Use of cognitive therapy for relapse prevention in chronic depression: cost-effectiveness study

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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
Cognitive therapy, in addition to antidepressants and clinical management, was compared with antidepressants and clinical management alone for relapse prevention in chronic depression. Clinical management comprised 30-minute appointments with a psychiatrist every 4 weeks during the treatment phase (20 weeks) and every 8 weeks during the 48-week follow-up phase. Cognitive therapy comprised 16 sessions over 20 weeks, with two subsequent booster sessions.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients with partially remitted major depression despite adequate clinical treatment. The participants were 21- to 65-year-old psychiatric outpatients with unipolar depression who gave informed consent and who had satisfied DSM-III-R criteria for major depression in an episode within the past 18 months, but not in the past 2 months. At randomisation, the patients were required to have current residual symptoms of at least 8 weeks' duration that reached 8 or more on the 17-item Hamilton Rating Scale for Depression (HRSD) and 9 or more on the Beck Depression Inventory (BDI). Patients were excluded if they had a past history of significant Axis I or Axis II co-morbidity, or other factors precluding participation in the study. They were also excluded if they had received prior cognitive therapy for more than five sessions.

Setting
The setting was not clearly stated, but it is likely to have been either local clinics or the participants' homes. The economic analysis was carried out in the UK.

Dates to which data relate
The dates to which the effectiveness data related were not reported. The resources used were estimated from a variety of sources available in 1998 and 1999. All the unit costs were adjusted to 1998 - 1999 prices using the relevant price indices.

Source of effectiveness data
The effectiveness data were gathered from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on a sub-group (86%) of the patient sample used in the effectiveness analysis. Resource utilisation questionnaires were available on 86% of the patients in each group.

**Study sample**

A total of 230 patients were invited to participate. The pre-sample size was 160 patients (80 per treatment group). This, by the log-rank test at \( p=0.05 \), gave 80% power to detect a reduction in relapse rates from 40% in one group to 20% in the other. All the patients were receiving antidepressants at a minimum dose equivalent to at least 125-mg amitriptyline. The patients were then randomised to receive clinical management alone (control group) or clinical management plus cognitive therapy (cognitive therapy group). Since cost information was available for only 77 patients in each group, the clinical analysis was performed on these patients (\( n=154 \)). The two treatment groups were closely comparable on all key variables. For example, the mean age (standard deviation, SD) was about 43 years, 43.3 years (SD=11.2) in the control group (c) versus 43.2 (SD=9.8) in the cognitive therapy group (ct). About 50% were male, 47% (c) versus 54% (ct). Finally, the severity ratings were in the middle of the residual depression range, with a mean HRSD score above 12 (c: 12.2, SD=2.9; ct: 12.1, SD=2.7) and a mean BDI of 22 (c: 22.3 SD=8.0; ct: 21.9; SD=7.7).

**Study design**

This was a randomised controlled study, which was carried out in a single centre. The duration of the follow-up was 68 weeks (20 weeks for the treatment phase and 48 weeks for the follow-up phase).

**Analysis of effectiveness**

The primary health outcomes were the relapse rates for the cognitive therapy group and the control group. The analysis of the clinical outcomes was conducted on an intention to treat basis. Relapse rates were defined as either:

- Meeting the DSM-III-R criteria for major depressive disorder for a minimum of 1 month, and also having a score of 17 or above on the HRSD at two successive face-to-face assessments at least 1 week apart; or

- Having residual depressive symptoms that persisted between two successive ratings 2 months apart, reaching a score of at least 13 on the HRSD on both occasions combined with a level of distress or dysfunction at which withholding additional active treatment was not justified.

Cox regression was used to analyse the relapse rates. This included, as covariates, the stratification variables used in the randomisation and other relevant demographic and clinical variables.

**Effectiveness results**

The actuarial cumulative relapse rates for the cognitive therapy and control groups were 10% (ct) and 18% (c) at 20 weeks, and 29% (ct) and 47% (c) at 68 weeks (adjusted hazard ratio 0.51; 95% confidence interval, CI: 0.32 - 0.93).

**Clinical conclusions**

Cognitive therapy is more effective than intensive clinical treatment in reducing significantly the risk of relapse in patients with chronic depression, who are resistant to standard treatment.

**Measure of benefits used in the economic analysis**

The authors did not develop a summary benefit measure. The primary health outcome, the reduction in relapse rate, was expressed as benefits.

**Direct costs**

The direct health care costs were assessed. These were for treatment, clinical management, inpatient, day hospital,
general practitioner and social worker, psychiatric nurse and therapist, group and marital therapy, and medication. Information on health and social care utilisation was collected using a questionnaire adapted from the Client Service Receipt Inventory. The costs were discounted at the annual rate of 6%. The unit costs were obtained from a variety of sources, including the relevant local providers, the Personal Social Services Research Unit and the British National Formulary. The cognitive therapy costs were calculated using a cost per minute taken from the mid-point of the relevant 1998 - 1999 salary scales, and included the employers' national insurance and superannuation contributions and overhead costs. The additional cost of non-face-to-face activities was estimated using a ratio provided by each therapist. A similar bottom-up approach was used to assess the unit cost of other therapies. The costs and the quantities were not reported separately. The prices used were for 1998 - 1999.

**Statistical analysis of costs**
The results of the cost analysis were reported as mean (median) values with SDs and as mean differences with 95% CIs. A non-parametric bootstrapping method (1,000 replications) was performed to test the robustness of the parametric assumptions on mean differences in the costs, and then parametric CIs were reported. Since the fully completed resource utilisation questionnaires were only available for 65% of the patients, the analysis imputed the missing assessments by using the last value carried forward at the previous assessment.

**Indirect Costs**
The indirect costs were not assessed.

**Currency**
UK pounds sterling ()

**Sensitivity analysis**
A one-way sensitivity analysis was carried out on the method of handling the missing data. Two alternative imputation methods were used, mean imputation and multiple imputation.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
Two separate analyses of the total costs were undertaken. First, the direct costs were considered but the additional costs of cognitive therapy were excluded. The second analysis included the cognitive therapy costs in the cost analysis.

The mean direct health care costs (excluding the cognitive therapy costs) were significantly lower in the cognitive therapy group (734) than in the control group (1,119). This was due to savings on inpatient admissions (161, 95% CI: 35 - 356) and day-patient services (206, 95% CI: 54 - 466).

Cognitive therapy resulted in a mean cost-saving of 385 (95% CI: 1 - 769; p<0.05).

When cognitive therapy costs were included, patients receiving cognitive therapy were 779 (95% CI: 387 - 1,170; p<0.01) more costly than those receiving standard clinical treatment. However, the incremental cost incurred by these patients (779) was lower that the overall mean therapy cost of cognitive therapy (1,164).

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratio (ICER) of cognitive therapy was 4,328 per relapse averted or 12.5 per additional relapse-free day. Based on the cost-effectiveness-acceptability curve for cognitive therapy, if the decision-maker would be prepared to pay 6,000, the probability of cognitive therapy being cost-effective would be over 60%,
and at 8,500, the probability would be over 80%. The ICER increased to 4,667 using the mean imputation method and to 5,028 using non-parametric multiple imputation. The results were relatively robust to the choice of the method used to impute the missing value.

In contrast to the imputation approaches, the ICER increased to 7,056 per relapse prevented using only the 65% of patients in the complete case analysis. The results were highly sensitive to the decision to impute the missing value.

Authors' conclusions
In individuals with depressive symptoms that are resistant to standard treatment, adjunctive cognitive therapy is more costly but more effective than intensive clinical treatment alone.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear. The comparator was chosen because it represented the routine care provided for patients with chronic depression. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The estimates of the measure of effectiveness are likely to be valid due to the randomisation and the accounting for the effects of confounding variables. However, the authors did not report the methods of randomisation, although it is apparent that stratification was used and some blinding was present. More detail of these facts would have enhanced the internal validity of the study. The authors stated that the estimates should be seen as a "worst-case" scenario, given that the study assumed that the primary health outcome from cognitive therapy came to an abrupt end at 17 months. This may have led to an overestimation of the ICER. Power calculations were conducted, although the final sample fell slightly short of the number required.

Validity of estimate of measure of benefit
The authors did not develop a summary benefit measure. The authors noted that a more appropriate measure of benefits, like quality-adjusted life-years, would have been relevant to compare the findings with other cost-effectiveness studies of physical disorders.

Validity of estimate of costs
The authors reported that the costs were estimated from the NHS perspective and, as such, the indirect costs were not reported. The exclusion of the indirect costs could have biased the results in favour of the standard treatment. As the authors noted, it is widely reported that effective treatment of depression often produces even greater reductions in indirect costs. The resource quantities were not reported, but the unit costs and the price year were. Statistical analyses of the mean differences in costs were conducted. However, no sensitivity analysis of the prices was conducted. The problem of missing values on resource utilisation arose due to the small size of the study sample. Missing data were compensated for using relevant imputation methods.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability of the results to other settings or countries was not specifically discussed. The authors do not appear to have presented their results selectively. The study enrolled patients with chronic depression despite clinical treatment and this was reflected in the authors’ conclusions. The robustness of the results was partially addressed using sensitivity analyses on the method of handling the missing data. However, further sensitivity analyses would only have strengthened the findings. In additional, only limited data were available on treatments (dose and medication usage).

Implications of the study
According to the authors, structured psychological therapies such as cognitive therapy, interpersonal therapy and similar approaches appear to have a major role to play in the treatment of residual depression. The authors strongly support the application of cost-effectiveness-acceptability curve techniques to randomised controlled trials of structured psychological therapies.

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**Other publications of related interest**


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