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Notes

Depression and anxiety disorders CHAPTER 3 Notes ■ ■ Tools such as the Montgomery-Asberg Depression Rating Scale (MADRS)¹² and the HAM-D¹³ are used in trials to assess drug effect. The HAM-D is now somewhat anachronistic and few clinicians are familiar with the MADRS (although it is probably the best scale to measure severity and change). The Patient Health Questionnaire-9¹⁴ is simple to use and is recommended for assessing symptom change in depression (although it better measures frequency rather than severity of symptoms). All rating scales should be treated with caution: someone with an HAM-D score of 30 is not twice as depressed as someone with a score of 15. That is, these scales are not linear and items are not weighted – on most scales insomnia scores more than a suicide attempt. ■ ■ Choice of antidepressant is governed largely by patient and clinician preference, but most authorities recommend an SSRI, or mirtazapine where sedation is required. A large network meta-analysis¹⁵ suggested that drugs with effects on both norepinephrine and serotonin uptake are the most effective (five of the top six ranked drugs are dual action) whereas agomelatine and SSRIs have the lowest dropout rates. A 2018 network meta-analysis¹⁶ of newer antidepressants suggested few, if any, clear advantages over older drugs for levomilnacipran, vilazodone and vortioxetine. ■ ■ Assessment at 2 weeks has some utility in determining eventual outcome.¹⁷ Only around 30% of those not reaching accepted symptom score threshold for improvement at 2 weeks will ultimately respond. Even fewer people go on to respond if there is no improvement at all or deterioration at 2 weeks. ■ ■ Switching between drug classes in cases of poor tolerability is supported by some studies¹⁸ and has a strong theoretical basis. Having said that, in practice, many patients who cannot tolerate one SSRI will readily tolerate another. ■ ■ In cases of non-response, there is some evidence that switching within a drug class is effective,^{8,19–22} but switching between classes is, in practice, the most common option and is supported by some analyses.²³ The American Psychiatric Association recommends both options.² The 2022 NICE guidelines⁹ suggest that there is little cogent evidence for switching between antidepressants (an observation in another analysis²⁴) and that combining antidepressants or adding a second-generation antipsychotic (SGA) are better-supported options at this stage. The strongest evidence in support of switching after the failure of one treatment is probably for vortioxetine.¹⁰ The most compelling evidence for combination antidepressants is for an SSRI plus mirtazapine.²⁵ ■ ■ There is minimal evidence to recommend increasing the dose of most SSRIs above the minimum therapeutic dose, at least when severity is measured using total rating scale scores.²⁶ Examining only the mood item on the HAM-D suggests some dose-response relationship for SSRIs.²⁷ Other evidence suggests that increasing the dose of venlafaxine, escitalopram and tricyclics may be helpful.^{3,28} Generally speaking, gains in efficacy afforded by dose increases are small (SSRIs, venlafaxine) or non-existent (e.g. mirtazapine above 30mg/day) while effects on tolerability are reliably and starkly detrimental.²⁹ ■ ■ Switch treatments early (e.g. after

1-2 weeks) if adverse effects are intolerable or if no improvement at all is seen after 2-3 weeks. Opinions on when to switch vary somewhat but it is clear that antidepressants have a fairly prompt onset of action³⁰⁻³² and that non-response at 2-6 weeks is a good predictor of overall non-response.³³⁻³⁵ The absence of any improvement at all by 2-3 weeks should normally provoke a change

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