutic relationship is to develop, doctors must acknowledge that, despite the current lack of understanding of the underlying cause and mechanisms of chronic fatigue, the symptoms are real and the suffering and associated disability is genuine."

"The notion of "abnormal illness behaviour" is contentious, and the term should not be used as a diagnostic label."

4.1.8 Secondary gain.

"In the absence of evidence of malingering, speculative judgements about unconscious motivation should be avoided. The psychoanalytic concept of "secondary gain" has been misused in medicolegal settings and does not rest on a solid empirical base. In evaluating patients with CFS, hypothesised secondary gains should be weighed against manifest secondary losses."

(UK psychiatrists and psychologists specialising in CFS also seem to specialise in making damaging and unfounded allegations about their patients. One psychologist,Professor Richard Bentall, has suggested, on very little evidence, that CFS/ME patients are motivated by secondary gain.[20] That is, they want to benefit financially from being ill. The Australian and Canadian guidelines make short work of that notion).

Canada.

The compilers of the Canadian National Guidelines[21] believe that patients should be respected and empowered. They strongly reject imposed top-down approaches which disrespect patients' opinion. They have many serious doubts on the validity of the UK evidence base. They strongly reject the British psychogenic hypothesis.

4.2.2 Patient Support and Well-Being:

Patient support and well-being are the top priorities: Above all, one must consider and support the well-being of the patient who is embedded in the climate of confusion and uncertainty that surrounds this poorly understood chronic illness, both in the social and medical context. Begin to reduce uncertainty by establishing a positive diagnosis, reassuring continuity of care, and realistic hope based on as

accurate an assessment of the patient's individual prognosis as possible.

4.2.3 Patient Participation and Empowerment:

The rules of healing differ from those of curing and must come from within. A starting point for empowerment is to validate the patients' self-experience and knowledge, as that is an integral part of their healing process.

Empower the patient through respect. The autonomy of patients is vital to their physical and psychological health.

It is most important that the ME/CFS patient has a sense of control over the pacing of their program. This will increase the likelihood of success and continued commitment.

4.2.4 The Patient Knows Best:

Patients are directly and potentially more accurately aware of their own bodies than anyone else. Early warning signs of a pending 'crash' must be respected. Patients can suffer severe and prolonged exacerbation of their illness if they transgress their activity boundaries

too deeply or too often.

Encourage patients to accept themselves with their limitations, get out of unfavourable situations before symptoms exceed coping powers, and learn to say "No."

4.2.5 Doubts about UK evidence base & clinical practice.

"Many therapies used for ME/CFS have not undergone well-controlled clinical trials and may not yet be

sufficiently scientifically confirmed."

"ME/CFS is not synonymous with depression or other psychiatric illnesses. The belief by some that they are the same has caused much confusion

in the past, and inappropriate treatment."

"As few as 5% of ME/CFS patients meet the criteria for somatization disorder."

"No known therapy helps all patients but some are helpful for some patients."

"Exercise programs must be entered cautiously as clinical studies have indicated that symptoms worsened

in approximated half of the ME/CFS patients."

4.2.6 Imposed regimes rejected.

"Externally imposed programs may not respect the patient's autonomy and impede self-direction. We must be very careful concerning any program that presupposes that patients are merely wrongheaded about their illness and activity limits."

4.2.7 Rejection of secondary gain thesis.

"Most patients are well motivated to improve their condition and have lost much more than they could possibly ever gain from becoming ill."

4.2.8 Emphatic rejection of the Wessely/Sharpe psychogenic hypothesis.

"This hypothesis is based on the premise that the patient's impairments are learned due to wrong thinking, and considers the pathophysiology of CFS to be entirely reversible and perpetuated only by the interaction ofcognition, behavior, and emotional processes. According to this model, CBT should not only improve the quality of the patient's life, but could be potentially curative".

"There is much that is objectionable in this very value-laden hypothesis, with its implied primary causal role of cognitive, behavioral and emotional processes in the genesis of ME/CFS. This hypothesis is far from being confirmed, either on the basis of research findings or from its empirical results."

"Nevertheless, the assumption of its truth by some has been used to influence attitudes and decisions within the medical community and the general cultural and social milieu of ME/CFS."

"To ignore the demonstrated biological pathology of this illness, to disregard the patient's autonomy and experience and tell them to ignore their symptoms, all too often leads to blaming patients

for their illness and withholding medical support and treatment."

New Zealand.

Preliminary work on CFS/ME Guidelines for New Zealand commenced in 2003. The Guidelines Group (NZGG) considered existing guidelines formulated in America,[22] Australia, Canada, and the UK.

They rejected certain aspects of the 2002 CMO's Working Group guidelines:

4.3.2 Psychiatric bias.

"It was felt that there was possible over-representation from psychiatry on the team, leading to too strong an emphasis on psychological issues and approaches;

Another *"weakness"* of the report was that *"it still recommends CBT and GET, albeit acknowledging the paucity of research support for these approaches. However, the potential for harm from GET is not adequately discussed, nor is the controversy surrounding CBT."*

They had the same complaint against the Australian guidelines, even after they had been revised.

"… this guideline had too strong a psychological approach. Many people with CFS find a strong emphasis on the psychological aspects of CFS insulting, and such emphasis can create barriers to effective care."

4.3.3 CBT & GET "outdated".

They regarded CBT & GET as "outdated management practices", and that GET was potentially harmful.

"Possibly resulting from the psychiatric bias, or from the outdated research base from which the (Australian) guideline is drawn, it was felt that this guideline showed a bias towards the now outdated management practices of Cognitive Behavioural Therapy (CBT) and Graduated Exercise Therapy (GET)."

4.3.4 The Canadian and American guidelines both *"adopted a more balanced (and thereby more acceptable to people with CFS) biopsychosocial model of CFS, and that it had useful management suggestions which reflect both benefits and risks of various treatments for people with CFS."*

4.3.5 UK research base Anglocentric & antiquated.

They regarded both the British and Australian research bases as outdated and inadequate.

(Australia) *"... the research about CBT is ambiguous and inconsistent; GET may cause relapses and is thereby potentially harmful."*

(UK) *"A shortcoming of the CMO report is the Anglocentric nature of the research base, and the consequent omission of potentially relevant recent evidence from certain international studies."*

They found no such fault with the New Jersey Consensus Manual,[23] where

"the evidence base was felt to be both up-to-date and adequate, with no noticeable gaps."

4.3.6 Consumer involvement.

They approved the British "trident" approach employed by the CMO group.

"The'trident approach': formulating conclusions based on research, consumer experience and clinical experience; the clear incorporation of professional expertise and consumer views was noted as a strength."

Similarly they approved the way

"consumer feedback is comprehensively incorporated into the content of the (Australian) guideline, and clearly identified throughout."

They thought that if a group compiling guidelines had *"under-representation of groups such as ancillary health professionals, and lack of consumer representation"*, then it could not do its job properly.

4.3.7 Respect for patients.

"The reviewers felt that a particular strength of the CMO report was the unambiguous acknowledgement of the reality of CFS as a chronic illness, together with the strong urging for more respectful treatment of people with CFS. Similarly, the report explicitly affirms the importance of a

good rapport between the person with CFS and the person managing their treatment and care.""The reviewers also found the Canadian guideline to be written with compassion and understanding for people with CFS, and liked the fact that it stressed that treatment and management must be patient-focused."

Similarly they praised the *"compassionate approach of the specialist authors*" of the New Jersey Consensus Manual.

4.3.8 Adverse consumer reaction.

Fearing any consumer rejection of their planned guidelines, the NZGG were interested in

"the reception of the guidelines by the populations for whom they were intended."

"'buy-in' by both people with CFS and health professionals is an important aspect of the success of any guideline."

They noted that the original draft of the Australian guidelines was attacked on account of psychiatric bias, and was revised for that reason.

"The draft Australian guidelines generated considerable controversy, being perceived as being biased towards a strongly psychological model of CFS, and promoting psychological therapies at the expense of addressing the physical aspects of the condition. The guidelines were revised considerably as a result of the public feedback."

They were aware too, of adverse patient reaction to the CMO Group's guidelines.

"This report was the source of both professional and consumer controversy both during development and upon its publication. … The report as a whole was somewhat overshadowed by extreme professional and consumer positions. … The controversy persists."

4.3.9 Danger of consumer rejection.

The NZGG is anxious to ensure that their proposed new guidelines are not rejected by the patient community, which would create great difficulties with implementation. At all costs they want to avoid the kind of controversy generated after new guidelines were introduced in the UK and Australia. To prevent this, they want open and transparent consultation with consumers.

"The major risk to implementation of a guideline is that its intended audiences (clinicians and people with CFS) would find it unacceptable. If the people with CFS reject the content and recommendations of the guideline, it can cause considerable difficulties. "

"An example of this occurred when the Australian guidelines and UK's CMO report recommended GET."

"It is also important that there is an open and transparent consultation process prior to release of the guideline to ensure a consumer focus is maintained, and to proactively identify (and have the ability to address) any points of contention."

4.3.10 Summary:

The compilers of CFS/ME guidelines in Australia, Canada and New Zealand have strenuously sought to engage the patient community, with some success. They emphatically reject much of the philosophy underlying the dominant UK treatment strategy. They see a lot of current British practice as poorly researched, antiquated, and guaranteed to alienate the patient community. The NZGG admire the compassion of doctors who compiled American and Canadian guidelines, and approve of the respect they have for their patients.

Key Messages for NICE from Australia, Canada and New Zealand:

Engagement of consumers is a *sine qua non*. If there is no consultation, then there is no implementation, and the efforts of NICE will have been wasted.
British psychiatric management of CFS/ME is a poorly-informed, counterproductive, parochial aberration.

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5. Publication Bias.

Bagnall et al. (2005) and Bagnall et al. (2001) have markedly different approaches to the same data.

In 2001 Bagnall et al. suspected that the generality of papers they reviewed suffered from publication bias. But in 2005, they confined their suspicions to just one study. Publication bias is the tendency for studies that show certain results, usually beneficial effects, to be published.

None of the trials found an overall negative effect from the intervention, suggesting that there may be bias toward publication of trials showing a positive effect.

Due to heterogeneity of outcomes and interventions it was not possible to assess the extent of publication bias using funnel plots.

Insufficient data were available to assess publication bias using standard methods (eg, funnel plots), and it was therefore discussed narratively.

(Bagnall et al. JAMA 2001).

These 2001 caveats, applying to all papers discussed, have been removed from the 2005 version.

5.2 Negative findings.

There is in fact one RCT (Lloyd 1993), which showed negative results for CBT. If publication bias is suspected in the CBT RCTs, then Lloyd's study provides a basis for comparison.

This is how Bagnall et al. reported on Lloyd in 2001:

This *"RCT, which also included immunologic therapy, did not find overall beneficial effects of CBT".*

In 2005, the Bagnall report is mixed, and harder to interpret:

"The RCT which investigated the effects of both leukocyte extract and CBT showed a significantly greater effect on general health in the group receiving both leukocyteextract and CBT compared to the other groups. No differences were found between groups (including CBT alone) for the other outcomes investigated."

5.3 Negative American findings.

A little lateral thinking would have led Bagnall et al. to a large American trial of CBT for Gulf War Syndrome, a condition which along with fibromyalgia, shares many similarities to CFS/ME. It was reported that this "recent large trial of treatment of Gulf War syndrome found no significant differences between CBT and control treatments (Donta et al, 2003)."

This was not surprising, considering that "A recent systematic review showed '... psychosocial treatments have not yet been shown to have a lasting and clinically meaningful influence on the physical complaints of polysymptomatic somatisers' (Allen et al, 2002)."
(Quotations from Professor Peter White).[24]

5.4 Exaggeration.

There is evidence that some UK CFS researchers exhibit bias, in exaggerating the beneficial effects of their treatments.

It is useful to note the way some British CFS/ME clinicians tailor their comments to cater for different audiences. When presenting their findings to a British audience, they claim "substantial" - almost curative - benefits. However in the American forum the same individuals will say that the benefits are only "modest", and "not a panacea".

Wessely in the UK. *"substantial improvements in measures of fatigue and physical functioning."*[25]

Wessely in the USA. *"modestly effective"; "neither approach is remotely curative"*; *"not the answer to CFS"*.[26]

Sharpe in the UK. *"the overall treatment effect was substantial"; "a return to normal functioning (albeit often with continuing fatigue) is possible in most cases"*.[27]

Sharpe in the USA. *"CBT is not a panacea"; "many, if not most, patients continue to complain of excess fatigue."*[28]

In America they face more robust peer review from heavyweight rivals, and are more circumspect in their claims. A number of leading US researchers are sceptical of their claimed results, in any case.

Key Message: UK research on CBT & GET may suffer from bias. NICE should not take it findings at face value.

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6. Imposed Top-Down Therapy Initiatives areRejected by CFS/ME Patients.

Evidence-based medicine is not "cook-book" medicine. ... it requires ***a bottom-up approach*** *that integrates the best external evidence with individual clinical expertise and* ***patient-choice****; it means the thoughtful identification and compassionate use of individual* ***patients'*** *predicaments****, rights, and preferences*** *in making clinical decisions about their care* - David Sackett.

6.2 Patient Dissatisfaction.

Bagnall et al. (2005) are aware of consumer dissatisfaction, as filtered through medical personnel, and as more accurately recorded in surveys by patient support groups. But they publish no realistic indication of the depth of patient alienation. This "ostrich" approach is inadequate and untenable, and will not assist NICE deliberations. Debate about treatment options occurs at academic as well as consumer level, and should fall within the purview of systematic reviewers.

6.3 The elephant in the room.

It will be pointless for NICE to formulate guidelines if therapies proposed encounter strong consumer resistance. The current disharmony between CFS/ME doctors and patients is a prominent feature in the landscape. It cannot be discounted or airbrushed out of sight. Provider/consumer acrimony is an elephant in the room. It must be acknowledged and dealt with, or it will continue to inhibit progress.

6.4 Psychiatrists refuse to engage with patients.

The handful of psychiatrists who have assumed - or hijacked - the leadership of CFS/ME research in the UK, are not comfortable with consumers. Far from consulting patients compassionately about their "rights, preferences and choices", they make every effort to elude consumer scrutiny. (See the "Lancet" Editor's strictures on their conduct at the end of this paper).

Their refusal to engage with the patient community was most memorably displayed in 2002, at the end of deliberations of the CMO's Group on CFS/ME. When the psychiatrists on this committee failed to get their way completely, some joined a petulant mass resignation. [29] Before the CMO's report was published, they began briefing against it in the pages of the BMJ. To assist their campaign of negative spin, they imported a pliable American former CFS/ME researcher, who obligingly railed against patient involvement, in a BMJ editorial.[30]

6.5 Coercion, not persuasion.

With consumers, psychiatrists have used every means to promote their agenda - except persuasion. They have lobbied the medical community, the Benefits Agency, the insurance industry, and the MRC - but they don't lobby patients.

As astute medical politicians, they have succeeded in imposing their agenda throughout a great part of the NHS. Their prejudices have become pervasive among many British doctors. Many of the new CFS/ME referral centres are based in psychiatric units.
The effect (and it may be the intention) is to coerce patients into psychiatric care. The only option offered those who refuse to attend such a centre, is to forego specialist treatment altogether.

There are many instances of more overt coercion of CFS/ME patients, or their relatives, by psychiatrists. The most notorious was the case of Ean Proctor in the Isle of Man in 1988. There are many more recent examples. In 2002 a consultant paediatrician was brought before the GMC, for failing to respect the right of two parents to give or withhold consent. [31] He had insisted that their child have psychiatric management, against their wishes. The GMC affirmed that the parents "were entitled to have the treatment of their choice for their child".[32]

6.6 Coercion fatal to guideline implementation.

The New Zealand Guidance Group were aghast that coercion was used in the UK in the treatment of CFS/ME patients: *"Such a situation would be a disaster if it were to occur in NZ."*

The NZGG see coercion as very damaging to the doctor/patient relationship, and fatal to the implementation of national guidelines.

"In countries where guidelines recommend GET, there have been cases where children have been removed from their parents because of it."
"This occurs when children or their parents on behalf of them has refused this treatment. The

guidelines are then cited as proof of a worthwhile treatment which is being refused."
"Such a situation would be a disaster if it were to occur in NZ."

6.7 Source of friction.

One of the most potent sources of friction between patients and doctors is the hypothesis floated in the "Lancet" by Wessely and Sharpe in 1999, that CFS/ME is a psychiatric condition, characterised by a history of emotional disorder and childhood abuse.[33]
This outlandish theory has done untold long-term damage to the relationship between the medical community and the CFS patient population. Wessely[34] and Sharpe[35] have retreated slightly from their original position. Despite that, the wounding allegation of mental illness still stands. In the words of psychiatrist Peter White:

"A general functional somatic syndrome can be consistent only with psychogenesis".[36]

The theory that CFS is a "Functional Somatic Syndrome" has been rejected by most CFS/ME researchers in the US, including those in the mental health sector. In the UK it is rejected by two prominent mental health professors specialising in the treatment of CFS/ME, Richard Bentall and Peter White.

The concept of a general functional somatic syndrome is unhelpful in understanding illness, aetiology, treatment and outcome, thus failing four of Kendell's tests of clinical validity", says White.[37]

Patients angrily reject the suggestion that they are mentally ill, confident that they are supported in this position by most of Wessely & Sharpe's American peers.

But medical sceptics, some of them occupying senior academic positions, have eagerly seized on the "Functional Somatic" hypothesis, using it to bolster their belief that CFS/ME is not a genuine clinical entity.[38]

6.8 Permanent loss of trust.

By promoting this damaging hypothesis, and by offering intellectual justification to the most prominent sceptics, Professors Wessely and Sharpe have irretrievably blighted their relationship with the community of CFS/ME patients, in the UK and farther afield. So pervasive is this loss of trust that these two doctors can now have little long-term future in CFS/ME medicine.

As well as damaging themselves, Professors Wessely and Sharpe have damaged the cause of psychiatric medicine. By falsely labelling all CFS/ME patients as mentally ill, they have alienated much of that patient population from mental health professionals.

6.9 Implication for treatment options.

In the minds of a large percentage of patients, the most frequently recommended treatments (CBT & GET) are now indissolubly linked to these two clinicians. The distrust and aversion extended to these individuals is now projected on to the treatments they advocate.

6.10 Why CFS/ME patients reject CBT & GET.

CBT is a valuable therapeutic tool in mental health medicine. It usefulness in CFS/ME is less clear, and controversial.
For their part, many patients reject CBT and GET because of the intrinsic demerits of these therapies, as applied in their own situation.

1. The therapies don't work for all patients.

(b) They make many patients worse.[39]

2. Even when they do work, the beneficial effect is marginal.

Patients are puzzled when researchers claim these treatments are "effective". Patients try CBT and GET, but are disappointed by the results. In lay terminology, "effective" means something like "curative". But these therapies are not "effective", not in the same way that paracetamol is effective for headache, or antibiotics are for a chest infection. There is a suspicion that, when they use the word "effective", CFS researchers are resorting to semantic manipulation.

6.11 Results are disappointing.

The principal promoters of these therapies, Professors Wessely and Sharpe, very rarely admit how limited their effect is. However, they have indeed made such admissions, on the record. They say the effects are "modest", but "not remotely curative", "not a panacea". They are "not the answer to CFS". (For details see para. 5.4).

The authors of the Australian National Guidelines concur that the effects of GET and CBT are "modest".

"There have now been a number of controlled or partially controlled studies of the various components of cognitive behavioural management approaches. …improvement has not been observed in all patients or in all studies and, when observed, may be modest."

In their 2001 JAMA systematic review, Bagnall et al. noted a lack of objective evidence of efficacy. Five years later that evidence has not been produced.

6.12 Secondary reasons for rejection.

Rejection of these therapies also occurs for secondary reasons. Patients refuse co-operation because they would see acceptance as reinforcement of the psychogenic hypothesis.

The authors of the Australian guidelines were aware that patients reject these therapies for these reasons, and commented:

"Contrary to popular myths, the (CBT) approach does not simplistically impose a psychological model of causation."

UK patients remain unconvinced, with good reason.

6.13 The Hidden Agenda with CBT & GET.

In January 2002, in the wake of the controversy over the CMO Group's report, psychiatrists and some patient representatives used the pages of the "Lancet" to announce a mutual 'ceasefire'.[40]

However in August the previous year, patients had made an unwelcome discovery. Professor Wessely's department was attempting to persuade WHO to reclassify CFS/ME as a psychiatric condition. Typically, this was done in clandestine fashion, without public announcement or consultation with patients groups - who found out only after the fact.

Dr. Wessely was not easy to stop. It took more than two years of patients' lobbying at the DSS and WHO, for the reclassification attempt to be abandoned. If Professor Wessely intended a new *entente cordiale* between patients and psychiatrists, as he had announced, he chose a strange way to promote it. His WHO initiative, coming soon after proposed reconciliation, was seen as a betrayal reinforcing existing distrust.

From this and many other examples, UK patients are convinced that Dr. Wessely and colleagues, despite disclaimers, are intent on classifying CFS/ME as a psychiatric disorder, to be treated by psychiatric therapies, in psychiatric centres. This is the "hidden agenda" referred to by the authors of the Canadian Guidelines, (p.49). Despite the weakness of their evidence base, and long before there is an international medical consensus, and in the teeth of prolonged and determined opposition from patients, the psychiatrists have succeeded in imposing their agenda throughout many parts of the NHS.

The handful of UK psychiatrists who specialise in CFS/ME show no sign of learning from their mistakes. It has never struck them that a treatment initiative cannot be implemented, and associated hospital centres cannot survive, unless endorsement by patients is secured, and unless patients' rights to consent and to choice are respected.

Key Message: A top-down initiative by NICE to promote CBT & GET will fail. There are primary and secondary reasons for rejection by patients.

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7. Counselling.

Some CFS/ME patients improve or recover with little medical intervention. For unrecovered patients, and in the continuing absence of a cure or effective treatment, the requirements are clear. And they are actually quite simple:

They need guidance on how to cope with the limitations of an intractable debilitating illness. This can come from various sources, lay and professional.

They need emotional support, from family, friends, fellow-patients, clergy, professionals.

They need practical assistance, financial and domestic, from family and the state benefits sector.

They want to be freed from unwarranted psychiatric labelling and stigma.
They need the knowledge that a cure is being sought, through worthwhile research.

7.2 CBT option unfeasible.

For all practical purposes, the CBT option for CFS/ME patients has now been discredited in the UK. (The NZGG also see it as outdated). In the minds of British patients, CBT is now associated with the imposition of a psychiatric diagnosis, together with the accompanying stigma. In the words the Canadian Guidelines, British mental health professionals dealing with CFS/ME patients will always be suspected of trying to introduce their own "hidden agenda".

The use of Counselling may be a solution to this impasse. One UK RCT has established that counselling is a viable and cheaper alternative to CBT, and equally effective. This paper was noted by the CMO's Working Croup on CFS, who recommended that this alternative be explored further.

4.4.3 The use of counselling

The principle is to create a supportive environment by the way in which the practitioner relates and responds to the patient, to provide them with the opportunity to explore, clarify, and makeprogress on personal issues with the goal of increasing resourcefulness towards improving wellbeing.

Clinical wisdom suggests that some form of counselling on coping with a longterm illness is an important part of the ongoing approach to management of CFS/ME.

Further research is warranted in the form of a larger, randomised, controlled trial to examine the possible benefits of counselling compared with other rehabilitative approaches in patients who have CFS/ME.

Key references

5 Ridsdale L, Godfrey E, Chalder T, et al. Chronic fatigue in general

practice; is counselling as good as cognitive behavioural therapy? A UK randomised trial. Br J Gen Pract 2001; 51: 19-24.

6 Chisholm D, Langley E, Ridsdale L, et al. Chronic fatigue in general

practice: economic evaluation of counselling versus cognitive behavioural therapy. Br J Gen Pract 2001; 51: 15-18.

In the 4 years since, no one has taken up the suggestion that further research be conducted. It may be relevant to note that Professor Wessely has an aversion to professional counsellors.[41]

7.3 The Counselling option.

The Counselling option has much to recommend it. Cognitive Behavioural therapists are in short supply, expensive to employ, and difficult to recruit and train. There is rapidly increasing demand for them in the mental health sector, which in itself will be difficult to meet. Lord Layard has said that the NHS could usefully employ an extra 10,000 CBT therapists.[42]

Counsellors are cheaper to employ, can be recruited directly to the CFS/ME service, and acclimatised by local professionals and patient groups.

Above all, they are not so closely connected with the mental health sector, and may bring with them no damaging suggestion that CFS/ME is a psychiatric condition.

The New Zealand Guidance Group knew it was pointless to make impracticable, unimplementable recommendations on therapy.

"One such risk is that guideline contains recommendations for tests and/or therapeutic interventions that are not available or not affordable. Resolving this issue can only be done by making the recommended treatments available, or by offering more available and affordable alternatives."

One RCT on the value of counselling for CFS/ME was included in the Bagnall et al. (2001) in their JAMA review.

"One RCT compared CBT with counselling and found that both interventions had a similar effect for patients with CFS". (This RCT is ref. 5 in the CMO extract above).

For some inexplicable reason mention of this counselling trial has been deleted by Bagnall et al. (2005)

Key Message: CBT therapists are scarce, expensive, and will face resistance. Counsellors are cheaper, easier to recruit, and more readily accepted.

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8. Treatment Choice - The Australian Model.

Evidence-based medicine is not "cook-book" medicine. … it requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and ***patient-choice*** - David Sackett.

Many UK Health Authorities, irrespective of an individual patient's mental health status, provide referral centres for CFS/ME patients only within a psychiatric setting. This ill-conceived strategy has profound social and ethical implications. Some day it will return to haunt those who commissioned such services.

8.2 UK patients robbed of choice and consent.

Firstly, in the eyes of most doctors and all members of the public, treatment in a psychiatric unit implies that a patient has a mental health condition. It follows that officials commissioning such services are implicitly suggesting that CFS/ME is a psychiatric entity.

No amount of disclaimers will alter this fact.

Secondly, it deprives patients of choice. In January 2006 it was announced that NHS patients must be offered four treatment options.[43] Only one, frequently unpopular, form of treatment is available for many CFS/ME patients.

Thirdly, it deprives patients of the right of free consent. Many patients attend such centres unwillingly. They come because the lack of an alternative compels them to. They must either attend a psychiatric centre - with the attendant risk of psychiatric stigma - or go untreated.

This is not a true exercise of consent, freely given, to a medical intervention. As Jason observed in the "Lancet", it leads to a situation where many patients disengage from the medical community, and go without medical care:

following "*antagonism between CFS patients and the traditional medical establishment, many CFS patients have dropped out of the medical care system*." [44]

There is no suggestion being made that psychiatric professionals be excluded from the care of all CFS/ME patients in all circumstances. But there is widespread unease about the psychiatric near-monopoly in the UK, in respect of research, publication, and treatments.

8.3 Three treatment options.

Australian practitioners are alert to these problems, and their national guidelines enshrine the patients' right to a range of treatment options.

Their code of practice is an example which must be followed by NICE when drafting UK guidelines. Here is an excerpt:

"Management principles.[45]

These management principles can be applied within any of the following conceptual frameworks, depending on the preferences of the patient and the expertise of the doctor:

1. A cognitive behaviour therapy model

This tends to suit practitioners and patients who are comfortable working with an overtly behavioural approach to managing CFS. Some patients find psychological terminology alienating, believing it to imply that their symptoms and disability are imaginary, contrived or "psychosomatic". Such beliefs are unfounded.

When properly used, a cognitive behavioural management approach promotes active patient participation with self-monitoring, and takes account of previous experiences, both beneficial and adverse.

2. A disease education model

This approach is used in other chronic and relapsing conditions such as diabetes or asthma, and therefore best suits patients and practitioners who are most comfortable with an overtly "medical" management model.

As with many other chronic medical disorders, it is better for patients with CFS to be empowered through appropriate self-management and self-monitoring techniques rather than passively submitting to fruitless investigations and marginally effective medical interventions.

3. A rehabilitation model

This is akin to approaches used for disabling medical conditions such as brain or spinal injury, stroke, or chronic heart and lung diseases. In the context of CFS, this model is best suited to doctors and patients who feel most comfortable focusing primarily on physical aspects of management."

Key Message for NICE: Any therapeutic strategy that denies CFS/ME patients the right of choice, or the right to freely-given consent, will fail.

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9. Many reports of adverse events with GET have been excluded by Bagnall et al.

One remit of Bagnall et al. was to determine **"How effective and safe are interventions for the treatment and/or management of CFS/ME in adults and children?" (Question 3).**

They have signally failed to address either issue in this heading.

We are left with a bald one-word assessment that GET is "promising". The reviewers demonstrate no curiosity respecting high drop-out rates. There is no risk-benefit analysis. We are not told whether GET is "safe", or even whether Bagnall et al. have an opinion.

For answers to this fundamental issue, we must look beyond the 2005 York review.

9.2 United States.

Dr. Leonard Jason does not share his British colleague's enthusiasm for GET:

"Our reluctance to endorse graded activity arises from our vastly different clinical experience in the United States." [46]

"Our clinical experience suggests that GA/CBT for clients who do not exhibit fear-based avoidance may be counterproductive and trigger symptom flareups."[47]

Dr. Jason is the author most cited by Bagnall et al. Their reference page lists 17 of his publications, an indication of his international stature as a researcher. When Bagnall et al. consult him so frequently, why did they fail to mention his reservations about GET?

9.3 Canada.

"Exercise programmes must be entered cautiously as clinical studies have indicated that symptoms worsened in approximated half of the ME/CFS patients."

(Canadian National Guidelines).

9.4 Australia.

"Many (CBT & GET) studies have significant refusal and drop-out rates, which may reflect on the acceptability of the treatment regimens."

(Australian National Guidelines).

Bagnall et al. list the Canadian and Australian guidelines among their references. Why then do they fail to discuss their contents?

The Australian guidelines express significant reservations about GET and CBT. Why are these concerns not reflected by Bagnall? The guidelines were endorsed by theRoyal Australasian College of Physicians, subjected to a long period of public consultation, and published in the peer-reviewed Medical Journal of Australia. What possible exception could Bagnall et al. take to their comments on GET?

9.5 New Zealand.

"GET may cause relapses and is thereby potentially harmful."

(New Zealand Guidance Group)

9.6 Eminent critical comment excluded.

Bagnall et al. are assumed to be neutral assessors. They are expected to canvass and assess a wide variety of expert opinion, and assist their clients to a balanced judgement. But what in fact seems to have happened, is that only positive comment on GET has been included. All negative comment, no matter how eminent the source, has been excluded.

9.7 Bagnall et al. suspend critical faculties.

There are times when Bagnall et al. (2005) seem to suspend their critical faculties entirely. Referring to the multicentre Prins trial (on CBT), they say this "RCT showed very high drop out rates of between 20 and 40%. Drop out rates were highest in the CBT group. Reasons for drop outs were not stated and no adverse effects from treatment were reported." (Reasons for drop out were in fact stated). They then make no further comment.

A review team charged with ascertaining treatment efficacy and safety, might have shown more curiosity about a drop out rate of 40%. One reason for high refusal rates was reported explicitly in the body of the article. "Many CFS patients eagerly expect a medical solution for their complaints and are quite sceptical about psychological treatments", said the authors. Consumers had so little faith in the therapy, that 99 (26% of those eligible) refused to enter the trial from the beginning. This pushed the overall refusal and drop out rate to 50.66%.

(Small wonder that there are no recent RCTs on GET and CBT. Investigators are probably reluctant to repeat their past catastrophes).

Well-motivated investigators of efficacy or safety would have found no lack of material in the Prins paper. But, not for the first time, Bagnall et al. seem unfamiliar with the internal dynamics of the studies they purport to analyze. (See also their failure on Deale et al. 2001, paras 2.11 & 2.12).

9.8 British reports on efficacy and adverse effects of GET.

As for GET, again Bagnall et al. take a rose-tinted view. GET trials had a high drop out rate of 18%. We have that figure from Bagnall et al. (2001), but curiously Bagnall et al. (2005) omit mention of it. There are other examples of their creative approach to GET statistics. Referring to the Wearden GET trial, they state that "11 participants dropped out". Examination of tables elsewhere in the document reveals that in the treatment arm there were in fact 25 drop outs, an attrition rate of 36%.

The damaging effects of GET is an important issue for CFS/ME patients in the UK. If clinicians do not report adverse events, then patients do. In 2000 one well-conducted British survey found that 12.9% of CFS patients received major benefit from graded exercise, but 38.8% found it harmful.[48] This survey was organised by the UK's main CFS/ME patient groups. It is cited by Bagnall et al. among their references, but they fail to discuss its contents. Had they acquainted themselves with the patient experience, they might have concluded that GET is not really so "promising".

9.9 Self-censorship.

In their older JAMA systematic review, doubtless subject to rigorous American peer scrutiny, Bagnall et al. (2001) were more forthright on the implications of high withdrawal rates with GET and CBT:

"Dropout rates may be important indicators of the acceptability of an intervention."

"Where dropout rates are higher in the intervention group than in the control group it may be the case that there is something about the intervention that trial participants find unacceptable."

"When deciding what treatments should be given to patients it is important to take adverse effects, especially those which are so severe as to cause patients to discontinue treatment, into consideration."

Not only have these caveats disappeared from the 2005 version, but citation of the JAMA article in which they appeared, has also been deleted. In 2001 Bagnall's work appeared in one of the world's most prestigious medical journals. But now she disowns it. What rationale could possibly underlie this astonishing act of self-censorship?

9.10 Improper External Influence.

There are a number of intriguing hints that Bagnall et al. have been subjected to covert external influence.

1. On p. 28 they refer to "depression and fibromyalgia" as illnesses "related" to CFS. In fact, depression and CFS/ME have long been differentiated (see Buchwald's comment in para. 3.2 above). But there is a well-known school of psychiatry in London which insists they are linked.

Reviewers are required to have knowledge of a range of opinions, without adopting them.

So who inoculated an unfounded assumption into the thinking of Bagnall et al.?

2. On p. 37 they assert that "graded activity is normally considered an integral part of CBT for CFS/ME." This is not the case, and prominent American researchers take a different approach.

But, as before, there is a school of psychiatry in London which promotes this characteristic view.

3. Bagnall first made the same Anglocentric gaffe in the pages of JAMA.

Describing a controlled trial by one of Jason's associates, Bagnall et al. (2001) remarked:

"The CBT used in the controlled trial differed from that used in the four RCTs, focusing more on limiting activities rather than trying to increase activity, and so it is questionable as to whether it should be classified as CBT."

This pejorative and uninformed comment betrayed an unfamiliarity with North American practice - and with the nature of CBT. (See the current "Treatment" page for CFS on the US's CDC web site, and p. 46 of the Canadian CFS Guidelines beginning "Two hypotheses underlying the CBT model of CFS").

Again, Bagnall et al. (2001) seem to have adopted the distinctive opinions of a familiar English psychiatrist.

9.11 Implications for York Centre for Review.

It would be most unfortunate if a powerful outside influence has been able to impose his own concepts on a team of supposedly neutral reviewers.

In his seminal 1996 BMJ editorial on Evidence-Based Medicine, David Sackett referred to the Cochrane Collaboration and the York Centre for Review and Dissemination, as national standard bearers.

The York Centre should not allow anything to put at question their independence, integrity, and authority.
Unfortunately there is abundant evidence that in 2005 Bagnall was prevailed upon to dilute or delete opinions she held in 2001.

Key Messages for NICE:

Internationally, a number of prominent researchers have strong reservations about GET.

Bagnall et al. have either failed to locate these references, or have failed to include them in their review.
Concealing evidence of adverse clinical events constitutes research misconduct.

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10. York - The Dog That Did Not Bark

There are a number of disturbing features in the Bagnall et al. (2005) review.

10.1

(1) In confining themselves to RCTs and CTs, the authors have in fact committed themselves to just a small number of papers, of some antiquity and of questionable scientific validity, the bulk of them originating in Great Britain, and all restricted to one treatment option and its associated philosophy. They have denied themselves a much larger archive of expert opinion, most of it the USA, with some in Australia, Canada and New Zealand.

The authors may have been restricted by their remit. But if that is the case, then the inadequacies of their brief have now been exposed. Other compilers of CFS/ME guidelines knew they had to cast their nets much wider, and NICE must now make the same accommodation.

Be that as it may, it was still the duty of Bagnall et al. to point out how small and dated the RCT evidence base was, and to draw attention fully to the internal limitations of each paper, and conclusions that might be drawn from them.

(2) In 2001 another Bagnall et al. review team surveyed the same corpus of research. As was required of them, they commented in detail both positively and negatively on each paper, and its

clinical implications.
It is blatant that in the 2005 version, all positive comment on the GET and CBT RCTs has been retained, and much negative comment has been deleted.

(3) In the 2001 Bagnall review, Counselling was mentioned as a viable treatment option. In the 2005 version, an important reference to a counselling RCT has been omitted.

(4). Bagnall et al. (2005) were asked to establish the safety of potential treatments. They almost completely failed to mention the known adverse effects of GET.

10.2 One lobby benefits.

All of these curious omissions and restrictions become more coherent, if one considers the possibility that they are calculated to benefit the interests of one interested party - the psychiatric lobby.

The defects of the British CFS/ME research base have been widely discussed internationally, and are admitted by its own authors.

But in 2005, Bagnall et al. gave it a clean bill of health. Eminent international criticism of therapies endorsed by the UK psychiatric lobby has been excluded. All mention of counselling - a viable cheaper alternative to psychiatric treatments - has vanished.

If a medical researcher concealed negative findings, or failed to alert colleagues to adverse events, this would constitute research misconduct. What are we to think of the authors of a systematic review making similar omissions?

10.3 Déjà vu.

In 1996 the current Editor of the "Lancet" made unfavourable comment on dubious tactics used by psychiatrists in formulating the Royal Colleges' report on CFS/ME.

"The authors of the report included 8 psychiatrists out of a membership of 16."

"The College representatives interpreted every piece of evidence pointing to a biological cause - for instance a virus - in a negative light."

"The evidence shows a total failure of antidepressants in these patients. Surprisingly, though, the Royal Colleges 'endorse the use of antidepressants' ."

"The last word of an American review on chronic fatigue is "compassion". One struggles to find this word in the UK report."

"Medical paternalism seems alive and well in Britain today".[49]

An astringent editorial in the same vein followed in the "Lancet".[50]

"Psychiatry has won the day for now."

"A decade hence, when an organic cause for at least some cases of CFS may have emerged, it would be tempting to ask the committee to reconvene."

"We believe that the report was haphazardly set-up, biased, and inconclusive, and is of little help to patients or their physicians.

The Lancet."

Ten years on, nothing has changed for the CFS/ME community in the UK.

The same individual doctors, displaying the same attitudes, are making the same mistakes, with the same negative consequences for CFS patients. A decade has been wasted, and they are hell-bent on wasting another.

Key Message: NICE should beware of repeating the debacles of 1996 & 2002. They should treat Section 3 of the Bagnall et al. (2005) systematic review with extreme caution.

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References

1 Reid, Wessely Chalder et al., Clinical review , Chronic fatigue syndrome, Extracts from "Clinical Evidence" BMJ 2000;320:292-296 (29 January) .

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See Also

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Work to support the NICE Guidelines

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October 2005

http://www.meactionuk.org.uk/NICE_draft_summary.html