Schizophrenia


**DEFINITION**
Schizophrenia is characterised by the positive symptoms of auditory hallucinations, delusions, and thought disorder, and by the negative symptoms of demotivation, self neglect, and reduced emotion.2 People are defined as being resistant to standard antipsychotic drugs if, over the preceding 5 years, they have not had a clinically important improvement in symptoms after 2–3 regimes of treatment with standard antipsychotic drugs for at least 6 weeks (from at least 2 classes at doses equivalent to or greater than 1000 mg/day chlorpromazine) and they have had no period of good functioning.2,3 Approximately 30% (10–45%) of people with schizophrenia meet these criteria.

**INCIDENCE/PREVALENCE**
Onset of symptoms typically occurs in early adult life (average age 25 years) and is earlier in men than women.4,5 Prevalence worldwide is 2–4/1000. One in 100 people will develop schizophrenia in their lifetime.

**AETIOLOGY/RISK FACTORS**
Risk factors include a family history (although no major genes have been identified); obstetric complications; developmental difficulties; central nervous system infections in childhood; cannabis use; and acute life events.6 The precise contributions of these factors and ways in which they may interact are unclear.

**PROGNOSIS**
About three quarters of people suffer recurrent relapse and continued disability, although the proportion of people who improved significantly increased after the mid 1950s (mean 48.5% from 1956–1985 v 35.4% from 1895–1956).6 Outcome may be worse in people with insidious onset and delayed initial treatment, social isolation, or a strong family history; in people living in industrialised countries; in men; and in people who misuse drugs.7 Drug treatment is generally successful in treating positive symptoms, but up to a third of people derive little benefit and negative symptoms are notoriously difficult to treat. About half of people with schizophrenia do not adhere to treatment in the short term. The figure is even higher in the longer term.7

**WHAT ARE THE EFFECTS OF TREATMENTS?**
Most evidence is from systematic reviews of RCTs that report disparate outcomes. There is a need for larger RCTs, over longer periods, with well designed end points, including standardised, validated symptom scales. No intervention has been found to consistently reduce negative symptoms. 

**Beneficial**
**Continuation of antipsychotic drugs for 6–9 months after an acute episode to reduce relapse rates**
Systematic reviews have found that continuing antipsychotic drugs for at least 6 months after an acute episode reduces relapse rates compared with no treatment or placebo, and that some benefit of continuing antipsychotics is apparent for up to 2 years.

**Multiple session family interventions to reduce relapse rates**
One systematic review found that multiple session family interventions reduced relapse rates at 12 months compared with usual care, single session family interventions, or psychoeducational interventions.

**Psychoeducational interventions to reduce relapse rates**
One systematic review has found that psychoeducation reduces relapse rates at 9–18 months compared with a control intervention.

**Likely to be beneficial**
**Behavioural therapy to improve adherence**
One RCT found that behavioural interventions improved adherence to antipsychotic medication over 3 months compared with usual treatment. Two RCTs found limited evidence that behavioural interventions may improve adherence more than psychoeducational therapy.

**Compliance therapy to improve adherence**
Two RCTs found limited evidence that compliance therapy may increase adherence to antipsychotic drugs at 6 and 18 months compared with non-specific counselling.

**Psychoeducational interventions to improve adherence**
One systematic review found limited evidence that psychoeducation improved adherence to antipsychotic medication compared with usual care. Two RCTs found limited evidence that psychoeducational therapy may improve adherence less than behavioural therapy.

**Trade off between benefits and harms**
**Chlorpromazine**
One systematic review has found that, compared with placebo, chlorpromazine reduces the proportion of people who have no improvement, or have marked or worse severity of illness at 6 months on a psychiatrist rated scale. The review found that chlorpromazine caused more adverse effects, such as sedation, acute dystonia, and parkinsonism, than placebo.

**Clozapine**
Two systematic reviews found that clozapine improved symptoms over 4–10 weeks compared with standard antipsychotic drugs. However, RCTs found that clozapine may be
associated with blood dyscrasias. Three systematic reviews of small RCTs provided insufficient evidence to compare clozapine versus other new antipsychotic drugs. One systematic review in people resistant to standard treatment found that clozapine improved symptoms after 12 weeks and after 2 years compared with standard antipsychotic drugs. RCTs provided insufficient evidence to compare clozapine versus other newer antipsychotics in people resistant to standard antipsychotic drugs.

**Depot bromperidol decanoate**
RCTs found no significant difference in the proportion of people who needed additional medication, left the trial early, or had movement disorders over 6–12 months between depot bromperidol decanoate and oral haloperidol, but it may have been too small to exclude a clinically important difference. Haloperidol is associated with acute dystonia, akathisia, and parkinsonism.

**Haloperidol**
One systematic review has found that haloperidol increases physician rated global improvement at 6 and 24 weeks compared with placebo but is associated with acute dystonia, akathisia, and parkinsonism.

**Thioridazine**
One systematic review has found that thioridazine improves global mental state over 3–12 months compared with placebo.

**Amisulpride; loxapine; molindone; olanzapine; pimozide; quetiapine; risperidone; sulpiride; ziprasidone; zotepine**
Systematic reviews have found that these newer antipsychotic drugs are as effective in improving symptoms as standard antipsychotic drugs, and have different profiles of adverse effects.

**Unknown effectiveness**
Cognitive behavioural therapy to reduce relapse rates
Limited evidence from a systematic review of two RCTs found no significant difference in relapse rates between cognitive behavioural therapy plus standard care and standard care alone.

**Multiple session family interventions to improve adherence**
One systematic review found that “compliance with medication” over 9–24 months was higher in people who received multiple family interventions compared with usual care, single family interventions, or psychoeducational interventions, but the difference did not quite reach significance.

**Perazine**
RCTs provided insufficient evidence to assess perazine.

**Social skills training to reduce relapse rates**
One systematic review of small RCTs provided insufficient evidence to assess social skills training.

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SL has been paid for speaking about critical appraisal by employees of the manufacturers of amisulpride, olanzapine, risperidone, and ziprasidone, and has been paid to speak about the management of schizophrenia by employees of the manufacturers of amisulpride, olanzapine, risperidone, and clozapine. AM and ZN; none declared.


**Other articles noted**

The journals that are reviewed and the criteria for selecting articles from these journals for inclusion in Evidence-Based Mental Health are set out in the purpose and procedure in each issue. All articles that meet our criteria in the reviewed journals are cited in Evidence-Based Mental Health, but there is not enough space to abstract them all. The following articles passed all criteria but were not abstracted because, in the judgment of the editors, their findings were less widely applicable to clinical practice in the area of mental health.

**THERAPEUTICS**


Jorm AF, Griffiths KM, Christensen H, et al. Providing information about the effectiveness of treatment options to


**AETIOLOGY**


**PROGNOSIS**
