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Schizophrenia (Maintenance Treatment)

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One in 100 persons will develop schizophrenia; about 75 percent of persons have relapses and continued disability, and one third fail to respond to standard treatment.

- Positive symptoms include auditory hallucinations, delusions, and thought disorder. Negative symptoms (anhedonia, social withdrawal, affective flattening, and demotivation) and cognitive dysfunction have not been consistently improved by any treatment.

Continuation of antipsychotic drugs for at least six months after an acute attack reduces the risk of relapse compared with no treatment, although no one drug seems to be more effective than others at preventing relapse.

- The definition of relapse varies widely among studies, and in many cases is synonymous with rehospitalization, although this reflects social variables as well as symptom exacerbation.

Where available, multiple sessions of family interventions or psychoeducational interventions can reduce relapse rates compared with usual care.

- We do not know whether cognitive behavior therapy or social skills training is also beneficial.

In persons who are resistant to standard

Clinical Questions

What are the effects of treatments to reduce relapse rates in persons with schizophrenia?

Beneficial	Continuation of antipsychotic drugs (when given for at least six months after an acute episode)
	Family interventions
	Psychoeducational interventions
Unknown effectiveness	Cognitive behavior therapy
	Social skills training

What are the effects of interventions in persons with schizophrenia who are resistant to standard antipsychotics?

Beneficial	Clozapine (compared with first-generation antipsychotics)
Unknown effectiveness	Clozapine (insufficient evidence to compare effectiveness versus other second-generation antipsychotics)
	Second-generation antipsychotics other than clozapine (insufficient evidence to compare effectiveness of drugs in this class or to compare their effectiveness versus first-generation antipsychotics)

What are the effects of interventions to improve adherence to antipsychotic medication in persons with schizophrenia?

Likely to be beneficial	Behavior therapy
	Psychoeducational interventions (brief group psychoeducational intervention may be more effective than usual care)
Unknown effectiveness	Compliance therapy
	Multiple-session family interventions

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antipsychotic drugs, clozapine may improve symptoms compared with first-generation antipsychotic agents, but there is limited evidence on its effectiveness compared with other second-generation antipsychotic agents.

- There is limited evidence to indicate that any antipsychotic other than clozapine is effective in persons with treatment-resistant schizophrenia.
- We do not know how second-generation antipsychotic agents other than clozapine compare with each other or with first-generation antipsychotic agents.

Behavioral interventions, compliance therapy, and psychoeducational interventions may improve adherence to antipsychotics compared with usual care.

Definition

Schizophrenia is characterized by three semi-independent symptom domains: positive symptoms, such as auditory hallucinations, delusions, and thought disorder; negative symptoms, including anhedonia, social withdrawal, affective flattening, and demotivation; and cognitive dysfunction, particularly in the domains of attention, working memory, and executive function. Schizophrenia is typically a lifelong condition characterized by acute symptom exacerbations and widely varying degrees of functional disability.

Maintenance antipsychotic drug regimens for schizophrenia are intended to limit the frequency and severity of relapses, maximize effects of treatment for persistent symptoms, and enhance adherence to recommended regimens. Antipsychotic medications are primarily effective for positive symptoms, and most persons require psychosocial interventions to manage the disability that often results from negative symptoms and cognitive dysfunction.

Adherence to prescribed antipsychotic regimens is typically low, and several psychosocial interventions have been developed to enhance adherence. About 20 percent of persons with schizophrenia are resistant to standard antipsychotics, as defined by lack of clinically important improvement in symptoms after two to three regimens of standard antipsychotic drugs for at least six weeks. An additional 30 to 40 percent of persons improve but are residually symptomatic despite antipsychotic treatment. Several pharmacologic strategies have been explored for these persons. This review focuses on the three key aspects of the management of schizophrenia.

Incidence and Prevalence

One in 100 persons will develop schizophrenia, and worldwide one-year prevalence rates vary from two to seven per 1,000 persons. Onset of symptoms typically occurs in early adult life (average age of 25 years) and occurs earlier in men than in women.

Etiology

Risk factors for schizophrenia include a family history, obstetric complications, developmental difficulties, central nervous system infections in childhood, cannabis use, and acute life events. The precise contributions of these factors and the ways in which they may interact are unclear.

Prognosis

About three fourths of persons with schizophrenia have recurrent relapse and continued disability, although the proportion of persons with significant improvement increased after the mid-1950s (mean: 48.5 percent from 1956 to 1985 versus 35.4 percent from 1895 to 1956). Outcome may be worse in persons with insidious onset and delayed initial treatment, social isolation, or a strong family history; persons living in industrialized countries; men; and persons who misuse drugs. Pharmacologic treatment is generally successful in treating positive symptoms, but up to one third of persons derive little benefit, and negative symptoms are notoriously difficult to treat. About one half of persons with schizophrenia do not adhere to treatment in the short term. The figure is even higher in the longer term.

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