

# Treatments and outcomes in bipolar disorder

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i sal 2119 Hälsovetarbacken, Arvid Wallgrens backe, hus 2, den 20 november, kl. 13.00

av Erik Joas

Fakultetsopponent:

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## Avhandlingen baseras på följande delarbeten

- I. Erik Joas, Alina Karanti, Jie Song, Guy M. Goodwin, Paul Lichtenstein & Mikael Landén. (2017). Pharmacological treatment and risk of psychiatric hospital admission in bipolar disorder. *The British Journal of Psychiatry*, 210 (3), 197-202.
- II. Jie Song, Arvid Sjölander, Erik Joas, Sarah E. Bergen, Bo Runeson, Henrik Larsson, Mikael Landén & Paul Lichtenstein. (2017). Suicidal behavior during lithium and valproate treatment: a within-individual 8-year prospective study of 50,000 patients with bipolar disorder, *American Journal of Psychiatry*, 174 (8), 795-802.
- III. Caroline Hansson, Erik Joas, Erik Pålsson, Keith Hawton, Bo Runeson & Mikael Landén. (2018). Risk factors for suicide in bipolar disorder: a cohort study of 12 850 patients. *Acta Psychiatrica Scandinavica*, 138 (5), 456-463.
- IV. Erik Joas, Kristoffer Bäckman, Alina Karanti, Timea Sparding, Francesc Colom, Erik Pålsson & Mikael Landén. (2020). Psychoeducation for bipolar disorder and risk of recurrence and hospitalization—a within-individual analysis using registry data. *Psychological Medicine*, 50 (6), 1043-1049.
- V. Erik Joas, Lina Jonsson, Alexander Viktorin, Erik Smedler, Erik Pålsson, Guy M. Goodwin & Mikael Landén. Effect of CYP2C19 polymorphisms on antidepressant prescription patterns and treatment emergent mania in bipolar disorder. Manuscript.

**SAHLGRENSKA AKADEMIN  
INSTITUTIONEN FÖR  
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# Treatments and outcomes in bipolar disorder

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## **Abstract**

Bipolar disorder is defined by recurring mood episodes and patients have a markedly increased risk of suicide. Pharmacological and psychological treatments for bipolar disorder have proven efficacy in clinical trials yet the generalizability of current evidence to routine clinical practice is contested. This thesis presents studies on treatments and outcomes relevant to bipolar disorder patients using data from national registers. In study I, II, IV, we studied the effectiveness of different treatments using within-individual study designs to reduce the impact of confounding-by-indication. In study I, we showed that commonly used drugs, such as lithium, several anticonvulsants, and atypical antipsychotics, were associated with a reduced risk of psychiatric hospital admissions. The association between treatment and hospital admission was stronger for lithium compared to the atypical antipsychotics olanzapine and quetiapine. This differs from previous clinical trial evidence. In study II, we showed that lithium, but not valproate, was associated with a lower risk of suicide-related behaviour. In study III, we studied risk factors for completed suicide in the Swedish National Quality Register for Bipolar Disorder (Bipolär). We identified several risk factors for suicide, e.g., recent affective episodes and psychiatric comorbidity. In study IV, psychoeducation was associated with a reduced risk of recurrence and hospital admission in Bipolär. Finally, in study V, we studied the impact of CYP2C19 polymorphisms on antidepressant treatment patterns as well as the risk for treatment emergent mania using a large sample of patients with bipolar disorder. The mainly negative results suggest that information on CYP2C19 genotype has limited clinical value. These studies showcase the possibility of conducting psychiatric treatment research in national registers to fill important knowledge gaps. The studies can be used as supporting evidence when there is a lack of evidence on the effectiveness of different treatments in routine clinical care. We also underline the unique position of lithium in bipolar disorder treatment and extend current knowledge on risk factors for suicide.

Keywords: bipolar disorder, lithium, psychoeducation, CYP2C19, antidepressants, epidemiology, valproate, quetiapine, olanzapine, suicide