North Wales randomized controlled trial of cognitive behaviour therapy for acute schizophrenia spectrum disorders: two-year follow-up and economic evaluation

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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
Patients with schizophrenia admitted to an acute psychiatric hospital were given cognitive-behavioural therapy (CBT) in addition to treatment as usual (TAU). Details of the CBT were given in an earlier study (Startup et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details), which described how patients offered CBT were supposed to commit themselves to at least 12 sessions, but were offered 25 weekly sessions, each session lasting around 90 minutes. A comparator group of patients was given TAU, which consisted of pharmacotherapy, nursing care during hospitalisation, and community care after discharge.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 65, admitted to an acute psychiatric hospital with a clinical diagnosis of a schizophrenia spectrum disorder, who were suffering from an acute psychotic episode and showing no evidence of organic mental disorder. Reasons for exclusion were diagnosis could not be confirmed according to the American Psychiatric Association's DSM-IV criteria (1994), intelligence quotient of below 80, dependency on alcohol or illicit drugs during the last year, and more than 28 days had elapsed since their admission.

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

Dates to which data relate
The resource evidence was from the period 1996 to 2002. The price year was 2001 (originally 1996).

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

Link between effectiveness and cost data
The same patients provided both the cost data and the effectiveness data. The costing was carried out retrospectively, with much of the data gathered at interviews at the three follow-up periods.

Study sample
Power calculations were reported in the parent study (Startup et al. 2004). These indicated that a total sample of 90 would be needed to give adequate power (0.8) to detect an effect size of 0.6 standard deviations (SDs). All patients meeting the inclusion criteria and willing to participate in the study were included. Ninety patients met the inclusion criteria, of which 43 were assigned to the TAU group and 47 to the CBT group. In the parent study (Startup et al. 2004), it was stated that 100 patients refused to participate in the study, 38 were excluded because more than 28 days had passed since they were admitted to hospital, and 51 did not meet the inclusion criteria.

**Study design**
This was a multi-centred, randomised controlled trial in which patients were randomly assigned to either CBT or TAU. The follow-up period was 2 years. The actual CBT received by patients followed a trimodal distribution (see Startup et al. 2004); patients either had 2 or 3 sessions, 12 sessions or 25 sessions. The mean number of sessions was 12.9 (SD=9.4) and the median was 12. Twenty-one of the 47 patients terminated the treatment. At 2 years, 30 patients were unavailable for interview. Follow-up assessments were not blinded to the treatment assignment.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. Information on comparability at baseline was given in the parent study (Startup et al. 2004). This showed that the two groups were comparable at baseline, apart from the Global Assessment of Functioning (GAF) score which was higher in the TAU group. The primary health outcomes used in the analysis were the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS). Global ratings for hallucinations and delusions were summed to form a score for psychotic symptoms, while global ratings for all the SANS items were summed to form a score for negative symptoms. Patients were assessed on the Social Functioning Scale (SFS) and on the Global Assessment of Functioning (GAF). The readmission rates to hospital and the mean survival time were also assessed. Trained assessors and best informants were used to derive these scores.

**Effectiveness results**
Two years after treatment, the mean SAPS psychotic score was 3.39 (standard error, SE=0.55) in the CBT group and 4.37 (SE=0.57) in the TAU group, (p=0.22).

The total SANS score was 4.32 (SE=0.65) in the CBT group and 7.09 (SE=0.67) in the TAU group, (p=0.004).

The SFS score was 104.00 (SE=1.63) in the CBT group and 97.81 (SE=1.66) in the TAU group, (p=0.009).

The GAF score was 56.2 (SE=2.57) in the CBT group and 49.17 (SE=2.64) in the TAU group, (p=0.06).

The GAF results were analysed further. Bounds of +/- 8.7 were used for a reliable change and a cut-off of 57 was chosen for a clinically significant change.

In the CBT group, one patient showed a reliable deterioration, 7 no reliable change, 9 a reliable improvement, and 17 a clinically significant improvement.

In the TAU group, 8 patients showed a reliable deterioration, 6 no reliable change, 11 a reliable improvement, and 9 a clinically significant improvement.

The association between treatment group and categorical outcome was significant (chi-squared (3, n=70) = 8.44, p<0.04).

Sixty-one per cent of the CBT group were readmitted to hospital during the 2 years, compared with 70% of the TAU group.

The mean survival time in the CBT group (401 days, 95% confidence interval, CI: 312 to 489) was longer than in the TAU group (331 days, 95% CI: 237 to 425). However, the difference in survival time was not statistically significant.
These results showed that the advantage of CBT over TAU shown at 1 year, as reported in the parent study (Startup et al. 2004), had diminished with respect to GAF and SAPS delusions and hallucinations. However, the advantage in social functioning and SANS negative symptoms was maintained.

**Clinical conclusions**

The different measures give a conflicting picture as to the long-term benefits of CBT, although the CBT patients were still doing better at 2 years than the TAU group and the size of the advantage was much greater for social functioning and SANS negative symptoms than for GAF and SAPS delusions and hallucinations. The advantage of CBT over TAU at 2 years was less marked than at 1 year, and was only seen in some of the measures of effectiveness. The authors suggested booster sessions of CBT to maintain its effectiveness.

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

No summary measure of benefits was included in the analysis. The costs and effects were left disaggregated and the study was therefore classified as a cost-consequences analysis.

**Direct costs**

Discounting was not carried out since the costs were estimated for less than 2 years. The costs were derived from actual data obtained by the Service Utilisation Schedule (SUS), which interviews the key worker looking after the patient and obtains information on the time spent by the key worker and other health services used by their client during the previous month. Hospital records and records of institutions giving residential care were used to obtain their costs. The quantities and the costs were not analysed separately in a comprehensible manner. The costs of hospital inpatient days, residential care days, antipsychotic medication, key worker hours, psychiatric consultations, general practitioner consultations, day hospital days, day centre days and support worker hours were measured. The original price year was 1996. The prices were converted into 2001 prices.

**Statistical analysis of costs**

Statistical analyses of the costs were performed using a Mann-Whitney U-test. The mean costs and CIs were reported.

**Indirect Costs**

No indirect costs were estimated.

**Currency**

UK pounds sterling (£).

**Sensitivity analysis**

No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**

No estimated benefits were calculated.

**Cost results**

The mean cost was 27,535 (SD=17,705; 95% CI: 21,584 to 33,486) in the CBT group and 27,956 (SD=19,716, 95% CI: 20,900 to 35,012) in the TAU group. The difference in costs was not significant (Mann-Whitney U = 504, p=0.94).

The costs were estimated for 2 years and the costs of adverse events were taken into consideration.
Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Although improvements in the cognitive-behavioural (CBT) group compared with the treatment as usual (TAU) group were not as great at 2 years as at 1 year, there was still an advantage in some of the symptoms and there was no increase in costs. The authors concluded that CBT did have a beneficial effect overall.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparator, TAU. It represented current practice in the NHS. You should decide if it represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study design might not have been ideal; indeed, the authors themselves noted in the introduction that earlier studies had been unable to distinguish between the effect of CBT and that of individual counselling. Thus, it may be that this study was not ideal to measure CBT specifically, rather it measured the effect of having additional individual psychological treatment of a particular kind. As the amount of CBT received by the patients was so variable, the results showed the effect of offering CBT rather than the effect of receiving it. The study sample was representative of the type of patient chosen to be studied but, with the exclusion criteria of alcohol and drug abuse, it was unclear whether they were representative of schizophrenics as a whole. The earlier paper had shown the patient groups to be comparable in most respects. The analysis of effectiveness was handled credibly. However, the authors acknowledged that the absence of blinded assessments was a main limitation of the analysis. There were no other sources of the effectiveness data.

Validity of estimate of measure of benefit
No measure of benefit used.

Validity of estimate of costs
From the cost perspective adopted (i.e. the health system), all the relevant costs were included. The costs and the quantities were not reported separately in a comprehensible manner. It was unclear what the unit cost of CBT was and, therefore, what the marginal cost of increasing the amount of CBT would be. Resource use quantities were taken from a single study, while the unit costs were taken from the authors' setting and published sources. A statistical analysis of the quantities was carried out, but there was no statistical, sensitivity or any other kind of analysis of the prices. Originally 1996 prices were used, but these were converted to 2001 prices using estimates from the NHS Executive. This will assist any future reflation exercises. Discounting was appropriately not carried out since the study had a very short-term time horizon.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was not addressed, and the fact that so many patients were unwilling to participate in the study means that generalisability to other settings is an issue. The authors did not present their results selectively and their conclusions generally reflected the scope of the analysis. However, the authors did not deal with the issue that patients assigned to CBT received very different amounts of CBT.

The authors reported several limitations of their study. First, the follow-up assessments were not blind to the treatment received by the patient. Second, a large proportion of participants (33%) were unavailable for follow-up interviews. The estimation of resources was largely based on use during the previous month only. In addition, the authors acknowledged that very large samples would be required to provide adequate power for the cost analysis.
Implications of the study
The authors concluded that, in terms of negative symptoms and social functioning, this type of schizophrenic patient was better off with CBT after 2 years than if they had received TAU. Further research that assessed the effect of different amounts of CBT, and also compared it with another kind of psychotherapy or counselling, would be very interesting.

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Bibliographic details

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Other publications of related interest
Startup M, Jackson MC, Bendix S. North Wales randomised trial of cognitive behaviour therapy for acute schizophrenia spectrum disorders: outcomes at 6 and 12 months. Psychol Med 2004;34:413-22.

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