Real-world effectiveness of pharmacological treatments in severe unipolar depression in a nationwide cohort of 123,712 patients

Jari Tiihonen, M.D., Ph.D., Markku Lähteenvuo, M.D., Ph.D., Fabian Hoti, Ph.D., Pia Vattulainen, M.Sc., Heidi Taipale, Ph.D., Antti Tanskanen, Ph.Lic.

ABSTRACT

Background: Very little is known about the comparative effectiveness of long-term pharmacological treatments of severe unipolar depression.

Method: We studied the risk of re-hospitalization during 1996–2012 among all patients who had been hospitalized because of unipolar depression in Finland (N = 123,712; mean follow-up time 7.7 years), by using nationwide databases for hospitalization and purchased medications. The primary analysis was within-individual analysis, in which each individual was used as his/her own control to eliminate selection bias. The effect of concomitant psychotropic medications and the temporal order of exposure and non-exposure periods were adjusted.

Results: Lithium use was associated with a markedly lower risk of re-hospitalization due to mental disorders (HR 0.47, 95% CI 0.40–0.55), while antidepressant treatments (1.10, 1.06–1.13) and antipsychotic treatments (1.16, 1.12–1.20) were not associated with any beneficial effect in this regard. Risk of re-hospitalization was lower during sole lithium therapy (0.31, 0.21–0.47) than its concomitant use with other antidepressants (0.50, 0.43–0.59). Analysis among incident cases (N = 30,004) showed slightly lower re-hospitalization risks during antidepressant (0.87, 0.82–0.93) and antipsychotic (1.03, 0.94–1.13) use, and markedly lower risks for lithium (0.31, 0.18–0.54) than in the total cohort. The only specific agent approaching the effectiveness of lithium was clozapine (HR 0.65, 0.46–0.90 in the total cohort; 0.33, 0.19–0.58 in the incident cohort). Sensivity analyses for all-cause hospitalizations and for controlling protopathic bias showed the same rank order as the primary analysis.

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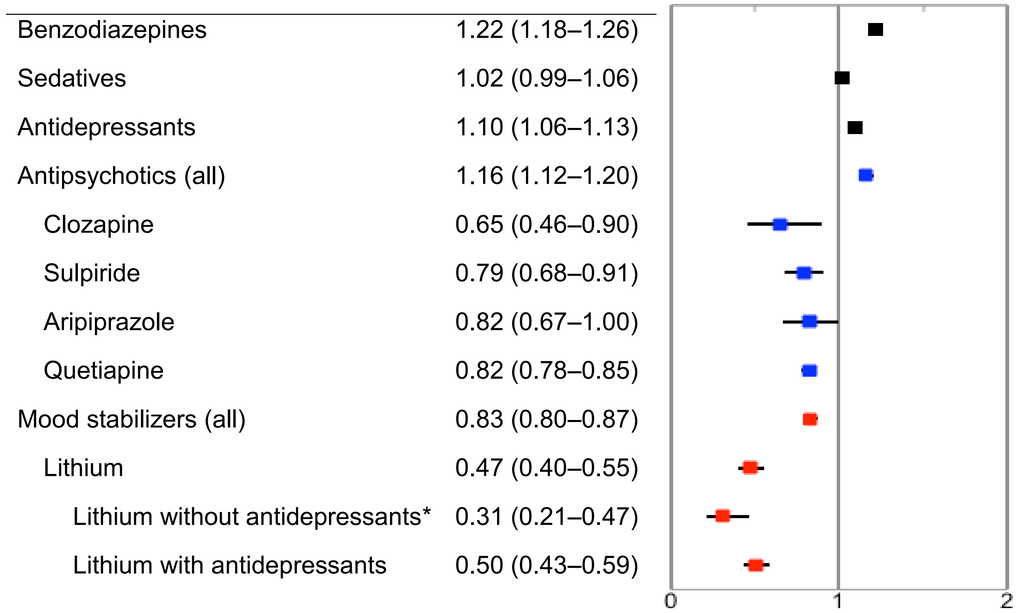
Figure. The risk of re-hospitalization due to mental disorder in the total cohort.



The adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for re-hospitalization due to mental disorder during use vs. no use of each pharmacological treatments in the total cohort of patients with unipolar depression (N = 123,712). Results are based on the within-individual Cox PH model, and are adjusted for time since diagnoses, temporal order of treatment, current use of other treatments, and polypharmacy. Mental disorder refers to any other disorder except schizophrenia of bipolar disorder (those patients who had ever had these diagnoses were excluded from the cohort).

*p = 0.02 for difference between lithium without concomitant antidepressant vs. with concomitant antidepressant use.

CONCLUSION

Lithium, and especially without concomitant antidepressant, is the most effective long-term treatment for severe unipolar depression. It is obvious that the effectiveness of antidepressants and ordinary antipsychotics in the maintenance treatment of severe unipolar depression is substantially lower when compared to lithium or clozapine.

Karolinska Institutet

Stockholms läns landsting

Karolinska Institutet
Jari Tiihonen
Professor
Department of Clinical Neuroscience
Stockholm, Sweden
jari.tiihonen@.ki.se