Sertraline and/or interpersonal psychotherapy for patients with dysthymic disorder in primary care: 6-month comparison with longitudinal 2-year follow-up of effectiveness and costs

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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
The health interventions examined in the study were Sertraline (SER), a selective serotonin reuptake inhibiting (SSRI) antidepressant (starting dose: 50 mg daily); Interpersonal Psychotherapy (IPT); and a combination of both (SER-IPT) for the treatment of adult patients with dysthymia. Patients were treated for six months with one of the three alternative interventions, which was then followed by an additional naturalistic 18-month follow-up. However, patients receiving SER would continue taking their medication until the end of the follow-up period. Patients receiving IPT (alone or in combination with SER) received a package of up to twelve 1-hour IPT counselling sessions to be completed before the end of the first six months.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients aged 18-74 years who screened positive for a DMS-IV dysthymic disorder, with or without major depressive disorder as a chronic or acute episode. A detailed list of exclusion criteria was given in the paper.

Setting
The setting was primary care. The economic study was carried out in a primary care university-affiliated Health Service Organization (HSO) located in Southern Ontario, Canada.

Dates to which data relate
No dates for effectiveness or resource use were reported. The price year was not given.

Source of effectiveness data
The effectiveness evidence came from a single study.

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

Study sample
Power calculations were not performed. Patients were recruited from the 11,000-patient roster of the HSO based on screening for a DMS-IV dysthymic disorder. Self-referral was encouraged through a publicity campaign. A total of 10,812 patients were contacted initially but an initial study sample of 707 eligible patients was enrolled in the analysis and allocated equally to the study groups.

**Study design**

This was a prospective, randomised, single-blind, clinical trial carried out in a single centre. Patients were allocated to study groups using a computerised randomisation schedule, which was generated prior to the recruitment of subjects. Each of the six physicians participating in the study received a box containing sealed opaque envelopes. Patient follow-up lasted two years and each patient was retained in the original randomised group. Outcome evaluation was blinded with independent interviewers, who were masked to patient allocation to study group, conducting study assessments at baseline, 6 months, 1 year, and 2 years. The overall loss to follow-up in the three study groups was 17% after six months. At the two-year evaluation, loss to follow-up was 11.8% in group 1, 13.1% in group 2, and 33.5% in group 3, (p=0.02). The authors reported that most of the patients left the study due to non-medical reasons: too busy, lived too far away, or other personal reasons. Hence 586 patients were retained at the 6 month assessment and only 525 patients were retained at the final assessment (after 2 years). Final groups were as follows: 196 subjects receiving SER (group 1), 212 patients receiving SER-IPT (group 2), and 178 subjects receiving IPT alone (group 3).

**Analysis of effectiveness**

The basis of the clinical analysis was stated to have been intention to treat, but only patients whose data were available at the follow-up assessment were used. Thus it appears that a per-protocol analysis was carried out. The authors reported that subjects were not dropped from the analysis if they did not comply with treatment and that patients were analysed according to their original group allocation.

The primary health outcome was mood, as measured by the Montgomery Asberg Depression Rating Scale (MADRS) at 6 months and later for 1- and 2-year follow-up assessments. Secondary health outcomes were response to treatment (defined as a 40% reduction in MADRS score), quality of life (Social Adjustment Scale-self rating (SAR-SR) to measure adult social adjustment in eight areas of work, family, and leisure roles; and McMaster Family Assessment Device to measure family function); Center for Epidemiologic Studies Depression Scale (CES-D), Visual Analogue Scale (VAS), compliance at six months (defined as 80% or more adherence to the prescribed regimen), and adverse events.

At baseline, age and initial MADRS score were statistically different across the study groups (excluding those lost to follow-up before the 6-month assessment) and, to adjust for potential confounding factors, baseline MADRS scores were used in the statistical analysis as a covariate. There was no statistically significant difference in the MADRS score, male to female ratio, insurance condition, or employment status between patients remaining in the study for the two-year assessment and those who were lost to follow-up. However, completers were significantly older, with more children, more education, and with a better perception of their own physical and mental health.

**Effectiveness results**

MADRS scores were as follows:

At six months: group 1, 14.3 (+/- 9.8); group 2, 15 (+/- 10.4); and group 3, 16.8 (+/- 10.6).

At two years: group 1, 11.7; group 2, 12.3; and group 3, 14.3. (All these differences reached statistical significance).

Treatment response was as follows: group 1, 59.7%; group 2, 57.5%; and group 3, 46.6%, (p=0.021).

SAR-SR improvements were as follows:

At six months: group 1, 0.19; group 2, 0.20; and group 3, 0.21.

At two years: group 1, 0.27; group 2, 0.26; and group 3, 0.26, (p=0.95).
Family function improvements were as follows:

At six months: group 1, 0.108; group 2, 0.107; and group 3, 0.156.

At two years: group 1, 0.21; group 2, 0.14; and group 3, 0.11, (p=0.27).

CES-D scores at six months were as follows: Group 1, 16; Group 2, 17; and Group 3, 18, (p=0.13).

The VAS scores at six months were: Group 1, 61; Group 2, 59; and Group 3, 56, (p=0.13).

Compliance at six months was as follows:
71.4% in group 1; 70.8% with SER and 78.3% with IPT in group 2; and 79.8% in group 3.

And finally, adverse events were mild in both SER groups and the proportion of patients reporting serious adverse events was 3.5% in group 1 and 4.3% in group 2.

Clinical conclusions
The effectiveness analysis showed that at six months patients in both SER groups (SER alone and SER-IPT) experienced a greater reduction in dysthymia symptoms than patients receiving IPT alone. This difference persisted over two years of follow-up.

Measure of benefits used in the economic analysis
Health outcomes were left disaggregated and no summary benefit measure was used, thus a cost-consequences analysis was carried out.

Direct costs
Health service and patient direct costs and transfer costs were included. Health service costs included primary care, emergency room, specialists, hospital episodes, hospital days, other health professionals and laboratory services. Patient costs included out of pocket expenditures for medications and supplies. Transfer costs included unemployment insurance, social assistance, family benefits and workers' compensation. Costs were discounted in the second year at 3% rate. Unit costs were not reported separately from quantities of resources used. The cost/resource boundary adopted in the study was that of society. The estimation of quantities was based on actual data derived from subjects' utilisation information. This was collected using a self-report inventory developed by Browne et al (1990). The estimation of costs was based on a health and social services database, developed and updated by the research team over the previous ten years. The period of data collection was not mentioned and no price year was reported.

Statistical analysis of costs
Statistical analyses were conducted to test for statistical significance of difference in total costs. The Kruskal-Wallis nonparametric test was used, as large standard deviations and heterogeneity of variances were observed.

Indirect Costs
Indirect costs were included as lost wages due to illness. Unit costs were not reported separately from quantities of resources used. The estimation of costs and resource consumption was conducted using the same methods as those used for direct costs (please see above). A 3% discount rate was used for costs incurred in the second year. No price year was reported.

Currency
Canadian dollars (Can$).
Sensitivity analysis
No sensitivity analyses were carried out.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results reported earlier.

Cost results
For two years of follow-up, per patient treatment and health care services costs were as follows:

Group 1, Can$4,922; Group 2, Can$4,898; and Group 3, Can$3,717, (p<0.05).

Social services costs were:

Group 1, Can$2,575; Group 2, Can$2,044; and Group 3, Can$1,665.

Indirect costs were:

Group 1, Can$369; Group 2, Can$446; and Group 3, Can$273.

Total discounted per patient costs over the two-year period were:

Group 1, Can$7,866; Group 2, Can$7,386; and Group 3, Can$5,657, (p<0.05).

Synthesis of costs and benefits
Not relevant as a cost-consequences analysis was conducted.

Authors’ conclusions
The authors concluded that the treatments based on SER (both SER alone and SER-IPT) were more effective than IPT alone for the treatment of patients with dysthymia. Although costs in the IPT alone group were lower than costs in both SER groups, overall expenses were similar in the two SER groups.

CRD COMMENTARY - Selection of comparators
The inclusion of SER and ITP and the exclusion of placebo in the study were justified by the authors. However, the authors did not state if they were the only relevant alternatives. You, as a user of this database, should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on a randomised controlled trial, which was appropriate for the study question. The overall validity of the study is likely to be quite good. The authors did not report any power calculations so it is possible that the results were due to chance. However, the sample size seemed quite large. Selection bias should be low as patients were randomised with good procedures. There is a possibility of attrition bias as loss to follow-up was a significant percentage of the total sample size and it was significantly different between the groups. Furthermore, per-protocol analysis was performed which does not account for loss to follow-up. Measurement bias is likely to have been low as the independent outcome raters were blinded to the subjects’ group status. There is a possibility of confounding as the baseline characteristics were significantly different between the groups.

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 (see Validity of effectiveness comments above).
Validity of estimate of costs
The analysis of costs was carried out from a societal perspective and the appropriate costs were included. Average actual costs were used, which enhances the study's internal validity. However, no discounting was reported and that was required given that costs were incurred over a period greater than 2 years. The fact that unit costs and quantities of resources used were not reported separately and no price year was given limits the reproducibility of the results to other settings. Unit cost data came from an institute's database and resource data from a primary study. Uncertainty in the cost results was investigated through statistical tests.

Other issues
The internal validity of the economic study was, in the main, increased through the full presentation of results, the authors' conclusions reflected the scope of the analysis and through observing some of the limitations of their analysis. These have been described above. The external validity of the study was improved through comparison of the study results with other selected studies and by addressing the generalisability of the study by specifying that the results were only valid for people with DSM-IV dysthymic disorders with or without depression, in primary care.

Implications of the study
The study suggested that SER-IPT should be used for the treatment of adult patients with dysthymia. The authors suggested that further studies should explore the effects of altering the mix and intensity of different treatments provided to patients with dysthymia and that subgroup analyses would be appropriate to identify the profile of individuals who may benefit from the interventions.

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Other publications of related interest

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