Which doses of atypical and typical antipsychotic drugs produce a near maximal response with minimal side effects in people with schizophrenia or schizoaffective disorder?

**CONCLUSIONS**

The doses reported are approximate (see notes) and treating people with schizophrenia empirically by varying doses is still recommended. Clinicians tend to use higher doses of typical antipsychotics than are needed. High doses have a no better or worse response than medium doses.

**NOTES**

The range for individual patients may be wider than the estimated dose range for pharmacokinetic or pharmacodynamic reasons, or for patients in an acute exacerbated episode. There is also little information on people who are too psychotic to give informed consent, and different doses may be required in these situations.

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**METHODS**

**Design:** Systematic review with meta-analysis.


**Study selection and analysis:** Double blind, randomised controlled trials of people with schizophrenia or schizoaffective disorder comparing two or more doses of typical or atypical antipsychotics were eligible. Dose response curves were plotted and the median effective dose, defined as 50% of the maximal response (ED50), and the near maximal effective dose range (ED85 to ED95) was established for each drug. Estimated equivalent doses were based on ED50. Meta-analysis determined whether medium and high doses vary in efficacy. The last-observation-carried-forward method and intent-to-treat sample were used for the meta-analysis. The possibility of other biases was explored using sensitivity analyses.

**Outcomes:** Median effective dose (ED50) and the near maximal effective dose range (ED85 to ED95). Schizophrenia symptoms were assessed in studies with the Positive and Negative Syndrome Scale (PANSS), the Brief Psychiatric Rating Scale, or the Clinical Global Rating Scale.

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**MAIN RESULTS**

The near maximal effective dose was determined for each drug (see http://www.ebmentalhealth.com/supplemental for table). **Typical antipsychotics:** the near maximal effective dose range for haloperidol was 3.3–10 mg/day. There was no evidence that higher doses of first generation antipsychotics were more effective than medium doses (3.3–10 mg/day haloperidol or equivalent). **Atypical antipsychotics:** the near maximal efficacy dose for aripiprazole was 10 mg/day, clozapine 400 mg/day, olanzapine possibly >16 mg/day, risperidone 4 mg/day, and ziprasidone 120 mg/day. Daily doses of 2 mg risperidone were about 30% less effective than higher doses. For olanzapine, 6 mg/day was 33% less effective than higher doses. For both atypical and typical antipsychotics, there was no evidence that higher doses were less effective, arguing against a “therapeutic window”.

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Review: high doses of antipsychotic drugs are no more or less effective than medium doses in people with schizophrenia

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