06 - Prescribing for depression in children and ad

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Prescribing in children and adolescents CHAPTER 5 meta-analysis comparing several treatments for depression in children and adolescents also found that combined fluoxetine and CBT was no more effective than fluoxetine alone but found that this combination was more effective than CBT alone.16 Prescribing for depression in children and adolescents Before prescribing ■ ■Undertake a comprehensive assessment: Establish a clinical diagnosis of depression. Exclude differential diagnoses, including psychiatric disorders (such as bipolar affective disorder), medical disorders (such as endocrine disorders) and medication-related effects (such as steroid adverse effects). Identify any comorbid psychiatric or medical conditions. Consider contraindications to SSRIs and potential interactions. Assess risk of harm to self and others. Formulate considering factors that could predispose, precipitate and perpetuate depression, such as family history of psychiatric disorders (including depression and bipolar affective disorder) and environmental stressors (including victimisation and other adverse experiences). If any co-occurring problems are identified, these should be addressed and prioritised based on a comprehensive formulation. ■ ■Measure baseline severity: Measures of depression symptoms include the clinician- administered Children’s Depression Rating Scale-Revised (CDRS-R)17,18 and the childand parent-reported Mood and Feelings Questionnaire (MFQ)19 or Revised Children’s Anxiety and Depression Scale (RCADS).20 Measures of functional impairment include the Children’s Global Assessment Scale (CGAS).21 ■ ■Obtain informed consent: Discuss the nature, course and treatment of depression, potential adverse effects of medication, delay in onset of treatment effects, plan for monitoring and maintenance of medication and potential discontinuation effects. ■ ■Develop a safety plan: In all but exceptional circumstances, a parent or carer should be responsible for the secure storage of medication for a child or adolescent. Advise the young person and their parent/carer of professionals or services they should contact if they experience significant adverse effects, risk of harm or worsening symptoms. What to prescribe ■ ■Fluoxetine is the recommended first-line

medication for depression in children and adolescents.3,4 It has the strongest current evidence for efficacy,6,9,11,16,22,23 showing moderate effects in reducing depression symptoms versus placebo (standardised mean difference = 0.51).16 In the UK, NICE states that fluoxetine is the only antidepressant for which clinical trial evidence shows that benefits outweigh risks.4 Fluoxetine should be started at a dose of 10mg daily which can be increased after 1 week to the minimum therapeutic dose of 20mg daily. Higher doses (up to 40–60mg daily) may be considered, particularly in older children of higher body weight or when, in severe illness, an early clinical response is considered a priority.4,5,15,24 The long half-life of fluoxetine may be beneficial for adolescents because it confers a reduced risk of discontinuation effects or relapse if doses are delayed or missed.25 Fluoxetine is approved for treatment of depression in patients aged 8 years and over by the US Food and

 (FDA), and by the European Medicines Agency and the UK Medicines and Healthcare products Regulatory Agency (MHRA) if the young person has moderate to severe depression and has not responded to psychological therapy.26 ■ ■Sertraline and escitalopram have also been found to be more effective than placebo for treating depression in young people6,22 and should be considered as alternatives if fluoxetine is not tolerated. Sertraline and escitalopram should also be started at low doses (25–50mg daily and 5–10mg daily, respectively) and titrated to therapeutic doses (50–-200mg daily and 10–20mg daily, respectively). The half-lives of sertraline, escitalopram and some other antidepressants may be shorter in young people than adults, so twice daily dosing could be considered to prevent discontinuation symptoms.27 Escitalopram is approved by the FDA for treatment of depression in patients aged 12 years and over. ■ ■Duloxetine and venlafaxine may be effective but are relatively poorly tolerated.28 ■ ■Agomelatine was more effective than placebo in children aged 7–11 years and showed similar efficacy to fluoxetine. A dose of 10mg seems to be effective. Agomelatine is extremely well tolerated but not licensed for children or adolescents. Liver function test (LFT) changes occurred in 1% of participants.29 Vortioxetine was no more effective than placebo in a large study of 12–17-year-old children.30 ■ ■For children and adolescents who have significant depressive symptoms resulting in distress or impairment despite an adequate trial of an SSRI alone, consider combination SSRI and psychological therapy. There is some limited evidence that combination treatment may be more beneficial than SSRI alone for some young people.6,31–33 ■ ■For children and adolescents who have significant depressive symptoms resulting in distress or impairment despite adequate trials of an SSRI (fluoxetine) and psychological therapy, consider a switch to a different SSRI (sertraline, escitalopram).4,31 This guidance is largely based on the Treatment of Resistant Depression in Adolescents (TORDIA) trial,24 the only RCT that has examined the comparative efficacy of different treatment strategies for SSRI-resistant depression in young people.24 This trial found that many participants improved when switched to another SSRI or venlafaxine (response rate 47% and 48%, respectively) and improved even more when this medication switch was combined with starting concurrent CBT (response rate 55% vs 41% without CBT) after 12 weeks of treatment. A switch to an SSRI was just as efficacious as a switch to venlafaxine but had less frequent and severe side effects, so an SSRI switch is preferred. ■ ■If limited response despite adequate trials of these medications and psychological therapy, consider augmenting SSRI treatment with another medication such as a second-generation antipsychotic or lithium. (Also consider augmentation if there has been partial response to an SSRI.31) Alternatively, consider switching to an antidepressant from a different class, for example mirtazapine34 – especially if poor sleep is a problem. There are no RCTs testing the effectiveness of these strategies in children or adolescents, and so this guidance is largely

based on evidence from studies of adults with treatment-resistant depression, in addition to very limited follow-up of TORDIA participants receiving open-label treatment.31,35 ■ ■Finally, if still no response to these medications and the young person’s depression is very severe, ketamine, repetitive transcranial magnetic stimulation (rTMS) or electroconvulsive therapy can be considered. These interventions have an evidence base and

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