

Chronic schizophrenia and the role of the general practitioner



Judy Hope, Nicholas Keks



Background

Chronic schizophrenia affects many Australians and is frequently managed in primary healthcare settings such as general practice. Physical health monitoring and management, especially of metabolic syndromes associated with new treatments, is a major focus of general practice care.

Objectives

The objectives of this paper are to describe the long-term treatments available to patients with chronic schizophrenia and to outline important physical health monitoring issues.

Discussion

Management of patients with chronic schizophrenia requires familiarity with antipsychotic medications, including efficacy and side effect profiles, knowledge of psychosocial interventions and physical healthcare. Physical care includes monitoring for metabolic syndrome, QTc interval, movement disorders, dental problems and hyperprolactinaemia, discussing smoking cessation strategies, and sexual health counselling.

Schizophrenia is a mental health disorder that affects around 30,000 adult Australians,¹ with a median lifetime risk of 7.2 per 1000 in the population.² Worldwide, schizophrenia is responsible for 1% of the global burden of disease.³

Chronic schizophrenia is an enduring syndrome of delusions, hallucinations, flatness of affect, poverty of speech or incoherence of speech.⁴ Other symptoms may occur, including mood symptoms, cognitive problems and movement disorders.

Symptoms of schizophrenia may be episodic or continuous. Some patients have excellent inter-episode remission and preservation of function. Others demonstrate treatment resistance, often with chronic negative symptoms and cognitive dysfunction.⁵ In some patients, negative symptoms (eg lack of motivation and minimal speech) predominate. Two-thirds of people with schizophrenia demonstrate impairment of self-care as well as social and occupational disability.¹

There are related disorders that can be included in the 'schizophrenia spectrum': schizoaffective disorder, psychotic bipolar disorder and psychotic depression. Chronic treatment-resistant illness can also occur with these disorders and management principles largely overlap with those for schizophrenia.

Physical health in schizophrenia

Up to 90% of people with schizophrenia have a chronic physical illness.³ There is a two-to-three-fold increase in mortality from suicide, accidents and medical disease.⁶ Obesity, smoking, diabetes, hypertension, dyslipidaemia and metabolic syndrome are present at rates of 1.5–5 times greater than the general population.^{7,8} Management of other physical health disorders, such as malignancy and complications of antipsychotic medication, is sometimes difficult in patients with schizophrenia.^{9,10} Physical health monitoring has been identified as inadequate in patients with severe mental illness.¹¹

Chronic schizophrenia and general practice

The majority of mental health disorders in Australia are managed in general practice.¹² Eighty-eight per cent of people with psychosis visited their general practitioner (GP) in the past 12 months.¹

Ideally, people with chronic schizophrenia should have ongoing access to specialist services, such as a private psychiatrist or public mental health services. These services should work in partnership with GPs. In this situation, the role of the GP is primarily to look after the physical health of patients while also monitoring treatment and mental state. GPs are, additionally, well placed to provide family support, as well as possible drug and alcohol intervention.¹³

Some people with chronic schizophrenia are managed solely by their GP. Many patients struggle to find specialist services that are available, accessible, affordable and acceptable.^{10,14} Access is often complicated by environmental factors, such as rural settings, service factors (eg complexity of pathways of care) and patient factors (eg level of insight and motivation to seek specialist treatment).¹⁵

Pharmacotherapy in schizophrenia

Antipsychotic medication continues to be the cornerstone of treatment in schizophrenia. In chronic schizophrenia, antipsychotics maintain symptom control and minimise exacerbations of illness, presumably through the blockade of dopamine D2 receptors. Antipsychotic medications are commonly classified as typical and atypical. They are available in various presentations, including tablets, capsules, wafers, and both short- and long-acting injectable preparations.

Oral antipsychotics

Atypical antipsychotics are now the most frequently used medications in the management of schizophrenia. Atypical antipsychotics differ substantially from each other in side effect profiles (Table 1).¹⁴ Aripiprazole and ziprasidone are less likely to cause weight gain than other atypical antipsychotics, but more likely to cause extrapyramidal side effects (EPSE). Olanzapine and clozapine are most likely to cause weight gain. Risperidone, paliperidone and amisulpride are more likely to cause hyperprolactinaemia and EPSE than other atypical antipsychotics, but they have no anticholinergic effects, such as dry mouth and constipation. Quetiapine is the most likely to cause sedation, anticholinergic effects and postural hypotension. QTc prolongation can occur with any atypical antipsychotic, but is more likely with amisulpride, ziprasidone and quetiapine.¹⁴

Atypical antipsychotics also differ in efficacy.¹⁴ Clozapine stands out as the most effective antipsychotic in treatment-resistant illness but has the most troubling side effects, including agranulocytosis. Amisulpride, risperidone and olanzapine appear to be more potent as antipsychotics than the remaining atypical antipsychotics. Risperidone, olanzapine and asenapine are available as dispersible oral formulations, which may aid adherence in some situations.¹⁴

Typical oral antipsychotics include chlorpromazine, haloperidol, trifluoperazine, pericyazine and zuclopenthixol. As EPSE occur

commonly at therapeutic doses with typical antipsychotics, these drugs are now used less frequently than atypical antipsychotics. Chlorpromazine is strongly sedative and tranquilising, but also have anticholinergic effects and are likely to cause postural hypotension. Haloperidol is not especially sedative, anticholinergic or likely to cause postural hypotension, but is likely to cause EPSE and hyperprolactinaemia.¹⁴

Depot antipsychotics

Typical depot antipsychotic preparations are all associated with increased tardive dyskinesia rates. Zuclopenthixol is more sedating than others and flupenthixol decanoate is sometimes more activating. Haloperidol decanoate can be used every four weeks.

Several new atypical depot preparations have become available recently. Risperidone long-acting injection is given fortnightly, and paliperidone and aripiprazole depot preparations are used monthly. Olanzapine can be used fortnightly or monthly. Test doses of oral medication should be used prior to depot administration to ensure safety (Table 2).

Non-pharmacological treatment in schizophrenia

Many GPs know their patients well and provide continuous care for them over many years. This provides an excellent base for supportive psychotherapy care. Problem solving and lifestyle advice provided by GPs can be very useful for patients with deficits in working memory and other executive functions. Writing down information or instructions is a practical intervention.

Specific psychological treatments can be helpful in patients with schizophrenia. Cognitive behavioural therapy (CBT) can be used to treat persistent auditory hallucinations.¹⁶ CBT treatment is available through referral to a psychologist using the Better Access initiative for six sessions in each referral, with up to 10 sessions per year. Psychological therapy can now be delivered by online services (eg Centre for Clinical Interventions, a Western Australian website). The Hearing Voices Movement run support groups for people living with chronic auditory hallucinations.

Support for families and carers through education and supportive therapy can also be a key role of GPs. Psychoeducation for patients and families is also possible through reliable websites such as SANE, Mental Illness Fellowship and the Centre for Clinical Interventions.

Social and vocational rehabilitation focuses on establishment or return of functional capacity in relation to relationships, study, work, travel and activities of daily living. This is now provided by non-government organisations, such as the Mental Illness Fellowship. In some areas, disability support workers providing this service may assist people with chronic schizophrenia to attend their GP or access other services.

Other treatment modalities in schizophrenia may be helpful. Regular daily exercise is known to be beneficial.¹⁷ Socialising and befriending programs are available in some urban settings, such as the successful Compeer Program.¹⁸

Table 1. Atypical antipsychotic formulations available in Australia (in order of likelihood of weight gain, least to most)¹⁵

Medication	Starting dose	Usual dose	Notable side effects
Ziprasidone	40 mg bd	40–80 mg bd	Movement disorder, may prolong QTc
Aripiprazole	5–10 mg mane	10–30 mg mane	Akathisia in 8% of users, usually little sedation
Amisulpride	100–200 mg daily	200–800 mg daily	Movement disorder, hyperprolactinaemia, may prolong QTc, usually little sedation
Asenapine	5 mg nocte	5–20 mg nocte	Sublingual preparation, unpleasant taste, transient perioral paraesthesia, mild weight gain, mild sedation
Paliperidone	3–6 mg nocte	6–12 mg nocte	Mild sedation, mild weight gain, mild EPSE, stuffy nose
Risperidone	0.5–1 mg nocte	2–6 mg nocte	Mild sedation, moderate risk of weight gain, mild EPSE, stuffy nose
Quetiapine	12.5–25 mg nocte	200–750 mg nocte	Postural hypotension, sedation, anticholinergic effects, moderate risk of weight gain
Clozapine	200–900 mg nocte		Weight gain common (often marked), sedation, constipation, postural hypotension, hypersalivation, seizures, agranulocytosis (1/100 risk), myocarditis/cardiomyopathy (rare, but requires specific physical health monitoring)
Olanzapine	5–10 mg nocte	10–20 mg nocte	Sedation, mild anticholinergic effects, weight gain common (often marked)

EPSE, extrapyramidal side effects

Table 2. Depot antipsychotic formulations available in Australia²⁴

Medication	Intramuscular dose and frequency	Notes
Haloperidol	50–200 mg every 4 weeks	Monthly preparation EPSE
Flupenthixol	20–40 mg every 2 weeks	Activating in some patients EPSE Weight gain
Zuclopenthixol	200–400 mg every 2 weeks	Sedating EPSE Weight gain
Fluphenazine	12.5–50 mg every 2 weeks	EPSE Weight gain
Aripiprazole depot	300–400 mg every 4 weeks	Reduce dose to 300 mg if known low metabolizer Continue oral aripiprazole for 14 days
Paliperidone palmitate	150 mg day 1 100 mg after 1 week 25–150 mg every 4 weeks thereafter	Similar side effects to oral preparation
Risperidone long-acting microspheres injection	25–50 mg every 2 weeks	Similar side effects to oral preparation
Olanzapine pamoate	Dosage varies depending on the oral dose of olanzapine previously prescribed. For example, if the oral dose of olanzapine was 10 mg, the dose of intramuscular olanzapine is 210 mg every 2 weeks for 2 months, then 150 mg every 2 weeks thereafter. ²⁴	Patient must be observed for 2 hours post-injection as risk of collapse Can be given monthly

EPSE, extrapyramidal side effects

GPs should also be aware of Recovery, a new paradigm in mental health. Recovery is the notion that the journey and outcomes following an episode of ill health can be defined by the person who is experiencing it themselves.¹⁹ Recovery is not the resolution of symptoms, but rather the person's self-defined pathway to restoration of the self. The ideas of Recovery include hope, dignity, self-determination and autonomy.

In practice, this manifests as a collaborative relationship between the healthcare provider, in which the health professional is the expert in their field, and the patient, who is acknowledged as an expert about themselves. Although many practitioners have practised this model for many years, the formalisation of Recovery practice will hopefully lead to a greater sense of empowerment and optimism in people with chronic schizophrenia.

Physical health monitoring in schizophrenia

Metabolic syndrome has become more prevalent due to the use of newer antipsychotics, which have been associated with greater weight gain and higher fasting glucose, cholesterol and lipid levels.¹¹ This places some patients at increased risk of diabetes and heart disease. Suggestions for monitoring are given in Table 3.

Some atypical antipsychotics may induce metabolic syndrome in patients who take them. Of the commonly used antipsychotics, olanzapine carries the greatest risk in this respect. One strategy is to switch to an antipsychotic medication with less metabolic risk (eg ziprasidone or aripiprazole). This is not always feasible or advisable, as switching carries a risk of relapse of the underlying disorder.

Diet and exercise are important in the management of obesity and metabolic syndrome. Barriers to this management (eg lack of knowledge, poor motivation and low disposable income) are possible to overcome in urban settings (this is more difficult to achieve in rural and remote settings) through the use of psychosocial services. Disability support workers can aid access to exercise programs. Dietitians and diabetes educators can be accessed through GP Management Plans, although these plans only allow for five allied health appointments per year. GPs may be able to use the Chronic Disease Health Assessment items 701–07.

Evidence now favours the use of metformin to prevent weight gain and the onset of hyperglycaemia in patients taking antipsychotic medications.²⁰ Metformin is now prescribed in patients without diabetes who are at risk of metabolic syndrome. Doses of 1000 mg daily are used prophylactically. Statins should be considered when lipid parameters are abnormal (Table 3).

Smoking cessation is a key intervention as 66% of patients with chronic schizophrenia smoke.² Psychological strategies are generally safest, followed by nicotine replacement therapies. Care should be taken with varenicline and bupropion in patients with schizophrenia, as mood and psychotic symptoms can uncommonly be precipitated.²¹

Electrocardiogram (ECG) monitoring should be undertaken annually in patients taking antipsychotic medication. The maximum acceptable QTc length is 450 ms for women and 430 ms for men.²²

Table 3. Suggested physical health monitoring in Australian general practice²⁷

	Frequency	Reason/intervention
Smoking status	Baseline, every visit	Motivational interviewing or QUIT program
Weight		Intervene if body mass index >25 kg/m ²
Waist circumference		Intervene if >94 cm for males and >80 cm for females
Blood pressure	Baseline, every 3 months for first year, then every 6 months	Intervene if systolic blood pressure is >130 mmHg and diastolic blood pressure is >85 mmHg
Fasting glucose		If fasting blood sugar levels 5.6–7 mmol/L then glucose tolerance test
Fasting cholesterol and lipids		Intervene if triglycerides >1.7 mmol/L, high-density lipoprotein <1.03 mmol/L in male and <1.29 mmol/L in female
Prolactin	Baseline, then annually	If high and symptomatic, refer to endocrinologist
ECG	Baseline, then annually in addition to at each change of antipsychotic dose	If QTc prolonged, refer to cardiologist
Liver function tests	Baseline, then annually	Antipsychotic induced transaminitis
Neurological examination	Baseline, then annually	Movement disorder
Eye examination	Biannually	Detection of cataracts, especially if on quetiapine and chlorpromazine
Contraception review (women only)	Annually	Counselling for prevention of unwanted pregnancy

Movement disorders may occur spontaneously in chronic schizophrenia or as a result of treatment. Acute dystonias generally occur rapidly after initiation of treatment, followed by Parkinsonism within weeks. Akathisia may occur fairly early in treatment, causing tormenting inner restlessness. All of these EPSE require dosage reduction or change of drug. Anticholinergic medication may also help.

Tardive movement states can occur at any time. Tardive states are complex and are best managed by a psychiatrist, sometimes in collaboration with a neurologist. Management options include reduction or cessation of the provoking agent, antioxidant supplements, tetrabenazine for tardive dyskinesia and botulin injections for chronic dystonias.²³

Many antipsychotic medications cause dry mouth, which predisposes to dental caries. Dental hygiene can be poor in people with chronic schizophrenia, which also contributes to dental disease. Access to low-cost dental services can be vital, but many people may not be able or willing to access these services. In this case, the GP is well placed to educate patients about the role of dental health in overall health, as well as providing general advice on regular brushing, the use of dental floss, and the importance of using gum or alcohol-free mouthwash to reduce dry mouth.

Some antipsychotic medications, particularly paliperidone, risperidone, amisulpride and haloperidol, can produce hyperprolactinaemia. Hyperprolactinaemia causes amenorrhoea in about 30% of women on these drugs, and sexual dysfunction also often occurs in both men and women.²⁴ Breast enlargement, tenderness and galactorrhoea will occur infrequently. If possible, lowering the dose of the drug or switching to an alternative antipsychotic may be tried, but must be weighed against the risk of relapse. Referral to an endocrinologist may be helpful. Although there is concern that osteoporosis could result from elevated prolactin, the evidence is not yet clear.²⁵

With the advent of antipsychotic medications that do not cause elevated prolactin, many more women with schizophrenia are fertile and require counselling about contraceptive choices. It is important that contraception is considered in women of childbearing age, especially those on medications of unknown teratogenicity, such as ziprasidone. Exogenous oestrogen can increase the stability of psychosis in some women, which is an important consideration if a combined oral contraceptive is preferred by a woman.²⁶ Progesterone intrauterine devices or progesterone implants may be preferable where exogenous oestrogen is contraindicated. Pap smears, sexual health counselling and screening for sexually transmissible diseases should be offered and encouraged where appropriate.

In summary, GPs have a vital role in caring for people with schizophrenia in conjunction with other health professionals. As outlined, GPs should be involved in the monitoring of both mental and physical health of people with schizophrenia.

Key points

- Monitor and manage physical health issues.
- Foster therapeutic alliance.
- Liaise with a specialist psychiatrist if the patient has insufficient symptom control or problematic side effects.
- Ensure referral is made to specialist services if the condition worsens or risk is apparent.
- Identify, educate and refer when drug and alcohol issues become apparent.
- Be aware of, and encourage, engagement with community-based services.
- Support family and/or carers.
- Consider practical needs (eg housing).
- Consider language and cultural barriers.
- Be flexible and adaptable where psychiatric illness factors may otherwise impede access to physical healthcare.
- Encourage optimism, hope and recovery.

Case 1. Mark

Mark, 45 years of age, is a single man living with his parents, who receives a disability support pension. He has chronic schizophrenia, which is managed with clozapine through a private psychiatrist. He continues to experience some low-level auditory hallucination and persecutory ideation, despite effective treatment. He has a disability support worker who helps him to attend a social group and encourages him to be active outside his home.

Mark sees his GP about once every three months. He smokes 20 cigarettes per day and is overweight. Today, he attends with his disability support worker who has driven him for a double appointment to receive blood test results. The disability support worker asks Mark for his permission to come into the consultation.

During the appointment, his GP weighs Mark, measures his height and his blood pressure, which is 115/80 mmHg. His latest blood tests results, ordered by the private psychiatrist, show high cholesterol and an impaired fasting glucose.

The GP discusses the results with Mark, showing him that he is at risk of developing diabetes, and has already developed high cholesterol and lipid levels. He explains that this will predispose Mark to heart disease and increases the risk of stroke. The GP asks what this might mean to Mark, to explore his understanding.

The GP, Mark and the disability support worker make a collaborative plan that includes:

- referral to a dietitian under a GP management plan for chronic disease
- daily exercise from walking the family dog
- the support worker offering to bike ride with Mark during their weekly appointments
- commencing on 500 mg mane of metformin to address the impaired fasting glucose

- considering stopping smoking – the GP remarks that Mark could reduce his clozapine dose by 25–50% if he stops smoking
- reviewing the effectiveness of the plan for reducing cardiovascular risk in six months' time.

The plan is written down, and copies are given to all of the stakeholders, including the family and the private psychiatrist, with Mark's permission.

The GP now sees Mark monthly. Three months later, Mark has lost 3 kg, his glucose readings are normal and he enjoys walking the dog. He is strongly contemplative about ceasing smoking as he recognises that smoking makes him less fit. The GP and patient then set another plan for smoking cessation with nicotine patch replacement and fortnightly appointments to monitor his progress.

Case 2. Donna

Donna, 32 years of age, is a woman living in supported rental accommodation on a Disability Support Pension. She has chronic schizophrenia. She is treated with paliperidone depot by the local area mental health service, under a community treatment order as a result of poor insight and adherence to treatment. Despite this, she is active in her community, attends church once a week and volunteers at the local op shop once a week.

Donna attends her GP every month for her depot injection. Each time, the GP faxes a note to the mental health service indicating the injection has been given. This month, Donna tells her GP that she has commenced sexual activity and requests advice about contraception. The GP notes that on her previous annual blood tests, her prolactin level was elevated at 1543 mIU/L. She has been amenorrhoeic despite never having been on contraception.

Donna's GP discusses contraceptive choices with her. He encourages the use of condoms, partly to prevent sexually transmissible diseases, as well as for contraception. He discusses the use of the oral contraceptive pill and recommends one that is available on the Pharmaceutical Benefits Scheme because of her financial constraints. The GP also suggests that Donna consider changing her depot medication to aripiprazole, and that she may wish to discuss this with her specialist mental health service.

The following month, Donna presents with signs of relapse. Although she remains on the paliperidone depot, she has commenced using cannabis with her new boyfriend. She has become paranoid, and has stopped attending church and her volunteer job. There are no acute risks to herself or others.

The GP explains the relationship between cannabis use and recurrent psychosis, and the need to both cease cannabis and increase her medication temporarily. The GP phones the area mental health service psychiatrist, and they agree to treat with 1 mg of oral risperidone and 5 mg diazepam twice daily, as required. Risperidone is chosen because low-dose tablets are available and its first metabolite is paliperidone so

that, effectively, antipsychotic monotherapy is maintained. A referral is made to the crisis intervention service to supervise the risperidone each day for two weeks and to monitor Donna's mental state.

Four weeks later, Donna has returned to her baseline function. The relapse has given her an opportunity to talk through her symptoms with her case manager and she is developing some insight into her condition. Consideration has been given to switching Donna's medication to aripiprazole in view of Donna's very high prolactin levels. She has also embarked on both an early warning sign and response plan, as well as a Recovery-inspired model of developing her own ideas around re-establishing hope and meaning in her life.

Donna continues to find that the long-term relationship with her GP provides understanding and support, and is appreciative that they both take an active role in her physical health management.

Authors

Judy Hope MBBS (Hons), MPM, PhD, FRANZCP, Deputy Director, Centre for Research and Education, Delmont Hospital, Consultant Psychiatrist Eastern Health, Adjunct Lecturer, Monash University, VIC. jhope1@bigpond.net.au
 Nicholas Keks MBBS, MPM, PhD, FRANZCP, Professor, Director, Centre of Education and Research, Delmont Private Hospital, Adjunct Professor of Psychiatry, Monash University, VIC

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correspondence afp@racgp.org.au