

Extract

Schizophrenia in primary care

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KEY MESSAGES

- Schizophrenia is a treatable disorder and some patients are able maintain employment despite persisting symptoms and/or disability.
- Although it is often necessary to admit these patients to hospital, care in the community should be arranged where possible, with close collaboration with the mental health service.
- Antipsychotic drugs should suppress the positive symptoms of the disorder, and should be offered to all patients. No single drug is clearly preferable to others.
- Patients who fail to respond to conventional treatments should be offered treatment with clozapine after two other drugs have been tried.
- Family interventions reduce the risk of relapse and reduce the level of symptoms. Other effective interventions include cognitive-behavioural therapy modified for psychosis (CBTp), and arts therapy.
- Those caring for these patients in the community should pay special attention to their social adjustment and ensure that they live in a social context that is as normal as possible.

Introduction

Schizophrenia is the name given to a group of mental disorders in which delusions and hallucinations predominate, and there are alterations in a person's perception, thoughts, feelings and behaviour. Each person with the disorder will have a unique combination of symptoms and experiences. Typically, there is a *prodromal period*, often characterised by some deterioration in personal functioning. This period may include memory and concentration problems, unusual behaviour and ideas and disturbed communication and affect.

Schizophrenia affects approximately 7 per 1000 people from adolescence onwards. It is an illness with low incidence and high prevalence, due to the effects of chronicity, and is of importance to primary care because of a shortage of mental health specialists globally, especially in low and middle-income countries.¹ In most countries, whatever their income, primary care will be the first contact for many people who suffer from mental health conditions.²

Historical background

Schizophrenia has been noted in all cultures throughout recorded history. In the 19th century, the French psychiatrist Benedict Morel, who observed rapid intellectual deterioration in a young teenage boy from a good student to one with confused thoughts and grossly disorganised behaviour over a few months, named the disorder *démence précoce*.³ In 1893, the fourth edition of Emil Kraepelin's textbook *Psychiatrie* introduced dementia praecox under the heading of 'Psychic degenerative processes'.⁴

In 1911, Eugene Bleuler replaced the term 'dementia praecox' with 'schizophrenia', because he believed the cognitive impairment associated with the disorder arose from splitting of psychic function.⁵ Bleuler identified four disturbances, known as 'the four As', as fundamental to the disorder. These were affective blunting, loosening of association, autism and ambivalence. He considered hallucinations and delusions as non-specific to the diagnosis of schizophrenia, since they occurred in patients with other conditions such as manic-depressive (bipolar) illness.

In 1959 Kurt Schneider, a German psychiatrist, drew attention to the importance of psychotic symptoms in the diagnosis of schizophrenia and identified certain 'first rank' psychotic symptoms as diagnostic, thus introducing greater objectivity and specificity into the diagnostic process.⁶ First-rank symptoms included thought insertion, thought withdrawal, thought broadcasting, delusions of control, audible thoughts, voices arguing about the subject, voices commenting on actions in the third person and delusional perception.

Epidemiology of schizophrenia

Schizophrenia is an illness with an unclear aetiology, which is likely to be both complex and multifactorial and to involve a gene and environment interaction. The best way to consider this in a primary care setting is by adopting a life-course approach, which begins from genetics, obstetric complications, childhood adversity, adolescent adversity and other life events of adulthood.

There is an association between schizophrenia and family history, as having a first-degree relative with schizophrenia increases a person's likelihood of experiencing schizophrenia ten-fold, while having two affected parents or an affected twin confers a likelihood of 50%.⁷ There is also evidence that prenatal infections can be associated with schizo-

phrenia; these include rubella,⁸ influenza⁹ and toxoplasmosis.¹⁰ One of the theories proposed to explain this association is the role of cytokine and chemokines as mediators of the host response to infection.¹¹ In addition to obstetric infections, other obstetric complications may be associated with an increased incidence of schizophrenia.¹² There is evidence that childhood trauma may be associated with psychosis;¹³ however, Morgan and Fisher are of the opinion that a number of conceptual and methodological issues need to be addressed before a definite conclusion can be reached.¹⁴

Adolescent and adult psychosocial stressors, including first and second-generation migration,^{15,16} inner-city environment,¹⁷⁻¹⁹ and, in some cases, substance misuse,²⁰⁻²² are all associated with onset, maintenance and relapse of schizophrenia.

The incidence of schizophrenia is higher in men than in women.^{23,24}

Key lessons for primary care are summarised in Box 1.

Positive and negative symptoms

There are two main groups of symptoms, and both may be present simultaneously or each can occur on their own. The prodromal period is usually followed by an acute episode marked by *positive symptoms* such as hallucinations, delusions and behavioural disturbances, accompanied by agitation and distress. *Negative symptoms* may take the form of social withdrawal, apathy and reduced interest in daily activities. In those with prolonged illnesses, there may be some cognitive decline over many years.

Box 1 Lessons for primary care

- There is a need for a bio-psycho-social approach to the management of schizophrenia.
- Prevention starts with:
 - genetic counselling for those parents who have a high genetic risk
 - prevention of infections in the prenatal period
 - good obstetric care during delivery
 - prevention of childhood trauma and deprivation
 - support for migrants
 - good environmental planning to decrease the stress of living in inner cities.

Acute episodes and persistent states

The International Classification of Diseases (ICD)-11 for primary health care (ICD11-PHC) is due to be released by the World Health Organization (WHO) in 2014. It distinguishes between acute episodes of psychosis and persistent psychotic states, where the illness has not resolved fully and may display both positive and negative features. The concept of 'acute psychosis' includes transient psychotic states that last less than one month, as well as schizophrenia, which is the name given to illnesses that have lasted more than one month. For primary care purposes, the broader concept is preferable, as an individual primary care clinician is more likely to see cases of transient psychotic states than first onset of schizophrenia. Since schizophrenia is often a long-lasting disorder, primary care clinicians are most likely to see cases of persistent psychotic illness.

Acute psychotic disorder

Presenting symptoms and complaints

Patients can present with sudden onset of severe disturbance, characterised by strange beliefs and grossly abnormal behaviour. They may be apprehensive, confused or extremely suspicious. Acute psychosis can be very transient in nature, lasting for a few hours to a few days, or can last for a few weeks. Complete recovery is the norm. *Schizophrenia should not be diagnosed until the disorder is still present after four weeks.* It is often very difficult to know the extent to which drugs may be responsible for psychotic experiences, and patients should always be asked what drugs they have used in recent weeks.

Diagnostic features

Acute psychotic disorder is a diagnostic label given to patients with unusual symptoms of sudden onset, usually with florid disturbance and lasting from a few days to a few weeks. While complete recovery is the norm, a minority of patients can have a relapse with similar presentations.

The unusual experiences, abnormal beliefs and behaviours may include:

- required symptoms:
 - delusions (strange beliefs may involve being persecuted or poisoned, of special powers, of one's spouse's infidelity, of being controlled or of being talked about by strangers)
 - hallucinations (hearing voices or seeing visions).

- other common symptoms:
 - withdrawal
 - agitation
 - restlessness or disorganised behaviour
 - muddled thinking,
 - incoherent or irrelevant speech
 - labile emotional states.

Differential diagnosis

- Bipolar disorder – the manic phase and psychotic forms of depression may have many similar features; patients may develop symptoms of classical mania and depression or may go on to become chronic, mandating a change in diagnosis over time
- Drug-induced psychotic states
- Exacerbations of a persistent psychosis, with a total duration of illness of more than three months
- Medical conditions such as delirium, with systemic or cerebral infections, and epilepsy

Persistent psychotic disorder

Presenting symptoms and complaints

The presentations include abnormal beliefs, hearing voices or seeing visions and may involve abnormal behaviour. Patients can also present with lack of energy for daily chores, lack of motivation to work, difficulty in concentrating, apathy and withdrawal from family, friends and colleagues.

Diagnostic features

Acute exacerbations include:

- delusions (strange beliefs of being persecuted or poisoned, of special powers, of one's spouse's infidelity, of being controlled or of being talked about by strangers)
- hallucinations (hearing voices and seeing things that others cannot see)
- restlessness and agitation
- grossly abnormal behaviour.

Persistent problems include:

- lack of energy or motivation to carry out daily chores and work
- apathy and social withdrawal
- strange and abnormal speech
- poor personal care or neglect.

Differential diagnosis

- Bipolar disorder – the manic phase may have many similar features
- Psychosis can also be associated with medical illnesses (e.g. infections and tumours of the brain, head injury, epilepsy, thyroid disorder)
- Dementia – organic psychoses (e.g. dementia) can have similar features
- Substance use – e.g. alcohol, cannabis, opioids, etc.

Interviewing and assessing a psychotic patient

Time is always short in primary care, and you may have to speed up your assessment. Some basic strategies follow.

The patient must perceive you as their own doctor, rather than the agent of their parents. If the patient is accompanied, start your interview with the patient, and only take a history from others with the patient's consent. Listen to the patient's account of the present problem, with sympathy and encouragement. If the patient is not sure why he or she has come, ask what has worried other people and suggested that they visit. If you are still not making much progress, ask whether the patient has had any experiences they could not account for, or has had any recurrent thoughts that troubled them.

If odd experiences are described, ask if they were taking any drugs at the time, or whether they have experimented with them in the last few weeks. If you are still making little progress and they are accompanied, ask if they mind asking the person with them what they have noticed that worries them.

In any case, you will need to take control of the interview and do a quick *mental state examination*. How are they feeling at present? Are they worried about themselves? Have they felt that life isn't worth living? (*If so, have they had thoughts about harming themselves?*) Have they found that they can hear things that other people don't seem to hear? Or have they seen things that they couldn't account for? (*Have they had auditory or visual hallucinations: can they describe what they have heard/seen?*) Have they had any problems with their thinking (*thoughts inserted, or controlled by others?*) Can they tell you where they are, what date/day of week it is, and who you are (*orientation*)?

Management of schizophrenia in primary care

The management of schizophrenia requires an integrated approach that recognises the central importance of the patient, their family and carers, is holistic, and focuses on developing patient strengths and promoting recovery.

Management of schizophrenia requires a recognition that the person with schizophrenia is an individual who should be treated with respect and empowered to manage the illness, so that they can maintain hope and obtain treatment in the least restrictive environment possible, and live a satisfying, hopeful and contributing life, despite the limitations caused by illness.²⁵

As with all other mental health conditions, it is important to invest in manpower to improve patient access to treatment, so that mental and physical health needs are addressed in an integrated way that can deliver the best possible outcomes.

It is known that not all people with schizophrenia will visit primary care, as illustrated by Goldberg and Huxley;²⁶ therefore, a systematic approach to the management of schizophrenia that takes into account prevention, the subtype of schizophrenia and its course is necessary.

Low and middle-income countries

In *middle-income countries* where secondary care mental health services are less well developed, general practitioners and family physicians should form an alliance with their local psychiatrist so that they can readily elicit support and advice to help them better manage early-onset cases of schizophrenia and those who have not responded to the usual treatment interventions. This approach can be better supported where locally agreed management guidelines have been jointly developed by primary care physicians and secondary care psychiatrists, as this will provide a clear guideline on when it is appropriate to ask for extra help or refer to the local mental health service. Liaison with mental health services can be further enhanced by organising regular meetings between primary care staff and the local psychiatrist at the primary care clinic, where complex cases can be brought and discussed. Many middle-income countries have a network of local district general hospitals that provide a range of services. General practitioners and family physicians should negotiate admission rights for psychiatric patients requiring inpatient care, supported by a clear admission guideline and treatment protocol.

In such circumstances, the role of the psychiatrist is to assist in developing evidence-based treatment protocols and guidelines, regular educational support and ongoing coaching to medical staff who are managing people with schizophrenia.

In *low-income countries*, where primary care services and secondary care mental health services are poorly developed, the roles of the general practitioner or family physician are different, as, not only are they the first point of contact, they also have to take on the role of local specialist for a range of mental health disorders. In such situations, it is even more important for primary care to develop very detailed schizophrenia protocols and guidelines to follow. If there are other general practitioners or family physicians in the area, they should form an alliance of mutual support or cooperation, including co-mentoring and peer support. They should develop the role of healthcare workers to support their mental health interventions, and work with local opinion leaders and advocates to address stigma and promote access. In some countries where traditional healers play a role, general practitioners and other health professionals working in primary care should work with their local health boards to generate a list of local traditional healers, so that they can provide them with mental health education and support, and their usefulness can be harnessed as part of the extended primary healthcare team.

In all countries, there is a need to develop a local formulary of a range of medications that are affordable, and of proven benefit in the treatment of schizophrenia, so that access to pharmacological interventions can be guaranteed.

The key to delivering good health is to keep the patient and their family or carer at the centre of the service.

Specific interventions for the treatment of schizophrenia

Once a history has been taken and a diagnosis made, an intervention plan should be developed using the following headings.

General

The person presenting with schizophrenia should be provided with a diagnosis and explanation of the disorder in a form that they can easily understand.

All people with schizophrenia should be assessed for risk to self and others. (For more details, please refer to Chapter 11 'Risk assessment and the management of suicidality in primary care mental health'.)

The prodromal phase

In many parts of the world, specialised early intervention services are not available, and primary care staff must use their own judgement in deciding what assistance to offer the person in a prodromal phase. If there is access to a local mental health service, it may sometimes be helpful to refer the patient, provided that he or she agrees to this. Where available, there are three components to the assistance a mental health service provides: firstly, early identification and therapeutic engagement of people in the prodromal phase; second, provision of specialised pharmacological and psychosocial interventions during or immediately following a first episode of psychosis; and third, education of the patient and his or her family and the wider community to reduce obstacles to early engagement in treatment.

An acute episode of psychosis

- For people with newly diagnosed schizophrenia presenting with positive symptoms, offer *oral antipsychotic medication*. Provide information and discuss with the service user the benefits and side-effect profile of any drug you intend to use, bearing in mind the relative potential of individual antipsychotic drugs to cause extrapyramidal side-effects (including akathisia), metabolic side-effects (including weight gain) and other side-effects (including unpleasant subjective experiences). In nine randomised controlled trials (RCTs) with a total of 1801 participants with first-episode or early schizophrenia (including people with a recent onset of schizophrenia and people who had never been treated with antipsychotic medication), the evidence suggested there were no clinically significant differences in efficacy between the antipsychotic drugs examined.²⁷ These medications are effective in reducing all florid symptoms, and in reducing excited behaviour.
- Referral to a specialised *mental health service* will depend upon local availability of such a service. Patients with grossly disturbed behaviour, or where there is thought to be a danger to either the patient or to others, are usually referred. If possible, all first episodes of acute psychosis should be referred to the specialist service.
- If patients are to be *managed in the community*, it is advisable for them to be visited by a mental health nurse who is able to give advice and support to carers. Interface with the local mental health service is facilitated if there is a *written care plan* that has been agreed between the two services and the service user and his or her family. Such care plans typically include details of symp-

toms both in relapse and admission, the usual medication and an acceptable alternative, details of any mental health nurse allocated to the case, and information on how to arrange readmission if this becomes necessary. There should be opportunities to have *case discussions* between primary care and mental health staff, especially at times of crisis.

- When the crisis of an acute episode is resolved, offer *family intervention* to all families of people with schizophrenia who live with or are in close contact with the service user. This is a specialised procedure best carried out by someone who has been trained to deliver such interventions. Family interventions aim to reduce the level of expressed emotion in the family and to decrease critical comments towards the patient, as well as to help carers deal with problems and to improve knowledge about the illness in both the service user and his or her family. Therapists are most likely to be a mental health professional. In 32 RCTs including 2429 participants, there was robust and consistent evidence for the efficacy of family intervention.²⁷ When compared with standard care family interventions have been shown to reduce the risk of relapse and to produce a lower level of active symptoms for up to two years after the intervention.^{28,29}
- The National Institute for Health and Clinical Excellence (NICE) recommends that general practitioners and other primary healthcare professionals should *monitor the physical health* of people with schizophrenia at least once a year. You should focus on cardiovascular disease risk assessment as described in the NICE guideline *Lipid modification*, but bear in mind that people with schizophrenia are at higher risk of cardiovascular disease than the general population. A copy of the results should be sent to the care co-ordinator and/or psychiatrist, and put in the secondary care notes.³⁰
- *Do not* initiate regular combined antipsychotic medication, except for short periods (for example, when changing medication).

Interventions for people with schizophrenia whose illness has not responded adequately to treatment

- First, review the diagnosis. Other possible explanations for symptoms include intoxications with drugs or alcohol and organic brain disease.
- Next, try to establish whether there has been adherence to antipsychotic medication, prescribed at an adequate dose and for the correct duration.

- Review engagement with and use of psychological treatments and ensure that these have been offered.
- If there is access to a specialist mental health service, ask for an opinion on which drug to try next. At least one of the drugs should be a non-clozapine second-generation antipsychotic.
- If trained staff are locally available to administer *cognitive behavioural therapy adapted for schizophrenia* (CBTp), suggest this as next step. When compared with standard care, CBTp was effective in reducing both the rate of readmissions to hospital and the duration of admissions. Negative symptoms were reduced at one-year follow-up.³¹ Early CBT trials tended to be particularly symptom focused, helping service users develop coping strategies to manage hallucinations.³¹ Since then, however, CBTp has evolved and now tends to be based on a manual. It should take place over a series of sessions, and establish links between the patient's thoughts, feelings or actions and their current or past level of functioning, and allow the patient to re-evaluate how their perceptions, beliefs or reasoning relate to the target symptoms.
- Offer *clozapine* to people with schizophrenia whose illness has not responded adequately to treatment despite sequential use of adequate doses of at least two different antipsychotic drugs. In 18 RCTs including 2554 participants whose illness had not responded adequately to treatment, clozapine had the most consistent evidence for efficacy over the first-generation antipsychotics included in the trials.³² A number of patient-related factors have been reported to increase the variability of plasma clozapine concentrations, with sex, age and smoking behaviour being the most important.

Patients with persistent psychotic states

Patients may reach a relatively stable state, with some residual positive symptoms in addition to some negative symptoms. Positive symptoms may reappear when the patient has experienced a stressful life event, or when they have stopped taking their medication. The advice given above will apply to management of the positive symptoms.

The use of depot medication

Consider this only where there is clear evidence that antipsychotic drugs are effective in controlling symptoms, and where there is evidence that the patient repeatedly relapses when medication is not taken, and agrees to receiving depot medication.

Combining clozapine with another antipsychotic

In six RCTs including 252 participants with schizophrenia whose illness had not responded adequately to clozapine treatment, there was some evidence that clozapine augmentation with a second antipsychotic might improve both total and negative symptoms if administered for an adequate duration.^{33,34}

Negative symptoms

There is no consistent evidence that one antipsychotic drug is any better at relieving negative symptoms than the others. In ten RCTs including 1200 participants with persistent negative symptoms, there was no evidence of clinically significant differences in efficacy between any of the antipsychotic drugs examined.²⁷ Careful clinical assessment is warranted, to determine whether such persistent features are primary or secondary, and may identify relevant treatment targets, such as drug-induced parkinsonism, depressive features or certain positive symptoms.³² However, if clozapine is augmented with another antipsychotic drug, there is some evidence of efficacy, as discussed above.

There are also social and psychological treatments that are effective to some extent. *Arts therapies*, which allow expression of emotions, whether by drama, by pottery or by painting, have been shown to have such an effect. There is consistent evidence that arts therapies are effective in reducing negative symptoms when compared with any other control.³² There is some evidence indicating that the medium to large effects found at the end of treatment were sustained at up to six months' follow-up.³² *CBTp* may also reduce negative symptoms.

Social care and rehabilitation

A *social assessment* is necessary to ensure that an individual is obtaining whatever social benefits are available, and has somewhere to live that provides shelter from adverse weather and adequate food. Social interventions for schizophrenia should include supported employment, including opportunities for volunteering,³⁵ access to education and leisure activities and appropriate housing. Supported employment programmes may provide assistance to people with schizophrenia who wish to return to work or gain employment. However, they should not be the only work-related activity offered when individuals are unable to work or are unsuccessful in their attempts to find employment. Patients with persistent psychotic disorders need to *structure their*

time usefully, and gain help and support from regular social contacts, perhaps in a group setting.

Re-referral to the specialist mental health services

For a person with schizophrenia being cared for in primary care, consider referral to secondary care again if there is a poor response to treatment, non-adherence to medication, intolerable side-effects from medication, coexisting substance misuse, or risk to self or others.

Reducing the risk of relapse and the promotion of recovery

The NICE guideline showed that in 17 RCTs including 3535 participants with schizophrenia, the evidence suggested that, when compared with placebo, all of the antipsychotics examined reduced the risk of relapse or overall treatment failure.²⁷ Although some second-generation antipsychotic drugs show a modest benefit over haloperidol, there is insufficient evidence to choose between antipsychotics in terms of relapse prevention.

Conclusions, prognosis and future developments

It cannot be emphasised enough that the schizophrenic cluster of psychoses are by no means always chronic disorders. In the WHO ten-country study, it was found that, even in high-income countries, of those satisfying criteria for schizophrenia, about 37% may expect to have a remitting course and eventually to recover. In low and middle-income countries, the outlook is much more positive, with 63% having such a favourable course.³⁶ This is despite the fact that in the former patients were on antipsychotic drugs for more than 75% of the two-year follow-up, while in the latter the corresponding figure was 16%. Primary care staff are therefore urged to take a positive, even modestly optimistic view of the prognosis, and this is especially true for transient psychotic disorders.

Indicators of a poor outlook are a slow, gradual onset over months or years, a long duration of untreated psychosis, a poor premorbid adjustment, and a schizoid personality. One or more of Schneider's 'first rank' symptoms (see earlier, 'Historical background') mean that the patient will have a three-fold increased risk of relapse.³⁶ The best predictor of relapse is failure to continue to take antipsychotic

medication,³⁷ and those using cannabis are also at greatly increased risk of relapse.³⁸

In contrast, a sudden onset, a severe precipitating life event, and a good adjustment during adolescence, being married, having close friends and avoiding street drugs all indicate a more favourable course.³⁹

Future developments include a continuing tendency to avoid caring for these patients in large institutions, and instead to look after them in as normal as possible a social context. Negative symptoms accumulate in unstimulating environments, and they are strikingly less evident in those cared for in the community. It is likely that further advances will be made in identifying the genetic basis for schizophrenia, and, in particular, in our understanding of the social environments that interact with these genes.

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