

RECOGNISING BIPOLAR DISORDERS IN PRIMARY CARE

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SUMMARY

Bipolar disorder, previously called 'Manic-depression', is a complex group of conditions characterised by recurrent changes in mood and energy. Crucially, the intensity and duration of these changes go beyond normal fluctuations and personality traits. Bipolar Disorder is a mental health disorder, but physical health manifestations (Smith 2013, Westman 2013, Fagiolini 2008, Young 2013) and complications are just as important. GPs have a key role in the recognition and management, in conjunction with secondary care colleagues.

Diagnosis is often difficult and may take several years (Smith 2011, Angst 2005, Manning 2010), because patients usually seek help for anxiety, depression or fatigue, not hypomania/mania, which they may not recognise. Individuals with a first episode of mania are more likely to present directly to secondary care, sometimes via a third party alerting the emergency services.

There is also debate around the classification, diagnosis and treatment of individuals with brief and milder mood changes ('bipolar spectrum disorder') (Faravelli 2009, Spence 2011). In the UK, the recent NICE Guidelines (2014) 1 only included Bipolar I and Bipolar II for these reasons.

A particular challenge for GPs is that whilst most people who have Bipolar Disorder (and especially Bipolar II) are depressed, most people with depression within a Primary Care setting do not have Bipolar Disorder.

Thus, a brief pragmatic screen is recommended in Primary care: ask about a family history of Bipolar Disorder and screen for a history of mania/hypomania in individuals with anxiety, depression or irritability, especially if there are recurrent episodes, suicidal thoughts or a previous suicide attempt. For suspected cases, formal diagnosis should not be made within Primary Care but individuals should be referred for Psychiatric assessment, ideally to a Mood Disorders specialist.

Key words: Bipolar Disorder - Primary Care

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INTRODUCTION

Brief historical Background

Mania and severe depression were recognised in antiquity. Esquirol (1819) characterised 'melancholia and mania' and in 1899 Kraepelin (Kraepelin 1899) conceptualised 'manic depressive insanity'. The term 'Bipolar Disorder' was used by Neele (1949) & Leonhard (1957). Cade (1949) and Schou (1954) demonstrated the efficacy of lithium in mania. In 1976, Dunner et al. (Dunner 1976) first formally described Bipolar II: recurrent severe depression interspersed with periods of hypomania. Crucially, in contrast to patients with unipolar depression, individuals with Bipolar II had a family history of bipolar disorder, a severe illness course and a far higher suicide rate – even higher than BD-I (Dunner 1976).

This classification is complex but important because there are key management and prognostic differences between the subtypes of Bipolar Disorder, the predominant symptom ('pole') of the illness at the time and whether the context is acute or prophylactic treatment. However there remain areas of uncertainty in both diagnosis and treatment.

Classification

Bipolar Disorder is classified as Bipolar I (mania and depression, previously 'manic-depression') and Bipolar II (hypomania and depression). Some individuals with Bipolar I may develop psychosis, when manic or depressed. Diagnostic criteria (see abbreviated

selected criteria, table 1) are ICD-10 (WHO 2010) (being updated to ICD-11) and DSM5 (American Psychiatric Association 2015) (used clinically in the USA and in most research studies). An important feature of hypomania and mania, recently recognised in DSM5, is an increase in energy levels.

In both of these subtypes, some individuals experience 'mixed' states, with concurrent mania/hypomania and depression. Mixed states are associated with impulsivity and a high suicide risk (Benazzi 2007, Akiskal 2005, McElroy 2006, Benazzi 2005). Diagnosing bipolar disorder in children is controversial and UK guidance (NICE 2014) is conservative.

There is debate regarding whether patients with brief hypomania (less than 4 days) and less severe depressive symptoms (including Cyclothymia and so called 'subthreshold bipolar' or 'Bipolar Spectrum') should be diagnosed and treated as Bipolar Disorder (Vieta 2008, Ghaemi 2004, Pies 2007, Akiskal 2000, Angst 2005, Faravelli 2009).

Patient numbers in Primary Care

An average UK GP with a list size of ~ 1600 will have about 16 patients with Bipolar I (~ 1% prevalence) and 16-32 with Bipolar II (1-2%) (Smith 2011, Merikangas 2011, Merikangas 2010, Angst 2011). Importantly, a proportion (perhaps 5-20%) of those with recurrent 'unipolar' depression or treatment resistant depression may also have bipolar disorder (typically Bipolar II) (Smith 2011).

Table 1. Abbreviated and selected diagnostic criteria (after DSM5). See ICD-10 and DSM5 for full details

<i>Mania (Bipolar I disorder)</i>	
A sudden change from normal behaviour, with increased energy, irritability and goal-directed behaviour, lasting more than 7 days or needing hospitalisation. With:	
3 (or more) of the following symptoms (4 if the mood is only irritable)	Comment, examples
Reduced need for sleep	Waking after only a few hours sleep, but feeling full of energy
Flight of ideas or a feeling that thoughts are racing	
Increased speech/pressure of speech	Puns and jokes, which may be inappropriate. Difficult to interrupt, speech may be so fast as to be unintelligible.
Inflated self esteem or grandiosity	A normally quiet individual becoming overly confident and acting inappropriately
Involvement in pleasurable activities with resultant harms	Overspending, unwise business ventures, sexual indiscretions
Increase in goal-directed activity or psychomotor agitation	Muti-tasking, hyper-focused
Distractibility	Can't concentrate - tasks started but not completed
<i>Hypomania</i> has the same symptoms as mania, but they do not significantly interfere with function. Hypomania may occur in both Bipolar I and Bipolar II, but mania only occurs in Bipolar I.	
<i>Bipolar II</i> can only be diagnosed if hypomania lasts more than 4 days, with recurrent major depression.	

Symptoms

Bipolar Disorder typically starts in adolescence, with low mood, anxiety/depression, fatigue, mood swings, and/or irritability. These features may evolve over several years and at some point, an escalation to the first obvious (so called 'index') episode may occur. This is typically mania or hypomania, though may be severe depression. Triggers to an 'episode' (there may be none) include stress, sleep deprivation, antidepressants, steroids, substance misuse, pregnancy and the post-partum, jet lag and seasonal changes.

Recurrence and prognosis is highly variable: some individuals may only suffer occasional episodes and be relatively well in between, but others may have frequent 'cycling', on-going 'subthreshold' symptoms or persistent, severe treatment resistant symptoms requiring multiple medications and long periods in hospital.

The psychological impact of Bipolar Disorder is of great importance. Given that Bipolar Disorder affects individuals in the prime of their lives, many mourn for the loss of their 'self' and unfulfilled promise.

Complications

Premature cardiovascular disease (Smith 2013, Westman 2013), suicidality and functional impairment (including fatigue, cognitive difficulties, sick leave, financial loss and relationship difficulties) are important. The risk of suicide is >20x the general population (Tondo 2003, Rihmer 2002). Mixed symptoms (depression + mania/hypomania) are common and increase the risk of suicide (Benazzi 2007, Akiskal 2005). Lifespan may be reduced by around 10 years on average, but correct diagnosis and management improves lives and reduces cardiovascular risk and suicide.

Does an accurate diagnosis matter?

Yes: a delay in the diagnosis and management of Bipolar Disorder can have serious consequences including increased depressive and manic symptoms as well as a poorer quality of life (Gazalle 2005).

Is Bipolar Disorder over-diagnosed?

Mania is usually a straightforward diagnosis, but the diagnosis of Bipolar II and 'Bipolar Spectrum Disorder' has been debated both in the medical literature and in the wider media. Although diagnostic criteria have evolved in recent years (Angst 2005, Angst 2011, ECNP 2007) there are still no reliable biomarkers. However, provided that meticulous assessment is carried out, there is good evidence that Bipolar II is under-recognized, undertreated and mistreated (typically with antidepressants) (Angst 2005, Angst 2011, Rihmer 2005, Merikangas 2010, Young 2011). This matters because of the high suicide rate of Bipolar Disorder and differences in treatment compared to unipolar depression.

It may be helpful to view this debate in the context of the wider discussion around the possible over-diagnosis of depression per se, an increase in antidepressant prescriptions (Moscrop 2012) and debate around efficacy and appropriateness of psychopharmacology. Added to this are problems with the accuracy of diagnostic tools in medicine (Barracough 2012) and increasing evidence of the harmful effects of over-investigation and over-diagnosis in medicine as a whole (Moynihan 2012). Thus a pragmatic approach to a suspected diagnosis of Bipolar Disorder would be advocated: it matters most where there is unexplained functional impairment and distress.

Not all mood swings are Bipolar Disorder

Mood swings are not a diagnostic term and may occur in many situations e.g. adolescence, menstrual cycle changes, the menopause, anxiety disorders, ADHD, in organic brain syndromes (e.g. fetal alcohol syndrome, multiple sclerosis, Parkinson's disease, frontal lobe tumours, dementia) personality disorders and following a head injury.

Borderline Personality Disorder (BPD) is a complex entity that is sometimes confused with Bipolar Disorder (Paris 2012). Some patients may be diagnosed with both and it has been suggested that BPD may be part of the Bipolar Spectrum (Smith 2004). Advances in neuroscience, imaging and genetics may clarify this issue. Key differences (Parker 2011) are that patients with BPD have rapidly unstable emotions and impulsivity, and do not have severe depression or hypomania. Individuals with BPD respond poorly to medication but may be helped by behavioural therapy.

MAKING A DIAGNOSIS

Diagnosing Bipolar Disorder is usually challenging and may take several years

GPs have a key role in recognising possible Bipolar Disorder, utilising the test of time that is so important in Primary Care. This is important, because GPs will see many patients with fatigue, low mood or anxiety, fewer with major depression and fewer still with bipolar disorder. However, if treated as apparent unipolar depression, antidepressants can be ineffective or harmful (Spence 2011, Esquirol 1819, Kraepelin 1899, Neele 1949).

GPs should be aware of an important diagnostic paradox: anxiety, depression and fatigue are the commonest symptoms of Bipolar Disorder, but the diagnosis rests on the presence of mania or hypomania. This side of

Bipolarity may only be apparent in retrospect, or via a third party, because individuals would be unlikely to see their GP if they felt energised, euphoric and not needing sleep. However, irritability (common in depression, hypomania, mania and mixed states) and persistent insomnia (especially middle insomnia, waking with irritable restlessness) may result in relationship and employment issues, leading to a visit to the GP.

From a consultation perspective, the irritability of individuals with hypomania/mania (especially if the diagnosis is unrecognised) may prove challenging. GPs should be aware of 'projective identification' and its effect on the Dr-patient relationship.

There is no current biological test and the diagnosis is clinical, based on specific criteria (ICD-10 or DSM5). Screening tools for a history of previous mania/hypomania ('mood questionnaires') may aid clinical assessment but are not diagnostic and NICE (2014) recommends that GPs do not use them.

Differential Diagnosis

See Table 2.

Bipolar Depression (rather than unipolar depression) is more likely (Angst 2005, Angst 2011, Mitchell 2008) if there is:

- A family history of Bipolar Disorder
- So-called 'atypical' depression symptoms (psychomotor retardation, hypersomnia, hyperphagia, 'lead-like' physical heaviness, marked fatigue)
- Pathological guilt
- Psychotic depression
- No response to >3 antidepressants
- Hypomania/mania with antidepressants
- Borderline Personality Disorder
- Post partum psychosis

Table 2. Differential Diagnosis

Normal: Be wary about medicalising normal mood reactions, personality traits and temperaments. Where necessary, review the patient to assess further.

Borderline Personality Disorder, ADHD, Impulse control disorder

Schizophrenia & Schizoaffective Disorder: Psychosis may be present in severe mania and also in Schizophrenia - but hallucinations, delusions and thought disorder are usually only present in schizophrenia or Schizoaffective Disorder. In first episode psychosis, a formal underlying diagnosis may be deferred until subsequent developments clarify the situation.

Organic pathology: Hyperthyroidism (mania) hypothyroidism (depression) Cushings (mania) Addisons (depression, fatigue) anaemia, renal failure, delirium (e.g. meningo-encephalitis) metabolic (e.g. hyponatraemia, hypercalcaemia, liver dysfunction, B12 deficiency), frontal lobe lesions, dementia, cerebral lupus, multiple sclerosis, HIV. Rarely: pheochromocytoma and porphyria.

Iatrogenic: Many drugs affect mood:

Mania/hypomania: corticosteroids, L-dopa, stimulants (e.g. methylphenidate, cocaine, amphetamines)

Depression: corticosteroids, beta-blockers, calcium channel blockers alpha-blockers and statins.

Consider a trial off relevant medication if possible.

Chronic Fatigue Syndrome, Sleep disorders: Primary insomnias; Sleep apnoea causing fatigue and behavioural changes

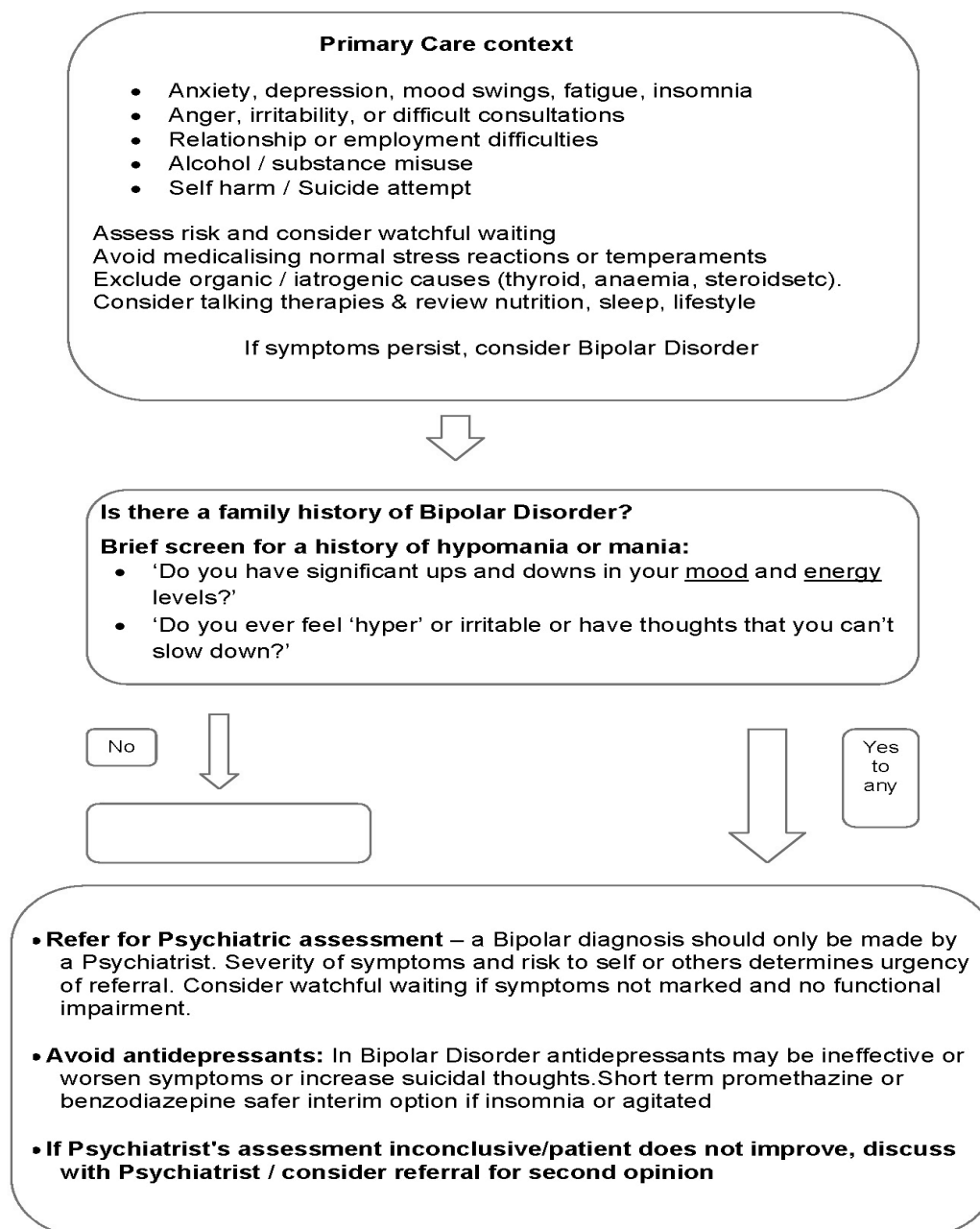


Figure 1. Flow chart for Primary Care

In these situations consider the following screening questions (see figure 1):

- *Is there a family history of Bipolar Disorder?'*
- *Do you have significant ups and downs in your mood and energy levels?*
- *Do you ever feel 'hyper' or irritable or have thoughts that you can't slow down?*

Formal diagnosis should not be made in Primary Care

Referral to a Psychiatrist, ideally with expertise in Mood Disorders (Young 2011), for formal assessment and management is essential, although watchful waiting may be appropriate for patients with milder symptoms.

Prompt referral is essential if there are any concerns about risk to self or others (suicidality or overactive, disinhibited or violent behaviour). Given the diagnostic challenges, a discussion with the Psychiatrist and/or a referral for a second opinion should be considered if an initial assessment proves inconclusive or if the patient does not respond to treatment.

FURTHER MANAGEMENT IF DIAGNOSIS CONFIRMED

In brief, this should involve a comprehensive care plan formulated by secondary care, which is usually refined over time. GPs will usually play a key role in on-going prescribing, monitoring and review.

Management includes:

- Compassion and holistic support to help build resilience.
- Risk assessment: hospitalisation may be required for mania or severe depression, sometimes via compulsory admission.
- Bipolar-specific Psychoeducation (Colom 2009): Understanding mood triggers, the importance of sleep, and regular daily routines. Self management strategies, mood monitoring and triggers, stress management, exercise, sleep, avoiding alcohol and substance misuse
- Dietary interventions (Sarris 2015, Sarris 2014) are increasingly thought to be important, including: increasing omega 3 essential fatty acids (Sarris 2012, Parker 2014, Lin 2012), ideally from marine sources (antidepressant and anti-inflammatory effects) and reducing sugars and processed foods.
- Talking therapies: bipolar-specific CBT, interpersonal and social rhythm therapy, family therapy, psychotherapy
- Pharmacotherapy: e.g. lithium, anticonvulsants, anti-psychotics, benzodiazepines. Hypomania/mania is usually far more responsive to pharmacological treatment than bipolar depression, which remains an important unmet need (Fountoulakis 2012). Different strategies may be required for acute versus prophylactic treatment. Individuals with ‘milder’ symptoms may opt for occasional ‘prn’ medication, or none; but others may benefit from long-term medication, and those with severe symptoms may warrant complex polypharmacy. Risk/benefit assessments are difficult. There is debate about the exact role of antidepressants in Bipolar Disorder (Berk 2005, Mitchell 2008, Sachs 2007, Perlis 2011), but in contrast to unipolar depression, antidepressants are often ineffective and in some individuals may precipitate hypomania, mania and suicidality (Akiskal 2005, McElroy 2006, Berk 2005). In situations where a trial of antidepressants is deemed necessary, a ‘mood stabiliser’ should usually be taken at the same time.
- ‘Physical treatments’: e.g. ECT for severe symptoms.
- Physical health monitoring is essential, especially for cardiovascular complications, obesity and type II diabetes.

CONCLUSION

Bipolar Disorder is complex and challenging for affected individuals, their relatives and for healthcare providers. Prompt diagnosis, meticulous treatment and good psychosocial support can help these individuals and significantly improve their quality of life. GPs can make a real difference here.

Acknowledgements:

This overview is primarily intended for GPs. Readers should refer to NICE guidance (NICE 2014) and expert literature for further information.

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