Psychodynamic psychotherapy and clomipramine in the treatment of major depression
Burnand Y, Andreoli A, Kolatte E, Venturini A, Rosset N

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
Two 10-week treatments for patients suffering from major depression were examined, a combined treatment comprising psychodynamic psychotherapy and clomipramine (antidepressant) versus clomipramine treatment alone. Clomipramine was administered at a dose of 25 mg on the first day, gradually increasing to 125 mg on the fifth day. Psychodynamic psychotherapy involved individual sessions, which were aimed at providing emphatic listening, guidance, support, and facilitation of an alliance by one carefully designated caregiver (trained nurses). The clomipramine protocol was identical in both study groups.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with major depression. The inclusion criteria were a diagnosis of major depressive episode on the basis of the Structured Clinical Interview for DMS-IV (SCID), whatever the severity of any concurrent suicidal ideation, personality psychopathology, or past resistance to treatment. Also, a score of at least 20 on the Hamilton Depression Rating Scale (HDRS), which ranges from 0 to 52 (higher scores indicate more severe disease). The exclusion criteria were bipolar disorder, psychotic symptoms, severe substance dependence, organic disorder, mental retardation, history of severe intolerance to clomipramine, and poor command of the French language.

Setting
The setting was secondary care. The study investigated patients referred to a community mental health centre. The economic study was carried out at the University of Geneva Psychiatric Center, Geneva, Switzerland.

Dates to which data relate
The effectiveness and resource use data were gathered from 1994 to 1996. No price year was reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

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

Study sample
Power calculations to determine the sample size were not reported. Of the 390 consecutive patients identified by four independent psychologists at the study hospital from 1994 to 1996, 110 were eligible. Ten patients were diverted to another study and 5 patients dropped out before randomisation. Thus, the final study sample comprised 95 patients for allocation to the study groups. However, 21 patients (12 in the combined treatment group and 9 in the clomipramine alone group) were excluded from the analysis. A sample of 74 patients was therefore enrolled, of which 35 were in the combined treatment group and 39 in the clomipramine alone group. The patients in the combined treatment group were aged 36 (+/- 9.5) years and 66% were women. The patients in the clomipramine alone group were aged 36.7 (+/- 10.4) years and 56% were women.

**Study design**

This was a randomised controlled trial, which was carried out in a single centre. Randomisation was carried out after stratification by presence of personal disorders, past major depressive syndrome, and gender. The patients were followed for 10 weeks. Twelve patients in the combined treatment group and 9 in the clomipramine alone group were lost to follow-up. This was due to patients not returning for treatment, patients dropping out against medical advice, and the discovery of exclusion criteria not detected at the study entry. All outcome raters were independent, and the nurse and clinical staff did not participate in the outcome assessment. The psychologist who made the assessment was blinded to the patient allocation. However, the authors stated that there was no blinding when it came to the measurement of severity of depression and the Health-Sickness Rating Scale (HSRS) score, because the patients were receiving intensive care.

**Analysis of effectiveness**

The basis for the analysis of the clinical study was treatment completers only, but an intention to treat analysis was also conducted. The primary health outcomes used in the effectiveness analysis were the severity of depression (HDRS) at intake and at 10 weeks, the Global Assessment Scale (GAS) score at intake and discharge, the number of days of hospitalisation and sick leave, and the actual number of hospitalisation episodes. The study groups were comparable at baseline in terms of the demographics and disease conditions. The authors also stated that patients lost to follow-up were comparable with those who remained in the study.

**Effectiveness results**

At baseline, the HDRS score was 24.3 (+/- 3.2) in the combined treatment group and 24 (+/- 2.9) in the clomipramine alone group. The corresponding scores at 10 weeks were 8.9 (+/- 7) (combined treatment) and 9.7 (+/- 7.3) (clomipramine alone), respectively.

At baseline, the GAS score was 43.3 (+/- 3.7) in the combined treatment group and 43.1 (+/- 4.1) in the clomipramine alone group. The corresponding scores at discharge were 62.8 (+/- 6.8) (combined treatment) and 58.3 (+/- 7.2) (clomipramine alone), respectively, (p=0.006).

The number of days of hospitalisation was 1.1 (+/- 2.2) in the combined treatment group and 3.2 (+/- 5.9) in the clomipramine alone group, (p=0.04).

The duration of sick leave was 46.1 (+/- 37.1) days in the combined treatment group and 57.9 (+/- 38.6) days in the clomipramine alone group, (not significant).

The actual number of hospitalisation episodes was 2 (6%) in the combined treatment group and 9 (23%) in the clomipramine alone group, (p=0.05).

The study results were unchanged when an intention to treat analysis was performed.

**Clinical conclusions**

The effectiveness analysis showed that the combined treatment was more effective than clomipramine alone in improving the patients’ health condition and in reducing hospitalisation and sick leave.
Measure of benefits used in the economic analysis

The health outcomes were left disaggregated and no summary benefit measure was used in the economic study. A cost-consequences analysis was therefore carried out.

Direct costs

The cost/resource boundary adopted in the analysis of the direct costs was not reported. The health service costs included in the economic evaluation were nurse visits, psychotherapy session, psychoeducation, psychiatric examination (by resident or attendant psychiatrist), clinical supervision, psychotherapy supervision, days of hospitalisation and additional outpatient treatment. The authors assumed that some specific expenses, such as clomipramine administration, equipment and assessment, were similar for both treatment groups. Discounting was not relevant since the time horizon of the study was 10 weeks. The unit costs were not reported separately from the quantities of resources used. Resource consumption was estimated using data collectively gathered from the same sample of patients as that used in the effectiveness trial from 1994 to 1996. The source of the unit cost data was not explicitly reported. No price year was given.

Statistical analysis of costs

The costs were treated descriptively.

Indirect Costs

The indirect costs were included. Thus, it appears that a societal perspective has been adopted in the analysis. The unit cost of a workday lost and the number of workdays lost were reported. The costs were estimated from the public health section of the Geneva Bureau of Statistics. Days of sick leave equalled the days spent at treatment. No price year was reported. No discounting was applied since the costs were incurred over a short time period.

Currency

US dollars ($). The costs were converted from Swiss francs (SFr) into American dollars. The conversion rate was SFr 1.40 = $1.

Sensitivity analysis

Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis

See the 'Effectiveness Results' section.

Cost results

The total direct costs were $2,976 (+/- 835) in the combined treatment group and $3,441 (+/- 966) in the clomipramine group.

The total indirect costs were $7,211 (+/- 5,804) in the combined treatment group and $9,057 (+/- 6,038) in the clomipramine group.

The total costs per patient were $10,187 (+/- 2,859) in the combined treatment group and $12,498 (+/- 3,057) in the clomipramine group.

Synthesis of costs and benefits

Not relevant due to the cost-consequences design.
Authors' conclusions
The adjunct of psychodynamic psychotherapy to standard antidepressant therapy was cost-effective for the treatment of patients with major depression.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Clomipramine treatment alone was selected as the basic comparator because it represented the standard care for patients with major depression, and the aim of the study was to evaluate the active value of adding psychodynamic psychotherapy to standard care. You should decide whether antidepressant therapy represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a randomised controlled trial, which was appropriate for the study question. The study sample was representative of the study population. Power calculations were not reported, and the sample size was not large. It is therefore possible that the results were due to chance. Selection bias should have been low due to randomisation. Confounding is likely to be limited due to randomisation and because the study groups were comparable at baseline. Performance bias should have been low, as the authors stated that there was adequate quality control of treatment provision and careful monitoring of drug administration. There was some loss to follow-up, but attrition bias should be low since the patients who were lost to follow-up were not statistically significantly different from those who were evaluated at the final assessment. The basis of the analysis of the clinical study was treatment completers only, but an intention to treat analysis was also conducted. A blinded outcome assessment was conducted, except for the measurement of severity of depression and HSRS score for patients receiving intensive care.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The perspective adopted in the study was not reported, but it appears to have been societal as the indirect costs were included in the analysis. The unit costs were reported separately from the quantities of resources used. A detailed breakdown of the costs was provided. Statistical analyses of the costs and quantities were generally not provided, with the exception of hospital stay and days of sick leave. The cost estimates were specific to the study setting.

Other issues
The authors did not explicitly compare their findings with those from published studies. They also did not address the issue of the generalisability of the study results to other settings. Thus, the external validity of the analysis was low. The study referred to patients with major depression and this was reflected in the conclusions of the analysis. The authors noted some strengths and limitations of their analysis. The major limitations, as stated by the authors, included the lack of blinding and that the therapists involved in the treatment were not certified psychotherapists.

Implications of the study
The study results suggest that psychodynamic psychotherapy should be added to standard antidepressant therapy for the treatment of patients with major depression.

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