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Maintenance treatment with antipsychotic drugs for schizophrenia.  
*Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD008016.  
DOI: [10.1002/14651858.CD008016.pub2](https://doi.org/10.1002/14651858.CD008016.pub2).

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[Intervention Review]

# Maintenance treatment with antipsychotic drugs for schizophrenia

Stefan Leucht<sup>1</sup>, Magdolna Tardy<sup>1</sup>, Katja Komossa<sup>2</sup>, Stephan Heres<sup>1</sup>, Werner Kissling<sup>1</sup>, John M Davis<sup>3</sup><sup>1</sup>Klinik und Poliklinik für Psychiatrie und Psychotherapie, Technische Universität München Klinikum rechts der Isar, München, Germany.<sup>2</sup>Klinik und Poliklinik für Psychosomatische und Medizin und Psychotherapie, Technische Universität München, Klinikum rechts der Isar, München, Germany. <sup>3</sup>University of Illinois at Chicago, Chicago, USA**Contact address:** Stefan Leucht, Klinik und Poliklinik für Psychiatrie und Psychotherapie, Technische Universität München Klinikum rechts der Isar, Möhlstr. 26, München, 81675, Germany. [Stefan.Leucht@lrz.tu-muenchen.de](mailto:Stefan.Leucht@lrz.tu-muenchen.de).**Editorial group:** Cochrane Schizophrenia Group.**Publication status and date:** New, published in Issue 5, 2012.**Citation:** Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Davis JM. Maintenance treatment with antipsychotic drugs for schizophrenia. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD008016. DOI: [10.1002/14651858.CD008016.pub2](https://doi.org/10.1002/14651858.CD008016.pub2).

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## ABSTRACT

### Background

The symptoms and signs of schizophrenia have been firmly linked to high levels of dopamine in specific areas of the brain (limbic system). Antipsychotic drugs block the transmission of dopamine in the brain and reduce the acute symptoms of the disorder. This review examined whether antipsychotic drugs are also effective for relapse prevention.

### Objectives

To review the effects of maintaining antipsychotic drugs for people with schizophrenia compared to withdrawing these agents.

### Search methods

We searched the Cochrane Schizophrenia Group's Specialised Register (November 2008), with additional searches of MEDLINE, EMBASE and clinicaltrials.gov (June 2011).

### Selection criteria

We included all randomised trials comparing maintenance treatment with antipsychotic drugs and placebo for people with schizophrenia or schizophrenia-like psychoses.

### Data collection and analysis

We extracted data independently. For dichotomous data we calculated relative risks (RR) and their 95% confidence intervals (CI) on an intention-to-treat basis based on a random-effects model. For continuous data, we calculated mean differences (MD) or standardised mean differences (SMD) again based on a random-effects model.

### Main results

The review currently includes 65 randomised controlled trials (RCTs) and 6493 participants comparing antipsychotic medication with placebo. The trials were published from 1959 to 2011 and their size ranged between 14 and 420 participants. In many studies the methods of randomisation, allocation and blinding were poorly reported. Although this and other potential sources of bias limited the overall quality, the efficacy of antipsychotic drugs for maintenance treatment in schizophrenia was clear. Antipsychotic drugs were significantly more effective than placebo in preventing relapse at seven to 12 months (primary outcome; drug 27%, placebo 64%, 24 RCTs, n=2669, RR 0.40 CI 0.33 to 0.49, number needed to treat for an additional beneficial outcome (NNTB 3 CI 2 to 3). Hospitalisation was also reduced, however, the baseline risk was lower (drug 10%, placebo 26%, 16 RCTs, n=2090, RR 0.38 CI 0.27 to 0.55, NNT 5 CI 4 to 9). More participants in the placebo group than in the antipsychotic drug group left the studies early due to any reason (at 7-12 months: drug 38%, placebo 66%, 18 RCTs, n=2420, RR 0.55 CI 0.46 to 0.66, NNTB 4 CI 3 to 5) and due to inefficacy of treatment (at 7-12 months: drug 20%, placebo 50%, 18 RCTs,

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n=2420, RR 0.36 CI 0.28 to 0.45, NNTB 3 CI 2 to 4). Quality of life was better in drug-treated participants (3 RCTs, n=527, SMD -0.62 CI -1.15 to -0.09). Conversely, antipsychotic drugs as a group and irrespective of duration, were associated with more participants experiencing movement disorders (e.g. at least one movement disorder: drug 16%, placebo 9%, 22 RCTs, n=3411, RR 1.55 CI 1.25 to 1.93, NNTH 25 CI 13 to 100), sedation (drug 13%, placebo 9%, 10 RCTs, n=146, RR 1.50 CI 1.22 to 1.84, number needed to treat for an additional harmful outcome (NNTH) not significant) and weight gain (drug 10%, placebo 6%, 10 RCTs, n=321, RR 2.07 CI 1.31 to 3.25, NNTH 20 CI 14 to 33). The results of the primary outcome were robust in a number of subgroup, meta-regression and sensitivity analyses, the main exception being that the drug-placebo difference in longer trials was smaller than in shorter trials.

### Authors' conclusions

The results clearly demonstrate the superiority of antipsychotic drugs compared to placebo in preventing relapse. This effect must be weighed against the side effects of antipsychotic drugs. Future studies should focus on outcomes of social participation and clarify the long-term morbidity and mortality associated with these drugs.

## PLAIN LANGUAGE SUMMARY

### Maintenance treatment with antipsychotic drugs for schizophrenia

Antipsychotic drugs are the mainstay of treatment of schizophrenia. The current report presents the first systematic review comparing the effects of all antipsychotic drugs compared to placebo for maintenance treatment, that is relapse prevention after the acute phase. Randomised controlled trials (RCTs) since the 1950s have consistently shown that antipsychotic drugs effectively reduce relapses and need for hospitalisation. Conversely, they are, as a group, associated with a number of side effects such as movement disorders, weight gain and sedation.