

# Depression: guide to detection and recommended management

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**Depression is a common condition and practitioners need to be alert to its possibility. Our Drug review discusses current diagnostic criteria and treatment guidelines, including the initiation of antidepressants, followed by sources of further information and an analysis of prescription data.**

Depression is a common and debilitating condition<sup>1</sup> and is mainly treated in primary care.<sup>2</sup> The criteria for a major depressive episode are outlined in the Diagnostic Statistical Manual (DSM) IV (see Table 1). Recent guidelines,<sup>3-5</sup> which inform this review, make reference to this classification system in preference to the World Health Organization's International Classification of Disease (ICD-10).

Both systems agree with regard to the range and duration of symptoms but differ according to the number of symptoms required to diagnose a clinically significant depressive episode: for DSM-IV five symptoms are required and for ICD-10 four. Key symptoms of depression are emphasised differently also. DSM-IV stipulates that within the five symptoms experienced, either depressed mood or anhedonia must be included, while ICD-10

describes the typical features of depression as lowering of mood, reduction of energy and decreased activity.

The National Institute of Health and Clinical Excellence (NICE) have adopted the DSM-IV criteria.<sup>3,4</sup> A Consensus Meeting in 2008<sup>5</sup> stressed the need for clinicians to have a working knowledge of the criteria for major depression.

## Detection

The effective treatment of depression meets an immediate hurdle: detection. Around 50 per cent of individuals with significant depressive symptoms will not have their condition recognised by primary-care doctors<sup>6</sup> due to a range of factors including the characteristics of patients, clinicians, and healthcare systems.<sup>7</sup> It is not surprising, therefore, that NICE guidelines on the treatment and



CPD questions available for this article. See page 32

## Depression

5 (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least 1 of the symptoms is either 1 or 2 (see below). Symptoms should be present most of the day or nearly every day.

1. depressed mood
2. markedly diminished interest or pleasure in all, or almost all, activities
3. significant weight loss when not dieting or weight gain (eg a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4. insomnia or hypersomnia
5. psychomotor agitation or retardation (observable by others)
6. fatigue or loss of energy
7. feelings of worthlessness or excessive or inappropriate guilt (not merely self-reproach or guilt about being sick)
8. diminished ability to think or concentrate, or indecisiveness (either by subjective account or as observed by others)
9. recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

The symptoms are not due to the direct physiological effects of a substance or a general medical condition.

The symptoms are not better accounted for by bereavement, *ie* after the loss of a loved one.

The symptoms persist for longer than 2 months or are characterised by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation.

**Table 1.** DSM-IV-TR criteria for major depressive disorder (adapted from the American Psychiatric Association)

management of depression in adults (CG90)<sup>3</sup> and on depression with a chronic physical problem<sup>4</sup> emphasise a need to be alert to the possibility of depression. This is particularly the case for individuals with a chronic physical condition or a previous history of depression.

NICE suggests that where there is a possibility of depression, the following two screening questions should be applied:

- During the last month, have you often been bothered by feeling down, depressed or hopeless?
- During the last month, have you often been bothered by having little pleasure or interest in doing things?

A 'yes' response to either of these questions prompts further, more comprehensive investigation. This process forms the initial stage of recommended management outlined in Figure 1. It is suggested<sup>3,4</sup> that a validated questionnaire be used to assist with this process. Establishing severity of symptoms is considered important because different treatments are advocated according to severity (see Figure 1).

### **Treatment considerations**

#### *Psychological and pharmacological options*

NICE guidelines advocate either high-intensity non-pharmacological interventions – specifically cognitive behavioural therapy (CBT) and interpersonal therapy (IPT), when delivered by competent practitioners and

in keeping with the relevant treatment manual – or antidepressant therapy for depression of at least moderate severity. Options pursued will depend upon patient preference, availability and previous successful treatment experience.

A generic SSRI at an effective dose is recommended where antidepressant therapy is indicated (see Figure 1 and Table 2). Taking into account efficacy, acceptability and cost, sertraline has been proposed as a first-line choice of antidepressants based on meta-analysis of 12 new-generation antidepressants.<sup>9</sup>

#### *Co-morbidities*

There is insufficient evidence for guidelines to recommend specific drugs for the treatment of depression

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in specific physical health conditions.<sup>4,8</sup> However, there is some evidence for avoiding certain antidepressants in particular situations. A synthesis of appropriate antidepressant treatments is presented in Table 2, along with minimum effective starting doses in Table 3.

Reboxetine (Edronax) has been found to be no better than placebo<sup>10</sup> and inferior to other antidepressants.<sup>9,10</sup> It is therefore only recommended as an option where patients have experienced significant sexual dysfunction with other antidepressants.

Where individuals with chronic physical conditions have not responded to either high-intensity psychological treatment, pharmacological treatment or their combination, collaborative care is advocated. Such programmes involve a co-ordinated, long-term approach

from a multidisciplinary team, which includes case management, close collaboration between primary care, secondary care and specialist mental health services and a range of psychological and pharmacological interventions.

#### *Inadequate treatment response*

With antidepressant treatment it is necessary to ensure that the dose, duration and adherence are sufficient to maximise the likelihood of an adequate treatment response. This is particularly important because the likelihood of there being an adequate response decreases as the number of changes to treatment strategies increases. Although Figure 1 outlines a course of action where response to treatment has not been adequate, it

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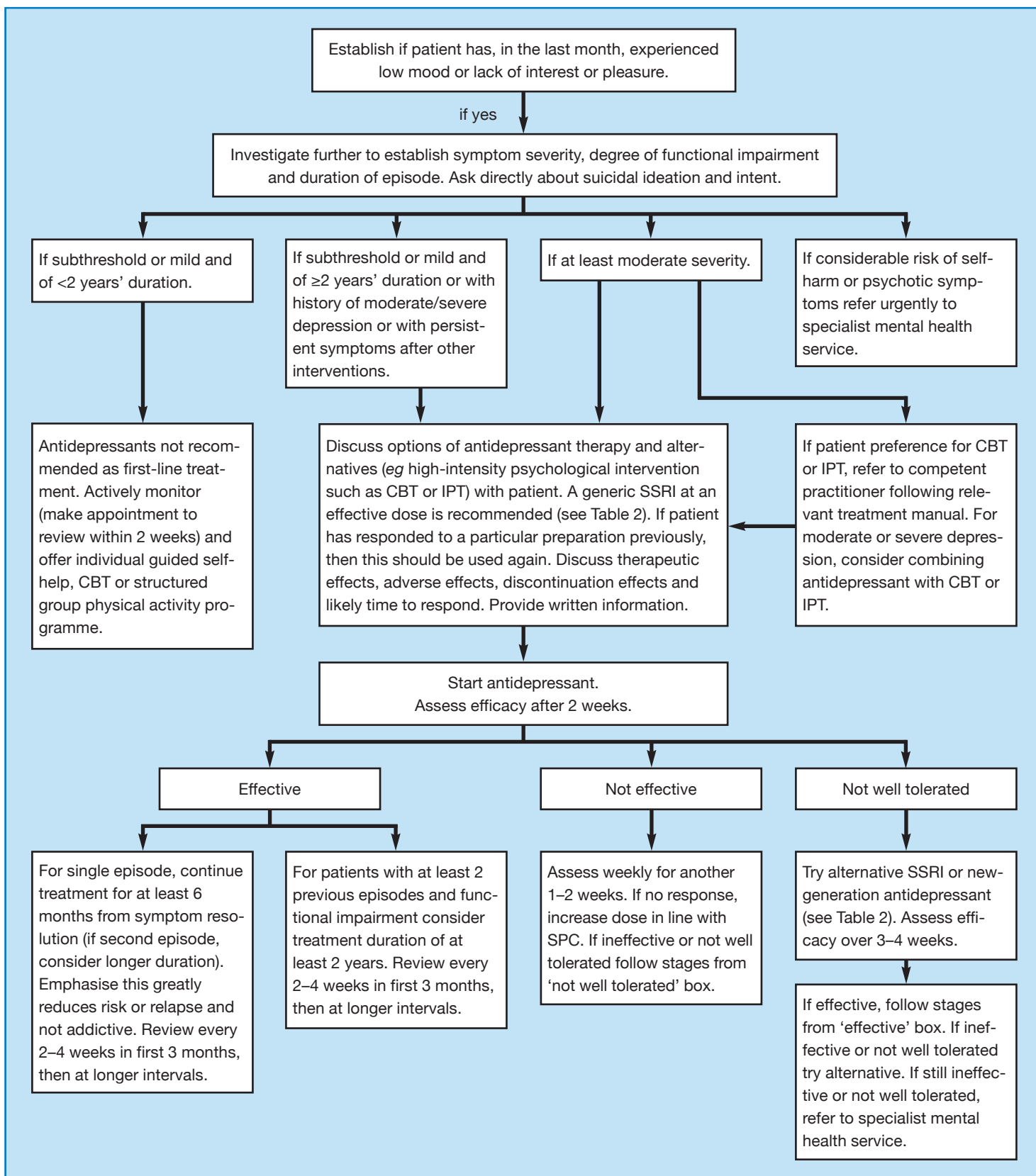


Figure 1. Depression – recommended management and treatment algorithm

is also acknowledged that further research is needed to identify optimal management strategies for such circumstances.<sup>3</sup> It is our view that if a dose increase is not effective within four weeks, practitioners should not delay further in considering an alternative antidepressant.

### *Recurrent depression*

Current guidelines emphasise the importance of continuation with antidepressant treatment after symptom remission for at least six months in a first episode and for longer periods where risk factors are present. Risk factors include having previous episodes of depression, presence of residual symptoms, concurrent physical health problems and psychosocial difficulties.

Continuing treatment in this manner has been demonstrated to reduce relapse rates by up to two-thirds.<sup>11</sup> The risk of relapse is greatest in the first few months after discontinuation regardless of duration of treatment.

### *Stopping and reducing*

When stopping antidepressant therapy, patients should be advised regarding discontinuation effects. Treatment should be gradually reduced over a four-week period (for preparations other than fluoxetine which does not require a gradual process given the long half-life of the active metabolite norfluoxetine). A period of longer than four weeks is advised for stopping paroxetine or venlafaxine due to their shorter half-life.

Co-morbidity	Antidepressant*	Comment
<i>No co-morbidity</i>	sertraline citalopram fluoxetine	consider mirtazapine or short-term benzodiazepine if sedation required
<i>Older adults</i>	citalopram mirtazapine	consider lower starting dose
<i>Cardiovascular disease</i>	fluoxetine sertraline	sertraline is the drug of choice post-MI avoid tricyclics
<i>Hepatic impairment</i>	citalopram paroxetine	dose reduction may be necessary avoid fluoxetine and lofepramine
<i>Renal impairment</i>	citalopram sertraline	dose reduction may be necessary avoid fluoxetine, lofepramine and venlafaxine
<i>Severe renal or hepatic disease</i>	seek specialist advice	
<i>Epilepsy</i>	citalopram	avoid tricyclics – seizure risk dose related
<i>Pregnancy</i>	fluoxetine (consider risk-benefit ratio)	consider withdrawal in third trimester avoid paroxetine refer to NICE guideline 45 consider specialist advice
<i>Breast feeding</i>	sertraline	refer to NICE guideline 45
<i>Sexual dysfunction</i>	mirtazapine reboxetine	
<i>Children and adolescents under 18 years</i>	fluoxetine	consider specialist advice
* see Table 3 for minimum effective doses		

**Table 2.** Choosing an antidepressant (from Cornhill Medicines Group, NHS Grampian 2010)

When reviewing patients on longer-term antidepressants it is necessary to consider factors such as age, co-morbid conditions, presence of residual symptoms, number of previous episodes, duration and degree of treatment resistance of the most recent episode, and severity.

### Tips and pitfalls

In clinical practice, gauging the severity of depressive symptoms in a manner that informs rational treatment decisions is challenging. NICE guidelines suggest the use of a validated questionnaire to facilitate this process. The GP contract Quality and Outcomes Framework (QOF) has advocated the use of several measures in primary care since 2006. These are the Patient Health Questionnaire (PHQ-9), the Hospital Anxiety and Depression Scale, Depressive Subscale (HADS-D) and the Beck Depression Inventory (BDI-II).

Unfortunately, the QOF endorsed scales were never validated for severity measurement in this setting and have now been shown not to align adequately with the Hamilton Rating Scale for Depression (HRSD-17), the severity measure used to inform the evidence base.<sup>12</sup> As a result, we cannot recommend them here, and it seems likely that these measures will be 'retired' in future iterations of the QOF and its successors.

The HRSD-17 has been applied in research – mainly assessing changes in mean scores across time following interventions, rather than to categorise the severity of depressive symptoms. Even this 'gold-standard' scale is of limited value as there is a lack of agreement between NICE<sup>3</sup> and the American Psychiatric Association<sup>13</sup> on severity cut-off points across scores. In any case, more research attention is required to assess the efficacy of antidepressants in milder depression as there are insufficient data to properly assess this, with previous meta-analyses extrapolating only from findings relating to patients with more severe symptoms.<sup>14</sup> It has been assumed that the potential harms of antidepressants outweigh their effectiveness in mild depression, but this has never been formally demonstrated.

While most guidelines give similar advice on the monitoring of antidepressants in the acute stage, guidance is less clear for longer-term prescribing. NICE states that people commencing an antidepressant should normally be reviewed at two- to four-weekly intervals in the first three months and then at longer intervals if response is good. Observation of monitoring in the longer term would suggest that, for people in the second or subsequent years of treatment, scheduled reassessment should occur routinely.<sup>15</sup>

Greater social adversity is associated with higher rates of depression<sup>16</sup> and lower rates of remission.<sup>17</sup> Little

Antidepressant	Minimum effective dose
citalopram	20mg daily
fluoxetine	20mg daily
paroxetine	20mg daily
sertraline	50mg daily
mirtazapine	30mg daily
reboxetine	8mg daily
venlafaxine	75mg daily

**Table 3.** Minimum effective doses (from the *Maudsley Prescribing Guidelines*<sup>8</sup>)

guidance is currently offered to direct clinicians as how best to address such issues. Nonetheless, it is important to recognise that adverse circumstances in themselves need not constitute a barrier to antidepressant treatment when significant mood disorder is present; improving depressive symptoms will play an important role in promoting more effective coping strategies.

There is an emphasis on taking into account patient preference in devising a treatment plan for depression. Many individuals will welcome the option of nonpharmacological treatments. Initiatives such as Improving Access to Psychological Therapy (IAPT) in England ([www.iapt.nhs.uk](http://www.iapt.nhs.uk)) and the Health Efficiency Access and Treatment Target (HEAT) to improve access to psychological therapies in Scotland ([www.evidenceintopractice.scot.nhs.uk](http://www.evidenceintopractice.scot.nhs.uk)) should help to implement the NICE guidelines, but it remains to be seen whether supply will be able to meet demand or, indeed, whether delivery is truly effective.

As with chemical antidepressants, it is by no means certain that the efficacy of psychological therapies demonstrated in the rarefied atmosphere of clinical trials, where selected patients are treated by expert enthusiasts, will translate into effectiveness in real-world settings.

### Conclusion

Practitioners should remain alert to the possibility of depression, especially in those at particular risk. Psychological and/or pharmacological treatment options may be considered and should be delivered with reference to the existing evidence base (in terms of dose, duration, training, *etc*) in order to maximise response. Further research is necessary to inform management strategies where there is inadequate response, where long-term treatment is advocated and in addressing issues of social adversity.

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#### Declaration of interests

Isobel Cameron and Dr Gauld have nothing to declare. Professor Reid has received honoraria from AstraZeneca UK.

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## Resources

### Guidelines

*Depression – management*. NHS Clinical Knowledge Summaries. [www.cks.nhs.uk/depression](http://www.cks.nhs.uk/depression).

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Evidence-based guidelines for treating depressive disorders with antidepressants. Consensus statement from the British Association for Psychopharmacology. Revised 2008. *Journal of Psychopharmacology* 2008; 22:343–96.

*The treatment and management of depression in adults with chronic physical health problems (partial update of CG23)*. CG91. NICE, October 2009.

## Prescription review

Prescribing of all antidepressant classes has been rising steadily over the past five years, with SSRIs showing strongest growth due to increased prescribing of citalopram. Costs were falling slowly until 2011, when spending on SSRIs almost doubled due to increased costs for citalopram and sertraline.

Amitriptyline is the only tricyclic to show significant volume growth and now accounts for 70 per cent of prescriptions and 45 per cent of costs for this class. Dosulepin, which the *BNF* classes as less suitable for prescribing due to its toxicity in overdose, is the next most frequently prescribed tricyclic and accounts for one in eight prescriptions in this class.

Mirtazapine overtook venlafaxine as the most frequently prescribed ‘other antidepressant’ in 2008, with 50 per cent volume growth in the past three years.

	Items (000)	Cost (£000)
citalopram	12 573	45 585
amitriptyline	9 118	16 863
fluoxetine	5 400	18 610
mirtazapine	3 564	10 020
sertraline	3 212	26 555
venlafaxine	2 648	67 516
paroxetine	1 579	7 264
escitalopram	1 244	24 138
duloxetine	675	18 942

**Table 4.** Prescribing of selected antidepressants in England, year to June 2011

Use of duloxetine has doubled in the last three and a half years, albeit from a low baseline, but its cost is also rising whereas spending on both mirtazapine and venlafaxine is falling.

## CPD: management of depression

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### 1. Which one of these statements about diagnostic criteria for depression is false?

- a. DSM-IV and ICD-10 do not agree with regard to the range and duration of symptoms
- b. For a diagnosis of depression, five symptoms are required by DSM-IV and four by ICD-10
- c. NICE has adopted the DSM-IV criteria
- d. DSM-IV requires the presence of depressed mood or anhedonia

### 2. One of these statements is false – which is it?

- a. Doctors in primary care do not recognise depression in 50 per cent of individuals with significant depressive symptoms
- b. Patients in primary care in whom depression is suspected can be screened for depression using two simple questions, which if positive prompt further investigations
- c. Symptom severity does not influence the choice of treatment
- d. Patients with suspected depression should be asked directly about suicidal ideation and intent

### 3. One of these statements is false – which?

- a. Antidepressant therapy is recommended for depression of at least moderate severity
- b. Sertraline is a suitable first-choice antidepressant
- c. Collaborative care is advocated for individuals with chronic physical conditions who have not responded to either high-intensity psychological treatment, pharmacological treatment or their combination
- d. Reboxetine should be avoided in patients who experienced sexual dysfunction with other antidepressants

### 4. Which one of these statements is false?

- a. If a patient does not respond to an antidepressant and a dose increase is not effective within four weeks, an alternative antidepressant should be considered

- b. The likelihood of an adequate treatment response decreases as the number of changes to treatment strategies increases
- c. Citalopram is a suitable antidepressant for patients with impaired renal or hepatic function
- d. Current guidelines emphasise the importance of continuation with antidepressant treatment after symptom remission for at least three months in a first episode of depression

### 5. Regarding discontinuing antidepressant therapy, which one of these statements is false?

- a. The risk of relapse is greatest in the first few months after discontinuation, regardless of duration of treatment
- b. When discontinuing fluoxetine, the dose should be tapered down over four weeks
- c. When discontinuing treatment with venlafaxine, the dose should be tapered down over a period of more than four weeks
- d. The number of previous episodes is one of the factors that should be considered when contemplating discontinuing antidepressant therapy

### 6. One of these statements is false – which is it?

- a. Questionnaires recommended in QOF to assess symptom severity do not correlate well with the HRSD-17
- b. NICE states that people commencing an antidepressant should normally be reviewed at two- to four-weekly intervals in the first three months and then at longer intervals if response is good
- c. NICE and the American Psychiatric Association agree that the cut-off point in HRSD-17 that signifies severe depression is a score of 12
- d. The minimum effective dose of mirtazapine is 30mg daily

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