

15 - Efficacy

Efficacy

Schizophrenia and related psychoses CHAPTER 1 High-dose antipsychotic medication: prescribing and monitoring 'High-dose' antipsychotic medication can result from the prescription of either a single antipsychotic medication at a dose above the recommended maximum or two or more antipsychotic medications concurrently that, when expressed as a percentage of their respective maximum recommended doses and added together, results in a cumulative dose of more than 100%.¹ In clinical practice, antipsychotic polypharmacy and prn antipsychotic medication are strongly associated with high-dose prescribing.^{2,3} Efficacy There is no firm evidence that high doses of antipsychotic medication are any more effective than standard doses for schizophrenia. This holds true for the use of antipsychotic medication for rapid tranquillisation, relapse prevention, persistent aggression and the management of acute psychotic episodes.¹ Nevertheless, the prescription of high-dose antipsychotic medication remains relatively common in clinical practice.^{4–6} In the UK, the national audit of schizophrenia in 2013, reporting on prescribing practice for over 5,000 predominantly community-based patients, found that, overall, 10% were prescribed a high dose of antipsychotic medication.⁷ A 2022 audit of adult inpatients in mental health services⁸ found that in over 4,000 patients on acute adult wards, just under 10% were prescribed high-dose antipsychotic medication, and for over 2,000 patients on forensic wards, the respective figure was 13%. In both settings, a high-dose prescription was predominantly a consequence of combined antipsychotic medications. Examination of the dose-response effects of a variety of antipsychotic medications has not found any evidence of greater efficacy for doses above accepted licensed ranges.^{9,10} Efficacy appears to be optimal at relatively low doses, such as 4mg/day risperidone,¹¹ 300mg/day quetiapine,¹² and olanzapine 10mg.^{13,14} Similarly, treatment with LAI risperidone at a dose of 100mg 2-weekly offers no benefits over 50mg 2-weekly,¹⁵ and 320mg/day ziprasidone¹⁶ is no better than 160mg/day. All currently available antipsychotic medications (with the possible exception of clozapine) exert their antipsychotic effect primarily through antagonism (or partial agonism) at post-synaptic dopamine receptors. But there is increasing evidence that refractory symptoms in some patients with treatment-resistant schizophrenia may not be driven by dysfunction of dopamine pathways,^{17–20} so prescribing a higher dosage to increase dopamine blockade in such patients would seem to be of uncertain value. Dold and colleagues²¹ conducted a meta-analysis of RCTs that compared continuation of standard-dose antipsychotic medication with dose escalation in patients whose schizophrenia had proved to be unresponsive to a prospective trial of standard-dose pharmacotherapy with the same antipsychotic medication. In this context, there was no evidence of any benefit associated with the increased dosage. In a study of patients with first-episode schizophrenia, increasing the dose of olanzapine up to 30mg/day and the dose of risperidone up to 10mg/day in those cases where the illness was non-responsive to treatment with standard doses yielded only a 4% absolute increase in

overall response rate. Switching to an alternative antipsychotic, including clozapine, was considerably more successful.²²

Revision #1

Created 2026-01-04 20:12:50 UTC by Omar Ayman

Updated 2026-01-04 20:12:50 UTC by Omar Ayman