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Discontinuation of medium- and long-term antidepressants

398 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 (approximately equal to a halving of the absolute risk). A later meta-analysis of 54 studies suggested that odds of relapse were reduced by 65%.12 The risk of relapse is greatest in the first few months after discontinuation and this holds true irrespective of the duration of prior treatment.13 Benefits persist at 36 months and beyond and seem to be similar across heterogeneous patient groups (first episode, multiple episode and chronic). An RCT of maintenance treatment in elderly patients, many of whom were first episode, found continuation treatment with antidepressants beneficial over 2 years, with a similar effect size to that seen in younger adults.14 One small RCT (n = 22) demonstrated benefit from prophylactic antidepressants in adolescents.15 Many patients who might benefit from maintenance treatment with antidepressants do not receive them.16 Assuring optimal management of long-term depression vastly reduces mortality associated with the condition.17 An alternative view is that the prophylactic effects of antidepressants have been overestimated because of confounding in maintenance trials. Effective drug treatment may be abruptly withdrawn, and it is the manner of this withdrawal (not necessarily the withdrawal itself) which increases the risk of relapse.18,19 Most of the apparent relapse after stopping antidepressants occurs in the first 6 months.20 Abrupt discontinuation increases the risk of relapse and exacerbates withdrawal symptoms (see below). It may be that at least part of the advantage reported for continuation treatment is derived from suboptimal treatment in patients switched to placebo. Some studies employ longer periods (a month or more) of withdrawal from active treatment21 but even this may not be long enough to allow complete abolition of the negative effects of withdrawal.22 There is also a minority school of thought which posits that antidepressants may ultimately worsen the conditions they treat.23 Some tenuous support for this theory comes from the observation that response to antidepressants reduces in line with the number of antidepressants previously prescribed.24 Other disadvantages of long-term antidepressants include an increased risk of GI and cerebral haemorrhage (see section on SSRIs and bleeding in this chapter) and an additional risk of

interaction with co-prescribed drugs likely to increase risk of bleeding or hyponatraemia. These observations, alongside awareness that maintenance trials have been conducted largely in those in remission, strongly suggest that antidepressant treatment should be continued only where there is clear evidence of substantial efficacy. This may seem like an obvious point, but clinical experience suggests that long-term, ineffective or partially effective antidepressant treatment is commonplace. The aim of treatment should be the achieving and maintenance of remission. Residual symptoms portend poor outcome and higher risk of relapse.25 Discontinuation of medium- and long-term antidepressants Stopping antidepressants in remitted patients clearly increases the risk of relapse compared with continuing with antidepressants.26 However, as already noted, many studies may be confounded by abrupt discontinuation of active treatment, which worsens risk of relapse27 and increases risk of withdrawal symptoms (which may mimic relapse).28 Two studies have tried to address these confounding influences. In the ANTLER trial, patients who were well after at least 2 years of treatment were randomised to continue

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Revision #1
Created 2026-01-04 20:15:37 UTC by Omar Ayman
Updated 2026-01-04 20:15:37 UTC by Omar Ayman