

Summary Australian and New Zealand clinical practice guideline for the treatment of schizophrenia (2003)

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Objective: To provide a summary of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) Clinical Practice Guideline for the Management of Schizophrenia.

Conclusions: Schizophrenia is a complex and misunderstood illness with a poor public image, but it is more treatable than ever before. A new generation of medication and psychosocial therapies, combined with a first generation of service reform, have created an evidence-based climate of realistic optimism. However, the potential for better outcomes and quality of life for people with schizophrenia has not been translated into reality. The gap between efficacy and effectiveness is wider for schizophrenia than for any other serious medical disorder. These guidelines distil the current evidence and make recommendations based on the best available knowledge. They are based on systematic meta-analyses and comprehensive reviews of the evidence, and their validity is supported by their congruence with several recent rigorous and independent guideline statements from the UK and North America.

Key words: clinical guidelines, evidence-based medicine, schizophrenia.

INTRODUCTION

Schizophrenia is a complex and misunderstood illness with a poor public image. It usually emerges during the critical period of transition to adulthood. Recognition and treatment is often suboptimal, yet over the past decade schizophrenia has become more treatable than ever. A new generation of drug therapies, a renaissance of psychological and psychosocial interventions and a first generation of reform within Australia's and New Zealand's specialist mental health systems have combined to create an evidence-based climate of realistic optimism. Exponential neuroscientific advances hold out the strong possibility of more definitive biological treatments in the near future.

This potential for greatly improved outcomes and quality of life contrasts starkly with the day-to-day reality for many people with schizophrenia. There is a large gap between the proven efficacy of treatments for schizophrenia and the effectiveness achieved in the 'real world',¹ resulting from factors such as underresourcing of services, inefficiency in the use of the resources, a failure to continue vital reform of psychiatric services, poor morale and divisions within the mental health workforce, and a continuing lack of professional and community concern and support for people with schizophrenia. The gap could be bridged by implementing optimal evidence-based treatment.

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This publication provides a summary of new Australian and New Zealand evidence-based clinical practice guidelines for the treatment of schizophrenia in adolescents and adults, including first-episode psychosis. The summary emphasizes general principles and major recommendations but, inevitably, much detail has been omitted from this version.

Key recommendations are summarized in Table 1.

METHOD

The guidelines were developed under the auspices of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) for use by all specialist disciplines delivering mental health care. The College received funding for the guidelines through the National Mental Health Strategy (Australia) and the New Zealand Ministry of Health.

Table 1: Key recommendations

General

Foundations for effective care include

- Optimism and partnership

- A stable and secure social environment, including a pleasant home environment, family and peer support, financial security and a meaningful social role

- Therapeutic engagement and continuity of care

Specific

Early detection and comprehensive treatment of first episodes of schizophrenia is a priority because it can minimize the psychosocial – and possibly biological – impact of illness and may improve long-term outcomes.

Comprehensive and sustained intervention should be provided during the initial years following diagnosis because the course of illness is strongly influenced by what occurs during this ‘critical period’. Patients should not have to ‘prove chronicity’ before they gain consistent access to specialist mental health services.

Antipsychotic medication is the cornerstone of treatment but there is great scope for further improvement in the expert use of these medications. The treatment of choice for most patients is the atypical antipsychotic medications because of their superior tolerability, probable greater efficacy in relapse prevention and, in particular, reduced risk of tardive dyskinesia. In first-episode psychosis atypical agents should be used as first-line therapy.

Conventional antipsychotic medications in low dosage may still have a role to play in a small proportion of patients, where there has been full remission and good tolerability, where atypicals are poorly tolerated, or where depot medication is unavoidable. However, the indications are shrinking progressively.

Clozapine should be prescribed early, if there is incomplete remission of positive symptoms following treatment with at least two other antipsychotic medications. Clozapine may also be considered where there are pervasive negative symptoms or a significant and persistent risk of suicide.

Psychosocial interventions should be available routinely for all patients within an integrated hospital and community service, and provided by appropriately trained mental health professionals. Appropriate interventions include family interventions, CBT, vocational rehabilitation and therapy for comorbid conditions, particularly substance use disorders.

Interventions should be tailored to the phase and stage of illness, and to the gender and cultural background of the person.

Consumers and relatives should be closely involved in the development and provision of services.

Maintenance of good physical health and the prevention and early treatment of medical illness in people with schizophrenia has been neglected.

General medical care for people with schizophrenia should become an active focus.

General practitioners should be closely involved in the care of people with schizophrenia in a ‘shared care’ model. Sole care by a GP with minimal or no specialist involvement is not an acceptable standard of practice, despite the challenges of Australia’s geography.

The specialist mental health system urgently needs to be strengthened and the complementary role of general practice expanded. Psychosocial rehabilitation services in particular need major updating, expansion and better integration with specialist and primary care services.

An increased research effort is urgently required to develop more effective and better tolerated drug therapies, more effective interventions to reduce comorbidity, particularly harmful substance use, and improved community understanding and support for people with schizophrenia.

CBT, cognitive behavioural therapy; GP, general practitioner.

Clinicians should consider, but not be limited to, the recommendations. The guidelines are not absolute and should not necessarily be interpreted as standards of practice. Mental health professionals care for patients with schizophrenia in many different settings, some of which are isolated and highly challenging, where it may not be feasible to apply all of the recommendations.

The development team included Australian and New Zealand clinical and research experts from psychiatry, clinical psychology, social work, psychiatric nursing and epidemiology. Consumers and carers reviewed drafts and their input was incorporated. The process for grading the recommendations on the basis of best available evidence has been described in Boyce *et al.*²

AN OVERVIEW OF SCHIZOPHRENIA

What is schizophrenia?

Schizophrenia is a psychotic disorder that is defined in terms of a variable confluence of positive and negative symptoms without the sustained presence of major mood disturbance. Cognitive impairment and disability are common additional concomitants. The boundaries and validity of the concept, especially in the onset phase, remain problematic. Schizophrenia overlaps with other psychotic disorders phenotypically and in terms of underlying risk factors.

Aetiological basis of schizophrenia

Schizophrenia arises from a combination of risk factors, mainly in genetically vulnerable people. The genetic vulnerability is complex and is now regarded as involving a variable combination of multiple genes of small effect. Environmental risk factors are also necessary and some operate early in life, creating a neurodevelopmental vulnerability state. Other contributory risk factors include gender, socioeconomic disadvantage and urban birth. Recently it has become clearer that more proximal risk factors and pathophysiological processes operating closer to the onset of the syndrome are also required. This second set of factors putatively involves either endogenous central nervous system (CNS) processes such as increased neuronal dysfunction with reduced connectivity, or extrinsic candidates such as substance abuse, viral infections and developmental stress. How specific these putative risk factors are for schizophrenia is not clear. With advances in neuroscience, there is now extensive evidence of mild structural and significant functional abnormalities in the CNS of people with schizophrenia, although none of these are specific. While they confirm that schizophrenia is associated with brain dysfunction and can be firmly regarded as a brain disease, there is still no laboratory test to confirm the diagnosis of schizophrenia.

Impact of schizophrenia

The lifetime prevalence is approximately 1% and it occurs in all known cultures. The course of illness is

highly variable,³ although despite much better recovery rates than generally appreciated, significant disability does occur in a large subgroup and life expectancy is substantially reduced by suicide and chronic medical diseases.⁴⁻⁶ In Australia, despite an initially encouraging process of national mental health service reform, the impact of schizophrenia remains a serious and neglected public health problem.¹ Although the cost of treating schizophrenia already appears high,⁷ these expenditure levels remain insufficient to meet more than the most basic needs of patients and families. The impact of schizophrenia could be substantially reduced through a combination of increased resources and evidence-based practice.⁸

CURRENT TREATMENT EVIDENCE

The management of schizophrenia is best considered in stages or phases: the prepsychotic or prodromal phase, first-episode psychosis, recurrent or persistent schizophrenia (including prevention and treatment of relapse), maintenance therapies, and treatment-resistant schizophrenia.

Prepsychotic or prodromal phase

Background

In most patients a prolonged period of symptoms and increasing disability, commonly termed the 'prodrome', occurs before the onset of severe and persistent positive psychotic symptoms that are sufficient to allow the diagnosis of schizophrenia or first-episode psychosis. Such psychosocial damage is always difficult to reverse. Recently it has also been shown that active neurobiological change may occur during this period.⁹ The prepsychotic phase is an active focus of research¹⁰ and more evidence is required before definitive guidelines can be developed, but in the meantime the following recommendations are offered.

Recommendations

- The possibility of psychotic disorder should be considered in any young person who is becoming more socially withdrawn, performing more poorly for a sustained period of time at school or at work, behaving in an unusual manner for them, or becoming more distressed or agitated yet unable to explain why [V-1].
- Subthreshold psychotic features combined with the onset of disability, especially if there is a family history, indicate very high risk.¹¹ The young person and the family should be actively engaged in assessment and regular monitoring of mental state and safety. This should be carried out in a home, primary care or office-based setting if possible, to reduce stigma [V-1].
- Concurrent syndromes such as depression and substance abuse, and problem areas such as interpersonal, vocational and family stress, should be appropriately managed [III-3].

- Information about the level of risk should be carefully provided, conveying a sense of therapeutic optimism. It should emphasize that current problems can be alleviated, that progression to psychosis is not inevitable, and if psychosis does occur then effective and well-tolerated treatments are readily available. Engagement at this early stage will help to reduce any subsequent delay in accessing treatment for first-episode psychosis [III-3].
- The use of antipsychotic medication during the prodrome is the subject of research.^{10,12-14} At present it should be reserved for patients who are clearly psychotic [V-1].

First-episode psychosis

Background

Two key issues in first-episode psychosis (FEP) are the timing of intervention (and thus the duration of untreated psychosis (DUP)¹⁵) and its quality (the sustained provision of comprehensive phase-specific treatment).¹⁶⁻²¹

There are often prolonged delays in initiating effective treatment for first-episode psychosis. Prolonged DUP is associated with poorer response and outcome.^{15,22,23} Early identification of people in the earliest phases of psychotic disorders combined with optimal treatment is very likely to reduce the burden of disease while it is active.²⁴ Any improvements in long-term outcome should be seen as a bonus, rather than as a prerequisite for improving clinical standards during early illness.²⁵

First-episode psychosis tends to be more responsive to treatment than subsequent episodes and later phases of illness but it can be more demanding because of the range of clinical issues to be addressed. Syndromes, and hence diagnoses, tend to be unstable and may evolve over time. The umbrella term 'psychosis' allows this syndromal flux and comorbidity to be accommodated, and treatment commenced for all prominent syndromes, before a stable diagnosis such as schizophrenia needs to be applied. Whether or not core 'schizophrenia' can be diagnosed or not is not crucial for effective treatment in FEP. Treatment-relevant syndromes are positive psychosis, mania, depression, substance abuse and the negative syndrome. Cannabis use in particular is common in FEP and can cause confusion and delay in treating the psychotic episode. Significant cannabis use appears to be a risk factor for onset of schizophrenia²⁶ as well as an aggravating factor for subsequent course.²⁷

Recommendations

- Strategies to improve the treatment of FEP include better mental health literacy, more informed primary care, and greater responsiveness of public and private psychiatry to possible cases. Community-

wide education systems should be developed to improve understanding of how psychotic disorders emerge in a hitherto healthy person and how to seek and obtain effective advice, treatment and support [III-1].^{28,29}

- A high index of suspicion and a low threshold for expert assessment should be set for FEP [V-1].
- Entry and retention within specialist mental health services is often based on a reactive crisis-orientated model in which individuals must reach a threshold of behavioural disturbance, risk, disability or chronicity. This resource-poor model creates unnecessary trauma, demoralization and therapeutic nihilism in patients, families and clinicians. Instead, services should aim for proactive retention of patients throughout the first 3-5 years of illness, combining developmental (youth) and phase-specific perspectives [III-3].^{19,20}
- Initial treatment should be provided in an outpatient or home setting if possible.³⁰ Such an approach can minimize trauma, disruption and anxiety for the patient and family, who are usually poorly informed about mental illness and have fears and prejudices about inpatient psychiatric care. Inpatient care is required if there is a significant risk of self-harm or aggression, if the level of support in the community is insufficient, or if the crisis is too great for the family to manage, even with home-based support [V-1].
- Inpatient care should be provided in the least restrictive environment. Optimal inpatient units should be streamed by phase of illness and developmental stage, be relatively small in size, and be adequately staffed so that 1:1 nursing of highly distressed, suicidal or agitated young people is possible without locking sections of the unit or secluding the patient, unless this is absolutely necessary. The use of traditional psychiatric 'intensive care', a pragmatic intervention that lacks a solid evidence base, is especially traumatic for these patients.³¹⁻³³ Where streaming is not possible, a special section may be created in a general acute unit for young recent-onset patients [III-3].
- Pharmacological treatments should be introduced with great care in medication-naïve patients, to do the least harm while aiming for the maximum benefit. Appropriate strategies include graded introduction, with careful explanation, of low-dose antipsychotic medication³⁴⁻³⁶ plus antimanic or antidepressant medication where indicated. Skilled nursing care, a safe and supportive environment, and regular and liberal doses of benzodiazepines are essential to relieve distress, insomnia and behavioural disturbances secondary to psychosis, while antipsychotic medication takes effect [III-3, V-1].

- The first-line use of atypical antipsychotic medication is recommended on the basis of better tolerability and reduced risk of tardive dyskinesia. In the longer term, the risk–benefit ratio may change for some patients, for example if weight gain or sexual side-effects associated with the atypical agents develop. Typical antipsychotic medications may then be one of the options considered [I].^{21,37,38}
- A baseline computed tomography (CT) scan, neurocognitive screen, neurological examination for movement disorder, electrocardiogram (ECG), weight (body mass index; BMI) and fasting serum glucose should be included in the initial assessment [V-1].
- Psychosocial interventions, especially cognitive behavioural therapy (CBT), are an important component of early treatment, providing a humane basis for continuing care, preventing and resolving secondary consequences of the illness, and promoting recovery.³⁹ Cognitive behavioural therapy may also be helpful for comorbid substance use, mood and anxiety disorders and improving treatment adherence [III-3].⁴⁰
- Families and, whenever possible and appropriate, other members of the person's social network should be actively supported and progressively educated about the nature of the problem, the treatment and the expected outcomes. If there are frequent relapses or slow early recovery, a more intensive and prolonged supportive intervention for families is required [I].^{41,42}
- If recovery is slow and remission does not occur despite sustained adherence to two antipsychotic medications (at least one of which is an atypical medication) for 6 weeks each, early use of clozapine and intensive CBT should be seriously considered [I].^{21,43}
- Early use of clozapine should also be considered if suicide risk is prominent or persistent [II].⁴⁴

Recommended interventions in FEP are summarized in Table 2.

Recovery and relapse: treating schizophrenia in the critical period

Background

Relapses are common during the first 5 years after a first episode of psychosis,⁴⁵ a phase that has been termed the 'critical period'.^{17,46} Young people naturally find it difficult to accept the lifestyle change of taking daily medication, especially if they have substantially recovered. Poor adherence often contributes to one or more relapses, which are risky, disruptive and may confer an increased chance of treatment resistance. Secondary consequences such as worsening substance abuse, vocational failure, family

stress and homelessness are common during this phase, as the social fabric of the young person's life is put under severe strain.

It is essential that high quality and intensive biopsychosocial care is provided continuously and assertively during this critical period. In practice, though, patients are rapidly discharged to primary care and must typically experience acute relapse, a suicide attempt or manifest severe disability and collateral psychosocial damage, before further specialist care is provided, often in a reactive 'too little, too late' manner. Services currently tend to disengage at precisely the time when they are most needed and could be of most value. Typically they become reinvolved only during increasingly brief acute episodes of care, superimposed on a low base of so-called 'shared care'. This minimalist model is highly inappropriate for the needs of patients during this often stormy critical period of illness.

Recommendations: recovery from first-episode psychosis

- In fully remitted patients, antipsychotic medication should be continued for at least 12 months and then an attempt made to withdraw the medication over a period of at least several weeks. Close follow up should be continued with specialist review for a further period of at least 12 months, and any relapse rapidly identified and treated [V-1].
- Approximately 10–20% of patients fail to fully remit after a trial of two antipsychotic medications. They should be considered as manifesting treatment resistance (see specific guidelines following [III-3]).
- Even in fully remitted patients, a range of psychological, family and vocational issues need to be addressed. Comorbidity, especially substance abuse, depression, posttraumatic stress disorder (PTSD) and social anxiety, is common and should be treated [V-1].
- Every patient has the right to a safe, secure and agreeable home environment [V-1].
- Family support and intervention should be consistently provided during this phase [I].⁴⁷
- Suicide risk must be actively monitored and addressed [II].^{44,48}
- Vocational recovery interventions should be offered once a stable clinical state has been achieved [II].^{49,50}
- Most patients should remain principally within specialist mental health care throughout the early years of illness, rather than discharged to primary care on improvement of acute symptoms. Optimal treatment in this phase is complex, but true 'shared care' arrangements that are driven by clinical

Table 2. Recommended interventions in first-episode psychosis

<i>First-episode non-affective psychosis</i>	<i>Pharmacological interventions</i>	<i>First-episode schizoaffective psychosis</i>	<i>Psychosocial interventions</i>
<p>24–48 h observation (no antipsychotics, but use benzodiazepines for anxiety and sleep disturbance) [V-1]</p> <p>Start low dose atypical [II]</p> <p>Increase within 7 days to initial target dose (risperidone 2 mg, olanzapine 10 mg, quetiapine 300 mg, amisulpride 400 mg) and hold for next 3 weeks [III-2, V-1]</p> <p>If no response increase dose slowly over next 4 weeks (8 weeks in total) to 4 mg, 20 mg, 800 mg and 800 mg respectively [III-2, V-1]</p> <p>If response occurs, continue for 12 months, and if remitted stop gradually over a few months with close follow up</p> <p>Side effects (e.g. weight gain) may be grounds to consider switch to typical agent.</p> <p>If no response, assess reason. For poor adherence, discuss, analyse reasons, optimize dose, try compliance therapy [V-2]</p> <p>Non-response: Switch to another atypical and assess over 6–8 weeks [V-1]</p> <p>If no response or poor adherence, or persistent suicide risk, positively recommend clozapine, informing patient and family of benefits and risks. If reluctant, further trials of atypicals or typicals may be justified. An injectable atypical preparation, namely risperidone, has recently become available. This may be considered by patient as an alternative to clozapine for poor adherence [V-2]</p> <p>If no response or poor adherence with frequent relapse, try low dose typical depot trial for 3–6 months. Currently, unless specifically preferred by the patient, this is a last resort option because of reduced tolerability, greater restrictiveness and associated stigma. This recommendation may partially change with the availability of atypical injectables [V-2]</p>	<p>24–48 h observation (no antipsychotics, but use benzodiazepines for anxiety and sleep disturbance) [V-1]</p> <p>If manic type: Start with mood stabilizer plus low-dose atypical antipsychotic (add benzodiazepine if sedation required) [V-1]</p> <p>If no response switch to another atypical [V-1]</p> <p>If depressed type: Start with low dose atypical and SSRI [V-1]</p> <p>If response, continue for 12 months and discontinue gradually [V-1]</p> <p>If cyclothymic or family history of bipolar add mood stabilizer [V-1]</p> <p>If no response switch to another atypical. If no response to SSRI try SNRI [V-1]</p> <p>If still no response try tricyclic antidepressant then consider ECT [V-1]</p>	<p>Prepsychotic period</p> <p>Engagement</p> <p>CBT [V-1]</p> <p>Stress management [V-1]</p> <p>Vocational rehabilitation [V-1]</p> <p>Family intervention [V-1]</p> <p>NB SSRIs where indicated</p> <p>First episode acute phase</p> <p>CBT [II]</p> <p>Psychoeducation and emotional support for both the patient and family/carers [V-1]</p> <p>Debriefing for patient and carers (especially where the admission involved traumatic events) [V-2]</p> <p>Address comorbidity (e.g. substance use, mood and anxiety disorders, trauma) [V-1]</p> <p>Case management aimed at coordinating care, reversing downward social drift, vocational repair, reduction in environmental stressors, engagement in and acceptance of treatment, lifestyle and social environment [V-1]</p>	

CBT, cognitive behavioural therapy; SNRI, selective noradrenaline re-uptake inhibitor; SSRI, selective serotonin re-uptake inhibitor.

rather than cost imperatives should be actively developed [V-2].

Recommendations: managing acute relapse

Table 3 summarizes strategies for acute relapse. A solid therapeutic relationship and a staged approach is essential.^{51,52} Good adherence to antipsychotic medication and specific psychosocial interventions, particularly family interventions, can reduce the risk of relapse.⁵³⁻⁵⁵ A significant advantage of an atypical antipsychotic over a typical agent in the prevention of relapse has recently been demonstrated.⁵⁶ Poorly engaged, frequently relapsing patients benefit most from intensive case management or assertive community treatment (ACT) models of care.⁵⁷ Comorbid substance abuse commonly contributes to relapse, and interventions based on CBT and motivational interviewing show early promise, although this is likely to remain a challenging issue.⁵⁸

Prolonged schizophrenia: maintenance treatment and care

Background

Long-term issues in schizophrenia include lifestyle problems and the physical and mental consequences of chronic illness, such as poverty, poor housing, a strained relationship with family members, social isolation and unemployment. Clinical issues include ongoing relapse prevention, reducing the demoralizing effects of persistent psychotic symptoms, depression and suicide, substance abuse, smoking, family relationships and vocational rehabilitation.^{49,50} The personal relationship with the patient is critical and a staged approach to recovery essential.^{51,52} Hence psychosocial intervention is always an essential element in addition to pharmacotherapy. Monotherapy with atypical antipsychotic medication, following consultation with the patient and family, is the treatment of choice, unless there has been full remission and good tolerability with a typical agent, or the atypical medications have produced unacceptable side-effects.²¹ Physical morbidity must not be neglected.^{5,59} The emergence of obesity, impaired glucose tolerance, tardive dyskinesia, hypertension and cardiovascular disorders should be regularly considered. Although the risk of tardive dyskinesia has been reduced with the atypical antipsychotics, the risk of obesity, diabetes mellitus and sexual side-effects has increased. Preventive health care should be offered early and consistently. No conclusive evidence could be found at this stage to support more widespread introduction of cognitive remediation or social skills training programmes.^{54,60}

Recommendations [all V-1]

- Actively maintain and enhance the patient's social environment and social capital within a case management framework, addressing issues such as access to paid work or pension support, housing,

social relationships. Attend to clinical issues such as active personal and family support, medication adherence, depression, monitoring suicide risk and substance use.

- In conjunction with general practitioners, ensure full annual physical check-ups that cover weight, blood pressure, lipid profile, ECG and fasting blood glucose, and usual preventive medicine activities such as appropriate screening for cervical, breast, bowel, skin and prostate cancer.
- Encourage smoking cessation and reduction or cessation of substance misuse, and promote exercise and a healthy diet.
- Regularly review sexual function.
- Regularly (6-monthly) examine for signs of tardive dyskinesia.
- Check for signs of late remission and review the need for continuing antipsychotic medication.
- Actively encourage and facilitate meaningful social role development and maintenance, especially through 'in vivo' vocational rehabilitation.

Treatment-resistant schizophrenia

Background

Symptoms persist in a substantial minority of people with schizophrenia despite apparently adequate treatment. While 15% of first-episode patients manifest treatment resistance, this rises with the passage of time and 'enrichment' of clinical samples to 30-50%.⁶¹ It is important for clinicians to remain hopeful of positive change rather than becoming nihilistic, and recognize that late remissions can occur despite treatment resistance.³ Treatment resistance can be defined narrowly in terms of persistent positive symptoms, or more broadly to include the persistence of negative symptoms and disability. Complacency, therapeutic nihilism and service gaps have meant that many such patients have not been exposed to clozapine, CBT or active psychosocial interventions.⁶² Conditions that may resemble 'treatment resistance' include marked but subtle extrapyramidal symptoms, unrecognized depression, inadequate psychosocial rehabilitation, poor adherence, substance abuse, drug interactions and inappropriate drug therapy.

Recommendations

- Identify and address contributing factors such as poor adherence, extrapyramidal side-effects, depression, substance abuse, polypharmacy, or poor social environment and support [V-2].
- Ensure that the patient has received two adequate trials (at least 6 weeks of maximum well-tolerated dose) of antipsychotics, of which at least one should be atypical [V-1].

Table 3: Recommended interventions in acute relapse

<i>Oral</i>	<i>Pharmacological interventions</i>	<i>Depot</i>	<i>Psychosocial interventions</i>
<p>Ascertain reason for relapse. Distinguish between relapse linked to poor adherence and relapse despite good adherence [V-1]</p> <p>Optimize medication dose and review polypharmacy [V-1]</p> <p>Re-start medication if relapse due to non-adherence after understanding the reasons [I]</p> <p>If on typical antipsychotic, switch to atypical if response not optimal or if there are tolerability problems. If relapse has occurred despite good adherence, switch to an atypical medication. If patient has been in remission with good quality of life and has no tolerability problems with typical agent, re-start or continue the typical medication. If tolerability problems with the atypical, especially weight gain, offer switch to another atypical or typical [III]</p> <p>If on depot, consider relapse as a learning experience and an opportunity to review need for depot within a psychoeducational framework [V-1]</p> <p>If treatment resistance is evident, and two antipsychotic agents (at least one an atypical) have been tried, switch to clozapine [I]</p> <p>Consider depot as a last resort only, unless patient prefers this. This situation may change with the advent of atypical depots, which could be considered prior to clozapine where compliance is uncertain [V-2]</p>	<p>Prior to starting or continuing depot consider potential reversible factors in current relapse (e.g. extrapyramidal side-effects) [V-1]</p> <p>If a depot is considered essential, consider using the lowest dose possible and maximum dosing interval</p> <p>Depot should be used in conjunction with psychosocial interventions [I]</p> <p>Short-term benzodiazepine or oral neuroleptic supplementation may be required [III]</p>	<p>Support and counselling for consumer and carers about relapse, especially for a second episode [I]</p> <p>Structured family interventions [I]</p> <p>Address comorbidities using CBT [III]</p> <p>Psychoeducation [III-1]</p> <p>Compliance therapy [III]</p> <p>Case management [V-1]</p> <p>Assertive community treatment [I]</p> <p>Vocational rehabilitation [I]</p> <p>Relapse prevention [I]</p> <p>Harm minimization for substance use disorders [III]</p>	

CBT, cognitive behavioural therapy.

- Clozapine is the treatment of choice for clearly defined treatment resistance [I].
- Depot antipsychotics can be considered if there has been poor adherence, but clozapine may be preferable because the required monitoring often enhances adherence. This recommendation may soon need to be reviewed when atypical injectables become available [V-1].
- Cognitive behavioural therapy should be offered either in conjunction with clozapine or as an interim alternative to it if the patient is unwilling to consent to clozapine. In this situation every effort should be made to inform the patient and family of the disabling consequences of the illness if symptoms do not remit, restate the risks and benefits of clozapine and evidence for its use, and enable them to reach an informed choice.
- If treatment resistance persists despite treatment with clozapine, reinstate the best previous antipsychotic and try an appropriate adjunctive therapy, such as lithium. Cognitive behavioural therapy should always be provided should clozapine fail. There is no firm evidence that combining antipsychotics in such patients is useful and tends to increase the side-effect burden [V-2].
- Personal, family and social support, vocational rehabilitation and a safe and fulfilling lifestyle are critical for this group of patients, who are at risk of being marginalized and demoralized [I].
- Use typical antipsychotics only as a last resort in emergency tranquillization because of the extremely high risk of extrapyramidal side-effects. Even in multiepisode patients, the doses of typical neuroleptics required for tranquillization greatly exceeds the threshold for extrapyramidal side effects (EPS).⁶³
- If the patient is non-combative, try oral therapy with benzodiazepines (e.g. lorazepam 1–2 mg or diazepam 5–10 mg) followed by oral olanzapine wafers (5–10 mg) as the next option. High doses of benzodiazepines may be required for some patients, especially those with severe substance dependence. The use of haloperidol is very difficult to justify because it is non-sedative and is associated with severe EPS and dysphoria in most cases.
- If the patient is openly combative, remains aggressive while consistently refusing oral medication, if the initial response to oral medication is inadequate, or if rapid tranquillization is required because of escalating aggression, then parenteral medication will be necessary. Start with 5 mg midazolam i.m. When any parenteral medication is administered, resuscitation facilities must be available and the patient must be directly observed for at least 2 hours.
- If the aforementioned steps have been ineffective, consider the following: (i) after an oral benzodiazepine and atypical antipsychotic, try chlorpromazine 25–100 mg orally; (ii) after i.m. therapy, consider droperidol, though due to the risks associated with QT prolongation, an ECG should be performed after administration (and if feasible, beforehand). Access to cardiopulmonary resuscitation (CPR) and defibrillation must also be assured; (iii) where repeated injections are occurring, consider zuclopenthixol acetate (use low doses, especially in patients not previously treated with antipsychotics, because EPS are very common); and (iv) after parenteral tranquillization, monitor temperature, pulse, blood pressure and respiratory rate every 5–10 min for 1 hour, then half-hourly until the patient is ambulatory.
- After remission of symptoms, the patient should normally be maintained on the lowest effective dose of an atypical antipsychotic. Debriefing for patients, staff, family members or other caregivers should always be provided.

Managing acute emergencies in schizophrenia

Background

Key goals in managing emergencies involving patients with schizophrenia are summarized in Table 4.

Key recommendations

- A range of preventive strategies aimed at reducing the likelihood, severity and sequelae of acute emergencies should be actively promoted.

Table 4: Key goals in managing emergencies

Primary prevention of emergency situations and the need for restraint
Prevention of physical harm to the patient, other patients or staff
Prevention of psychological trauma to patients and staff arising from the management of emergencies
Prevention of adverse events from physical or pharmacological restraint during emergencies
Prevention of sequelae of emergency restraint

CONCLUSION

These guidelines are inevitably a 'work in progress'. The evidence base continues to grow steadily and, despite gaps and the lack of uniform level I evidence, is relatively clear as judged by the degree of consensus between these guidelines and those from other countries that have produced similar documents. Despite the untested claims of "assumption based medicine",⁶⁴ there is scope for great real world improvement in the treatment of schizophrenia, and an urgent priority

is to translate the knowledge we already have into routine clinical practice. Treating schizophrenia inadequately is already a costly exercise.^{4,7} To achieve better outcomes and quality of life will require a renewed wave of reform at the service level as well as at the level of individual clinical practice. This will cost substantially more. Such increased funding should be directed to the 'best buys' as identified in this summary report.

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APPENDIX I

Selected meta-analyses and Cochrane reviews

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APPENDIX II

National Institute for Clinical Excellence (NICE) guidelines

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