Background
Schizophrenia affects about 1% of the world’s population. Central to its treatment are antipsychotic drugs, probably the most widely used of which is haloperidol.

Haloperidol’s efficacy as an antipsychotic, however, seems to vary, and there has always been concern and debate surrounding its long-term use.

In accordance with the recommendations of drug regulatory authorities, haloperidol is increasingly used as a comparator drug in clinical trials. Thus haloperidol is often the benchmark by which other antipsychotics are measured.

Estimates of the effects of haloperidol are currently based on traditional reviews that lack both methods and quantification.

Objectives
To evaluate the clinical effects of haloperidol for the management of schizophrenia and other similar serious mental illnesses compared to placebo.

Search strategy

Selection criteria
Study methodology - randomised trials
Participants - people with a diagnosis of schizophrenia or ‘serious/chronic mental illness’ or ‘psychotic illness’
Interventions – haloperidol versus placebo

Trial selection and data analysis
Studies were independently inspected and quality assessed

Relevant data were extracted and synthesised within RevMan Software.

Intention-to-treat analyses were undertaken for dichotomous data and relative risk (RR) and numbers needed to treat/harm (NNT/H) calculated.

Results
Seventy-four trials were identified but only 20 could be included.

Outcome: No global improvement

Outcome: Leaving the study early

Outcome: Acute movement disorders

Outcome: Mental state – no clinical improvement (>20% reduction in BPRS, 0-6 weeks

Outcome: Not in remission at 1 year

Outcome: Adverse effects - non-acute

More people allocated haloperidol improved in the first six weeks of treatment than those given placebo (3 trials, n=159, RR failing to produce a marked improvement 0.44 CI 0.3 to 0.6, NNH 3 CI 2 to 5).

A further eight trials (n=308) also found a difference favouring haloperidol across the 6-24 week period (RR no marked global improvement 0.68 CI 0.6 to 0.8 NNH 3 CI 2.5 to 5) but this may be an over estimate of effect as small negative studies were not identified.

About half of those entering studies failed to complete the short trials, although, at 0-6 weeks, 10 studies found a difference that favoured haloperidol (n=688, RR 0.82 CI 0.7 to 0.95, NNH 8 CI 5 to 17).

Limited adverse effect data do, nevertheless, support the clinical impression, that haloperidol is a potent cause of movement disorders, at least in the short term. Haloperidol promotes acute dystonia (3 trials, n=93, RR 4.7 CI 1.7 to 14, NNH 5 CI 3 to 9), akathisia (3 trials, n=126, RR 6.9 CI 1.3 to 38, NNH 6 CI 4 to 14) and parkinsonism (4 trials, n=163, RR 11.7 CI 2.9 to 47, NNH 3 CI 2 to 5).

Conclusions
Haloperidol is a potent antipsychotic drug but with a high propensity to cause adverse effects.

Given no choice of drug, use of haloperidol to counter the damaging and potentially dangerous consequences of untreated schizophrenia is justified. If a choice of drug is available, however, people with schizophrenia and clinicians may wish to start another antipsychotic with less likelihood of causing parkinsonism, akathisia and acute dystonias.

For countries where haloperidol is not widely used, it should not be a control drug of choice for randomised trials of new antipsychotics.