Cognitive-behavioural therapy and motivational intervention for schizophrenia and substance misuse - 18-month outcomes of a randomised controlled trial


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
The use of an integrated programme of cognitive-behavioural therapy (CBT) combined with motivational intervention (MI) plus routine care (RC), versus RC alone, for the treatment of patients with dual diagnosis of schizophrenia and substance misuse.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Individuals were entered into the trial as patient and carer pairs. The inclusion criteria were:

an ICD-10 (World Health Organization) and DSM-IV (American Psychiatric Association) diagnosis of schizophrenia, schizoaffective disorder or delusional disorder;

a DSM-IV diagnosis of substance dependence or misuse;

in contact with catchment-area-based mental health services in the north-west of England;

aged between 18 and 65 years; and

face-to-face contact with a carer for a minimum of 10 hours per week.

Patients were excluded if there was evidence of organic brain disease or learning disability. Patients were accepted for the study only if both the patient and carer consented.

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

Dates to which data relate
It is likely that the effectiveness and resources use data were collected between 1998 and 1999, although the exact dates of the clinical trial were not reported. Prices relating to 1998/1999 were used.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
The participants in the study were selected from patients at three National Health Service hospital trusts that met the inclusion criteria. The paper did not report whether power calculations were used to determine the sample size. Initially, 66 pairs of patients-carers were eligible. However, 30 pairs (23 patients and 7 carers) refused to give consent. Thus, 36 pairs were finally randomised, 18 being allocated to each group (intervention and control). Patients who refused to participate were significantly older, had a longer duration of illness dating from their first admission, and had fewer admissions in the past 3 years.

Study design
The study was a randomised controlled trial (RCT) that was carried out in one centre over three sites in the UK. Further details of the study were provided elsewhere (see Other Publications of Related Interest). The unit of randomisation was the patient-carer pair. The patients and carers were assessed on multiple measures for their initial clinical and emotional condition before randomisation. A third party, who had no affiliation to the study, allocated the pairs to the groups. A computer-generated randomisation list stratified for patient gender and three types of substance use (alcohol alone, drugs alone, or drugs and alcohol) was used.

The intervention period was 9 months. The total follow-up period was 18 months for the patients and 12 months for the carers. Seventeen patients and 15 carers in the intervention group, and 15 patients and 12 carers in the control group, were followed up until the end of treatment (9 months). Fifteen patients in the intervention group and 13 in the control group were followed up until the end of the study (18 months), while 14 (intervention) and 11 (control) carers, respectively, completed the 12-month follow-up. Independent assessors who were blinded to the treatment allocation conducted all of the assessments. Blinded allocation was achieved using separate rooms and administrative procedures for project staff, multiple coding of treatment allocation, and by asking the participants not to disclose information about their treatment.

Analysis of effectiveness
The basis of the analysis was intention to treat. The primary patient outcome evaluated was the change in the Global Assessment of Functioning Scale (GAF). The secondary patient outcomes included measures of:

patient symptomatology, using the Positive and Negative Syndrome Schedule (PANSS);

social functioning, using the Social Functioning Scale;

patient substance use, using timeline follow back; and

the frequency and duration of relapses.

The inter-rater reliability for all assessments was checked and found to be good (inter-rater correlation coefficient was 0.65 for the GAF measure). The carer functioning was assessed using several questionnaires and appropriate schedules. The two groups of patients (intervention and control) were comparable in terms of any measured demographic and illness history variables, and for the distribution of alcohol and drug use. Carers in the two groups were also reported to be comparable for emotional status and other variables examined.

Effectiveness results
To compare the effects of the intervention between the groups, analyses of covariance were used with the pretreatment scores entered as the covariate.

The mean GAF scores for the two groups were:
at 0 months, 49.67 (standard error, SE=11.96) for the intervention group and 53.33 (SE=13.53) for the control group; at the 18-month follow-up, 60.12 (SE=18.96) for the intervention group, and 53.44 (SE=13.00) for the control group. The adjusted values at the end of the follow-up were 61.68 (SE=3.32) for the intervention group and 51.77 (SE=3.42) for the control group, (p=0.048).

The average improvement on GAF scores was 22.5% for the intervention group versus no change for the control group. For the secondary outcomes, the differences were either not statistically significant, or only indicated a trend towards a statistically significant difference, (p>0.05). The exception was one PANSS sub-scale score, for which the intervention proved to be more effective.

Clinical conclusions
The treatment group had significantly superior GAF scores at the 18-month follow-up. Advantages for negative symptoms were also found. CBT-MI resulted in significant improvements in patient functioning in comparison with routine treatment, and the benefits persisted for up to 18 months.

Measure of benefits used in the economic analysis
The outcome measure used in the economic analysis was the mean GAF score at the end of the 18-month follow-up.

Direct costs
The study perspective was societal. All the relevant costs were included in the analysis. The estimated costs were for the actual intervention (individual CBT, family or carer intervention and family support services), hospital services, primary care services (visits to general practitioners or practice nurses), community or domiciliary services (e.g. social workers and occupational therapists), day services (e.g. drop-in centres), medication and the costs to the patient (e.g. travel and other out-of-pocket payments). The quantities and the unit costs were reported separately where relevant.

The direct health service resource use items were based on actual data, recorded prospectively in the trial. Details of the primary care and community-based services, as well as the direct patient costs, were obtained from the patients' self-reported data using an adapted version of the Client Service Receipt Inventory. The unit costs were collected from the financial departments of the participating hospitals. Where these were not available, data from the national literature, drug formularies, national salary scales and statistical surveys were used. The costs were discounted at an annual rate of 6%, as they were incurred during more than one year (18 months). Although not explicit, it would appear that the quantity of resources used was measured in 1998 to 1999. Prices relating to 1998/1999 were used.

Statistical analysis of costs
The costs were treated stochastically, with mean values and standard deviations (SDs) presented. The mean differences in all cost elements between the two groups were also provided, along with the 95% confidence intervals (CIs). Since the costs were not distributed normally, the robustness of the parametric assumptions about mean differences in the costs was tested using non-parametric bootstrapping methods (1,000 replications of the original data).

Indirect Costs
Indirect costs (productivity losses) were also included in the analysis. They were obtained from the patients' self-reported data using an adapted version of the Client Service Receipt Inventory. The quantities were not reported separately from the costs. The costs were discounted at a rate of 6%. Prices relating to 1998/1999 were used.

Currency
UK pounds sterling (£).
Sensitivity analysis
One-way sensitivity analyses were undertaken on the base-case results. These explored the impact of several assumptions about the costing. In particular, changing the discount rate, excluding the costs of family support visits when the patient was not at home, and including the cost of inpatient days of leave during the hospital stay.

Estimated benefits used in the economic analysis
Apart from the results presented (Effectiveness Results), no additional effectiveness data were reported. The measure of benefit used in the economic analysis was the mean GAF score at the end of the 18-month follow-up.

Cost results
The mean total costs from baseline to the 18-month follow-up were 8,753 (SD=4,804) for the intervention group and 10,013 (SD=10,717) for the control group. The difference between the costs was -1,260 (95% CI: -6,978 - -4,459). This was not statistically significant, (p=0.25).

A further analysis was carried out, in which the costs of the experimental treatment were excluded. The mean total costs were then -6,205 (SD=4,580) for the intervention group and -9,453 (SD=10,773) for the control group. The difference between the costs, -3,248 (95% CI: -8,957 - 2,460), was still not statistically significant, (p=0.25).

The costs were discounted at a rate of 6%.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was calculated. This expressed the difference in mean costs between the two groups divided by the difference in the mean GAF scores at the end of the follow-up. However, the result was not reported in the paper.

A cost-acceptability curve was used to incorporate the uncertainty around the sample estimates of the mean costs and outcomes, and the uncertainty about the maximum ICER that a decision-maker would consider acceptable. The graph was presented. The probability of the intervention being less costly than routine care (willingness-to-pay of 0) was 69.3%. According to the authors, this exceeded the "50% decision rule”. If the decision-maker were prepared to pay at least 20 per point increase in the GAF score, then the probability of the treatment programme being cost-effective increased to 70%. Finally, at a willingness-to-pay of 655 per point increase in the GAF score, this probability rose to 90%. The sensitivity analysis showed that the results were robust to the different scenarios adopted in the costing analysis.

Authors’ conclusions
Compared with routine treatment, the integrated programme of cognitive-behavioural therapy (CBT) combined with motivational intervention (MI) for patients with psychosis and substance use resulted in significant improvements in patient functioning. In addition, the benefits persisted for up to 18 months. The experimental intervention was no more costly than routine care (RC), and there was a high probability of it being cost-effective.

CRD COMMENTARY - Selection of comparators
The justification for the choice of the comparator was clear. The comparator represented RC for patients with psychosis and substance use. You should consider whether the RC described represents current practice in your setting.

Validity of estimate of measure of effectiveness
The estimate of measure of effectiveness was based on an assessor-blind RCT, which is the "gold standard” method for the evaluation of effectiveness. The method of randomisation is likely to have limited the possibility of selection bias. However, the study sample was small and was not representative of the study population. The authors acknowledged that eligible patients who refused to participate in the study were significantly different from those who consented. This
fact may limit the generalisability of the results. It was stated that the patient groups were comparable in their baseline characteristics. The data were analysed on an intention to treat basis. Appropriate statistical analyses were conducted to account for potential biases and confounders. Overall, the internal validity of the effectiveness estimates is likely to have been high.

Validity of estimate of measure of benefit
One measure of benefit from among those evaluated in the RCT was used in the economic analysis. The choice of this estimate was justified.

Validity of estimate of costs
A societal perspective adopted and, as such, all the categories of costs relevant to this perspective appear to have been included in the economic analysis. The costs and the quantities were reported separately, where appropriate, which will aid reproducibility in other settings. A statistical analysis of the quantities was performed. Sensitivity analyses were conducted, to explore the impact of different assumptions in the costing analysis. A range of prices was provided, where relevant. Discounting was undertaken, as appropriate. The year to which the prices referred was reported, which will aid reflation.

Other issues
The authors compared their results with findings from other studies, but the issue of generalisability to other settings was not explicitly addressed. The results for the cost-effectiveness analysis were not adequately reported. The authors acknowledged that the small sample size represented a limitation of the study. However, they stated that the characteristics of the study sample were similar to other substance-misusing psychosis groups cited in the literature. It was recognised that the special contact characteristics of the patients with their family or carers might prevent the generalisability of the results to patients who live alone and are without contact with their families, although the baseline characteristics between these two categories of patients were found to be similar in the literature. The authors also suggested that the small sample size might have led to some potentially clinically significant results not achieving statistical significance. Finally, the authors reported that the benefits attributed to the intervention may have been due to additional contact time per se, as the study design did not control for the additional staff time allocated to the intervention group.

Implications of the study
The authors recommended further research to clarify the nature of the interaction between psychosis and substance use. Moreover, they suggested that additional trials with larger sample sizes and more specific interventions for patients and carers are needed, to identify the most effective therapy for patients with psychosis and substance use.

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Other publications of related interest
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