

IN THE HIGH COURT OF JUSTICE
QUEEN'S BENCH DIVISION
ADMINISTRATIVE COURT CO/1040/2007

BETWEEN:

THE QUEEN

On the application of:

(1) DOUGLAS FRASER

(2) KEVIN SHORT

Claimants

-and-

**THE NATIONAL INSTITUTE FOR
HEALTH AND CLINICAL EXCELLENCE**

Defendant

-and-

BB

(by his mother and litigation friend JB)

Interested Party

SKELETON ARGUMENT OF
INTERESTED PARTY

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SKELETON ARGUMENT OF THE INTERESTED PARTY

1. The Interested Party supports the Claimants' position as set out in the 'Grounds of Claim' and the remedy sought.
2. The Interested Party makes the following additional challenge to the Defendant's guidance for 'Chronic Fatigue Syndrome' and 'Myalgic Encephalomyelitis' ('CFS/ME').
3. The guidance under challenge is the recommendation by the Defendant of Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) as treatment for CFS/ME. which can be found in various places in different versions of the guidelines as explained by the Defendant at paragraph 19.24 of the grounds of resistance. The guidance under challenge is found in the following places:
 - (a) The NICE clinical guideline 53 at 1.6.2.4 states that: '*cognitive behavioural therapy*

(CBT) and/or graded exercise therapy (GET) should be offered to people with mild or moderate CFS/ME and provided to those who choose these approaches, because currently these are the interventions for which there is the clearest research evidence benefit. This paragraph is repeated at page 10 and in the “Full Guidelines” at the same paragraph number of 1.6.2.4 and page 30. All are challenged. Paragraph 1.6.2.5 of NICE Guidelines and the “Full Guidelines” are also under challenge for the same reasons. In so far section 6.3 of the “Full Guidelines” is premised upon the recommendation of CBT and GET, this is also challenged for the reasons set out below.

(b) The “Quick Reference Guide”, which is commonly used by healthcare professionals, repeats the above guidance at pages 17 to 20 (with reference to CBT and GET as recommended treatment at page 14). At page 17 it is stated: ‘*Offer... CBT and... GET to people with mild or moderate CFS/ME, and provide them for those who choose them, because these are the interventions for which there is the clearest research evidence of benefit... etc.*’ This is also challenged for the reasons set out below.

4. In summary, the Interested Party contends that the Defendant is *required* to consider the cost-effectiveness of any healthcare intervention recommended in its guidance and has failed to do so in respect of Graded Exercise Therapy (‘GET’) at all, while its appraisal of the cost-effectiveness of Cognitive Behavioural Therapy (‘CBT’) is *Wednesbury* unreasonable, irrational and flawed.
5. In support of this challenge the Interested Party relies upon the statement of Dr Malcolm Kendrick dated 1 April, which is annexed to the ‘Detailed Grounds’ of the Interested Party prepared by Kate Marcus, in particular paragraphs 27 to 50.

Requirement for the Defendant to evaluate cost effectiveness

6. Under paragraph 2(1) Directions and Consolidating Directions to the National Institute for Health and Clinical Excellence 2005 (‘the 2005 Directions’) (page 490 to 494 of the bundle) the Defendant is directed to: ‘*exercise the following functions in connection with the promotion of clinical excellence and the effective use of available resources in the health service – (a) to appraise the clinical benefits **and costs** of such health care interventions as*

may be notified by the Secretary of State and to make recommendations...’ (emphasis added).

7. In 2004 the Secretary of State required NICE to provide a Guideline in respect of ‘Chronic Fatigue Syndrome’ and ‘Myalgic Encephalomyelitis’ (‘CFS/ME’). The role of drawing up guidance on the treatment of these conditions was ultimately delegated to a Guideline Development Group (‘GDG’).
8. By virtue of paragraph 2(4) of the 2005 Directions, when appraising the benefits and costs of possible treatments for CFE/ME, the Defendant was required to have regard to ‘(a) *the broad balance of clinical benefits **and** costs; (b) the degree of clinical need of patients with the Condition or disease under consideration*’ (emphasis added).
9. By virtue of the above Directions, therefore, the Defendant has a statutory duty to appraise cost-effectiveness in respect of any recommended ‘*healthcare interventions*’. A failure to do so at all, or to do so on an irrational or *Wednesbury* unreasonable basis, is properly a subject of review.

Purported evaluation of cost effectiveness

10. In the ‘Full Guidelines’ on CFS/ME published in 2007, it is said in relation to the interventions for CFS/ME that ‘*these interventions can be costly, often involving input from more than one member of a multidisciplinary team.*’
11. The Defendant has purported to evaluate the clinical benefits and cost-effectiveness of CBT and GET at 6.3.2 to 6.3.4 of the Full Guidelines (see pages 183 onwards).
12. The GDG made a search for cost-effectiveness literature, which apparently ‘*yielded 60 unique records. The abstracts were reviewed, three papers ordered and their results extracted*’.
13. The only study used for the purposes of evaluating cost-effectiveness was a Dutch study, (Severens et al) which is said to have looked at the cost effectiveness of CBT for CFS/ME patients.

14. Using only this report, the GDG concluded that the cost per quality-adjusted life year (QALY) for people with CFS/ME treated by CBT relative to no-protocol medicine is £16,036 (see 6.3.2.6 at page 183 and 6.3.5.2 at pages 191 to 193). This, it is said, ‘*lies below the £20-£30,000 per QALY willingness to pay threshold and would therefore be considered cost effective*’ (see page 193 of the Claimants’ bundle).

15. No effort was made to evaluate of the cost effectiveness of GET at all.

Wednesbury unreasonable / irrational

16. The Interested Party contends that the conclusions reached by the Defendant in respect of GET were *Wednesbury* unreasonable or irrational:

(a) The Defendant has failed to make any attempt to appraise the cost-effectiveness of GET for the purposes of paragraph 2(1) of the 2005 Guidance or to consider ‘*the broad balance of clinical benefits **and costs***’ as it must under paragraph 2(2) of the 2005 Guidance.

(b) Without considering the cost-effectiveness of GET as a treatment for CFS/ME at all, the Defendant has thereby failed to take into account something it is legally required to do when recommending GET as a treatment for CFS/ME in the ‘NICE clinical guideline 53’ used by health care professionals.

(c) In these circumstances the guidance in respect of the recommendation for GET as a treatment for should be quashed and the matter referred back to NICE for fresh consideration.

17. In respect of CBT, the Defendant has purported to appraise cost-effectiveness. The conclusions reached on the evidence used, however, are *Wednesbury* unreasonable or irrational:

(a) The GDG has only relied upon one study, ‘the Severens Study’, in considering cost-effectiveness of CBT. The data of the report relied upon could not provide a rational basis for the conclusions reached by the GDG:

- i) There was a difference in the measured quality of life of the control group and the CBT group at the start of the trial, i.e. one group enjoyed a higher quality of life than the other. The quality of life was measured at 0.486 for the CBT group and 0.526 for the control group.
- ii) This gave a difference of 0.04 in quality of life between the control group and the CBT group at the *start* of the trial.
- iii) At the end of the trial, the difference between the groups was 0.0015.
- iv) This massive uncorrected bias was not corrected in the original study.
- v) The GDG noted this deficiency and potential bias at page 201 of the guidelines (see page 200 and 201 of the Guidelines at page 186 and 187 of the bundle). They state that '*Sensitivity analysis was carried out to test the robustness of the result when the incremental health gain is reduced*' (see 6.3.5.4 of the Full Guidance).
- vi) The GDG made no attempt to correct the bias because, as they admit at page 209 of the Full Guidelines, they did not have access to the trial data.
- vii) Although they could not correct for a potential bias they also make the point that their sensitivity analysis shows that if baseline differences are corrected, there *could* be a significant impact on the results.
- viii) Dr Kendrick states at paragraph 37 of his statement that if baseline differences were corrected there *would* have been a significant impact on the results, and questions why this was not done.
- ix) In reality, Dr Kendrick says, no rational analysis is possible in these circumstances (see paragraph 38 of his statement):
 - (1) If there are two groups which are supposedly randomised, yet one group is significantly different to the other at baseline, further analysis is invalid.
 - (2) It could, for example, be the case that the control group which started with the

higher quality of life would have found it difficult to improve from that condition.

Dr Kendrick says this is reflected by the fact that the CBT group only reached the point 0.0015 higher than the control group at the end of the study after 14 months, which he says is *'a figure so small as to be completely statistically insignificant, and for a patient absolutely clinically insignificant'* (see paragraph 39).

(3) The GDG have accepted this difference, and accepted at page 196 of the Full Guidelines that *'When the baseline difference is equalised, the ICER [per QALY] shoots up to £283,421. This emphasises the importance of correcting differences at baseline for future guideline updates as regression to mean effect could have a significant impact on the cost effectiveness result'*.

(4) As Dr Kendrick says, at paragraph 41 of his statement, the £283,421 figure represents the only figure which can be used without bias. The cost per QALY for CBT, when taking account of the bias, is therefore £283,420.81, vastly more than the £20,000 to £30,000 per QALY 'willingness to pay threshold' that would be considered 'cost-effective' (see page 207 of the Full Guidelines, page 193 of the Claimant's bundle).

18. The conclusions that the GDG reached in the Full Guidelines were also based on obvious mathematical errors:

(a) The improvement in the CBT group was recorded in table 4 as 0.0737¹, when it was in fact 0.1155 (the difference between 0.5257 and 0.5999 in table 2)².

(b) The improvement in the control group was recorded in table 4 as 0.0458, when it was in fact 0.0742 (the difference between 0.5257 and 0.5999).

(c) The figure established as the difference between the two groups is therefore also wrong, as is the figure of £16,035.84 per QALY. The 'Severens utility increment' should have been 0.0413 and the 'cost effectiveness ratio' would have been £10,833 per QALY,

¹ See page 207 of the Full Guidelines / page 192 of the Claimants' bundle.

² See page 201 of the Full Guidelines / page 187 of the Claimants' bundle.

although such a figure is invalid for the reasons already given.

19. In the above circumstances, no reasonable GDG could have come to the conclusion that the QALY for CBT was in fact £16,036 as found at 6.4.2.6. This figure could not rationally have been the basis for recommending CBT as a cost-effective treatment, as it was plainly both in error and the reasoning behind it fundamentally flawed. When taking into account of the bias recognised as such by the GDG the cost of the treatment goes beyond the ‘willingness to pay’ threshold by a factor of 10. The guidelines recommending CBT as treatment should therefore be quashed and the matter referred back to the Defendant for fresh consideration.
20. Despite realising in the Full Guidelines that the sole report on which this cost-effectiveness analysis was based was flawed, the GDG did not attempt to consider any other evidence in relation to the cost-effectiveness of CBT:
 - (a) The GDG failed to consider, for example, a study which has reviewed the cost-effectiveness of CBT which was unable to show the benefit of the treatment (see the statement of Dr Kendrick paragraph 32). It thereby failed to take into account relevant material in its appraisal of cost-effectiveness in circumstances where the material in fact considered was extremely limited in value (as below).
 - (b) Despite recognising the extremely limited value of the report relied upon, given the evidential bias, no other research was carried out. No reasonable GDG could have taken this approach.

Conclusion

21. The Defendant has therefore failed entirely to consider the key criteria of cost-effectiveness for GET, and has come to conclusions which are irrational, wrong and which no reasonable GDG could reach in respect of the cost-effectiveness of CBT. In so doing, it has failed to adhere to the requirements of the 2005 Directions.
22. As a consequence, the Defendant’s guidelines ‘NICE clinical guideline 53’ used by health

care professionals recommends CBT and GET at 1.6.2.4 without having properly, or at all, considered the cost-effectiveness of such treatment.

23. The Defendant's *Wednesbury* unreasonable appraisal of the cost-effectiveness of CBT and failure to consider the cost-effectiveness of GET at all potentially has a significant impact on the public in the following ways:

- (a) Public money better spent elsewhere may well be wasted. Avoidance of such waste is in the general public interest.
- (b) In so far as the Defendant has unreasonably exaggerated the clinical benefits of CBT and GET for CFS/ME sufferers (see the Claimant's grounds for review), the money earmarked by Trusts for treatment of these conditions is being spent ineffectively at the expense of other possible treatments. This is to the detriment of sufferers of CFS/ME, including the Claimants and the Interested Party.

The Defendant's grounds of resistance

24. The Defendant has set out its 'detailed grounds for resistance' in relation to the above at paragraphs 60 to 64.

25. It is said that this ground is predicated on the assertion that the recommended treatments are not clinically effective, and that the Claimants impermissibly invite the Court to substitute its view for that of the GDG in relation to clinical effectiveness. This is incorrect:

- (a) The challenge to the Defendant's conclusions as to cost-effectiveness are based upon:
 - i) Their failure to consider cost-effectiveness at all in relation to GET (contrary to the assertion made at paragraph 62 that this was in fact done).
 - ii) Their irrational conclusions reached upon the evidence *in fact* used by the GDG when considering the cost-effectiveness of CBT.
 - iii) Their reliance upon a sole report when considering the cost-effectiveness of CBT, despite the admitted knowledge of the limited evidential value of that report.

(b) These challenges are free-standing, and relate to the Defendant's failure to carry out their statutory duty to consider cost-effectiveness of the respective treatments. They do not go behind the Defendant's evaluation of clinical effectiveness.

26. At paragraph 63 of the grounds of resistance it is said that the Claimants invite the Court to substitute their view for that of the GDG in relation to cost-effectiveness. This is not correct, at least for the Interested Party. Rather, the Interested Party requests the Court to consider the lawfulness of the guidelines in light of the Defendant's failure to take into account of information that they must by law take into account (i.e. in relation to the cost-effectiveness of GET), and to consider whether, in relation to the appraisal of the cost-effectiveness of CBT, the Defendant has reached irrational or *Wednesbury* unreasonable conclusions. The Interested Party does not seek the Court's view of the cost-effectiveness of these treatments, but seeks for the matter to be referred back to the Defendant for lawful consideration.

27. It is said at paragraph 64 of the grounds of resistance that it is not the function of the court to review the logical and mathematical errors exposed by Dr Kendrick in his statement. This is wrong:

(a) Where a public body makes important decisions which affect a significant number of people on the basis of obvious logical and mathematical errors, it is the function of the court to review such decisions where they are irrational and therefore unlawful.

(b) Were the Court to decline to do so simply because the logical and mathematical errors occur in detailed analysis, public decision making would not be subject to effective scrutiny.

(c) It is difficult to see how the simple and obvious mathematical errors in the cost-effectiveness analysis can come down to '*one or more doctors' disagreement with the approach adopted by those in the GDG*' as suggested by the Defendant.

(d) As to the 'logical errors', it is again difficult to see how the GDG's conclusions on the cost-effectiveness on CBT could have been arrived at rationally for the reasons outlined by Dr Kendrick. This is not a matter of reasonable disagreement. If the GDG's

conclusions are in the Court's view irrational then they are properly the subject of review and the guidance in so far as it is based upon these conclusions should be quashed.

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27th of January 2009