



# Treatment Patterns and Risk of Switch to Mania in Bipolar Depressive Patients Treated with Antidepressants: A real world study using the OHDSI Network

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## Background

Bipolar disorder is a recurrent and chronic affective disorder, throughout the course of the disease, depression episodes accounted for 72% of the duration of the illness, and it also takes a longer time to remission. However, the use of antidepressants (AD) in bipolar depressive episodes treatment remains controversial due to the potential risk of inducing a switch from depression to hypomania or mania (McGirr et al., 2016). In this study, we conducted a large-scale, retrospective, observational study across five databases standardized to Observational Medical Outcomes Partnership Common Data Model (OMOP CDM) to investigate the treatment patterns for the bipolar depression and risk of switch to mania amongst the patients treated with antidepressants.

## Methods

**Data sources:** Four electronic health record (EHR) databases and one administrative claims database from the USA, Germany, France, and China.

**Participants:** Patients with diagnosis of bipolar disorder current episode depression were included in the study. They should not have diagnosis or history of schizophrenia, psychotic disorders, dementia, neurodegenerative disease, or psychiatric disorders due to substances.

**Treatment:** The study population was classified into subgroups on the basis of treatments whether ADs were used or not. AD group was further stratified as AD concurrent with antipsychotic or mood stabilizer (AD-con) group or antidepressant monotherapy (AD-mono) group.

**Outcome:** The occurrence of switch to mania was defined as outcome after prescriptions of AD. Incidence rate ratio (RR) of manic switch in both acute and maintenance phase were calculated by comparing the patients treated with (AD group) with those who were not (Non-AD group).

## Results

A total of 2.8 million patients from the five databases were included for the analysis, 70% of whom received AD as initial treatment for bipolar depression. Proportion of AD-mono ranged from 19.6% to 46.9% across the databases. Data from China showed a wider spread of therapies which indicated more treatment alternatives and combinations. AD group had lower incidence rates of manic switch than Non-AD group in both acute and maintenance phase. Furthermore, incidence rates of manic switch were lower in AD-mono group than AD-con group in both acute and maintenance phase.

## Conclusions

This study indicated that AD had been widely used in clinical practice to treat bipolar depression, even as initial treatment. The use of AD did not increase the risk of manic switch when compared to non-AD treatment, whether alone or in combination with mood stabilizers or atypical antipsychotics. Therefore, AD could be used as a safe and effective alternative treatment for bipolar depression and be recommended as first-line treatment.



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## Abstract

**Aims.** The use of antidepressants (AD) for treating bipolar depression remains controversial due to the potential risk of inducing switch to mania. This multinational, large-scale, observational study is to describe the use of AD among bipolar depressive patients, and the potential risk of manic switch associated with the use of AD alone or in combination with antipsychotic or mood stabilizer.

**Methods.** Four electronic health record databases and one administrative claims database from four countries were used in this retrospective, observational study. Demographic characteristics of the bipolar depressive patients and their treatment pathways were described. Incidence rate ratio (RR) of manic switch was calculated by comparing the patients treated with AD group with those who were not AD group in 0-3 months (acute phase) and in 3-9 months (maintenance phase) after the treatment. Patients were further categorized to AD monotherapy (AD-mono group) and AD in combination with antipsychotics or mood stabilizers (AD-con group). Rate ratios comparison were used to evaluate the protective effects of concurrent treatments on manic switch.

**Results.** 2.8 million patients from the five databases were included for the analysis, 70% of whom received AD as initial treatment for bipolar depression. Proportion of AD monotherapy ranged from 19.6% to 46.9% across the databases. AD group had lower incidence rates of manic switch than Non-AD group in both acute and maintenance phase. Furthermore, incidence rates of manic switch were lower in AD-mono group than AD-con group in both acute and maintenance phase.

**Conclusions:** AD had been widely used in clinical practice to treat bipolar depression. The use of AD did not increase the risk of manic switch when compared to non-AD treatment.

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## Results

A total of 2.8 million patients from the five databases were included for the analysis, 70% of whom received AD as initial treatment for bipolar depression. Proportion of AD monotherapy ranged from 19.6% to 46.9% across the databases (Fig.1). Data from China showed a wider spread of therapies which indicated more treatment alternatives and combinations. AD group had lower incidence rates of manic switch than Non-AD group in both acute and maintenance phase. Furthermore, incidence rates of manic switch were lower in AD-mono group than AD-con group in both acute and maintenance phase.

## Results

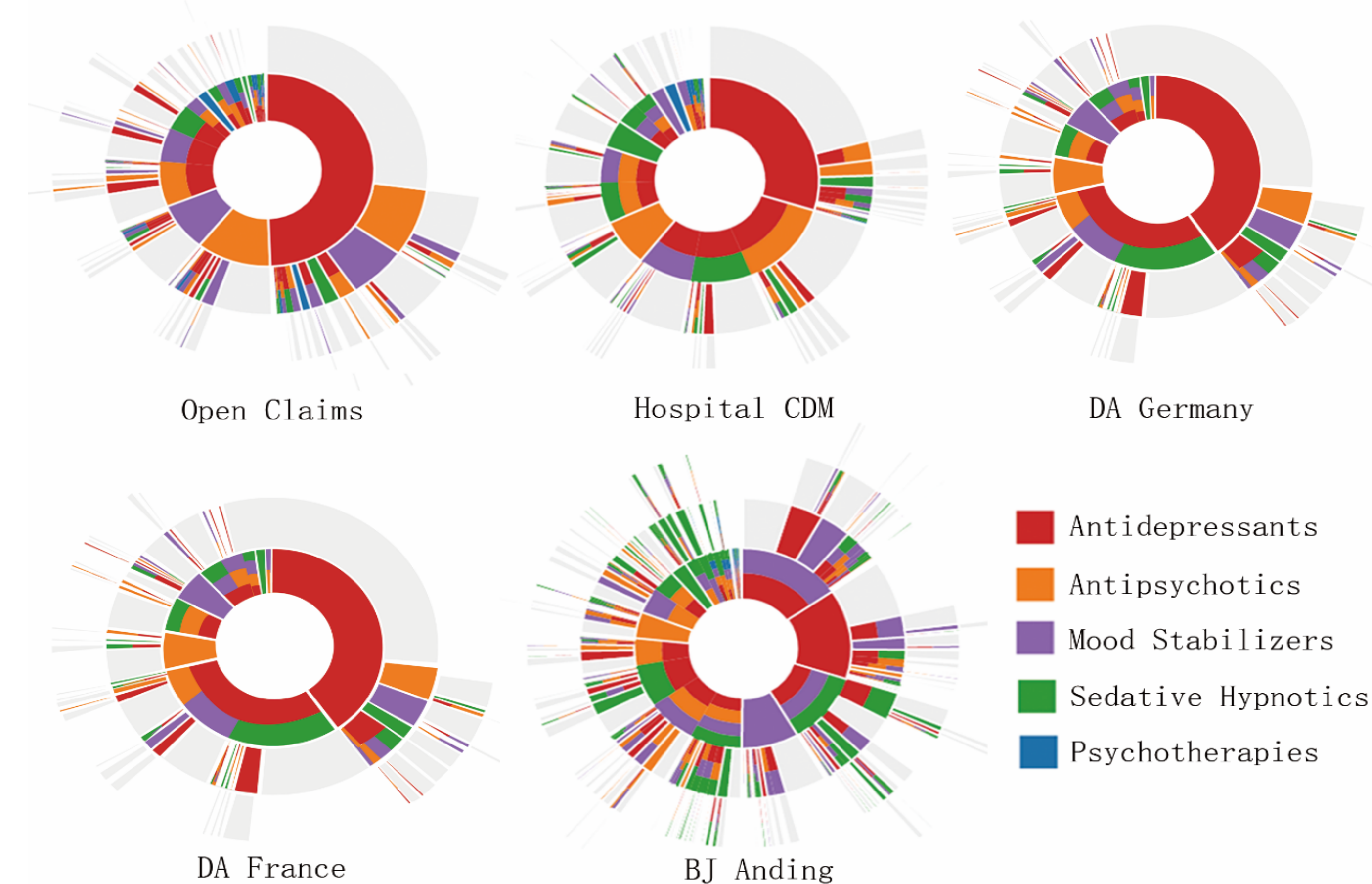


Fig. 1: Treatment pathways for all data sources. The inner circle shows the first relevant medication that the patient took, the second circle shows the second medication, and so forth.

## Conclusions

This study indicated that antidepressants had been widely used in clinical practice to treat bipolar depression, even as initial treatment. The use of antidepressants did not increase the risk of manic switch when compared to non-antidepressants treatment, whether alone or in combination with mood stabilizers or atypical antipsychotics. Therefore, antidepressants could be used as a safe and effective alternative treatment for bipolar depression and be recommended as first-line treatment.