



Title	Randomized Controlled Trials of Conventional Antipsychotic Versus New Atypical Drugs, and New Atypical Drugs Versus Clozapine, in People With Schizophrenia Responding Poorly to, or Intolerant of, Current Drug Treatment
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Aim

To determine the clinical and cost effectiveness of different classes of antipsychotic drug treatment in people with schizophrenia responding inadequately to, or having unacceptable side effects from, their current medication.

Conclusions and results

In people with schizophrenia whose medication was being changed because of intolerance or inadequate response, there was no disadvantage in quality of life or symptoms over one year in commencing conventional antipsychotic drugs rather than new atypical drugs. On the quality of life scale (QLS) and symptom measures, participants in the conventional arm showed a trend toward greater improvement. Participants reported no clear preference for either class of drug. Net costs of care over the year varied widely with a mean of GBP 18 800 in the conventional drug group and GBP 20 100 in the new atypicals group, not a statistically significant difference.

New atypicals compared with clozapine in people with more narrowly-defined treatment resistance showed an advantage for commencing clozapine in QLS at trend level ($p=0.08$) and in symptoms (PANSS), that was statistically significant ($p=0.01$), at one year. Clozapine showed approximately a 5-point advantage on PANSS total score. Participants reported at 12 weeks that their mental health was significantly better with clozapine than with new atypicals ($p<0.05$). Net costs of care varied widely, with a mean of GBP 33 800 in the clozapine group and GBP 28 500 in the new atypical group, not a statistically significant difference. Of these costs, 4.0% and 3.3% respectively were due to antipsychotic drug costs. The increased costs in the clozapine group appeared to reflect the licensing requirement for inpatient admission for commencing the drug.

Recommendations

In people with schizophrenia whose medication is being changed because of intolerance or inadequate response,

there is no disadvantage in terms of quality of life and symptoms, or associated costs of care, over one year in commencing conventional antipsychotic drugs rather than new atypical drugs.

In people with schizophrenia whose medication is being changed because of narrowly defined treatment resistance, there is a statistically significant advantage in terms of symptoms, but not quality of life, over one year in commencing clozapine rather than new atypical drugs.

Methods

Two pragmatic, randomized, controlled trials (RCTs) were undertaken. The first compared the class of older, inexpensive conventional drugs to the class of new atypical drugs in people with schizophrenic disorders, whose current antipsychotic drug treatment was being changed either because of inadequate clinical response, or due to side effects. The second RCT compared the new (non-clozapine) atypical drugs with clozapine in people whose medication was being changed because of poor clinical response to two or more antipsychotic drugs. Both RCTs were 4-center trials with concealed randomization and 3 followup assessments over one year, blind to treatment.

Further research/reviews required

- Randomized trial of NICE antipsychotic treatment guidance using atypical versus conventional drugs in the context of careful management of schizophrenia outlined in this document
- Randomized trial of antipsychotic drug maintenance vs early drug withdrawal plus psychological treatment after the first episode of schizophrenia
- Development of a valid measures of utility in serious mental illness
- Randomized trial of low dose "conventional" vs new atypical in first episode schizophrenia
- Randomized trial of sodium valproate plus antipsychotic drug treatment in acute schizophrenia.