II. Bipolar Disorder

Frye et al.*1

Retrospective review of outcomes among women with bipolar disorder (BD) and intramural study participants (n = 178).

Adepong et al.*2

Cross-sectional review of 2 regional Nigerian outpatient settings (n = 278).

Adli et al.*3

3-month survey of German outpatient academic centers and specialty software captured a mean of 114.7 days of treatment (n = 480).

Assen et al.*4

Retrospective study of 10 German clinics (n = 10).

Bak et al.*5

BD I or II patients across 10 Korean academic hospitals since 2009 (n = 1,447).

Golding et al.*6

Longitudinal cohort study of discharge of inpatients with bipolar disorder from the Institute of Living (n = 2,712).

Gonzalez-Pinto et al.*7

2-year naturalistic follow-up after index manic episode in Bipolar II (BD II) (n = 1,312).

Pesold et al.*8

2-year naturalistic follow-up after index manic episode in New York state (n = 407).

Goldberg et al.*9

Patterns of lithium, anticonvulsants, antipsychotics, and antidepressants examined from bipolar disorder subjects entering START-BP: Systematic Treatment Enhancement Program for Bipolar Disorder (n = 1,400) in 1999-2000. (n = 6,035).

Levine et al.*10


Post et al.*11

Naturalistic treatment outcomes in the Stanley Bipolar Network.

Weinstock et al.*12

Retrospective chart review from Brown University/Butler Hospital (n = 230).

Quanto et al.*13

2006–2010 outpatient 3-month epidemiologic study (n = 356).

Lyall et al.*14

Prescription data from electronic Scottish Mortality Registry (n = 22,133).

Baldessarini et al.*15

2005 prospective study of adherence from 780 patients with BD I or II, randomly selected prescribing psychiatrists (n = 429).

Baldessarini et al.*16

US national health claims to 2000 from 24 states examining prophylaxis and adherence to lamotrigine (n = 7,100).

Baer et al.*17

Self-reported daily medication analysis over 6 months (n = 68).

Baer et al.*18

Self-reported mood and medication adherence over 48 weeks from 314 patients (n = 12,261).

Bjerkund et al.*19

Cohort study from annual cross-sectional examination of medication use (1995-2012) in The Danish Psychiatric Central Research Database (n = 20,616).

Garver et al.*20

Retrospective claims database (1996-2004) comparing racial differences in prophylaxis (n = 1,113).

Jarcz et al.*21

Chart review of discharges from 3 psychiatric facilities in Poland (n = 127).

Peh and Tay*22

Record of two private outpatient practices in Singapore from 1999 to 2003 (n = 127).

Sachs et al.*23

Cross-sectional assessment of abnormal features and polymorphic activity in consecutive patients with bipolar disorder (n = 89).

Kupfer et al.*24


Fung et al.*25

Secondary analysis of adult bipolar disorder patients from CHICOS (CHICOS II) (n = 1,312).

Adachi et al.*26

Cross-sectional nationwide survey of 176 bipolar patients (n = 42,500) in Japan.

Howland et al.*27

Cross-sectional assessment of depressed inpatients and outpatients across 6 sites within Western Psychiatric Institute and Clinic (n = 69).

Increasing numbers of medications needed to achieve remission over successive years from 1974 to 1996.

92% took 2 medications; any polypharmacy in 21% of affective disorder patients across Europe.

93.4% received at least simple polypharmacy (mean = 3.8 medications). Most (72.5%) had bipolar disorder (BD; mean = 2.4 hospitalizations; 28% died disabled and institutionalized).

75% took 2 medications. Antipsychotics were used in 87%-97% of patients with bipolar disorder or schizophrenia disorder.

In all phases, polypharmacy picked for initial treatment in >80% (most favored was mood stabilizer and antipsychotic). Antipsychotics prescribed in >90% across all treatment scenarios.

Lithium use not associated with complex polypharmacy.

Comparable (nonsignificantly different) rates of improvement with either augmentation; lithium better tolerated than quetiapine.

Among 204 subjects taking ≥3 medications (lithium plus divalproex plus an atypical antipsychotic, risk for treatment switch, discontinuation), evaluation was lower than those taking antipsychotic monotherapy. An earlier analysis*4 showed that hospitalization rates 1 year after an index manic episode were comparable in patients taking lithium and divalproex, but not valproate monotherapy.

Significantly higher relapse rates at 2 years for taking ≥3 medications (41.9%) or mood stabilizers (43.8%) than those taking 1 mood stabilizer (22.4%).

No differences observed in monotherapy or simple complex polypharmacy regimens (lamotrigine, mood stabilizer; medication, marital status, clinical outcomes not reported).

A mean of 2.08 medications was needed over 18 months to achieve remission for at least 6 months; respondents took fewer antidepressants or antipsychotics than nonresponders.

Risk of complex polypharmacy increased if subjects had ever taken an atypical antipsychotic, more severe depressive episode, attempted suicide, and had an annual income of 575,000 or more.

Complex polypharmacy rates changed minimally from 2009 (5%) to 2016 (7%).

Complex polypharmacy patients took an antidepressant. No pattern found between stable drug combinations.

No significant association between adherence and daily number of medications reported, presence of side effects, or switching or concomitant medications than non-taking individuals.

No differences were found in the rare characteristics of polypharmacy.

Complex polypharmacy increased significantly from 1997 (15.5%) to 2012 (20.9%) except in patients over age 70 years. The proportion receiving lithium, lamotrigine, and valproic acid increased from 25.5% in 1997 to 12.1% in 2012, and monotherapy decreased from 47.7% to 23.9%.

Complex polypharmacy rates were higher than expected.

In 46% of patients, mood stabilizers, antidepressants, and antipsychotics were prescribed in a discordant diagnosis >2 years.

More Black individuals received 2 medications from different classes (11.1% vs. 5.5%). Simple polypharmacy is the most common simple polypharmacy (46.4%) in this population, while age and duration of illness, and global improvement

More than a third took complex polypharmacy; half had attempted suicide.

Complex polypharmacy found in 48% and associated with noncompliance but not treatment side effects.

16% of complex polypharmacy patients achieved remission. Remission was less likely in polypharmacy, comorbid social or generalized anxiety disorder, or BD II vs Ix diagnoses.

Patients took a mean of 3.5 ± 0.8 medications. Number of drugs was associated with no difference in adherence, psychiatric symptoms, psychiatric hospitalizations, and duration of illness.

Polypharmacy more common among patients with psychiatric; antipsychotic use

II. Bipolar Depression

Grell et al.*28

Observational cross-sectional prescription data from European psychiatric hospitals in inpatients from 1994 to 2002 (n = 2,231).

81.3% received antipsychotics (73.8% as monotherapy), 57.9% anticonvulsants, 51.1% antipsychotics, 57.9% tricyclic antidepressants, and 39.2% selective serotonin reuptake inhibitors (SSRIs). Use was decreasing with lithium and increased for antipsychotics, anticonvulsants, and tranquilizers; was found for antidepressants; and increased for quetiapine, lamotrigine, and valproate.