

**Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care**

**NICE guideline**

**Draft for consultation, April 2014**

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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## Introduction

Bipolar disorder is a potentially lifelong and disabling condition characterised by episodes of mania (abnormally elevated mood or irritability and related symptoms with severe functional impairment or psychotic symptoms for 7 days or more) or hypomania (abnormally elevated mood or irritability and related symptoms with decreased or increased function for 4 days or more) and episodes of depressed mood. It is often comorbid with other disorders such as substance misuse, personality disorders and attention deficit hyperactivity disorder (ADHD).

The peak age of onset is 15–19 years, and there is often a substantial delay between onset and first contact with mental health services. The lifetime prevalence of bipolar I disorder (mania and depression) is estimated at 1% of the adult population, and bipolar II disorder (hypomania and depression) affects approximately 0.75% of adults. Bipolar disorder in children under 12 years is very rare.

Since the publication of the previous guideline (NICE clinical guideline 38) in 2006, there have been some important advances in our knowledge of the care pathway and treatment approaches that are most likely to benefit people with bipolar disorder. All areas of NICE clinical guideline 38 have been updated.

This guideline covers the recognition, assessment and management of bipolar disorder in children, young people and adults. It includes specific recommendations for diagnosis in children and young people because presentation in these age groups can be complicated by other conditions such as ADHD. The recommendations apply to people with bipolar I, bipolar II, mixed affective and rapid cycling disorders. Non-bipolar affective disorders are not covered because these are addressed by other guidelines, and this guideline does not make specific recommendations about other mental disorders that commonly coexist with bipolar disorder.

### ***Drug recommendations***

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The service user (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

## Person-centred care

This guideline offers best practice advice on the care of adults, children and young people with bipolar disorder.

Service users and healthcare professionals have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Service users should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the service user is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the [Department of Health's advice on consent](#). If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) and the supplementary [code of practice on deprivation of liberty safeguards](#).

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#).

NICE has also produced guidance on the components of good service user experience. All healthcare professionals and social care practitioners working with people using adult NHS mental health services should follow the recommendations in [Service user experience in adult mental health](#).

If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's [Transition: getting it right for young people](#).

Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with bipolar disorder. Diagnosis and management should be reviewed throughout the transition process, and

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there should be clarity about who is the lead clinician to ensure continuity of care.

## **Strength of recommendations**

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most service users would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the service user about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Person-centred care').

### ***Interventions that must (or must not) be used***

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

### ***Interventions that should (or should not) be used – a 'strong' recommendation***

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of service users, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most service users.

### ***Interventions that could be used***

We use 'consider' when we are confident that an intervention will do more good than harm for most service users, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the

service user's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the service user.



## **Update information**

This guidance is an update of NICE clinical guideline 38 (published July 2006) and will replace it.

## Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in [section 1](#).

### ***Care for adults, children and young people across all phases of bipolar disorder***

#### **Support for carers of people with bipolar disorder**

- As early as possible negotiate with the person with bipolar disorder and their carers about how information about the person will be shared. When discussing rights to confidentiality, emphasise the importance of sharing information about risks and the need for carers to understand the person's perspective. Foster a collaborative approach that supports both people with bipolar disorder and their carers, and respects their individual needs and interdependence<sup>1</sup>. [1.1.15]

### ***Recognising and managing bipolar disorder in adults in primary care***

#### **Managing bipolar disorder in primary care**

- Offer people with bipolar depression:
  - a manualised psychological intervention specifically developed for bipolar disorder **or**
  - a high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with the NICE clinical guideline on [depression](#).

Monitor mood carefully and if there are signs of hypomania or deterioration of the depressive symptoms, liaise with or refer the person to secondary care. If the person develops mania or [severe depression](#), refer them urgently to secondary care. [1.2.5]

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<sup>1</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

## ***Managing mania or hypomania in adults in secondary care***

### **Pharmacological interventions**

- If a person develops mania or hypomania and is not taking an antipsychotic or mood stabiliser, offer haloperidol, olanzapine, quetiapine or risperidone, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity and previous response to treatment). Follow the recommendations on using antipsychotics in section [1.10](#). **[1.5.3]**
- If the person is already taking lithium, check plasma lithium levels to optimise treatment (see recommendations [1.10.11](#) and [1.10.12](#)). Consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment. **[1.5.7]**

## ***Managing bipolar depression in adults in secondary care***

### **Psychological interventions**

- Offer people with bipolar depression:
  - a manualised psychological intervention specifically developed for bipolar disorder **or**
  - a high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with [recommendations 1.5.3.1–1.5.3.5](#) in the NICE clinical guideline on depression.

Monitor mood carefully for signs of mania or hypomania or deterioration of the depressive symptoms. **[1.6.1]**

### **Pharmacological interventions**

- If a person develops moderate or severe bipolar depression and is not taking a drug to treat their bipolar disorder, offer fluoxetine combined with olanzapine<sup>2</sup>, or quetiapine on its own, depending on the person's preference and previous response to treatment.

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<sup>2</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the

- If the person prefers, consider either olanzapine (without fluoxetine) or lamotrigine<sup>3</sup> on its own.
- If there is no response to fluoxetine combined with olanzapine, or quetiapine, consider lamotrigine on its own.

Follow the recommendations on using antipsychotics in section [1.10](#).

### **[1.6.3]**

- If a person develops moderate or severe bipolar depression and is already taking lithium, check their plasma lithium level and:
  - if their plasma lithium level is inadequate, increase the dose of lithium
  - if their plasma lithium is at maximum level, add either fluoxetine combined with olanzapine<sup>4</sup> or quetiapine, depending on the person's preference and previous response to treatment. If there is no response or the person prefers, consider olanzapine (without fluoxetine) or lamotrigine<sup>3</sup>.

Follow the recommendations in section [1.10](#) on using lithium and antipsychotics. **[1.6.4]**

## ***Managing bipolar disorder in adults in the longer term in secondary care***

### **Psychological interventions**

- Offer a structured, manualised psychological intervention (individual, group or family) designed for bipolar disorder to prevent relapse or for people who have some persisting symptoms between episodes of mania or bipolar depression. **[1.7.3]**

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decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

<sup>3</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), lamotrigine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

<sup>4</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

## Pharmacological interventions

- Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder and:
  - if lithium is ineffective, consider adding [valproate](#)<sup>5</sup>
  - if lithium is poorly tolerated, consider valproate or olanzapine instead or, if it has been effective during an episode of mania or bipolar depression, quetiapine.

Discuss with the person the possible benefits and risks of each drug for them. [1.7.6]

## ***Recognising, diagnosing and managing bipolar disorder in children and young people***

### Recognition and referral

#### ***Diagnosis and assessment***

- Diagnosis of bipolar disorder in [children and young people](#) should be made only after intensive monitoring and by a specialist in bipolar disorder in children and young people. [1.11.4]

### Management in young people

#### ***Mania***

- For the treatment of mania or hypomania in young people consider following the recommendations for adults in section [1.5](#)<sup>6</sup>. Aripiprazole is also a treatment option in line with NICE technology appraisal guidance on

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<sup>5</sup> Although its use is common in UK clinical practice, at the time of publication (September 2014), sodium valproate did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Semi-sodium valproate is licensed for this indication if the person responded to treatment for mania.

<sup>6</sup> At the time of publication (September 2014), olanzapine, risperidone, haloperidol, quetiapine, lamotrigine, lithium and valproate did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

[aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder](#). Refer to the [BNF for children](#) to modify drug treatments, be aware of the increased potential for a range of side effects, and do not continue antipsychotic treatment for longer than 12 weeks.

**[1.11.10]**

- Do not offer valproate to girls of childbearing potential. **[1.11.11]**

***Bipolar depression***

- Offer a structured, manualised psychological intervention (individual cognitive behavioural therapy or interpersonal therapy) to young people with bipolar depression. The intervention should be of at least 3 months' duration. **[1.11.12]**

## 1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) [\[hyperlink to be added for final publication\]](#) gives details of the methods and the evidence used to develop the guidance.

The recommendations cover children, young people and adults with suspected or diagnosed bipolar disorder and apply to bipolar I, bipolar II, mixed affective and rapid cycling disorders.

### ***Terms used in this guideline***

**Children** People aged 12 years and under.

**Depression** The severity of bipolar depression is defined in line with the NICE clinical guideline on [depression](#) as follows:

*Mild depression* Few, if any, symptoms in excess of the 5 required to make the diagnosis, with symptoms resulting in minor functional impairment.

*Moderate depression* Symptoms or functional impairment that are between mild and severe.

*Severe depression* Most symptoms, with symptoms markedly interfering with functioning. Can occur with or without psychotic symptoms.

**Older people** People aged 65 years and over.

**Young people** People aged 13–18 years.

**Valproate** Refers to 3 formulations of valproate available in the UK: sodium valproate and valproic acid (licensed for the treatment of epilepsy) and semi-sodium valproate (licensed for the treatment of acute mania and continuation treatment in people whose mania responds to treatment). Both semi-sodium and sodium valproate are metabolised to valproic acid (also known as valproate), which is the pharmacologically active component.

## **1.1 *Care for adults, children and young people across all phases of bipolar disorder***

### **Improving the experience of care**

- 1.1.1 Use this guideline in conjunction with the NICE clinical guidance on [service user experience in adult mental health](#) to improve the experience of care for adults with bipolar disorder using mental health services.
- 1.1.2 Follow the recommendations in [general principles of care](#) in the NICE clinical guideline on psychosis and schizophrenia in children and young people to improve the experience of care for [children and young people](#) with bipolar disorder.

### **Treatment and support for specific populations**

- 1.1.3 See the NICE clinical guideline on [antenatal and postnatal mental health](#) for guidance on the management of bipolar disorder in women of childbearing potential.
- 1.1.4 Ensure that people with bipolar disorder and a coexisting learning disability are offered the same range of treatments and services as other people with bipolar disorder.
- 1.1.5 Ensure that [older people](#) with bipolar disorder are offered the same range of treatments and services as younger people with bipolar disorder.
- 1.1.6 Offer people with bipolar disorder and coexisting disorders, such as personality disorder, anxiety disorders or substance misuse treatment in line with the relevant NICE clinical guideline, in addition to their treatment for bipolar disorder. See the NICE clinical guidelines on [antisocial personality disorder](#), [borderline personality disorder](#), [generalised anxiety disorder](#) and [psychosis with coexisting substance misuse](#).



- 1.1.7 Offer people with rapid cycling bipolar disorder the same interventions as people with other types of bipolar disorder because there is currently no strong evidence to suggest that people with rapid cycling bipolar disorder should be treated differently.

### **Information and support**

- 1.1.8 Consider identifying and offering assistance with education, financial and employment problems that may result from the behaviour associated with bipolar disorder, such as mania and hypomania. If the person with bipolar disorder agrees, this could include talking directly with education staff, creditors and employers about bipolar disorder and its possible effects, and how the person can be supported.
- 1.1.9 Consider encouraging people with bipolar disorder to develop advance statements while their condition is stable, in collaboration with their carers if possible.
- 1.1.10 Consider providing information and discussing making a lasting power of attorney with adults with bipolar disorder and their carers if there are financial problems resulting from mania or hypomania.

### **Treatments that are not recommended for bipolar disorder in any phase**

- 1.1.11 Do not offer gabapentin or topiramate to treat bipolar disorder.

### **Support for carers of people with bipolar disorder**

- 1.1.12 Offer carers of people with bipolar disorder an assessment (provided by mental health services) of their own needs and discuss with them their strengths and views. Develop a care plan to address any identified needs, give a copy to the carer and their GP and ensure it is reviewed annually<sup>7</sup>.

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<sup>7</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

1.1.13 Advise carers about their statutory right to a formal carer's assessment provided by social care services and explain how to access this<sup>8</sup>.

1.1.14 Give carers written and verbal information in an accessible format about:

- diagnosis and management of bipolar disorder
- positive outcomes and recovery
- types of support for carers
- role of teams and services
- getting help in a crisis.

When providing information, offer the carer support if necessary<sup>9</sup>.

1.1.15 As early as possible negotiate with the person with bipolar disorder and their carers about how information about the person will be shared. When discussing rights to confidentiality, emphasise the importance of sharing information about risks and the need for carers to understand the person's perspective. Foster a collaborative approach that supports both people with bipolar disorder and their carers, and respects their individual needs and interdependence<sup>9</sup>.

1.1.16 Review regularly how information is shared, especially if there are communication and collaboration difficulties between the person and their and carer<sup>8</sup>.

1.1.17 Include carers in decision-making if the person agrees<sup>9</sup>.

1.1.18 Offer a carer-focused education and support programme, which may be part of a family intervention for bipolar disorder, as early as possible to all carers. The intervention should:

- be available as needed

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<sup>8</sup> From [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

<sup>9</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- have a positive message about recovery<sup>10</sup>.

1.1.19 Identify children, young people and vulnerable adults who are dependent on, living with or caring for a person with bipolar disorder and:

- review the need for an assessment according to local safeguarding procedures for children or adults as appropriate
- offer psychological and social support as needed.

## **1.2 *Recognising and managing bipolar disorder in adults in primary care***

### **Recognising bipolar disorder in primary care and referral**

1.2.1 When adults present in primary care with depression, ask about previous periods of overactivity or disinhibited behaviour. If the overactivity or disinhibited behaviour has lasted for 4 days or more, consider referral for a specialist mental health assessment.

1.2.2 Refer people urgently for a specialist mental health assessment if mania or [severe depression](#) is suspected or they are a danger to themselves or others.

1.2.3 Do not use questionnaires in primary care to identify bipolar disorder in adults.

### **Managing bipolar disorder in primary care**

1.2.4 When working with people with bipolar disorder in primary care:

- engage with and develop an ongoing relationship with them
- support them to carry out care plans developed in secondary care and achieve their recovery goals
- follow crisis plans developed in secondary care and liaise with secondary care specialists if necessary

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<sup>10</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- review their treatment and care, including medication, at least annually.

1.2.5 Offer people with bipolar depression:

- a manualised psychological intervention specifically developed for bipolar disorder **or**
- a high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with the NICE clinical guideline on [depression](#).

Monitor mood carefully and if there are signs of hypomania or deterioration of the depressive symptoms, liaise with or refer the person to secondary care. If the person develops mania or severe depression, refer them urgently to secondary care.

1.2.6 Psychological therapists working with people with bipolar depression in primary care should have training in and experience of working with people with bipolar disorder.

1.2.7 Do not start lithium in primary care to treat bipolar disorder, except under shared-care arrangements.

1.2.8 Do not start [valproate](#) in primary care to treat bipolar disorder.

1.2.9 If bipolar disorder is managed solely in primary care, re-refer to secondary care if any one of the following applies:

- there is a poor or partial response to treatment
- the person's functioning declines significantly
- treatment adherence is poor
- comorbid alcohol or drug misuse is suspected
- the person is considering stopping any medication after a period of relatively stable mood
- a woman with bipolar disorder is pregnant or planning a pregnancy.

## Monitoring physical health

- 1.2.10 Develop and use practice case registers to monitor the physical and mental health of people with bipolar disorder in primary care<sup>11</sup>.
- 1.2.11 GPs and other primary healthcare professionals should monitor the physical health of people with bipolar disorder when responsibility for monitoring is transferred from secondary care, and then at least annually. The health check should be comprehensive, focusing on physical health problems that are common in people with bipolar disorder. Include all the checks recommended in recommendation 1.2.12 and refer to relevant NICE guidance on monitoring for cardiovascular disease, diabetes, obesity and respiratory disease. A copy of the results should be sent to the care coordinator and psychiatrist, and put in the secondary care records<sup>11</sup>.
- 1.2.12 Ensure that the physical health check for people with bipolar disorder includes:
- weight or BMI, diet, nutritional status and level of physical activity
  - cardiovascular status, including pulse and blood pressure
  - metabolic status, including fasting blood glucose, glycosylated haemoglobin (HbA<sub>1c</sub>) and blood lipid profile
  - liver function
  - renal function for people taking long-term lithium.
- 1.2.13 Identify people with bipolar disorder who have hypertension, have abnormal lipid levels, are obese or at risk of obesity, have diabetes or are at risk of diabetes (as indicated by abnormal blood glucose levels), or are physically inactive, at the earliest opportunity. Follow NICE guidance on [lipid modification](#), [preventing type 2 diabetes](#),

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<sup>11</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

[obesity](#), [hypertension](#), [prevention of cardiovascular disease](#) and [physical activity](#)<sup>12</sup>.

- 1.2.14 Offer treatment to people with bipolar disorder who have diabetes and/or cardiovascular disease in primary care in line with the NICE clinical guidelines on [lipid modification](#), [type 1 diabetes](#), [type 2 diabetes](#) and type 2 diabetes – newer agents<sup>12</sup>.

### **1.3 *Assessing suspected bipolar disorder in adults in secondary care***

- 1.3.1 Assessment of people with suspected bipolar disorder should be conducted in early intervention in psychosis services.
- 1.3.2 When assessing suspected bipolar disorder in secondary care:
- undertake a full psychiatric assessment, documenting a detailed history of mood, episodes of overactivity, disinhibition or other episodic and sustained changes in behaviour, symptoms between episodes, triggers to previous episodes and patterns of relapse, and family history
  - assess social and personal functioning and current psychosocial stressors
  - assess for potential mental and physical comorbidities
  - assess the person's physical health and review medication and side effects, including weight gain
  - discuss treatment history and identify interventions that have been effective or ineffective in the past
  - encourage people to invite a family member or carer to give a corroborative history
  - discuss possible factors associated with changes in mood, including relationships, psychosocial factors and lifestyle changes.

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<sup>12</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- 1.3.3 Take into account the possibility of differential diagnoses including schizophrenia spectrum disorders, personality disorders, drug misuse, alcohol-use disorders, attention deficit hyperactivity disorder and underlying physical disorders such as hypo- or hyperthyroidism.
- 1.3.4 Carry out a risk assessment in conjunction with the person, and their carer if possible, focusing on areas that are likely to present possible danger or harm, such as self-neglect, self-harm, suicidal thoughts and intent, risks to others, including family members, driving, spending money excessively, financial or sexual exploitation, disruption in family and love relationships, disinhibited and sexualised behaviour, and risks of sexually transmitted diseases.
- 1.3.5 Following diagnosis, the management of bipolar disorder should be conducted in early intervention in psychosis services for the first 3 years.

#### **1.4 *Managing crisis, risk and behaviour that challenges in adults with bipolar disorder in secondary care***

- 1.4.1 Develop a risk management plan jointly with the person, and their carer if possible, covering:
- identifiable personal, social, occupational, or environmental triggers and early warning signs and symptoms of relapse
  - a protocol for increasing doses of medication or taking additional medication (which may be given to the person in advance) for people at risk of onset of mania or for whom early warning signs and symptoms can be identified
  - agreements between primary and secondary care about how to respond to an increase in risk or concern about possible risk
  - information about who to contact if the person with bipolar disorder and, if appropriate, their carer, is concerned or in a

crisis, including the names of healthcare professionals in primary and secondary care who can be contacted.

Give the person and their GP a copy of the plan, and encourage the person to share it with their carers.

1.4.2 Offer crisis services to support people with bipolar disorder who are in crisis, in line with [recommendations 1.4.1.1–1.4.1.4](#) in the NICE clinical guideline on psychosis and schizophrenia in adults.

1.4.3 If people with bipolar disorder pose an immediate risk to themselves or others during an acute episode, see the NICE guidance on:

- [violence](#) and [service user experience in adult mental health](#) for advice on managing imminent violence and on rapid tranquillisation **or**
- [self-harm](#) for advice on managing acts of self-harm or suicide risk.

## **1.5 *Managing mania or hypomania in adults in secondary care***

### **Support and advice**

1.5.1 Ensure that people with mania or hypomania have access to calming environments and reduced stimulation. Advise them not to make important decisions until they have recovered from mania or hypomania and encourage them to maintain their relationships with their carers if possible.

### **Pharmacological interventions**

1.5.2 If a person develops mania or hypomania and is taking an antidepressant (as defined by the [British national formulary \(BNF\)](#)) as monotherapy, stop the antidepressant and start an antipsychotic as set out in recommendation 1.5.3.



- 1.5.3 If a person develops mania or hypomania and is not taking an antipsychotic or mood stabiliser, offer haloperidol, olanzapine, quetiapine or risperidone, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity and previous response to treatment). Follow the recommendations on using antipsychotics in section [1.10](#) .
- 1.5.4 If the first antipsychotic is poorly tolerated at any dose (including rapid weight gain) or ineffective at the maximum licensed dose, offer an alternative antipsychotic from the drugs listed in recommendation 1.5.3, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity and previous response to treatment).
- 1.5.5 If an alternative antipsychotic is not sufficiently effective at the maximum licensed dose, consider adding lithium. If adding lithium is ineffective, consider adding [valproate](#)<sup>13</sup> instead.
- 1.5.6 If a person develops mania or hypomania and is taking an antidepressant (as defined by the [BNF](#)) in combination with a mood stabiliser, consider stopping the antidepressant.
- 1.5.7 If the person is already taking lithium, check plasma lithium levels to optimise treatment (see recommendations [1.10.11](#) and [1.10.12](#)). Consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment.
- 1.5.8 If the person is already taking valproate or another mood stabiliser as prophylactic treatment, consider increasing the dose, up to the maximum level in the [BNF](#) if necessary, depending on clinical

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<sup>13</sup> Although its use is common in UK clinical practice, at the time of publication (September 2014), sodium valproate did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Semi-sodium valproate is licensed for mania if lithium is not tolerated or is contraindicated.

response. If there is no improvement, consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment.

1.5.9 If the clinical presentation is of a mixed affective state, characterised by both manic and depressive symptoms, follow recommendations [1.5.1–1.5.8](#) for the treatment of mania, and monitor closely for the emergence of depression.

1.5.10 Do not offer lamotrigine to treat mania.

### **Reviewing treatment for mania**

1.5.11 At 4 weeks after resolution of symptoms, discuss with the person, and their carers if appropriate, whether to continue treatment for mania or start long-term treatment (see section [1.7](#)). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment.

1.5.12 If the person decides to continue with treatment for mania, offer it for a further 3–6 months, and then review.

## **1.6 *Managing bipolar depression in adults in secondary care***

### **Psychological interventions**

1.6.1 Offer people with bipolar depression:

- a manualised psychological intervention specifically developed for bipolar disorder **or**
- a high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with [recommendations 1.5.3.1–1.5.3.5](#) in the NICE clinical guideline on depression.

Monitor mood carefully for signs of mania or hypomania or deterioration of the depressive symptoms.

- 1.6.2 Psychological therapists working with people with bipolar depression should have training in, and experience of, working with people with bipolar disorder.

### Pharmacological interventions

- 1.6.3 If a person develops [moderate or severe bipolar depression](#) and is not taking a drug to treat their bipolar disorder, offer fluoxetine combined with olanzapine<sup>14</sup>, or quetiapine on its own, depending on the person's preference and previous response to treatment.

- If the person prefers, consider either olanzapine (without fluoxetine) or lamotrigine<sup>15</sup> on its own.
- If there is no response to fluoxetine combined with olanzapine, or quetiapine, consider lamotrigine on its own.

Follow the recommendations on using antipsychotics in section [1.10](#).

- 1.6.4 If a person develops moderate or severe bipolar depression and is already taking lithium, check their plasma lithium level and:

- if their plasma lithium level is inadequate, increase the dose of lithium
- if their plasma lithium is at maximum level, add either fluoxetine combined with olanzapine<sup>14</sup> or quetiapine, depending on the person's preference and previous response to treatment. If there is no response or the person prefers, consider olanzapine (without fluoxetine) or lamotrigine<sup>15</sup>.

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<sup>14</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

<sup>15</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), lamotrigine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

Follow the recommendations in section [1.10](#) on using lithium and antipsychotics.

1.6.5 If a person develops moderate or severe bipolar depression and is already taking [valproate](#), consider increasing the dose. If the maximum tolerated dose has been reached and there is a limited response to valproate, add fluoxetine combined with olanzapine<sup>16</sup> or add quetiapine, depending on the person's preference and previous response to treatment.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine<sup>17</sup> to valproate
- If there is no response to adding fluoxetine combined with olanzapine, or adding quetiapine, stop the additional treatment and consider adding lamotrigine to valproate.

Follow the recommendations in section [1.10](#) on using valproate.

1.6.6 Follow the recommendations on using antipsychotics in section [1.10](#) and be aware of the potential interactions between valproate and fluoxetine, lamotrigine and olanzapine.

1.6.7 Take into account toxicity in overdose when prescribing psychotropic medication during periods of high suicide risk. Assess the need to limit the quantity of medication supplied to reduce the risk to life if the person overdoses.

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<sup>16</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information

<sup>17</sup> Although this use is common in UK clinical practice, at the time of publication (September 2014), lamotrigine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

### **Reviewing treatment for bipolar depression**

- 1.6.8 At 4 weeks after resolution of symptoms, discuss with the person, and their carers if appropriate, whether to continue treatment for bipolar depression or start long-term treatment (see section 1.7). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment.
- 1.6.9 If the person decides to continue with acute treatment, offer it for a further 3–6 months, and then review.

## **1.7 *Managing bipolar disorder in adults in the longer term in secondary care***

### **Discussing long-term treatment**

- 1.7.1 After each episode of mania or bipolar [depression](#), discuss with the person, and their carers if appropriate, managing their bipolar disorder in the longer term. Discussion should aim to help people understand that bipolar disorder is commonly a long-term relapsing and remitting condition that needs self-management and engagement with primary and secondary care professionals and involvement of carers. The discussion should cover:
- the nature and variable course of bipolar disorder
  - the role of psychological and pharmacological interventions to prevent relapse and reduce symptoms
  - the risk of relapse after stopping medication for an acute episode
  - the potential benefits and risks of long-term medication and the need for monitoring
  - the potential benefits and risks of stopping medication, including for women who may wish to become pregnant
  - the person's history of bipolar disorder, including:

- the severity and frequency of episodes of mania or bipolar depression, with a focus on associated risks and adverse consequences
- previous response to treatment
- symptoms between episodes
- potential triggers for relapse, early warning signs, and self-management strategies
- possible duration of treatment, and when and how often this should be reviewed.

Provide clear written information about bipolar disorder, including NICE's [information for the public](#) [\[hyperlink to be added for final publication\]](#), and ensure there is enough time to discuss options and concerns.

### **Psychological interventions**

- 1.7.2 Offer a family intervention to people with bipolar disorder who are living, or in close contact, with their family in line with [recommendation 1.3.7.2](#) in the NICE clinical guideline on psychosis and schizophrenia.
- 1.7.3 Offer a structured, manualised psychological intervention (individual, group or family) designed for bipolar disorder to prevent relapse or for people who have some persisting symptoms between episodes of mania or bipolar depression.
- 1.7.4 Individual and group psychological interventions for bipolar disorder to prevent relapse should consist of between 9 and 25 sessions and:
- provide information about bipolar disorder
  - consider the impact of thoughts and behaviour on moods and relapse
  - include self-monitoring of mood, thoughts and behaviour
  - address relapse risk, distress and how to improve functioning

- develop plans for relapse management and staying well
- consider problem-solving to address communication patterns and managing functional difficulties.

In addition:

- individual programmes should be tailored to the person's needs based on an individualised assessment and psychological formulation
- group programmes should include discussion of the information provided with a focus on its relevance for the participants.

### **Pharmacological interventions**

1.7.5 When planning long-term pharmacological treatment to prevent relapse, take into account drugs that have been effective during episodes of mania or bipolar depression. Discuss with the person whether they prefer to continue this treatment or switch to lithium, and explain that lithium is the most effective long-term treatment for bipolar disorder.

1.7.6 Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder and:

- if lithium is ineffective, consider adding [valproate](#)<sup>18</sup>
- if lithium is poorly tolerated, consider valproate or olanzapine instead or, if it has been effective during an episode of mania or bipolar depression, quetiapine.

Discuss with the person the possible benefits and risks of each drug for them.

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<sup>18</sup> Although its use is common in UK clinical practice, at the time of publication (September 2014), sodium valproate did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Semi-sodium valproate is licensed for this indication if the person responded to treatment for mania.

- 1.7.7 Before stopping medication, discuss with the person how to recognise early signs of relapse and what to do if symptoms recur.
- 1.7.8 If stopping medication, do so gradually (see section [1.10](#)) and monitor the person for signs of relapse.
- 1.7.9 Continue monitoring symptoms, mood and mental state for 2 years after stopping medication. This may be undertaken in primary care (see recommendation [1.9.3](#)).

## **1.8 *Monitoring physical health in secondary care***

- 1.8.1 Healthcare professionals in secondary care should ensure, as part of the care programme approach, that people with bipolar disorder receive physical healthcare from primary care as described in recommendations [1.2.10–1.2.14](#)<sup>19</sup>.
- 1.8.2 People with bipolar disorder, especially those taking antipsychotics, should be offered a combined healthy eating and physical activity programme by their mental healthcare provider<sup>19</sup>.
- 1.8.3 If a person has rapid or excessive weight gain, abnormal lipid levels or problems with blood glucose management, offer interventions in line with the NICE guidance on [obesity](#), [lipid modification](#), or [preventing type 2 diabetes](#)<sup>20</sup>.
- 1.8.4 Routinely monitor weight and cardiovascular and metabolic indicators of morbidity in people with bipolar disorder. These should be audited in the annual team report<sup>19</sup>.
- 1.8.5 Trusts should ensure compliance with relevant guidelines on the monitoring and treatment of cardiovascular and metabolic disease in people with bipolar disorder through board-level performance indicators<sup>19</sup>.

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<sup>19</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

<sup>20</sup> From [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).



## **1.9 Promoting recovery and return to primary care**

### **General principles**

1.9.1 Continue treatment and care in early intervention in psychosis services or refer the person to a specialist integrated community-based team. This team should:

- offer the full range of psychological, pharmacological, social and occupational interventions recommended in this guideline
- be competent to provide all interventions offered
- place emphasis on engagement rather than risk management
- provide treatment and care in the least restrictive and stigmatising environment possible, and in an atmosphere of hope and optimism in line with the NICE clinical guidance on [service user experience in adult mental health](#)<sup>21</sup>.

1.9.2 Consider intensive case management for people with bipolar disorder who are likely to disengage from treatment or service<sup>22</sup>.

### **Return to primary care**

1.9.3 Offer people with bipolar disorder whose symptoms have responded effectively to treatment and remain stable the option to return to primary care for further management. If they wish to do this, record it in their notes and coordinate transfer of responsibilities through the care programme approach<sup>22</sup>.

1.9.4 When making transfer arrangements for a return to primary care, agree a care plan with the person, which includes:

- clear, individualised social and emotional recovery goals
- a crisis plan indicating early warning symptoms and triggers of both mania and depression relapse and preferred response during relapse, including liaison and referral pathways
- an assessment of the person's mental state

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<sup>21</sup> From [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

<sup>22</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- a medication plan with a review date, frequency and nature of monitoring for effectiveness and adverse effects, and what should happen in the event of a relapse.

1.9.5 Review the need for a meeting with the person's GP before discharge and transfer.

### **Employment, education and occupational activities**

1.9.6 Offer supported employment programmes to people with bipolar disorder who wish to find or return to work. Consider other occupational or educational activities, including pre-vocational training, for people who are unable to work or unsuccessful in finding employment<sup>23</sup>.

## **1.10 *How to use medication***

1.10.1 Discuss the use of alcohol, tobacco, prescription and non-prescription medication and illicit drugs with the person, and their carer if appropriate. Explain the possible interference of these substances with the therapeutic effects of prescribed medication and psychological interventions<sup>23</sup>.

1.10.2 When offering psychotropic medication to [older people](#), take into account its impact on cognitive functioning in older people and:

- be aware of the need to use medication at lower doses
- be alert to the increased risk of drug interactions
- be aware of the negative impact that anticholinergic medication, or drugs with anticholinergic activity, can have on cognitive function
- ensure that medical comorbidities have been recognised and treated.

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<sup>23</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

## Using antipsychotic medication

### ***Starting antipsychotic medication***

1.10.3 Before starting antipsychotic medication, measure and record the person's:

- weight or BMI
- pulse
- blood pressure
- fasting blood glucose or HbA<sub>1c</sub>
- blood lipid profile<sup>24</sup>.

1.10.4 Before starting antipsychotic medication, offer the person an electrocardiogram (ECG) if:

- it is specified in the drug's summary of product characteristics (SPC) **or**
- a physical examination has identified a specific cardiovascular risk (such as hypertension) **or**
- there is a family history of cardiovascular disease, a history of sudden collapse, or other cardiovascular risk factors such as cardiac arrhythmia **or**
- the person is being admitted as an inpatient<sup>24</sup>.

1.10.5 Treatment with antipsychotic medication should be considered an explicit individual therapeutic trial. Include the following:

- Discuss and record the side effects that the person is most willing to tolerate.
- Record the indications and expected benefits and risks of antipsychotic medication, and the expected time for a change in symptoms and appearance of side effects.
- At the start of treatment prescribe a dose that is appropriate for the phase and severity of the illness.

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<sup>24</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- Do not routinely prescribe a dose above the maximum recommended in the [BNF](#) or SPC.
- Justify and record reasons for doses outside the range given in the [BNF](#) or SPC, and inform the person that such treatment is unlicensed.
- Record the rationale for continuing, changing or stopping medication, and the effects of such changes<sup>25</sup>.

### ***Monitoring antipsychotic medication***

1.10.6 Monitor and record the following during dose titration and then regularly and systematically throughout treatment:

- pulse and blood pressure after each dose change
- weight or BMI weekly for the first 6 weeks, then at 12 weeks
- blood glucose or HbA<sub>1c</sub> and blood lipid profile at 12 weeks
- response to treatment, including changes in symptoms and behaviour
- side effects and their impact on functioning
- the emergence of movement disorders
- adherence<sup>25</sup>.

1.10.7 The secondary care team should maintain responsibility for monitoring the efficacy and tolerability of antipsychotic medication until the person's condition has stabilised<sup>25</sup>.

1.10.8 If out-of-range test results are reported at any stage of treatment, the healthcare professional who ordered the tests should ensure that the person is offered further investigations and treatment as needed.

1.10.9 'As required' (p.r.n.) prescriptions of antipsychotic medication should be made as described in recommendation 1.10.4. Review clinical indications, frequency of administration, therapeutic benefits and side effects each week or more often if needed. Ensure that

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<sup>25</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

p.r.n. prescriptions have not unintentionally led to a total antipsychotic dosage above the maximum specified in the [BNF](#) or SPC<sup>26</sup>.

- 1.10.10 Do not start regular combined antipsychotic medication, except for short periods (for example, when changing medication)<sup>27</sup>.

## Using lithium for long-term treatment

### *Starting lithium*

- 1.10.11 When starting lithium as long-term treatment:

- advise the person that poor adherence or rapid discontinuation may increase the risk of relapse
- measure the person's weight or BMI and arrange tests for urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR), thyroid function and a full blood count
- arrange an ECG for people with cardiovascular disease or risk factors for it
- ensure the person is given the information they need to take lithium safely, for example the National Patient Safety Agency's [information on lithium](#) or a locally developed equivalent
- establish a shared-care arrangement with the person's GP for prescribing lithium and monitoring adverse effects.

- 1.10.12 Measure serum lithium levels 1 week after starting lithium and 1 week after every dose change, and weekly until the levels are stable. Aim to maintain serum lithium level between 0.6 and 0.8 mmol per litre in people being prescribed lithium for the first time.

- 1.10.13 Consider maintaining serum lithium levels at 0.8–1.0 mmol per litre for a trial period of at least 6 months for people who:

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<sup>26</sup> Adapted from [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

<sup>27</sup> From [Psychosis and schizophrenia in adults](#) (NICE clinical guideline 178).

- have had a relapse while taking lithium in the past **or**
- are taking lithium and have subthreshold symptoms with functional impairment.

1.10.14 Advise people taking lithium to:

- seek medical attention if they develop diarrhoea or vomiting or become acutely ill for any reason
- ensure they maintain their fluid intake, particularly after sweating (for example, after exercise, in hot climates or if they have a fever), if they are immobile for long periods or if they develop a chest infection or pneumonia
- talk to their doctor as soon as possible if they become pregnant or are planning a pregnancy.

1.10.15 Warn people taking lithium not to take over-the-counter non-steroidal anti-inflammatory drugs and avoid prescribing these drugs for people with bipolar disorder if possible; if they are prescribed, this should be on a regular (not p.r.n.) basis and the person should be monitored closely.

### ***Monitoring lithium***

1.10.16 Measure the person's serum lithium level every 6 months.

1.10.17 Consider measuring serum lithium levels every 3 months for:

- older people
- people taking drugs that interact with lithium
- people who are at risk of renal, thyroid or other complications
- people who have poor symptom control
- people with poor adherence.

1.10.18 Measure the person's weight or BMI and arrange tests for urea and electrolytes including calcium, eGFR and thyroid function every 6 months, and more often if there is evidence of impaired renal function.

- 1.10.19 Monitor lithium dose and blood serum levels more frequently if urea and creatinine levels become elevated or eGFR declines over 2 or more tests, and assess the rate of deterioration of renal function.
- 1.10.20 When discussing whether to continue lithium, take into account clinical efficacy, other risk factors for renal impairment, and degree of renal impairment; if needed seek advice from a renal specialist and a clinician with expertise in managing bipolar disorder.
- 1.10.21 Monitor the person at every appointment for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels of lithium.

### ***Stopping lithium***

- 1.10.22 Lithium should be stopped gradually over at least 4 weeks, and preferably up to 3 months, even if the person has been started on another antimanic drug.
- 1.10.23 During dose reduction and for 3 months after lithium treatment is stopped monitor the person closely for early signs of mania and depression.

### **Using valproate for long-term treatment**

#### ***Starting valproate***

- 1.10.24 When starting [valproate](#) as long-term treatment, measure the person's weight or BMI and carry out a full blood count and liver function tests.
- 1.10.25 Do not offer valproate to women of childbearing potential.
- 1.10.26 Advise people taking valproate, and their carers, how to recognise the signs and symptoms of blood and liver disorders and to seek immediate medical help if any of these develop. Stop valproate immediately if abnormal liver function or blood dyscrasia is detected.

- 1.10.27 When prescribing valproate, be aware of its interactions with other anticonvulsants (particularly carbamazepine and lamotrigine) and with olanzapine and smoking.

***Monitoring valproate***

- 1.10.28 Do not routinely measure valproate blood levels unless there is evidence of ineffectiveness, poor adherence or toxicity.
- 1.10.29 Measure the person's weight or BMI and carry out liver function tests and a full blood count again after 6 months of treatment with valproate and repeat annually.
- 1.10.30 Be aware of the need for more careful monitoring of sedation, tremor and gait disturbance in older people.

***Stopping valproate***

- 1.10.31 If stopping valproate, reduce the dose gradually over at least 4 weeks to minimise the risk of relapse.

***1.11 Recognising, diagnosing and managing bipolar disorder in children and young people***

**Recognition and referral**

- 1.11.1 Do not use questionnaires in primary care to identify bipolar disorder in [children or young people](#).
- 1.11.2 If bipolar disorder is suspected in primary care in children or young people aged under 14 years, refer them to child and adolescent mental health services (CAMHS).
- 1.11.3 If bipolar disorder is suspected in primary care in young people aged 14 years and over, refer them to a specialist early intervention in psychosis service or specialist CAMHS. Both services should be multidisciplinary and have:
- engagement or assertive outreach approaches



- family involvement and family intervention
- access to structured psychological interventions and psychologically informed care
- vocational and educational interventions
- access to pharmacological interventions
- professionals who are trained and competent in working with young people with bipolar disorder.

### ***Diagnosis and assessment***

- 1.11.4 Diagnosis of bipolar disorder in children or young people should be made only after intensive monitoring and by a specialist in bipolar disorder in children and young people.
- 1.11.5 When diagnosing bipolar disorder in children or young people take account of the following:
- mania must be present
  - euphoria must be present on most days and for most of the time, for at least 7 days
  - irritability is not a core diagnostic criterion.
- 1.11.6 Do not make a diagnosis of bipolar disorder in children or young people on the basis of depression with a family history of bipolar disorder but follow them up.
- 1.11.7 Do not diagnose bipolar II disorder in children or young people.
- 1.11.8 When assessing suspected bipolar disorder in children or young people, follow recommendation [1.3.2](#) for adults, but involve parents or carers routinely and take into account the child or young person's educational functioning.

### **Management in young people**

- 1.11.9 When offering treatment to young people with bipolar disorder, take into account their cognitive capacity, emotional maturity and developmental level.

### **Mania**

1.11.10 For the treatment of mania or hypomania in young people consider following the recommendations for adults in section [1.5](#)<sup>28</sup>.

Aripiprazole is also a treatment option in line with NICE technology appraisal guidance on [aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder](#). Refer to the [BNF for children](#) to modify drug treatments, be aware of the increased potential for a range of side effects, and do not continue antipsychotic treatment for longer than 12 weeks.

1.11.11 Do not offer [valproate](#) to girls of childbearing potential.

### **Bipolar depression**

1.11.12 Offer a structured, manualised psychological intervention (individual cognitive behavioural therapy or interpersonal therapy) to young people with bipolar [depression](#). The intervention should be of at least 3 months' duration.

1.11.13 If after 4 to 6 sessions there is no response to cognitive behavioural therapy or interpersonal therapy, carry out a multidisciplinary review.

1.11.14 After the multidisciplinary review, if there are coexisting factors such as comorbid conditions, persisting psychosocial risk factors such as family discord, or parental mental ill-health, consider:

- an alternative psychological intervention for bipolar depression for the young person, their parents or other family member **or**

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<sup>28</sup> At the time of publication (September 2014), olanzapine, risperidone, haloperidol, quetiapine, lamotrigine, lithium and valproate did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

- an additional psychological intervention for any coexisting mental health problems in line with relevant NICE guidance for the young person, their parents or other family member.

1.11.15 After the multidisciplinary review, if the young person's bipolar depression is moderate to severe, cautiously consider a pharmacological intervention in addition to a psychological intervention. Follow the recommendations for pharmacological interventions for adults in section [1.6](#)<sup>29</sup> but refer to the [BNF for children](#) to modify drug treatments, and do not continue antipsychotic treatment for longer than 12 weeks.

### ***Long-term management***

1.11.16 Consider a structured individual or family psychological intervention for managing bipolar disorder in young people in the longer term.

## **2 Research recommendations**

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline.

### **2.1 *Psychological interventions for young people with bipolar depression***

What is the clinical and cost effectiveness of structured psychological interventions for [young people](#) with bipolar [depression](#)?

#### **Why this is important**

There has been very little research regarding the clinical effectiveness of structured individual and group psychological interventions for [children](#) and

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<sup>29</sup> At the time of publication (September 2014), olanzapine, quetiapine and lamotrigine did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information.

young people with bipolar disorder. Research on unipolar depression in children and young people supports the effectiveness of cognitive behavioural therapy (CBT), interpersonal therapy (IPT) and short-term family therapy. However there have been no published trials investigating clinical and functional outcomes for young people with bipolar depression. Given the increasing emphasis on early interventions in related conditions such as psychosis and unipolar depression, it is important to know the form of psychological therapy that can benefit young people with bipolar disorder.

A high-quality, non-inferiority randomised controlled trial (RCT) should recruit young people during an acute episode of bipolar depression who are treated with structured psychological interventions (CBT versus IPT). Interventions should be offered over 6–9 months, with a 9-month follow-up period. Key outcomes should include clinical recovery, symptom change, personal recovery or functional outcomes at the end of treatment and at 9-month follow-up, and cost effectiveness.

## **2.2      *Maintenance treatment***

In the maintenance treatment of bipolar disorder, what is the relative effect on quality of life of lithium, an antipsychotic (haloperidol, olanzapine, quetiapine or risperidone), or a combination of lithium and an antipsychotic?

### **Why this is important**

Lithium and antipsychotic medication are known to reduce the risk of relapse when used long-term in people with bipolar disorder. Relapses do still occur and the response is usually to add another mood-stabilising drug. However, lithium and antipsychotics are associated with a number of side effects, some of which can adversely affect physical health. The relative effects of lithium, an antipsychotic or a combination of these drugs, regarding efficacy, tolerability, cost effectiveness and quality of life are unknown. Such information is important to people with bipolar disorder to help them make an informed choice about the treatment options available to them, and to the NHS to inform the best use of resources.

The suggested programme of research should involve a pragmatic 3-arm RCT comparing lithium monotherapy with antipsychotic monotherapy (haloperidol, olanzapine, quetiapine or risperidone) and a combination of lithium and an antipsychotic. The study should last at least 1 year with the primary outcome being quality of life. Symptom control, relapse, function and economic outcomes should also be measured.

### **2.3 *Antidepressants combined with antimanic medication in bipolar depression***

What is the clinical and cost effectiveness of fluoxetine combined with olanzapine versus an alternative selective serotonin reuptake inhibitor (SSRI) combined with olanzapine in the treatment of moderate to severe bipolar depression?

#### **Why this is important**

Bipolar depression occurs 3 times more frequently than mania and is associated with suicide and impaired function and quality of life. The 2014 NICE clinical guideline on bipolar disorder found that the combination of fluoxetine and olanzapine was the most clinically and cost-effective treatment for bipolar depression. Antidepressants (imipramine, paroxetine and moclobemide) alone were ineffective compared with placebo. Olanzapine alone was an effective treatment for bipolar depression but not as effective as olanzapine and fluoxetine in combination. However, for many people some antidepressants are ineffective or cannot be tolerated. For these people the NICE clinical guideline on [depression in adults](#) recommends changing to another antidepressant from the same or a different class.

A 2-arm non-inferiority RCT of the combination of fluoxetine and olanzapine within BNF therapeutic levels versus an alternative SSRI and olanzapine for moderate or severe bipolar depression with a 12-week follow-up period should be carried out. The primary clinical outcome should be depression response. Secondary outcomes should be depression remission, function, anxiety symptoms, emergent mania or hypomania symptoms, other adverse outcomes, quality of life and cost effectiveness.

## **2.4      *A specialised collaborative care service for people with bipolar disorder***

What is the clinical and cost effectiveness of a specialised collaborative care service for people admitted to hospital with bipolar disorder versus treatment as usual delivered by generic care services?

### **Why this is important**

There is moderate-quality evidence of the effectiveness of a specialised collaborative care service compared with treatment as usual in reducing hospitalisation in 2 studies (from Denmark and the USA). There is no overall evidence of an effect on relapse or other outcomes. An economic analysis from 1 study showed that better clinical outcomes were achieved at two-thirds of the overall cost of treatment as usual. If similar results were obtained in England, then better care for a substantially reduced cost might be achieved.

A 2-arm multicentre RCT of a specialist collaborative care service for people admitted to hospital with bipolar disorder compared with treatment as usual, with follow-up of at least 2 years, is needed. Community alternatives to hospitalisation should be included. The specialist intervention should be based on collaborative care principles, including group or other psychoeducation to promote self-management, care coordination and algorithm-derived psychotropic medication (compatible with the 2014 NICE clinical guideline on bipolar disorder) under the direction of a psychiatrist. Feasibility and acceptability development work should involve collaborating with service users and professionals to demonstrate sustainable service delivery and recruitment, and identify and address possible barriers to such a service. Clinical outcomes should include time to next bipolar episode, mania and depression symptoms, function, recovery and quality of life. Economic outcomes should consider health, social care and personal costs.

## **2.5      *Cognitive behavioural therapy for the long-term management of bipolar disorder***

What is the clinical and cost effectiveness of face-to-face CBT versus internet-facilitated CBT in the long-term management of bipolar disorder?

### **Why this is important**

The 2014 NICE clinical guideline on bipolar disorder found that individual structured psychological interventions are clinically effective. Studies support the efficacy of individual CBT but evidence for long-term benefits of internet-based interventions is less conclusive. Internet-facilitated CBT has the potential to deliver the key components of face-to-face CBT in a more cost-effective and accessible format. If this proves to be the case then increased access to cost-effective psychological care could be rapidly achieved.

The proposed research programme would have two phases: (1) software development of internet-facilitated CBT including alpha, beta and feasibility and acceptability testing to confirm that the intervention is safe, acceptable and used by potential patients; (2) a 2-arm non-inferiority RCT comparing internet-facilitated CBT with individual face-to-face CBT designed for bipolar disorder. Participants should be aged 16 years and over and be in a state of euthymia when recruited. The primary outcomes should be personal recovery and quality of life at 12-month follow-up. Secondary outcomes should be time to relapse, social and occupational functioning, and cost effectiveness.

## **3 Other information**

### **3.1 *Scope and how this guideline was developed***

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

#### **How this guideline was developed**

NICE commissioned the National Collaborating Centre for Mental Health to develop this guideline. The Centre established a Guideline Development Group (see section 4), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

### **3.2      *Related NICE guidance***

Details are correct at the time of consultation on the guideline (April 2014).

Further information is available on [the NICE website](#).

#### **Published**

- [Psychosis and schizophrenia in adults](#). NICE clinical guideline 178 (2014).
- [Social anxiety disorder](#). NICE clinical guideline 159 (2013).
- [Psychosis and schizophrenia in children and young people](#). NICE clinical guideline 155 (2013).
- [Patient experience in adult NHS services](#). NICE clinical guidance 138 (2012).
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- [Antenatal and postnatal mental health](#). NICE clinical guideline 45 (2007).
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- [Violence](#). NICE clinical guideline 25 (2005).
- [Self-harm](#). NICE clinical guideline 16 (2004).
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### **Under development**

NICE is developing the following guidance (details available from [the NICE website](#)):

- Antenatal and postnatal mental health. NICE clinical guideline. Publication expected December 2014.
- Violence and aggression. NICE clinical guideline. Publication expected April 2015.

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