Cost-effectiveness of cognitive behavioural therapy, graded exercise and usual care for patients with chronic fatigue in primary care

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three strategies for the treatment of patients with chronic fatigue syndrome (CFS) were examined. The strategies were cognitive-behavioural therapy (CBT), graded exercise therapy (GET), and usual general practitioner (GP) care plus a self-help booklet (BUC).

CBT (6 sessions of 45 minutes) included an initial assessment, activity planning, homework, and the establishment of a sleep routine. GET aimed for a gradual increase in aerobic activities, especially walking. Trained cognitive behavioural therapists delivered CBT, while physiotherapists delivered GET.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with unexplained fatigue that had lasted for more than 3 months.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were gathered from January 1999 to June 2001. 2000/2001 prices were used for the cost analysis.

Source of effectiveness data
The effectiveness evidence was derived from a single study, the main details and results of which had been published elsewhere (Ridsdale et al. see 'Other Publications of Related Interest' section for bibliographic details).

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the clinical study.

Study sample
The authors stated that sample size was determined on the basis of power calculations to show significant differences in clinical outcomes. Limited information on the process of sample selection was reported. Of the 144 patients included in
the first comparison between GET and CBT, 123 received the study interventions. A further group of 40 of the 47
initially identified patients entered the BUC group (7 patients refused to participate). However, the final study sample
comprised 50 patients (66% women) in the GET group, 52 patients (71% women) in the CBT group and 30 patients
(77% women) in the BUC group, because cost-effectiveness data was available for a smaller group of patients than that
initially considered. The mean age of the patients was 40 (+/- 10.7) years in the GET group, 40 (+/- 12.8) years in the
CBT group and 36.9 (+/- 10.7) years in the BUC group.

Study design
This was a prospective study in which the patients were initially allocated to the two therapy options (GET versus CBT)
in a randomised fashion. GET and CBT patients were then grouped (therapy group) and compared with BUC patients
who were identified in a non-randomised fashion. The patients were recruited at 22 general practices in London and the
South East of England. The length of follow-up was 8 months. The outcomes were assessed at baseline and 3 and 8
months. Details of the loss to follow-up were unclear.

Analysis of effectiveness
The analysis of the clinical study was restricted to patients whose cost-effectiveness data were available. The primary
outcome measure used was the change in fatigue. This was assessed using a validated 11-item Likert instrument (for
each item, 0 represented fatigue less than usual and 3 much more than usual), with higher scores representing higher
levels of fatigue. The three groups of patients were comparable in terms of their demographics and the baseline values
of the outcome measures. However, when GET and CBT patients were grouped, the therapy group had a higher
proportion of non-white patients and significantly higher baseline fatigue, symptom and depression scores.

Effectiveness results
For GET versus CBT, the mean decrease in fatigue score for the GET group relative to the CBT group was 0.71 points,
but this difference was not statistically significant. The data showed that 73% of GET patients and 79% of CBT
patients had a decrease in fatigue of at least 4 points. The mean unit change was 2.4 (+/- 2.2) in the GET group and 2.7
(+/- 2.1) in the CBT group.

For therapy (GET or CBT) versus BUC, the outcomes were significantly better for therapy over BUC, with the mean
difference being 4.38 points on the fatigue scale. In addition, only 60% of the BUC patients showed clinically
significant improvements compared with 76% of the therapy group. The mean number of four-unit changes was 1.2
(+/- 1.9) and 2.6 (+/- 2.2), respectively.

Clinical conclusions
The effectiveness analysis showed that GET and CBT were equally effective, but therapy (either GET or CBT) was
significantly more effective than BUC.

Measure of benefits used in the economic analysis
The summary benefit measure was the change in fatigue score, which was derived directly from the clinical analysis.
The authors also considered two variations in this outcome measure for the economic evaluation. First, a variable that
scored 1 if a clinically significant reduction in fatigue of at least 4 points was achieved. Second, a variable equal to the
total change in the fatigue score divided by four to measure the units of change, with a 1-unit change being equal to
four points on the original scale.

Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe. The unit costs were not reported
separately from the quantities of resources used, but the unit costs were provided for the majority of items. The health
services included in the economic evaluation were GET, CBT, BUC, GPs, other clinicians, nurses, inpatient stays,
physiotherapists (additional to those providing GET), counsellors, nutritionists, social services and complementary
therapy, and informal care time spent in specific tasks. The specific tasks in the latter related to personal support, child care, help in or around the house, help outside the home, or other tasks.

The perspective adopted in the study might have been that of society since costs relevant to the health care service, as well as the economic impact of informal care, were included. Resource use was estimated using patient-level data collected alongside the effectiveness study. The data were gathered 3 months before baseline and at 8 months’ follow-up. The costs came mainly from national figures. Other published sources were used for CBT and GET services, while the cost of informal care came from rates of home care workers. A fixed cost for the booklet used in the BUC group was used. The prices used referred to 2000/2001 figures.

Statistical analysis of costs
A multiple regression analysis was carried out to examine the statistical significance of differences in the estimated costs, so as to adjust for patient characteristics. Owing to the non-normal distribution of the costs, bootstrapping with 5,000 samples was used. Thus, confidence intervals (CIs) were generated.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
UK pounds sterling (€).

Sensitivity analysis
Sensitivity analyses were carried out to examine the robustness of the cost-effectiveness results to variations in some cost estimates. In particular, the analysis was re-run assuming that the cost of information care was equal to the national minimum wage or equal to zero. The cost of therapy was varied between one third higher and one third lower.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
For GET versus CBT (with sample differences controlled for), the total mean cost was 519 (90% CI: -814 - 1,904; p=0.552) higher for the CBT than the GET group at baseline. However, at the follow-up assessment, it was 193 (90% CI: -946 - 458; p=0.620) less for the CBT. The difference in total costs did not reach statistical significance.

For therapy versus BUC (with sample differences controlled for), the baseline costs for the therapy group were 385 (90% CI: -811 - 1,702; p=0.664) greater than for the BUC group. At follow-up, the therapy group was 149 (90% CI: -708 - 1,011; p=0.791) more expensive. Again, the difference in total costs did not reach statistical significance.

Synthesis of costs and benefits
The costs and benefits were combined using the net-benefit (NB) approach. Alternative values for the society's willingness to pay for an improvement in the benefit measure were used. These ranged from 0 to 10,000 at 500 increments. Cost-effectiveness acceptability curves were generated.

For GET versus CBT, if society placed a zero-value on a clinically significant decrease in fatigue, then the probability that CBT would be more cost-effective over GET was 0.589. This probability increased to 0.766 if society valued a clinically significant change at 5,000. At all values considered, CBT was more cost-effective. With a zero-value placed on a 4-point change in the Likert-scale, the probability that CBT would be more cost-effective was 0.663.
For therapy versus BUC, therapy produced greater benefits at a non significantly higher cost. With a zero-value placed on decrease of fatigue, the probability that therapy was more cost-effective than BUC was 0.237. This probability was 0.818 when the value placed on fatigue was 4,500. If a 4-point change in the Likert-scale was valued at 500, then the probability that therapy is more cost-effective than BUC was 0.819.

The sensitivity analysis showed that the base-case results were quite robust. If the cost of informal care was 0, then the probability that therapy was cost-effective was 0.880, which became 0.894 with a unit cost of 4.10.

If the cost of therapy increased by one third, the probability that therapy was the most cost-effective option fell to 0.797 with a willingness to pay of 4,500. If the cost fell by one third, then the probability value was 0.836.

**Authors’ conclusions**
Cognitive-behavioural therapy (CBT) was slightly more cost-effective than graded exercise therapy (GET) for the treatment of patients with chronic fatigue syndrome (CFS), although outcomes and service use were quite comparable. The probability that usual care plus a booklet (BUC) was cost-effective over either therapy option was low. The cost of informal care played a key role in the cost-effectiveness analysis. Whether the improvement achieved for patients with CFS was worthwhile depended on society's willingness to pay.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparators was appropriate as usual care and two alternative therapy options were considered. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from a published study, which was in part randomised. However, the comparison between therapy and BUC was not randomised and the study groups were not comparable at baseline. Thus, the impact of selection bias and confounding could not be ruled out. The authors noted that assessment bias was minimal since all patients were drawn from the same practices and the same instruments were used. In fact, the multi-centre design and the use of power calculations (which were carried out in the primary study) enhanced the internal validity of the analysis.

**Validity of estimate of measure of benefit**
The summary benefit measure is specific to the disease considered in the study. Thus, it is not comparable with the benefits of other health care interventions. The impact of the interventions on quality of life was not reported. The authors noted that the interpretation of a unit change on the fatigue scale was difficult.

**Validity of estimate of costs**
The authors stated that a broad perspective was adopted in the analysis. Indirect costs were not included on account of controversy on their inclusion and measurement. The economic impact of informal care was considered and different rates were used in the sensitivity analysis. The unit costs were reported for the majority of cost items. Typical National Health Service sources were used and some uncertain cost estimates were tested. Statistical analyses were carried out on the costs. The price year was reported, which aids reflation exercises. The authors noted that the measurement of informal care costs was an issue in the literature, but sensitivity analyses were carried out to consider alternative values.

**Other issues**
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Limited sensitivity analyses were carried out (only on the cost side). The study referred to patients with CFS and this was reflected in the authors’ conclusions. The authors highlighted some limitations of the analysis. For example, the non-randomised study and the difficulty in assigning an economic value to changes in fatigue scale.
Implications of the study
The study results suggested that the use of therapy to treat CFS depended on how much society valued improvements in the benefit measure. The authors stressed that future studies should assess such a willingness to pay for patients with fatigue and other disorders.

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Other publications of related interest


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