INTRODUCTION

■ Bipolar disorder type I (BD-I) is characterized by at least one manic episode; major depressive episodes can occur as well, however, they are not necessary for diagnosis of BD-I.

■ The primary goal of this study was to perform a systematic review of the literature on real-world data from observational studies about the treatment of bipolar disorder (BD-I), especially the patterns-of-care, adherence, and clinical outcomes of second-generation atypical antipsychotics (SGA).

■ The secondary objectives were to describe and evaluate the types of observational studies and databases available for BD-I in the US.

METHODOLOGY

■ A systematic review was performed using MEDLINE, EMBASE, the National Health System Economic Evaluation Databases (NHS EED) and the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) database.

■ The search strategy was developed to include all observational studies in US (specified in eligibility criteria) that involved at least one treatment, regardless of type, objective and quality. This strategy was robust enough to address all objective questions (patterns of care, adherence and clinical outcomes).

■ The search was limited to a 10-year period (2006-2016). Inclusion criteria: original research in the US population; patients with BD-I: at least one type of therapy in use; studies of patients of care; studies of adherence to treatment; studies of specific therapies (atypical antipsychotics) evaluating clinical outcomes.

■ Exclusion criteria: sample size lower than 100 patients; safety, quality of life, heterogeneous outcomes; randomized controlled trials, naturalistic studies in which the intervention was determined by the study protocol; psychotherapy, social therapy, nutrition, alternative medicine and ECT (electroconvulsive therapy); studies of specific therapies other than atypical antipsychotics (i.e., studies of lithium or valproate).

■ A total of 53 studies were included (Figure 1). They addressed pattern of care and adherence, and also clinical outcomes.

RESULTS

■ Patterns of care:
  - Research has shown that about 45% of patients with BD received pharmacological treatment in 12-month period, and this proportion seemed to be consistent throughout the last decade.
  - More current data estimated that SGA monotherapy was prescribed for about 45% of patients with BD as the first antipsychotic.
  - Considering all patients currently receiving medication for BD, SGAs are prescribed (as monotherapy or as a component of a polytherapy) for approximately 45% to 50% of that population.

■ Data on mood stabilizers (e.g.: lithium, anticonvulsants) showed that they were prescribed to 10% to 20% of patients with BD during their follow-up.

■ Most patients were treated according to recommendations from clinical practice guidelines. Adherence to guidelines was reported to range from approximately 35% to 85% of patients.

■ Adherence:
  - Medication possession ratio (MPR), defined as the ratio of the number of dose dispensed relative to the dispensing period, was the most commonly used measure of adherence.
  - MPR of 80% was considered as a marker for appropriate adherence to therapy.

■ Although some research reported higher median adherence rates (mean MPR of only 15% to 28% and MPR of 40% to 65% in 10% to 15% of patients receiving SGAs, most studies reported a somewhat lower adherence (from 40% to 47%) to 75% MPR.

■ The mean duration of SGA use ranged from 170 to 290 days over a 12-month observation period, but persistence (defined as the time from starting an index therapy to the date of the last dispensing) to 30-60 days in prescription life (usually) is described as around 100 days.

■ Reasons for nonadherence were diverse, but the most consistent ones were:
  - Young age;
  - Baseline substance use disorder;
  - Higher disease burden, with a greater number of symptoms;
  - Side effects as a cause for frustration;
  - Comorbid anxiety or obsessive-compulsive disorder.

■ Clinical Outcomes:
  - Clinical outcomes were defined as any therapy benefit for the patient directly linked to the disease and not regarding safety, resource use or cost.
  - The main outcomes evaluated addressed hospitalization risk and rate of hospitalization, time to hospitalization and length of hospitalization.

  - A total of 19 studies were included and subdivided in two groups: studies clearly described to obtain the value of a single SGA and studies that evaluated the SGA class (Tables 1 and 2).

DISCUSSION

■ Bipolar disorder (including BD-I) is a chronic condition, and clinical practice guidelines recommended treatments for both acute episodes and as a maintenance therapy for prevention of recurrences. However, only 45% of the patients received treatment.

■ There were several limitations observed in the research addressing patterns of treatment for BD.

■ Most studies described only data about BD-I as a broadly defined condition, with few specifically addressing BD-I.

■ Most studies covered a wide time span, including periods in which some antipsychotics were approved by the FDA, which limited our observation of a reliable assessment of more current medication choices.

■ Moreover, there were no data addressing each treatment phase (i.e., acute episode or maintenance therapy).

■ Finally, there were scarce data on prevalence of long-acting injectable (LAI) antipsychotic prescription and adherence or persistence patterns for these agents.

■ The majority of the available inpatient retrospective claims database and very few chart reviews were detected. Claims analyses bring valuable information but insufficient clinical details that can hinder our understanding of outcome drivers and identification of confounding variables.

■ Most common SGAs had at least one publication, however, for risperidone, there were no published studies.

■ Reasons for these findings could be related to the high success rates of inpatient treatment in BD and higher in SGA group.

■ Higher inpatient success rates are related to the higher risk of AC and PR hospitalization.

■ It is possible that our findings are biased by the use of older therapies, however, we may be not analyzing many of the most current data.

■ The incidence of suicide events was not found.

■ No statistically significant differences were found.

■ Total health care cost: aripiprazole was associated with significantly lower health care resource use than quetiapine.

■ Aripiprazole vs. quetiapine:
  - N=1,127.
  - Aripiprazole used as monotherapy.

■ Quetiapine XR vs. quetiapine IR:
  - N=3,049.
  - Quetiapine XR medication used as monotherapy.

Conclusions:

- Observations from real-world evidence are essential components in economic model development and the decision-making process. This review showed which patterns of care are adopted in clinical practice for the treatment of patients with BD (including those with BD-I) as well as adherence and clinical outcomes studied.

REFERENCES