Primary Care Mental Health 2006;4:00–00

International research

Management of bipolar disorder: developments relevant to primary care

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ABSTRACT

Bipolar disorder is a serious mental illness characterised by recurrent episodes of manic and depressive moods that can each last weeks or months. The symptoms of bipolar disorder typically reduce opportunities for employment and education, adversely affect finances and relationships, and produce a markedly elevated risk for suicide.

As discussed in this paper, primary care physicians (PCPs) have a unique and wide-ranging role in the care of patients with bipolar disorder because PCPs frequently are the first to identify patients with bipolar disorder and to refer them to specialist mental health services. Following establishment of a care plan, PCPs may be the only healthcare professionals in regular contact with patients during their long-term care, particularly in terms of monitoring their wider healthcare needs. A number of guidelines have been produced to better inform healthcare professionals on the diagnosis and treatment of patients with bipolar disorder. This article reviews current understanding of the optimal management of bipolar disorder based on recent research and guidelines, with particular reference to the diverse role of PCPs.

Keywords: to come?

The burden of bipolar disorder

Bipolar disorder is a serious, lifelong illness characterised by recurrent manic and depressive mood episodes interspersed with periods of more normal mood. The episodes of manic or depressive symptoms may persist for weeks or months and be of sufficient severity to affect employment, finances, and relationships, while placing considerable burdens on family and other caregivers.[1–3] Illustrating this, 73% of patients participating in a US survey reported problems at work or school, 55% financial difficulties, and 80% difficulties in relationships.[4] Concurrent physical health problems were reported by 46%, and 37% described alcohol or substance abuse.[4] The burden from the symptoms of bipolar disorder contributes to an elevated risk of suicide, reported in some studies as up to 15%.[5]

As may be expected, the economic burden to society is enormous. NHS costs of managing bipolar disorder have been estimated at £199 million annually, while indirect costs due to unemployment, absenteeism, suicide, and caregiver costs, while only roughly quantifiable, may reach £2055 million each year.[6]

Diagnosis of bipolar disorder

Bipolar disorder is relatively common in the community, with a lifetime prevalence up to 3.7% according to a large screening survey utilising the Mood Disorder Questionnaire.[7–10] Despite this high prevalence, awareness of bipolar disorder remains low among healthcare professionals, including primary care physicians (PCPs). Although patients with

bipolar disorder typically experience both manic and depressive symptoms over time, they most usually present to their PCP during a depressive episode.[11–13] The reason may be that episodes of depression are more frequent and of longer duration than episodes of mania (see Figure 1).[14] Another explanation is that, in contrast to depressive episodes, milder manic symptoms may not be considered a problem.[17] For the same reason, it may be difficult to obtain a history of manic episodes in order to confirm the diagnosis, and for this enlisting comments from a family member may help.[18,19]

During a depressive episode of bipolar disorder, the symptoms may mistakenly be attributed to unipolar depression.[11,20–23] In confirmation of this, a large survey questioned 600 patients with bipolar disorder in 1992 and found that 73% had initially been misdiagnosed.[4] A repeat of the survey in 2000 indicated little improvement, as 69% of patients with bipolar disorder were initially misdiagnosed, typically with 3–4 incorrect diagnoses prior to the correct one. Before establishing the final diagnosis of bipolar disorder, physicians who were approached by patients with bipolar symptoms included a psychiatrist (62%) or a physician, family doctor or obstetrician/gynaecologist (54%). In the 2000 survey, patients consulted a mean of four physicians before receiving an accurate diagnosis. Unipolar depression was the most common misdiagnosis (60%), followed by anxiety disorder (26%) and schizophrenia (18%). Some misdiagnosis is inevitable in the early stages of any psychiatric illness, because some symptoms are non-specific. Accordingly, it remains unclear how far the reported delay experienced by patients can reasonably be expected to fall, but the failure to see a larger change in the intervening period is disappointing, given efforts to increase awareness among health professionals.

Despite the similarity in symptoms between unipolar depression and bipolar depression, establishing the correct diagnosis is important because different treatments are recommended for the two disorders. Patients with unipolar disorder are usually treated initially with an antidepressant.[24,5] For patients with bipolar depression, however, this approach is not advised because there is the potential risk that antidepressant monotherapy may induce a manic episode,[25–27] or accelerate mood cycles.[22,28]

Besides unipolar depression, bipolar disorder must be distinguished from a number of alternative diagnoses such as psychotic disorders, attention deficit hyperactivity disorder, conduct disorder, antisocial personality disorder, and borderline personality disorder, mood disorder due to a general medical condition (e.g. multiple sclerosis, stroke, hypothyroidism, or brain lesion), and substance-induced mood disorder (e.g. due to drug or alcohol abuse). Patients with bipolar disorder very frequently suffer comorbidities including anxiety disorders, substance abuse disorders, and personality disorders, and these may complicate diagnosis as well as treatment.[23,27]

A number of diagnostic tools have been developed to assist healthcare professionals to identify bipolar disorder based on its characteristic symptoms. The recent National Institute for Health and Clinical Excellence (NICE) guideline recommends that patients should be suspected to have bipolar disorder if they exhibit either of the following: (1) periods of overactive, disinhibited behaviour lasting $\geq$4 days with or without periods of depression; (2) $\geq$3 recurrent depressive episodes in the context of a history of overactive, disinhibited behaviour.[27] Patients exhibiting these symptoms should be referred to specialist care, and this is essential if the symptoms are so severe as to pose a risk to self or others.

Patients with an established diagnosis of bipolar disorder should be considered for specialist referral in the event of an acute exacerbation of manic or depressive symptoms or an increase in risk to self or others while on therapy. Other reasons for specialist review are the presence of comorbid alcohol or drug dependence and a patient's expressed intention to stop medication after successful mood stabilisation.[27]

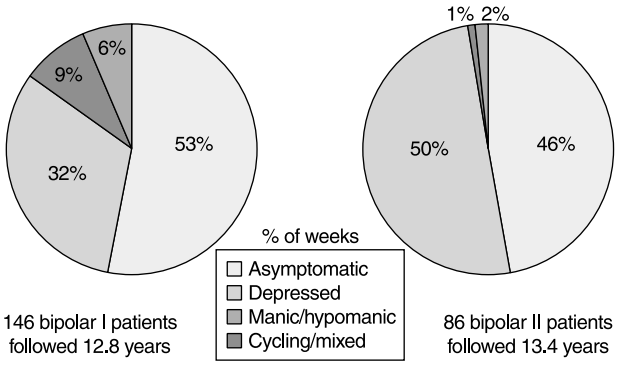

Figure 1 Patients with bipolar disorder (I or II) spend longer periods in the depressive phase than in the manic phase of the illness[15,16]

Confirmation of a diagnosis of bipolar disorder is typically based on criteria such as those in the *International Classification of Disease-10* (ICD-10) or the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV).[29,30] The ICD-10 and the abbreviated version for primary care physicians (ICD-10 PHC) are produced by the World Health Organization and often used in Europe, while the DSM-IV is by the American Psychiatric Association and is widely used in the USA[29]. Although broadly similar, the ICD-10 and DSM-IV do differ in definitions of manic and depressive episodes, as described in Table 1.[29,30,32]

Classification of bipolar disorder

Following a diagnosis of bipolar disorder, patients are typically classifiable into subtypes. Allocating patients to the appropriate category is important because there is evidence that different categories are associated with different courses of illness and responses to treatment.[3]

The DSM-IV recognises the subtypes: bipolar I, bipolar II, cyclothymic disorder, and bipolar disorder not otherwise specified (NOS). Bipolar I disorder is characterised by a history of manic or mixed episodes. Depressive episodes may have occurred but they are not required for allocating patients to the bipolar I category. Bipolar II disorder requires a history of depressive episodes and at least one episode of hypomania. Cyclothymic disorder requires a history of hypomanic episodes intermingled with depressive episodes that do not meet full criteria for major depressive episodes. Patients not meeting the criteria for any of the other subtypes receive a diagnosis of bipolar disorder NOS.[30]

The ICD categorises bipolar disorder in a different manner and generates more categories than the DSM, based on the characteristics described in Table 1: current episode hypomanic, manic without psychotic symptoms, manic with psychotic symptoms, mild or moderate depression, severe depression without psychotic symptoms, severe depression with psychotic symptoms, mixed, in remission, other bipolar affective disorders, and unspecified.[29,30,32] There is little research that has made the ICD distinctions useful.

Treatment of bipolar disorder

The management of bipolar disorder has conventionally been based on medications including lithium (see Box 1), anti-epileptics such as valproate, and typical antipsychotics including haloperidol. Based on recent trial evidence, the pharmacological options in bipolar disorder have expanded to include the atypical antipsychotics and additional anti-epileptics.[33] The atypical antipsychotics (including olanzapine, risperidone, quetiapine, aripiprazole and ziprasidone) have been associated with improved safety and tolerability profiles compared with typical antipsychotics, but side-effects associated with some of the newer agents, such as weight gain and metabolic disturbance, should be taken into consideration when formulating a patient's treatment plan.[27,33] The characteristic properties of medications commonly used in the treatment of bipolar disorder are summarised in Table 2.

Based on these properties, a number of guidelines have been developed to advise on optimal therapy in bipolar disorder, including those produced by BAP[26,54] and, more recently, NICE.[27] All guidelines emphasise that medication choice should be influenced by the patient's current status preferences as well as responses to previous treatments.

For the treatment of acute mania there are extensive data in support of a range of medication choices. Recommendations by NICE for the treatment of acute mania are summarised in Table 3.

Treatment choices for acute bipolar depression are not as well defined as those for acute mania, in part because there are fewer medications with proven efficacy, and recommendations in guidelines frequently differ. Recommendations for bipolar depression from the NICE guideline are summarised in Table 4. As mentioned above, it is advised that antidepressant therapy is used with caution in patients with depressive symptoms of bipolar disorder and should not normally be given to those with rapid cycling (i.e. with four or more mood episodes in a year), a recent hypomanic episode, or recent rapid mood fluctuations accompanied by functional impairment because of elevated risk of symptom exacerbation.

Bipolar disorder is a chronic relapsing and remitting condition, and patients require long-term treatment to maximise functioning and quality of life and reduce the likelihood of relapse. Recommendations for long-term therapy from the NICE guideline are summarised in Table 5.[27] The recommended duration of long-term therapy is two or more years after an episode of bipolar disorder and five or more years if risk factors for relapse persist. These risk factors include a history of frequent relapses, severe psychotic episodes, substance abuse, stressful life events, and poor social support. Patients who decline while receiving long-term medical therapy should be regularly reassessed.[27]

Medical therapy is frequently supplemented with psychological and psychosocial interventions as

Table 1 Characteristics of manic, hypomanic, depressive, and mixed episodes of bipolar disorder

DSM-IV criteria[30]	ICD-10 criteria[29]
Manic episode	
• Abnormally and persistently elevated, expansive, or irritable mood lasting ≥1 week • ≥3 of the following (4 if the mood is irritable): – inflated self-esteem or grandiosity – decreased need for sleep – more talkative than usual or pressure to keep talking – flight of ideas or racing thoughts – distractibility – increase in goal-directed activity or psychomotor agitation – excessive involvement in pleasurable activities with high risk for negative consequences • Symptoms not caused by medication, drug abuse, or other treatment or by a general medical condition • Psychotic features (in some severe cases) • Mood-congruent: delusions or hallucinations consistent with manic themes • Mood-incongruent: persecutory delusions, thought insertions, and delusions of being controlled	• Without psychotic symptoms: mood elevation out of keeping with circumstances – mood varies from carefree joviality to almost uncontrollable excitement – increased energy resulting in overactivity, pressure of speech, and decreased need for sleep – attention cannot be sustained; marked distractibility – inflated self-esteem with grandiose ideas and overconfidence – loss of normal social inhibitions which may lead to reckless, foolhardy, or inappropriate and out-of-character behaviour • With psychotic symptoms: – symptoms as above along with delusions (usually grandiose) or hallucinations (usually voices speaking directly to patient) – excitement, excessive motor activity, and extreme flight of ideas making patient incomprehensible or inaccessible to ordinary communication
Hypomanic episode • A distinct period of persistently elevated, expansive, or irritable mood lasting ≥4 days • ≥3 symptoms listed for the manic episode (4 if the mood is only irritable) • Episode is associated with an unequivocal and uncharacteristic change in functioning observable by others • Episode is not severe enough to cause significant impairment in social or work functioning, does not necessitate hospitalisation, and there are no psychotic symptoms • Symptoms not caused by medication, drug abuse, or other treatment or by a general medical condition	• Persistent mild elevation of mood, increased energy and activity • Over-familiarity, increased sexual energy, and decreased need for sleep but not to the extent that it disrupts work or social interactions • Irritability, conceit, and boorish behaviour may be present instead of euphoric sociability • Absence of hallucinations or delusions
Depressive episode • ≥5 of the following during the same 2-week period (≥1 symptom must be depressed mood or loss of interest or pleasure; symptoms must be present nearly every day): – depressed mood most of the day – diminished interest or pleasure in all or almost all activities of the day significant weight loss when not dieting or weight gain or increase or decreased in appetite – insomnia or hypersomnia – psychomotor agitation or retardation – fatigue or loss of energy – feelings of worthlessness or excessive or inappropriate guilt – diminished ability to think or concentrate or indecisiveness	• Lowered mood, reduced energy, and decreased activity • Reduced capacity for enjoyment • Reduced concentration • Easily fatigued • Sleep disturbances • Reduced self-esteem and self-confidence and some ideas of guilt or worthlessness often present • Mood varies little from day to day and is unresponsive to circumstances • Somatic symptoms may be present: loss of interest and pleasurable feelings, early awakening, worsening of depression during morning hours, marked psychomotor retardation, agitation, loss of appetite and weight loss, loss of libido

Table 1 Continued

– recurrent thoughts of death, recurrent suicidal ideation, specific plan for committing suicide, or a suicide attempt – symptoms cause significant distress or impairment in social or work functioning • Symptoms not caused by medication, drug abuse, or other treatment or by a general medical condition	
Mixed episode • Patient meets criteria for both a manic episode and a major depressive episode nearly every day for ≥1 week • Mood disturbance causes significant impairment in social or work functioning or necessitates hospitalisation, or psychotic features are present • Symptoms not caused by medication, drug abuse, or other treatment or by a general medical condition	• A mixture or a rapid alteration of manic and depressive symptoms

Box 1 Lithium use in bipolar disorder – recommendations from the NICE guideline[27] and British Association for Psychopharmacology (BAP) guideline[26]

Lithium remains a medication used in the management of bipolar disorder, frequently as a component of combination therapy. Lithium may be effective, but requires careful monitoring because of potentially toxic effects at high serum concentrations (see Table 2). Patients should be warned that careful compliance to lithium therapy is critical for efficacy and safety. Dehydration may elevate serum lithium concentrations and patients should be cautioned to ensure that fluid intake is maintained during episodes of diarrhoea or vomiting or under circumstances of excessive sweating (due to fever, exercise, or in hot climates). Warning signs for neurotoxicity from lithium include paraesthesia, ataxia, tremor, and cognitive impairment. Readers are referred to NICE[27] and BAP[26] guidelines for a more detailed discussion. While general practitioners typically do not initiate lithium therapy, their responsibility in shared care may include monitoring for abnormal symptoms, adverse effects, and changes in serum levels as described below, and seeking specialist support in cases of abnormalities.

Initiating lithium

- BAP advises that the highest dose that produces minimal side-effects should be employed.
- NICE suggests that target serum lithium levels should be between 0.6 and 0.8 mmol/l over at least six months (assessed weekly at initiation and every dose change until levels stabilise). For patients who have relapsed previously on lithium or continue to experience subthreshold symptoms, serum levels between 0.8 and 1.0 mmol/l may be considered.

Monitoring lithium, other measures

- Serum lithium levels should normally be monitored every three months.
- Monitoring of lithium levels should be more frequent in the presence of clinical deterioration, abnormal results, elevation in urea or creatinine levels, or change in risks factors (e.g. initiation of angiotensin-converting enzyme (ACE) inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), or diuretics).
- Older patients require close monitoring for symptoms because of increased susceptibility to lithium toxicity.
- Serum urea and creatinine should be measured every six months.
- Thyroid and renal function tests should be performed every six months.

Stopping lithium

- BAP advises that lithium should be reduced only after complete remission of symptoms and preferably after eight or more weeks of euthymia.
- Lithium should be stopped gradually, preferably over a period of up to three months, to reduce the risk of relapse.

Table 2 Medications used to treat patients with bipolar disorder

Benefits	Drawbacks
Lithium	
• A long history of clinical use (≥50 years) for bipolar disorder[34] • Effective for treatment of pure mania[35] • Beneficial for bipolar depression[35] • Long-term use can prevent mood episode recurrence and reduce suicide risk[35]	• About half of patients do not respond fully to monotherapy[36] • Adverse events: tremor, weight gain, cognitive dysfunction, sedation/lethargy, impaired co-ordination, gastrointestinal distress[36]
Valproate	
• Efficacy for mania similar to that for lithium[37] • Effective for treating bipolar depression[37]	• Efficacy for mania not as good as that of olanzapine[37] • Not as effective as lithium for bipolar depression[34] • Not to be used in female patients of child-bearing potential[27] • Adverse events: sedation, gastrointestinal distress, hair loss, increased appetite, and weight gain[36]
Lamotrigine	
• Increasing role in bipolar depression, especially for preventing recurrence[35,38,39] • May be effective for rapid cycling[35]	• Slow dose titration necessary to avoid rash[38] • Adverse events: headache, nausea, infection, dry mouth[36] • Small risk for serious rashes (particularly when combined with valproate) including Stevens–Johnson syndrome[36]
Carbamazepine and oxcarbamazepine	
• Carbamazepine is effective in acute mania and may be modestly effective in bipolar depression[40] • Patients unresponsive to lithium or valproate may respond[36] • Oxycarbamazepine is better tolerated than carbamazepine[41]	• Adverse events: agranulocytosis, aplastic anaemia[36] • Potential drug interactions via potent induction of CYP 3A4 enzymes • Drug interactions with oral contraceptives necessitating higher estrogen doses Efficacy for bipolar disorder is poorly documented[41] Drug interactions with oral contraceptives necessitating higher oestrogen doses[41]
Antidepressants	
• May be useful for bipolar depression[27]	• Monotherapy to be avoided because of the risk for treatment-emergent mania and cycle acceleration[32] • Tricyclics appear to pose a greater risk for disease destabilisation than SSRIs[34]
Atypical antipsychotics	
• Quetiapine, olanzapine, and risperidone are currently approved for treatment of acute mania in the UK.[27] Ziprasidone and aripiprazole are also approved in other countries • Can be combined with valproate or lithium for greater efficacy[42–44] • Efficacy of quetiapine and olanzapine as monotherapy for bipolar depression demonstrated in 8-week, placebo-controlled trials[45–47]	• Metabolic side-effects are under investigation[48] • Risk for weight gain, diabetes and dyslipidemia probably greatest with olanzapine and clozapine[48] • Quetiapine side-effects: sedation[49] • Risperidone side-effects: prolactin elevation and dose-related extrapyramidal symptoms[50,51] • Ziprasidone side effects: QTc prolongation[52] • Aripiprazole side effects: akathisia[53]

SSRI, selective serotonin reuptake inhibitor

Table 3 Treatment for acute mania – recommendations from the NICE guideline[27]

Recommended agents	Relevant clinical situation and additional information
Patients not currently taking an antimanic agent	
• Atypical antipsychotic: olanzapine, quetiapine, or risperidone	• Choice reflects risk factors for side-effects • Augment with valproate or lithium in patients with severe symptoms or behavioural disturbances
• Lithium	• Use in patients with previous good response and compliance • Do not use in patients with severe symptoms because of the slow onset of action
• Valproate	• Use in patients with previous good response and compliance • Not recommended for female patients of child-bearing potential
• Benzodiazepines	• Use as short-term add-on therapy in patients with acute behavioural disturbances or agitation
Current agent	**Recommended action**
Patients currently using an antimanic agent who experience a manic episode	
• Atypical antipsychotic	• Check dose and increase if necessary • Augment with valproate or lithium
• Lithium	• Check plasma lithium level – if below 0.8 mmol/l, increase dose to reach a maximum plasma level of 1.0 mmol/l • If mania is severe, consider adding an atypical antipsychotic while slowly increasing lithium dosage
• Valproate	• Increase dosage until symptoms improve or side-effects limit further increases • Consider adding an atypical antipsychotic if there are no signs of improvement or if mania is severe
• Carbamazepine	• Do not routinely increase dose • Consider adding an atypical antipsychotic • Investigate possible interactions with other agents

components of long-term care. As pointed out in the NICE guidelines, patients who may benefit most from these interventions are typically stable after an acute episode but with residual mild-to-moderate affective symptoms. Psychological therapy includes education about the nature of bipolar illness, how to monitor mood and detect early warning signs, and methods to prevent progression of episodes. The importance of adherence to medical therapy and the role of a regular daily routine with adequate sleep are also emphasised. Psychological therapy, administered by trained therapists, has normally continued over at least 16 sessions (i.e. six to nine months) in controlled studies.[27]

Family therapy courses over periods of approximately nine months have shown benefits in improved depressive symptoms, reduced recurrence and hospitalisation rates, and greater medication adherence. Family therapy may be particularly beneficial for patients from families with high expressed emotion. Finally, user groups can provide useful support and information about bipolar disorder and its treatment. A useful overview of psychological interventions in bipolar disorder is provided by Culver *et al*.[55]

Continuing care and the role of the PCP

The National Service Framework (NSF) *for Mental Health* provided a structure for the provision of services to patients with psychiatric illnesses in the UK.[56] The NSF stipulates that most mental health care be provided in the primary care setting, within

Table 4 Treatment for bipolar depression – recommendations from the NICE guideline[27]

Recommendation	Additional information
Patients not taking antimanic agent[a]	
• Patients currently taking an antidepressant should be prescribed an antimanic drug[a] • Antidepressant agents should be used with caution	• Choice of antimanic drug should reflect side-effects and whether the patient is a woman of child-bearing potential • Antidepressants should be avoided when there are symptoms of: – rapid cycling – recent hypomanic episode – recent functionally impairing rapid mood episodes • Patients should be informed of the risk of switching to mania and the benefits of combining therapy with an antimanic agent • Patients unwilling to use an antimanic agent must be carefully monitored • Treatment should be initiated at a low dose and increased slowly if necessary
Patients taking an antimanic agent who experience a depressive episode[a]	
Recommended actions • Verify that the agent is being taken at the appropriate dose • Adjust dose if necessary	
Patients with mild depressive symptoms	
Recommended actions • Assess patient within 2 weeks of symptom onset if: – previous bipolar depression did not become severe or chronic – the patient is not at risk for severe depression	
Patients with moderate-to-severe depressive symptoms	
Recommended agents	Relevant clinical situation and additional information
• SSRI antidepressant	• SSRIs are considered to pose a lower risk for switch to mania than tricyclic antidepressants • Paroxetine is not to be used in pregnant women
• Add-on therapy with quetiapine	• For patients already taking an antimanic agent that is not an antipsychotic

[a] The NICE guideline utilises the term 'antimanic' to include agents with antidepressive activity in bipolar disorder
SSRI, selective serotonin reuptake inhibitor

the context of a multidisciplinary team that includes specialist care and support from social service agencies. Unipolar depression and schizophrenia received specific attention in the NSF, while the service needs of patients with bipolar disorder were largely neglected.[57,58]

The recent NICE guideline represents the most comprehensive direction on the care of patients with bipolar disorder in the UK to date, including diagnosis, treatment, pathways to care, and monitoring of physical health. NICE also explores the responsibilities of the PCP. However, these recommendations are essentially formulaic. They are not based on a pragmatic investigation of what works best for bipolar patients.

Table 5 Long-term treatment for patients with bipolar disorder – recommendations from the NICE guideline[27]

Drug choices	Additional information
General recommendations • Lithium • Olanzapine • Valproate	Choice reflects: • response to previous therapy • relative risk of mania versus depression • physical risk factors (e.g. obesity, diabetes, renal disease) • patient preference and adherence history • sex – valproate should be avoided in women of child-bearing potential in the elderly, a brief assessment of cognitive function
Choices	**Additional information**
Patients with frequent relapses or continuing symptoms causing functional impairment • Switch to different monotherapy • Add-on therapy with a second agent	Possible combinations: • Lithium + valproate • Lithium + olanzapine • Valproate + olanzapine Requires close monitoring of clinical state, side-effects and blood levels (in the case of lithium)

Integrated programmes to co-ordinate primary and secondary care are recommended for managing all patients with bipolar disorder. These programmes should establish individual responsibilities among primary and secondary care team members, provide regular reviews of the patient's mental state and personal and social functioning, include detailed protocols for provision of pharmacological, psychosocial and psychological interventions, and provide written treatment plans to promote self-management by the patient.[27]

Fundamental to the principles of patient-centred care is establishing and maintaining a treatment alliance between physician, patient, and family. Through education and discussion, patients and caregivers can gain awareness of the importance of adherence to medical therapy, the role of stressors and sleep disturbance in relapse, and early warning signs of relapse.[27,59] Participation in self-help groups can provide valuable information and support to patients, particularly at first diagnosis.

Based on revisions to the general medical services contract for PCPs in the UK for 2006–2007, all patients who are registered in general practice with a diagnosis of bipolar disorder (i.e. ICD-10 code F31 or Read code Eu31 – discussed above) are to be included in a register for severe mental illness. In addition, a comprehensive care plan must be established for each patient that includes details on current health status and social care needs, social support from family and other caregivers, occupational status, early signs of relapse from the patient's perspective, the course of action in case of relapse, and the co-ordination arrangements with secondary care.

Referral to secondary care is advised for patients who experience frequent relapses or inadequate symptom control, pose a danger to themselves or others, are unable to adhere to treatment plans, or have chronic alcohol or substance-abuse problems.

In part as a consequence of the burden of bipolar disorder symptoms, the physical health of patients is frequently overlooked or is managed suboptimally.[27] Poor physical health reflects, in part, the lifestyle and habits, as well as symptoms of patients with bipolar symptoms, such as greater risk taking during manic episodes and increased sedentary behaviour during depressive episodes, although a range of other medical conditions present more frequently than in the general population.[60–62] Cardiovascular risk factors or diseases occurring at elevated incidences include hypertension, dyslipidaemia, and diabetes.[60,63,64] Pulmonary conditions such as asthma and chronic obstructive pulmonary disease are also recorded at higher rates.[4,60] Migraine is twice as common in patients with bipolar disorder as in the general public.[65] The reason for these elevated incidences of comorbidity is not entirely clear, but they certainly contribute to the burden of disease and increase mortality.[66,67] Screening for physical comorbidities is therefore appropriate, such as annual checks on blood pressure, pulse, cholesterol levels, blood glucose or urinalysis, peak flow rates and body mass index. Hyperprolactinaemia secondary to the use of neuroleptics is also a growing concern and, in

addition, the use of anticonvulsants is associated with metabolic bone disease. It is appropriate to offer advice on diet, cessation of smoking and substance abuse, and avoidance of risk-taking behaviour that elevates the likelihood of HIV and hepatitis B infection.[68]

Although all healthcare professionals take responsibility for monitoring the physical health of patients with bipolar disorder, PCPs play a pivotal role in long-term management and monitoring, including the effects of medications. Initial assessments should include measurements of vital signs, height, and weight, a full blood count, blood glucose level, serum lipid profile, thyroid, liver, and renal function, smoking status, and alcohol use. Drug screening should also be considered if indicated by the patient's history or clinical presentation. NICE recommendations for follow-up monitoring include annual measurements of lipid profile, glucose levels, weight, smoking status, alcohol use, and blood pressure. Additional follow-up requirements reflect the medications chosen. Recommendations derived from the NICE guideline are shown in Table 6.

Table 6 Follow-up monitoring according to medication – recommendations from the NICE guideline[27]

Test or measurement	Antipsychotics	Lithium	Valproate	Carbamazepine
Thyroid function		At start and every 6 months, more often if evidence of deterioration		
Liver function			At start and at 6 months	At start and at 6 months
Renal function		At start and every 6 months, more often if evidence of deterioration or drugs such as ACE inhibitors, diuretics or NSAIDs are started		Urea and electrolytes every 6 months
Full blood count		Only if clinically indicated	At start and 6 months	At start and at 6 months
Blood (plasma) glucose	At start and 3 months (and 1 month for olanzapine), more often if evidence of elevated levels			
Lipid profile	At start and at 3 months, more often if evidence of elevated levels			
Prolactin	Risperidone only: at start and if symptoms of raised prolactin develop			
ECG	At start if risk factors for or existing cardiovascular disease	At start if risk factors for or existing cardiovascular disease		

Table 6 Continued

Weight and height	At start and every 3 months for first year, more often if patient gains weight rapidly	At start and when needed if patient gains weight rapidly	At start and at 6 months if patient gains weight rapidly	At start and at 6 months if patient gains weight rapidly
Serum levels of drug		1 week after initiation and 1 week after every dose change until levels stable, then every 3 months	If evidence of ineffectiveness, poor adherence or toxicity	Every 6 months

ACE, angiotensin-converting enzyme; ECG, electrocardiogram; NSAID, non-steroidal anti-inflammatory drug

Conclusions

PCPs are at the frontline of care for patients with bipolar disorder. The recent recommendations from NICE on diagnosis and management incorporate recent findings on medications newly investigated in bipolar mania and bipolar depression and an increased understanding of the need for behavioural change by patients themselves. These conceptual and practical advances promise to enhance care, with significant benefits for the outcome of patients with bipolar disorder. However, the recommendations from NICE increase the responsibilities of PCPs without a clear basis for their preferred service model, which is largely borrowed from that recommended in schizophrenia. While this poses problems, it is also an opportunity to think creatively about the form ideal services should take and how the expertise required to look after a complicated illness can be nurtured and shared. Service delivery for bipolar patients should assume an increased priority for health services research.

ACKNOWLEDGEMENTS

We thank Bill Wolvey, BSc (PAREXEL MMS), who provided medical writing support on behalf of AstraZeneca.

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CONFLICTS OF INTEREST

None.

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