

## Managing and preventing depression in adolescents

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Depressive disorder affects 1-6% of adolescents each year worldwide,<sup>1 2</sup> and early onset heralds a more severe and persistent illness in adult life.<sup>3</sup> Effective treatment is available, but best treatment practice is controversial because of concerns about the use of antidepressants in young people and inconsistencies in evidence. This review provides guidance for non-specialists on the assessment and management of adolescent unipolar depression and considers emerging evidence on prevention strategies.

### Why is it important to identify adolescent depression?

Evidence from prospective community studies suggests that rates of underdiagnosis and undertreatment of depression are higher in adolescents than in adults.<sup>4</sup> Large scale, longitudinal population based and clinical cohort studies have consistently shown that rates of depression rise sharply after puberty, especially in girls, with immediate and long term risks.<sup>5 6</sup> Clinical depression adversely affects schooling, educational attainment, and relationships,<sup>7</sup> and it has long term negative consequences on adult physical health and functioning.<sup>8</sup> Although most affected adolescents show initial remission, 50-70% of them will have a recurrence within five years of initial diagnosis.<sup>5</sup> Large prospective studies have also shown that adolescent depression is associated with a raised risk of suicide (odds ratio 11 to 27),<sup>9</sup> and suicide represents the third leading cause of death in this age group (aged 14-19 years).<sup>10</sup>

### SOURCES AND SELECTION CRITERIA

We searched for papers published between 1990 and 2009 using key index terms (adolescent depression, treatment, and prevention) on PubMed (Medline and life science journals). In addition, we consulted the Institute of Medicine report "Preventing mental, emotional and behavioral disorders among young people: progress and possibilities" (published by National Academies Press 2009), NICE guidelines on adolescent depression, Cochrane systematic reviews, and *BMJ Clinical Evidence*. This was supplemented by reviews and our own knowledge.

### Which adolescents are most at risk of developing a depressive disorder?

Evidence from clinical and epidemiological studies shows that three groups are at increased risk of developing a depressive disorder. Firstly, adolescents who have raised levels of depressive symptoms but fall below the diagnostic threshold have a two to three times greater risk of developing future depressive episodes than those without such symptoms.<sup>8</sup> Secondly, the adolescent offspring of parents with a history of depression are three to four times more likely than those of parents with no psychiatric history to develop depression.<sup>11</sup> Thirdly, in adolescents who have previously had depression, recurrence rates are high.<sup>8</sup>

### How is adolescent depression diagnosed?

Diagnostic criteria from either ICD-10 (international classification of diseases, 10th revision) (box) or the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV) are currently used; these two sets of criteria are similar.

The criteria for depression in adolescents are the same as for adults (although the DSM-IV criteria allow "irritable" (easily annoyed and provoked to anger) instead of "depressed" mood in children and adolescents). Thus the clinical questioning approach with adolescents should be similar to that used in adults. In this age group, it is helpful to question both the adolescent and the parent(s) about specific symptoms and to check whether the symptoms of depression are associated with impairment—for example, an adolescent with depression may stop going out with friends or show deterioration in school work. Irritability may be a prominent symptom. In this age



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"We're doing a large study at the moment, of 340 families, where the parents have had recurrent depression, and we're following up the adolescents over four years to look at factors that improve outcomes as well as risk pathways, and hopefully that will help us to understand more, so we can devise better prevention and intervention programmes"  
Author Anita Thapar talks about her paper in a podcast  
<http://podcasts.bmj.com/bmj>

### SUMMARY POINTS

Depression affects 1-6% of adolescents each year worldwide

Diagnostic criteria for depression are the same as for adults, but the primary presenting concern may be different (for example, behavioural problems, refusal to go to school)

For mild depression, cognitive behavioural therapy seems to be effective. Because such treatment is a scarce resource, less specialised supportive treatment and guided self help can be used initially

For moderate-severe depression, fluoxetine and routine specialist (child and adolescent mental health service) clinical care or fluoxetine plus cognitive behavioural therapy is recommended

Suicidal risk must be carefully monitored

Parental depression needs to be treated

group, comorbidity with other psychiatric disorders—notably disruptive behaviour disorders (20-40%) and anxiety disorders—is common (occurring in 30-75% of cases), as is association with deliberate self harm and suicidality (odds ratio 5.1).<sup>12</sup> Depression may be missed if the primary reported features are behavioural problems, substance misuse, anxiety symptoms, refusal to go to school, academic failure, or unexplained physical symptoms—especially musculoskeletal pains<sup>13</sup>—all of which are significantly associated with adolescent depression (reported odds ratios 10 to 29).<sup>14</sup>

Questionnaires can be used for screening and monitoring changes in the depression symptom score. The Mood and Feelings Questionnaire (MFQ; <http://devepi.duhs.duke.edu/mfq.html>) is one of the most well established screening instruments for adolescent depression,<sup>15</sup> and it has been validated in clinical and community samples. If a parent raises the initial concerns, their reports on the adolescent can be helpful as a first screen, and the above questionnaire has both a parent version and a child version. Other questionnaires are also available.<sup>16</sup> It is important to ask the adolescent about suicidal thoughts and intent.

### Which treatments work for adolescent depression?

Inconsistent evidence and guidelines have made best treatment practice of depression in adolescents controversial.<sup>17,18</sup> Most published evaluation studies have focused on the short term effectiveness of newer generation antidepressant drugs or cognitive behavioural therapy (CBT), or both. Evidence on long term efficacy and prevention of relapse is lacking.

### Psychological treatments

The two most commonly investigated treatments are CBT and interpersonal psychotherapy. The evidence on CBT is mixed. One meta-analysis suggests that CBT is effective for adolescent depression, although effect sizes are mod-

### CRITERIA FOR DEPRESSIVE EPISODE, ACCORDING TO ICD-10

Two of the first three symptoms listed below must be present. In addition, at least four symptoms (for mild episode), six symptoms (for moderate episode), or eight symptoms (for severe episode) must be present during the same two week period.

- Depressed mood for most of the day and almost every day
- Loss of interest or pleasure in activities
- Decreased energy or increased fatigability
- Loss of confidence or self esteem
- Unreasonable feelings of self reproach or excessive inappropriate guilt
- Recurrent thoughts of death or suicide, or any suicidal behaviour
- Reduced ability to think or concentrate
- Change in psychomotor activity, agitation, or retardation
- Sleep disturbance
- Change in appetite with corresponding weight change

est (0.3).<sup>19</sup> A recent systematic review and meta-analysis also shows that CBT is modestly effective for adolescent depression, but that effect sizes are smaller in more recent better designed studies and in more complicated cases.<sup>20</sup> In contrast, a large randomised controlled trial (TADS) from the United States found that in moderate-severe depression, CBT alone was no better than placebo,<sup>21</sup> and that it provided benefits only in combination with fluoxetine.

Interpersonal psychotherapy has been shown to be effective in treating adolescent depression in three randomised controlled trials.<sup>22</sup> However, good quality psychological treatments for adolescents are not widely available in many countries.

Taken together, the evidence on psychological treatments can be summarised as follows:

- CBT alone is probably most useful for mild depression
- Interpersonal psychotherapy, if available, is worthwhile.

### Drugs

The effectiveness of selective serotonin reuptake inhibitors for children and adolescents has been systematically reviewed.<sup>23</sup> Two systematic reviews suggest that fluoxetine is an effective treatment for adolescent depression (41-61% response to fluoxetine v 20-35% response to placebo, relative risk 1.86; treatment effect in terms of depression symptom scores -5.63). Consistent good quality evidence on other newer generation antidepressants is currently lacking.

### Treating mild depression in non-specialist settings

In most countries, including the United Kingdom, primary care plays a key part in the detection and initial management of adolescent depression, but few treatment studies are based in this setting. One randomised controlled trial in the US suggested that organisational changes in primary care through trained care managers who enhanced access to evidence based treatments (CBT and antidepressants) significantly reduced symptoms of adolescent depression in the short term.<sup>24</sup>

Simple, non-specific psychosocial strategies might also

### QUESTIONS FOR FUTURE RESEARCH

- Improved understanding of the early natural history of adolescent depression including risk factors and protective factors to guide new treatments
- Randomised controlled treatment trials of adolescent depression that are not sponsored by drug companies
- Randomised controlled treatment trials of psychological therapies that can be delivered without the need for expensive and intensive training (for example, guided self help, graded activities, and guided internet packages)
- Which subgroups of patients respond better to specific treatments?
- Which treatment and prevention approaches are most effective and feasible in low resource communities and developing countries?
- Does early intervention improve longer term prognosis?
- Which interventions prevent relapse?
- Randomised controlled treatment trials of simple psychosocial strategies for prevention in non-specialist settings
- Does improving management of parental depression reduce the risk of depression in adolescents?

**It is increasingly being argued that preventing, or at least delaying, the onset of depression in children and adolescents is a major public health and clinical priority**



be helpful as an initial treatment, although good quality evidence on these is lacking. Such first line pragmatic approaches deserve proper evaluation because specialised resources such as CBT are limited. Suggested strategies include providing parental support; recognising and treating parental mental illness; educating patients about depression (this may include the use of educational leaflets); problem solving; attending to recent family or peer group conflicts; dealing with comorbidity; and liaising with schools and other agencies while monitoring mental state and using an empathic reflective approach.<sup>25</sup> Advice on nutrition and diet, exercise (45 minutes to one hour three times week), sleep hygiene, and anxiety management, along with guided self help and non-directive supportive counselling are also recommended.<sup>17</sup>

#### Treating moderate-severe depression

Clinical guidelines on the treatment of adolescent depression differ between Europe and the US, and some guidance is based on consensus opinion rather than evidence. Currently, evidence on the best available treatment for moderate-severe adolescent depression comes from two randomised controlled treatment versus placebo trials. One study was based on UK NHS patients (ADAPT),<sup>25</sup> had

no sponsorship from a drug company, and found a significant treatment effect at 12 weeks. It compared fluoxetine alone (61% “much or very much improved” by 28 weeks) with CBT plus fluoxetine (53% much or very much improved); all patients received routine specialist clinical care. The other study (TADS) was from the US, and it compared 12 weeks of CBT alone (43% response), fluoxetine alone with no psychosocial care (61% response), and CBT plus fluoxetine (71% response) with placebo (35% response).<sup>21</sup> The evidence on treating moderate-severe depression can be summarised as follows:

- Fluoxetine is an effective treatment for adolescent depression<sup>21 23 25</sup>
- Evidence on the benefits of adding CBT to fluoxetine is mixed. The US study suggested that it accelerated the response to treatment and reduced suicidality,<sup>21</sup> whereas the UK study found no benefits.<sup>25</sup> This might have been because the UK study included more severe clinic derived cases and all patients received routine specialist care
- Consistent effectiveness data on newer generation antidepressants other than fluoxetine are lacking,<sup>23</sup> and they are currently not approved for use in patients under 18 years in the UK and Europe. Escitalopram has been approved by the US Food and Drug Administration, but consistent evidence on its effectiveness in adolescence is still limited.

Only around 60% of adolescents with depression show remission after treatment, so what about those who fail to respond to initial treatment? One large US randomised control trial of adolescents who had not responded to two months of initial treatment with a first selective serotonin reuptake inhibitor suggested that adding CBT and switching to another one of these drugs (paroxetine or citalopram) results in a higher response rate (54.8%) than switching drugs only (40.5%).<sup>26</sup> A switch to venlafaxine was not recommended because of adverse side effects.

#### Suicidal risk

One of the major concerns has been that new generation antidepressants seem to be associated with greater suicidal risk in adolescents than in adults.<sup>27</sup> Caution

#### A PATIENT'S PERSPECTIVE

J is a 15 year old boy who came to clinic with his mother and father. He has “always” had episodes of feeling low in mood but this has become sustained and problematic during the past 18 months and accompanied by other depressive disorder symptoms, including marked irritability. He has stopped going to school and his parents cannot get him to leave the house.

These are his own words: “I feel constantly down. I am feeling tormented. I feel sad, hate myself. This feels different from usual sadness and I can’t stop crying. I don’t want to go out and don’t like football or computer games any more. I can’t cope with activities such as rugby club. I can’t concentrate on computer games. I feel exhausted all the time and can’t go to school. I feel paranoid, that other people turn to look at me and I want to die. I feel I am torturing my family and I am jealous as other teenagers my age are better off. My future looks bleak.”

## TIPS FOR NON-SPECIALISTS

- Consider the possibility of adolescent depression even when the adolescent does not present primarily with mood symptoms
- Remember that depression can present with behavioural problems, unexplained physical symptoms, academic failure, refusal to go to school, anxiety, and substance misuse
- Ask about suicidal thoughts
- Ask parents with depression about concerns regarding their adolescent offspring
- When depression is diagnosed, provide the adolescent and his or her parents (or carers) with information on the disorder and guided self help strategies
- If moderate-severe depression, continued mild depression, complicating psychotic features, suicidality, or other psychiatric risk factors are present, refer to child and adolescent mental health services. Monitor carefully in the interim

## ADDITIONAL EDUCATIONAL RESOURCES

## Resources for healthcare professionals

Centre for Clinical Interventions ([www.cci.health.wa.gov.au](http://www.cci.health.wa.gov.au))—Although not specifically aimed at adolescent depression, this site has a section containing resources for general practitioners

National Institute for Health and Clinical Excellence ([www.nice.org.uk/CG28](http://www.nice.org.uk/CG28))—UK clinical guidance on depression  
 American Academy of Child and Adolescent Psychiatry ([www.aacap.org/cs/Depression.ResourceCenter](http://www.aacap.org/cs/Depression.ResourceCenter))—US clinical guidance on adolescent depression

## Resources for patients

Youthinmind ([www.youthinmind.com](http://www.youthinmind.com))—Website providing help for stressed children and teenagers and those who care for them

Samaritans ([www.samaritans.co.uk](http://www.samaritans.co.uk))—Confidential source of support—face to face, telephone, and email; the website also contains useful information

Depression in Teenagers ([www.depressioninteenagers.co.uk](http://www.depressioninteenagers.co.uk))—Aimed at teenagers; gives useful advice about depression and its treatment

Black Dog Institute ([www.blackdoginstitute.org.au/public/depression/inteenagersyoungadults.cfm](http://www.blackdoginstitute.org.au/public/depression/inteenagersyoungadults.cfm))—Useful information on depression for parents and young people

is needed in interpreting results, however, because untreated adolescent depression can itself lead to suicidality and the evidence is mixed.<sup>23-27</sup> A recent pooled analysis of 27 published and unpublished randomised placebo controlled trials of newer generation antidepressants in children and adolescents found that the benefits of antidepressants (number needed to treat 10) were greater than the risk of suicidal ideation and suicide attempts (number needed to harm 143).<sup>27</sup> Overall, the evidence supports careful monitoring for suicidal risk in adolescents with depression, regardless of treatment choice.

### Can we prevent or delay onset of depression in adolescents?

Given the serious burden of depression, the poor prognosis when onset is early, and the limited treatment options available, it is increasingly being argued that preventing, or at least delaying, the onset of depression in children and

adolescents is a major public health and clinical priority.

A meta-analysis of the evidence on this topic suggests that prevention strategies are likely to be effective only when given to high risk groups of adolescents rather than to the whole population.<sup>28</sup>

### What sorts of prevention strategies might be useful?

The most promising prevention programme has been targeted at three high risk groups—those with raised depression symptoms, a previous episode of depression, and whose parents have a history of depression. It consists of a group based CBT approach delivered to parents and children.<sup>29</sup> A recent high quality randomised controlled trial in the US found that this type of intervention resulted in significantly fewer depressive episodes at one year (21.4% v 32.7% in controls).<sup>29</sup> However, the intervention was less effective if the parents had current depression. This could simply reflect higher inherited risk for depression in the adolescents, but it could mean that adolescent depression can arise from the direct and indirect risk effects of being exposed to current parental depression. In support of current maternal depression being an important target, the largest treatment trial of adult depression, STAR\*D, found that successfully treating depression in mothers improved the mental health of children.<sup>30</sup> However, this finding requires confirmation. Nevertheless, these results highlight the importance of effectively monitoring and treating maternal depression and better integrating adult and child services. They also suggest future possibilities for prevention programmes.

### Conclusion

Depression in adolescents is common, severe, and leads to immediate and long term morbidity and mortality. It is important for clinicians who deal with young people and families to be aware of the problem, so that high risk adolescents can be screened, assessed, and offered appropriate treatment. Prevention strategies in high risk groups are likely to become increasingly important.

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**Parental consent obtained.**

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## ANSWERS TO ENDGAMES, p 269. For long answers go to the Education channel on bmj.com

### CASE REPORT A massive haematemesis

- 1 Decompensated alcoholic liver disease with portal hypertension leading to haemorrhage from gastro-oesophageal varices.
- 2 A safe airway should be secured, appropriate intravenous access obtained, and the critical care team involved. The patient requires immediate fluid resuscitation, including blood and blood products, and prophylactic antibiotics (such as cefotaxime).
- 3 Once stable he should undergo emergency gastroscopy for diagnosis and treatment. In view of the likely diagnosis, a vasoactive drug such as terlipressin or octreotide should be given while preparing him for endoscopy.
- 4 Patients with suspected portal hypertension should have a screening endoscopy and if varices are found be considered for either non-selective  $\beta$  blockade or prophylactic endoscopic treatment.
- 5 The key determinants of long term prognosis are the severity of his underlying liver disease and whether he stops drinking alcohol.

### STATISTICAL QUESTION Control groups

*b* and *c* are both true; *a* and *d* are false.

### PICTURE QUIZ Red in the face

- 1 A florid eruption composed of a sharply demarcated erythematous macular patch on the left side of her face with complete sparing of the contralateral side.
- 2 Phototoxic drug eruption, erysipelas, or unilateral rosacea. The nature of the eruption and the lack of systemic features suggested that the most likely diagnosis was a phototoxic drug reaction to doxycycline.
- 3 Firstly, review the drug history and stop the drug responsible, which in this case was doxycycline. Potent topical steroids can then be given short term to settle down the florid inflammatory reaction. It may also be necessary to institute photoprotective measures, such as moving the patient away from the window and providing adequate protective clothing and high SPF sunblock. The diagnosis can be confirmed by performing monochromator light testing.