Bipolar Disorder in Late Life

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Disclosures

We have no disclosures to be made.

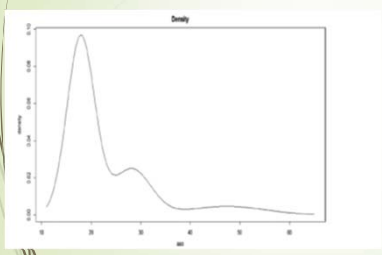
Who is in the audience?

International Society for Bipolar Disorders Task Force Definition of OABD

Older-Age Bipolar Disorder (OABD) = patients ≥50 years

- A report on older-age bipolar disorder from the International Society for Bipolar Disorders Task Force First published: 19 September 2015 https://doi.org/10.1111/bdi.12331

Age of onset of bipolar disorder



Onset over age 50 is about 5 – 10% of individuals with bipolar disorder.

Behdin et al. 2016

Age at diagnosis – is it the same disorder?

Early Onset BD

New onset mania <50 years

Family history of affective disorder is common

Late Onset BD

New-onset mania >50 years

Often associated with vascular changes or other brain pathology

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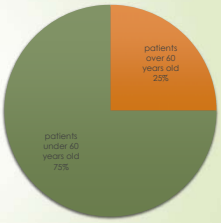
As the population ages . . .

The percent of bipolar patients who are over age 60 grows

- Currently about 25% of patients with bipolar disorder are > 60 years old. By 2030 this will be 50%.



Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62(6):593–602
Sajatovic M, Gyulai L, Calabrese JR, et al. Maintenance treatment outcomes in older patients with bipolar I disorder. Am J Geriatr Psychiatry 2005;13(6): 505–11.
A comprehensive nationwide study of the incidence rate and lifetime risk for treated mental disorders. JAMA Psychiatry. 2014 May;71(5):573-81.

Some more numbers…

In psychiatric outpatients, prevalence of late-life mania is 0.6 %
In psychiatric inpatients units it is 6% .

Patients with bipolar disorder tend to die young.
Most cases of OABD (70-95%) represent cases with onset age <50

Men with bipolar disorder die younger.
Geriatric bipolar patients are predominantly female, 69% women.
Younger bipolar adults; ratio of females to males was approximately 1:1.

The epidemiology of psychiatric disorders in Quebec's older adult population. Can J Psychiatry. 2008;53(12):822.
The prevalence of late-life mania: a review. Bipolar Disord. 2014;16(2):113. Epub 2013 Aug 6.
Cross-national associations between gender and mental disorders in the World Health Organization World Mental Health Surveys. Arch Gen Psychiatry. 2009;66(7):785.
Bipolar disorder in the elderly: different effects of age and of age of onset. J Affect Disord. 2009;114(3):176.
Diagnosis and management of bipolar disorder with comorbid anxiety in the elderly. J Clin Psychiatry. 2006;67 Suppl 1:21

Bipolar disorder is characterized by episodes of

- Major depression
- Mania
- Hypomania

Manic Episode DSM-5 Diagnostic Criteria

For a diagnosis of bipolar I disorder, it is necessary to meet the following criteria for a manic episode. The manic episode may have been preceded by and may be followed by hypomanic or major depressive episodes.

Manic Episode

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).

B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

- **Inflated self-esteem or grandiosity.**
- **Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).**
- **More talkative than usual or pressure to keep talking.**
- **Flight of ideas or subjective experience that thoughts are racing.**
- **Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.**
- **Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity).**
- **Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).**

C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

D. The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition.

Note: A full manic episode that emerges during antidepressant treatment (e.g., medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode and, therefore, a bipolar I diagnosis.

Note: Criteria A–D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

Hypomania – DSM-5 Diagnostic Criteria

Hypomanic Episode

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.

B. During the period of mood disturbance and increased energy and activity, three (or more) of the following symptoms (four if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree:

- Inflated self-esteem or grandiosity.
- Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
- More talkative than usual or pressure to keep talking.
- Flight of ideas or subjective experience that thoughts are racing.
- Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
- Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
- Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.

F. Effective August 2015The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition .The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition.

Note: A full hypomanic episode that emerges during antidepressant treatment (e.g., medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess, or agitation following antidepressant use) are not taken as sufficient for diagnosis of a hypomanic episode, nor necessarily indicative of a bipolar diathesis.

Note: Criteria A–F constitute a hypomanic episode. Hypomanic episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Major Depressive Episode – DSM 5 Diagnostic Criteria.

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, or hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
- Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
- Insomnia or hypersomnia nearly every day.
- Psychomotor agitation or retardation nearly every day (observable by others; not merely subjective feelings of restlessness or being slowed down).
- Fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
- Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

Note: Do not include symptoms that are clearly attributable to another medical condition.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or another medical condition.

Note: Criteria A–C constitute a major depressive episode. Major depressive episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Is it bipolar disorder?

Bipolar I Disorder

Bipolar II Disorder

The prevalence of misdiagnosis is high (48%-61%) in bipolar disorder. Misclassification decreases with age, but is still substantial.

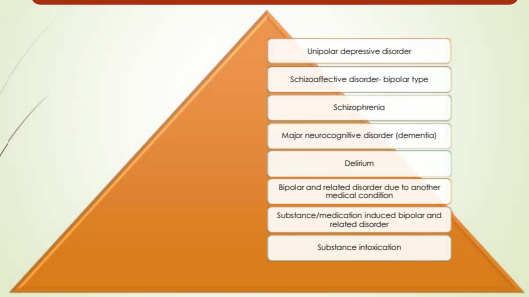
Bipolar Disorders, Volume: 17, Issue: 7, Pages: 689-704, First published: 19 September 2015, DOI: (10.1111/bdi.12331)

What does mania look like in Old Age Bipolar Disorder (OABD)?

- Hyperactivity
- Aggression
- Insomnia
- Cognitive impairment is **more** common
- Comorbid general medical illnesses **more** common
- Hypersexuality **less** common
- Comorbid anxiety and substance use disorders **less** common

Geriatric bipolar disorder. Psychiatr Clin North Am. 2011;34(2):319.
Comorbidity in bipolar disorder among the elderly: results from an epidemiological community sample. Am J Psychiatry. 2006;163(2):319.
Learning and memory in bipolar and unipolar major depression: effects of aging. Neuropsychiatry Neuropsychol Behav Neurol. 2000;13(4):246.

Differential Diagnosis of OABD



Medical causes of mania

Neurologic
- Dementia
- Head injury
- CNS tumor
- Multiple sclerosis
- Stroke
- Epilepsy
- Wilson's disease

Infectious
- HIV
- Syphilis
- Lyme disease
- Viral encephalitis

Sleep Apnea

Toxic
- Medications
  - Corticosteroids
  - Amphetamines
  - Other sympathomimetics
  - L-DOPA
- Other substances

Endocrine
- Hypo- or hyperthyroidism
- Hypercortisolemia

Vitamin B12 Deficiency

Cognitive dysfunction in OABD

Cognitive Dysfunction found in > 30% of people with OABD.

Does BD cause neuroprogression /dementia? **CONTROVERSIAL**

Cognitive outcomes are worse in late onset than in early onset bipolar disorder.

Some neurodegenerative diseases (like Frontal-Temporal Dementia) have clinical overlap with OABD, leading to misdiagnosis.

What to do?
1) Protect from CV risk factors.
2) Avoid medications that worsen cognition (e.g. benzodiazepines and anticholinergic drugs).

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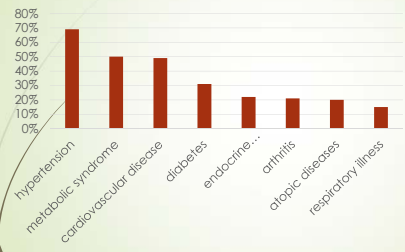
Medical comorbidities in OABD



Death occurs an average of 10 years earlier in bipolar patients than in the general population.

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Cerebrovascular risk in OABD

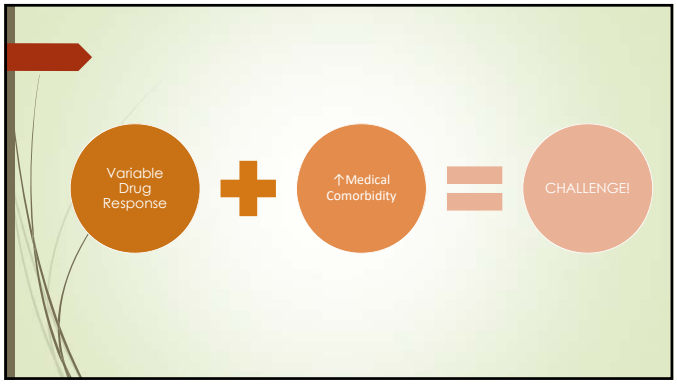
Silent cerebral infarctions
- present in over ½ of patients with OABD

Risk Factors
- Smoking
- Obesity
- Lack of Exercise

Treatment of OABD

Drug response in bipolar disorder is variable
- Not everyone responds in the same way to the same drug
- (What works for one person might not work for another)

Medical comorbidity can limit the treatment options for OABD because of
- Drug tolerability
- Drug-drug interactions
- Drug-disease interactions
- Altered metabolism



FDA approved medication for Management of Acute Mania and Hypomania

First line- Lithium, Valproate, Olanzapine, Quetiapine

Lithium compared with divalproex; the results indicate that the benefit of each drug is substantive and generally comparable. *GEBS-Ba: A Randomized Double-Blind Controlled Trial of Lithium and Divalproex in the Treatment of Mania in Older Patients With Bipolar Disorder.*

Points to remember which one to choose from

- past response to medications
- psychotic symptoms
- side effect profiles
- comorbid general medical conditions
- potential for drug-drug interactions
- patient preference, and cost

50-80% of older adults with mania will respond to a first-line treatment

Lithium

Start low and go slow in OABD

Baseline monitoring- CBC, CMP, TSH, EKG

Starting dose 150 mg. One to two times daily

- Increase as tolerated every 1-5days. Half life longer in older patients
- Rarely 900mg daily will be required.

Target dose is determined by 12-hour serum trough levels that should be drawn five to seven days after each dose increase.

Serum concentrations, from the International Society for Bipolar Disorders consensus practice guidelines for maintenance treatment in geriatric bipolar disorder and are based upon age :

- Patients 60 to 79 years old – 0.4 to 0.8 mEq/L (0.4 to 0.8 mmol/L)
- Patients 80 years and older – 0.4 to 0.7 mEq/L (0.4 to 0.7 mmol/L)

Lithium(Doesn't bind to proteins, Excreted in Kidneys, not metabolized)

Effective for

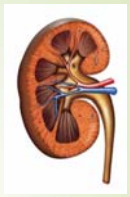
Bipolar Mania
Bipolar Depression
Bipolar Maintenance Treatment

Risks/Side effects

- Nausea/vomiting
- Sedation
- Weight gain
- Tremor
- Hypothyroidism (15%female and 4% male)
- Nephrogenic Diabetes insipidus- Polyuria and Polydipsia – Ultimate renal failure if not treated.
- Bradycardia, AV block – check EKG before starting
- Neurological- Confusion, ataxia, Stupor, Coma and even death in case of toxicity

Lithium and renal risk in OABD

- Co-prescription with
  - ACE inhibitors
  - Ca Channel Blockers
  - Diuretics- HCTZ, Loop
  - NSAIDs
- Co-morbid
  - Diabetes
  - Hypertension
  - Age related renal decline



Inadequate lithium monitoring → Increasing lithium levels → Worsening renal function

Anti-epileptic drugs for OABD

For acute mania	For bipolar maintenance treatment	For bipolar depression
• Carbamazepine • Valproate • (Gabapentin)	• Lamotrigine(Avoid using with valproate) • Valproate	• Lamotrigine (Off label use)

Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. Lancet. 2016 Apr 9;387(10027):1561-72

Valproate - 1

Start low and go slow in OABD

- Start at 125 to 500mg/day and increase slowly every one to five days.
- With 24-hour extended-release preparations, Blood levels checks after 18-24hrs later, prior to next dose. Bioavailability is 30% less with ER formulations.
- Serum level of 65 to 100 mcg/mL recommended (mean serum concentration 74 mcg/mL per GERI-BD), although some elderly patients will not tolerate the higher ranges.
- The half-life and free-plasma fraction of valproate may increase with age.

Target dose- 500 to 1500 mg/ day. (Mean dose 1200mg/day per GERI-BD)

Elderly patients may tolerate Depakote over Depakote ER due to less cognitive and renal side effects.

Valproate - 2

Baseline monitoring- CBC (White count and Platelets), BMP, LFTs, Lipase(If suspected acute abdominal pain) and wt.

Common side effects in older geriatric bipolar

- gastrointestinal distress,
- sedation,
- weight gain and hand tremor

Other Side Effects to know-

- Neutropenia,
- Thrombocytopenia,
- Pancreatitis,
- PCOS- Polycystic Ovarian syndrome ,
- Elevated LFTs- liver failure if untreated
- hair loss and
- Neural Tube Defect in Pregnancy(Less likely with Elderly)

Valproate in OABD (3)

Drug-drug interactions

- *Aspirin*
- *Warfarin*
- *Digitoxin*
- *Phenytoin*
- *Lamotrigine – valproate decreases clearance*

Ammonia levels can become elevated, even with normal valproate levels.

Atypical antipsychotics

For acute mania	For bipolar maintenance treatment	For bipolar depression
• Olanzapine • Quetiapine • Aripiprazole • Risperidone • Ziprasidone • Asenapine • Cariprazine (FDA approved for mixed episodes as well) • (Clozapine – not FDA approved)	• Aripiprazole • Olanzapine • Risperidone • Quetiapine • Ziprasidone	• Olanzapine + fluoxetine • Quetiapine • Lurasidone • Cariprazine

Atypical antipsychotic challenges in OABD

Many carry ↑ risk for metabolic syndrome.

Some carry risk of extrapyramidal or Parkinson-like effects.

Check EKG prior to starting

Comparative Efficacy between various agents.

lithium may be less effective than olanzapine or risperidone for reducing acute mania in patients with bipolar disorder- Cochrane Database Syst Rev. 2019 Jun 1;6:CD004048

lithium might be more effective than lamotrigine and appears similar to carbamazepine and valproate for improving acute mania in patients with bipolar disorder- Cochrane Database Syst Rev. 2017 Jun 1;6:CD004049

valproate appears to have efficacy similar to lithium and olanzapine for improving acute manic episodes in adults with bipolar disorder- Cochrane Database Syst Rev 2019 Oct 7;10:CD004052

oxcarbazepine and valproate may be similarly effective for patients with bipolar disorder- Cochrane Database Syst Rev 2011 Dec 7;(12):CD004857

second-generation antipsychotics may be more effective than mood stabilizers for acute mania- J Affect Disord 2011 Nov;134(1-3):14

aripiprazole may not be more effective than haloperidol or lithium for patients with acute manic or mixed episodes- Cochrane Database Syst Rev 2015 Dec 17;(12):CD005000

quetiapine and lithium appear similarly effective for improving symptoms, but quetiapine may have greater adverse effects in patients with bipolar I or II disorder- J Clin Psychiatry 2016 Jan;77(1):90

antipsychotics such as haloperidol, risperidone, or olanzapine may be more effective than mood stabilizers and anticonvulsants in patients with acute mania- Acta Psychiatr Scand. 2017 Oct;136(4):324

Combination Antipsychotic and Mood Stabilizer

combination of mood stabilizer (lithium or valproate) and second-generation antipsychotic (more evidence for younger patients)

- considered an alternative first-line option to monotherapy with either mood stabilizer or an antipsychotic by Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 recommendations
- may have faster onset of response than monotherapy- Lancet. 2016 Apr 9;387(10027):1561-72,
- may be more effective in reducing symptoms than single agent alone- Am Fam Physician. 2012 Mar 1;85(5):483-93full-text
- may increase adverse effects (Expert Opin Drug Saf 2015 Aug;14(8):1181)
- Can be used for patients with mania who are not adequately improving on lithium or valproate alone. Aust N Z J Psychiatry 2015 Dec;49(12):1215

Some Studies with information on combination use.

- ziprasidone to lithium or divalproex may not be associated with improved response in patients with acute mania- Randomized trial: J Clin Psychiatry 2012 Nov;73(11):1412
- addition of aripiprazole to lithium or valproate may improve mania symptoms- Randomized trial: Am J Psychiatry 2008 Oct;165(10):1316
- Addition **of olanzapine to lithium or valproate** may improve symptoms at 6 weeks in manic patients not adequately improving on lithium or valproate alone. Randomized trial: Arch Gen Psychiatry 2006 Jan;63(1):57
- Either risperidone or haloperidol may improve short-term response in acute mania when added to mood stabilizer (lithium or valproate). Randomized trial: Am J Psychiatry 2009 Jul;166(7):766
- olanzapine plus divalproex appears more effective than divalproex alone for reduction of manic and depressive symptoms in patients with bipolar I disorder with mixed episodes. Randomized Trial: J Clin Psychiatry 2009 Nov;70(11):1540

Electroconvulsive Therapy (ECT)

Can be an excellent option for OABD

https://youtu.be/-T0mwzXHgvI (can stop at 1:12min.)

Psychosocial interventions

Helping Older People Experience Success (HOPES)	Skills training and health management training	Improved social skills community functioning self-efficacy leisure recreation
Medication adherence skills training (MAST-BD)	Improved medication adherence depression quality of life indices	

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Take home points

National Institute for Health and Care Excellence (NICE) 2020 recommendations for use of psychotropic medication in patients ≥ 65 years old, consider

- lower doses of medications
- increased risk of drug interactions
- Assessing and managing comorbidities
- increased risk of detriment to cognitive function and mobility with anticholinergic medication or drugs with anticholinergic mechanisms

Patients > 60 years old may be more likely to have rapid cycling, fewer suicide attempts, and less manic and psychotic symptoms

Remember: antipsychotics are associated with increased risk of stroke, and greater rate of cognitive decline and mortality in patients with dementia

Caution while using antipsychotics due to risk of exacerbating or causing SIAD or Hyponatremia

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Any questions?

THANK YOU