

Submission to the RACP Working Group
regarding the
Chronic Fatigue Syndrome Draft Clinical Practice Guidelines
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Table of Contents

Abbreviations & Conventions	2
Introduction	3
Preamble	4
Missing Information	6
Terms Of Reference	6
Complementary & Alternative Medicine In CFS	7
Prevention	8
Placebo therapy	9
General & repeated faults of the DCPG	9
Cognitive Behaviour Therapy, and the “poor prognosis” related to belief in “exclusively physical” nature of the illness	9
Somatoform Disorder	12
Differences between science & practice in medicine	15
Specific Analysis & Critique Of DCPG	16
Quality of evidence ratings (QER) - Sect. 6 - P. 26	16
Specific QER issues	17
Bibliography	23
Evidence OF Scientific Misconduct or Fraud	24
Authors	27
Membership of Working Group	27
Preface	28
Clinical Overview	32
What is CFS?	45
How should people with fatigue be evaluated	50
Natural History of CFS	55
How should CFS be managed?	56
Associations between CFS & other disorders	60

1 ABBREVIATIONS & CONVENTIONS

CFS	Chronic fatigue syndrome
CPG	Clinical Practice Guidelines
DCPG	Draft Clinical Practice Guidelines
MCS	Multiple chemical sensitivities
NHMRC	National Health and Medical Research Council
QER	Quality of evidence ratings
RACP	Royal Australian College of Physicians
RCT	Randomised placebo-controlled trials
WG	The RACP Working Group

Please note that the document uses a left margin notation of page, column and paragraph so that the section of the DCPG referred to can be identified. Certain conventions are used, however, and these should be known before attempting such look-ups.

1. The paragraphs are numbered from the first *complete* paragraph in a column
2. Bulleted or numbered lists are considered part of the preceding paragraph
3. Where paragraphs cross pages or columns, they are dealt with in the reference to the page or column in which the paragraph commences.

Where proposals are made in the text of this document, they are made as indented italicised paragraphs, for convenience only. Many of the most important of these are extracted and included in the summary for ease of reading only.

References, abstracts and articles are included as separate documents. Although the majority of this document is evidence based, it was beyond the capabilities of the author to fully cross annotate the text for these references given the time and financial constraints. The document as it stands represents a considerable expenditure of effort and time without financial compensation of any type. Should the WG require, and allocate appropriate funding for the project, the document could be revised, annotated, cross referenced and indexed for the use of the Working Group. This request should be made formally and in writing.

Finally, the section numbering is not directly related to the section numbers in the DCPG. The order of dealing with the report required a logical, rather than sequential, approach. Thus, the QER and bibliography are dealt with before the body of the document, because many of the logical and conceptual faults lie in the QER alterations and the selected and unrepresentative bibliography. The numbering is used simply for convenience.

2 INTRODUCTION

This document is a formal response to the “Chronic fatigue syndrome - Draft Clinical Practice Guidelines”, and is intended as a critical review of the document as requested by the Working Group, divided according to the structure of the document it critiques.

It is the view of this author, however, that the DCPG are so seriously flawed in every area that piecemeal criticism is inadequate. In conception, appointment of members, process of evaluation of evidence, funding and conclusions, the DCPG are inadequate, often misleading, and do not address the very aspects of primary care in which they purport to provide expertise. The initiation, funding and appointment of members of the WG lack transparency, while the selective quoting and interpretation of the medical literature to support previously held beliefs of the committee would seem to constitute either misleading behaviour (bordering on scientific fraud), or an unfortunate convergence of opinion based less on evidence than on opinion. It is also clear that the DCPG, and indeed the current WG, do not enjoy the support of those who suffer from the illness, their personal carers, or the primary care practitioners who generally treat such patients. It would seem that, no matter what the intentions of the WG, the needs and views of stakeholders have not been adequately addressed, and that the document is paternalistic and divorced from the needs of sufferers. Failure to adequately address the issues which would result in improved care for sufferers defines the DCPG as a failure. The goal of the process was not to simply provide guidelines for their own sake, but to improve the quality of care of those suffering.

I therefore make the formal following proposals, that

- the current DCPG be abandoned,
- a new, representative and inclusive WG be constituted, and
- a new, appropriately funded effort be made to create CPG which better address primary care practice and patient needs

3 PREAMBLE

There are a large number of faults in the DCPG, and many appear to be faults of logic. The more serious flaws of conception, appointment to the WG, terms of reference, selective quoting of literature, and arbitrary alteration of the QER are dealt with elsewhere in this review.

The logical and conceptual flaws fall into a number of areas, namely:

- Assertion or opinion unsupported by the available evidence, but passed off as if evidence based,
- Uncritical acceptance of summarised literature (leading to quotation of much evidence unrelated to CFS), including studies in which there were no “true” control arms because of the nature of the intervention (eg CBT), and those in which there was no protection against researchers or practitioners intentionally or unintentionally breaking the coding,
- Illogical conclusions from available evidence,
- Selective presentation of data designed to bolster support for one (previously held) view over others.
- “Categorisation traps” - this is a situation in which there is no escape from a particular categorisation - especially noted in the many discussions regarding factors said to impede recovery. For example, the failure to accept possible psychological causes itself becomes a psychological diagnosis, forcing the sufferer into the category no matter what the “real” cause.
- “Unshared enlightenment” - the WG holds what it believes to be an enlightened view, but it is a view not shared by those outside the WG - especially apparent in the oft stated view that there should be no division between mind and body, rendering the concept of psychosomatic disease as irrelevant and outmoded. The flaw is that the world with which the WG is attempting to communicate may not hold such enlightened views, making misunderstanding inevitable. It does not appear to be the work of the WG to bring the rest of society to enlightenment. It is therefore necessary to deliver the message of the CPG to the “lowest common denominator” (ie those who hold, for whatever reason, that such a mind-body division exists, and who have an interest in determining the category into which CFS falls). It may be useful for the WG to note the varied attitudes, state what it believes to be the “enlightened position”, and then address the issue in terms which are clear, understood by all, and are least subject to confusion and misapplication.
- Inappropriate extrapolation from the general to the particular. This is especially risky in poorly defined and categorised illnesses. The poverty of distinction can lead to heterogenous groups in which any overall approach is statistically unlikely to succeed, but in which a careful clinical assessment may lead to a clear understanding of cause and appropriate management in the individual.

As an example, let us consider “pain” as the general category. If no categorisation were to take place, then even a well designed trial may find “no cause” and “no beneficial treatment” on a statistical assessment of outcomes. It would be incorrect

to say, however, that this means that no cause or treatment can be determined in an individual case. One person may suffer from low back pain due to disc rupture, another migraine headaches, and yet another anginal pain. A careful history would be required to determine the likely cause in each, and therapy would vary considerably in each. And each would benefit from therapeutic approaches unlikely to benefit the other two, and shown not to be effective in the management of pain generally.

The same applies in chronic fatigue syndrome, and the lack of primary care practice experience is clearly exposed in this inappropriate and illogical extrapolation. The clinical history and examination often provides clear evidence of cause in an individual's particular case, and particular testing is often helpful in confirming or supporting those clinical findings. This is the point of clinical medicine, as opposed to medical research. Were it not, every patient could be dealt with on a statistical, probabilistic basis, without the need for human judgement.

I put it to the WG that its biased composition, comprising mainly secondary and tertiary referral practitioners and researchers, has led to hold a "frequentist, probabilistic" assessment of CFS, and a failure to appreciate the nature of primary care practice, with a focus on the particulars of each individual, assessed one case at a time.

- Inappropriate extrapolation from the particular to the general. This occurs frequently throughout the paper where evidence from one or a few unrepresentative studies are appraised as if referring to all people with CFS.
- Prior known biases have not been carefully guarded against by the WG. The denial of the possibility of environmental illness, the arbitrary and unsupported dismissal of complementary medicine practices (and the exhaustive listing of these as unsupported therapeutic approaches), and the views on the positive value of research are well known to be associated with particular members of the WG. Such biases and opinions have no place in ostensibly objective approaches to the problem. Those with prior strong, often petrified, positions on particular issues should ensure that they do not force that personal viewpoint as a ready-made position of the WG. It is my own opinion that such members would do best to remove themselves from such discussions and determinations, so that the outcomes are more likely to become evidence-based, rather than opinion based.
- The WG has failed to distinguish between lack of data (evidence) and evidence of lack of efficacy. Had the WG been a little more inclusive of references from Ernst, for example, it would have arrived at the clear view that the problem with assessing the value of complementary medicine lies in the lack of data, and the paucity of funds directed towards research and publication in complementary medicine, rather than in evidence that it is not effective. This is an important flaw throughout the DCPG, in that there is a confusion between lack of evidence (ie need to gather more data) and evidence of lack of efficacy. The CPG needs to formally state which areas have accumulated adequate evidence of the type preferred by the WG, and separate those from areas in which the research is inadequate to arrive at a conclusion.

It is my opinion, having read and critically reviewed much of the literature, that the

majority of commonly used approaches in the diagnosis and management of CFS fall into the latter area, and that few approaches fall into the former area.

Under such circumstances, it would be more honest to admit that the biases introduced by allocation of funding to particular research approaches and experimental designs makes any broad assessment of the field of CFS impossible at present. Further, the CPG could make the useful recommendation that the paucity of uneven data be addressed in future research allocations for this important and expensive illness. This is an approach supported by Ernst generally in relation to complementary medicine, and I have included a document on complementary medicine with his references included.

It seems clear that the WG was left with the unenviable task of arriving at CPG in a situation in which the evidence was too thin, and the studies inadequately narrowly focused. Under such circumstances, it may have been preferable to overtly state the limitations, make a call for further appropriate primary care based studies, and abandon the creation of CPG until the evidence was more relevant and complete, possibly within the next few years.

As it stands, the WG has delved into speculative extrapolation from few data, and has demonstrated a type of arrogance which is unsupportable. In the absence of adequate formal research evidence, "experts" have less to offer in constructing primary care approaches than do primary care practitioners. Primary care practitioners have a deep understanding of approaches based on empirical evidence, often termed "can do" approaches in the American vernacular.

I would make the analogy of the NRMA (or similar on road support service) in the management of a broken down car. If the problem is unknown, and the job is to get the car back on the road, sophisticated understanding of the processes of combustion and fluid dynamics are of less use than the "string, wax and screwdriver" approach. If the car is in a garage with sophisticated diagnostic and repair services, then well and good. On the "road", however, in the absence of complete knowledge, the NRMA repairer and the primary care practitioners do the job which is needed, and do it cost-effectively and well.

4 MISSING INFORMATION

4.1 Terms Of Reference

The terms of reference for the DCPG are omitted. Dr Loblay has repeatedly claimed that there are no terms of reference. If this is so, it is a major flaw in itself. Without overtly stated terms of reference, the nature, purpose, limitations and outcomes from the report cannot be assessed or determined. This creates an environment of suspicion because of lack of transparency regarding the aims and limitations of the CPG. A report can only be considered in relation to its terms of reference or its stated goals. The soft, general goals

of “aiding the general practitioner” are imprecise and impossible to gauge.

I propose that the WG set down specific terms of reference for the CFS CPG, and create defined and assessable goals for the final CPG. Further, I propose that the WG employ a separate and credible third party as an independent auditor, to determine if the terms of reference were adhered to, and whether the goals were attained.

4.2 Complementary & Alternative Medicine In CFS

I have a particular concern related to the issue of the use of Complementary and Alternative Medicine in CFS. The majority of long term CFS sufferers either use or have used one or more complementary and alternative medicine modalities in their management. It is insufficient to simply dismiss these practices with an unrepresentative quote from a “patient support group”, and a table listing many practices as lacking scientific evidence.

The general issue needs to be addressed of the way in which scientific research (and therefore evidence) occurs. The implication inherent in a review of the scientific literature is that research is randomly distributed, and that as a result, all likely approaches are likely to have been assessed over time. The job, in such circumstances, would be simply to weigh the evidence, and decide on rational grounds as to which approaches were appropriate to which cases.

The truth is far from that. The majority of public research funding goes to orthodox and conservative researchers, a fact which has been recently addressed and shown to be as true in Australia as many other countries. In addition, the process of peer review of research applications means that there is a significant pressure upon “professional researchers” to pose orthodox and conservative questions in research. If they do not, then the peer review bias tends to remove research into unorthodox approaches, creating significant biases in the research proposed, and even larger biases in the research funded.

Thus, the statement that “scientific evidence is lacking” for a particular approach is nothing more than a recognition that funding for research has not been forthcoming to allow for studies to address the question. “No evidence of benefit” is an entirely different statement than “Evidence of no benefit”, and it is my opinion, having read the DCPG that these two concepts have been intentionally confused in order to imply that complementary medicine practices are of no value.

The fact that a high proportion of CFS sufferers seek management from complementary and alternative practitioners should be sufficient to make a recommendation that an observational study be undertaken in Australia, to assess the type of practices used by sufferers, their perception of the benefit of these practices (compared to their use and perceived benefit from orthodox medical approaches), and the aggregated experience of CFS consumer groups regarding the use and utility of such practices in managing CFS.

Although Ernst was referred to once (page 15) as being harshly critical of alternative medical approaches, this is in fact a misrepresentation of his published body of work. I

have included many of these references with my submission related to complementary and alternative medicine. In general, though, I would be more than happy to provide the WG the copies of Ernst's papers, just as he so kindly provided them to me. He recurrently makes the strong point that there is empirical evidence of benefit for many complementary medicine practices, and that there is an urgent need for allocation of funds for quality research in this area, precisely so that important and potentially valuable diagnostic, therapeutic and health care approaches are not abandoned simply because of lack of evidence. We need, as scientists, to do the research to fill the data gaps.

I propose that the report be amended, and that there be:

- *a recognition of the common use of complementary and alternative medicine by CFS sufferers generally*
- *a recognition of the lack of funding for quality research in this field, and the consequent paucity of data for consideration by the WG*
- *a clear statement that the "Lack of evidence" regarding complementary and alternative medicine is a direct result of a lack of publicly funded research, and that a priority should be to address the lack of evidence by making research into complementary medicine in CFS a priority.*
- *That an observational (data gathering) study be conducted as a matter of urgency to determine the extent and type of complementary medicine use by CFS sufferers, the reasons they choose complementary medicine, and the reported outcomes (as a means of identifying potentially beneficial modalities).*

4.3 Prevention

The DCPG fail to deal with the issue of prevention of CFS. It should deal with the known aspects of epidemiology and aetiology of CFS, and it may be worth noting the huge data gaps in this as well. It is clear that there are certain proximate causes which require mention, and a note should be made that caution is urged in such situations.

These reported factors include vaccination (especially hepatitis B vaccination), workplace or environmental exposure to toxic chemicals, work in the health care industry, nutritional disorders, and possibly allergy. Suggestions have been made that prolonged antibiotic use may lead to chronic, antibiotic resistant bacterial infections, and organisms such as staphylococci, mycoplasma, and others have been implicated,

In fact, the broad range of pathogens provides strong evidence that CFS may represent a disorder of host immune response. In such circumstances, it may be useful for the WG to affirm the value of maintenance of optimal health as a primary preventive principle. The basics of clean air, clean water, a high quality diet, and management of excessive stress should be emphasised in the absence of specific preventive data.

4.4 Placebo therapy

There is enormous potential for value in harnessing the value of placebo therapy in many illnesses, and in fact it is clear that modern medicine relies on this very effect for much of its benefit.

Many of the current approaches proposed by different practitioners work in part because of their strong placebo effect. Such effects may be gained from antidepressants, antibiotics, CBT, graded exercise, dietary supplements, and other interventions.

I would note that none of these are *necessarily* placebos, and may be found to have mechanisms which benefit certain subgroups. But until such evidence is available, they are best considered placebo therapy. The main aim should be to make certain that they have minimum risk of harm to the patient, and that they do not interfere with the natural history of recovery in the illness.

I include a copy of the recent Scientific American article on this very subject, and the proposals made for harnessing the placebo response are apposite in CFS, being a complex illness with no proven successful management.

5 GENERAL & REPEATED FAULTS OF THE DCPG

5.1 Cognitive Behaviour Therapy, and the “poor prognosis” related to belief in “exclusively physical” nature of the illness

The recurrent theme of the relationship between belief in the exclusively physical nature of the illness and poor prognosis is grossly flawed, and cannot be supported by studies (even those which purport to confirm this view) or by logic. I wish to address this once here, so that it can be referred to as it arises throughout the body of the DCPG.

Firstly, it is a basic tenet of science that there exists a physical basis for all observed phenomena. This is summed up in the quote, “The work of science is physics. The remainder is stamp collecting”. Put another way, the scientific axioms of causation and locality for objects outside the quantum realm are fairly well accepted. Humans, and illnesses, are not likely to be explicable by quantum phenomena, so it can be assumed that there are local factors which are causative in illness. That is, that there exists purely physical phenomena which lead to the final observed state of health. Thus, physics can in theory provide a relatively good description of the events leading to any pathology, from crush injury to schizophrenia to pain to heart attack.

All of human experience is a physical phenomenon, at least to the eyes of science. Science has no place for spirits, morality, or “ghosts in the machine”, and any scientific appraisal of illness generally, or of a particular illness must take extreme care not to cast the “unknown” factors onto some alternative to physical medicine. Psychiatry and

psychology have, in the past, proven a receptive dumping ground for the poorly understood aspects of medicine, and have tended to provide a dimension “outside science” for the handling of unknown factors or uncomfortable facts. Even the current fad of “biological psychiatry” is struggling to break the cartesian dichotomy, with much discussion of the “mind-body” interface showing just how deeply our prejudices can run.

Thus, at a profound level, all illness and all symptoms *do* have a physical basis, or they would not exist. The difficulty arises when we attempt, within a scientific framework, to relate “subjective experience” to “measurable, objective reality”. The observer, who does not *experience* the illness, looks to devices which remove the experiential component, or reduce the experience to an objective measurement. The experiment, observation or measurement becomes a “surrogate reality”, a single dimension of a complex experience. “Reality” lies in the original experience, or the thing being observed. There is nothing to suggest that it is able to be simplified beyond the actual experience, and if such an attempt is made, information is necessarily lost. The type and extent of information lost is dependent on the observation and the actions of the observer, and not on the experience itself.

CFS is a complex, multifactorial illness, with a broad range of symptoms experienced by sufferers. To consider experience anything other than perception of physical phenomena is absurd. In fact, even perception is a physical phenomenon, meaning that at all levels, illness and symptoms *are* purely physical.

One would struggle, therefore, to identify why it is that an accurate and scientifically credible view of one’s own illness (ie belief in exclusively physical basis for the illness and symptoms) could lead to a worse outcome for those holding this view.

There is a clear answer, however, and it relates more to the views and beliefs of the treater or measurer than to the views of the sufferer.

The prior assumptions and beliefs of the researchers who find this poor prognostic factor have something in common, and it is that the cause and process is *not* exclusively physical. What the other, nonphysical, factor or factors are, however, is never defined. In fact, such factors *cannot* be defined without bringing to light the prior assumptions and beliefs of the experimenters or observers. The unstated belief is that disorders of the mind *are not* physical in their nature, and possess a type of “ghost like” existence outside usual physical phenomena. In this light, practices such as CBT can be seen for what they are, namely a type of exorcism of evil spirits and wrong-thinking by the sufferer.

And here is the problem with this whole process. Poor recovery is predicted not so much by belief in the physical nature of the disease, as by a failure to adopt the peculiar (and often demonstrably faulty) beliefs of the doctor or experimenter! Conflict with the views of the doctor or experimenter leads to distress on the part of the sufferer, even when the sufferer is demonstrably more credible in their view.

This is not a new phenomenon. Throughout history, reduced suffering has always been

more likely for those who find a way to agree with authorities. In the extremes, death or miserable incarceration awaited those who refused to hold the orthodox view. One need only recall Copernicus, Galileo and Semmelweis to identify the risks of belief in a “physical basis” for something, when the authorities held a different view.

One can also address this problem a different way. Let us pretend that the mind-body division exists, that there is a continuum in CFS from those with almost purely “mind” problems to those with almost purely “body” (or physical) problems. I am aware of the stupidity of this, but it allows for a proof of the absurdity of the findings even within the terms of the experimenters.

Let us also assume that CBT addresses the “mind” aspect of the illness well, while addressing the “body” aspect of the illness poorly. Those from the “mind” end of the spectrum enter the program, do well, and are assessed as benefiting from CBT. Those from the “physical” end of the spectrum do poorly, and derive no benefit from CBT.

Does this suggest that “belief in a physical basis” for the illness is a poor prognostic factor generally? Clearly not. It simply means that there is no place for CBT for those who come from the physical end of the spectrum, or more generally, that CBT fails to address the “body” (physical) aspects of the illness.

In other words, CBT is inappropriate for one aspect of the illness, and for those people suffering from that aspect of the illness.

The demand that patients adopt the beliefs and values of researchers and doctors is a peculiar type of medical Fascism, and leads to a type of self-fulfilling, inescapable outcome for sufferers. If the person recants, and admits to the nonphysical nature of the illness, they gain the support and recognition required, and may even benefit from this in ways which have been well described in the past. The stresses are lowered, conflict is resolved (by capitulation), and support is restored.

If the person continues to hold the idea that their illness is physical in nature, they risk disapproval, stress increases, and support is denied. They become less well, reinforcing the prejudices of those with different beliefs, and a vicious loop is created, in which their health spirals down under the weight of medical disapproval. This is iatrogenic disease at its worst, subtle to the point of invisibility, yet profoundly adversely affecting the health of the sufferer.

It is not the work of medicine to identify and weed out belief systems which appear to be inappropriate, nor to bend the beliefs of suffering people to beliefs similar to those of their doctor. Medicine is, or should be, a science, agnostic before the facts. Doctors and researchers need to be very vigilant against the tendency to interpolate their beliefs or concepts *as if they were scientific axioms*, into the experimental design, or into the consultation and care of the patient.

CBT, as practiced and researched to date, is a philosophical rather than a scientific construct. Definitions, methods, mechanisms and hypotheses are totally lacking, the

experimental processes are not subject to placebo control (since the mechanism is unknown, there is no way to isolate the useful aspects of the process), and poor outcomes are ascribed to faulty beliefs on the part of the patient.

Worse, suffering people who do not fit the philosophy are subtly blamed for holding inappropriate beliefs which prevent a recovery which would otherwise have been achieved. The philosophy of CBT may thus stress and worsen the health of those who do not adopt its “belief system”.

The support of CBT by the WG is the rough equivalent of proposing “faith healing” in CFS. No one knows exactly what it is or how it works, there is no evidence of a scientific basis to the process, and those who fail to benefit can be described in retrospect as lacking faith or belief. Like faith healing, though, CBT may provide empirical benefit in some people. It may harm others by diverting them from arriving at an understanding of the physical basis of their illness. It must remain as unproven, and possibly unprovable, at least until the mechanisms are understood.

5.2 Somatoform Disorder

The issue of “somatoform disorders” needs to be explicitly dealt with in the CPG. The reason is that there remains a “loophole” for those (especially psychiatrists) who would seek to deny the valid diagnosis of CFS. In fact, the very definition of somatoform disorder makes it impossible to distinguish from CFS, as it relies on a range of medically unexplained symptoms to reach the diagnosis.

Somatoform disorder, to put it bluntly, has had its day, and has little place in the diagnostic armamentarium of modern medicine. Throughout our history, we have misinterpreted symptoms we do not understand as being evidence of a “defective patient” of some type. In other words, patients with symptom patterns which do not fit our categorisations are assumed to have no pathology. “Somatoform disorder” thus becomes a type of medical trash can, and varies over time arbitrarily and as knowledge of underlying disease processes grow.

I include an editorial from a recent BMJ on “Unexplained neurological symptoms” in support of this view. In the 1950s, these unexplained symptoms were assumed to be “conversion reactions”, physical symptoms of purely psychological origin. Doctors at the time were confident that no physical cause existed. Yet a follow up over 25 years found that the vast majority had a pathological basis (with the introduction of new diagnostic technologies, or at autopsy), and doctors, suitably chastised, tended to try to avoid making the same mistake in mislabelling after. Recall that at the time, they were all confident in the quality of their diagnosis, believing their diagnostic technologies were sufficiently powerful to come to that view.

We move on nearly fifty years, and we find ourselves repeating history! We are tossing those people in whom we can find no evidence of pathology to explain their complaints,

and label them “somatoform disorder”, a label designed to simplify the life and work of a doctor rather than to “help relieve the suffering and disability” of our patients. Yes, we are confident of our ability to identify existing pathology now, as we were in the 1950s. Each generation of medicine believes itself to be only a step away from absolute knowledge, yet with each advance we make, there are more things that we do not know or cannot explain than there were before the advance. This does not suggest that we know less, simply that as we learn more, we become more aware of the important gaps in our knowledge, and the areas which we do not yet understand.

This is especially a problem in complex, multi-system illnesses such as CFS. By *definition* CFS has a range of at least four symptoms unexplained by any other known medical disease or pathological process.

It is thus, logically, not possible to entertain the view that the diagnosis of somatoform disorder should take priority over that of CFS, when the diagnostic criteria for CFS or ICF have been fulfilled.

This issue of “priority of diagnostic labelling” is very important. In terms of the suffering and disability of the patient, it is arguably the *most important* issue in CFS. Too many CFS sufferers have, in the past, been mislabelled as “somatoform disorder”, “psychosomatic illness”, depression”, “neuroticism”, or “personality disorder” by doctors either unaware of the diagnostic criteria for CFS, or aware of them and opposed to the diagnosis of CFS on personal or professional grounds. On many occasions, I have been sent vindictive and defamatory letters from such doctors, or from the insurance companies or employers many of them work for, berating me for making the diagnosis, and demanding that I “recant” and accept their diagnosis instead. The basis for this request is most often that the practitioner is a psychiatrist, and claim priority because of “higher qualifications” than my own. Their employer or paymaster chooses to accept the “paid for” view of their own expert, who simply refuses to entertain the possibility of CFS as a diagnosis, and the CFS sufferer is left miscategorised, unpaid, and without any recognition of disability resulting from CFS.

The clear statement in the CPG should be that a chronically fatigued person who fulfils the diagnostic criteria proposed by Fuduka et al (1994) has CFS as the first, appropriate diagnosis. Any other diagnosis (psychiatric or otherwise) requires firm evidence by objective criteria before it could be accepted as a possible alternative diagnosis.

The final sentence of the first paragraph on page 13 of the DCPG is unhelpful and illogical in addressing the issue of somatoform disorders, and leaves the diagnosis as arbitrary and open to abuse. One would have to ask, in addition, how the medical approach to the patient (“excessive and poorly justified laboratory investigation and invasive medical treatments”) can in any way define the condition being assessed. The reference is circular, and is unhelpful.

The extra problem is the subjective nature of “excessive and poorly justified”. What is

indicated and justified for one doctor may be excessive and unjustified in the opinion of another, but this is judgemental, opinion-based medicine at its worst. Only the doctor in the consultation at the time of requesting such investigations is in any position to make this judgement. Others will have the advantage of retrospective review of those investigations, and such hindsight is invariably clearer than the vision when the tests were requested.

In addition, there exist serious differences of opinion within medicine regarding the need for and utility of certain investigations. The field of Occupational Medicine, for example, seeks to identify evidence of occupational damage from chemical exposure, and investigations required to support or refute this diagnosis would almost invariably be considered “excessive and poorly justified” by another doctor who considered the association unlikely. Of course, other physicians will tend to see mainly the patients whose cause and pathology has not so far been identified by other doctors, meaning that they will see a selected subgroup which will tend to support the view that prior investigations were excessive and poorly justified. They will not see the balance of patients, namely those in whom a cause or process was identified, and who are being successfully managed for that condition.

The same applies to invasive medical (or surgical) treatments. Where such treatments have been effective, and the patient recovers, the subject is no longer likely to see other doctors for assessment or management. Where it has failed, they seek other medical care, and the therapeutic failure is identified.

This same process occurs between the fields of orthodox and complementary medicine. Patients who are seen by one group and are well managed (especially when they recover) are unlikely to be seen by the other group. When poor management or therapeutic failure occurs, however, the patient is likely to seek help from practitioners “on the other side”. This leads to a situation in which each “side” sees the diagnostic and therapeutic failures of the other “side”, and tends to cement in the minds of both groups the poor quality of care and the poorly justified, excessive use of investigations and ineffective therapies.

Through this process, the division between the “sides” is widened, to the detriment of quality patient care.

In any event, opinions on the actions of the doctor can in no way reflect upon the likelihood of a suffering person falling into one category or another.

5.3 Differences between science & practice in medicine

The statistical outcome vs the consultation

There is a self-contradictory factor contained in these paragraphs which permeates the DCPG. The fact that CFS “identifies a heterogenous group of people”, does make it unlikely that any one test will prove of diagnostic benefit for the unselected group. Doctors, however, see patients one at a time, and not as a heterogenous group. Each individual patient has an individual story regarding the onset, symptoms, exacerbating and relieving factors in CFS, and these provide the data for the clinician to appropriately categorise each individual.

In fact, such categorising is the absolute norm of primary care practice, resolving the blurred uncertainty of research classifications to a highly detailed and specific picture in each individual case.

How can this be? It is dealt with elsewhere, but at its most basic, one must accept that research and statistics carry with them the problem of discarded data related to the individual, in order to determine overall patterns and tendencies of the group. Research is only as good as the data it retains, and the heterogeneity of CFS has been the direct cause for the low returns of research to date. The data lost in heterogenous groups is much greater than the amount lost in homogenous groups.

By contrast, heterogeneity or homogeneity make little difference in a medical consultation, where the missing data are gathered, and a picture is built up over time related to the specific patient being assessed.

There is no place in medical practice for discarding clinical judgement, and a complete history, simply because research on unselected groups has been unsuccessful. There is a need, however, for researchers to go back to the source of the original data, and to work with primary care practitioners, in order to gain a meaningful understanding of ways in which CFS subgroups can be made more homogenous.

Pathology testing which demonstrates no diagnostic benefit in unselected research groups may have enormous value in the setting of the primary care practitioner. Just as there is no universally useful tool for assessing the cause of pain, the individual consultation is able to distinguish the headache from the neck pain, from the abdominal pain, and instigate appropriate investigations which would be unsupportable from research in the unselected group of pain patients.

In short, decisions about the positive diagnostic value of tests should be left in the hands of the practitioner after the consultation, and researchers should be listening to those practitioners rather than attempting to regulate them.

As well, some doctors may have a special interest in some aspects of CFS, and their practice may attract a particular subgroup of CFS patients. Their diagnostic testing would be likely to be significantly different than those seeing other subgroups.

As an example, I have an interest in adverse chemical effects on health, and frequently see CFS patients whose illness has been triggered by such occupational or environmental exposure. Many of these agents are known to affect the nervous system, immune response, liver and even cause chromosomal damage. Assessment of the type and extent of damage caused by this exposure is clearly likely to be different than for those whose CFS followed a simple glandular fever infection. Yet if we were to find that the group of chemically exposed individuals accounted for only 5% of CFS, it is easy to see how their impact on an unselected clinical trial would be minimal, and the data from their testing lost in the general “noise” resulting from poor selection.

6 SPECIFIC ANALYSIS & CRITIQUE OF DCPG

6.1 Quality of evidence ratings (QER) - Sect. 6 - P. 26

The QER need to be addressed before any analysis of the CPG is possible, because they lie at the basis of many decisions and opinions expressed throughout the text.

There have been changes made to the QER from the original NHMRC recommendations, and although this is referred to in passing in the text of the document, there is no documentation of the precise changes made, and the reason for those changes. The acknowledgements at the base of page (ii) thank Helen Lapsley “for advice on guideline development and assessment of levels of evidence”. On page 26, the simple statement “The quality of evidence ratings chosen for these clinical practice guidelines were modified from existing guides.”

The statement which follows is effectively meaningless without supportive evidence. “The amendments provided an integrated system for evaluating epidemiological and laboratory-based pathophysiological studies, as well as controlled treatment trials, as the former are not usually included in existing guides, which focus on treatment interventions”.

It can be seen from this that the DCPG have been altered in a subtle but extremely significant way, making it different from other CPG in ways which appear arbitrary and fortuitously beneficial for those with a bent towards medical research (as opposed to improved clinical outcomes) in the WG.

There needs to be compelling, well argued, and broadly agreed reasons to change the rules for assessing evidence with regards CFS, and a frank discussion of the changes involved, the reasoning behind each change, and the anticipated alteration of findings which are likely to occur as a result of the changes. It is insufficient to claim (as Loblay has claimed to me in personal communications [available on request]) that Helen Lapsley attended an early meeting of the WG, and agreed that the changes may be useful. Such an opinion must have been sought for a reason, and the reason or reasons are not stated. In addition, Helen Lapsley may have been unable, at that point, to comprehend the

significance or effect of such a change. The changes, which may have seemed innocent and possibly useful in a spur of the moment decision, may be viewed a different way when the effects of the capricious changes are realised. Even if she did agree, both at the time and on reflection at a later time, this is far from a formal change in the QER required in such an important paper.

Stated briefly, if arbitrary and opinion based changes are made in the very way evidence is assessed and incorporated for the CPG, it is no longer possible to claim that the CPG are evidence based. The initial opinion and arbitrary nature of the change contaminates all subsequent aspects of the process and outcome. This initial error in process and judgement percolates through all areas of the report, arbitrarily excluding evidence, data and opinions which would otherwise have been incorporated. Worse still, the WG risks becoming "blind" to the introduced bias, proceeding in a covert, convergent acceptance of the changes, without any real examination or measurement of the effects of the change.

In a way, the process has a "chaotic" character, in that the final outcome has a "sensitive dependence on initial conditions". Had the original QER been adopted and utilised, the outcome would have been markedly different from the current document.

It is on this basis, firstly, that I request that the final outcome be discarded, and the process recommenced with either the original QER, or with any variations agreed upon by all parties after considered discussion and consensus. If no consensus is reached, then the original QER would need to remain.

6.1.1 Specific QER issues

6.1.1.1 General

It is my understanding that at least two ratings have been changed (III-3 and IV), that there is an arbitrary approach to escalation and deescalation of certain diagnostic and management approaches through the ratings, and that the guidelines themselves would support the logical view that, at present, no evidence could rate higher than Level III-2.

6.1.1.2 Change in wording of QER

QER rating III-3 has apparently been changed from "Evidence obtained from a single case study or a selected cohort study" to "Evidence obtained from a single case-control study or selected cohort study". I would regard this as a "researcher's variation" of a previously perfectly adequate QER.

Most data gathered in primary care practice are in the form of case studies or case series. There are serious ethical issues raised by the adoption of "case-control" studies in a clinical setting, just as there are massive practical difficulties in doing so. The obligation of the primary care practitioner is to his or her patient.

As the Austrian paediatrician, Béla Schick, wrote,

“First, the patient, second the patient, third the patient, fourth the patient, fifth the patient, and then maybe comes science. We first do everything for the patient; science can wait, research can wait.”

Aphorisms and Facetiae of Béla Schick

The work of medicine is not research, it is care for those who are suffering and seek our help as doctors. We make decisions, even in information vacuums, in what we believe to be the best interests of our patients, and we do not turn patients into laboratory animals. The first job of medical research is to gather and assess the variety of approaches so generated in individual patient care, and to propose hypotheses which may be suggested by those data. The testing of those hypotheses is performed by researchers in an experimental setting, which is of its nature, an attempt to control and constrain the messy variables with which primary care practitioners must struggle. The “case-control study” is a research tool, designed to refine and focus the observations of the primary carers, and derive useful approaches from those data. It is not an alternative to primary care.

The effect of this QER change is that the body of observational work performed by primary care practitioners is struck from consideration with a single word. Also banished are the case studies of nonmedical practitioners, and the aggregated case studies of sufferers and carers. This is an intolerable loss of essential information. It would be a travesty if the range and details of approaches used in the care of patients were discarded simply on the basis that controls were not included. It defeats the very process of science, which begins with careful observation by the prepared mind, and hypothesis formation. It seeks to turn the *test* of reality into *actual* reality. This is non-science, and clear nonsense.

Research, along with case-control studies, is a useful tool to test the validity of hypotheses derived from observations. It is neither the job of medicine, nor the reason for medicine. Research serves the achievement of improved patient care, or it is a waste of resources.

I would note in passing that the vast majority of research into management of CFS has been blighted by the appalling lack of data gathered from observation, and from a failure to utilise the expertise, experience and knowledge of sufferers, carers and primary care practitioners. Much expensive research and many useless trials could have been avoided if the experience and observations of the sufferers, carers and primary care practitioners had been sought before the question was posed. The money saved would have funded the support groups and practitioners in the gathering of data and outcomes from varied individual approaches, and the field would be far progressed compared to its current state.

I would go so far as to assert that in the past decade, the poorly conceived and expensive research have achieved little of benefit, and may actually have worsened the clinical outcomes of CFS management by diverting resources from the areas needed to those

reflecting the interests and biases of the researchers. Researchers may need to be made accountable for expensive waste of money and resources where it can be shown that the research was not based on firm observational data from the affected community, or from primary care practice.

I propose that the term "case-control" be removed from the QER III-3, and that it be replaced with the term "case".

I propose that the submissions of case studies by primary care practitioners be reviewed and included under this QER.

I propose further that the CPG make specific reference to the need for adequate observational data from primary care practice and from sufferers, and propose increased funding for support groups and primary care practitioners to achieve this.

QER IV, as far as I understand, has been changed from "Opinions of respected authorities, based on clinical experience and/or descriptive reports" to "Consensus opinions of respected authorities, based on clinical experience and/or descriptive reports". Again, the effect of an apparently minor change is very significant, while the arbitrary nature of the terms "respected" and "authorities" are problematic.

The DCPG suggest that there is little consensus and much disagreement on the issue of CFS at present. Consensus views may be appropriate when a clear consensus on an illness or disease exists, although even then, the dissenting views have proven throughout history to be valuable, if not essential, in progressing scientific understanding. It was the "consensus opinion of respected authorities" that dismissed Ignaz Semmelweis, damning a generation of babies to iatrogenic infection and premature death.

I propose that the "dissenting opinions" of a range of people with expertise and experience in CFS be recognised and recorded (rather than discarded), and that the term "Consensus" be deleted from QER IV.

The term "respected authorities" is undefined, and dangerously arbitrary. The question arises, "Respected by whom? On what basis?". It leaves a gaping and unexamined loophole in the QER, allowing for personal opinion and bias to determine entry or otherwise in this category. The term "respected" and the term "authority" both require definitions if one is to expunge opinion and personal conflicts from the CPG.

I would instance the submission of the proceedings and the consensus statement of the "Complementary Medicine in Chronic Fatigue Syndrome National Consensus Conference" (Sydney 1995). This conference was attended by over 200 primary care practitioners, many with considerable experience in the field of CFS. Most of the presenters had published in the peer reviewed scientific literature. The proceedings and consensus documents provided a gathering of experience of a broad range of acknowledged experts (including two in the current Working Group), and with no public funding, produced both proceedings and a clear consensus statement. This was submitted to the WG, yet no reference appears in the CPG to either the approaches proposed by the presenters or the consensus statement following from it.

I posed the question to Loblay as to what had been the fate of the (unmentioned) proceedings or consensus statement, and was given the reply (personal communications, available on request) that the WG had “considered” the documents, and that they *may* be represented in the final document. This did not address the reason for exclusion from the original DCPG. It was also disconcerting that in 1995, Loblay declined an invitation to attend the conference in question, and was quoted in the media on the day before as saying that the conference was “politically motivated”, with a prior view that it would create no contribution to better care.

In this context, it is possible that Loblay or other WG members may not “respect” the authorities presenting at the conference, and may exclude the opinions of those people on that basis. This arbitrary exclusion is incompatible with unbiased, quality science.

The second question is “Who is an authority?”. There is no generally accepted view on this, although it may be argued that a primary author of a peer reviewed publication on CFS may constitute adequate evidence of “authority”.

On this basis, the majority of the current Working Group would not be considered “authorities”. The members who, based on the bibliography, would not be considered “authorities” include:

- Loblay (co-convenor)
- Stewart (co-convenor)
- Bertouch
- Cistulli
- Darveniza
- Ellis
- Gatenby (paper on breast implants only)
- Gillis
- Phillips
- Phoon
- Steven
- Watson

Those who would be considered authorities include Hickie, Lloyd, Rowe and Wakefield, representing only one quarter of the membership of the WG.

The views of those who remain unpublished in the peer reviewed literature on CFS may therefore need to be discounted if it is hoped that the current CPG will achieve any QER.

I propose that the term “respected” be deleted from QER IV on the basis that it is arbitrary, and introduces an unacceptable level of opinion in determination.

I propose that “authorities” be defined as a person who is a primary author of at least one peer reviewed paper related directly to CFS, or the secondary author of more than one peer reviewed paper related directly to CFS.

I propose also that those members of the WG who are not considered “authorities” under this definition be replaced by others who do fulfil this definition.

6.1.1.3 Alteration of Level of Evidence

There has been a tendency throughout the DCPG to promote or demote particular evidence on an arbitrary basis. The most obvious case, and a major flaw in the DCPG, is the “brownian motion” associated with cognitive behavioural therapy (CBT).

On page 18, two positive and two negative studies are documented, placing the QER for CBT at III-4. In the table on page 19, it has been inexplicably promoted to QER II (with a poorly argued case for dismissing the contrary studies on page 20). In the box on page 17, it has achieved QER of I, or the highest level. The data are not consistent with the rating, and if an elevation in status is to be undertaken, then the reasons must be overwhelmingly compelling, the reasoning clear, and the precise rationale for discarding contrary data must be explicitly stated. Even in such circumstances, the process of arbitrary (rather than evidence based) change leaves the way open for other diagnostic or therapeutic approaches to become equally “slippery”. The integrity of the CPG is immediately lost under such arbitrary approaches.

I believe it is fair to say that the value of CBT is a strongly held belief by some in the WG, and that their strong advocacy for the approach has resulted in it’s promotion beyond its status. It could also (or otherwise) be that the WG was searching for something positive to offer from the CPG, and was simply filling the vacuum created by the report itself.

In contrast, other evidence has been demoted to either a mention in the CPG, or has been omitted entirely. These areas relate to certain issues which one or more of the WG members personally oppose or about which they have publicly stated their incredulity. This includes the relationship between chronic fatigue syndrome and multiple chemical sensitivities, where the references appear to be missing. MCS as an entity or trigger factor appears to have been excluded from the DCPG, as has the association between occupational or environmental chemical exposure and chronic fatigue syndrome. The latter is reduced in importance by separating one case-control study from other papers or studies addressing the relationship on page 24.

As well, the letters and opinions of those opposing the therapeutic options so embraced by the WG have been excluded, especially in relation to CBT and graduated exercise. I include some of these. These letters should be considered part of the peer reviewed medical literature for the purpose of assessing validity of, and consensus surrounding, a particular approach. Clearly, such letters should not constitute evidence that the author is “authoritative”.

In this way, the value of the DCPG are effectively reduced to zero, as placement in a category is more contingent on opinion and arbitrary exclusion of data than on evidence.

I propose that a thorough review of the available literature be undertaken to determine where the current “bibliography” is deficient, and that the bibliography be updated to reflect the broader range of the literature.

I also propose that the QER be adhered to, and that the proposals should not vary from the correct categorisation according to the data, other than the WG’s view of the validity of data.

Finally, regarding the QER, I would note that the body of the report repeatedly (and correctly, in my opinion) asserts that CFS may represent a number of distinct pathological processes, and is most likely not a single disease. I believe it is fair to say that no single diagnostic or therapeutic approach is likely to be effective across the different pathogenic processes.

If this is to be accepted, then it is difficult to conceive how any QER could rate above III-2, on the basis that it is unlikely (or at least we cannot be sure) that the study group is representative of CFS as a whole. This is further compounded by the fact that the research assessed emerges mainly through tertiary referral (with the inherent biases admitted in the body of the report on page 15).

In particular, I note the item in the bottom of the box on page 8, under "Specialist referral", which states:

"An experienced general practitioner should be able to make the confident diagnosis of CFS in most patients. Specialist medical or psychiatric referral is only required if the diagnosis remains in doubt (Level IV)"

If we assume that this has been true for some time, then this would lead to an important "skewing" of the population seen in secondary or tertiary referrals, who would then see a preponderance of patients in whom "the diagnosis remains in doubt". It would not, therefore, be surprising that these referred groups are not representative, and may lead to widely divergent views of the illness being held by different groups. In particular, the "referral because of doubt", rather than because of severity, would tend to make other diagnoses more likely, as the referred patient is unlikely to be a "classic" CFS case. This could explain the high rates of depression diagnosed, and may explain the apparent success of therapies like CBT, which may be likely to be less effective in "plain vanilla" CFS patients.

In addition, since technology at present does not allow for appropriate categorisation of the pathophysiology or appropriate subgrouping, there is no way of being confident that any patient sample is representative. In the absence of strong evidence of the sample being representative, one cannot assume that the sample is representative.

In a sense, this is analogous to resolution in microscopy. The resolution is inversely related to the wavelength of the imaging illumination. Resolution cannot exceed this limit, although people peering through a microscope may interpolate, based on their perception of the image seen. Our view of CFS is at present most fuzzy, and any type of certainty is likely to be opinion based on personal perception. We are assessing a most blurred image, and all are searching for ways to shorten the wavelength, to sharpen the image. We must be cautious not to interpolate the data based on our perceptions, then pass it off as if it were science.

I propose that it be overtly stated that there is no current evidence which can be rated higher than III-2, and that improvement of the QER will depend on future subdivision of patient samples into provably representative categories.

6.2 Bibliography

The Acknowledgements (page ii) thank “Andrew Lloyd, Ian Hickie and Christina Ricci for their comprehensive review of the published literature and preparation of preliminary drafts”.

This is of some concern to me.

Firstly, I would ask if this means that the responsibility for the gathering of literature evidence and preparation of preliminary drafts (leading to the DCPG) was left in the hands of this small subgroup of the WG? If so, I have concerns that two of the three named (Hickie and Ricci) are from a single institution, namely the School of Psychiatry, and would ask what efforts were made to ensure that the research related to psychiatry was not overly represented in the final references or DCPG? Was the work of these three members independently reviewed by others in the WG to ensure that no (intended or unintended) biases were introduced. If so, who reviewed this work?

If it has not been independently reviewed, it is possible that the expertise in psychiatry may have led to an increased comfort in the Medline search terms used in psychiatry, and a relative discomfort with terms used in medicine generally. As well, biases in the preliminary drafts would be considered likely to have occurred (because of the individual’s knowledge and expertise in those fields), and it is possible, given the limited funding of the WG, that such initial unexamined biases may have proceeded through to the DCPG finally published for comment.

It is my view that such biases in assessment and management are obvious in the DCPG. How would one ensure that my view was not a correct interpretation?

While it is commendable that the researchers (Hickie and Lloyd) have included the references to the broad range of their own research, there are gaps which are apparent in the bibliography even on a cursory reading. The failure to gather the articles relating CFS to multiple chemical sensitivities (MCS) is an obvious error. This may relate to the lack of experience in appropriate search terms for this area of medicine, and would most likely have been addressed if a broader range of researchers had been involved.

A brief search of Medline has turned up many references which were not included in the Bibliography. Even worse, there appears to have been systematic errors of omission, and the information omitted appears to relate primarily to studies which conflict with prior expressed or published views of some of the WG members. This is outlined below, but if proven to be intentional withholding of published evidence, would amount to scientific fraud. Under such circumstances, I have no doubt that all would agree that the integrity of the WG would be sufficiently called into question (as all members must be considered responsible for the conduct and publication of the DCPG) that an external, independent investigation would be required. Clearly, under such circumstances, the DCPG would need to be shelved while this apparent anomaly was pursued. If shown to be likely to be true, the DCPG would need to be discarded, with the process starting over.

The difficulty with such a bibliography lies not so much in assessing what is included, as what is left out. It is possible to argue with the included literature, but determining when data or references are omitted is extremely difficult. Acceptance of the references included then depends entirely on the available resources, the quality and the integrity of the few researchers involved. Intentional omission cannot be easily distinguished from unintentional omission.

Put bluntly, it is impossible to know if the assessment of the literature is complete or representative without an independent parallel literature search by researchers from another field, and matching (and combining) of the two outcomes.

I propose that an independent comprehensive review of the medical literature on CFS be undertaken, and that a comparison be made with the literature review provided. Explanations should be made regarding discrepancies, and the reviews combined.

6.2.1 Evidence of Scientific Misconduct or Fraud

It is of great concern when a supposedly independent expert or review committee abuses the trust which is placed in it by the medical and scientific community. While it is never possible to divorce the scientific method from human biases, such committees are meant to circumvent the problem by incorporating a diversity of expertise, opinion and evidence, and by the process of the committee catching and correcting potential biases as they occur. In this way, the medical community is able to place a high degree of trust in such processes, and this trust translates directly to the likelihood of incorporating the outcomes and recommendations into patient care.

It is thus extremely important that the WG correct any identified biases, and that they prevent such biases from entering the final recommendations or outcomes. Failure to do this would be considered, at least negligence, and at worst, scientific misconduct or fraud. Evidence of active withholding or other suppression of evidence, preventing the committee from performing its function, would almost certainly constitute evidence of scientific fraud.

It is my view, based on a review of the available medical literature regarding CFS, that there is strong evidence of selective literature quotation designed to support one view over others. It is also my view, based on the same review of the literature, that there is evidence of deliberate withholding of evidence (peer reviewed publications, trial outcomes, etc) where such evidence conflicts with the prior opinion of some of the members of the WG.

I appreciate the seriousness of such allegations, and do not make them lightly. Due to the constraints of time, and the large number of papers in both the medical literature and the bibliography of the DCPG, I have not been in a position to look at all aspects of these potential biases in the DCPG. However, I am confident that in the areas noted below that such manipulation of the evidence base has occurred. The fact is that the manipulation leads to loss of information which may otherwise conflict with the prior views of some of

the members of the WG. This is the reason that I believe that a case for scientific fraud can be made.

The secondary issue of the responsibility of each member of the WG for the conduct of the group as a whole is a separate and important issue. The use of public money from the Department of Health and Family Services carries with it a high responsibility for accountability of all members of the WG. It is not sufficient to say that the manipulation of evidence was not known, for all members are responsible for the group as a whole. All have allowed their name to be used in the DCPG, and all would presumably have been credited with the final CPG. It is therefore incumbent upon all members to ensure that the data and evidence are complete, unbiased and supportable, just as these same responsibilities fall upon all authors of papers published in the scientific and medical literature.

Firstly, I will deal with the evidence of selective quotation of the literature to support a particular viewpoint. The text refers on page 15 to a single reference from "Ernst, E", an article entitled "Complementary Medicine: from quackery to science". The single reference is one of many articles on this general issue, and all other papers by Ernst appear to have been ignored. This single paper is misquoted, appearing to support the view of no value of complementary medicine in CFS. In fact, this article does not relate to CFS, and is one of many authored by Ernst on the subject of evaluation of the safety and efficacy of complementary medicine. In the context in which it is quoted, it is also not representative of the paper in question, nor of the many other papers authored by Ernst regarding this issue. The use of an isolated reference to imply a lack of value for approaches or practices in complementary medicine is unsupportable, given that the point of the work by Ernst is to demonstrate that there is a similarity in the evidence base (or lack of it) for both orthodox and complementary medical practices.

Selective literature quotation is reprehensible in such documents, and it can even be argued that it constitutes a subtle type of scientific fraud, particularly when the quotation misleadingly purports to be representative of the author's views, or when a subset of the author's work is used to produce a picture not supported by the general work of that author.

I provide a general overview of the issue of complementary medicine, related to issues of safety, efficacy and research, with a selected bibliography. This paper is designed to put the case "for" the careful and considered safe use of complementary medicine, and I would ask that the references be included in the CPG.

I wish also to submit this paper for consideration by the WG of the place of complementary medicine in future CFS research, and its place in clinical practice.

The other selective quotation of the literature is the omission of the BMJ and other "Letters" responses to the studies of CBT and graduated exercise programs. The DCPG utilises the original studies, but fails to include the responses of the medical and scientific

community also published in the same Journal. This leads to a view that the original article was meritorious and generally accepted, when the fact is that there was significant and well reasoned criticism of the methods, case selection, categorisation of patients, and post hoc alteration of assessment criteria. While these letters are not RCT, they are found in any search of medline with the CFS search criteria. I have found these consistently reported using two different search engines. Thus, it appears to be true that there has been an active decision to exclude these dissenting views on practices which the WG escalated to QER of I or II. This would have been impossible if the content or the existence of these criticism had been made available to the WG.

Most seriously, though, I was concerned by the failure of the DCPG to mention at any point the issue of multiple chemical sensitivities, and its relationship with CFS. The further issue of environmental and workplace exposure to chemical agents was also virtually totally excluded. The issue of triggering or exacerbation of CFS following immunisation was also not addressed.

These data gaps concerned me, and I gathered the medical literature on these subjects. All were able to be found under the search criteria of CFS, and I include some of the references and abstracts which appear to have been intentionally excluded from the bibliography of the DCPG.

There is thus a likelihood that the references have been constructed to support the views and argument held by the WG and published in the DCPG, rather than the DCPG body being derived from an unbiased assessment of the totality of the medical scientific literature.

If this is the case, then it would seem that the DCPG is a misrepresentation of the available data, and suggests either incompetence or fraud. If the exclusion of relevant data has been intentional, for whatever motive, then it is an issue of scientific fraud rather than incompetence.

The following extract is from an email sent to me by Victoria Toulkidis, <policy@racp.edu.au> on 20/2/97 concerning the missing references:

The bibliography does not include all the references that have been reviewed, only those used in the guidelines according to their levels of evidence. If you have any further queries about this, please ask Rob [Loblay].

I believe that in total, and from the above information, it is clear that the references were selected to support the views expressed in the guidelines intentionally. I believe that this is a very serious matter, and requires independent investigation of the propriety of the WG generally, and the individuals responsible for the exclusion of scientific evidence in particular.

6.3 Authors

6.3.1 Membership of Working Group

Page (ii) of the DCPG provides a list of members of the WG. The information provided is inadequate, and requires expansion.

A preamble is required which addresses the details of how the WG came to be, and the processes by which its membership was constructed. A specific statement needs to be made as justification for the inclusion of each member of the WG.

The rationale for the choice or election of Convenors (Loblay and Stewart), and the process by which they became Convenors should also be stated in this area.

A brief CV related to CFS is required for each member of the WG. In particular, the following information is required so that those reading the report can adjudge the experience and expertise of each member in relation to CFS:

- Publications in peer reviewed literature related to CFS
- Specialty and type of clinical practice
- Number of new CFS patients seen per year in clinical practice
- The types of CFS patients commonly referred (ie referral base)
- The number of years experience in assessing and treating CFS
- Experience in primary care practice managing people with CFS

I understand that there were serious discrepancies in the degree of input and frequency of meeting attendance provided by the different members. To aid in assessing the relative contributions of the members of the group, the following information is also needed:

- Number of WG meetings attended, and which meetings were attended
- Reasons for nonattendance of other meetings
- Information provided by each member
- Information and/or submissions reviewed by each member
- The input of each member into the DCPG, as precisely as possible
- The income or reimbursements received by each member from the grant

As well, a brief statement of the accounting is required. An overt statement identifying all sources of funding for the document creation is required. How was that money allocated? What income did each member receive for the work done? How many hours of work (paid and unpaid) were contributed by each member of the WG.

There is a clear sex bias in the membership of the WG, with 15 of the 16 (94%) members male. How is this accounted for? Were steps taken to attempt to address this bias in the group? If not, why not?

There is a clear bias towards members of the RACP in the membership, and it seems to me that 12 of 16 (75%) are specialist physicians of various types. Two (13%) are general practitioners, one (6%) is a psychiatrist, and one (6%) is a consumer representative. How is this bias explained, given that the document is aimed at “assisting general practitioners”.

Finally, the Acknowledgements need to be somewhat more complete in the statement of the helpful actions performed by those within and without the WG. Specifically, the contributions of Lloyd, Ricci and Hickie, and that of Helen Lapsley need to be discussed or specified. These may be critical to an understanding of the problems which later arose in the DCPG.

6.4 Preface

Page iii

Col 1, Par 1 Change the line, “They are based on the best information available at the date of publication” to something like, “They are based largely on the evidence derived from an extensive Medline search of the literature at (date of literature review)”. There is no easy definition of “best” and no way to determine that there could have been no better way.

Change “...are intended to provide a general guide to appropriate practice” to “...are intended to provide a summary of the available peer-reviewed literature on the subject, and suggestions to improve the quality of care for CFS patients”. The term “appropriate practice” has a very definite technical meaning for the Health Insurance Commission (HIC, who funded the study). If this defines “appropriate practice”, it follows that all other approaches must represent “inappropriate practice”. Legislation currently exists which allows for Australian doctors to be referred to a powerful disciplinary body (a statutory body known as the Professional Services Review - PSR) on the arbitrary basis of suspected inappropriate practice. This can result in expulsion of the doctor from the Medicare system (ie their patients cannot claim for the doctor’s services under the public health insurance system), massive fines of up to twice the doctor’s yearly income, or both.

Dr Loblay has repeatedly and publicly asserted that the GPG is in no way intended to restrict clinical practice, and is not intended to be used by third parties for political ends. On direct questioning regarding the PSR, he has made public assurance that, despite funding of the WG by Medicare, the outcomes would not be able to be used by Medicare for referral of practitioners to the PSR. His stated view of the guidelines is that they should not allow for such use.

I find it more than coincidence, however, that the precise term, “appropriate practice”, should be used in the DCPG. The term would allow for such abuse of the guidelines by the Health Insurance Commission (Medicare) and by the PSR. It is more likely than not that it will allow for the CPG to be used in an attempt to restrict diagnostic and therapeutic

approaches in a misguided attempt to control Medicare costs. This will cause immense stress and suffering to doctors who do not adopt the approaches supported in the CPG.

I propose that the section of the paragraph "...and are intended to provide a general guide to appropriate practice", to "... and are intended to provide a summary of CFS research to date, in the hope that such information will allow for general practitioners to refine and improve patient care"

I further propose that the following be inserted at the end of the paragraph 1 of the Preface. "The CPG are not designed to restrict or override clinical judgement of medical practitioners in their care of people suffering CFS. They are therefore not to be used in any way to determine appropriate or inappropriate practice, and should not be used to identify, refer, or judge doctors whose practices may differ from those suggested in the CPG."

Finally, a statement in the first paragraph is required to recognise that the guidelines are a partial and very incomplete review of the available evidence (by nature of the restrictions in funds and time for their generation), and that they are out of date in this rapidly changing field by the time they are published. This is different from other areas of medicine, where CPG emerge from a stable body of knowledge of pathophysiology, and where on the whole, minor adjustments are all that is usually required.

I propose that the following be inserted after the first paragraph of the Preface: "The field of CFS research and practice is rapidly emerging at present, making it likely that the CPG are out of date even at the time of first publication. They should not in any way be considered complete, definitive, prescriptive or proscriptive. It is recommended that an ongoing commitment be made to allow for regular (say six monthly) review of the CPG, to allow incorporation of new evidence and information, revise information contained herein, and to delete information or references which are unsupported by subsequent data."

col 1, par 2 In the last sentence, it would be more accurate to say, in my opinion, "In 1994 a fully revised discussion paper prepared by Robert Loblay was circulated...". I have read the paper, and Loblay was the sole author. I am unaware that there was any formal election of Loblay to represent ASCIA, and it was certainly the opinion of the president of the RACP at the time that this was Robert Loblay's discussion paper.

col 1, par 3 More information is needed regarding the circumstances surrounding the decision "to develop an expert consensus position". Who were the individuals involved, and on what basis did they "represent" the RACP and ASCIA? Were they elected to those representative positions, and by what method in each case? It is my understanding that the people were not "representatives of" the bodies, but simply "members of" the bodies, who appointed themselves to the WG.

The last two sentences are of interest and need expansion.

Firstly, the "multi disciplinary Working Group ... was established under the auspices of the RACP to develop and disseminate evidence-based guidelines *following the procedures recommended by the NHMRC*" (my emphasis).

This seems like rudimentary “terms of reference”, and in the absence of other goals and terms, may need to be taken as such. If this is so, then there is no allowance for the WG to engage in variations of the procedures recommended by the NHMRC.

This would suggest that the arbitrary alterations of those guidelines, and in particular, the alterations to the quality of evidence ratings (QER) should not have occurred.

It is not adequate to state that Helen Lapsley (as a member of the NHMRC) agreed with the changes, any more than it would be adequate to change the definition of CFS with the agreement of the WG Convenor.

I propose that the DCPG be discarded on the basis that it failed to adhere to its own stated terms of reference, and made arbitrary alterations to the procedures recommended by the NHMRC.

The simple statement “The Commonwealth Department of Health and Family Services provided funding.” is inadequate, and needs to be both expanded and explained. The following issues, as a minimum, need to be addressed:

- What was the extent of the funding?
- From which area or division of the DHFS were the funds provided? Which budget within the department did it impact?
- What were the requirements of the WG, laid down by the funding body, regarding use of the money, accounting practices, auditing, and fiscal responsibility? Who was appointed auditor? What procedures were put in place to prevent misappropriation or waste of the funds?
- What was the nature and content of the contract agreed to for the funding? What were the expectations (stated or anticipated) by the funding body?

There are many issues regarding the propriety of accepting funds from a body which may have a financial or other vested interest in the outcome, and recent medical literature has adequately demonstrated that the source of funding can be a significant factor in determining the outcome of research in medicine. At the very least, a clear statement of the potential for such biases needs to be stated in the body of the report, and the issues of potential use or misuse of the document need to be stated.

As well, the study must overtly state the source of funding in sufficient detail for the reader to determine if a conflict of interest may exist, and the likely type, direction and extent of those conflicts.

I propose that the above issues related to funding and full disclosure be addressed, and that more extensive information on these matters be prominently included in the CPG. I further propose that a critical review of these statements be made by a trusted third party, agreed to by the WG and by other stakeholders (GPs, patient support group representatives, etc).

col 2, par 1

It is my view that the literature review is neither “exhaustive”, nor is much of the literature review “relevant”. This is a statement not backed by any evidence beyond the existence of an extensive bibliography. I have addressed this issue in a specific critique of the References elsewhere. This first sentence should be altered to read as follows. “Three members of the WG conducted a review of the medical literature on fatigue, prolonged fatigue, chronic fatigue and CFS.”

The first mention is made of the “modification” of the NHMRC schema, in apparent contradiction to the information in the previous paragraph. Further information is required on this matter, if the modifications are to have any validity. It is my view that the flaw in this arbitrary modification is so serious and pervasive that the DCPG are reduced to being an opinion based, useless document, unable to be compared to other CPG, and unable to be validated. To me, this means that the DCPG should be abandoned, and a fresh start made, which conforms to strict terms of reference.

The “variety of other local and international public domain documents” which were examined need to be explicitly listed. This type of “motherhood statement”, intentionally devoid of information, is common throughout the DCPG.

col 2, par 2

This paragraph relates to the same issues addressed in the paragraphs above. In particular, I have been unable to determine the fate of the submission by the Australian Comprehensive Medicine Association (ACMA), including the proceedings of the 1995 consensus conference on CFS, the consensus statements arising from the conference, or the documents on the “Cheney Clinic Protocols”, arising from a specific workshop on CFS conducted by Dr Paul Cheney in 1995. I would ask that the fate of these documents be explicitly addressed, and include information regarding which members of the WG were provided copies of the documents, and which members reviewed and summarised them for potential inclusion in the DCPG.

I propose that a complete listing of all submissions and documents be made, and be included with the body of the report along with details on the submitting body or individual. I also propose that the fate of each document, including a list of the WG members who read and assessed each document, be stated, and that information be provided as to whether the contents were considered, included in, or excluded from the DCPG. For those documents which were in part or whole excluded, clear reasons why should be provided. For those included, notes as to where they were included should be made.

Diagram

The diagram is meaningless without some descriptive legend. It is unclear what the boxes purport to convey, or in which category the WG falls. It appears that the WG’s DCPG relate only to the top centre box, “Research Evidence”, as the issues of “Clinical Expertise” and “Patient Preference” are not addressed by the WG in the DCPG.

I propose that the following caption be included below the diagram: The CPG address the area of “research evidence”, and informed decision making requires that further data be gathered and incorporated from “clinical expertise” and “patient preference”. The CPG do not address the last two issues.

6.5 CLINICAL OVERVIEW

There appear to be sections missing from the Clinical Overview. It would appear to be the place to address issues regarding the general context of the CPG, raising issues of the political issues of cost containment, evidence-based medicine (which requires a careful definition), social justice, and the problems of medical analytical approaches in dealing with complex illnesses.

As well, a discussion on the issue of suffering and disability, and the response of the general and medical community to these would be useful, as would a brief outline of the history of CFS in Australia.

I would suggest that this is also the area to initiate discussion on the divergent views on CFS, contrasting the differing views, experience and requirements of sufferers, family, community, primary care practitioners, specialists and researchers. It may also be useful here to note the very high use of complementary medicine by CFS sufferers, and the general failure of the orthodox medical profession to deal with the illness adequately.

The opportunity arises in this section to explore the ways in which the divergent needs of sufferers, carers, families, communities, government, business, doctors, and researchers could be simultaneously met. The issues of social justice, and nonjudgemental provision for disabilities are important.

The Overview is the place to overtly state the “philosophy” of the WG, especially in approaches which may otherwise lead to unnecessary confusion. An example would be the issue of mind-body division, and the concept of psychosomatic disease. A clear statement here could make an enormous difference in the potential for misuse or abuse of the document by “unenlightened” individuals or organisations who may have an interest in misusing the later material to categorise sufferers as suffering psychological or psychiatric disease. In passing, it needs to be recognised that the very existence of the specialty of psychiatry tends to encourage the perpetuation of that division. A call for cooperative “transdisciplinarity” (see accompanying Science Spectra editorial) may be useful. This may do some good in putting an end to the “turf wars” in which different specialties, and even complementary and orthodox medicine approaches, compete for the control of the illness, and ownership of the (eventually defined) disease.

I remain confused as to the reason for the interests of immunologists in an illness which is generally regarded as primarily neurological in nature. This could be explained.

I would suggest that a preliminary discussion on aetiology should be commenced in this section, especially addressing the likelihood that differing aetiologies may result in different pathological processes, requiring different management strategies, and with very different outcomes. The general areas of proximate apparent causes of CFS, including infection, environmental, post-vaccination, genetic, and metabolic causes should be nominated and briefly addressed. In addition, the current view of the CDC, derived from their trials, that CFS should be divided into broad categories of rapid and slow onset

needs to be addressed. It seems as though this division is useful, and the failure to make the division may be an important reason for the divergence of viewpoints in the literature.

The CDC case definition (Fuduka 1994) defines the diagnosis of chronic fatigue syndrome, and the basic criteria are outlined in the box on page 1. There appears to be a mistake in part 2 of the box, "Other Symptoms". On page 956 of the original Annals paper, the symptom list is seen at the bottom of column 1. Each of the symptoms is separated by a semicolon (;), and there are seven symptoms by this assessment, rather than eight identified in part 2 of the box. The reason is that in the original definition, "muscle pain, multijoint pain without joint swelling or redness;" occurs as a single symptom (presumably indicating that musculoskeletal pain is the symptom assessed), whereas in the DCPG, the muscle and the joint pain are listed as separate symptoms. This does make a material difference in the correct diagnosis of CFS, and this matter needs to be addressed and most likely corrected in the DCPG.

Page 1

- col 1, par 1 The second sentence should be changed from, "...and is accompanied by other constitutional and neuropsychiatric symptoms," to "...and is accompanied by other constitutional symptoms, with or without concomitant neuropsychiatric symptoms".
- The case definition can be fulfilled with only four of the seven core symptoms, making it quite possible to have CFS without neuropsychiatric symptoms. Clearly, fatigue cannot itself be termed an "other ... neuropsychiatric" symptoms, because it is the prior defining factor. Pain is not a neuropsychiatric symptom.
- col 1, par 2 Add to the end of the paragraph, "For this reason, it is unlikely that a single diagnostic or therapeutic approach can be generally applied to CFS, and the appropriate assessment and management of CFS must in the meantime remain an issue to be decided in each individual clinical setting."
- The error corrected is that of inappropriate extrapolation from the general to the specific. The aim of the addition is to recognise that while on a statistical basis in an undifferentiated CFS population, no single cause or treatment may be determined, in a clinical setting of an individual patient consultation, likely causes and useful management can be decided for the particular case.
- col 1, par 3 Add to the end of the paragraph, "Worse still, the suffering and disability is frequently increased by the failure of the doctor to recognise and diagnose the illness appropriately, or by the denial of the diagnosis of CFS by doctors who refuse to accept the reality of the illness. There is no place in medicine for such abuse of an already vulnerable and sick patient by a doctor."
- This addresses the iatrogenic component of the unaccepting attitude of the doctor, and the harm done by failing to diagnose and categorise sufferers.

col 1, par 4 The final sentence is poorly constructed, unclear and is potentially a source of considerable confusion. It appears to leave the choice between the diagnosis of CFS and the diagnosis of depression arbitrarily in the hands of the clinician, although it betrays a leaning towards CFS as the primary diagnosis. I believe the statement can be made clearer, and more in line with the CDC case definition (Fuduka 1994) by rephrasing along the following lines:

“CFS is often associated with feelings of depression in sufferers. In part, this depression arises as a result of the neurochemical changes caused by the illness, and in part as an expected consequence of suffering a chronic and disabling illness. Occasionally, the depression is accentuated by the failure of family, community or doctor to accept the diagnosis, or to appreciate the pain and disability associated with the illness. The diagnosis of CFS takes priority over the diagnosis of depression as a primary diagnosis, except in clear cases of major depression.”

col 2, par 1 It would be surprising if “major depression” were defined as “loss of motivation and pleasure” as suggested in this paragraph. If that is the definition, then it reflects simply the poverty of science in the field of psychiatry. Many CFS sufferers experience a “loss of motivation and pleasure”, as do sufferers of any chronic and debilitating illness, especially in those in which pain is present. This line can give the impression that this symptom is the hallmark of major depression, and could lead to the inappropriate diagnosis of major depression, and the failure to correctly diagnose CFS. It should be deleted, or restated in a way to avoid the possibility of misinterpretation.

col 2, par 2 Similarly, the issue of “prior episodes of depression or anxiety (vulnerability to psychiatric disorders” should be removed for the same reasons. I am unaware of any evidence that people suffer “a vulnerability to psychiatric disorder”. In what way can a person be proven or disproved to be so “vulnerable”. Does the subsequent emergence of psychological disorders support or confirm such “vulnerability”. This is opinion based, retrospective medicine at its worst, and may well result in mistaking long term mood alteration appropriate to poor personal or social situations with vulnerability to such psychiatric disorders, allowing for the underlying circumstances leading to the symptoms (poverty, work stress, etc) to be ignored

The issue of chemical exposure in the workplace, in agriculture, and in the environment generally needs to be addressed here. Clear, high dose toxic exposure suggests a preferable diagnosis of “toxic chemical poisoning” (and not CFS), while it is generally considered that moderate dose exposure to such agents should not preclude the diagnosis of CFS (Dunstan 1995).

A mention should be made of multiple chemical sensitivities (MCS) and its close relationship with CFS (literature references supplied). Exposure to volatile chemicals in MCS sufferers frequently triggers a rapid relapse of symptoms of CFS. As well, many people with CFS develop a heightened awareness of, and sensitivity to, the effects of low or moderate dose chemical exposure.

col 2, par 3

This is incorrect, and again is an error caused by extrapolating the general to the particular. The fact that there are no *consistent* clinical findings on physical examination of CFS sufferers in no way suggests that all CFS sufferers have no abnormalities on physical examination. In fact, it is my experience that most CFS sufferers do have abnormal signs on examination, although these signs vary greatly from individual to individual. The "Cheney Clinic Protocols" and the CFS Consensus conference proceedings (1995), both of which were submitted to the WG, list the types and frequency of physical abnormalities found in CFS sufferers. Primary among these are evidence of autonomic dysfunction (incl orthostatic hypotension), alterations of balance (without hearing loss, and usually without tinnitus), and inflammation of the pharynx and nasal mucosa. In addition, temperature is typically reduced by approximately 0.7 degrees celsius.

Page 2

col 1, par 3

Investigation.

The issue of investigation suffers again from the general flaw of inappropriate extrapolation from the general to the particular. While many studies have been performed involving the general group of patients with CFS, this is a very different matter to investigations in an individual with a specific history, symptoms and signs. By definition, a single patient cannot cross many categories of CFS, and therefore is a single member of a subgroup within CFS. A single patient does not suffer from the dilutional effect of a large group of poorly differentiated patients.

The clinical assessment and investigation, beyond the limitations described for poorly differentiated groups, is therefore not only possible, but is usual and expected. Clinical medicine should never be forced to await the completion of research before becoming involved in patient care and reducing suffering.

Thus, in the clinical setting, it is not necessarily true that the only purpose of testing is to exclude other disorders, even though that exclusion process is very important.

I provided the WG with a copy of the CFS Consensus Conference proceedings, and a copy of the Cheney Clinic Protocols. Each provides evidence from the literature that in a clinical setting, history and examination can suggest a categorisation within CFS (infectious, post vaccination, toxic, allergic, etc) which in turn becomes a provisional diagnosis. Specific testing is then able to improve the confidence in such a provisional diagnosis, suggesting that appropriate testing may be an aid to appropriate categorisation. In addition, abnormalities identified may be useful in assessing progression or regression over time, and in predicting prognosis more accurately than clinical assessment would allow.

I am aware that this view is repeatedly returned to throughout the DCPG, and in almost every case it betrays a lack of understanding of the differences between a statistical, frequentist approach to medicine, and the processes normally involved in primary

practitioner care of patients. Neither is more or less scientific - they simply represent different approaches to the solution of different problems.

Certainly, primary care approaches may need to be altered in the light of strong evidence which emerges from quality research in well defined illnesses. This is not the case with CFS, as the sufferers are heterogenous in nature, the quality and value of research to date is exceedingly poorly conceived and executed, and the homogeneity and appropriate categorisation of patients is almost non-existent.

col 1, par 4

The bulleted list is arbitrary, and simply lifted from the Fuduka 1994 paper without critical review. It is not evidence based, but opinion based. I would add at the very least cholesterol, and antinuclear antibody, on the basis of the high yield of abnormalities as a likely contribution to the fatigue.

There is always value in assessing organ function where clear evidence of dysfunction is elicited on history. Thus, clear neurological deficit may require central evoked response testing, especially in cases in which neurotoxin exposure is proven or likely. Hepatitis screening is useful in patients at risk of hepatitis, with tender and inflamed livers. Hormonal testing, assessing the path from cholesterol to sex hormones and cortisol, is worthwhile where evidence of hormonal dysregulation is clear. And allergy testing (IgE, skin testing) is required for the 30% to 40% of patients with clinically important allergy.

col 1, par 6

Specialist referral

I am unaware of any evidence which suggests that specialist referral to a physician or a psychiatrist results in any improved outcomes for patients, or in the formulation of an appropriate management plan. In the absence of such evidence, I would assert that such referral is likely to worsen outcomes and management plan, in part because the specialist(s) is/are likely to begin to "subdivide" the patient, with little regard for their overall wellbeing or best outcomes. In short, the CFS patient is probably benefited more by avoiding physicians or psychiatrists than by consulting them.

col 1, par 7

Under management, the issue of "spontaneous" resolution of prolonged fatigue is problematic. There is no evidence that the resolution is spontaneous, as it may occur as a result of active patient strategies designed to relieve the problem. The lack of knowledge of the mechanisms of "normal" recovery from fatigue is a tragedy of lost data, as people who recover tend not to return to their doctor, who loses them to follow up, and loses the data concerning those factors which encouraged resolution.

col 1, par 8

The first sentence needs to be changed from "Doctors who display empathy..." to "Doctors who are empathetic...". Sufferers are sophisticated and very sensitive to non verbal clues in communication. Generally, it will not help a patient if his or her doctor simply learns to display empathy and the other values.

It is my opinion that the doctor must enter the therapeutic relationship at a different level to be of value to the sufferer. This means that the emotional link must be authentic and not assumed for the purpose of patient manipulation.

I would note that this paragraph is another “motherhood statement”, and clearly applies to all illness, and not simply CFS.

col 2, par 2 The bullet points are opinion based, not evidence based, and this should be noted in the text. The fact that I agree with most of the points is irrelevant.

col 2, par 3,4 The two paragraphs under the heading, “Understanding the illness” are entirely opinion based, and have no evidence to support them. In addition they represent the personal views of at least one (and most likely a number) of the WG. Such assertions and use of CPG to perpetuate personal opinion is reprehensible, and has no place in such reports. Both paragraphs need to be removed from the report.

I refer to the general section regarding the flaws in the argument that a belief in the physical nature of the illness is a poor prognostic factor.

col 2, par 5 The conclusion drawn in the second sentence cannot be derived from the assertion in the first sentence. The first sentence should be amended to “No pharmacological agent has been reliably shown to be effective treatment for CFS generally, although it is likely that one or more agents may be of benefit in the individual clinical setting.”

Even if the original sentence were true, the second sentence is not true. Management strategies may be directed to symptom relief, social support, rehabilitation, or many other aspects beyond “minimising impediments to recovery”, as is stated. This needs to be changed.

As well, “management strategies” involve far more than “pharmacological agents”. They may involve surgery, physical therapy, counselling, access to social security or insurance, retraining, or any of dozens of other strategies.

And again, the confusion between lack of benefit for an unselected group in a research setting and benefit in an individual consultation is apparent.

graph page 2 The graph is inaccurate, and has no data to support it.

There are no data to determine if we are dealing with a homogenous single group, or a number of distinct sub populations. The true graph may well represent a series of overlapping normal distributions, especially given that the WG has suggested that CFS may represent a range of different medical causes and conditions.

In any event, it provides an unreasonably optimistic view of the outcomes in CFS to suggest that more than 50% of CFS patients (those who fulfil the criteria at 6 months after onset of the fatigue) no longer have these symptoms after a further year. This is not even supported in the text of the DCPG in Section 3 - Natural History of CFS. It seems more likely that the vast majority of people who have had CFS retain *some* symptoms of the CFS, even though they may improve in their health and capabilities over time. My reading of the literature is that more than 50% of correctly diagnosed CFS patients remain unwell with CFS two years after the onset of the symptoms. The honest appraisal of the literature is that it is inadequate to reach any firm conclusions of prevalence,

incidence or natural history of the illness at present, and that there exists an urgent need for data gathering from the primary care arena to determine all of these, and answer the question of whether or not the incidence is increasing over time.

It is also worth distinguishing recovery of the illness from the adaptation made by the person to reduce symptoms and disability. As an example, accidental amputation of a limb is an example of a pathological state which will not recover in any way, but in which the impact and disability caused by the pathology can be reduced over time, mainly from adaptation of the host to the permanent defect.

It is my own clinical experience, having talked with many people who have “recovered”, that they do not return to their former robust state of health, but remain impaired for many years with some of the symptoms of CFS. Their “recovery” is more often than not a complex of tissue repair, recovery of organ function, and adaptation to residual damage and disability.

In passing, the graph should either be removed, or a modified and more realistic graph (with riders regarding the speculative nature of the graph) should appear in Section 3, rather than on page 2.

page 3

col 1, par 1

There is no evidence that “loss of aerobic fitness” is an “impediment to recovery”. In fact, recent work at Adelaide (presented at the CFS 98 Conference in Manly, attended by Loblay and others of the WG) would tend to deny this. Again, it is an ill informed opinion, dressed up as if it were factual, or supported by research. An analysis of the studies which suggest the same makes it clear that this idea is nothing more than a “commonly held idea”, not based on data.

As well, the “disruption of the sleep-wake cycle”, and the “intercurrent depression and social isolation” can hardly be termed “impediments to recovery” in CFS. They are a direct consequence of the illness, and are observed in the majority of sufferers. They are, in a sense, the illness.

It would be absurd to say, for example, that “failure to speak properly, or move limbs on one side of the body” was an impediment to recovery in cerebrovascular accidents (stroke), or that chest pain was an impediment to recovery in cardiovascular disease.

This paragraph, in fact, demonstrates the confusion in the DCPG regarding causes, consequences, pathology, and associated factors in CFS. The confusion has permeated the entire document, and is, in my opinion, a significant factor in the generation of controversy and ill feeling between the WG and the sufferers, carers and primary care practitioners dealing with CFS.

If the WG were simply to revise the document with Occam’s razor somewhat sharper, excising those sections unsupported by reasonable and agreed upon data, and separating opinion-based from evidence-based material, then the document would be considerably

thinner, and would leave room for useful proposals on ways in which the data drought could be addressed.

I would refer the WG to the work of Ernst regarding a scientifically credible approach to addressing such data gaps, despite the fact that it addresses the broad field of complementary medicine.

The final absurdity of this paragraph is the idea that “a promotion of a clear understanding of the illness” would be of benefit. If the WG and experts have no “clear understanding” then the only way it can be gained is by gathering sufficient data to reach a “clear understanding”. This is impossible now.

It seems that *cognitive behavioural therapy* is defined here as “removing impediments to recovery” and “promoting a clear understanding of the illness”. If this is so, then CBT is impossible at present, in part because the “barriers to recovery” are the symptoms of the illness, and in part because no “clear understanding of the illness” exists.

This “fuzzy description” problem of CBT is dealt with elsewhere. It is insufficient to leave a therapeutic process so strongly advocated by the WG as undefined, unresolved, and without a clear statement of the method, mechanisms by which it works, and protocol. If this is not done, then the process of management gets into the realm of “spiralling empiricism”, a state abhorred in Loblay’s 1994 ASCIA paper to the RACP membership when applied to complementary medicine.

If the WG defines CBT as “an approach which works in most people with CFS”, then the reference is circular, and can be reduced to the statement, “The WG regards those approaches which work as approaches which work in CFS.” If any variety of undefined approaches appear to have benefit in many people with CFS, why not simply state this. It does appear that a basic component of every primary practitioner consultation or intervention could be termed CBT, and may well help minimise the illness and disability in *any* illness, but this helps little in defining an approach likely to be of benefit.

Passing it off as if it were a course of therapy, delivered by psychologists and psychiatrists, is dishonest and would tend to unnecessarily increase costs compared to the administration of the essential components within the medical consultation.

Unless it can be demonstrated that psychiatrists or psychologists need more clients, there can be little rationale for proposing CBT as a separate form of management. The therapy is lacking any scientific basis or credibility - there is no accepted definition of what it is, how it is performed, what its mechanism of action is, or how it differs from the emotional and medical support provided by good doctors as a usual part of the consultation. It is an unproven, and even worse, undisprovable therapy, as it shifts definition and implementation in a rather slippery way.

I am personally surprised that the WG, so ready to decry the lack of scientific basis or evidence for alternative medicine, should so gullibly accept a few poorly designed and implemented trials on an approach which is not scientifically conceived. To say that “it

works” is to miss the point. Exorcism may work, but would rightfully be rejected from consideration until, as Dr Lloyd put it, “some plausible scientific basis for its benefit” is established.

At present, CBT is a “black box” whose quality, definition, process and even existence is uncertain or unknown. That it is practised without this definition and information is more a tribute to the poor quality of the science of psychology and psychiatry than to the efficacy of CBT. That it is recommended by the WG in the DCPG is more a consequence of the desire of the WG to propose something positive in the vacuum of clinically relevant information, than to the value of CBT in CFS.

col 1, par 2

Physical Activity

It is not only in the early stages of the illness that this cycle occurs. The recovering CFS person, even years after the onset of the illness, is also subject to this “using up” of the returning energy levels. The paragraph should begin with, “At any stage of the illness, but particularly in the early stages and during recovery, ...”

There is no evidence to support this view that avoidance leads to increasing loss of activity. The Adelaide research suggests that this is not true, and that CFS has similar activity issues to those of sedentary employment. The failure of the WG to grasp the high variability of severity of CFS has led it to an arbitrary, and in my experience, untrue, assertion that the sufferer becomes a source of their own disability by avoiding activity. The alternative, obvious and preferable explanation would be that there is a natural variability of severity of the disease, and that the most disabled are those least likely to participate in activities, as admitted on page 11 of the DCPG. The long term avoidance is therefore described by severity, rather than avoidance practices.

By analogy, it could be argued that “failure to indulge in vigorous aerobic exercise” led to “activity avoidance” and a worse prognosis in patients with cardiovascular disease. The more likely explanation is that those with the most severe disease are less able to exercise, and the prognosis is related to disease state, rather than a consequence of that disease state.

col 1, par 4

There is no evidence that graded exercise programs are of benefit in improving aerobic capacity in CFS. Fulcher (1997) produced a flawed study in which more than half of the original “unselected” CFS referrals were screened out, based on less than well explained criteria. The authors used the Oxford rather than the CDC criteria, the control group entered a therapy (“flexibility treatment”) which appears to have worsened outcome compared to placebo, and the dividing line for “improvement” was set *after* completion of the trial. The trial was flawed in design with regards blindness (all subjects knew which type of treatment they were receiving), and may not have even been single blind according to normal definitions. The results cannot be accepted as useful under such circumstances

More generally, all similar approaches (CBT, positive thinking, graduated exercise programs, etc) suffer from a flaw that there is no real placebo group, since the “active” component of these vague therapies cannot be separated from the therapeutic process. In all of the studies I have seen, the study group have been proponents (before and after) of the approach taken, and they are clearly enthusiastic about the potential value of their approaches. The patients conscripted to the studies are fully aware of whether they are receiving the “active” or the “control” treatment (in Sharpe’s and other studies, the “control” was no intervention whatsoever, leaving such patients with a clear understanding that there was no attempt being made to help or treat them!), and the therapy in question is being administered by proponents of the therapy, or those with sufficient interest and belief in the value of the therapy to be involved.

Until these studies are replicated by researchers who are openly critical of the therapy, and until an appropriate vehicle for a true placebo-control trial can be constructed, validated and used, the results of these trials should be at best regarded as QER III-3. If one accepts that there are no control patients, however, they fit only as “single case series without control subjects”. Although they would have made it into the original NHMRC QER, the DCPG states on page 26 that these studies “provide little more than stimulus for subsequent hypothesis testing. Such reports were not included in the systematic analysis of evidence upon which these guidelines are based.”

In short, they have no place within the DCPG as currently defined, and all reference to them should be removed from the CPG, as should recommendations regarding their use.

I propose that all references to CBT and graduated exercise programs, as well as all other approaches to CFS in which control groups were either not present or were inappropriate, be removed from the report.

col 1, par 5 (incl bullet points)

If graduated exercise is to be undertaken, despite the total lack of scientific evidence for benefit, then any such exercise must be clearly patient regulated, with response to exercise used to define the process of such graduated exercise. Under any circumstances, if exercise induces fatigue on the day after the exercise, it needs to be ceased until recovery of baseline fatigue levels is regained, and should be recommenced at a reduced level.

col 1, par 7 **Sleep**

The fact that sleep alteration can cause symptoms in healthy people is irrelevant to the place of sleep disorders in CFS. By analogy, heavy exercise may induce shortness of breath in healthy people, but this is unrelated to the cause of shortness of breath in asthmatics, even ones who exercise. Reducing physical activity is unlikely to reduce asthma.

One is a physiological response, the other is a pathological response. The sleep disturbances in CFS are likely to be a result of the pathophysiological changes in CFS,

and may relate to gut flora alterations, chronic immune activation, or any of a number of other processes. This paragraph is meaningless, and should be deleted.

col 1, par 8

(incl bullet points)

There is no evidence to support these recommendations in CFS. Applying practices used in healthy poor sleepers to those with an illness is flawed, speculative, and may be as likely to be harmful as to be beneficial.

Either there should be evidence for each point made *in CFS patients*, or they should be removed, and included in a separate region of the paper dealing with speculation on “unproven approaches”.

In particular, the recommendation of sedative hypnotics to achieve sleep is at odds with later recommendations within the DCPG (page 21) that “behavioural approaches to managing these [sleep] difficulties are likely to be more successful than pharmacological approaches, as the latter do not induce normal sleep.”

Please explain!

col 1, par 9

There is no evidence to support this paragraph, unless one is suggesting that CFS patients are really sleep disorder patients in disguise. The concept of gaining the advice of a sleep physician (is there really such a specialty, or simply physicians with an interest in sleep disorders?) is utterly unsupported, as there is no good evidence of benefit for *any* patients with disordered sleep, let alone CFS patients, by such referral.

The tendency to suggest cross-referral to various specialist physicians needs to be carefully reviewed by the WG. There is absolutely no evidence that referral to a physician of any type in CFS is of any value with regards outcomes and prognosis. Without putting too fine a point on it, such recommendations (especially when contrasted with the recommendations not to use complementary medicine approaches) smacks of medical nepotism and incestuous cross referral among the brotherhood of the Royal Australian College of Physicians. Physicians should always be reminded that they are not the exclusive domain of truth in medical science, nor that practices they indulge in are necessarily more scientifically credible or useful simply because they lack humility.

col 2, par 2

Symptomatic drug treatment.

The entire section on symptomatic drug treatment lacks evidence, and should be recast as the opinions of the majority of the WG (if this is so), rather than as information gained from the scientific evidence.

The issue of increased susceptibility to the adverse effects of drugs is correct, but is not proven. It raises the more general issue of adverse effects from exposure to a range of chemical agents, including medications, inhaled volatile chemicals, and other chemical exposure. The issue of multiple chemical sensitivities (MCS) is related to this increased sensitivity, and this may be a point in which the MCS association with CFS is overtly stated.

- col 2, par 3 I have dealt with the convoluted way of differentiating depression from CFS earlier (dealing with page 1 of the DCPG), and would recommend that the same correction and restatement occur in this paragraph.
- The second sentence needs to be altered to read, "Hence, antidepressant drugs are generally ineffective in managing CFS". The reason is that, to say that they are not a panacea may suggest that they are nonetheless proven to be very useful. Antidepressants are generally not effective. In some patients, they provide some symptom relief, but we have no data which helps predict which patients will benefit.
- col 2, par 4,5 There is no evidence to support these paragraphs, and it should be overtly stated as an opinion, presumably supported by the majority of the WG. I am aware of no evidence to support the view that specialist physicians or psychiatrists are more effective than primary care practitioners in guiding the choice of therapy, or in monitoring the response. I would go so far as to say that the constant long term contact between the primary care practitioner and the CFS sufferer makes it more likely that the specialist physicians or psychiatrists would have little or no role.
- col 2, par 6 I do not know what the evidence is that these treatments are effective as stated in fibromyalgia. Even if they were, they may be of limited or no value in CFS.
- col 2, par 7 **Psychological and social support**
- CFS also affects primary school students, and the effects are often different to those of CFS in high schools. In particular, the issue of suspected "Munchausen's by proxy-like" abuse by parents on the part of the school and medical authorities needs to be addressed.
- In addition, the part played by exposure to chemical triggering chemical agents in the school, home and workplace needs to be addressed. Many people with multiple chemical sensitivities find that such exposure triggers symptoms of chronic fatigue syndrome. Conversely, many CFS patients find that they become very sensitive to various chemicals, smells and foods, and that exposure to these triggers severe symptoms, often exacerbating the illness in a way similar to excessive physical activity.
- col 1, par 8 It needs to be recognised that in some cases of CFS, the severity of the illness precludes rehabilitation, and that pushing on with attempted rehabilitation in these people may tend to worsen the illness, further reducing their chances of successful employment.

Page 4

- col 1, par 1 The words, "be prepared to" should be removed from the first sentence. Doctors should act as advocates for their sick patients. Always.
- There is also an artificial distinction made here between "advocacy" for the patient, and provision of medicolegal assessment (pages 13 & 14). Given that much of the advocacy requires the completion of legal documents (certificates, social security forms, etc), it is unclear how the doctor could do one and not the other.

In fact, the whole distinction is artificial, and based on a faulty belief that only specialist physicians are the only “experts” in CFS. That a group of RACP members would assert that expert witnesses should be “qualified as a specialist and have extensive experience with people with CFS” (page 13) is disappointing, but hardly surprising. There is nothing inherent in the process of postgraduate education of the College of Physicians which ensures increased expertise in CFS or any other medical condition. That members consider themselves in such a way is a tragic misrepresentation of reality in the case of CFS.

CFS is a primary care issue. The original CFS Review Committee stated this repeatedly. Physicians see cases rarely, and gain a skewed appreciation of the illness from the referrals they receive. Dr Loblay has stated that he “would see most CFS cases only once, or maybe once a year”(CFS 98 Conference, Manly). This seems to be likely to be the case for the majority of CFS referrals to specialist physicians. The people with the experience and understanding of each individual case of CFS are the primary care practitioners, and it is these who should be providing medicolegal assessments and expert opinions.

The reason is simple - there is little science at present related to CFS, and what is known can be easily digested and integrated by any doctor with an interest in CFS. The primary care practitioner, however, knows the individual’s details of history over time, disability, and other factors at a much deeper level than the specialist, and can best provide a view on origins, disability and prognosis based on this knowledge.

It could appear to a cynic that the suggestion that primary care practitioners act as advocates for patients in poorly compensated areas, while physicians should hold a monopoly in the highly profitable area of medicolegal assessment, is little more than a conceit on the part of the WG, and a conceit which robs the primary care practitioner of income and earned credibility.

col 2, *

The list of CFS support groups is utterly inadequate, and needs to be fully inclusive of all groups, even those who are openly critical of some of the medical approaches and research to date. To include only those groups which support the views of some of the WG is insupportable, if not reprehensible. Think of Oscar Wilde’s celebrated statement, “I define an agreeable person as a person who agrees with me”.

The FAQs

These questions and answers are excessively simplistic to the point of being either meaningless or inaccurate. They seem to have been used as a place to insert personal viewpoints without any pretence of evidence, and the risk is that these inadequate “snapshots” will be accepted uncritically by lazy doctors, and become a part of their practice and attitude. They have no place in the CPG, and seem more a regrettable consequence of the “ten second grab” of television, than of serious and considered science. Doctors who wish to gain a knowledge of CFS must not be allowed to become self-opinionated amateurs in the field. Either they take the time to read and assess the CPG, or they hand over care to someone in the practice who has done so.

I would pose this question. Why produce CPG if the whole can be reduced to such a trivial subset of questions and simplistic responses?

Specifically, there are large information gaps in every answer to every question. I am prepared to provide a critique of each question and response if requested, but will not do so here, as the table of FAQs needs to be surgically excised in its entirety.

6.6 What is CFS?

Page 5

The spectrum of fatigue states

col 1, par 1

There is no information which shows that CFS is a part of the spectrum of “normal” fatigue, from mild to severe, or from transient to prolonged. This concept revolves around the concept of a single normal distribution for a particular parameter. This cannot be assumed to be the case for complex multisystem illnesses. The reason is that CFS is not simply a fatigue state, and even if we were to assess only that one dimension, fatigue is a final outcome of many different pathological processes.

Allergy is an example of an illness in which symptom severity is not evenly distributed. One population, the majority, have little or no potential for allergy, no matter what the stimulus. The other population, the minority, not only have a potential for allergy, but response to allergen exposure is nonlinear. This means that there are at least two populations (and possibly more within the minority), and each may not be normally distributed.

The point is this - that knowing the responses or pathology in one population does not allow for statistical prediction of response or pathology in the other. Normal distribution cannot be assumed, but must be measured with a view to identifying different populations within the whole. If there are different subsets, it may be incorrect to describe responses as “lying along a continuum”.

It is *possible* that certain subsets of CFS lie along a continuum of “normal” fatigue states, but the evidence would suggest that this is unlikely. There is likely to be a distribution of fatigue for the general population, and another distribution of those susceptible to CFS.

This “discontinuity” within CFS seems apparent at the clinical level, suggesting some type of positive feedback process which separates CFS patients from the rest of the population. Patients frequently describe a state of “normal” variable health and fatigability prior to the event which was associated with the onset of CFS. The degree of fatigue then increases in a nonlinear way, resulting in massively increased fatigue and disability from a relatively small insult.

The metaphor which many CFS patients identify with is one of “falling off a cliff”, after having an “up and down” course in their health immediately prior to the fall. There is no “continuum” in the disintegration of health, and the nonlinear response suggests that many pathological processes may be involved, each escalating others.

It could, of course, be that this first paragraph is saying only that some people are very much affected and others not at all. If this is all that is meant, then the concept is obvious, trivial, and does not need to be included.

col 1, par 2

A disease is not usually classified by the underlying cause or pathophysiology, but rather by the observable lesion (if such can be observed). An example is duodenal ulcer, in which the concepts of pathophysiology and causative agents have changed over time, but the name of the disease has remained constant. The lesion exists, whatever its cause.

In fact, it is rare in medicine for us to have a complete understanding of either cause or pathophysiology. What appears certain at one time is utterly rejected at a later time. In addition, medicine most often concerns itself with proximate causes, rather than ultimate causes. We may focus, for example, on cholesterol levels originally, then on different types of cholesterol, then on apolipoproteins, then on oxidation of lipids, then on dietary factors involved in risk and protection, and so on. Neither the cause nor the pathophysiology is ever certain, being always subject to revision as further evidence comes to light. Despite this, the disease is constantly termed atherosclerosis, being more a description of the lesion than the cause or pathophysiology.

In states where there exists no directly observable simple lesion or pathology, diseases are often named in the absence of direct evidence of observable lesions. This is especially the case in diseases of the central nervous system, such as schizophrenia and major depression. These are examples of “syndromal diagnoses” which are nonetheless regarded as disease. Classification of a disorder as disease is the very much the province of opinion in medicine, being a reflection of the prevailing attitudes of the majority of the profession.

While the separation of the nosological construct (disease), the subjective state (illness), and the functional deficit (disability) may be of some value, the divisions are artificial, and relate to the tendency of the medical profession (and indeed humans generally) to classify and categorise continuous phenomena rather arbitrarily. We create categories as a result of our own need to create order in a random and chaotic universe. We should not, therefore, consider for a moment that the divisions referred to are “real” in any sense. They are created for the convenience of medicine.

The reason for this philosophical detour is to demonstrate that the categorising referred to in the paragraph may have the paradoxical effect of defeating the goal of physicians referred to in the final sentence of the paragraph.

We should not, as physicians, ignore the suffering we have caused as a result of our arbitrary classifications, bestowing disease status on some complaints or syndromes, while denying it in others. In the case of CFS, there is a strong view among sufferers that the failure to classify it as a disease increases suffering and disability. I agree that this is the case.

Disease status has enormous value for the suffering and sick person. It provides a name, a place in society, and a “badge” which is a confirmation of their suffering and disability, with no confusion or explanations required. Even universally fatal illnesses, in which the sufferer may be unconscious or vegetative, benefit from the labelling with a disease name. It allows for the family and the community to come to grips with the reality of the illness, circumscribes the illness, and insulates society from the fear engendered by mystery and superstition.

It is, of course, not a scientific issue, but a human issue. Throughout history, when faced with disease and mortality, humans have turned to shamans, healers, witch doctors and others to make sense of the process, converting the “objective” reality into a “culturally acceptable” reality. The work of the healer has generally been to make sense of suffering, illness and death, a job shared with the spiritual leaders in communities. On many occasions, the healer and priest were one and the same.

Many in medicine would suggest that these issues are merely quaint anachronisms, relics from a past unilluminated by the “modern science” of medicine.

This is utter hubris. Humans are still humans, and tend to form communities, with similar needs, desires and faults to those we have had through our history. The emergence of science as a means of describing and understanding the universe is a relatively recent historical phenomenon, and there is no evidence that humans have adopted this approach deeply into their social and spiritual paradigms. Medicine, as a healing art and the youngest science, must overtly recognise that it works within a social and human framework. It can only succeed by marrying the art with the science. If the science does not “help relieve suffering and disability, whatever the cause”, it fails both as science and as art.

However well considered the arguments are on the matter of disease status in CFS, they lead to increased suffering and disability by denying people with this complex and disabling illness the valuable social status of disease.

This denial leads to difficulties for the families of sufferers and their communities in their relationship with sufferers, who hover somewhere between “sick” and “malingering”, depending on the view or prejudices of those around them. The result is frequently a heartbreaking process of family breakdown, divorce, and even vilification within the intimate community.

Beyond those problems, the broader issues of social justice are poorly served by the failure to apply appropriate disease labelling. Insurers, employers, and government agencies use the lack of disease status to perpetrate doubts about the “reality” or “validity” of the condition, often manipulating the “disease, illness, disability” arguments to allow for denial of social justice to sufferers, or denial of financial support or payments.

These issues have been dealt with in many forums before, and I would draw the attention of the WG to Ivan Illich's classic critique of medicine, *Medical Nemesis*, as well as to the included articles on Placebo Therapy in January's *Scientific American*, and the *Annals of Internal Medicine* paper on the role of patients in the medical decision making process.

An statement regarding the harm caused by the denial of disease status to CFS sufferers, and the potential for abuse of the "disease, illness, disability" by certain medical practitioners, government agencies, and others with financial stakes in the outcome needs to be included.

col 1, par 3 There is no mention of the second category proposed by Fuduka et al for those with chronic fatigue who fail to satisfy the required criteria of CFS. This separate category is termed "idiopathic chronic fatigue" (ICF), and is a useful label for those people who would have been diagnosed as suffering from CFS were it not for one or two criteria. The value for the label is similar to those discussed previously regarding the status of CFS as a disease.

col 2, par 2 I have no data to support this view, but it is my strong impression that the suggested two thirds of patients with chronic fatigue have "another medical or psychiatric disorder that accounts for it". The five papers quoted do not support such a view, and I would hope that the WG would be aware of the shortcomings of the Manu studies, and the unrepresentative nature of the chronic fatigue patients in Buchwald's and Lawrie's studies.

col 2, par 3 The inclusion of the Fuduka category of ICF (see above) would make the suggestion in the last sentence of this paragraph possible.

col 2, par 4 This entire paragraph (extends onto page 6) is jargon and convoluted to the point of being meaningless. Having read it eight times, I cannot make any sense of it. I would respectfully suggest that it be rewritten in English, or removed.

Table page 5 None of the items in the epidemiology section achieve QER of either I or II. This is because none ensures that patient samples are representative of the broader CFS community.

In addition, the definition of "young adults" needs to be provided.

page 6

col 2, par 2 I am uncertain why this subsection has been included regarding "other names used for CFS". It seems more than anything else a place for well known biases, pet theories and faulty associations to be briefly expressed as if they were factually based.

The terms ME and CFIDS have grown from the vacuum caused by medicine's failure to deal with the illness. There are subgroups within CFS in whom there is evidence for brain involvement and inflammation, and in whom the immune response has become dysregulated. Thus, these labels apply to certain CFS patients, usually those most disabled, and each has evidence from the medical literature to back them.

The name CFS, while it may satisfy “research groups”, has been the subject of intense international discussion regarding the need for a name change in the past two years. It is the view of the majority of sufferers and their carers that the name CFS tends to trivialise a very debilitating illness, and contributes to the suffering, disability and prejudices surrounding the illness.

If “Our goal as physicians is ... to help relieve suffering and disability, whatever the cause” (page 5), and our patients tell us that the name is increasing suffering and disability, then we must accept their view (as they are the only ones who can experience these), and work with them to achieve a change in name which will help in community acceptance of the condition as a severely disabling illness, or a seriously disabling disease.

col 2, par 3 The paragraph on “neurasthenia” is neither useful nor relevant, although it is a pet subject of at least one of the authors of the DCPG. The phrase “...although its specific relationships with CFS, and common psychological disorders ... are not resolved” is sufficient evidence that the paragraph has no place in the report, and may only serve to confuse the issue.

page 7

col 1, par 1-3 The actual incidence and prevalence of CFS are unknown, and this should be clearly stated. The absurd variation between early figures and recent figures should give some pause to attempts to be dogmatic about claims in these areas. Even the massive difference in prevalence in a primary care setting (0.5% to 2.5%) requires explanation.

A measure of the difficulties in this field can be seen by the incompatible ranges of incidence and prevalence in studies performed to date.

col 2, par 1. There needs to be a more specific statement regarding the nature of the “common, nonspecific viral infections” which do not cause or trigger CFS, and the “specific infections” which “commonly do so”.

col 2, par 2 The cost to the community is underestimated, in part because the cost of medical management rose far more rapidly than CPI between 1989 and 1998. In addition, the community prevalence is more appropriately considered the mean or median of the estimates rather than the minimum.

It would be useful if the costs of CFS could be related to the costs of other, better known diseases such as atherosclerosis, diabetes, epilepsy or dementia,

6.7 How should people with fatigue be evaluated

page 8

- col 1, par 2 Many CFS patients, especially chronic patients suffering exacerbations, do experience “lack of motivation and loss of pleasure from usual daily activities”. In part, this is because the “usual daily activities” are markedly reduced, and in part because of the chronic pain. These factors do not differentiate CFS from depression as the primary diagnosis.
- col 1, par 4 This should be amended to read, “People with CFS also report a broad range of symptoms, including:”In addition, CFS sufferers experience short term memory loss rather than long term memory loss. This is of major importance, as long term memory changes may indicate other neurological disease.
- Also, “irritable mood” is more commonly referred to as “emotional lability”.
- col 2 table There are many factual errors, as well as miscategorisation to the inappropriate QER levels.
- The physical examination of people with CFS is not necessarily normal (point 3). It may be normal in some, while others show disturbances of balance, mild lymphadenopathy, pharyngeal redness, etc. Also, having CFS does not necessarily *protect* one against other illness, nor is the presence of another illness necessarily a reason for discarding the diagnosis of CFS. Under such circumstances, examination is not normal.
- Point 4 needs to be rephrased and demoted in strength of evidence. Hickie’s work has shown that the rate of depression in CFS is not greater than the rate for other chronic diseases. I would suggest the following: “People with CFS commonly suffer depression, as do all groups suffering from chronic or debilitating diseases. It arises from the disease process, and as a general consequence of chronic illness (level III-2)”
- Point 7 needs the first word changed from “The” to “One”, for reasons alluded to earlier. It would read “One purpose of laboratory investigation is to exclude other conditions that may cause fatigue (Level IV).

Page 9

- col 1, par 1 Include after the first sentence the following, which may clarify the diagnostic process: “It is the general constellation of symptoms typical of CFS, and the lack of symptoms and signs which would suggest an alternative diagnosis, which can lead a doctor to make the diagnosis of CFS with confidence”
- I refer to the earlier coverage of somatoform disorders, which should not take priority over CFS as a diagnosis.
- col 1, par 2 It is worth making the point that the history should cover issues of workplace or environmental chemical exposure or other hazards, and a good dietary history. Factors which may help identify those at risk of alteration of their host response mechanisms

(ie those which reduce health generally) needs to be assessed, as management of these are among the first principles of medical care when the cause or management of an illness is unknown.

At the end of the paragraph, when dealing with medications and substances of abuse, a further mention of chemicals (pesticides, solvents, etc) should be inserted, as these cause the same types of problems, most often by pathways similar to those mentioned.

col 2, par 3

It is simply incorrect to exclude the diagnosis of CFS in people successfully and stably managed for another medical condition. If the expectation of such successful management is that the person should not be fatigued (as happens with successful treatment of hypothyroidism by thyroxine), then the emergence of fatigue and the range of other symptoms of CFS would suggest a different illness.

Put another way, suffering from another medical illness does not protect against CFS, and when treatment is expected to cure or fully manage the disease, the emergence of another illness is possible and diagnosable.

col 2, par 4

Psychological evaluation is an intimate and integrated aspect of every primary care practitioner consultation. This paragraph, and the one which follows it on page 9, seem to suggest that a formal psychological or psychiatric evaluation should occur.

This is neither necessary, nor is it practicable. The primary care practitioner, especially when he or she is the person's usual doctor, is the person best placed to make such an assessment, and costly and unnecessary referral should be avoided if possible. I know of no evidence that suggests that CFS patients who have been assessed by a psychiatrist gain any benefits in terms of outcomes, suffering or disability. In fact, the opposite may be true, as the specialist psychiatrist may be more inclined to prescribe medications which in turn increases the risks of adverse effects (as suggested previously on this page of the DCPG).

As well, the DCPG tells us that the incidence of suicide in CFS is no higher than it is for the general community. While I hold a view that this is unlikely to be true, if that is the evidence we currently have, then the referral to psychiatrists is of no proven value.

As well, this paragraph uses the terms psychiatric and psychological interchangeably, referring to the need for "psychological evaluation" at one point, then defining the components of "psychiatric assessment". The terms are not interchangeable, and the WG needs to identify which it is referring to.

Page 10

col 1, par 3

It is important to note that person with CFS is highly susceptible to exacerbation of the illness due to a broad range of stressors, including infection, chemical exposure, sleep deprivation, physical injury, allergy, vaccination, or psychological stress, to name only a few. It is worth mentioning that the exacerbating factor provides no insight into the

original cause of the illness. The same, of course, is true for most diseases, including HIV, heart disease and diabetes, but it needs to be explicitly stated in the case of CFS. The reason is that thinly veiled prejudices exist among doctors and throughout the community for illnesses which have not yet achieved the status of accepted disease. Such people will interpret the sufferer's attempt to avoid exacerbating factors as evidence of "neurotic avoidance behaviour", and assume that whatever worsens the symptoms must have been the original cause. Often, these people attempt to "prove" their hypothesis that CFS is a psychological disorder by stressing the sufferer, intentionally or unintentionally, and interpreting subsequent exacerbation of symptoms as proof of the psychological nature of the illness. The same people would not do this to people suffering heart disease or cancer, because they implicitly accept the reality of those diagnoses, and would never consider a heart attack as evidence of the psychological nature of heart disease.

Until CFS gains a new name, and formal disease status, then the CPG should explicitly state that the illness can be worsened by exposure to a range of stressors, whatever the original cause and disability. A brief listing of those above may be useful to make the types of exacerbating factors reported more explicit.

Box 2.2

A caption is required for this box, making it clear that there is no evidence to support the flow chart, and that it is a proposed approach to the diagnosis and management, based on the opinion of the WG. Otherwise, it could be assumed to be evidence based.

Page 11

col 1, par 1

The issue of somatoform disorder and CFS is dealt with earlier.

col 1, par 2

This paragraph is arguably one of the worst, poorly constructed and illogical in the DCPG. It introduces the very arbitrary prejudices which the WG has attempted to abolish elsewhere. I think it could be consigned to the trash can with little loss to the DCPG.

Firstly, psychomotor slowing and cognitive impairment are commonly found in CFS patients, and some of the diagnostic criteria relate directly to these symptoms or signs. Odd interpersonal behaviour is also hardly unusual in a person who has been told for years that there is nothing wrong with them, and that the problem is "all in [their] mind". The degree of trust with doctors tends to become untrusting and suspicious. And hostile, angry or excessively irritable responses are a normal part of everyone's life. Expression of these emotional responses may not be liked or appreciated by doctors, but they are hardly evidence of a personality disorder, whatever that means.

Let us not confuse iatrogenic alterations of personality with either illness or a disease process! We would otherwise be treating the majority of the most creative and original iconoclasts in our community with drugs to "normalise" behaviour, indulging in a type of psychological eugenics program. Not only opinion based medicine, but dangerous and

culpable interpretation of the natural variability of humans as evidence of disease.

I would also ask the WG as to whether they would like to make some recommendation regarding suicide risk? Should sex change of hormonal feminisation be recommended for those males at risk, if being male is associated with increased risk?

col 1, par 4-5 The entire subcategory “How should the context of the illness be assessed?” is opinion based, and this needs to be stated. If the illness itself is so difficult to define, its “context” is an even slipperier entity. More importantly, the context is in a state of rapid change at present, and didactic statements on this issue are unlikely to stand up well in the future review of the illness.

I do agree with many of the issues raised. I simply note that they are a result of experience in the clinical consultation, and not a result of appropriately gathered evidence.

The last sentence, “At the severe end of the spectrum...” seems to directly contradict the recommendations regarding graduated exercise programs, and the value of this in recovery of function.

Page 12

col 1, par 2-5 The issue of the differences between research and clinical approaches is dealt with earlier. The priority needs to be on approaches which reduce “suffering and disability”, rather than on those which promote an understanding of the pathophysiology.

col 1, par 6 The issue of the association between CFS and multiple chemical sensitivities is a glaring omission from this section (Overlap with other illnesses). Many people develop CFS as a consequence of chemical exposure, and the subsequent development of multiple chemical sensitivities. In these people, exposure to certain volatile chemical agents is the single most notable cause of exacerbation of CFS.

In others with CFS from other causes, the development of multiple chemical sensitivities is a common occurrence, and this was previously alluded to in the DCPG when referring to the adverse response to medications and other chemical agents.

col 1, par 8 There are no reasonable data to support the view that two thirds of CFS sufferers have prior or concurrent major depression. Major depression clearly means different things to different people. My understanding is that it is related to the prior “diagnosis” of “endogenous depression” or “unipolar depression”. Maybe it would be useful for the WG to define “major depression”, and overtly identify the ways it is objectively identified. In addition, the “priority of diagnosis” issue arises, and I would propose that unless there is some type of psychotic or suicidal component, the diagnosis is of little value prognostically. If it is not helping the suffering and disability of the patient, it should be dropped.

Page 13

col 1, par 1 This section on the definition of somatoform disorders has been dealt with earlier, and is logically flawed.

col 2, par 1 This section on medicolegal assessment has been dealt with earlier in the response to page 4, Doctors as Advocates.

It is paternalistic, arrogant and arrant illogical nonsense, and is based solely upon the opinion of a group of specialist physicians who appear to suffer some delusions regarding the unique ability of RACP members to arrive at considered, evidence based medicolegal assessments.

Medicolegal assessment is based on a concept of cause “on the balance of probabilities”, and not on the concept of “beyond reasonable doubt”. This makes the statement on the next page, “Given that the pathophysiological basis of CFS is unknown, definitive statements on occupational risk factors is unwise”, irrelevant. Statements do not need to be definitive, but need to be based on a clear history, examination, knowledge of the literature evidence, and an opinion integrating these factors into a straightforward statement on the most likely cause *in a particular case*. The issue of whether all workers are involved, whether the average worker would be affected, and other scientific issues are not necessarily important in arriving at this conclusion.

As stated earlier, this assertion of medicolegal assessment being the sole turf of “specialists” (assuming that this means RACP members) needs to be better argued if the appearance of financial gain to RACP members from the opinion expressed is to be circumvented.

page 14

col 2, par 1 The two subsections regarding the “benefits” and “drawbacks” of diagnosing CFS are not evidence based (the papers quoted indulge on speculation on these very issues, and cannot be considered more than non-consensus opinion, meaning that they have no QER status in this CPG). Nonetheless, they may still be useful as a “discussion section” of the CPG, as long as it is clear that they are not evidence based.

col 2, par 3 There needs to be an addition to the sentence, so that it reads, “Making the diagnosis should mark the end of investigations to exclude alternative diagnoses, unless new symptoms or information from the patient or the medical literature leads to a revision of that diagnosis, and exclusion of other conditions which arise as a new possibility.”

col 2, par 4 This section regarding “myths” is opinion based. Since the pathophysiology is unknown, and the groups are heterogenous, it is likely that one or more of the “myths” will prove correct for a particular subgroup.

In addition, simple or simplistic concepts are useful in complex illnesses, as they may focus attention on details or approaches which may modify the course of the disease.

Atherosclerosis is a complex, multifactorial issue, yet simplifying the complexity to clear recommendations on diet, weight, exercise, and the like has an immense advantage for those who need to act in definable ways to minimise risk and disability.

6.8 Natural History of CFS

Page 15

col 1, par 2 The content of the first sentences leads directly to the outcome that no evidence in the medical literature can, in theory, achieve a QER higher than III-2. The biases in patient referral, and the lack of understanding of the degree to which the studied groups are “representative” means that higher levels of confidence in the research to date is not justified. There is no measure by which homogeneity of the subjects or bias of the referral process can be identified.

col 1, par 4 I would find it unlikely that the suicide rates in CFS were not raised, unless the studies done have defined anyone who may potentially be suicidal as not suffering from CFS, but from depression or some other diagnosis.

The general experience of the CFS community is that the suicide rate is considerably raised. This issue needs to be better and more explicitly addressed.

col 1, par 5 I have dealt elsewhere with this oft repeated phrase regarding the patient’s belief in the physical nature of their illness. This reflects little more than a poor prognosis being associated with a disagreement with the paradigm of the investigator.

It may be suggested that clinicians would do more good in understanding and working with the beliefs of the patients who consult them, than they would by arguing that the patient should adopt the belief of the doctor. If failure to adopt the doctor’s belief is associated with a poorer outcome, then the poor prognosis associated with this could rightfully be considered an iatrogenic worsening of CFS. At the least, the doctor can be said to be derelict in his or her duty to “reduce the suffering and disability” of the patient by insisting that they adopt a particular view of the disease.

col 2, par 1-2 Doctors need to *be* empathetic and accepting, not simply “display empathy and acceptance”. CFS sufferers are sensitive enough to pick the difference, on the whole. Simplistic notions and “unjustified medical labels” may be of value in the doctor’s work with a particular patient, even though they may appear “pseudoscientific” to researchers and specialists. Primary care practitioners need to understand the beliefs and understandings of the patients, and work with those to achieve the goals of “reducing suffering and disability”. This may not appeal to specialists or researchers, but is a fact of day to day medical practice, and a part of the long history of the art and science of healing. The arrogance of the “purely scientific position”, and the attempt to force the patient to adopt the belief systems of the doctor can not be justified. Firstly, asking patients to adopt the beliefs of a group with a very high suicide, alcoholism, divorce and

premature death rate is illogical. One could almost suggest that adoption of medical beliefs and dogma is itself a health hazard, based on studies of predictors of survival in cancer and heart disease. It is an approach which can only be maintained by doctors who can transfer care back to another when they fail to convert the patient. This process of “ending the relationship” between patient and doctor is a luxury *only* experienced by specialists. Primary care practitioners cannot “pass the patient on” when a disagreement arises over philosophy, beliefs or values.

The specialists on the WG may need to gain a better understanding of medicine “at the coal face” if they are to make recommendations on philosophical aspects of primary care medicine. Even better, they should incorporate a number and variety of primary care practitioners into the WG, discard the current DCPG, and commence the process again from a base incorporating experience, evidence and expertise of a range of practitioners.

The reference to Ernst (1996) is included here, and is a gross misrepresentation of the approach and information included in that paper, as well as being an unexplained selective quotation of the general publications and direction proposed by Ernst. His view, recurrently and consistently expressed, is that no view can be gained about the utility of complementary medicine until the research is commenced, and the data gathered. His call is for complementary medicine to become a research priority because of the suggested value of cost effective management of many illnesses, including CFS.

It is very naughty to selectively quote and misrepresent authors!

Box - p 15

None of the statements, and especially point 3 and 4, achieve a QER greater than III-2. Point 3 achieves a QER of III-4 because of conflicting medical literature (Hickie), while point 4 has no place in the QER, being entirely opinion based, and not a consensus of experts.

Page 16

The two tables are flawed, and the flaws are dealt with by other critics more than adequately (Martinovich, Shaw, etc).

6.9 How should CFS be managed?

page 18

The entire section on management is opinion based, with no quality evidence of benefit for any single approach whatsoever. This is recognised by the WG in recommending that no management is proven as yet apart from CBT. The issue of the flaws in the concept of CBT have been dealt with earlier, and will not be repeated here.

It may be of some benefit to reduce the complications of this section, and to enunciate the principles and goals of quality medical management for any poorly defined or complex illness.

The essential differences between the goals of researchers and those of doctors needs to be emphasised. Doctors often need to work in a scientific vacuum, and the skills needed by doctors in doing this are not well addressed by science at present.

The proposal could be made in the paper that there is an urgent necessity for the gathering of data about the various approaches used in the management of CFS patients, and the value of those approaches. I direct the WG to the paper I have included regarding the establishment of an “Antibiotics in CFS Special Interest Group”, which has arisen from the CFS 98 Conference at Manly. Many of the insights and suggestions, of course, arise from the work of others, and especially the work of Ernst in the UK.

I also direct the WG to the paper on placebos in medicine from a recent issue of Scientific American, addressing the issue of harnessing of the placebo response when scientific certainty or data are lacking.

col 1, par 4

There is no need for a discussion in the CPG on the needs or opinions of researchers, and this section smacks of arrogant preaching of well known scientific research principles to primary care practitioners. It is difficult to see any way in which this discussion “assists general practitioners in the management of CFS patients”.

The discussions of the importance of trials *may* impact future care of CFS patients, although it must be said that the past decade of research has done little or nothing in this regard. This is most likely because research did not run from a solid observational base, and reflected the interests and biases of researchers, rather than the needs of sufferers, carers or their primary care practitioners.

The section should be deleted, or included as a brief appendix.

Page 18

The table is flawed, including many studies unrelated to CFS. The quoted studies may simply reflect the interests and prior convictions of certain members of the WG, rather than being a critical assessment of appropriate controlled trials in CFS.

The defects are dealt with by other critics very adequately (Martinovich, Shaw, etc).

I would note, however, that none of the studies under “Behavioural treatments” were truly placebo controlled, and none were “double blind” in nature. In every case, the patient was aware of the activities they were involved in, and in no case was the “control” arm similar to the “treatment” arm.

In addition, at least one of the studies (Sharpe 1996) suffered from inadvertent unblinding, with a researcher aware of the allocation of patients between the groups, and responsible for referral to the assessing doctors.

Page 19

col 2, par 3

The additional statement needs to be made, “There is no evidence of consistent benefits derived from the use of antidepressants, and there is evidence of a higher than normal rate of adverse reactions or side effects among CFS sufferers. Under such circumstances, their use cannot be recommended. If they are to be used, a lower than usual dosage may need to be tried before a full dose program.

Table 4.2

CBT needs to be removed entirely, or demoted to QER III-4, to comply with the QER adopted in the DCPG, and based on the evidence tabled on page 18.

Page 20

col 1, par 1 For reasons dealt with extensively previously, the section of “Is there a role for behavioural treatment approaches” must be deleted, or can be responded to with the simple line, “Currently, there is no evidence to support the use or otherwise of behavioural treatment approaches.”

Table 4.3 This table or box stands as an absurd indictment of the prior views and prejudices of the WG members, as does the quote used above the table. The CPG is not an arena for WG members to abuse their position or power in an attempt to belittle or ban approaches which sufferers have found to be of benefit in the medical vacuum surrounding CFS.

The differentiation between “absence of evidence of benefit” and “evidence of absence of benefit” is addressed by Ernst, and in the paper I include with this report regarding complementary medicine. The confusion arises because of selective tables such as this, and represents a petty and unnecessary attack on complementary medicine.

The table should either be removed, or should include the vast range of medical approaches in common use for which there is also no evidence. These include, for example*, psychotherapy, amphetamines, benzodiazepines, cognitive behavioural therapy, antibiotics, antidepressants, diuretics, thyroxine, and a host of other drugs and approaches utilised on an ad hoc basis by doctors desperate to help their patients. It should be followed by a clear statement that the lack of evidence in no way implies that the approaches are not beneficial, and simply notes that there is a lack of suitable evidence at present by which a conclusion can be reached.

** not an exhaustive list*

page 21

col 1, par 1 There is no evidence that the management of sleep problems helps in any way in CFS. The changes in sleep are more likely to be a consequence of the illness than a cause of CFS.

col 2, par 1 Support groups

The approach seems to be that support groups are recommended only to the extent that they support the medical scientific approach to CFS promoted by researchers and specialists.

Support groups may arise in response to the problems caused by inappropriate medical approaches to the illness in question, and their focus and rationale is different than those of researchers, doctors or other stake holders.

Support groups can, therefore, set their own agenda with regards meeting patients needs, and it is the job of the medical profession to respond to those expressed needs. If they reinforce stereotypes, increase alienation from medical and government agencies, or encourage forms of treatment that lack scientific evaluation, then that is their prerogative. They represent the aggregated views of the suffering people, and take on a life of their own. That they may disagree with medical authorities, or promote

unscientific approaches is an issue for the profession to address, and to understand in what way it has failed to meet the needs of sufferers.

In passing, it is more than a little interesting to note the term “lack scientific evaluation”. The evaluation of a treatment can hardly be said to increase the value or efficacy of the treatment. I would assume that this was meant to read “lack scientific evidence of efficacy”.

On this basis, the WG may be said to be doing the same in promoting CBT, not only because it is not proven effective, but because it is undefined, the mechanism of action is unknown, and is based firmly on philosophical rather than scientific principles.

Box 4.4

The graphic is attractive, but is not based on any evidence. The opinion of the WG may indeed be valuable, as may a proposed conceptual framework, but it should be noted in the caption that this is not evidence based, and is a proposed conceptual framework.

In addition, the graphic provides a very confusing message. It seems to suggest that the use of the proposed management strategies leads to a downward spiral of health to inevitably greater disability. It would be hoped that the opposite were true, though there is no evidence for either view.

The graphic also creates the simplistic impression that disability increases over time, and that there is a progression through the different areas of symptoms over time. This is also untrue. Many people suffer social isolation and physical illness, even though their intellectual capacity has not changed.

Next, there is no evidence for the apparent “timing” of the interventions. In addition, as I hope I have demonstrated in this document, the therapeutic approaches recommended themselves have no solid scientific foundation or evidence.

Finally, the graphic in fact contradicts some basic premises in the body of the report, especially those regarding the necessity for management of the individual with CFS, rather than the illness known as CFS.

In all, therefore, although the graphic is certainly handsome, it is positively harmful to an understanding of the management, is based on opinion only, contradicts other sections of the report, and cannot be said to “assist general practitioners in their understanding of CFS”.

It is, in my personal view, a regrettable result of the easy access to sophisticated computer graphics programs that clarity and logic in diagrams is being sacrificed for special effects and attractive but difficult to comprehend pictures. The reader is left with the impression that such a sophisticated diagram must be important and must convey necessary information. The neophyte may even be tempted to attempt a clinical care program not based on clear logic, but on a complex, poorly defined and inappropriate path, such as that suggested in this particular diagram.

If the diagram does not support an improved understanding of the text and the logic, then

it should be left out. It is insufficient to say that sophisticated colour graphics are expected in such a document in order to gain the attention of the reader. The graphic which oversimplifies or confuses will only do more harm if it is attractive, and will distract the reader from the core information, which may not be so easily summarised.

6.10 Associations between CFS & other disorders

Page 22

This section is hopelessly deficient in addressing proposed mechanisms, associations, and related diseases. It is beyond the scope of this critique to cover the broad range of the missing material related to associated factors, although I will be delighted to if contracted by the WG to perform such an extensive task, with associated support from the scientific (as well as the medical) literature.

I would raise simply the following associations and factors which are currently missing from this section: post-antibiotic gut flora changes; mitochondrial damage; reduced gene expression for cytochrome p-450 enzyme function; multiple chemical sensitivities; adverse vaccination response (especially to Hep B vaccines); olfactory bulb disturbances; limbic system dysfunction; altered autonomic response; neurally mediated hypotension; mycoplasma infection; viral cardiomyopathy; rickettsial infection; chronic sinusitis; thyroid hormone resistance; staphylococcal infection; disturbance of 1-carbon metabolism; mould allergy; stealth virus encephalopathy. This list is far from exhaustive, and incorporates information from the CFS 98 conference at Manly a few weeks ago.

The section entitled "Gaps in our knowledge" is rather small, and should either be expanded or deleted. Our knowledge is minimal at present, and the section should logically include almost every aspect of CFS pathogenesis, diagnosis and management!

col 1, par 5

The fact that the authors state that one key confounding factor in studies is "the likely heterogeneity in patient groups being studied". This appears to be the case, and it follows logically that no CFS research can achieve a QER higher than III-2. The likely, but unmeasured, heterogeneity makes it impossible to be confident of the representative nature of the subjects, despite efforts at randomisation. In this way, CFS research is severely deficient when compared to research in other, better characterised fields of medicine. The result is a cacophony of research outcomes which may all appear impressive, but are not compatible with other impressive research findings. The greatest problem in research into CFS appears to be the identification and categorisation of more homogenous subgroups within CFS. Until that time has arrived and is generally accepted, all research is highly subject to the problem of non-representative samples.

col 1, par 6

The researchers within the WG, in attempting to place the horse before the cart, appear to have forgotten the wheels. The research efforts required are those of

basic data gathering and observational studies at a primary care practice level, or even at the community level. There is *no place* for educated hypothesising before the data are known, and have been interpreted appropriately. *After this*, research into pathophysiology, causes and management strategies may be undertaken. Without the basic data, research is very much like a game of darts played blindfolded - if the target is hit, it is only due to good luck. To date, not even the dart board has been threatened with the expensive darts of researchers.

Support for primary care practitioners, incorporating their work and observations into a research program, is essential. Many doctors are willing and ready to do this with minimal financial compensation. As well, money and resources provided to CFS patient support groups would allow for the cost-effective aggregation of an enormous volume of useful and usable data regarding apparent causes, diagnostic and therapeutic approaches perceived as useful, and the outcomes, including measures of patient suffering and disability.

col 2, par 1 The last sentence is dreadful jargon, and should either be deleted or expanded, with appropriate explanation of the concept.

Pages 23 and 24

Tables & boxes It is not clear to me why these have been created, unless they are simplified summaries of some of the available literature. They may be present simply so it is clear that more work has been done than is evident in the body of the document.

I do not see their value as they are. Either they provide information which should appear and be addressed in the body of the document, or they should be relegated to the appendices.

The comments at the base of each are simply opinions, most likely of a single member of the WG. They are not evidence-based, but are “impressions” of the general trend of the research referred to. There is no information provided on the studies quoted to determine whether the item was supported or countered by the literature. This should at least list the research which finds a positive result, and a separate list which did not. A brief explanation for the variation in outcomes would be helpful.

Page 25

Graphic

I am aware that certain members of the WG are very proud of this diagram. I find it difficult to comprehend, illogical in the construction, and lacking any sequence or hierarchy beyond the view that the brain is intimately involved. Most of the graphic is speculative, based on hypotheses of the author regarding various pathways and feedback mechanisms.

Many possible and reported risk factors are omitted, no mention is made of important and common symptoms of CFS (headache, chemical sensitivity, post exertional malaise), and the involvement and site of inflammation caused by specific infectious agents is almost ignored, as is the increased incidence of autoantibodies in CFS sufferers.

The graphic is deficient in important concepts and information, and is speculative in the information conveyed. It is not based on evidence, but on personal views of likely pathogenic pathways. The fact that it is labelled "Potential nervous system pathways to CFS" should be enough to exclude it from such an "authoritative" document until those pathways are better defined.

Signed,

A handwritten signature in black ink, appearing to be 'M. Donohoe', with a large, sweeping flourish extending to the right.

Dr Mark Donohoe MB BS
23/2/98