BJPsych | The British Journal of Psychiatry (2008)
193, 163–164. doi: 10.1192/bjp.bp.107.045708

Short report

# Maintenance pharmacotherapy for recurrent major depressive disorder: 5-year follow-up study

Irina A. K. Holma, K. Mikael Holma, Tarja K. Melartin and Erkki T. Isometsä

**Summary**
Practice guidelines endorse maintenance antidepressant treatment for recurrent major depressive disorder. In the Vantaa Depression Study, we followed 218 psychiatric patients with major depressive disorder for up to 5 years with a life-chart. Of these patients, 86 (39.4%) had more than three lifetime episodes and an indication for maintenance pharmacotherapy. However, of these, only 57% received treatment and only for 16% of the time indicated. Good adherence to pharmacotherapy in the acute phase independently predicted maintenance treatment. The tertiary preventive impact of maintenance treatment may remain limited, as many patients with major depressive disorder either do not receive it, or receive it for too short a period.

**Declaration of interest**
None. Funding detailed in Acknowledgements.

Major depressive disorder is usually recurrent. National practice guidelines recommend maintenance pharmacotherapy for most patients with a history of three or more major depressive episodes or who are vulnerable to future recurrences.[1–4] Maintenance treatment is an effective tertiary preventive intervention.[5] However, to our knowledge, there are no studies that have examined how successfully these recommendations are implemented. We investigated, in a 5-year prospective follow-up study of psychiatric patients with major depressive disorder in a Finnish city,[6] the prevalence, duration and predictors of maintenance treatment.

## Method

The Vantaa Depression Study is a collaborative depression research project between the Department of Mental Health and Alcohol Research of the National Public Health Institute, and the Department of Psychiatry, Helsinki University Central Hospital in Finland. The study is described in detail elsewhere.[6–9]

### Screening and baseline evaluation

In the first phase of the study, 806 psychiatric secondary care patients (aged 20–60 years) in the City of Vantaa, seeking treatment, referred to from primary care or already receiving psychiatric care but showing signs of deteriorating clinical state, were screened for the presence of depressive symptoms between 1 February 1997 and 31 May 1998.[7] Of the 703 eligible patients, 542 (77%) gave written informed consent and participated. In the second phase, researchers interviewed these patients using the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) version 2.0;[10] 269 patients were subsequently diagnosed with DSM–IV major depressive disorder[11] and included in the study. The diagnostic reliability of the diagnosis was excellent (kappa=0.86).[7]

### Follow-up

After baseline, participants were investigated at 6 and 18 months with SCAN, and at 5 years with Structured Clinical Interview for DSM–IV–TR Axis I Disorders (SCID–I/P),[12] plus several semi-structured scales.[6,8,9] The exact duration of the index episode, the timing of recurrences and treatment were examined by gathering all available data, a best estimate of which was integrated into a graphic life-chart. In addition to the follow-up interviews, patient records were also available. Questions related to important life events were asked to investigate changes in psychopathological state.

We classified the patients' follow-up time in the life-chart into three categories: (a) full remission (none of the 9 major depressive episode criteria symptoms), (b) partial remission (1–4 of the 9 symptoms) or (c) major depressive episode ($\geqslant$5 of the 9 symptoms). Recurrence was defined as return of symptoms sufficient to fulfil criteria for major depressive episode after at least two consecutive months of partial or full remission. Self-reported adherence and attitudes towards treatments were assessed by interviewing and rated on ordinal scales.[9] Specifically, adherence to antidepressant treatment during the first 6 months was used as a measure of acute-phase pharmacotherapy adherence and classified based on whether the patient used them: (a) regularly, treatment adherence adequate with respect to treatment goals; (b) somewhat irregularly, unclear whether this would affect treatment goals; (c) very irregularly, the treatment did not proceed according to plan; and (d) not at all, the treatment could not be implemented. Social relationships were investigated with the Interview Measure of Social Relationships.[13]

Of 269 participants initially included in the cohort, 198 participated in the 18-month interview and 182 (67.7%) in the 5-year interview. In all, information on 218 participants, followed for up to 60 months or until they left the study, was analysed. We defined an indication for maintenance treatment to exist after a major depressive episode among patients having already had more than three lifetime major depressive episodes and then achieving full remission for more than 2 months. Treatment was to commence 4 months after onset of full remission (i.e. after the continuation treatment phase).

### Statistical methods

We used SPSS software, version 14.0 for Windows, and $\chi^2$ (with Yates' correction), Fisher's exact, Mann–Whitney and Kruskal–Wallis tests, plus the two-sample *t*-test when appropriate. Logistic regression was used to investigate predictors for receiving maintenance treatment. From a predetermined set of twelve predictors covering the domains in the online Table DS1, the non-significant variables were eliminated from the final model, but age, gender and length of maintenance indication (months) were controlled for.

## Results

About half of the patients (57.0%, 49 out of 86) for whom maintenance treatment was indicated received it at least once during the follow-up. Their median time with an indication was 22.7 months (s.d.=17.7), but median duration of maintenance treatment received was only 2.8 months (s.d.=14.8). Of all patients with an indication, maintenance treatment was received for 15.9% (s.d.=43.7) of the total time with an indication (2961.4 patient-months), for a mean of once (s.d.=0.71). Patients receiving maintenance treatment visited psychiatrists more often than those not receiving treatment (median 4.0 (s.d.=5.72) *v.* 2.0 (s.d.=2.78); $z=-2.65$, $P=0.008$), among two-thirds (64.9%, 24 out of 37) of whom contact with secondary care facilities had ended prior to the onset of indication.

In univariate analyses, maintenance treatment was predicted by numbers of previous episodes, comorbid Axis I–III disorders and mental disorders, severity of anxiety, anxiety disorders, panic disorder, social phobia, avoidant personality disorder, positive medication attitude, good adherence during the acute phase and higher income (online Table DS1). However, in multivariate logistic regression analyses, only good antidepressant adherence in the acute phase (OR=3.18; 95% CI 1.12–9.03, $P=0.030$) independently predicted maintenance treatment.

## Discussion

Although national practice guidelines recommend maintenance treatment for tertiary prevention of depressive recurrences, to our knowledge, no previous study has investigated whether these recommendations are implemented. In this study of patients with major depressive disorder who had an indication for maintenance treatment, only about half received it and only for about a sixth of the time indicated. Maintenance treatment was best predicted by good medication adherence during the acute phase.

Our study had some major strengths. It comprised a cohort of patients representing psychiatric out- and in-patients with major depressive disorder in a Finnish city and is up to date in terms of the use of DSM–IV, modern antidepressants and maintenance treatment recommendations.[1–4,7,9] Structured and semi-structured measures plus life-charts, a prerequisite for this type of study, were used. However, limitations also exist. Those participants who left the study did not differ in their outcome, at least during the time they participated, from those who remained in the follow-up. Although we had full access to patient records, a long interval between the last two interviews (3.5 years) may have affected the accuracy of information regarding longitudinal outcome. We may have slightly underestimated the recurrence rate (and thus onset of maintenance indication) during this period.[6] Minor inaccuracies may also exist regarding treatment information; participants may not always have recalled information on treatment precisely or reported adherence honestly. However, data from participants or from their records were carefully compared and combined. Finally, we defined the indication for maintenance pharmacotherapy to begin after three lifetime major depressive episodes, and a different threshold could change the findings. However, setting it to lifetime fourth or fifth episodes in sensitivity analyses resulted in quite similar (61.5 and 62.9% respectively) proportions of patients having received maintenance treatment.

To ensure generalisability, replication of these findings is necessary. Nevertheless, they are important from a public health perspective. In secondary care, maintenance treatment is received by those able to adhere to their treatments, a finding which highlights the interactive nature of continuity of treatment. The tertiary preventive impact of maintenance treatment for major depressive disorder seems currently limited, as many patients may either not receive it or receive it for too short a period.

**Irina A. K. Holma**, MD, **K. Mikael Holma**, MD, Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki; **Tarja K. Melartin**, MD, PhD, Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, and Department of Psychiatry, HUCH, Peijas Hospital, Health Care District of Helsinki and Uusimaa, Vantaa; **Erkki T. Isometsä**, MD, PhD, Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, and Department of Psychiatry, Helsinki University Central Hospital, Helsinki, Finland

**Correspondence:** Erkki T. Isometsä, MD, PhD, Institute of Clinical Medicine, Department of Psychiatry, P.O. Box 22 (Välskärinkatu 12 A), 00014 University of Helsinki, Finland. Email: erkki.isometsa@hus.fi

First received 26 Sep 2007, final revision 15 Apr 2008, accepted 30 Apr 2008

## Acknowledgements

This study was supported by grants from the Academy of Finland, and the Healthcare District of Helsinki and Uusimaa.

## References

1 Depression Guideline Panel. *Depression in Primary Care. Volume 2: Treatment of Major Depression. Clinical Practice Guideline Number 5*. US Department of Health and Human Services, 1993.

2 American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry* 2000; **157** (suppl 4): 1–45.

3 National Collaborating Centre for Mental Health. *Depression. Management of Depression in Primary and Secondary Care*. National Institute for Clinical Excellence, 2004.

4 Isometsä E, Lindfors O, Pirkola S, Seppälä I, Salminen JK, Luutonen S, Marttunen M, Mattila M, Jäättelä A. The National Finnish Current Care Guidelines for the Treatment of Depression. An overview. *Psychiatr Fennica* 2003; **34**: 181–96.

5 Geddes JR, Carney SM, Davies C, Furukawa TA, Kupfer DJ, Frank E, Goodwin GL. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. *Lancet* 2003; **361**: 653–61.

6 Holma KM, Holma IA, Melartin TK, Rytsala HJ, Isometsa ET. Long-term outcome of major depressive disorder in psychiatric patients is variable. *J Clin Psychiatry* 2008; **69**: 196–205.

7 Melartin TK, Rytsala HJ, Leskela US, Lestela-Mielonen PS, Sokero TP, Isometsa ET. Current comorbidity of psychiatric disorders among DSM–IV major depressive disorder patients in psychiatric care in the Vantaa Depression Study. *J Clin Psychiatry* 2002; **63**: 126–34.

8 Melartin TK, Rytsala HJ, Leskela US, Lestela-Mielonen PS, Sokero TP, Isometsa ET. Severity and comorbidity predict episode duration and recurrence of DSM–IV major depressive disorder. *J Clin Psychiatry* 2004; **65**: 810–9.

9 Melartin TK, Rytsala HJ, Leskela US, Lestela-Mielonen PS, Sokero TP, Isometsa ET. Continuity is the main challenge in treating major depressive disorder in psychiatric care. *J Clin Psychiatry* 2005; **66**: 220–7.

10 Wing JK, Babor T, Brugha T, Burke J, Cooper JE, Giel R, Jablensky A, Regier D, Sartorius N. SCAN. Schedules for Clinical Assessment in Neuropsychiatry. *Arch Gen Psychiatry* 1990; **47**: 589–93.

11 American Psychiatric Association. *Diagnostic and Satistical Manual of Mental Disorders* (4th edn, text revision) (DSM–IV–TR). APA, 2000.

12 First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM–IV–TR Axis I Disorders, Research Version, Patient Edition with Psychotic Screen*. Biometrics Research, New York State Psychiatric Institute, 2002.

13 Brugha TS, Sturt E, MacCarthy B, Potter J, Wykes T, Bebbington PE. The Interview Measure of Social Relationships: the description and evaluation of a survey instrument for assessing personal social resources. *Soc Psychiatry* 1987; **22**: 123–8.

EXTRA CONTENT ONLINE



https://doi.org/10.1192/bjp.bp.107.045708 Published online by Cambridge University Press