The NICE Clinical Guideline: convincing evidence?

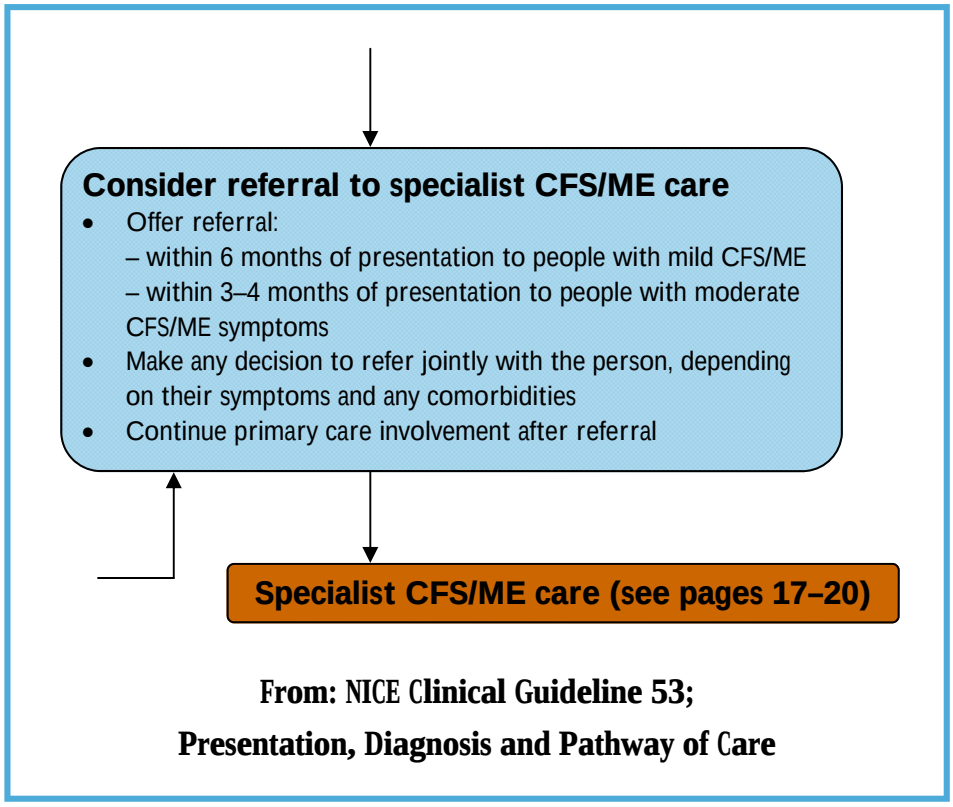
For the Judicial Review of the NICE Guideline on CFS/ME on the 11th and 12th of February 2009, at the High Court in London, Dr Neil Abbot provided an Expert Witness statement on the evidence base underpinning the main 'treatment' recommendations. In this article, he summarises his conclusions, mainly with reference to cognitive behavioural therapy (CBT), though many points also apply to graded exercise therapy (GET).

The National Institute for Clinical Excellence (NICE) is rightly respected for basing its treatment recommendations on evidence. In the case of the illness ME/CFS, its principal recommendations were cognitive-behavioural approaches for the specialist management of the illness because 'currently these are the interventions for which there is the clearest research evidence of benefit'.

However, cognitive-behavioural approaches are widely recognised, including by the NICE Guideline itself (section 6.3.8, page 252), to be non-curative for ME/CFS; and in other physical illnesses these approaches are used as adjuncts to but not substitutes for mainstream treatment. So, what was the evidence base for the central role of these approaches in the clinical management of the illness?

The table opposite shows that the evidence base for these cognitive-behavioural approaches consists of a small group of randomised controlled trials on adults (ten trials in all; seven with mild-to-moderately positive results and three with negative results). Focusing in on CBT (a form of psychotherapy used to treat a variety of psychological impairments), the first thing to note is that two out of five trials have a negative overall result (Whitehead, 2002; Lloyd, 1993). The remaining three trials have overall positive effects, and moreover have high 'validity scores', indicating that they are likely to have been well-designed and conducted. Nevertheless, the 'gold standard' evidence-base consisted of three mild-to-moderately positive randomised controlled trials only. It is instructive to compare this with the evidence base available for NICE Guideline 8 on multiple sclerosis, with many hundreds of trials.

Other key points to note are the following:



From: NICE Clinical Guideline 53; Presentation, Diagnosis and Pathway of Care

Patient numbers

The trials of CBT have relatively small numbers of patients; in four of the trials, analysis was performed on no more than 30 patients in the CBT groups, while the largest trial (Prins, 2001) analysed 92 patients in the CBT arm. Since only two of the trials (Deale, 1997; Prins, 2001) reported making a power calculation to determine the adequacy of sample size to determine a treatment effect, it is entirely possible that some samples were too small to determine a true effect.

Different kinds and duration of treatment

There is a difference between trials in the type and content of CBT delivered, as well as in the number, frequency and length of intervention sessions given. This makes it impossible to say that like was being compared with like as far as type and delivery of 'treatment' was concerned.

Diagnostic definitions

Case definitions of CFS differ, raising the question of whether homogeneous groups of patients are being compared between trials. Two of the positive trials recruited patients using the Oxford criteria (1991) which focuses on unexplained chronic fatigue and does not require additional symptoms. Given that the NICE Guideline itself recommends that post-exertional malaise and other symptoms such as cognitive difficulties,

sleep disturbance and chronic pain be present for a diagnosis to be made, it is entirely possible that new patients diagnosed by their GPs using NICE guidance constitute a different — most probably more sick — clinical group than those who took part in the original trials.

Comparison groups differ

As each trial employed a different comparison group (placebo injection, relaxation, standard medical care, guided support/natural course and no intervention), it is impossible to say that the CBT delivered was having a 'specific' treatment effect. For example, some people (including the authors of the Canadian Consensus document of 2003) wonder whether a program of formal CBT or GET adds anything to what is available in the ordinary medical setting under a good and concerned medical practitioner.

Long term effects

In four out of five trials, follow-up was relatively short, and so the relevance of the findings over the longer term remains unknown. This is particularly important in an illness which is a long-term condition, and tends to be chronic with serious debility in some; a moderate treatment effect in the short term might not show treatment-specific gains in the longer term. For example, the one trial (Deale, 1997) in which five-year follow-up results were reported revealed no significant difference in physical functioning and fatigue between CBT and a relaxation control group after five years, though other parameters were improved.

Serious commentators might consider that the conclusions about efficacy one could draw from this small group of trials are suggestive and tentative only. A recent Cochrane review (Price, 2008) found fifteen studies of CBT (including controlled clinical trials) for CFS/ME, and took a far more measured, cautious view of the evidence and its limitations than the authors of the NICE Guideline, as did a second recent review (Malouff, 2008).

The practical consequences of NICE's recommendations can be seen in the 'Quick reference guide' to the NICE Guideline, which (unfortunately) is the only part read by most healthcare professionals and GPs. On page 6, the Pathway of Care ends at a category called 'Specialist CFS/ME care' (see figure opposite), inside which CBT and/or GET are the principal 'treatments' alongside activity management.

Whatever the merits of these therapies in themselves for psychological illnesses, can it be reasonable for them to be enshrined in established national guidelines which feed into clinical care and government policy — at a potential cost to the country of £45.2 million over a five-year period — on the evidence available? ●

Summary of randomised controlled trials in adults

(source: Appendix 1, NICE Guideline; and Bagnall et al, 2007)

Author and year	Case definition	Treatment	Patient numbers	Comparison group	Overall effect of "treatment"
Lloyd, 1993	Australian	**CBT** (+ DLE injection)	90	Placebo injection only	None
Deale, 1997 & 2001	Oxford	**CBT**	60	"Relaxation"	Positive
Sharpe, 1996	Oxford	**CBT**	60	Standard medical care	Positive
Prins, 2001	CDC, 1994	**CBT**	270	"Guided support" and "natural course"	Positive
Whitehead, 2002	CDC, 1994	**CBT** by GP	65	"No intervention" control	None
Wearden, 1998	Oxford	**GET** & fluoxetine	136 (4 groups)	Review of activity diaries/placebo capsule	None
Fulcher, 1997	Oxford	**GET**	66	Flexibility exercises and relaxation therapy	Positive
Powell, 2001 & 2004	Oxford	**GET**	148 (4 groups)	Standardised medical care	Positive
Moss Morris, 2005	CDC, 1994	**GET**	49	Standard medical care	Positive
Wallman, 2004	CDC, 1994	**GET**	61	Relaxation/flexibility therapy	Positive