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Review Article

Bipolar disorder in older adults: a critical review

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Objectives: The goal of this article is to provide a comprehensive critical review of studies reporting the prevalence, features, age of onset, course, comorbidity, and neuropsychology of, as well as service utilization, in bipolar disorder in older age.

Methods: We searched the Medline, Pubmed, and PsycINFO databases using combinations of the keywords 'Bipolar', 'Manic/a', 'Manic Depression', 'Elderly', and 'Older'. We included English-language reports presenting quantitative data on the prevalence and/or any descriptive information about adults with bipolar disorder over age 50. Findings from similar studies were pooled when possible. A total of 61 studies met our broad criteria.

Results: Common methodological problems in the published studies included small sample sizes, retrospective chart review, lack of standardized measures, overemphasis on inpatients, and dearth of longitudinal data. Strong evidence indicates that bipolar disorder becomes less common with age, accounts for 8–10% of late life psychiatric admissions, is associated with neurologic factors in late-onset groups, and is a heterogeneous life-long illness. Weak or inconsistent evidence was found for a higher prevalence of mixed episodes in older adults, a lower treatment response, and the association with lower family history in late-onset groups. Minimal information is available on bipolar depression in late life.

Conclusions: Bipolar disorder in old age is a growing public health problem. Greater research on bipolar disorder in older people will assist in enhancing services to this group as well as inform research on bipolar disorder across the life span.

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As the population ages, the number of older adults with severe mental illnesses will increase dramatically over the next several decades (1). Concerted efforts have been made to increase the knowledge base on the characteristics of older people with depression (2), enhancing age-adapted services to depressed older adults as well as informing research on depression throughout the life span. However, the relative lack of knowledge about bipolar disorder in older people has been pointed out in a number of reviews of bipolar disorder (3, 4) and of affective disorders in older adults (2, 5–7). In the recent consensus statement from the Depression and Bipolar Support Alliance, Charney et al. (2) called for 'multi-center studies of the diagnosis and treatment of bipolar disorder in elderly patients' (p. 667). A recent report by an NIMH workgroup on Affective Disorders repeatedly cited the relative lack of information about bipolar disorder in elderly persons compared with late-life depression (8). To date, there have been no published large-scale multi-center studies of

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prevalence, etiology, or clinical features of bipolar disorder in late life, nor have there been any double-blind randomized controlled trials of pharmacologic treatments in this population.

Consequently, many clinical observations about bipolar disorder remain empirically unconfirmed. Kraeplin's (9) original notion of manic-depressive illness included its episodic (versus chronic) nature and better outcome relative to schizophrenia (dementia praecox). More recent authors have suggested that bipolar disorder often 'burns out' in the latter half of life (10), based primarily on the observation that few older people were present in large mixed-age studies. However, other authors have argued that bipolar disorder follows a progressively deteriorating course (11), which by extrapolation would suggest poor outcome for older people with bipolar disorder. Additionally, several authors have observed differences between younger and older bipolar patients. Rennie (12) concluded that aging with bipolar disorder was associated with longer episodes and shorter inter-episode intervals, and Blazer & Koenig (13) believed that recurrence was more likely in old age mania. Compared with mania in younger people, mania in older people has been qualitatively described as either less intense (14–15), or with more hostility, irritability, and mixed features (14, 16). It has been observed that mania in older people is more difficult to resolve (17), suggesting that medication may be less effective.

Thus, there is a need to consolidate our existing knowledge about late-life bipolar disorder, examine what existing data say about the unconfirmed observations made above, and identify significant gaps in the literature. Previous reviews of the literature on bipolar disorder in older adults have largely focused on the relationship between mania and cerebrovascular illness (18, 19), biologic factors (20), and clinical assessment and pharmacotherapy (21–29). Many of these reviews have been targeted toward the clinician, and they have relied heavily on extrapolating data from other psychiatric disorders in late life or from younger people with bipolar disorder. Reviews that have more systematically critiqued available data need to be updated (30–33).

The aim of this review is to provide a systematic and comprehensive critique of studies of older people with bipolar disorder. Specifically, the goals are to: 1) consolidate available findings in bipolar disorder patients over age 50, 2) critique methods used, 3) compare findings to data on younger people with bipolar disorder and older people with other psychiatric disorders, and 4) identify gaps in the literature and provide suggestions for addressing them. A related goal for this review is to present relevant data from studies in tabular format. Due to the complexity of pharmacotherapy in both older adults and those with bipolar disorder, we have chosen not to include studies of treatment in this review (see 24, 28, 34).

Method

A review of published studies was conducted using the electronic databases Pubmed, Medline, and Psychinfo with the keywords 'Bipolar', 'Manic/a', 'Manic-Depression', 'Elderly', and 'Older'. Articles were also found by cross-referencing identified articles, searching reference lists in geriatric psychiatry textbooks, and using the 'related articles' function on Pubmed. Our inclusion criteria for acceptable studies were deliberately broad. Studies were included in the review if they reported data on prevalence within a defined population (e.g. nursing home, community) or any descriptive information (e.g. age, age of onset, gender ratio), in patients with 'primary' mania or bipolar disorder who were over age 50. We chose age 50 as the youngest age that could reasonably refer to 'older adult', in order to be as inclusive of published papers as possible, particularly with respect to recent studies with samples of adults aged 50 and older with more rigorous methods (35, 36). Age 50 has been used by some as the beginning of middle age (37). We excluded reports that were published in non-English journals. With these methods, we identified 61 studies that met our broad criteria. Of these, 27 reported prevalence relative to a population (e.g. community, inpatient hospital; Tables 1 and 2), and 34 reported some demographic, psychiatric, functional, or clinical data on these patients (see Tables 3–6).

Results

A number of limitations of the published studies hinder the ability to conduct meta-analyses. Before summarizing findings from available studies, we will outline several recurring shortcomings we identified in the sampling, definitions, and methods used in these studies.

Samples

Small sample size. The mean sample size of the 35 descriptive studies reviewed was 54.8 (SD = 27.3), and the largest sample reported had 92 subjects. Studies focusing on neuropsychology or neuroimaging generally had even fewer participants. These smaller sample sizes clearly limit power in subgroup analyses, and may contribute to negative findings when, for example, comparing older adults

Table 1. Community prevalence of bipolar disorder in older adults

Study	Sample size	Setting	Prevalence	Diagnostic criteria	% Female	Comments
Weissman et al. (60)	18,263	ECA multisite study	0.4% (45–64 years) 0.1% (65 and older)	DSM-III (Diagnostic Interview Schedule)	59% (45–64 years) 62% (65 and older)	Range across five sites was 0–0.5
Unutzer et al. (64)	294,284	HMO	0.46% (40–64 years) 0.25% (65 and older)	DSM-IV; hierarchical administrative database scheme	N/A	Medicare patients might have been excluded
Klap et al. (63)	9,585	Community telephone survey	0.08% (65 and older)	DSM-III-R (Composite International Diagnostic Interview)	N/A	Sample included 'bipolar disorder or psychosis'
Hirschfeld et al. (61)	85,258	Community survey	1.6% (55–64 years) 0.5% (65 and older)	Mood Disorder Questionnaire	N/A	Younger adults (aged 18–24) eight times more likely than those aged 55 and older to screen positive for bipolar disorder

ECA = Epidemiological Catchment Area; HMO = Health Maintenance Organization; N/A = not available.

with younger adults or subdividing samples by early and late onset (38).

Overemphasis on inpatients. About 85% of the descriptive samples we reviewed derived from convenience samples of inpatient psychiatric populations from only one institution or site. However, the majority of older people with mental illness reside in the community, and many manage to avoid hospitalization altogether (39). Furthermore, inpatients are generally in acute states, such that their impairments may be overestimated. Sampling from inpatient populations also leads to a preponderance of study patients in the manic phase of the illness. Thus, relative to the features of acute mania, we know far less about community adjustment, inter-episode functioning, and bipolar depression in older adults.

Sample variability due to study chronology. We reviewed articles published across several decades, and their findings may reflect changes in length of stay and type of treatment settings, available medications, and differing non-psychiatric treatments. For example, as pointed out by Dhingra & Rabins (40), comparison of more recent data with the studies of Roth (15) or Wertham (41) may be problematic due to the effect of the introduction of lithium. The number of studies reviewed that were published in the past 10 years accounted for about 30–50% of the entire set of studies reviewed (eight of 24 studies on prevalence, and 16 of 34 with descriptive information). Therefore, combining older and more recent studies introduces variability when consolidating prevalence and clinical data.

Differing inclusion/exclusion criteria. Although most descriptive investigations had a shared focus on bipolar disorder in late life, inclusion criteria varied along a number of important dimensions. The minimum age varied from 50 to 65 years. Some studies only selected those in the manic phase (42–43), and others only selected those with later ages of onset (44). Furthermore, some articles excluded those with indications of 'organic' etiology (45), while others did not (46–47).

Definitions

Patient selection criteria. As noted in other reviews of bipolar disorder in older people (30, 32, 33), the definition of age of onset varied widely across studies in several ways, which likely contributes to inconsistency across investigations. Studies varied in whether they reported onset of affective symptoms, full-blown depression or mania, or psychiatric

Table 2. Studies reporting prevalence of bipolar disorder in non-community settings

Study	Total no. of patients	Setting	No. of patients with bipolar disorder	Diagnostic criteria	% Female	Comments
Roth (15)	464	Psychiatric hospital	6% had mania	Author's criteria; age >60, mania	N/A	Concluded that prognosis was poor, because at follow-up most had died
Spicer & Slater (91)	1,056 psychiatric admissions in England and Wales	First admissions to psychiatric hospital	Increasing rate of first admissions into late life	ICD-7 mania	Rates of first admission for mania rise in males but not females	Authors attribute increase in first admission rates in late life to neurologic disorders
Spar et al. (136)	155	Geropsychiatric unit	9.0%	DSM-II	N/A	
Stevick (137)	276	State geriatric facility	5.8%	N/A	8.5% of all women and 2.5% of all men	
Chacko et al. (138)	80	Outpatient geriatric clinic	8.75%	DSM-III; age >55	85.7%	
Glasser & Rabins (46)	N/A	Inpatient	4.9% of admissions for 60 and older	DSM-III mania; organic causes not excluded	57.1%	
Eagles & Whalley (90)	Scottish psychiatric hospital admissions (1969–1978)	Inpatient	Increasing slope of first admissions	ICD-8 mania	Significant increase in both genders into old age	Rate per 100,000 highest among those over age 75
Mei-Tal & Meyers (139)	112	Psychogeriatric unit	8%	DSM-III, bipolar, manic	88.8%	Mean age 68.8; 3/8 had organic brain syndrome
Yassa et al. (44)	217	Geropsychiatric unit	Bipolar, mania in 4.7% of all patients; 9.3% of affective disorders	DSM-III, organic mental disorder excluded; only index episode over 60 or first psychiatric admission after age 65	60%	
Moak (65)	124 consecutive admissions	State geropsychiatric hospital	18.5%	DSM-III, bipolar, manic	N/A	Non-demented patients only
Molinari (140)	390 consecutive admissions	Geropsychiatric unit	7.7% of discharges, not individuals	ICD-9 manic depressive psychosis	0% (Veteran's hospital)	43% of affective disorder discharges; a higher proportion of bipolar disorder patients were recidivists relative to unipolar
Sibisi (92)	United Kingdom psychiatric hospital admissions (1982–1986)	First admissions to psychiatric hospital	Rate of first admission stable across age groups	ICD-9 manic depressive psychosis	Rates of first admissions show preponderance of females for the first time after age 79	
Snowdon (98)	N/A	Psychiatric hospitals	12% of admissions to psychiatric hospital over age 60	DSM-III manic depression	69.3	0.3% of area residents over age 60 were admitted to a hospital for bipolar disorder per year

Table 2. Continued

Study	Total no. of patients	Setting	No. of patients with bipolar disorder	Diagnostic criteria	% Female	Comments
Speer (68)	187	Outpatient geriatric clinic	2%	DSM-III-R bipolar disorder	N/A	
Speer (68)	178	Residential	17.4%	DSM-III-R bipolar disorder	N/A	
Tariot et al. (71)	80	Nursing home	3%	DSM-III-R bipolar disorder	N/A	
Shulman et al. (72)	173	Psychiatric emergency room	17% of patients over age 60	DSM-III-R, bipolar disorder	N/A	Bipolar patients more likely to be 'known' in the hospital
Holyrod & Duryee (70)	140	Geriatric outpatient clinic	5%	DSM-IV, bipolar manic	N/A	
Meeks & Murrell (39)	346	Community mental health	25% had bipolar disorder I or II	RDC, over age 40 (SADS)	N/A	Study of middle to late-life severe mental illness
Rasanen et al. (89)	Finnish psychiatric hospital admissions (1987–1994)	First admissions to psychiatric hospital	19% had first admission for bipolar disorder after age 60	DSM-III-R bipolar disorder	Risk higher in males aged 50–59 and 80+; risk higher in females aged 60–79	Highest risk bracket was aged 50–59
Webster & Grossberg (141)	1,700	University psychiatric hospital	5% of late-onset psychosis admits	DSM-IV, bipolar disorder; late-onset psychosis (after age 65)	N/A	Late-onset bipolar more common than late-onset psychosis due to schizophrenia/ schizoaffective disorder
Ponce et al. (109)	378 consecutive admissions	Geropsychiatric unit	5%	DSM-III-R and IV bipolar disorder, manic	N/A	25% had concomitant dementia; 29% had additional Axis I; 24% were divorced; 19% had substance abuse diagnoses
Wylie et al. (45)	791	Geropsychiatric unit	8%	DSM-III-R bipolar I	59.3%	
Yang et al. (142)	520	Veteran's hospital in Taiwan	6.5%	DSM-III-R, bipolar, manic	N/A	Mean MMSE score = 22.94

MMSE = Mini-Mental State Examination; SADS = Schedule for Affective Disorders and Schizophrenia (143); N/A = not available.

Table 3. Studies providing descriptive information on bipolar disorder in older adults

Study	Sample size	Mean patient age (years)	Setting	Diagnostic criteria	% Female	Mean age of onset of illness (years)	Family history	% Neurologic comorbidity	Other findings	Comments
Carlson et al. (88)	20	60.3	Inpatient	Feighner's criteria; onset after 50	45%	50.6 with duration of 10.4 years	35% in first degree relatives	N/A	Higher frequency of rapid cycling in the late-onset compared with adolescent onset group; same episode frequency per year	
Himmelhoch et al. (112)	81	63.27	Inpatient	RDC bipolar disorder	48%	43; average duration of illness was 20.9	N/A	12% with dementia	33% abusing drugs	
Shulman & Post (55)	67	N/A	Inpatient	Feighner's criteria	73%; men had earlier first onset of mania and more likely to have neurologic comorbidity	First affective disorder = 48.9; first mania = 58.9; only 8% had onset of mania before 40	N/A	23.8%	62.7% had first episode as depression	
Molinari et al. (69)	7	68	Outpatient	DSM-III bipolar	85.7%	First mania = 55.7; first hospitalization = 54.1	57%	N/A	Average of 2.57 marriages; 6/7 had precipitating life events for current episode	
Glasser & Rabins (46)	42	N/A	Inpatient	DSM-III mania in people over 60; organic causes not excluded	57.1%	First affective disorder = 43.7; first mania = 51.1	23.8%	17% had cerebral impairment	59% had grandiose delusions and 11% had AH	Authors concluded that bipolar presents similarly to younger people
Mei-Tal & Meyers (139)	9	68.8	Inpatient	DSM-III, manic	88.8%	N/A	N/A	37.5% with organic brain syndrome		
Yassa et al. (44)	10	72.8	Inpatient	DSM-III onset of mania after 60	60%	First depression = 62; first mania = 71	30%	N/A	20% had paranoid delusions and 'mixed mania'	
Stone (47)	92	70.3	Inpatient	Feighner's criteria; all patients over age 65 with mania	68%; no gender differences in age of onset	57; 26% had no history of mental illness; 74% onset after age 50	27%	24%; eight had specific conditions, three were secondary mania		
Broadhead & Jacoby (38)	35	72.5	Inpatient	Feighner's criteria	N/A	First affective disorder = 42; first manic episode = 59	29%	43%; 2/35 demented; 0% of young group with cerebral impairment	17 years between first mania and first depression; older group more likely to have depressive episode on admission	Compared with younger bipolar group, less severity on mania scale but no item differences
Berrios & Bakshi (86)	19 patients with 'manic symptoms'	77	Geropsychiatric facility	ICD-9 affective psychoses; unclear how manic, depressed and other groups delineated	79%	N/A	N/A	N/A	Manic symptom group had increased behavior disorder, neuroleptic usage, bad outcome, worse cognition, and more psychosocial impairment	Manic patients may have been delirious

Table 3. Continued

Study	Sample size	Mean patient age (years)	Setting	Diagnostic criteria	% Female	Mean age of onset of illness (years)	Family history	% Neurologic comorbidity	Other findings	Comments
Dhingra & Rabins (40)	38 [follow-up of Glasser & Rabins (46)]	N/A		DSM-III mania in people over 60; organic causes not excluded	N/A	45; age of onset did not relate to gender ratio, mortality, or relapse rate	N/A	N/A	34% were deceased 5–7 years later; 72% of living were symptom free; 32% experienced rehospitalization	32% had MMSE scores <24 (0% at baseline); authors felt that prognosis was better than in Roth (15) study
Snowdon (98)	75	N/A	Psychiatric hospital	DSM-III	69.3%	First affective disorder = 46.5 episode; first mania = 58	35.6%	17.3%	3.65 hospitalizations in 10-year period; 16.4 year latency to mania in those with depression first; 58% had onset of affective disorder after age 45	
Shulman et al. (42)	50	N/A	Inpatient	DSM-III-R; bipolar, mania	70% women	First affective disorder = 56; first mania = 66	52%	36% versus 4% of depressed patients	Manic patients had higher mortality than depressed patients	
Bartels et al. (57)	20 NH; 39 community	76.8 NH; 69.5 community	NH and community (same community sample as above)	DSM-III-R; random sample received SCID	NH = 90.0%; community = 89.7%	N/A	N/A	N/A	10 and 23% had psychiatric admission within previous 6 months, significantly more than comparison schizophrenia group; bipolar patients had fewer positive and negative symptoms, greater cognition (MMSE); higher GAF and community living skills	
Noaghiul et al. (144)	21	70.5	Inpatient	DSM-IV bipolar, manic; all patients taking valproate	89%	45	42%	N/A	43% had impaired cognition on MMSE; 85% were psychotic	
Chen et al. (145)	59 patients on lithium or valproate monotherapy	70.3	Inpatient	DSM-III-R or DSM-IV bipolar disorder, manic	71% female	43.2	N/A	N/A	4.2 previous hospitalizations; 66% with psychotic features	
Meeks (35)	86	53.6 (age range 40–78)	Community mental health	RDC bipolar I (n = 74) or bipolar II (n = 12)	74.4%	First symptoms = 24.9; first hospitalization = 32.5; first mania = 34.9	N/A	N/A	Mean number of hospitalizations = 6.6; 20% with psychotic features; GAF scores predicted by number of depressive episodes	Most living alone (36%) and 72.8% below poverty level
Wylie et al. (45)	62	71.7	Inpatient	DSM-III-R bipolar I; organic mood disorder excluded	59.3%	46.4	N/A	53% had one or more cerebrovascular risk factor	58% with psychotic features	
Bartels et al. (56)	37 compared with 85 unipolar	69.7	Outpatient	DSM-III-R	89.2%	37.0; 69% onset affective disorder <40	N/A	N/A	32% residing in group home; compared with unipolar group: less depression, more positive symptoms, BPRS total, and lower community-living skills	Service utilization higher in bipolar group for inpatient, case management, day treatment, but lower for psychotherapy

Table 3. Continued

Study	Sample size	Mean patient age (years)	Setting	Diagnostic criteria	% Female	Mean age of onset of illness (years)	Family history	% Neurologic comorbidity	Other findings	Comments
Benazzi (36)	31	59.2	Outpatient private practice	DSM-IV bipolar II depression; age >50 (SCID)	61.2%	First major depression = 37.2	N/A	N/A	Bipolar II patients over 50 were more often psychotic and less often atypical than under 50; 70% rate of Axis I comorbidity; 48% had chronic course	
Beyer et al. (95)	29	60.1 (over age 50)	Inpatient and outpatient	DSM-IV (SCID)	72.4%	First depression = 28.8; first mania = 38.8	N/A	N/A	Older bipolar patients had fewer differences from age-matched controls in social support than younger bipolar compared with controls	
Young et al. (146)	57 (46 with out AAM and 11 with suspected AAM)	70.4	Psychiatric hospital	DSM-IV bipolar I and RDC mania; active substance abuse excluded	81% AAM; 70% non-AAM	Non-AAM: first mania = 51.3, first affective illness = 48.7; AAM: first mania = 65.1; first affective illness = 51.8	In non-AAM group 45.5% had family history of depressive disorder; 47.8% had family history of mania	N/A	3.1 prior manic episodes in non-AAM group	Only 25% of total sample were prescribed mood stabilizers at time of admission; data from pre-1990 (fewer SSRIs)

AAM = antidepressant associated mania; BPRS = Brief Psychiatric Rating Scale; GAF = Global Assessment of Functioning; MMSE = Mini-Mental State Examination; N/A = not available; NH = nursing home; SCID = Structured Clinical Interview for DSM; SSRI = selective serotonin reuptake inhibitor.

hospitalization. In addition, other reports simply reported 'age of onset' without specifying which type. Studies that divided samples by early and late onset defined the age cut-off anywhere between 30 (48) and 65 (49) years, which severely limits the ability to compare these studies. Criteria for co-occurring neurologic impairment and family history differed widely between studies, as well.

Diagnostic changes over the years. The studies we examined varied in whether cases were diagnosed using ICD (50), DSM-III (51), III-R (52), IV (53), Feighner's criteria (52), and RDC (54) criteria.

Lack of differentiation of bipolar spectrum. The vast majority of the studies we reviewed did not report distinctions between bipolar I, and bipolar II, and cyclothymia, nor did they report course or severity specifiers.

Methods

Retrospective chart review versus prospective investigation. The majority of the data from studies derived form retrospective reviews of case records, within one particular institution. Only a few prospective studies were identified (e.g. 38).

Longitudinal versus cross-sectional investigation. Only three studies (40, 42, 55) reported follow-up or outcome of an older cohort of bipolar patients beyond 5 years. Data from most studies were restricted to a single period of hospitalization.

Dearth of standardized measures of diagnosis or outcome. We identified few studies that reported diagnoses derived from structured clinical interviews (35, 36, 56, 57), thus increasing the probability of diagnostic inaccuracy. Furthermore, descriptive information generally did not include standardized measures (e.g. Young Mania Rating Scale; 58). In younger people with bipolar disorder, global ratings have been found to relate only weakly with symptom measures (59). Standardized assessment measures of psychiatric symptoms and functioning appear more in recent studies (45), yet these symptom scales (particularly for mania) have not been specifically validated in older adults with bipolar disorder.

Where possible, we attempted to pool data from the studies using sample weighting (i.e. weighting prevalence estimates by the number of cases in a given study). We have organized this review into the following areas: prevalence, clinical features, age of onset, course, comorbidity,

Table 4. Studies comparing early- and late-age onset bipolar disorder

Study	Sample	Age cut-off	% Family history of affective disorder	% Neurologic illness	Comments
Taylor & Abrams (48)	132	>Age 30 (first mania)	LOBP = 4.7% EOBP = 14.2% ($p < 0.0001$)	N/A	
Carlson et al. (88)	48 inpatients	<Age 20 (n = 28) versus >age 45 (n = 20) mania	EOM = 54% LOM = 35% NS (p = N/A)	N/A	Significantly more rapid cyclers in LOM group (6 versus 2)
James (147)	48	>Age 30	EOM = 26.0% LOM = 12.3% ($p < 0.01$)	N/A	
Baron et al. (148)	142	>Age 40 first episode	EOM = 31.6% LOM = 22.6% ($p < 0.001$)	N/A	
Glasser & Rabins (46)	42 inpatients	>Age 60 mania, no numbers	(No frequencies reported) NS (p = N/A)	N/A	Number of patients in onset groups not provided
Stone (47)	92 inpatients	N/A	N/A	N/A	Age of onset later in positive family history group and cerebrovascular impairment group
Broadhead & Jacoby (38)	35 bipolar inpatients; 14 EOM and 21 LOM	>Age 60 first mania	LOM = 14% EOM = 50% NS (p = N/A)	LOM = 57% EOM = 21% NS (p = N/A)	No differences in IQ, course, discharge disposition, or treatment
Tohen et al. (149)	50 bipolar inpatients; 14 late onset 36 early onset	>Age 65 (first mania)	LOM = 57% EOM = 36.1% NS (p = N/A)	LOM = 71.4% EOM = 27.7% ($p = 0.005$)	No differences in mortality, morbidity, gender ratio, or sociodemographic characteristics
Hays et al. (150)	74 outpatients	>Age 50 first symptoms	LOM = 83.3% EOM = 88.2% LOD = 67% EOD = 88.7% N/S (p = N/A)	Vascular morbidity LOM = 50% EOM = 17.6% LOD = 33% EOD = 19.7% Sig (p = N/A)	
Wylie et al. (45)	62 inpatients	>Age 49	N/A	N/A; LOM = 70% versus EOM = 43.8% ($p = 0.01$) Cerebrovascular risk/burden	Higher divorce rate in EOM; LOM more psychotic; no differences in treatment response between groups
Schurhoff et al. (93)	210 inpatients	>Age 40 in LOBP (n = 39); <age 18 EOBP (n = 58)	EOBP = 10.1% LOBP = 6.0% ($p = 0.0002$)	N/A	More mixed episodes, psychotic features, panic disorder and worse lithium response in the EOBP group

Table 4. Continued

Study	Sample	Age cut-off	% Family history of affective disorder	% Neurologic illness	Comments
Almeida & Fenner (49)	6, 182 public mental health users	>Age 65 (first contact with mental health system)	N/A	Organic brain syndrome: EOM = 0.7%; LOM = 2.8% ($p < 0.001$)	EOM more likely to have mixed episode and to live in economically disadvantaged area; mania more common in LOM group
Cassidy & Carroll (94)	366 inpatients, DSM-III-R manic or mixed	>Age 47 first hospitalization (23 LOM versus 343 EOM)	N/A	LOM = 88% EOM = 61% ($p = 0.026$) Two or more vascular risk factors	Fasting cholesterol higher in LOM group

EOM = early-onset mania; EOD = early-onset depression; EOBP = early-onset bipolar disorder; LOM = late-onset mania; LOD = late-onset depression; LOBP = late-onset bipolar disorder; Sig = significant; NS = non-significant; p = N/A = no p-value reported; N/A = not available.

neuropsychology/neurology, service utilization, and conclusions.

Prevalence

Community studies. Table 1 presents studies that have reported the prevalence of bipolar disorder among community-based/population-based samples. These studies consistently indicate that the prevalence of bipolar disorder declines in late life. Data from the Epidemiologic Catchment Area (ECA) survey (60) indicated a 1-year prevalence rate of 0.1% among adults over age 65. This is much lower than the prevalence among young adults (18–44 years; 1.4%) and middle-aged adults (45–64 years; 0.4%). According to the ECA data (60), depression and schizophrenia are about 14 and three times more common than bipolar disorder in the elderly, respectively. The ECA estimates across age groups in bipolar disorder show similar lower rates of the prevalence estimates among elderly groups diagnosed with schizophrenia and major depression.

In other community surveys with less rigorous diagnostic procedures, estimates of bipolar disorder in older adults were also lower compared with those in younger groups. Using the Mood Disorder Questionnaire (a brief screening measure derived from DSM-IV criteria), Hirschfeld et al. (61) found that 1.6% of people between ages 55 and 64 and 0.5% of people aged 65 and older screened positive for current bipolar disorder. Compared with the 18–29-year-old group, bipolar disorder was eight times less likely in the over-65 age group. In a telephone survey that used an adapted version of the Composite International Diagnostic Interview (CIDI) (62), a total of 0.08% of 1538 adults over age 65 screened positive for bipolar disorder or psychosis, compared with 1.17% of those between ages 30 and 64 (63). Finally, in a large HMO administrative database, the treated prevalence of clinically diagnosed bipolar disorder was 0.25% among adults over 65, compared with 0.46% of adults between 40 and 64 (64).

Taken together, community and population-based surveys indicate a marked decline in the prevalence of bipolar disorder in late life, which is similar in magnitude to the age-related changes in prevalence found in depression and schizophrenia.

Inpatient psychiatry samples. A total of 11 studies reported the relative proportion of older patients with mania and/or bipolar disorder in inpatient psychiatric settings (Table 2). All of these studies used chart review method. Estimates ranged from 4.7% (44) to 18.5% (65). The mean prevalence for

Table 5. Frequency of findings in studies comparing early- and late-onset bipolar disorder

Variable	Number of studies	Demonstrating association	Demonstrating little or no association
Strong evidence			
Neurological illness	6	Four studies showing LOM > EOM (45, 49, 149, 150)	Two studies (38, 94)
Weak or inconsistent evidence			
Family history of affective disorder	9	Four studies showing EOM > LOM (48, 93, 147, 148)	Five studies (38, 46, 88, 149, 150)
Mixed episodes	3	Two studies showing EOM > LOM (49, 93)	One study (94)
Treatment response	4	One study showing EOM < LOM (93)	Three studies (38, 45, 48)
Gender ratio	5		Five studies (45, 48, 88, 93, 149)
Minimal evidence			
Psychotic features	2	One study showing EOM > LOM (93) One study showing LOM > EOM (45)	
Predominant mania	2	One study showing LOM > EOM (49)	One study (88)
Course	2		Two studies (38, 45)
Divorce/social support	2	One study showing EOM > LOM (45)	One study (95)
Substance abuse	2		Two studies (49, 93)
Severity of mania	1		One study (38)
Severity of depression	1		One study (38)
Rapid cycling	1	One study showing LOM > EOM (88)	
Cognitive functioning	1		One study (MMSE) (45)
Panic disorder	1	One study showing EOM > LOM (93)	

EOM = early-onset mania; LOM = late-onset mania.

the 318 cases (of a total N of 3887) reported was 8.7% (SD = 3.7). This figure is likely to be an underestimation, as three of 11 reported only individuals in the manic phase, and Yassa et al. (44) only reported cases with onset after age 60. On the contrary, the highest percentage (18.5%) included only non-demented admissions to a psychiatric hospital (65). Therefore, a conservative estimate would be that 8–10% of psychiatric inpatients over age 55–60 are diagnosed with bipolar disorder.

Our pooled estimate of inpatient sites is fairly consistent with two large system-wide studies of psychiatric hospitalization. A study of Medicare patients admitted to the hospital for a primary psychiatric diagnosis reported that, of 240 000 admissions, bipolar disorder accounted for 6.7%, whereas schizophrenia accounted for 5.7% and unipolar depression was 28.1% (66). This study demonstrated a prevalence of 1.9% in bipolar disorder among admissions in the oldest group (age 85+). In this study, 10% of the bipolar sample was discharged to a nursing home and the mean length of stay was 17 days, rates, which were comparable with both schizophrenia and unipolar depression.

It may be that the proportion of bipolar diagnoses in psychiatric hospitals is roughly similar among younger and older patients. In a large database study of all psychiatric hospitalizations in Maryland in 1998, bipolar disorder was diagnosed in 9.6% of those over 65, compared with 11.5% of those under 65 (67). However, the over-65 group had double the length of stay compared with the younger group, suggesting that symptoms or medical comorbidity may take longer to resolve in the elderly. Therefore, the proportion of people with bipolar disorder in psychiatric hospitals appears to be relatively consistent across age groups.

Outpatient psychiatry. We identified only three studies that examined the prevalence of bipolar disorder among older users of outpatient clinics and/or community mental health services (Table 2). The percentage of older outpatients diagnosed with bipolar disorder appeared to be lower than the rate of bipolar disorder among inpatient settings, ranging from 2% (68) to 8% (69). Weighted prevalence for the three studies identified was 6.1% (SD = 1.5). This may be an underestimate, again due to lack of consideration of bipolar depression (70).

Other settings. Studies in other settings have also reported frequency of older bipolar patients (Table 2). Long-term care institutions are common settings for older individuals with chronic mental illnesses. One study reported the prevalence of

Table 6. Neurological/neuropsychological findings in older adults with bipolar disorder

Study	Sample size	Average age (years)	Diagnostic criteria	Findings	Comments
Savard et al. (123)	7 over age 40 with bipolar depression	>40	DSM-III (Spitzer Manic Criteria)	Compared with unipolar, normal control and younger bipolar patients, older bipolar patients had more category errors even after symptom resolution	
Broadhead & Jacoby (38)	35 patients over 60 compared with 35 younger patients	72.5	Feighner's Criteria	Patients with significantly more cortical atrophy than control group; early and late-onset groups not different; age correlated significantly with VBR and cortical atrophy in the manic group	
McDonald et al. (126)	12	68.3	DSM-III-R mania; onset after age 50; average age of onset of illness = 62; all 12 had cognitive dysfunction; 3/12 had family history of affective disorder	Increased number of subcortical white matter hyperintensities compared with normal control group; patient group had more lesions in the parietal lobe	
Fujikawa et al. (127)	20 LOM versus 20 EOA versus 20 LOD	61 averaged across groups	DSM-III-R; early onset <50; 17 of 20 LOM patients had previous depression	Silent cerebral infarctions >5 mm in 65% of the LOM group versus 55% in the LOD and 25% in the EOA	
Harvey et al. (124)	26 bipolar, 24 unipolar, 308 schizophrenia chronically hospitalized patients	N/A	DSM-III-R; new onset neurological disorders or evidence of cognitive decline excluded	Bipolar and unipolar patients showed no differences on CERAD battery; affective disorder patients showed higher scores on MMSE than schizophrenia patients but no other differences	
Young et al. (125)	30 patients and 18 controls	71.4	Spitzer Manic Criteria	Greater VBR and CSW in patients. CSW correlated with age of onset	
Burt et al. (122)	13 bipolar and 24 unipolar over 60 compared with younger groups	68.8 bipolar and 71.1 unipolar	RDC, all patients diagnosed via SADS	IQ and MMSE did not differ across diagnoses; delayed retrieval lower in older bipolar group compared with younger and older unipolar group	Patients were depressed and awaiting ECT

Table 6. Continued

Study	Sample size	Average age (years)	Diagnostic criteria	Findings	Comments
Rabins et al. (128)	14 patients with bipolar disorder compared to 14 with unipolar depression and 14 with schizophrenia compared to normal controls	73.0	DSM-III-R onset of illness after age 44	Bipolar group highly similar to unipolar group, but both distinguished from schizophrenia; abnormalities in bipolar group were found in cerebral sulci, lateral ventricle, temporal cerebral sulci	
Tsai et al. (117)	52	66.7	DSM-IV bipolar I, early onset (age < 40)	30.7% had MMSE scores below 24; first manic episode <age 40 and cerebrovascular disease risk/burden accounted for 16% of variance in MMSE score	

VBR = ventricle brain ratio; CSW = cortical sulcal widening; LOM/D/A = late-onset mania/depression/affective disorder; EOA = early-onset mixed affective disorder; CERAD = consortium to establish a registry for Alzheimer's disease.

bipolar disorder in a nursing home was 3% (71). Koenig & Blazer (5) reported that 9.7% of chronically institutionalized patients from the ECA were diagnosed with bipolar disorder. In the psychiatric emergency setting, Shulman et al. (72) conducted a chart review study indicating that 17% of people presenting to a psychiatric ER over age 60 were diagnosed with bipolar disorder. This compares closely to a mixed-age study that found 14% of psychiatric emergency room presenters were diagnosed with bipolar disorder (73). Finally, Speer (68) found that bipolar disorder was present in 17.4% of a residential psychiatric program for older adults.

Thus, bipolar disorder may be a relatively common diagnosis in nursing home, emergency, and residential mental health settings.

Multisite studies. The two largest ongoing multisite studies of bipolar disorder, Systematic Treatment Enhancement Program-Bipolar Disorder (STEP-BD) (74) and the Stanley Foundation Research Network (75) have relatively few exclusion criteria that might limit sampling of older adults (e.g. due to cognitive impairment and/or comorbid medical illnesses). Suppes et al. (76) reported that only 5% of the first 261 patients enrolled in the Stanley Foundation study were over age 65. Preliminary figures for the STEP-BD have not yet been published, but it has been estimated that fewer than 5–10% of those enrolled will be elderly (77).

In summary, it appears from existing data that bipolar disorder becomes less common with age in community samples. Data from several large-scale community surveys indicate that bipolar disorder in the older population is about one-third as common as it is in younger people. The magnitude of this age-associated decline in prevalence is similar to what is seen with depression and schizophrenia. Reasons for this decline in prevalence may include factors related to the disorder (e.g. excess mortality, recovery) and/or the interaction with aging and case-finding methods (e.g. institutionalization, cohort differences in symptom reporting). However, bipolar disorder appears to account for roughly the same proportion of admissions to psychiatric facilities among older adults as younger adults (approximately 8–10%), and possibly the same proportion of outpatient and psychiatric emergency diagnoses. Furthermore, even if prevalence does decline across the lifespan, the absolute number of older adults with bipolar disorder will certainly rise as the population ages (1). This shift toward greater numbers of older people with bipolar disorder may already be occurring. Among public mental health users in

Australia, Almeida & Fenner (49) reported that the number of adults over 65 with bipolar disorder increased from approximately 2% of all bipolar suffers in 1980 to about 10% in 1998.

Clinical features

Findings from the descriptive studies we identified are displayed in Table 3. Again, we have pooled descriptive data from these studies when possible. In an effort to place these findings in context, results are compared with an extensive review of mixed-aged studies of bipolar disorder (4).

Gender ratio. In 17 studies that reported the percentage of females in the sample, the weighted mean was 69% (range 45–89). As would be expected, the ratio of women to men in older samples is higher than the estimate of 55% among younger adults (4), roughly equivalent to the gender ratio among older adults in the general United States population (78). In comparison with the ECA data, the ratio of women to men is lower in bipolar disorder in older adults compared with major depression (3.5 female to male ratio) (4) and roughly similar to older patients with schizophrenia (three to two female to male ratio) (79).

Psychotic features. Of the five studies that reported the frequency of psychotic features (i.e. delusions or hallucinations) among older adult samples, the mean rate was 64% (range 20–85). This figure is remarkably similar to that found in mixed-age groups [63% (4)], but in contrast to clinical observation suggesting greater paranoia among older adults (13).

Family history. Family history of psychiatric disorder (in most studies 'affective disorder') was reportedly high in 10 studies. The pooled estimate was 39% (range 23–57%), which is much higher than the 24% reported across mixed-age samples(4). One would expect that family history of affective disorder would be *lower* among older adults, given the often cited association of late-life bipolar disorder with organic or environmental causes (19, 33). Methodological issues may explain this higher rate of family history. Family history may be higher in these studies because older probands more likely have a greater number of older first-degree relatives (including siblings and children), who subsequently have longer periods of exposure to the genetic and environmental influences that predispose people to psychiatric disorders. Older samples were largely derived from inpatient populations, which may lead to a preponderance of individuals with more severe forms of psychopathology. In addition, the range of rates of positive family history is broad across the studies we reviewed in older adults, suggesting that there are different definitions of positive family history across studies.

Studies comparing younger and older bipolar groups. We identified two studies that directly compared the symptoms of bipolar disorder in older individuals with younger people (38, 80). Broadhead & Jacoby (38) assessed 35 older bipolar inpatients and compared them with a younger bipolar cohort (n = 35). Overall, few differences were found. On the Blackburn Mania Rating Scale (81), older individuals had a lower total score, but only one significant item difference was present. The older manic group had a longer latency from the first depression to the onset of mania (17 years versus 3 years, respectively), and they were more likely to relapse into depression after mania. Furthermore, no differences were seen in the frequency of mixed episodes between younger and older groups (45% of older manic patients versus 48% of younger patients showed mixed features). No differences were detected in the duration of mania or psychiatric hospitalization. Young & Falk (80) examined the effect of age on Mania Rating Scale (58) items in a sample of 40 patients (aged 17–66). Significant negative correlations were seen with age and 'increased-activity' and 'language-thought disorder'. Older patients had smaller change in total score over a 3-day interval. However, the authors noted that the majority of this sample was younger than 60 years, which limited the strength of their conclusions about mania in older people.

Another study that examined differences in bipolar symptoms by age group derived from a subset of individuals who screened positive for bipolar disorder on the Mood Disorder Questionnaire in the population study described above (61, 82). A considerable proportion of these individuals were likely false-positive for actual bipolar disorder. Given this limitation, the authors examined days of experiencing bipolar symptoms in the past 4 weeks and past 12 months across different age segments (ages 18–34, 35–54, and 55 and older). The over-55 age group experienced 5.6 days of symptoms in the previous 4 weeks, and 53.3 days in the past 12 months. The latter figure was about half the days reported by the youngest group.

In summary, compared with the larger set of available data available on younger individuals with bipolar disorder, the presentation in older adults appeared to evidence only minor differences.

The most consistent finding was that older people with bipolar disorder were more likely to be women, by a ratio of about 2 to 1. A great majority of studies did not report ethnicity of their samples, and therefore the ethnic distribution in bipolar disorder in older age is uncertain. Older people appeared to evidence psychotic features at the same frequency as younger people. Contrary to clinical observations (14), mixed features were no more common in older people in one study (38). Family history of affective disorder was more common in older adults, which is a finding that deserves further investigation. In the few studies that have made direct comparisons between younger and older people, there was some evidence for mania to be less intense and there is a possible trend for more time spent asymptomatic in older age (although older adults may have longer stays in the hospital, possibly due to higher medical comorbidity).

Differences between bipolar and other late-life psychiatric disorders

Three studies directly compared older bipolar disorder patients' psychiatric and functional impairment with that in other diagnostic groups, although two of these reports derive from the same bipolar sample (42, 56, 57). Bartels et al. (57) compared a group of 39 community-residing and 20 nursing home residents with bipolar disorder to groups with schizophrenia having similar living situations. Relative to the schizophrenia group, bipolar patients had more depressive symptoms, but fewer positive and negative symptoms. Overall psychopathology [Brief Psychiatric Rating Scale; BPRS (83)] and cognition did not differ [Mini-Mental State Examination; MMSE (84)]. On a clinician-rated measure of functioning, bipolar patients had greater community-living and relationship skills, but were similar in basic activities of daily living (ADL) skills. In a separate study, Bartels et al. (56) compared the community bipolar sample to 85 unipolar outpatients. Bipolar patients had higher BPRS scores, more positive symptoms, and worse community-living skills. Global cognitive impairment, other functional abilities, and Global Assessment of Functioning [GAF (85)] did not differ across affective diagnoses.

Shulman et al. (42) compared 50 elderly inpatients with a diagnosis of mania to a sample of 50 unipolar inpatients. Patients with bipolar depression were excluded from the depression group. The manic patients had a significantly higher rate of mortality over a 3–10-year follow-up (manic 50% versus depressed 20%). The group with mania also had a significantly higher rate of neurologic disorders than the unipolar group (36% versus 8%, respectively). Berrios & Bakshi (86), in a study that did not employ diagnostic categories, compared geropsychiatric inpatients with 'predominant' symptoms of mania ($n = 19$), depression ($n = 31$), or neither ($n = 20$). The group with mostly manic symptoms had greater cognitive impairment, more cerebrovascular burden, more psychosocial problems, and worse outcome than the other groups.

Overall, the available data suggest that bipolar disorder in older adults is intermediate between schizophrenia and major depression with regard to psychiatric morbidity and functional impairment. In studies of younger adults, mixed-age patients with bipolar disorder demonstrate outcome that is better than that in schizophrenia but worse than in depression, as well (87). In general, these comparisons were based on global psychiatric and cognitive functioning, so we know little about finer grained differentiation in important domains between these disorders. For example, the difference in executive functioning or memory between diagnostic groups is unclear, as comparisons were based largely on measures of global cognitive functioning (e.g. MMSE scores).

Age of onset of illness

Age of onset across samples. The distribution of age of onset of illness in mixed-age samples of bipolar disorder appears to be unimodal, with a peak between ages 20 and 29 years (4). Mean age of onset of illness for mixed-age samples was 28.1 years (4) or earlier in the ECA data (60) (age 21). In a pooled sample of 1300 patients, fewer than 5% of individuals had their first age of onset of illness after age 60 (4). We identified 13 studies in older bipolar patients that reported age of onset of any psychiatric disorder (mostly affective) and eight studies that reported age of first onset of mania. Noting that the definition of onset may vary across studies, several consistencies are apparent. The sample-weighted mean age of these samples was 68.2 years ($SD = 3.9$; range 60–72). The weighted mean age of onset of any affective disorder was 48.0 years ($SD = 6.4$; range 28–65) and age of onset of mania was 56.4 years ($SD = 7.3$; range 38–70). Although some of these studies did not select individuals who had manic episodes before 50 (44, 88), the general trend is for 10-year intervals between first affective symptoms, mania, and time of the study. On one hand, these figures indicate that the average older person with bipolar disorder/mania has experienced affective

symptoms for 20 years. On the other hand, the age of onset for elderly people with bipolar disorder is substantially later than that in younger individuals.

Age at first admission. A surprising finding is that rates of first hospitalization for mania may be *higher* in older-age groups compared with younger adults, which is in contrast to what would be expected from epidemiologic investigations reviewed above. Three of the four studies that examined incidence of first hospitalization for mania or bipolar disorder (89) identified higher frequency of first-hospitalization for mania among older age groups (89–92). The high incidence of first-admission mania in older adults has been attributed to the increasing rate of dementia or other neurologic disorders with age (91). However, we identified one study (89) that described incidence of first-admission DSM-III-R *bipolar disorder* (thus excluding secondary mania), which reported higher incidence of first-admission bipolar disorder among those aged 50–70 relative to those aged 20–29. In this study, 20% of individuals in Finland who were hospitalized for the first time with bipolar disorder were older than age 60. Therefore, the unexpectedly high incidence of first hospitalization for mania/bipolar disorder in older age may be only partly explained by the presence of secondary mania.

Comparison of 'early' versus 'late' onset groups. We identified 12 studies that compared 'early onset' with 'late-onset' bipolar disorder (Table 4). A listing of the frequency of specific findings (e.g. family history, gender ratio) is displayed in Table 5. Some of these studies were not restricted to older bipolar patients but are included here. Across these studies, the age cut-off that defined onset groups ranged from 30 to 65 years. The most common comparison between early and late-onset patients in these studies involved presence of family history of affective disorder and presence of neurologic risk/impairment. Of the nine studies that compared family history of affective disorder in early and late-onset bipolar disorder, four reported significant differences between early and late-onset groups (all showing late onset with less familial risk). In the studies not showing significant differences ($n = 5$), three showed trends for higher familial risk in the late-onset group. Therefore, the literature is far from conclusive about rates of familial affective disorder by age of onset in older adults.

The relationship of late-onset bipolar disorder to neurologic illness was more consistent across studies. Comorbid neurologic illness/risk was defined differently across studies, with terms such as 'organic brain syndrome', 'cerebrovascular risk/burden', and 'neurologic illness'. Of the six studies reporting rates of neurologic illness/risk, four showed significantly higher rates in the late-onset group, and the other two reported trends in that direction.

In terms of other characteristics, gender ratio was equivalent between early and late-onset groups in all five studies reporting it. A higher frequency of mixed episodes was found in early onset bipolar patients in two reports (49, 93), but not in another study (94). Psychotic features were found to be more common in late-onset bipolar disorder in one investigation (45), and less common in another study (93), although the sampling and onset definitions of these reports were different. Wylie et al. (45) also found no differences in treatment response between early and late-onset groups. Finally, Beyer et al. (95) found no differences in social support between older early and late-onset bipolar groups.

Taken together, the consistent findings are that older adults report a later onset of affective symptoms and mania than mixed-age groups. Although their onset is considerably later, older adults report experiencing some form of affective disturbance for a mean of 20 years. Several studies indicate an increase in the prevalence of first admission for mania among older age groups, although community data would suggest that bipolar disorder in older people is less common than in younger people. The definition of late and early onset across studies is highly variable. However, even when considering only the direction of findings, the evidence for greater family history in early onset older bipolar groups is inconclusive. In contrast, a consistently higher rate of neurologic illness was present in late-onset mania/bipolar disorder. Other differences, such as presence of psychotic features, social support, mixed episodes, and treatment response are reported in too few studies to allow firm conclusions.

Course

Long-term studies of younger cohorts. Studies of the long-term course of bipolar disorder have been rare, yet it is likely that bipolar disorder does not 'burn out' in old age, nor does it follow a progressively deteriorating course. In perhaps the best existing long-term follow-up study that reported outcome of bipolar disorder into old age, Angst & Presig (96) followed a cohort of 209 Swiss psychiatrically hospitalized patients with bipolar disorder over 40 years until a median age of 68. Of these patients, only 16% had fully recovered (had

no episodes within the previous 5 years). A total of 26% had GAF scores below 60 without experiencing episodes in the past 5 years, and 36% were still suffering from recurring episodes. Another 16% displayed a chronic course and 7% had committed suicide. Compared with the outcome of the group with unipolar depression, the bipolar group was roughly similar, except that bipolar patients were less likely to recover. A slightly better long-term outcome for manic patients was reported by Tsuang et al. (87) who followed a cohort of manic, depressed, and schizophrenic patients for 30–40 years. Age at time of final assessment for the manic group was 65. Half of the manic patients had 'good' psychiatric outcome (lack of current diagnosis), which was similar to the unipolar group, but far better than the schizophrenia group in which only 20% attained good outcome.

Angst & Preisig (97) found that the bipolar group had experienced an average of 10 episodes (versus four for unipolar patients) although only 56% of these episodes were associated with hospitalization. Relative to unipolar, schizoaffective-manic, and schizoaffective depressed patients, bipolar patients were less likely to be hospitalized for an episode.

Follow-up of older cohorts. In the studies that followed older bipolar patients, three reported long-term outcomes longer than 5 years (40, 42, 55). Shluman et al. (42) and Dhingra & Rabins (40) found higher mortality rates in manic patients, compared with age-matched patients with unipolar depression and normal controls, respectively. Shulman et al. (42) found that 50% of bipolar manic patients had died and 20% of unipolar patients had died at follow-up. In neither study was there a preponderance of suicide in the bipolar groups. All three studies examined rehospitalization after discharge, from 3 to 7 years post-admission, 30–50% of surviving patients were readmitted. Shulman et al. (42) found that readmission rates for unipolar bipolar patients were similar. Finally, Shulman & Post (55) found that 13% of their sample followed a chronic course, which is comparable with 16% found in the 40-year follow-up described above (96).

Retrospective analysis of course in older bipolar patients. Course prior to hospitalization has been reported in a number of the descriptive studies in Table 2. A recurring finding is that depression occurred as the first episode slightly more often in older adults (ranging 40–69%, mean 57%) than in younger patients (4) (approximately 50%). Among patients who had depressive episodes first, the mean difference between onset of depression and mania was upwards of 15 years in three studies (38, 42, 55). Three studies reported that about half of patients with depressive onset had three or more depressive episodes before onset of mania (38, 55, 98). Therefore, older bipolar patients included a subgroup of approximately 20–30% who were unipolar patients, but converted to bipolarity after recurring depressive episodes.

Finally, a number of case reports have identified rapid cycling patterns in geriatric patients (99–102). Whether rapid cycling is more or less common, presents differently, or responds to treatment differently in older people is not known.

Taken together, the long-term outcome of early onset bipolar disorder shows that the majority has recurring or residual symptoms, with an equal chance of recovery or chronic course. Thus, the most likely scenario is that bipolar disorder is a life-long illness, perhaps slightly more persistent than moderate to severe unipolar depression. Even if a proportion of older adults does show syndromal or symptomatic recovery, it is likely that far fewer show full *functional* recovery as is true of younger adults with bipolar disorder (103). There appears to be a broad range of course-defined subtypes in older people. For example, there is a subgroup of older people with bipolar disorder who have switched to mania after recurring depressive episodes. The distinguishing characteristics of these 'depressed-course' individuals from other types of bipolar disorder in late-life is unknown. There are also rapid-cycling older people with bipolar disorder, although the prevalence, characteristics, and differences from younger rapid-cyclers are unknown. Little evidence to date confirms that older people have more frequent or longer episodes, as suggested by clinical observations (12).

There is a lack of quantitative data about the precipitants of episodes in older adults, although some retrospective studies have indicated that negative life events precipitated a majority of psychiatric admissions (44, 69). In addition, no information on the quality and severity of subsyndromal symptoms is available, which is particularly important given recent life-chart based studies that indicate a surprisingly small percentage of time that mixed-age bipolar patients spend free of symptoms (75). Finally, the high risk of suicide in older people and in bipolar disorder would seem to be additive. However, in a study of suicide in bipolar disorder across the life span, Tsai et al. (104) found that highest risk for completed suicide was in 7–12-year post-onset and in those under age 35, which parallels the relationship of age and suicide in

schizophrenia (105). Older early onset bipolar patients may thus belong to a 'survivor cohort'.

Comorbidity

Psychiatric comorbidity. Bipolar disorder frequently occurs alongside other psychiatric disorders, and among the most common ones in the latter category are substance abuse, anxiety disorder, and personality disorder. The rate of substance abuse co-occurrence in bipolar disorder is the highest of any Axis I condition (106). In National Comorbidity Survey data, presence of any substance use disorder occurred in 61% of the bipolar sample (107). In a large mixed-age sample, approximately two-thirds of 392 hospitalized bipolar patients had a co-occurring Axis I disorder (108). However in that same study, the rate of lifetime substance abuse in those over 60 was 29%, which was significantly lower than that in the younger cohorts. This concurs with the retrospective findings of Ponce et al. (109) and Sajatovic et al. (110), who identified a comorbid substance use disorder in 25% of 19% older bipolar inpatients, respectively. Among older adults in the Cassidy et al. (108) sample, those with a lifetime history of substance abuse appeared to have a greater number of hospitalizations.

Ponce et al. (109) reported that 29% of their small sample had comorbid Axis I disorders. Only one study has examined the rate of Axis II disorders among elderly BD patients (111). Using a structured interview, Molinari & Marmion (111) found a 70% rate of personality disorder among 27 geropsychiatric inpatients and outpatients with bipolar disorder. We identified no studies that examined presence of anxiety disorder or other psychiatric disorders in older people with bipolar disorder.

Neurological illness. We found eight studies that reported the presence of neurologic illness/risk/burden (see Table 2). Definition of neurologic illness varied across studies, with some studies reporting the prevalence of cerebrovascular risk factors (45), other studies reporting incidence of frank dementia (112), and still others describing neurologic disorders (42). In eight studies, the sample-weighted prevalence of neurologic illness/risk was 23.1% (SD = 9.1; range 12–43%). In the one study that made a direct comparison with unipolar depression, Shulman et al. (42) found significantly higher rates of neurologic illness in manic patients (36% versus 8%). Wylie et al. (45) found that 24% of their sample had more than two cerebrovascular risk factors.

Medical comorbidity. Medical comorbidity in older people with affective disorders is extremely common (2). A study of psychiatric admissions in Maryland reported that 20% of elderly bipolar patients had seven or more comorbid medical diagnoses (67), which was slightly higher than the prevalence in schizophrenia. In terms of specific conditions, some existing data indicate that risk for diabetes may be high in this population. Regenold et al. (113) reviewed psychiatric inpatient records of mixed-diagnosis patients aged 50–74. Type II diabetes was present in 26% of bipolar inpatients, significantly more than among those with depression, schizophrenia, or dementia. The prevalence of diabetes in the Regenold et al. (113) study was substantially higher than that in a mixed-age study of bipolar patients that reported a rate of diabetes of 12% (114).

In summary, psychiatric comorbidity seems to be a rule rather than an exception in bipolar disorder. However, older people appear less likely to abuse substances, and substance abuse is a significant source of excess disability in younger people with bipolar disorder. Two caveats are that substance abuse may be harmful at lower level of intensity in older adults, and the cohort differences in lifetime substance abuse between younger and older groups may lessen as the baby boom generation replaces the current cohort of older people. There are few data to determine whether older people have different rates of other psychiatric comorbidities. Medical comorbidity is likely higher in older adults with bipolar disorder compared with younger cohorts, with some data demonstrating a high rate of diabetes in this population relative to those with other psychiatric diagnoses. What we do not know is how psychiatric, medical and neurologic comorbidities affect the health-related quality of life in this population.

Neuropsychology/neuropathology

A significant focus in reviews of mania in late life has been the role of organic or neurologic factors in late-life bipolar disorder, particularly late-onset mania. So-called secondary mania, which arises as the direct result of a known organic factor, has been reviewed elsewhere (115, 116). A sizeable proportion of older people with bipolar disorder have concomitant neurologic risk factors/illnesses, with later-onset groups more at risk as reviewed above (Table 3). Studies that have investigated neuropsychologic functioning and neuroimaging are displayed in Table 6.

The prevalence of dementia in older people with bipolar disorder has received inadequate attention. Within four inpatient samples, the incidence of concomitant dementia was highly variable, ranging from 3% to 25% (38, 47, 109, 112). In an inpatient sample, Tsai (117) found 30.7% of 52 early onset patients (onset of illness younger than age 40) had MMSE scores below 24 (indicating substantial cognitive impairment). Furthermore, Broadhead & Jacoby (38) found that 25% of patients scored in the demented range on a neuropsychologic battery. A number of case studies have described patients who presented with dementia-like symptoms that were later determined to be cognitive manifestations of bipolar disorder (118–120). Delirium in bipolar patients has also been reported (121).

Neuropsychological testing. A few studies have investigated neuropsychologic performance among older bipolar patients. Burt et al. (122) assessed inpatients with unipolar and bipolar depression referred for ECT, comparing bipolar and unipolar elderly to a group of younger patients with affective disorders. Older unipolar and bipolar patients did not differ in global measures. In examining age-group differences, younger bipolar patients had the best performance and the older bipolar patients had the worst performance on measures of delayed recall. Relatively poor performance by older bipolar patients compared with unipolar patients was reported on the Category test, as well (123). Harvey et al. (124) compared a group of 26 chronically institutionalized bipolar disordered patients with 24 unipolar patients. Those with new-onset neurologic illnesses were excluded. No differences were seen in MMSE scores, word list learning, or delayed recall. Furthermore, no differences were seen in construction or naming. The affective disorder group was also similar in cognitive functioning to a larger group of institutionalized patients with schizophrenia.

Neuroimaging. Several studies have reported results of structural neuroimaging in late life bipolar disorder. Two studies found evidence for increased ventricle brain ratio (VBR) in bipolar disorder compared with age-matched adults without psychiatric disorders via computed tomography (38, 125). Broadhead & Jacoby (38) found no differences between early and late-onset groups in VBR. In a sample of 30 geriatric patients with mania, Young et al. (125) found greater cerebral sulcal widening (CSW), and positive correlations between CSW, age of onset and age of first manic episode within the bipolar group. In relation to a normal comparison group, McDonald et al. (126) found among 12 late-onset (> 50 years) manic patients greater frequency and size of white matter hyperintensities on MRI.

Two studies have examined whether brain changes in older people with mania are specific to the diagnosis. Fujikawa et al. (127) compared MRI data on 20 late-onset (> onset after age 50) bipolar patients with 20 late-onset unipolar patients and 20 early onset affective disorder patients (mixed unipolar and bipolar). Silent cerebral infarctions were found in 65% of the late-onset manic patients versus 55% of the late-onset unipolar patients and only 25% of the early-onset affective disorder patients. Rabins et al. (128) compared 14 late-onset schizophrenia (> age 44) with 14 late-life bipolar and 14 unipolar patients. These diagnostic groups were then compared with an age- and gender-matched control group. The age of onset of affective disorder patients was not reported. In relation to normal subjects, affective disorder patients showed high concordance in patterns of atrophy. Both affective disorder groups showed more atrophy in cerebral sulci and lateral ventricle, whereas the schizophrenia group showed atrophy in the sylvian fissure, third ventricle, and temporal horn.

Taken together, available neuroimaging studies indicate that older people with bipolar disorder may show increased signs of atrophy and cerebral vascular lesions compared with normal age-matched control subjects. Late-onset groups again had higher risk for neurologic impairment. A central unanswered question is whether increased brain atrophy and/or cerebrovascular lesions in these studies were attributable to the pathophysiology of bipolar disorder or to secondary factors (e.g. lifestyle, substance abuse, medication). Comparisons between bipolar disorder and other diagnoses would be helpful in indicating the long-term specific effects of the bipolar disorder.

Service utilization

High use of mental health services, particularly inpatient psychiatric hospitals, is characteristic of younger bipolar patients, adding greatly to the societal cost of this disorder (129). In two retrospective studies that examined hospitalization over a 10-year period, older adults with bipolar disorder were hospitalized approximately four times (98, 110). In the Sajatovic et al. (110) report, bipolar patients were hospitalized at the same rate as older patients with schizophrenia, although their length of stay was shorter than that of a comparison group with schizophrenia. Bartels et al. (56) found that 35 older outpatients with bipolar

disorder used four times the amount of outpatient services than a comparison sample of unipolar patients. Specifically, bipolar patients used more inpatient hospitalization, case management, skills training, and partial hospitalization. In contrast, bipolar patients used less psychotherapy than the unipolar group. In another study comparing the same bipolar sample to a group with schizophrenia, bipolar patients were significantly more likely to be hospitalized within the past 6 months (57).

Brennan et al. (130) examined a cohort of 10,678 older veterans with substance use disorder and found that having a comorbid bipolar diagnosis was associated with increased probability of mental health care and readmission. This effect was stronger than that with depression, but less than that with schizophrenia. In contrast to the high rate of mental health service usage in this group, Cradock-Oleary et al. (131) found that having bipolar disorder was associated with *fewer* medical visits among veterans over age 50.

As the above reports were cross-sectional, it is unclear how service utilization changes across the lifespan in bipolar disorder. In depression and schizophrenia in late life, older age is often associated with reduced usage of mental health services. It is unclear whether these age-related patterns are apparent in older patients with bipolar disorder.

Clinical and research implications

Conclusions from the published data can be organized into gradations of certainty: strong evidence, weak or inconsistent evidence, and minimal evidence. We defined strong evidence by a majority of four or more studies showing statistically significant and consistent results. Weak or inconsistent evidence was from two or three studies or a minority of consistent significant findings. Minimal evidence was distinguished by one study or lack of consistent significant findings in two studies. The number of studies and the total number of patients across the studies is listed in parentheses after each conclusion.

Strong evidence. It does seem that the community prevalence of bipolar disorder declines with age (four studies; total n = 407,390). It is unclear whether this decline can be attributed to excess mortality, diagnostic or residential shift, and/or sampling biases. Although less common in the community, bipolar disorder is present in roughly the same proportion of older psychiatric inpatients, which we estimate to be 8–10% of all inpatients over age 55 (11 studies; total n = 318). Older bipolar patients have a later age of onset of illness than younger individuals on average (13 studies; total n = 700), and later onset of mania is associated with more neurologic impairment (four of six studies; total n = 586). Substance abuse, a significant and disabling comorbidity in younger individuals, is considerably less common in older cohorts (four studies; total n = 173). Finally, there is likely a greater degree of heterogeneity in presentation and course in older people with bipolar disorder. For instance, individuals may have developed new-onset mania associated with vascular changes, some may have become manic after recurrent depressive episodes, and some may have been diagnosed with bipolar disorder at an early age and have survived to old age with the illness. The way in which this heterogeneity in course relates to treatment response is unknown.

Weak or inconsistent evidence. Conclusions are much more tentative about other factors. Mania may be less intense in older adults, but likely presents with more similarities than differences from younger adults (two studies; total n = 75). There is little evidence that older adults have more mixed episodes or more psychotic features (five studies; total n = 194), but one large study did indicate longer hospital stays (one study; total n = 287). A majority of studies found later onset to be associated with lower family history of affective disorder (four studies; total n = 268), yet five reports did not find a difference in family history across age of onset groups. Greater cortical atrophy and white matter hypertensities may be more common in older people with bipolar disorder than in normal comparison groups (three studies; total n = 51). It is unclear how these brain changes arise, whether they relate directly to psychopathology or to lifestyle factors, and whether they are specific to bipolar disorder. Older adults may use a high rate of inpatient and other mental health services relative to unipolar depression or schizophrenia (two studies; total n = 59), but it is not known how service utilization changes across the lifespan within bipolar disorder patients.

Minimal evidence. From the data we reviewed, we know virtually nothing about the presentation and features of bipolar depression in older adults (one study; n = 31). We also know very little about how individuals function between inpatient stays, and what factors predict whether individuals maintain residence in the community versus require placement in inpatient or residential facilities. Furthermore, we do not know about the frequency of subsyndromal symptoms in this population. For

clinical purposes, we do not know about the psychometric properties of existing instruments in the assessment of bipolar disorder in older adults, as few studies have utilized these instruments in describing samples. Few studies have reported the frequency of different ethnic groups among patients with bipolar disorder in late life, and so ethnic differences among older bipolar patients are unknown.

Aging is associated with substantial changes in several areas that have great relevance to bipolar disorder in younger adults. In particular, changes in normal adults such as reduced sleep quality (132), higher risk of suicide in males (2), and increased medical morbidity likely negatively affect the functioning of older people with bipolar disorder. On the contrary, psychosocial changes such as decreased social conflict (133), decreased emotional reactivity (134), and increased lifestyle regularity (135) may serve as protective factors for some older people with bipolar disorder. The effects of these and other developmental trends are promising but mostly untapped avenues for research in bipolar disorder in late life.

Suggestions for future research. At present there are more gaps in empirical knowledge than there are answers, and more empirical studies of bipolar disorder need to be undertaken. The following are suggestions for improving the quality and quantity of future research with this group:

1. Collaboration among sites, such as by pooling data from multiple sites (e.g. outpatient clinics) with similar standardized outcome measures, would provide more statistical power to detect differences among subgroups of bipolar disorder.
2. Increasing emphasis on effectiveness studies with broad inclusion criteria, exemplified by the Stanley Foundation studies (75) and the STEP-BD (74), may make participation in clinical research more available to older bipolar patients with complicated medical comorbidity and/or cognitive impairment.
3. Given that most older bipolar patients reside in the community (39), more research should be conducted on outpatients addressing the predictors of successful (and less successful) community functioning.
4. Much of the existing knowledge base in older bipolar patients relates to the manic phase of the illness, although depression may be more pernicious to functioning over the course of the illness (35). Thus, more research should address the symptoms, severity, and neuropsychology of bipolar depression in late life, in comparison with younger adults with bipolar disorder and with older adults with major depression.
5. Given that bipolar disorder is largely treated in the public mental care system, use of administrative databases will be helpful in elucidating the effect of aging on service utilization. This research will provide an indication of the quantity and quality of services used by older bipolar patients, as well as a rough indication of changes in psychopathology across the life span.
6. We found a lack of a consistent definition of early and late-onset bipolar disorder across studies. Age of onset of illness should be analyzed as continuous as well as a categorical variable, and investigations should report multiple definitions of onset (age at first hospitalization, symptoms, psychosis, etc.), both of which will increase comparability across different samples.
7. We know little about the correlates of the long-term course of bipolar disorder in older people. Longitudinal studies with life-chart methods (75) or temporally continuous methods (e.g. actigraphy) may assist in validating subtypes of older bipolar patients, as well as identifying which older patients may be particularly vulnerable to negative outcomes.

Empirical research into bipolar disorder in older adults will not only help to improve the care of this vulnerable and growing group, but will also inform research on the consequences and treatment of bipolar disorder throughout the lifespan.

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