Schizophrenia

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Schizophrenia is a mental illness that is among the world’s top ten causes of long-term disability. The symptoms of schizophrenia include psychosis, apathy and withdrawal, and cognitive impairment, which lead to problems in social and occupational functioning, and self-care. About 1% of the population is affected by schizophrenia, with similar rates across different countries, cultural groups, and sexes. The illness tends to develop between the ages of 16 and 30 years, and mostly persists throughout the patient’s lifetime. The cause of schizophrenia is unknown, but evidence suggests that genetic factors, early environmental influences (eg, obstetric complications), and social factors (eg, poverty) contribute. No biological alterations are pathognomonic of schizophrenia, although several pathophysiological differences exist in a wide range of brain structures. Antipsychotic medications are the mainstay for managing schizophrenia. A range of psychosocial treatments are also helpful, including family intervention, supported employment, cognitive-behaviour therapy for psychosis, social skills training, teaching illness self-management skills, assertive community treatment, and integrated treatment for co-occurring substance misuse.

Schizophrenia is a major mental illness characterised by psychosis, apathy and social withdrawal, and cognitive impairment, which results in impaired functioning in work, school, parenting, self-care, independent living, interpersonal relationships, and leisure time. Among psychiatric disorders, schizophrenia is the most disabling and requires a disproportionate share of mental health services. For example, patients with schizophrenia occupy about 25% of all psychiatric hospital beds and represent 50% of admissions to hospital. The total costs of treating schizophrenia are high, estimated to be US$44·9 billion in the USA for the year 1994, £2·6 billion in the UK for 1996, and CAN$2·35 billion in Canada for the same year. The combined economic and social costs of schizophrenia place it among the world’s top ten causes of disability-adjusted life-years, accounting for an estimated 2·3% of all burdens in developed countries, and 0·8% in developing economies.

Although schizophrenia is a life-long disorder requiring substantial care, great advances have been made in treatment and many patients can now live rewarding and meaningful lives in the community. In this article we provide an introduction to schizophrenia, including epidemiology, diagnosis and clinical description, etiology, onset and course, and clinical management.

Epidemiology

The annual incidence of schizophrenia is 0·2–0·4 per 1000, with a lifetime prevalence (risk) of about 1%. The incidence of schizophrenia is the same across sexes, although women tend to have a later age of onset than men, and a more benign course of illness, including fewer hospital admissions and better social functioning. The later age of onset in women is associated with higher attainment of social role functioning before illness, which confers a better outcome. The mechanism underlying the later illness onset in women has been postulated to be the effects of oestrogen on reduced sensitivity of D₂ receptors in the central nervous system.

Substantial variations in the prevalence and incidence of schizophrenia across different countries and cultural groups have been reported. However, these differences are reduced when stricter diagnostic criteria for schizophrenia are used. In a WHO study, the incidence of schizophrenia was shown to be quite similar across ten countries. Research by WHO across multiple countries also indicates that the clinical syndrome of schizophrenia is similar across a wide range of cultures and countries, including in developed and developing nations.

Diagnosis and clinical description

Modern notions of schizophrenia are based on the work of Kraepelin, who focused on the long-term deteriorating course of the illness, and Bleuler, who emphasised the core symptoms of the disorder as difficulties in thinking straight (loosening of associations), incongruous or flattened affect, loss of goal-directed behaviour or ambivalence due to conflicting impulses, and retreat into an inner world (autism).

Search strategy

To identify recent advances in understanding the nature, causes, and treatment of schizophrenia, we searched PubMed for journal articles in English published over the past 5 years with the keywords schizophrenia plus epidemiology, diagnosis, etiology, pathophysiology, neurodevelopmental, onset, course, treatment, pharmacology, psychosocial, rehabilitation, first episode, developing nation, or stigma. This search was supplemented by reading chapters in recently published compilations on schizophrenia, and consulting reference lists of articles and chapters to identify additional research contributions.
two major diagnostic systems for schizophrenia in common use are the *Tenth Revision of the International Classification of Diseases* (ICD-10)\(^1\) and the *Diagnostic and Statistical Manual*, Fourth Edition (DSM-IV).\(^1\) Both systems objectively define symptoms and characteristic impairments of schizophrenia in a similar way, and have improved the reliability of diagnostic assessments over more subjectively based approaches. The major differences between the systems are the DSM-IV requirements of social or occupational dysfunction (not included in ICD-10) and a 6-month duration of illness (versus 1 month for ICD-10), resulting in a somewhat narrower definition of the disorder in DSM-IV. Reliability of diagnoses between the two systems is high.\(^1\)

The stability of diagnosis over time is moderate, with most variability immediately after onset of the disorder; 21–30% of patients treated for a first episode have no symptom relapses over the next 5 years.\(^2\) Schizophrenia is characterised by three broad types of symptoms, including psychotic symptoms, negative symptoms, and cognitive impairment.\(^2\) Psychotic symptoms involve the loss of contact with reality, including false beliefs (delusions), perceptual experiences not shared by others (hallucinations), or bizarre behaviours. Various different types of hallucinations occur in schizophrenia, including auditory, visual, olfactory, gustatory, or tactile hallucinations, with auditory hallucinations most common. Common delusions in schizophrenia include persecutory delusions, delusions of control (eg, the belief that others can interfere with one's thoughts), grandiose delusions (eg, the belief that one is Jesus Christ), and somatic delusions (eg, the belief that one's brain is rotting away). The presence and severity of psychotic symptoms tend to be episodic over time.

Negative symptoms are deficit states in which basic emotional and behavioural processes are diminished or absent. Common negative symptoms include blunted affect (eg, immobile facial expression, monotonous voice tone), anhedonia (lack of pleasure), avolition or apathy (diminished ability to initiate and follow through on plans), and alogia (reduced quantity or content of speech). Negative symptoms are more pervasive and fluctuate less over time than psychotic symptoms,\(^2\) and are strongly associated with poor psychosocial functioning.\(^2\) Because it is less readily apparent to other people that negative symptoms are manifestations of a psychiatric illness, patients are often perceived by relatives and others to be lazy and willfully unengaged in bettering their lives.\(^2\)

Cognitive impairment in schizophrenia includes problems in attention and concentration, psychomotor speed, learning and memory, and executive functions (eg, abstract thinking, problem solving). A decline in cognitive abilities compared with premorbid functioning is present in most patients with schizophrenia, with cognitive functioning after onset of the illness relatively stable over time.\(^2\) Despite this decline, some patients' cognitive functioning is in the normal range. Like negative symptoms, cognitive impairment is strongly associated with functional impairment, including community living and work.\(^2\)

Impaired role functioning or substantial change in personal behaviour are also included as diagnostic criteria for schizophrenia. Problems in these areas include reduced ability to work, attend school, parent, have close relationships, take care of oneself, and enjoy leisure time, with difficulties emerging several years before psychotic symptoms.\(^2\) Impairment in functioning can be profound, resulting in the need for disability entitlements and assistance in meeting basic living needs, such as housing, medical care, food, and clothing. Improving functioning remains the single most important challenge for the management of schizophrenia.

In addition to symptoms and impaired role functioning, schizophrenia affects many other areas of living. Patients are at increased risk of alcohol and drug problems,\(^2\) infectious diseases (eg, hepatitis C, HIV infection),\(^2\) violent victimization,\(^2\) post-traumatic stress disorder,\(^2\) housing instability and homelessness,\(^2\) smoking-related and other illnesses,\(^2\) and negative emotions, such as anxiety,\(^2\) depression,\(^2\) and hostility.\(^2\) The net result of exposure to these risks is an increased mortality due to suicide (estimated about 5%),\(^2\) accidents, and illnesses such as respiratory and cardiovascular diseases.\(^2\)

### Aetiology

Both genetic and environmental factors appear to play a role in the aetiology of schizophrenia.

#### Genetic factors

Rates of schizophrenia are higher among relatives of patients than in the general population. Adoption and twin studies have shown that this increased risk is genetic, with a tenfold increase in risk associated with the presence of an affected first-degree family member. This genetic risk increases with each affected relative, to nearly 50% when both parents are affected,\(^3\) and 60–84% when a monozygotic twin is affected.\(^3\) The genetic transmission does not appear to follow simple Mendelian single-gene inheritance patterns. More probably, there are multiple susceptibility genes, each with small effect and acting in concert with epigenetic and environmental factors. At least seven genes have shown to be associated with schizophrenia.\(^3\)

#### Environmental factors

Environmental risks for schizophrenia include biological and psychosocial factors. The risk of development of schizophrenia is increased by prenatal and perinatal events—including maternal influenza, rubella, malnutrition, diabetes mellitus, and smoking during pregnancy—and obstetric complications.\(^4\) Obstetric complications associated with hypoxia are particularly related to increased risk, which might be mediated by excitotoxic effects of hypoxia on the fetal neonatal brain.\(^4\) Since most cases of obstetric complications do not lead to schizophrenia, such complications might interact with genetic vulnerability to increase risk of the illness.\(^4\) However, it is not yet known whether the high frequency of obstetric complications in schizophrenia is the result of abnormal brain development associated with genetic vulnerability, or an additive environmental factor towards the development of schizophrenia.

Several sociodemographic factors are associated with increased risk of schizophrenia.\(^4\) Poverty and lower social class have long been linked to higher rates of schizophrenia.\(^4\) Two hypotheses have been advanced to account for this association: social causation (ie, stressful environmental conditions increase risk of schizophrenia) and downward social drift (ie, schizophrenia reduces social and occupational functioning), both of which have received support.\(^4,5\)

Individuals born in urban areas are more likely to develop schizophrenia than those in rural areas.\(^4\) Although the incidence of the condition is similar across different ethnic groups,\(^4\) increased rates are present in some ethnic minority populations, such as second generation Afro-Caribbean people in the UK,\(^4\) Dutch Antillean and Surinamese immigrants in Holland,\(^4\) and
African-American people. These differences might reflect the stressful effects of being an ethnic minority in a social environment, which may increase vulnerability to schizophrenia in biologically predisposed individuals.

**Pathophysiology**

The most frequently confirmed neurobiological finding in schizophrenia is enlargement of the ventricular system, specifically the lateral and third ventricles, in some patients compared with healthy controls. Ventricular enlargement is accompanied by overall reductions in brain volume and cortical grey matter. Regions such as the frontal lobes, amygdala, hippocampus, parahippocampus, thalamus, and medial temporal lobe, cingulate gyrus, and superior temporal gyrus have decreased volumes in patients with schizophrenia compared with controls. Ventricular enlargement and brain volume reductions are not explained by illness chronicity or treatment, as they are evident in newly diagnosed patients and occur in unaffected relatives at risk for the illness.

Positron emission tomography (PET), which allows examination of cerebral bloodflow and receptor function in vivo, has been used to identify different and possibly dysfunctional neural circuitry used in cognitive tasks. Abnormalities in bloodflow have been shown in frontal regions, thalamus, and cerebellum in PET studies of patients with schizophrenia performing tasks involving executive functions, memory, and sustained attention. Reduced prefrontal bloodflow during cognitive tasks, or hypofrontality, has been noted in schizophrenia and linked to diminished dopamine activity, which is involved in the pathology of the disorder. The PET scans in figures 1 and 2 show frontal lobe activation in patients with schizophrenia compared with other patients or unaffected controls.

Functional imaging techniques such as functional MRI (fMRI), which uses deoxygenated haemoglobin as an endogenous tracer, allow assessment of activity in specific brain regions while patients perform cognitive tasks, such as remembering information. Abnormalities in neural activity compared with controls have been shown in frontal and temporal areas during cognitive imaging. Thus far, fMRI findings in schizophrenia suggest a disruption in functional circuits rather than localised dysfunction in single brain regions such as the prefrontal cortex. Neuroimaging studies showing structural and functional abnormalities in first-episode, never-treated patients suggest that these abnormalities are not secondary to treatment and chronicity of the illness. Deficits in social cognition (ie, the ability to accurately process social information such as emotions), which are especially prominent in schizophrenia, are related to abnormalities in the left prefrontal cortex. fMRI has also been used for longitudinal assessment of psycho-pharmacological effects on cerebral physiology. Honey and colleagues showed significantly enhanced frontal functioning in patients with schizophrenia performing a memory task after substitution of risperidone, a novel antipsychotic, for conventional antipsychotic drugs, an effect hypothetically due to increased dopaminergic transmission to the frontal cortex.

Diffusion tensor imaging has been used to characterise the structural integrity of white matter. This method measures the sum of the vectors of water diffusion within axons or myelin sheaths. This sum reflects the coherence of the structures within a given region, or the anisotropy of the tissue. Tissue that is aligned along a consistent axis or plane has high anisotropy, whereas tissue with a less uniform orientation has low anisotropy. Similarly, the anisotropy of axons and myelin directed towards white matter structures can be understood as a measure of the coherence of white matter in that region. Decreased anisotropy has been found in schizophrenia in a number of brain regions, including the prefrontal cortex and in fronto-temporal and fronto-parietal tracts. Pathology in white matter myelination in schizophrenia has been proposed as an explanation for problems with connectivity between brain regions, and is consistent with some of the symptoms and cognitive deficits of the illness. Psychosis and cognitive impairments are associated with other demyelinating disorders, such as metachromatic leucodystrophy and multiple sclerosis. Psychotic symptoms occur more often in metachromatic leucodystrophy, which—like schizophrenia—often begins during late adolescence or early adulthood, compared with multiple sclerosis, which usually has a later age of onset. The timing of the onset of metachromatic leucodystrophy, multiple sclerosis, and schizophrenia and the emergence of psychosis suggests that demyelination during...
adolescence or early adulthood may be critical to the development of psychosis.

**Neurodevelopmental model**

Several lines of evidence suggest that structural changes are likely to result from abnormal early brain development. The emergence of psychosis many years after early structural brain changes led to the hypothesis that schizophrenia is a neurodevelopmental disorder.79 As previously mentioned, structural changes are apparent before the first episode and in first-degree biological relatives,62 indicating that such abnormalities are not restricted to the pathological process of psychosis but are a manifestation of familial risk factors, the most likely candidates being genes affecting neurodevelopment. Additionally, morphological abnormalities occurring in early brain development arise at higher frequency in schizophrenia, such as aqueduct stenosis, arachnoid and septal cysts, agenesis of the corpus callosum, and absence of, or reversal of, normal structural cerebral asymmetries.77 Further evidence that neuropathological changes in schizophrenia are prenatal rather than postnatal comes from the absence of glial reactions in the brains of people with schizophrenia.78 Glial reactions are common sequelae to most adult-onset brain injuries and neurodegenerative conditions such as Alzheimer’s disease, but not with neuropathological events that occur early in development.

Furthermore, cortical cytoarchitectural abnormalities have been shown in postmortem histological studies, which implicate a defect in the formation of the cortical plate. These types of abnormalities can only occur early during brain development. Findings in this area indicate defective cellular organisation where the laminar distribution of cortical neurons is displaced inwards.79 As previously mentioned, structural changes are apparent before the first episode and in first-degree biological relatives,62 indicating that such abnormalities are not restricted to the pathological process of psychosis but are a manifestation of familial risk factors, the most likely candidates being genes affecting neurodevelopment. Additionally, morphological abnormalities occurring in early brain development arise at higher frequency in schizophrenia, such as aqueduct stenosis, arachnoid and septal cysts, agenesis of the corpus callosum, and absence of, or reversal of, normal structural cerebral asymmetries.77 Further evidence that neuropathological changes in schizophrenia are prenatal rather than postnatal comes from the absence of glial reactions in the brains of people with schizophrenia.78 Glial reactions are common sequelae to most adult-onset brain injuries and neurodegenerative conditions such as Alzheimer’s disease, but not with neuropathological events that occur early in development.

The actual mechanism accounting for the delayed onset of psychosis in adolescence or early adulthood is unclear. It has been speculated that excessive synaptic pruning occurs in schizophrenia, which leads to psychosis when it reaches a threshold.80,81 Substantial synaptic elimination occurs during adolescence, which may account for the onset of schizophrenia around this time.82 The age of onset may be further lowered when genetic vulnerability is compounded by neuronal loss due to hypoxia-associated obstetric complications.48

**Onset and course of illness**

Schizophrenia typically has its onset between the ages of 16 and 30 years, and infrequently after the age of 45 years.83 The disorder usually has a gradual, insidious onset that takes place over an average of 5 years, beginning with the emergence of negative and depressive symptoms, followed shortly by cognitive and social impairment, which is then followed several years later by the emergence of psychotic symptoms and first psychiatric contact.84 The course of the illness is most strongly predicted by the level of social development attained at the onset of psychosis, which is related to the age psychosis develops.45 Once schizophrenia has developed, some impairment is usually present throughout most life, although many patients experience remissions of symptoms late in life.20

The course of schizophrenia tends to be less severe in developing countries than developed ones.18 For example, in a multinational WHO study,77 patients in ten of 13 treatment centres in developing countries had better outcomes than those in developed countries. The mechanisms responsible for the better outcome in developing countries are unclear, although differences in social structures, the central role of the family, and beliefs about the origins of mental illness have been postulated to be important.89

Psychotic symptoms tend to be episodic over time, with their emergence or worsening associated with a potential risk to self or others, often requiring temporary hospitalisation. Because of the disruptive effects of relapses on patients’ lives, and the high cost of inpatient treatment, relapse prevention is a major goal of treatment. Negative symptoms and cognitive problems tend to be more stable over time, and contribute significantly to functional impairment.20

**Stress-vulnerability model**

The course of schizophrenia can be understood with the stress-vulnerability model.88 According to this model, schizophrenia is caused by an underlying psychobiological vulnerability, determined early in life by genetic and early environmental (eg, perinatal) effects. Once the vulnerability is established, the onset of the illness and its course, including relapses, is determined by the dynamic interplay of biological and psychosocial factors, as illustrated in figure 3. Among the biological factors that affect the course of schizophrenia, medication and substance abuse are the most critical. Antipsychotic medications can reduce severity of symptoms and susceptibility to relapses, whereas substance abuse can worsen symptoms and contribute to relapses. Among psychosocial factors that can influence schizophrenia, stress, coping skills, and social support are most important. Stress can impinge on biological vulnerability, worsening symptoms and triggering relapses. However, coping skills (eg, problem-solving and social skills) can minimise the harmful effects of stress by moderating stress and preventing relapse. 

![Figure 3: Stress-vulnerability model of schizophrenia](image-url)
Pharmacotherapy is the mainstay of treatment, without pharmacological treatment losing its ability to cope. The stress-vulnerability model provides a useful heuristic in guiding treatment for the management of schizophrenia. Important treatments include medication to reduce biological vulnerability, minimisation of substance misuse and environmental stress, enhancement of patients’ coping skills, and improved social support.

Management
The management of schizophrenia can be divided into pharmacological and psychosocial treatment.

Pharmacological treatment
Pharmacotherapy is the mainstay of treatment, without which most psychosocial treatment would not be possible.

Antipsychotics are the primary medication for schizophrenia, with major effects on the reduction of psychotic symptoms and prevention of relapses. By contrast with their dramatic effects on psychotic symptoms, antipsychotics have more modest effects on negative symptoms and cognitive impairment.

Before the 1990s, the primary antipsychotics available were the typical or conventional antipsychotics, with the exception of clozapine, an atypical antipsychotic introduced in 1958 but not widely used or available in many places until recently. Conventional antipsychotics, although relatively effective at treating psychotic symptoms, can also produce problematic side-effects, including Parkinsonian/extrapyramidal symptoms (eg, muscle stiffness, akathisia, tremors) and tardive dyskinesia (a neurological syndrome involving involuntary movements in the extremities such as fingers, toes, or oral-facial region). Since the 1990s, various

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<tr>
<th>Goals</th>
<th>Treatment</th>
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<td>Assertive community treatment</td>
<td>Engage patients in treatment who do not regularly attend outpatient clinics</td>
<td>Reduced symptoms and readmissions</td>
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<td>Improve co-ordinated delivery of services to patients who are prone to frequent relapses or readmission, and former long-term residents in institutions who now live in the community</td>
<td>Improved housing stability and quality of life</td>
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<td>24-h responsibility for patients</td>
<td>High patient satisfaction with services</td>
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<td>Shared caseloads among clinicians</td>
<td>Less costly for high service users</td>
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<td>Family psycho-education</td>
<td>Establish a collaborative relationship between family and treatment team</td>
<td>Reduced relapses and readmissions</td>
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<td>Improve monitoring of psychiatric illness and response to early signs of relapse</td>
<td>Decreased family stress and burden of care</td>
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<td>Reduce burden of care on family</td>
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<td></td>
<td>Increase family support for patient</td>
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<tr>
<td>Supported employment</td>
<td>Help patients obtain and keep competitive work in integrated community settings</td>
<td>Improved rates of competitive employment, hours worked, wages earned</td>
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<td>Rapid job search rather than extensive pre-vacational assessment and skills training</td>
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<td>Integration of vocational and clinical services</td>
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<td>Provision of follow-along supports</td>
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<td>Attention to patient preferences in job type and employment support</td>
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<td>Social skills training</td>
<td>Increase social skills such as having conversations, making friends, resolving conflict, expressing feelings, assertiveness, dealing with problems at work, and developing leisure and recreational activities</td>
<td>Improved social and leisure functioning</td>
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<td>Skills taught based on social learning theory: modelling, role playing, positive and corrective feedback, homework</td>
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<td>Group skills training over at least several months</td>
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<td>Community trips to practice skills</td>
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<td>Training in illness management skills</td>
<td>Improve understanding of schizophrenia and its management</td>
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<td>Increase medication adherence</td>
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<td>Prevention of relapses and readmissions</td>
<td>Fewer relapses and readmissions</td>
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<td>Enhance coping with distressing symptoms</td>
<td>Reduced distress due to symptoms</td>
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<td>Cognitive behaviour therapy for psychosis</td>
<td>Reduce severity of persistent psychotic symptoms</td>
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<td>Psychoeducation about illness</td>
<td>Reduced severity of negative symptoms</td>
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<td>Development of strategies for taking medication regularly</td>
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<td>Teaching recognition of early warning signs of relapse</td>
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<td>Development of relapse prevention plans</td>
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<td>Cognitive-behavioral strategies for coping with symptoms</td>
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<td>Integrated treatment for comorbid substance abuse</td>
<td>Decrease substance abuse</td>
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<td>Treatment of schizophrenia and substance abuse by same team of clinicians</td>
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<td>Outreach to engage reluctant patients</td>
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<td>Motivation-based interventions to retain patients in treatment</td>
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<td>Focus on reduction of harmful consequences of substance abuse</td>
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Summary of psychosocial interventions for schizophrenia supported by empirical evidence

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other atypical antipsychotics have been developed that have a more favourable side-effect profile. Evidence suggests that atypical antipsychotic medications are more clinically effective than conventional antipsychotics, although some of this apparent benefit might be due to the relatively high dosages of conventional antipsychotics used in many studies. Clozapine has unique potency for the treatment of persistent psychotic symptoms, negative symptoms, and suicidality. A drawback to clozapine is that it can lead to agranulocytosis, a dramatic lowering of the white blood-cell count that can be fatal if not detected in time. Substantial clinical experience indicates that clozapine can be safely used in schizophrenia when patients’ white blood-cell count is routinely monitored. Atypical antipsychotics have also been found to have beneficial effects on cognitive functioning compared with conventional antipsychotics.

Other pharmacological treatments are frequently used in the management of schizophrenia, including antidepressants, mood stabilisers (eg, lithium, valproic acid, carbamazepine), and benzodiazepines. Limited evidence supports the effectiveness of adjunctive medication in the treatment of schizophrenia, including the recent trend towards combination therapy with different antipsychotics. Despite this, polypharmacy has become common in the treatment of schizophrenia.

Non-adherence
Non-adherence to antipsychotic medications is common, with estimates of non-compliance in the range of 50%, and even higher soon after the onset of the disorder. Several strategies have been developed to improve adherence. First, some antipsychotic medications can be given as an injectable depot once every 2–4 weeks, including fluphenazine, haloperidol, and risperidone. Second, adherence can be improved by simplifying the regimen (taking fewer medications fewer times per day) and by behavioural tailoring (teaching patients how to incorporate medication into their daily routines). Third, medication adherence can be improved by direct delivery and monitoring of medication ingestion in patients’ homes.

Psychosocial treatment
Psychosocial intervention seeks to improve the management of schizophrenia (eg, coping with symptoms, relapse prevention) and to enhance functioning in areas such as independent living, relationships, and work. Specific interventions that have been shown to improve the outcome of schizophrenia include assertive community treatment, family psychoeducation, supported employment, social skills training, teaching illness management skills, cognitive-behaviour therapy for psychosis, and integrated treatment for comorbid substance abuse (table).

Assertive community treatment
Patients with severe schizophrenia often fail to follow through on outpatient treatment, resulting in medication non-adherence and poor monitoring of the illness, and leading to frequent relapses, rehospitalisations, and housing instability. To address this problem, multidisciplinary assertive community treatment teams have been developed for patients with the most difficulty sustaining stable community living. These teams are characterised by lower staff-to-patient ratios (one-to-ten instead of one-to-30 or higher), provision of most services in patients’ usual environments instead of the clinic, direct provision of most services by the team rather than brokering services to other providers, 24-h coverage, and shared rather than individual caseloads. Research on this strategy, including more than 30 controlled studies done mainly in the USA and Australia, suggests that compared with traditional approaches assertive community treatment reduces symptoms and rehospitalisations, stabilises housing in the community, and improves subjective quality of life.

Controlled research on intensive case management in England (reduced staff-to-patient ratios compared with standard case management) has failed to find effects on reduced hospitalisations and improved functioning. One large, seemingly experimental study in England comparing intensive community services with standard treatment failed to find better outcomes with the more intensive approach, although this study has been criticised on methodological grounds. Although intensive case management is not the same as assertive community treatment, the benefits of both approaches are probably attenuated in well co-ordinated and adequately staffed systems of care.

Family psychoeducation
Many patients live with family members or have continuing contact with relatives. Caring for or maintaining a close relationship with a person with schizophrenia is associated with high levels of burden in relatives. Additionally, family stress can impinge on the patient’s biological vulnerability, precipitating relapses and rehospitalisation. Family psychoeducational programmes have been developed to reduce burden of care and family stress, and to improve the management of schizophrenia. Family programmes led by professionals focus on teaching relatives and patients about schizophrenia and the principles of its treatment, reducing stress, and improving the ability of the family to work towards individual and shared goals. Research on family psychoeducation, including over 20 controlled studies, indicates that long-term programmes are effective at reducing cumulative relapse and rehospitalisation rates from about 60% over 2 years to less than 30%.

Supported employment
Rates of competitive employment among individuals with schizophrenia are low, typically ranging between 10% and 20%, yet the majority of patients want to work. To address this problem, supported employment programmes have been developed that emphasise rapid job search, competitive work in integrated community settings, provision of follow-along supports, attention to patients’ preferences about job type and nature of support, and integration of vocational and clinical services. Nine controlled studies have shown that supported employment programmes are more effective at improving competitive work outcomes than other approaches.

Social skills training
Social dysfunction, characterised by poor relationships with others, few friends, and lack of social reciprocity, is pervasive in schizophrenia and contributes to a poor quality of life and worse outcome. Social skills training addresses social functioning by systematically teaching patients new interpersonal skills, such as starting conversations and expressing feelings, using social learning strategies such as modelling, role playing, and homework. Social skills training has been the focus of extensive research, and the results of several controlled trials indicate that it improves social recovery in patients who have been hospitalised. Additionally, incorporation of specific skills into the community to practise skills has been found to further increase the beneficial effects of training on social functioning.
Teaching illness-management skills
It is now widely accepted that patients with schizophrenia can become active participants in their own illness management, and programmes have been developed to achieve this.10,12 Illness management includes several different treatment components, each of which has been found to improve knowledge or outcome in several controlled studies.8 First, patients benefit from learning information about schizophrenia and the principles of its treatment so they can make informed decisions about their care.12 Second, patients can be taught how to monitor the early warning signs of relapse, and helped to develop plans to respond to these signs and prevent relapses.14 Third, patients can be taught more effective coping skills to deal with persistent symptoms.11 Teaching coping strategies involves a careful analysis of the situations in which symptoms are most problematic, the selection and practice of new coping skills in session, and at-home practice.

Cognitive behaviour therapy for psychosis
About 25–40% of patients experience persistent psychotic symptoms, despite optimal pharmacological treatment.15 Psychotic symptoms are associated with high levels of distress,15 and can contribute to functional impairment, such as reduced ability to work.12 Cognitive behaviour therapy for psychosis involves developing a collaborative relationship with the patient, examining the circumstances in which delusional beliefs or hallucinations emerged, and exploring alternative interpretations that may be more adaptive and accurate, and result in less distress.15 More than seven controlled studies, most of which were done in Great Britain, have shown that cognitive behaviour therapy for persistent psychotic symptoms is effective in reducing the severity of those symptoms, with additional benefits including reduced relapse rates and negative symptoms.13

Integrated treatment for co-occurring substance misuse
The most common co-occurring disorder in schizophrenia is substance misuse.14 Previous attempts to treat substance misuse in schizophrenia by referring patients to substance-use specialists were unsuccessful because of difficulties these services had in engaging and retaining patients with schizophrenia in treatment.15 Programmes in which substance misuse and schizophrenia are treated simultaneously by the same individuals have shown better outcomes.12 Other features of effective, integrated treatment programmes for substance misuse in schizophrenia include outreach to engage patients in treatment, motivation-based interventions that first instil the desire to change substance misuse, and efforts to minimise the negative consequences of substance misuse at the earliest possible time. Research on integrated treatment for dual disorders supports the effectiveness of integrated programmes at reducing substance abuse.15

Early intervention for schizophrenia
Over the past decade, interest has grown in identifying and rapidly treating schizophrenia at the earliest possible stage, either during the prodromal phase or immediately after the frank emergence of psychotic symptoms. Enthusiasm for early intervention has been based on three findings. First, patients benefit from learning information about schizophrenia and the principles of its treatment so they can make informed decisions about their care.12 Second, patients can be taught how to monitor the early warning signs of relapse, and helped to develop plans to respond to these signs and prevent relapses.14 Third, the development of schizophrenia is associated with an arrest in social development and attainment of usual social roles, which at earlier ages contributes to a worse clinical and social prognosis.11 These results have stimulated the hope that more effective methods for detecting first-episode schizophrenia, combined with rapid pharmacological intervention and comprehensive psychosocial treatment, could improve the long-term outcome, reduce burden on relatives, and reduce the cost of treatment. To date, several programmes have been developed that target first-episode patients in Europe, Australia, and North America.12,13 The long-term benefits of early intervention are unknown, but controlled studies have shown promising results for pharmacological and psychosocial treatments.

In addition to efforts to more rapidly treat first episodes of psychosis, work has focused on identifying and treating schizophrenia before it develops during the prodromal phase. Standardised methods have been established that identify patients with prodromal symptoms who are likely to develop schizophrenia over the next 6–12 months.14 One study found that antipsychotic medication was more effective than placebo in reducing the severity of prodromal symptoms over 6–8 weeks.17 Another group reported that the combination of antipsychotics with cognitive-behaviour therapy reduced the likelihood of patients with prodromal symptoms developing schizophrenia over 6 months.11 This research bodes well for the potential to intervene early and prevent the emergence of psychosis in vulnerable people.

Schizophrenia in developing nations
Since the prevalence of schizophrenia is similar in developing and developed countries, the majority of people in the world with the illness live in developing nations where they face particular challenges. First, the detection of schizophrenia may be complicated by the higher presence of infectious, parasitic, and nutritional diseases that result in psychotic symptoms. Second, most people with schizophrenia in developing nations live with family members, but receive no formal treatment, resulting in a high burden of care on relatives. The integration and provision of mental health services in primary health-care settings has shown some promise as a strategy for increasing access to treatment (especially antipsychotic medication) for people with schizophrenia.14 Third, the effectiveness and need for adaptation of pharmacological and psychosocial treatment methods supported by rigorous research in developed countries largely remain to be determined for developing countries. A partial exception to this is family psychoeducational programmes, which have been implemented successfully and shown to be effective in controlled research in China.15

Stigma
Stigma has long been recognised as a major challenge for people with mental illness,19 with schizophrenia among the most stigmatising disorders.19 Widely held myths about people with schizophrenia and other severe mental illnesses are that they are frequently violent, childlike, or irresponsible,19 with exaggerated beliefs about danger contributing most strongly to negative attitudes.19 People with mental illness are held more responsible for their disorders than people with other disabilities,19 resulting in discrimination in areas such as work19 and housing,19 and self-stigma leading to poor self-esteem and demoralisation.19 Aside from these direct effects, stigma can also contribute to denial of the illness by patients, which can lead them to delay seeking help and reduce their adherence to treatment recommendations.19 Widespread, inaccurate
media depictions of mental illness in the media seem to be at least partly responsible for these negative attitudes. Recognition of the effects of stigma has led to research aimed at understanding its roots and exploring strategies for reducing it. Methods with promise for destigmatisation include education about mental illness, facilitation of positive contact with people with a mental illness, legislation (e.g., the Americans with Disabilities Act), and campaigns against negative stereotypes in the media. The importance of addressing stigma has also led to large-scale campaigns aimed at reducing stigmatisation and discrimination, the most notable of which is the World Psychiatric Association Worldwide Programme to Fight Stigma and Discrimination Because of Schizophrenia.

Conflict of interest statement
None declared.

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