

Bipolar disorder is less common in the older adult population. However, the quality of life for older adults with bipolar disorder is significantly impacted. Older patients with bipolar disorder have more cognitive and functional impairment than younger patients. Studies show that older adults with bipolar disorder also have an increased risk of suicide, dementia, and medical illness, as well as a higher mortality rate. This article provides a review of the epidemiology, clinical features, suicide risk, comorbidities (including dementia), and management of bipolar disorder in older adults.

Key words: bipolar disorder, mania, bipolar depression, treatment

Diagnosis and Management of Bipolar Disorder in Older Adults

Patricia Hall, MD, Department of Psychiatry, University of Western Ontario, London, ON.

Verinder Sharma, MB, BS, FRCPC, Professor, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON.

Introduction

The prevalence of bipolar disorder in the general population is approximately 1.0%.¹ Bipolar disorder becomes less common with age, with a prevalence of 0.1–0.5% in adults 65 and older.² Bipolar disorder in the older adult accounts for 8–10% of all late-life psychiatric admissions.² The Epidemiologic Catchment Area (ECA) study reported the mean age of onset for bipolar disorder as 21 years.³ It is reported that 10% of bipolar disorder patients develop the disorder after the age of 50.⁴ This late onset of symptoms is more likely to occur in female patients.⁵ Goodwin *et al.* found two peak periods of onset of mania in women—one in early adult life and a second around the time of menopause.⁶ Some researchers have demonstrated that men show an increase in mania in the eighth and ninth decade of life.⁷

Neurotransmitter dysfunction and neuroradiologic changes have been associated with bipolar disorder in the general population.⁸ Patients with late-onset bipolar disorder have fewer relatives with the illness when compared to bipolar disorder that occurs earlier in life.⁹ Late-onset bipolar disorder may be influenced by both genetic and environmental factors.⁷ One environmental risk factor reported is neurological disease. Several studies have documented that 17–43% of older patients with bipolar disorder have cerebral organic disorders.⁸ Studies have shown that patients with late-onset symptoms tend to have an increase in cerebrovascular risk factors and subtle evidence of cerebrovascular disease on neuroimaging.⁷ Several

researchers have also provided a link between mania and cerebrovascular accidents, particularly of the right hemisphere.⁷ Shulman found that increased vulnerability to brain insults played a stronger role than life events in precipitating late-onset mania.¹⁰ A study by Hays *et al.* suggests that patients who have a younger age of symptom onset have more of a psychosocial component, whereas organic factors are important to symptom onset in later life.⁹

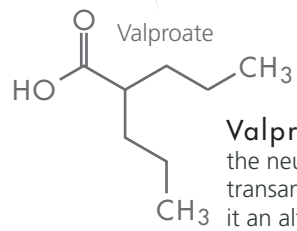
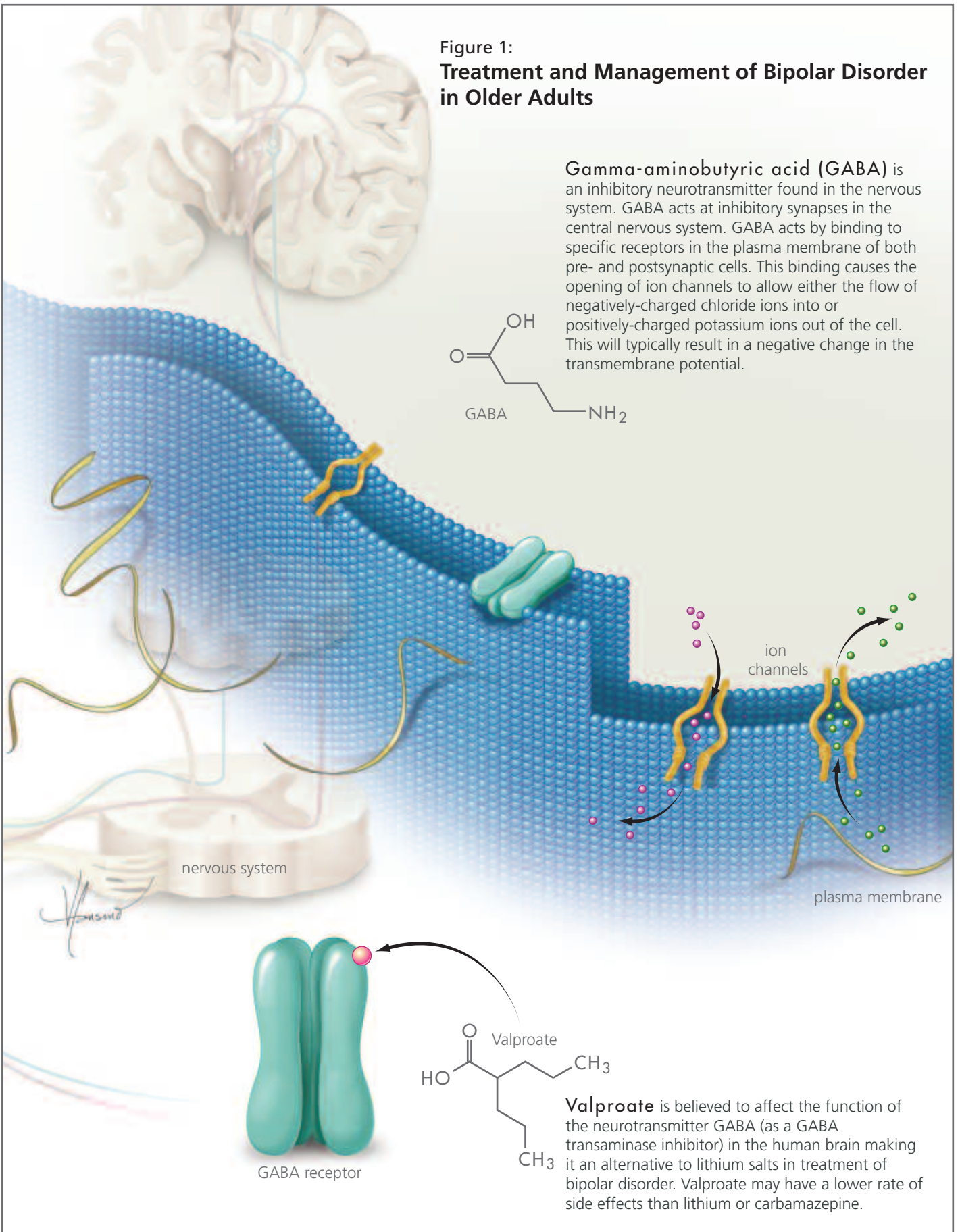
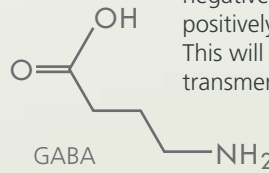
Clinical Features

No single symptom of bipolar disorder is considered characteristic in the older adult.¹⁰ Older age is associated with longer episodes of mania with shorter intervals between manic episodes.¹¹ Older adults with bipolar disorder also require longer hospitalizations¹² and have a poorer response to pharmacotherapy than younger patients with bipolar disorder.^{13,14}

There are many studies focusing on whether late onset of bipolar disorder is a distinct subtype of bipolar disorder. Studies have shown that older adults with late-onset mania are more than twice as likely to have an underlying neurological disorder, most commonly stroke, than older adults who have been diagnosed with bipolar disorder at an early age.¹⁵ In terms of symptoms, studies show that the early onset group have more psychotic features,¹⁴ more mixed episodes,^{14,16} and greater comorbidity with panic disorder.¹⁴ Studies also show older patients present with more functional and cognitive impairment.¹⁷ One study reported that older patients with

Figure 1:
**Treatment and Management of Bipolar Disorder
 in Older Adults**

Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter found in the nervous system. GABA acts at inhibitory synapses in the central nervous system. GABA acts by binding to specific receptors in the plasma membrane of both pre- and postsynaptic cells. This binding causes the opening of ion channels to allow either the flow of negatively-charged chloride ions into or positively-charged potassium ions out of the cell. This will typically result in a negative change in the transmembrane potential.



Valproate is believed to affect the function of the neurotransmitter GABA (as a GABA transaminase inhibitor) in the human brain making it an alternative to lithium salts in treatment of bipolar disorder. Valproate may have a lower rate of side effects than lithium or carbamazepine.

Management of Bipolar Disorder

bipolar disorder present with lower global functioning scores than younger patients.¹⁷ However, there are also reports that there is little difference in the clinical presentation of early-onset versus late-onset groups. Depp found few meaningful differences between early-onset and late-onset groups when comparing psychopathology, cognitive functioning, and medication use.¹⁸

Comorbidity

Neurological illness is found in 23% of older adults with bipolar disorder.² Studies have found that patients with bipolar disorder have a higher prevalence of neurological illness (36%) compared to age- and sex-matched cases of depression (8%).¹⁹ Other medical comorbidities, such as diabetes, are also common.² Bipolar disorder is associated with several risk factors—among which are obesity, smoking, unhealthy diet, and poor utilization of primary health care²⁰—that contribute to medical problems. Anxiety disorders and personality disorders are frequent comorbidities in the general bipolar population.¹² Unfortunately, there are no data examining the rate of these disorders in the older adult with bipolar disorder. The Epidemiological Catchment Area (ECA) study reports alcohol abuse or dependence in 46% of all patients with bipolar disorder compared to 13% in the general

Table 1: Differential Diagnosis of Manic Symptoms in the Older Adult

Delirium
Agitated depression
Agitated dementia
Bipolar disorder
Mania due to a general medical condition
Substance-induced mania
Late onset delusional disorder
Schizoaffective disorder
Schizophrenia

Source: Adapted from McDonald, 2000⁷ and Brooks, 2005.¹⁵

population.^{21,22} However, older patients with bipolar disorder are less likely to have comorbid substance abuse, which occurs at a rate of 20–30%.^{17,23,24}

Dementia

The Canadian Study for Health and Aging Working Group reported that the prevalence of dementia in Canada was 8% of Canadians aged 65 and over. The female-to-male ratio in the study was 2:1.²⁵ Dementia is an important cause of hospital admissions, disability, and death.²⁶ Some studies suggest that patients with depressive or bipolar disorder may be at increased risk for developing dementia.²⁷ It remains unclear whether patients with late-onset mania are at greater risk for the development of dementia than older patients with early onset.¹⁰ Kessing and Anderson did a case register study and found that the rate of diagnosis of dementia was significantly related to the number of previous affective episodes. On average, the rate tended to increase by 6% with every episode leading to a hospital admission with bipolar disorder and by 13% for depressive episodes when adjusted for differences in age and sex.²⁷ Another study reported that patients with bipolar disorder seem to have an increased risk of developing dementia compared to patients with osteoarthritis or diabetes.²⁸ Studies have reported that bipolar disorder may also be secondary to dementia.^{29,30} Patients with dementia have an increased risk of being admitted to hospital for a depressive or manic episode.³⁰

Suicide Risk

Statistics Canada reports that in 1998, suicide was the cause of death for 3,699 (12.2 per 100,000) Canadians. Out of those 3,699 deaths, 457 were aged 65 and over. In those who are 70 years old or older, men are hospitalized for suicide attempts at a greater rate than women. The mortality rate from suicide increases in both men and women over the age of 80.¹² The majority of older adults who commit suicide have a mental illness.³¹ The most common precipitants for suicide in the older adult are physical illness and loss.³²

Suicide in the older adult is also associated with social isolation and alcohol abuse.³³

Another study compared multiple medical and psychiatric diagnoses and the risk of suicide in older adults over age 66. The study reported that bipolar disorder had the highest risk for suicide out of the illnesses that were reviewed.³⁴ Results from a long-term survey indicate that the highest risk occurs in the first 7–12 years

Table 2: Assessment of Manic Symptoms in the Older Adult

Thorough psychiatric history
Thorough medical history
Physical exam including neurological check-up
Rule out neurological insults
Rule out endocrine abnormalities
Rule out drugs that can cause secondary mania
Laboratory testing should include
Complete blood count
Creatinine and urea
Electrolytes including calcium and magnesium
Liver function tests
Thyroid panel
Venereal Disease Research Laboratory screening
Vitamin B12 and folate
Urinalysis
Toxicology screen
Electrocardiogram
Serum level of medication if clinically indicated
Neuroimaging if clinically indicated
Lumbar puncture if clinically indicated

Source: Adapted from McDonald, 2000⁷ and Khouzam, 1994.³⁷

Table 3: Selected Drugs Used to Treat Bipolar Disorder: Dosages, Side Effects, and Recommendations

Drug	Dosage	Common Side Effects	Recommended Use
Lithium	Average healthy adult: 900–1,200 mg/d	Weight gain, tremor, loss of coordination, hypothyroidism, alopecia, acne, psoriasis, nausea, loose stools, nephrogenic effects including polyuria, polydipsia Less Common: ankle edema, electrocardiogram changes, including: sinus node dysfunction, sinoatrial block, bundle branch block, ventricular arrhythmia	First-line treatment of acute bipolar mania First-line treatment of acute bipolar depression First-line maintenance therapy
Anticonvulsants			
Divalproex	200–2,500 mg/d	Tremors, weight gain, sedation, reduction in platelets, reduction in white cell count, nausea, vomiting, alopecia Rare: hepatotoxicity, pancreatitis	First-line treatment of acute bipolar mania First-line treatment of acute bipolar depression (in combination with lithium or an SSRI or bupropion) First-line maintenance therapy
Carbamazepine	200–1,200 mg/d	Dizziness, sedation, ataxia, diplopia, nystagmus, mild rash Rare: Stevens-Johnson syndrome, agranulocytosis, aplastic anemia, thrombocytopenia, lowered plasma levels of other drugs including anticonvulsants, antipsychotics, antidepressants and oral contraceptives	Second-line treatment of acute bipolar mania Third-line treatment of acute bipolar depression Second-line maintenance therapy
Lamotrigine	50–400 mg/d	Headache, ataxia, dizziness, tremors, nausea, somnolence, diplopia, blurred vision, benign rash Less Common: serious rash (0.1%)	First-line treatment of acute bipolar depression First-line maintenance therapy
Atypical Antipsychotics			
Olanzapine	10–30 mg/d	Sedation, dizziness, weight gain, diabetes mellitus, hyperlipidemia, orthostatic hypotension, constipation Less Common: elevated liver transaminases, extrapyramidal side effects	First-line treatment of acute bipolar mania—may use alone or in combination with lithium or divalproex First-line treatment of acute bipolar depression when combined with an SSRI First-line maintenance therapy

Table 3 continued: Selected Drugs Used to Treat Bipolar Disorder: Dosages, Side Effects, and Recommendations

Drug	Dosage	Common Side Effects	Recommended Use
Risperidone	2–6 mg/d	Sedation, anxiety, insomnia, nausea, constipation, mild weight gain, decreased libido, erectile dysfunction, galactorrhea Less common: Prolonged corrected QT interval, Extrapyramidal side effects	First-line treatment of acute bipolar mania—may use alone or in combination with lithium or divalproex Second-line maintenance therapy when combined with lithium or divalproex
Quetiapine	50–500mg/d (some patients require higher doses up to 800mg/d)	Sedation, Tachycardia, Orthostatic hypotension, Weight gain, Dry mouth, Constipation Less common: Extrapyramidal side effects	First-line treatment of acute bipolar mania—may use alone or in combination with lithium or divalproex Second-line therapy for acute bipolar depression—may use alone or in combination with an SSRI Second-line maintenance therapy when combined with lithium or divalproex

Abbreviations: SSRI = Selective Serotonin Reuptake Inhibitor

Source: Adapted from Yatham, 2005;²⁹ Moore, 2004;⁵² Singh, 2005;⁵³ and Sajatovic, 2001.⁵⁴

of bipolar disorder onset and in those under age 35.³⁵ A study by Ahrens *et al.* reported that in patients with bipolar disorder, the suicide risk remains steady and does not decline as a patient ages.³⁶

Issues in Assessment and Treatment

Principles for the differential diagnosis of older patients with mania are described in Tables 1 and 2. General principles for treating bipolar disorder in the older adult are similar to those for younger adults.^{29,38}

Pharmacological Treatment

Therefore, the older adult usually requires lower doses of medications (Table 3).

Aging is associated with physiological changes that decrease the rate of renal clearance of medications and the volume of distribution.³⁹ Common medical comorbidities like heart failure, as well as commonly used medications in the older adult, can also alter metabolism and excretion.¹¹ Older patients usually require

lithium doses 45–50% lower than younger patients.⁴⁰ Older adults may be at a higher risk of developing cognitive and neurological side effects on lithium than younger patients.⁸ However, lithium is generally well tolerated and, with proper precautions and monitoring, it can be safely administered to older adults with bipolar disorder.⁴¹ Valproate may have a lower rate of side effects than lithium or carbamazepine.⁴² Some antidepressants and antipsychotics cause orthostatic hypotension, increasing the risk of falls in the older adult.⁴³ Older patients are more at risk of developing extrapyramidal side effects (EPS) with antipsychotics than younger patients; however, the atypical antipsychotics have a lower rate of EPS than traditional antipsychotics.⁴⁴ There is one retrospective study that reports that when high doses of atypical antipsychotics are used, the risk of developing parkinsonian side effects are similar to the risk of the typical antipsychotics.⁴⁵ Some antipsychotic agents also have increased anticholinergic side effects and may cause cognitive impairment.^{46,47} The FDA

recently issued a black box warning on the increased risk of mortality with atypical antipsychotics in the treatment of older patients with dementia (FDA, April 11, 2005). However, there are no reports of increased risk of mortality when atypical antipsychotics are used in older patients with bipolar disorder.

Studies have shown that both lithium and valproate are effective antimanic drugs in the older adult.²⁹ Valproate should be considered in mixed mania, rapid-cycling mania, and secondary mania as well as in patients unresponsive to lithium.⁸ There are no controlled trials of atypical antipsychotic drugs, but preliminary reports on the use of clozapine, risperidone, olanzapine, and quetiapine suggest that there is a positive response to these agents in older adults with bipolar disorder.⁴⁸

For bipolar depression, a small open trial demonstrated that lamotrigine was effective as an add-on to lithium or valproate.⁴⁹ Antidepressant monotherapy is generally not recommended due to the risk of induction of

Table 4: Key Characteristics of Bipolar Disorder Among Older Adults

Bipolar disorder becomes less prevalent with age.
Patients with late-onset bipolar disorder are more likely to be female.
Later average age of illness onset corresponds with lower rate of family members with the illness.
Older age is associated with longer episodes of mania with shorter intervals between manic episodes, medical illness, neurological insults, and longer hospitalization time.
There is ongoing debate about whether late-onset bipolar disorder should be considered a different subtype of bipolar illness.
Older bipolar patients have more cognitive and functional impairment, and less substance abuse, than younger patients.
Some studies have shown bipolar patients have an increased risk of developing dementia. Both dementia and secondary mania must be ruled out.
Bipolar disorder increases the risk of suicide in older adults.
Physiological changes in the older patient alter pharmacokinetics.
There are reports of the effectiveness of lithium, divalproex, lamotrigine, and atypical antipsychotics in treating bipolar disorder in older adults.

mania or rapid cycling.⁵⁰ There is a paucity of data on maintenance treatment of bipolar disorder, but a randomized controlled trial showed that both lithium and lamotrigine were effective.⁵¹

Although pharmacotherapy is essential in the treatment of bipolar disorder, there is an important role for psychotherapy and psychoeducation. Common issues in the older adult include loss of societal status and employment, physical illness, and the loss of interpersonal relationships and bereavement.⁴ Sajatovic reported that the psychotherapies that have shown some benefit for older adults include cognitive behavioural therapy, group therapy, and family therapy.⁴

Conclusion

Bipolar disorder significantly impacts the quality of life for older adults with the illness. Older adults with bipolar disorder have an increased risk of suicide, dementia, medical illness, and a higher mortality rate. More research is needed in all areas reviewed in order to enhance health services to this population.



No competing financial interests declared

References

- Tohen M, Angst J. Epidemiology of bipolar disorder. In: Tsuang MT, Tohen M, editors. *Psychiatric epidemiology*. New York: Wiley Liss, 2002: 427–44.
- Depp CA, Jeste DV. Bipolar disorder in older adults: a critical review. *Bipolar Disord* 2004;6:343–67.
- Hirschfeld RMA, Williams JBW, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the mood disorder questionnaire. *Am J Psychiatry* 2000;157:1873–5.
- Sajatovic M. Treatment of bipolar disorder in older adults. *Int J Psychiatry* 2002;17:865–73.
- Sajatovic M, Bingham CR, Campbell EA, et al. Bipolar disorder in older adult inpatients. *J Nerv Ment Dis* 2005;193:417–9.
- Goodwin FK, Jamison KR, Post RM, et al, editors. *The natural course of manic-depressive illness: neurobiology of mood disorders*. Baltimore, MD: Williams & Wilkins, 1984.
- McDonald WM. Epidemiology, etiology, and treatment of geriatric mania. *J Clin Psychiatry* 2000;61(13 Suppl):3S–11S.
- VanGerpen MW, Johnson JE, Winstead DK. Mania in the geriatric population: a review of the literature. *Am J Geriatr Psychiatry* 1999;7:188–202.
- Hays JC, Krishnan KR, George LK, et al. Age of first onset of bipolar disorder: demographic, family history and psychosocial correlates.

- Depress Anxiety 1998;7:76–82.
- Alexopoulos GS. Late-life mood disorders. In: Sadavoy J, Jarvik LF, Grossberg GT, et al, editors. *Comprehensive textbook of geriatric psychiatry*. New York, NY: W.W. Norton & Company, 2004: 609–54.
- Young RC, Klerman GL. Mania in late life: focus on age at onset. *Am J Psychiatry* 1992;149:867–76.
- Health Canada. *A report on mental illnesses in Canada*. Ottawa, ON: Health Canada, 2002.
- Kenig HG, Blazer DG. Mood disorders. In: Blazer DG, Steffens DC, Busse EW, editors. *The American psychiatric publishing textbook of geriatric psychiatry*, 3rd ed. Arlington, TX: American Psychiatric Publishing, Inc., 2004: 241–68.
- Schurhoff F, Bellivier F, Jouvent R, et al. Early and late onset bipolar disorders: two different forms of manic depressive illness? *J Affect Disord* 2000;58:215–21.
- Brooks JO, Hoblyn JC. Secondary mania in older adults. *Am J Psychiatry* 2005;162:2033–8.
- Almeida OP, Fenner S. Bipolar disorder: similarities and differences between patients with illness onset before and after 65 years of age. *Int Psychogeriatr* 2002;14:311–22.
- Depp CA, Lindamer LA, Folsom DP, et al. Differences in clinical features and mental health service use in bipolar disorder across the life span. *Am J Geriatr Psychiatry* 2005;13:290–8.
- Depp C, Jin H, Mohamed S, et al. Bipolar disorder in middle aged and elderly adults: is age of onset important? *J Nerv Ment Dis* 2004;192:796–9.
- Shulman KI, Tohen M, Satlin A, et al. Mania compared with unipolar depression in old age. *Am J Psychiatry* 1992;142:341–5.
- McIntyre RS, Konarski JZ, Misener VL, et al. Bipolar disorder and diabetes mellitus: epidemiology, etiology, and treatment implications. *Ann Clin Psychiatry* 2005;17:83–93.
- Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiological Catchment Area (ECA) Study. *JAMA* 1990;264:2511–18.
- Regier DA, Boyd JH, Burke JD, Jr, et al. One-month prevalence of mental disorders in the United States: based on five Epidemiologic Catchment Area sites. *Arch Gen Psychiatry* 1988;45:977–86.
- Kilbourne AM. General-medical conditions in older patients with serious mental illness. *Am J Geriatr Psychiatry* 2005;13:250–4.
- Kessler RC, Rubinow DR, Holes C, et al. The epidemiology of DSM-III-R bipolar I disorder in a general population survey. *Psychol Med* 1997;27:1079–89.
- Canadian Study of Health and Aging Working Group. Canadian study of health and aging: study methods and prevalence of dementia. *Can Med Assoc J* 1994;150:899–913.
- Hill GB, Forbes WF, Lindsay J, et al. Life expectancy and dementia in Canada: the Canadian study of health and aging. *Chronic Diseases in Canada* 1998;18:166–7.
- Kessing LV, Andersen PK. Does the risk of developing dementia increase with the num-

Management of Bipolar Disorder

- ber of episodes in patients with depressive disorder and in patients with bipolar disorder? *J Neurol Neurosurg Psychiatry* 2004;75:1662–6.
28. Kessing LV, Nilsson FM. Increased risk of developing dementia in patients with major affective disorders compared to patients with other medical illnesses. *J Affective Disorders* 2003;73:261–9.
 29. Yatham LN, Kennedy SH, O'Donovan C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: consensus and controversies. *Bipolar Disord* 2005;7(3 Suppl):S5–69.
 30. Nilsson FM, Kessing LV, Sorensen TM, et al. Enduring increased risk of developing depression and mania in patients with dementia. *J Neurol Neurosurg Psychiatry* 2002;73:40–4.
 31. Preville M, Hebert R, Boyer R, et al. Physical health and mental disorder in elderly suicide: a case-control study. *Aging Ment Health* 2005;9:576–84.
 32. Cattell H. Suicide in the elderly. *Adv Psychiatr Treatment* 2000;6:102–8.
 33. O'Connell H, Chin AV, Cunningham C, et al. Recent developments: suicide in older people. *BMJ* 2004;329:895–9.
 34. Juurlink DN, Herrmann N, Szalai JP, et al. Medical illness and the risk of suicide in the elderly. *Arch Intern Med* 2004;164:1179–84.
 35. Tsai SY, Kuo CJ, Chen CC, et al. Risk factors for completed suicide in bipolar disorder. *J Clin Psychiatry* 2002;63:469–76.
 36. Ahrens B, Berghofer A, Wolf T, et al. Suicide attempts, age and duration of illness in recurrent affective disorders. *J Affect Disord* 1995;36:43–9.
 37. Khouzam HR, Emery PE, Reaves B. Secondary mania in late life. *J Am Geriatr Soc* 1994;41:85–7.
 38. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. American Psychiatric Association practice guideline for the treatment of patients with bipolar disorder. *Am J Psychiatry* 2002;159(4 Suppl):S1–50.
 39. Sproule BA, Hardy BG, Shulman KI. Differential pharmacokinetics of lithium in elderly patients. *Drugs Aging* 2000;16:165–77.
 40. Mulsant BH, Pollack BG. Psychopharmacology. In: Blazer DG, Steffens DC, Busse EW, editors. *The American Psychiatric Publishing Textbook of Geriatric Psychiatry*, 3rd ed. Arlington, TX: American Psychiatric Publishing, Inc., 2004: 387–412.
 41. Chacko RC, Marsh BJ, Marmion J, et al. Lithium side effects in elderly bipolar outpatients. *Hillside J Clin Psychiatry* 1987;9:79–88.
 42. Gnam W, Flint AJ. New-onset rapid-cycling bipolar disorder in an 87-year-old woman. *Can J Psychiatry* 1993;38:324–6.
 43. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta analysis, 1: psychotropic drugs. *J Am Geriatr Soc* 1999;47:30–9.
 44. Caligiuri MR, Jeste DV, Lacro JP. Antipsychotic-induced movement disorders in the elderly: epidemiology and treatment recommendations. *Drugs Aging* 2000;17:363–84.
 45. Rochon PA, Stukel TA, Sykora K, et al. Atypical antipsychotics and parkinsonism. *Arch Intern Med* 2005;165:1882–8.
 46. Mirchandani IC, Young RC. Management of mania in the elderly: an update. *Ann Clin Psychiatry* 1993;5:67–77.
 47. McDaniel JS, Johnson KM, Rundell JR. Mania. In: Rundell JR, Wise MG, Editors. *Textbook of consultation-liaison psychiatry*, 1st Ed. Washington, DC: American Psychiatric Press, 1996:347–67.
 48. Sajatovic M, Madhusoodanan S, Coconcea N. Managing bipolar disorder in the elderly: defining the role of the newer agents. *Drugs Aging* 2005;22:39–54.
 49. Robillard M, Conn DK. Lamotrigine use in geriatric patients with bipolar depression. *Can J Psychiatry* 2002;47:767–70.
 50. Bittman BJ, Young RC. Mania in an elderly man treated with bupropion. *Am J Psychiatry* 1991;148:541.
 51. Sajatovic M, Gyulai L, Calabrese JR, et al. Maintenance treatment outcomes in older patients with bipolar I disorder. *Am J Geriatr Psychiatry* 2005;13:305–11.
 52. Moore DP, Jefferson JW. Moore and Jefferson: handbook of medical psychiatry, 2nd ed. Philadelphia, PA: Mosby Inc, 2004.
 53. Singh V. Anticonvulsants in bipolar disorder. *Psychiatr Clin North Am* 2005;28:301–23.
 54. Sajatovic M, Brescan DW, Perez DE, et al. Quetiapine alone and added to a mood stabilizer for serious mood disorders. *J Clin Psychiatry* 2001;62:728–32.