

Australian and New Zealand Journal of Psychiatry Grading of Recommendations, Assessment, Development and Evaluations (GRADE) guidelines for the management of schizophrenia

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Abstract

Objective: The current Guidelines aim to provide evidence-based management recommendations for treatment of people living with schizophrenia in Australia and Aotearoa New Zealand.

Methods: The *Australian and New Zealand Journal of Psychiatry* (ANZJP) commissioned a panel of experts to establish these Guidelines. The existing literature was reviewed to address key health questions. The certainty of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach, and the strength of the recommendation was determined by the panel.

Results: The ANZJP GRADE Guidelines examined the current evidence base for a range of areas relevant to treatment for people with schizophrenia including: initial physical health assessment; pharmacological treatment; psychological and psychosocial interventions; family, whānau and carers; psychiatric comorbidities; physical health and lifestyle interventions; and special populations.

Conclusions: It is hoped that the current Guidelines provide useful recommendations in important aspects of care for people living with schizophrenia and their family, whānau and carers in Australia and Aotearoa New Zealand, both at the individual and systemic levels.

Keywords

Schizophrenia, GRADE, guidelines

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Introduction

The current Guidelines were commissioned by the *Australian and New Zealand Journal of Psychiatry* (ANZJP). These Guidelines are informed by the two previous Royal Australian and New Zealand College of Psychiatrists (RANZCP) clinical practice guidelines (Galletly et al., 2016; Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders, 2005). In formulating the recommendations, we employed the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach to develop and evaluate the key health questions (Guyatt et al., 2011a, 2011b; Lewin et al., 2015). In areas where there was an absence of quantitative research available, the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research) (Lewin et al., 2015) and the World Health Organization Qualitative Evidence Synthesis Framework (Downe et al., 2019) approaches were used to synthesise the evidence from qualitative studies. As such, the current Guidelines are more limited in scope than previous RANZCP clinical practice guidelines. It is important to emphasise that schizophrenia is a syndromal diagnosis with considerable heterogeneity in both the presentation and prognosis. While we hope that the current Guidelines help inform the delivery of care for people living with schizophrenia, each clinician needs to apply evidence appropriately and specifically to each person with schizophrenia within the context in which they work (Greenhalgh et al., 2014). The current Guidelines should be used in conjunction with an individualised, collaborative formulation to provide the optimal care for the person living with schizophrenia and their family, whānau and carers.

Schizophrenia

Schizophrenia is characterised by psychotic symptoms (i.e. delusions, hallucinations and disorganised thinking and speech), negative symptoms (including reduced emotional expression or motivation), cognitive impairment and abnormal motor behaviour (Jauhar et al., 2022; McCutcheon et al., 2020). The symptom profile and severity of symptoms can vary between individuals. The diagnostic criteria for the two main international classification systems (American Psychiatric Association, 2022; World Health Organization, 2022) are outlined in Table 1. Despite the ever-expanding body of work in the area (Jauhar et al., 2022), no objective measures, such as serum markers, neuroimaging and cognitive testing, are confirmatory in diagnosing schizophrenia. Thus, the diagnosis of schizophrenia remains clinical, based on comprehensive psychiatric assessment, collateral information and exclusion of other conditions that may imitate similar symptoms. The lifelong prevalence of schizophrenia is estimated to be around 0.7%

globally (McGrath et al., 2008), with variations observed depending on study design, geographic region, time of assessment and study quality, as well as case identification methods. While these estimates remain relatively stable (Simeone et al., 2015), the raw global prevalence (14.2–23.6 million) and associated disability-adjusted life years (9.1–15.1 million) have increased significantly since 1990 (Solmi et al., 2023b). These findings indicate that although schizophrenia remains a low-prevalence disorder, its burden of disease globally is substantial and increasing (Charlson et al., 2018).

General principles in working with people with schizophrenia

Shared decision-making. A shared decision-making process of ensuring that the person with schizophrenia is the primary driver for the care should be implemented as much as possible. Whenever appropriate, their family, whānau and carers should be invited and involved in their care. Person-centred care is an important element in building strong and inclusive mental health systems and service cultures that value diversity and promote safety in service contact for all in the community. This also includes treating people from diverse backgrounds with appropriate cultural sensitivity within a culturally informed care model.

Working with family, whānau and carers. All mental health professionals, including psychiatrists and psychiatry trainees, should be mindful of how we work with family, whānau and carers to build our capability in family-focused care, and improve our confidence in managing confidentiality issues. We should also be proactive in recognising the emotional support needs of family, whānau and carers, while maintaining respect for the privacy and rights of the person receiving care. This is a crucial element in building strong and inclusive mental health systems and service cultures.

Adequate training of clinicians. Psychological, psychosocial and lifestyle interventions recommended in these Guidelines need to be provided by adequately trained and/or credentialed clinicians with appropriate supervision.

Medication considerations. When trialling a new medication, the dose should be reviewed proactively and adjusted according to its effectiveness and side effects in collaboration with the person with schizophrenia. The optimal dose should be the lowest effective dose with a tolerable adverse effect profile, taking into account the individual's age, sex and ethnicity, as pharmacokinetic and pharmacodynamic differences exist among demographic groups (Halstead et al., 2025; McCutcheon et al., 2025). If an agent's intolerability exceeds benefits, then switching to another medication should be

Table 1. Diagnostic criteria for schizophrenia in DSM-5-TR and ICD-11.

DSM-5-TR (American Psychiatric Association, 2022)	ICD 11 (World Health Organization, 2022)
A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be delusions, hallucinations or disorganised speech: • Delusions • Hallucinations • Disorganised speech (e.g. frequent derailment or incoherence) • Grossly disorganised or catatonic behaviour • Negative symptoms (i.e. diminished emotional expression or avolition) B. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet the above criteria (i.e. active phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested only by negative symptoms or by two or more symptoms listed above present in an attenuated form. C. For a significant portion of time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or selfcare is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is a failure to achieve expected level of interpersonal, academic, or occupational functioning). D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either (1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or (2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness. E. The disturbance is not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication) or another medical condition. F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated). <i>Specify if:</i> The following course specifiers are only to be used after a 1-year duration of the disorder and if they are not in contradiction to the diagnostic course criteria. • First episode, currently in acute episode: First manifestation of the disorder meeting the defining diagnostic symptom and time criteria. An acute episode is a time period in which the symptom criteria are fulfilled.	<i>Essential (Required) Features:</i> At least two of the following symptoms must be present (by the individual's report or through observation by the clinician or other informants) most of the time for a period of 1 month or more. At least one of the qualifying symptoms should be from item a) through d) below: a) Persistent delusions (e.g. grandiose delusions, delusions of reference, persecutory delusions). b) Persistent hallucinations (most commonly auditory, although they may be in any sensory modality). c) Disorganised thinking (formal thought disorder) (e.g. tangentiality and loose associations, irrelevant speech, neologisms). When severe, the person's speech may be so incoherent as to be incomprehensible ('word salad'). d) Experiences of influence, passivity or control (i.e. the experience that one's feelings, impulses, actions or thoughts are not generated by oneself, are being placed in one's mind or withdrawn from one's mind by others, or that one's thoughts are being broadcast to others). e) Negative symptoms such as affective flattening, alogia or paucity of speech, avolition, asociality and anhedonia. f) Grossly disorganised behaviour that impedes goal-directed activity (e.g. behaviour that appears bizarre or purposeless, unpredictable or inappropriate emotional responses that interferes with the ability to organise behaviour.) g) Psychomotor disturbances such as catatonic restlessness or agitation, posturing, waxy flexibility, negativism, mutism, or stupor. Note: If the full syndrome of Catatonia is present in the context of schizophrenia, the diagnosis of Catatonia Associated with Another Mental Disorder should also be assigned. The symptoms are not a manifestation of another medical condition (e.g. a brain tumour) and are not due to the effects of a substance or medication (e.g. corticosteroids) on the central nervous system, including withdrawal effects (e.g. from alcohol). <i>Course specifiers for schizophrenia:</i> The following specifiers should be applied to identify the course of schizophrenia, including whether the individual currently meets the diagnostic requirements of schizophrenia or is in partial or full remission. Course specifiers are also used to indicate whether the current episode is the first episode of Schizophrenia, whether there have been multiple such episodes, or whether symptoms have been continuous over an extended period of time.

(Continued)

Table 1. (Continued)

DSM-5-TR (American Psychiatric Association, 2022)	ICD-11 (World Health Organization, 2022)
- First episode, currently in partial remission: Partial remission is a period of time during which an improvement after a previous episode is maintained and in which the defining criteria of the disorder are only partially fulfilled. - First episode, currently in full remission: Full remission is a period of time after a previous episode during which no disorder-specific symptoms are present. - Multiple episodes, currently in acute episode: Multiple episodes may be determined after a minimum of two episodes (i.e. after a first episode, a remission and a minimum of one relapse). - Multiple episodes, currently in partial remission - Multiple episodes, currently in full remission - Continuous: Symptoms fulfilling the diagnostic symptom criteria of the disorder are remaining for the majority of the illness course, with subthreshold symptom periods being very brief relative to the overall course. - Unspecified <i>Specify if:</i> - With catatonia (refer to the criteria for catatonia associated with another mental disorder for definition). <i>Specify current severity:</i> - Severity is rated by a quantitative assessment of the primary symptoms of psychosis, including delusions, hallucinations, disorganised speech, abnormal psychomotor behaviour and negative symptoms. Each of these symptoms may be rated for its current severity (most severe in the last 7 days) on a 5-point scale ranging from 0 (not present) to 4 (present and severe).	Schizophrenia, first episode: The first episode specifier should be applied when the current or most recent episode is the first manifestation of schizophrenia meeting all diagnostic requirements in terms of symptoms and duration. If there has been a previous episode of Schizophrenia or Schizoaffective Disorder, the 'multiple episodes' specifier should be applied. - Schizophrenia, first episode, currently symptomatic - Schizophrenia, first episode, in partial remission - Schizophrenia, first episode, in full remission - Schizophrenia, first episode, unspecified Schizophrenia, multiple episodes: The multiple episodes specifier should be applied when there has been a minimum of two episodes meeting all diagnostic requirements of Schizophrenia or Schizoaffective Disorder in terms of symptoms, with a period of partial or full remission between episodes lasting at least 3 months, and the current or most recent episode is schizophrenia. Note that the 1-month duration requirement for the first episode does not necessarily need to be met for subsequent episodes. During the period of remission, the diagnostic requirements of schizophrenia are either only partially fulfilled or absent. - Schizophrenia, multiple episodes, currently symptomatic - Schizophrenia, multiple episodes, in partial remission - Schizophrenia, multiple episodes, in full remission - Schizophrenia, multiple episodes, unspecified Schizophrenia, continuous: The continuous specifier should be applied when symptoms fulfilling all diagnostic requirements of schizophrenia have been present for almost all of the course of the disorder during the person's lifetime since its first onset, with periods of subthreshold symptoms being very brief relative to the overall course. In order to apply this specifier to a first episode, the duration of schizophrenia must be at least 1 year. - Schizophrenia, continuous, currently symptomatic - Schizophrenia, continuous, in partial remission - Schizophrenia, continuous, in full remission - Schizophrenia, continuous, unspecified Other specified episode of Schizophrenia Schizophrenia, episode unspecified

DSM-5-TR = *Diagnostic and Statistical Manual of Mental Disorders* (5th ed., text rev.); ICD-11 = *International Classification of Diseases*, 11th Revision.

considered. If another psychotropic agent is added for augmentation or combination, then both the effectiveness and tolerance should be monitored regularly. The additional agent should be withdrawn if no benefits are seen within 3 months to reduce the risks associated with polypharmacy. In accordance with existing national and international guidelines (Firth et al., 2019; Galletly et al., 2016; Halstead et al., 2025; Lambert et al., 2017; McCutcheon et al., 2025), people with schizophrenia should be screened and monitored for cardiometabolic abnormalities and modifiable lifestyle risk

factors (e.g. substance use, physical inactivity, poor diet) regularly. This should begin from the outset of diagnosis and antipsychotic medication prescription, especially given the increased prevalence of multimorbidity observed among young adults with schizophrenia (Halstead et al., 2024a, 2024b). In addition, non-pharmacological and lifestyle interventions should also be offered at treatment commencement and all stages of treatment for people with schizophrenia to both enhance the effectiveness of interventions provided and mitigate the physical side effects of pharmacotherapy.

Methods

Guidelines panel

The authorship group (the Panel) was developed through the identification of clinical experts across Australia and Aotearoa New Zealand, including a psychiatry trainee and experts with lived experience. The Panel first met in January 2024 and subsequently met on a monthly to bi-monthly frequency, chaired by the senior author (D.S.). Representation across psychiatric career stages, including trainee representation, was considered in selecting the Panel. Potential conflicts of interest were documented, and management of such was discussed by consensus (Table 2).

Consumer consultation group

The consumer consultation group comprised seven individuals with lived experience of schizophrenia. Four meetings were held between August 2024 and August 2025, each attended by three to four group members alongside two Panel members (S.S. and N.K.). These meetings sought targeted input on the formulation of topics for inclusion in the Guidelines and the development of key health questions. Draft findings and recommendations were presented to the group for feedback and refinement. Table 3 summarises selected feedback provided during these consultations.

GRADE methodology

In short, the GRADE approach provides a structured method to assess the level of certainty in the existing evidence base (very low, low, moderate or high) and the strength of the recommendation (weak or strong) (Guyatt et al., 2011a; Prasad, 2024) (Table 4). For section 4 (Family, whānau and carer involvement), the GRADE-CERQual (Lewin et al., 2015) and the World Health Organization Qualitative Evidence Synthesis Framework (Downe et al., 2019) approaches were used to synthesise the evidence from qualitative studies given the absence of randomised controlled trials (RCTs) specifically examining family, whānau and carer involvement. Judgements were based on the overall certainty of the evidence, the balance of benefit and harm and the inferred values and preferences of people with schizophrenia supported by the consumer consultation group (Andrews et al., 2013). The Panel decided on either a strong recommendation (i.e. most people with schizophrenia should be offered the recommended intervention), or a weak recommendation (i.e. different choices would be appropriate for different people, depending on their values and preferences) (Andrews et al., 2013). The GRADE evidence and recommendations were independently reviewed by two authors (C.G. and D.K.) who had not been involved in the original evidence review process.

The topics for the relevant clinical sections were developed through consensus discussions and reviews of existing guidelines, as well as seeking additional input from the consumer consultation group. Following the GRADE framework, key health questions were developed by section leads, reviewed by consensus and discussed with a consumer consultation group on two separate occasions to establish relevance and priorities. The key health questions are presented in Table 5.

To answer each of the key health questions, a database review was performed to identify the most recent and complete evidence. We searched databases, including PubMed, Google Scholar and Cochrane, from inception to March 2024, and the results were updated in June 2025. The evidence was selected based on the hierarchy of evidence levels (i.e. umbrella review > systematic review > RCTs). When multiple studies provided data for the same outcome, we selected the most comprehensive recent study. If identified evidence based on hierarchy was over 5 years old, more recent studies from the next level of evidence were also considered, unless a study older than 5 years was deemed to be more relevant than more recent studies. The Panel also decided to translate the confidence level directly from the findings from Cochrane reviews and Confidence in Network Meta-Analysis (CINeMA) ratings. Furthermore, the previous RANZCP clinical practice guidelines (Galletly et al., 2016) as well as other national/international guidelines and associated papers (Barnes et al., 2020; Buchanan et al., 2025; Castle et al., 2017; Correll et al., 2022; Falkai et al., 2025; Hasan et al., 2017, 2020; Keepers et al., 2020; McCutcheon et al., 2025; Remington et al., 2017) were consulted. The recommendations, along with their associated strengths and certainty of evidence, are summarised in Tables 6–10 with the overall summary of recommendation presented in Table 11. The GRADE summary of findings is presented in Supplemental Appendix Tables 1–19 with the definitions of estimate/magnitude of effect presented in Supplemental Appendix Table 20.

Section I: physical health assessment

People with schizophrenia have poor physical health and premature mortality of approximately 15 to 20 years compared to the general population (Hjorthøj et al., 2017). The majority of years lost are due to cardiometabolic disease, which is associated with modifiable lifestyle risk factors (e.g. physical inactivity, poor diet, smoking) (Goldfarb et al., 2022; Firth et al., 2019). A comprehensive clinical assessment can help identify treatable physical health comorbidities early.

Secondary physical health, or organic, causes of psychosis have been identified in around 5% of individuals on first presentation (Blackman et al., 2025; Crede et al., 2011; Johnstone et al., 1987). The initial physical health

Table 2. Potential conflicts of interest.

Author	Conflict – potential, perceived, actual
Shuichi Suetani	SS is an employee of Institute for Urban Indigenous Health SS is an associate editor of the ANZJP and Therapeutic Advances in Psychopharmacology SS is a section editor of the British Journal of Psychiatry SS was a deputy editor of Australasian Psychiatry between 2021 and 2024 SS has received an honorarium from SAGE Publishing (2025) SS was on the Seqirus medication advisory board for cariprazine (2020 to 2022) SS has received honorarium from Inside Practice Psychiatry (2021) and GroupH (2021)
Frances Dark	FD is an employee of Metro South Addiction and Mental Health Service in Brisbane, Queensland
Susanna Every-Palmer	SEP is an employee of Te Whatu Ora Health New Zealand and of The University of Otago SEP is a deputy editor of the ANZJP SEP serves on the Committee for Research of the RANZCP SEP is Vice President of the Pacific Rim College of Psychiatry SEP has not received any funding from the pharmaceutical industry
Cherrie Galletly	CG is on Advisory Boards for Boehringer Ingelheim, Lundbeck and Servier Laboratories
Brian O'Donoghue	BOD is an employee of University College Dublin with portions of his time attributed to St Vincent's University Hospital and Dublin South East mental health service. BOD previously received a fellowship from the NHMRC and currently holds funding from the Health Research Board in Ireland BOD has never received funding or financial support from the pharmaceutical industry BOD is an associate editor of the Irish Journal of Psychological Medicine and Early Intervention in Psychiatry
Sean Halstead	SH is an employee of Queensland Health SH has not received any funding from the pharmaceutical industry. SH has been supported by a Research Training Program scholarship from 2023 to 2025, as well as a RANZCP Foundation Partners Scholarship from 2025
Dolores Keating	DK is an employee of St John of God University Hospital DK has never received financial support from the pharmaceutical industry DK has been a collaborator on research grants received from the Health Research Board in Ireland
Nicole Korman	NK is an employee of Metro South Addiction and Mental Health Service in Brisbane, Queensland NK has received funding from Otsuka to deliver an educational conference on lifestyle interventions NK has previously received support from an RANZCP novice investigator grant NK received a University of Queensland grant to fund consumer involvement in the development of these Guidelines
Julia M Lappin	JL is an employee of UNSW Australia and New South Wales Health JL is an associate editor of ANZJP JL serves on the Committee for Research of the RANZCP JL has not received any funding from the pharmaceutical industry
Sharon Lawn	SL serves on the Committee for Research of the RANZCP SL served on the Steering Group for the Future Development of Clinical Practice Guidelines as the lived experience representative of the RANZCP
Andrew Thompson	AT is an employee of Parkville Youth Mental Health and Wellbeing Service AT is an employee of the Orygen, the University of Melbourne AT is a chief investigator on grants from the NHMRC and MRFF AT has received honorarium for independent educational talks for Servier, Lundbeck and Otsuka AT has received an unrestricted neuroscience research grant from Pfizer AT has been on an advisory board for Lundbeck AT has been an associate editor of the ANZJP
Nicola Warren	NW is an employee of Queensland Health NW is an employee of The University of Queensland NW is an associate editor of the ANZJP NW serves on the Committees for Research; Foundation; Awards and Recognition; Practice, Policy and Partnerships; Queensland Branch of the RANZCP NW has received honorarium for independent educational talks from Lundbeck
Dan Siskind	DS is an employee of Queensland Health DS is a deputy editor of the ANZJP DS serves on the Committee for Research of the RANZCP DS has served on the Viatrix Quality Assurance Committee and received honorarium for independent educational talks from Servier, Viatrix and Lundbeck DS has an NHMRC Investigator Grant GNT1194635 and is a chief investigator on grants from the NHMRC and MRFF

No action was deemed to be required to manage the above potential conflicts of interest. ANZJP = Australian and New Zealand Journal of Psychiatry; MRFF = Medical Research Future Fund; NHMRC = National Health and Medical Research Council; RANZCP = Royal Australian and New Zealand College of Psychiatrists; UNSW = University of New South Wales.

Table 3. Selected feedback from consumer consultation group meetings.*Clinical guidelines in general:*

'Yeah, absolutely [psychiatrists need guidelines]. I just think that it will maintain the relationship between patients and the psychiatrist, like a guideline would definitely help with the treatment of the goals of the patient'.

'They (psychiatrists)'ll have a path to follow. And it can be safer. More predictable too'.

'I think a good thing about guidelines is that they don't have to be strictly followed, but they can be flexible as well in order to adapt to the situation the patient is in'.

Medication:

'I think my story, I was sort of given it [antipsychotic medication] without metformin, because I've been putting on quite a bit of weight and stuff like that and that wasn't really being treated'.

'I had a very similar experience. I also gained a significant amount of weight in the first six months of taking olanzapine. And the other side effect was fatigue, lack of energy throughout the day'.

'I prefer the injection than the tablets. Because with the tablets, you have to remember every day or whatever. With the injection, you get it done once and then for two to three months you don't have to take tablets just come back again to the injection'.

Talking therapy:

'[Psychoeducation] gives them power to know what they can go through and, you know, like me, suffer. So, they know how to deal with the illnesses that they go through'.

'You can learn about your problem more. You can learn like with the thinking and skills you can relate to the topics that you talk about'.

'It's good to have the theory side to the practical'.

Family involvement:

'I think it's good to get [family] involved and educated because it just helps the person being treated have extra support from them. And I think that support's going to help the long-term outcome'.

'You feel stronger with your family. You know, like you've got someone, you're not lonely and stuff like that. And they've got their opinion as well on different situations. You can get some advice from your own family as well. Someone to bounce ideas off about what to do'.

'[Having family involved in care] might fill in the blanks for them. And might erase some myths that they might have about the illnesses too'.

Lifestyle interventions:

'I think that is good to look at you're looking at the patient holistically. And that holistic intervention is good. Because it should, it's not just the symptoms but the cause, potential causes of sort of weight gain, stuff like that'.

'My mum also had schizophrenia, and I think I would have liked her to have also given up smoking, and I think anything that can sort of help with that for that kind of stuff would have been good'.

'As you say, helping the general population with sort of smoking and nicotine addiction is good'.

'[Having peer workers involved] is a good idea. So when you're going through it, when you get in contact with the peer, friend or whatever, you won't be in the dark. So you can see what's your future or whatever it might be. And whatever the peer person gonna bring to the table will be important for the client, for the patient'.

assessment should also consider the higher prevalence of comorbid physical health conditions that present earlier in life for people with schizophrenia (Halstead et al., 2024a). A tailored physical health history and examination is key. Although clinically significant laboratory results are uncommon, it is reasonable to consider initial broad screening investigations of electrolytes, renal, liver and haematological functioning (Conigliaro et al., 2018; Eskelinen et al., 2020). Baseline and continued monitoring of metabolic parameters are also necessary (Castle and Li, 2023; Lambert et al., 2017), but the requirement for fasting samples may not be essential in the prediction of cardiovascular disease for most individuals (Nordestgaard et al.,

2016; Selvin et al., 2010). Thyroid function tests are frequently indiscriminately ordered. Although psychotic symptoms have been shown in up to 15% of individuals with hypothyroidism, retrospective studies of both inpatient psychiatric admissions and community based populations demonstrate very low rates of clinically relevant abnormal thyroid results, many of which were already identified on physical assessment (Arce-Cordon et al., 2007; Garnier et al., 2016). Thus, thyroid function should only be requested when history and examination indicate clinical concern. Hyperprolactinaemia most commonly occurs as a consequence of antipsychotic use or pituitary prolactinoma (Cookson et al., 2012). Given the frequency

Table 4. Certainty of evidence and strength or recommendation definitions.

Certainty of evidence	
High	The Panel believes the available evidence provides a high level of confidence in the estimate of the effect, and the true effect lies close to that of the estimate.
Moderate	The Panel believes the available evidence is sufficient to support a conclusion, but future research may impact the confidence. The true effect is likely to be close to the estimate, but there is a possibility that it is substantially different.
Low	The Panel believes that the available evidence is limited, and the true effect may be substantially different from the estimate of the effect.
Very low	The Panel believes that the available evidence is insufficient to support any firm conclusion, and the true effect is unknown.
Strength of recommendation	
Strong	The Panel believes that the desirable effects of an intervention clearly outweigh the undesirable effects, or when the undesirable effects clearly outweigh the desirable effects. These recommendations apply to most individuals or populations and should be followed as a standard of care.
Weak	The Panel believes that the desirable and undesirable effects are closely balanced, or the available evidence is of low certainty. Different options may be appropriate for different individuals and/or situations.

Table 5. Key health questions.

Section 1: Physical health assessment
What are the important organic differential diagnoses to assess for people in first-episode psychosis?
What investigations should be conducted for people with first-episode psychosis?
What are the common physical health comorbidities in people with schizophrenia?
What investigations for physical health disorders should be conducted throughout the course of schizophrenia?
Section 2: Pharmacological treatment
How should considerations for side effects and tolerability feature in the recommendation of appropriate first-line antipsychotics?
What factors should be considered in choosing medication to treat people with schizophrenia?
What potential side effects should be monitored and managed for people with schizophrenia throughout the course of illness?
Section 3: Psychosocial and psychosocial interventions
What psychological and psychosocial interventions are indicated for people with schizophrenia?
What psychological and psychosocial interventions are effective for specific symptoms associated with schizophrenia (positive psychotic symptoms, negative psychotic symptoms, concurrent depressive symptoms, cognitive difficulties/ deficits and poor functioning)?
What psychological and psychosocial interventions are effective when individuals have declined antipsychotic medications?
What novel psychological and psychosocial interventions are now available that may either have an evidence base or require further evidence?
Section 4: Family, whānau and carer
What interventions are indicated for people with schizophrenia and their family, family, whānau and carer?
What factors should be considered in involving family, whānau and carer in providing care for people with schizophrenia?
Section 5: Psychiatric comorbidities
What are important psychiatric comorbidities for people with schizophrenia and what interventions are indicated for those conditions?
What interventions are indicated for people with schizophrenia and comorbid substance misuse?
What interventions are indicated for people with schizophrenia and substance-related psychosis?

(Continued)

Table 5. (Continued)

What interventions are indicated for people with schizophrenia and anxiety?
What interventions are indicated for people with schizophrenia and obsessive-compulsive disorder?
What interventions are indicated for people with schizophrenia and depression?
What interventions are indicated for people with schizophrenia and trauma?
Section 6: Physical health and lifestyle interventions
What lifestyle interventions are indicated for people with schizophrenia?
What lifestyle interventions are effective for specific symptoms associated with schizophrenia (positive symptoms, negative symptoms, concurrent depressive symptoms, cognitive difficulties/deficits and poor functioning)?
What lifestyle interventions are effective for potential factors/medication side effects associated with schizophrenia (smoking, sleep, dental issues, weight gain)?
Section 7: Special populations
What are the prevalence and mental health outcomes for Māori and Aboriginal and Torres Strait Islander peoples with schizophrenia, and how do they differ from non-Indigenous people?
What is the evidence around service delivery models that facilitate engagement and improve outcomes for Māori and Aboriginal and Torres Strait Islander peoples with schizophrenia in a culturally safe way?
What are the important issues related to caring for people with schizophrenia in rural areas?
Footnotes:
GRADE ratings were completed for the outcomes relevant to each key health question by two independent authors, with a consensus discussion held with the Panel for any discordant findings. Section leads nominated key findings based on a GRADE assessment and confirmed them through a consensus review with the Panel.

GRADE = Grading of Recommendations, Assessment, Development and Evaluation.

and consequences of hyperprolactinaemia, expert consensus and more recent guidelines recommend prolactin testing at baseline, 3 months after initiation or changes to dose or medication, and when indicated by abnormal menstrual, sexual, or neurological assessment (Peveler et al., 2008; Grigg et al., 2017).

In the case of suspected intracranial pathology, with a history of headaches, nausea or vomiting, seizure-like activity, childhood (<12 years) or older age (>40 years) onset of symptoms, rapid onset or fluctuation of psychosis, significant neurocognitive deficits, catatonia and/or neurological examination findings, neuroimaging with magnetic resonance imaging (MRI) should be conducted. Clinical assessment should guide targeted serum anti-neuronal antibody testing and consideration of lumbar puncture for cerebrospinal fluid (CSF) analysis (Scott et al., 2018). For individuals with first-episode psychosis and no atypical features, neuroimaging and further investigations, such as an electroencephalogram (EEG), are less clearly indicated. They should be guided by collaborative discussions with the person and their family, whānau and carers, with further consideration given during future physical health assessments. While there may be a future role for advanced neuroimaging and other biomarkers to guide personalised treatment (Schmidt and Borgwardt, 2020; Warren et al., 2024), currently the frequency of neuroimaging abnormalities that have established causality with psychosis has been

estimated at 0.4% (Forbes et al., 2019). The recommendations for the first-episode psychosis workup are summarised in Table 12.

Section 2: pharmacological treatment

First-episode psychosis

Most previous international clinical guidelines have not been prescriptive as to which antipsychotics are preferred first-line agents for first-episode psychosis (Correll et al., 2022). Given that all antipsychotic medications demonstrate gradual rather than discrete differences in efficacy (Huhn et al., 2019; Oh et al., 2015; Zhu et al., 2017), the decisions on the first agent to trial should be individualised based on tolerability and side effect profile as well as individual preference (McCutcheon et al., 2025; Scott et al., 2022). In terms of long-acting injectable (LAI) formulations, an umbrella review (Etienne and Verdoux, 2025) suggested that LAIs may be useful in selected individuals with early psychosis; however, a meta-analysis found no clear benefit over oral formulations overall (Vita et al., 2024b). It has been noted that the benefits may be more likely to occur when the potential benefits and risks are discussed in a collaborative manner involving the individuals and families (Kane et al., 2021). For these reasons, we recommend initiating with one of the following antipsychotic medications

Table 6. Recommendation summary for pharmacological and physical interventions.

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We recommend that people with schizophrenia should be given oral second-generation antipsychotic medications with a favourable cardiometabolic side effect (including hyperprolactinemia) profile as the first-line treatment (i.e. aripiprazole, brexpiprazole, cariprazine, lurasidone).	I and 2	Huhn et al. (2019), Zhu et al. (2017) and Pillinger et al. (2020)	Strong
Judgement: Most antipsychotic medications have low to moderate certainty evidence for largely moderate size for overall changes, positive symptoms, and negative symptoms, and small effect size for depressive symptoms (Huhn et al., 2019). They also have moderate to high certainty evidence for tolerability (all-cause discontinuation rates) (Huhn et al., 2019). The Panel believes that given the relatively comparable efficacy of all available antipsychotic medications (except for the superiority of clozapine) (Huhn et al., 2019), the side effect burden, especially the cardiometabolic side effects, should be the primary consideration for choosing the first-line antipsychotic option (Huhn et al., 2019; McCutcheon et al., 2025; Scott et al., 2022). Given the risks of untreated schizophrenia and the high certainty of evidence supporting antipsychotic medication use in the maintenance stage, reducing both relapse and hospitalisation (Ceraso et al., 2020), the Panel believes that the better-tolerated antipsychotic medication should be offered from the onset of illness. Four agents are recommended based on the balance of benefit and harm, acknowledging that individuals experience side effects differently.			
We suggest that people with schizophrenia in the early stages of the illness may be offered long-acting injectable antipsychotic medications.	3	Vita et al. (2024b)	Weak
Judgement: The Panel reviewed the best available evidence for comparison of relapse rate and tolerability in early-stage schizophrenia and found very low certainty evidence for both outcomes for long-acting injections vs oral antipsychotic medications. Both relapse and all-cause discontinuation rates for people in the early stage of illness (within 5 years) did not show clinically significant differences between oral or long-acting injectable formulations (Vita et al., 2024b). The Panel believes that while there might be a subgroup of people with schizophrenia (e.g. those who find it challenging to adhere to daily medication intake) who may benefit from the long-acting injectable form of antipsychotic medication (Efthimiou et al., 2024), for many people the current evidence base does not suggest superiority of the injectable form in the earlier stages of illness (Vita et al., 2024b). Therefore, a weak recommendation is made as an early-stage option.			
We recommend that people with schizophrenia in the maintenance stages of the illness should be offered long-acting injectable antipsychotic medications as a treatment option.	3 and 5	Kishimoto et al. (2021) and Ceraso et al. (2020)	Strong
Judgement: There is a very small benefit of the long-acting injectable form over oral medication in terms of relapse/hospitalisation rate without having any difference in tolerability between the two groups (Kishimoto et al., 2021). The Panel believes that given the magnitude of potential adverse consequences of a relapse, potential benefits of long-acting injectable formulation seen in cohort studies (Aymerich et al., 2025; Efthimiou et al., 2024), combined with the fact that there seems to be no significant differences in tolerability between the two forms of medications (Kishimoto et al., 2021), people with schizophrenia should be offered the long-acting injectable antipsychotic medication in the maintenance phase. It is also worth highlighting that compared to placebo, antipsychotic medications as a group (either oral or long-acting injectable) were associated with reduced risk of relapse, hospitalisation, as well as improved quality of life and functioning in the maintenance phase (Ceraso et al., 2020). Therefore, a strong recommendation is made as a maintenance stage pharmacological option.			
We recommend that people with treatment-resistant schizophrenia should be offered clozapine.	I and 4	Dong et al. (2024) and Huhn et al. (2019)	Strong
Judgement: Overall, indirect evidence (with very low to low certainty) from a network meta-analysis showed that clozapine was more efficacious than all first-generation antipsychotic medications examined for the overall symptoms of schizophrenia (Dong et al., 2024). They were also more efficacious than quetiapine but not significantly superior compared to other second-generation antipsychotic medications, including olanzapine, risperidone and ziprasidone (Dong et al., 2024). Clozapine also showed the most efficacy (with a large effect size but low certainty) for overall improvement in symptoms in acute phases (Huhn et al., 2019). The Panel believes that as clozapine was significantly less likely to be discontinued due to inefficacy than olanzapine (Dong et al., 2024), the sensitivity analysis including only double-blind studies using high clozapine doses in very resistant patients showed clozapine's superior efficacy (Dong et al., 2024), and given accumulated evidence on effectiveness from observational studies (Siskind et al., 2025b), clozapine should be chosen as the treatment of choice for those with treatment-resistant schizophrenia. Therefore, a strong recommendation is made for those with treatment-resistant schizophrenia.			

(Continued)

Table 6. (Continued)

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We suggest that people with treatment-resistant schizophrenia may be offered electroconvulsive therapy.	4	Sinclair et al. (2019)	Weak
Judgement: A Cochrane review found moderate certainty evidence to support improved response to treatment for those with treatment-resistant schizophrenia receiving electroconvulsive therapy compared to those who received standard care only after 8–12 weeks (Sinclair et al., 2019). The risk ratio was modest at 2.06. Although the review found no clear superiority over clozapine treatment (low certainty) (Sinclair et al., 2019), a more recent small randomised control trial (Mishra et al., 2022) showed that the maintenance electroconvulsive therapy was superior to clozapine treatment over 6 months. While there are significant short-term and long-term adverse effects associated with electroconvulsive therapy, given the difficulty associated with obtaining clinical benefits among people with treatment-resistant schizophrenia, the Panel believes that electroconvulsive therapy should be offered as a treatment option in those with treatment-resistant schizophrenia. Therefore, a weak recommendation is made.			
We recommend that people with schizophrenia should be offered lifestyle and non-pharmacological interventions at all stages of treatment to mitigate the cardiometabolic side effects of antipsychotic treatment.	19	Fernández-Abascal et al. (2021)	Strong
Judgement: There is moderate certainty evidence for multimodal lifestyle interventions being efficacious for weight loss for people with schizophrenia, with a moderate effect size (Fernández-Abascal et al., 2021). While lifestyle interventions alone may not be sufficient to resolve all cardiometabolic side effects, the Panel believes that a strong recommendation is warranted given the broad spectrum of health benefits associated with lifestyle interventions and the low risk of adverse events related to non-pharmacological modalities (Firth et al., 2019).			
We suggest that medications used to treat people with schizophrenia may be rationalised when cardiometabolic side effects occur through switching to a more metabolically neutral antipsychotic agent.	6	Siskind et al. (2021), Speyer et al. (2021), Taylor et al. (2017) and Kanagasundaram et al. (2021)	Weak
Judgement: There is very low to low certainty evidence that switching to a more metabolically neutral antipsychotic (primarily aripiprazole) is effective at reducing antipsychotic-induced weight gain (Siskind et al., 2021; Speyer et al., 2021), as well as lowering total cholesterol (Kanagasundaram et al., 2021), but not for hyperglycaemia (Taylor et al., 2017). Any antipsychotic medication switching is associated with the potential risk of destabilisation with worsening of symptoms. Therefore, the Panel believes that the decision to switch should consider the potential benefits versus risks for each individual, and a weak recommendation is made.			
We recommend that people with schizophrenia should be offered adjunctive metformin for the management of antipsychotic-induced weight gain. Early utilisation of metformin should be prioritised for people receiving any antipsychotic medication, and co-commencement of metformin on initiation of olanzapine or clozapine is recommended for weight gain prevention.	6	Yu et al. (2024), Jiang et al. (2020) and Carolan et al. (2025)	Strong
Judgement: Metformin is the most widely studied pharmacological adjunct for antipsychotic-induced cardiometabolic disturbances. The most recent meta-analytic evidence for mitigating weight gain and increased fasting blood glucose (Yu et al., 2024) is moderate certainty for the outcome of preventing weight gain; there is also moderate certainty evidence for improved total cholesterol with metformin (Jiang et al., 2020). Older meta-analyses also exist with low certainty evidence for treating weight gain (Agarwal et al., 2022; Wang et al., 2021), very low evidence for hyperglycaemia (Taylor et al., 2017; Zheng et al., 2015). The Panel believes that, as a generally well-tolerated and accessible agent, early utilisation of metformin is recommended for its benefits to cardiometabolic parameters, particularly antipsychotic-induced weight gain. Its potential benefits should nevertheless be considered against possible adverse effects, including gastrointestinal side effects, vitamin B12 deficiency and lactic acidosis; metformin is contraindicated in individuals with renal impairment. Co-commencement of metformin is recommended when starting either clozapine or olanzapine as high-risk agents, as per recent international guidelines published (Carolan et al., 2025; McCutcheon et al., 2025).			

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Table 6. (Continued)

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We suggest that people with schizophrenia may be offered the use of a glucagon-like peptide-1 receptor agonist to manage antipsychotic-induced weight gain.	6	Bak et al. (2024) and Khaity et al. (2023)	Weak
Judgement: Glucagon-like peptide-1 receptor agonists (GLP-IRAs) have very low certainty evidence (Bak et al., 2024; Khaity et al., 2023) for the mitigation of antipsychotic-induced weight gain, as well as very low certainty evidence for the reduction of total cholesterol (Khaity et al., 2023). While the included studies in the meta-analyses used first-generation GLP-IRAs (e.g. liraglutide and exenatide), a more recent randomised controlled trial of second-generation GLP-IRAs (e.g. semaglutide) show a larger effective size (Siskind et al., 2025a). GLP-IRAs are generally well tolerated, with gastrointestinal side effects being the most common. As such, the Panel believes that where available, GLP-IRAs should be considered for treatment in addition to metformin for antipsychotic-induced weight gain, particularly when a cardiometabolic-adverse agent such as olanzapine or clozapine has been prescribed.			
We suggest that people with schizophrenia may be offered adjunctive low-dose propranolol or low-dose mirtazapine for the treatment of akathisia experienced during treatment with antipsychotics, particularly after attempts to rationalise the offending antipsychotic medication have been made.	7	Furukawa et al. (2024a) and Gerolymos et al. (2024)	Weak
Judgement: Only very low certainty evidence is available to support the efficacy of propranolol (Gerolymos et al., 2024) and mirtazapine (Furukawa et al., 2024b) in network meta-analysis for the reduction of akathisia symptom severity. While no meta-analytic evidence is available, clinical practice guidelines routinely recommend that the offending antipsychotic is rationalised and switched to an alternative agent with lower propensity for akathisia given the distressing nature of akathisia. The Panel believes that to assist with the reduction of akathisia symptoms, both propranolol and mirtazapine should be considered as adjuncts after the medication rationalisation, with consideration of the adverse effects of both agents and potential contraindications.			
We suggest that people with schizophrenia may be offered vesicular monoamine transporter 2 inhibitors, valbenazine or deutetrabenazine, if available, followed by Vitamin E supplementation for the treatment of tardive dyskinesia symptoms after attempts to rationalise the offending antipsychotic agent.	7	Solmi et al. (2018, 2025)	Weak
Judgement: Moderate certainty evidence is available to support the small efficacy of vesicular monoamine transporter 2 inhibitors (VMAT-2I) valbenazine or deutetrabenazine for the reduction of tardive dyskinesia (Solmi et al., 2018). However, at the time of publication of this guideline, these agents were not available in New Zealand nor Australia. Very low certainty evidence is available, in contrast, that suggests a potential benefit of Vitamin E supplementation in preventing further deterioration of tardive dyskinesia symptom burden (Bergman et al., 2017; Solmi et al., 2025). Similar to akathisia, clinical practice guidelines recommend that the antipsychotic be switched to an alternative agent with a lower risk for tardive dyskinesia. While VMAT-2I has emerging moderate evidence, its current availability and licensing for the treatment of tardive dyskinesia are limited, and adverse effects should be considered. Vitamin E is demonstrably less efficacious but likely more accessible with minimal adverse effects of note. Given these factors, the Panel makes a weak recommendation for VMAT-2I and Vitamin E after medication rationalisation.			
We suggest that people with schizophrenia may be offered adjunctive aripiprazole if antipsychotic-induced hyperprolactinaemia persists and is clinically significant after attempts at antipsychotic rationalisation have been made.	8	Lu et al. (2022)	Weak
Judgement: Only very low (Zhang et al., 2021) to low (Lu et al., 2022) certainty evidence is available that supports the role of adjunctive aripiprazole in the management of antipsychotic-induced hyperprolactinaemia. However, given the frequent occurrence of antipsychotic-induced hyperprolactinaemia, adjunctive treatment with aripiprazole should be considered with respect to potential risks and benefits, depending on whether rationalisation strategies have already been trialled. The Panel believes that the clinical threshold to treat antipsychotic-induced hyperprolactinaemia should take into account whether it is symptomatic, and potential long-term complications from untreated hyperprolactinaemia (e.g. reduced bone density) (Grigg et al., 2017; Solmi et al., 2023).			

(Continued)

Table 6. (Continued)

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
Footnotes:			
• Certainty of evidence (high, moderate, low or very low) was assessed using the GRADE approach with consideration of risk of bias, precision, directness, consistency, publication bias, dose-response relationships and large effect sizes. The best available evidence was used to rate the certainty of the evidence, with additional resources, such as other clinical practice guidelines and large cohort studies, considered in the evidence-to-decision process. Where GRADE assessments had been conducted by a Cochrane group, these were accepted. CINeMA assessments from network meta-analysis informed certainty of evidence judgements. • Definitions of the estimate/magnitude of effect are described in Supplemental Appendix Table 20. The Panel considered a small effect size to be a minimal clinically meaningful benefit for most outcomes. • The evidence-to-decision framework considered the certainty of the evidence, the balance of benefits and harms, and the values and preferences of people with schizophrenia. Other considerations for some recommendations included feasibility, resource requirements and acceptability. • Values and preferences of people with schizophrenia and their supporters were incorporated through the panel judgement of the balance of benefit, harm and burdens of therapy. The Panel included an expert by experience, and input was also sought from a consumer consultation group.			

for people with first-episode psychosis: D2 partial agonists (e.g. aripiprazole [oral rather than LAI formulation], brexpiprazole, or cariprazine), or lurasidone due to their broadly more tolerable adverse effect profiles, including lower metabolic risks (McCutcheon et al., 2025; Pillinger et al., 2023). Given the increased sensitivity of those with first-episode psychosis to antipsychotics compared to those with established courses of illness, lower doses may be more effective at eliciting clinical response (Zhu et al., 2017). Thus, we recommend starting low and going slow (e.g. titrating the dose up at 1–2 week intervals if inadequate response and agent well tolerated) for those with first-episode psychosis. Assertive mental state monitoring should be provided on the initiation of medication (e.g. weekly), with attention to adherence to medication in a non-judgment manner (non-adherence often refined as taking less than 80% of prescribed dose or absent plasma level; McCutcheon et al., 2025), and the dose should be reviewed based on effectiveness and side effects (McCutcheon et al., 2025; Scott et al., 2022).

Optimisation of antipsychotic treatment

Adherence to antipsychotic medication as a group (oral or LAI) is associated with reduced risk of relapse and hospitalisation, as well as improved quality of life and functioning in the maintenance phase (Ceraso et al., 2020). It is important to discuss and, if necessary, address treatment adherence with the person with schizophrenia in an open and non-judgmental manner, particularly if there is a partial or no response to the initial medication. Where appropriate, consideration may be given to obtaining collateral reports from family, whānau and carers, as well as measuring serum concentration if feasible (McCutcheon et al., 2025).

If there is no response within 2 weeks despite dose within target range and confirmed treatment adherence, it is unlikely that the person will respond to a more extended trial of the same medication (Samara et al., 2015c). At this stage, there is limited evidence on the optimal treatment strategy for those who do not respond to initial antipsychotic medication (Samara et al., 2018b). Thus, there remains no clear evidence to suggest whether it is better to switch antipsychotics or to continue the same antipsychotic in people with schizophrenia who did not respond to their initial treatment (Samara et al., 2025b). Therefore, we recommend changing the initial antipsychotic medication to another agent if (1) there is no response at all to the initial agent after 2 weeks at dose within target range with confirmed adequate adherence, or (2) there is a suboptimal response to the maximum recommended dose of the initial agent after 2–4 weeks with confirmed adequate adherence, or (3) the individual is not able to tolerate the adverse effects of the initial agent at any dose.

In choosing the second antipsychotic medication, there are several considerations. First, although a network meta-analysis of RCTs found no significant difference in efficacy in terms of relapse prevention between different non-clozapine antipsychotic medications either in oral or LAI formulation in the maintenance phase of schizophrenia (Schneider-Thoma et al., 2022), when observational studies have been included in analyses, individuals who are treated with LAIs displayed a lower risk of relapse and hospitalisation compared to those on oral antipsychotic medication (Kishimoto et al., 2021). Similar to the acute phase of treatment (Huhn et al., 2019), different antipsychotic medications exhibited varying tolerability profiles during the maintenance phase (Schneider-Thoma et al., 2022). Among different LAI antipsychotic medications, a network

Table 7. Recommendation summary for psychological and psychosocial interventions.

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We suggest that people with schizophrenia may be offered relapse prevention interventions.	9	Bighelli et al. (2021)	Weak
Judgement: There is low certainty evidence to suggest that relapse prevention interventions were associated with a moderate effect size in reducing relapse at 12 months and a large effect size in reducing the risk of relapse at 12 months and longer (low certainty evidence) (Bighelli et al., 2021). Given the potentially devastating impact that a relapse can have and that there is minimal risk associated with the intervention, the Panel makes a weak recommendation for the intervention.			
We recommend that people with schizophrenia should be offered psychoeducation.	9	Bighelli et al. (2021)	Strong
Judgement: Psychoeducation has a small effect on reducing relapse with moderate certainty evidence (Bighelli et al., 2021). Psychoeducation does not require a high skill level to be delivered. Although it only has a small effect on reducing relapse, given the serious consequences of relapse and considering the intervention is low risk, the Panel believes that most individuals with schizophrenia would wish to be offered this intervention.			
We recommend that people with schizophrenia should be offered cognitive behavioural therapy for psychosis.	9, 10	Bighelli et al. (2021) and Jauhar et al. (2014)	Strong
Judgement: Cognitive behavioural therapy for psychosis has moderate certainty evidence indicating a small effect on reducing relapse (Bighelli et al., 2021) and improving positive symptoms and overall psychiatric symptoms. It is also associated with a very small effect size for negative symptoms (Jauhar et al., 2014). The Panel believes that although cognitive behavioural therapy requires an adequately trained clinician to deliver the intervention, it is a low-risk intervention that has a benefit, albeit small, across a number of domains. Therefore, it should be offered to most people with schizophrenia.			
We recommend that people with schizophrenia should be offered cognitive remediation therapy, particularly those who have cognitive deficits/difficulties or poor functioning.	10	Vita et al. (2021, 2024a)	Strong
Judgement: Cognitive remediation therapy has a very small effect on improving positive symptoms, negative symptoms and overall psychiatric symptoms (Vita et al., 2021) as well as a small effect on cognition and functioning in people with schizophrenia (Vita et al., 2021, 2024a). The most important outcome for people with schizophrenia engaging in cognitive remediation therapy is improvements in cognitive symptoms. The Panel considered high certainty evidence for a small effect size for this outcome. There is also moderate certainty evidence for improvement in overall psychiatric symptoms. The Panel believes that these domains can be very challenging to improve, and even a slight improvement could make a meaningful difference in the quality of life for the individual. Thus, although cognitive remediation therapy requires a high level of skills and training to deliver, it should be offered to most people with schizophrenia, particularly those who have cognitive deficits/difficulties or poor functioning.			
We recommend that people with schizophrenia should be offered meta-cognitive therapy, particularly those who have persisting positive and negative symptoms of psychosis.	10	Melville et al. (2024)	Strong
Judgement: Meta-cognitive therapy has a small effect on positive (high certainty) and negative symptoms (high certainty), as well as functioning (moderate certainty) (Melville et al., 2024). The Panel believes that although the clinician requires a high level of skill and training to deliver this intervention, meta-cognitive therapy should be offered to individuals who have residual symptoms or only partially treated symptoms.			
Footnotes: • Certainty of evidence (high, moderate, low or very low) was assessed using the GRADE approach with consideration of risk of bias, precision, directness, consistency, publication bias, dose-response relationships and large effect sizes. The best available evidence was used to rate the certainty of the evidence, with additional resources, such as other clinical practice guidelines and large cohort studies, considered in the evidence-to-decision process. Where GRADE assessments had been conducted by a Cochrane group, these were accepted. CINeMA assessments from network meta-analysis informed certainty of evidence judgements. • Definitions of the estimate/magnitude of effect are described in Supplemental Appendix Table 20. The Panel considered a small effect size to be a minimal clinically meaningful benefit for most outcomes. • The evidence-to-decision framework considered the certainty of the evidence, the balance of benefits and harms, and the values and preferences of people with schizophrenia. Other considerations for some recommendations included feasibility, resource requirements and acceptability. • Values and preferences of people with schizophrenia and their supporters were incorporated through the panel judgement of the balance of benefit, harm and burdens of therapy. The Panel included an expert by experience, and input was also sought from a consumer consultation group.			

Table 8. Recommendation summary for family, whānau and carers.

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We suggest that family/whānau/carers may be offered family-based interventions.	11	Chien et al. (2024)	Weak
Judgement: Family-based interventions have low to moderate certainty of evidence for reducing relapse and caregiver burden (Chien et al., 2024). While the size of evidence base remains relatively small, the Panel believes that when the individual with schizophrenia agrees, their family/whānau/carers may be offered family-based interventions.			
We recommend that the decision to include family/whānau/carers should be negotiated collaboratively and with transparency between providers, people with schizophrenia and family/whānau/carers, and always with the consent of the person with schizophrenia, where possible.	12	Cameron et al. (2023), Iswanti et al. (2023), Landeweer et al. (2017), Tham and Solomon (2024) and Vasava et al. (2023)	Strong
Judgement: The benefits of family/whānau/carers involvement in providing emotional support, practical support for everyday psychosocial needs, and decision-making, information retention and engagement support are based on moderate confidence in evidence (Cameron et al., 2023; Iswanti et al., 2023). Consent is an important consideration, given that there is also moderate evidence for negative impacts of family/whānau/carers involvement (e.g. privacy and concern for autonomy) for some individuals with schizophrenia (Cameron et al., 2023; Landeweer et al., 2017; Vasava et al., 2023). The Panel believes that respect for autonomy and privacy of the person with schizophrenia is paramount in building trust, engagement and recovery.			
We recommend that family/whānau/carers be offered general information about the nature, potential causes, psychosocial needs, and support and management of mental health difficulties related to a schizophrenia diagnosis.	12	Cameron et al. (2023), Iswanti et al. (2023), Landeweer et al. (2017), Tham and Solomon (2024) and Vasava et al. (2023)	Strong
Judgement: The evidence, with moderate confidence, suggests that many families seek information on how to support their family member (Cameron et al., 2023). The evidence also explores the complexities of families and their relationships with one another, the individual with schizophrenia, and their broader network (Landeweer et al., 2017; Vasava et al., 2023; Tham and Solomon, 2024). The Panel believes there is benefit in family/whānau/carers being offered general information about schizophrenia, such as myths and assumptions (to address stigma), potential adverse impacts, general strategies for how to support individuals with this diagnosis, and clarity in communication of information with family/whānau/carers, to build consistency and partnership across treatment, care and support.			
We suggest that psychoeducation be delivered individually to family/whānau/carers to assist them to better understand and support a person with personal recovery and management of their schizophrenia, and for family peer support. Psychoeducation should also be offered in group contexts with other family/whānau/carers.	12	Cameron et al. (2023), Iswanti et al. (2023), Landeweer et al. (2017), Tham and Solomon (2024) and Vasava et al. (2023)	Weak
Judgement: There is moderate confidence in evidence for the value of psychoeducation for family/whānau/carers (Cameron et al., 2023; Iswanti et al., 2023). However, given there is much heterogeneity to the experiences of family/whānau/carers, and what they find helpful and supportive (Cameron et al., 2023; Landeweer et al., 2017; Vasava et al., 2023; Tham and Solomon, 2024), likely to due to the nature of the role, the potentially enduring nature of schizophrenia, and the lack of sufficiently powered research, the Panel makes a weak recommendation for psychoeducation to family/whānau/carers.			
Footnotes: • Certainty of evidence (high, moderate, low or very low) was assessed using the GRADE approach with consideration of risk of bias, precision, directness, consistency, publication bias, dose-response relationships and large effect sizes. The best available evidence was used to rate the certainty of the evidence, with additional resources, such as other clinical practice guidelines and large cohort studies, considered in the evidence-to-decision process. Where GRADE assessments had been conducted by a Cochrane group, these were accepted. CINeMA assessments from network meta-analysis informed certainty of evidence judgements. • For Supplemental Appendix Table 12, confidence in evidence (high, moderate, low or very low) was assessed using the GRADE-CERQual. Methodological limitations, coherence, adequacy of data and relevance of study findings were considered. Confidence is the extent to which a finding from a review of qualitative evidence is considered a reasonable representation of the phenomenon of interest. • Definitions of the estimate/magnitude of effect are described in Supplemental Appendix Table 20. The Panel considered a small effect size to be a minimal clinically meaningful benefit for most outcomes. • The evidence-to-decision framework considered the certainty of the evidence, the balance of benefits and harms, and the values and preferences of people with schizophrenia. Other considerations for some recommendations included feasibility, resource requirements and acceptability. • Values and preferences of people with schizophrenia and their supporters were incorporated through the panel judgement of the balance of benefit, harm and burdens of therapy. The Panel included an expert by experience, and input was also sought from a consumer consultation group.			

Table 9. Recommendation summary for treatment of comorbid psychiatric conditions.

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We recommend that people with schizophrenia and comorbid depression should be offered an antidepressant medication.	15	Gregory et al. (2017) and Helfer et al. (2016)	Strong
Judgement: Systematic reviews (Gregory et al., 2017; Helfer et al., 2016) have shown a small but significant benefit to antidepressant medication use for people with schizophrenia for depression (moderate certainty evidence). The Panel believes there is benefit in being offered antidepressant treatment, acknowledging that this treatment will not lead to improvement in depressive symptoms for everyone, number needed to treat = 5 in one review (Gregory et al., 2017). There does not appear to be any one antidepressant that is more efficacious than others.			
We suggest that people with schizophrenia with comorbid substance use may be offered psychosocial interventions for substance use.	13	(Siddiqui et al., 2024)	Weak
Judgement: There is limited evidence to guide psychosocial interventions with low certainty evidence, finding no effect when comparing all psychosocial interventions together as a group (Siddiqui et al., 2024). The Panel believes that despite the lack of apparent efficacy currently, given the very low risk of harm, psychosocial interventions may be offered to people with comorbid substance use.			
We suggest that people with schizophrenia and comorbid anxiety may be offered cognitive behaviour therapy.	14	Jones et al. (2018)	Weak
Judgement: Moderate certainty evidence indicates no clinically significant benefit of cognitive behavioural therapy plus standard care over standard care alone for reduction in anxiety symptoms among people with schizophrenia (Jones et al., 2018). The Panel believes that despite the lack of apparent efficacy currently, given the very low risk of harm, cognitive behavioural therapy may be offered to people with comorbid anxiety.			
We suggest that people with schizophrenia and comorbid post-traumatic stress disorder may be offered trauma-based psychotherapy.	16	Brand et al. (2018) and Reid et al. (2024)	Weak
Judgement: Trauma-based psychotherapies showed no clinically significant benefit in reducing post-traumatic stress disorder symptoms (Brand et al., 2018). Some therapy types may be more effective than others, but the current evidence is not conclusive (Reid et al., 2024). Although the efficacy of trauma-based psychotherapy is currently equivocal, many of them, when provided by trained clinicians, are well tolerated (Reid et al., 2024). Thus, the Panel believes trauma-based psychotherapies may be offered to people with comorbid post-traumatic stress disorder.			
Footnotes: • Certainty of evidence (high, moderate, low or very low) was assessed using the GRADE approach with consideration of risk of bias, precision, directness, consistency, publication bias, dose-response relationships and large effect sizes. The best available evidence was used to rate the certainty of the evidence, with additional resources, such as other clinical practice guidelines and large cohort studies, considered in the evidence-to-decision process. Where GRADE assessments had been conducted by a Cochrane group, these were accepted. CInEMA assessments from network meta-analysis informed certainty of evidence judgements. • Definitions of the estimate/magnitude of effect are described in Supplemental Appendix Table 20. The Panel considered a small effect size to be a minimal clinically meaningful benefit for most outcomes. • The evidence-to-decision framework considered the certainty of the evidence, the balance of benefits and harms, and the values and preferences of people with schizophrenia. Other considerations for some recommendations included feasibility, resource requirements and acceptability. • Values and preferences of people with schizophrenia and their supporters were incorporated through the panel judgement of the balance of benefit, harm and burdens of therapy. The Panel included an expert by experience, and input was also sought from a consumer consultation group.			

Table 10. Recommendation summary for physical health and lifestyle interventions.

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
We recommend that people with schizophrenia should be offered physical activity programmes to improve psychiatric symptoms of schizophrenia, including positive symptoms, negative symptoms and global cognition.	17	Kim et al. (2023) and Shimada et al. (2022)	Strong
Judgement: Of psychiatric symptoms, positive (moderate certainty, small effect size) and negative symptoms (moderate certainty, moderate effect size), as well as global cognition symptoms (moderate certainty, small effect size) had the most consistent evidence from physical activity programmes (Kim et al., 2023; Shimada et al., 2022). The majority of evidence is derived from aerobic interventions of at least moderate to vigorous intensity, delivered by exercise professionals. Overall, the certainty of the evidence for physical activity to improve positive symptoms, negative symptoms and global cognition is moderate. The Panel believes that a strong recommendation is warranted as the majority of people with schizophrenia would want to be offered this intervention, and it is associated with minimal harm.			
We recommend that people with schizophrenia should be offered physical activity programmes to improve global functioning and quality of life.	17	Korman et al. (2023) and Rissmayer et al. (2024)	Strong
Judgement: Current evidence suggests a small clinically meaningful benefit for global functioning (moderate certainty) (Korman et al., 2023) and a moderate benefit for quality of life (moderate certainty) (Rissmayer et al., 2024). The Panel believes that a strong recommendation is warranted as the majority of people with schizophrenia would want to be offered this intervention, and it is associated with minimal harm.			
We recommend that people with schizophrenia should be offered multimodal lifestyle interventions for the management of antipsychotic-induced weight gain from the outset of prescription and throughout all stages of illness.	18	Fernández-Abascal et al. (2021), Rissmayer et al. (2024) and Rocks et al. (2022)	Strong
Judgement: Physical activity and dietary interventions on their own did not appear to lead to significant weight loss (Rissmayer et al., 2024; Rocks et al., 2022) but multimodal lifestyle interventions that include components such as dietary intervention, weight management, physical activity, health education, motivational interviewing and cognitive behavioural therapy have been associated with weight loss (Fernández-Abascal et al., 2021). Note that a subgroup analysis found modest effects for dietary interventions offered by diet professionals (Rocks et al., 2022). With moderate certainty evidence, the Panel believes that a strong recommendation is warranted for multimodal lifestyle interventions as it is associated with minimal harms, and antipsychotic-induced weight gain is one of the most distressing side effects.			
We recommend that people with schizophrenia should be offered physical activity programmes to improve their physical health, including cardiorespiratory fitness and strength.	18	Gallardo-Gomez et al. (2023)	Strong
Judgement: Current evidence suggests no significant benefit of physical activity for cardiorespiratory fitness (low certainty) and a moderate benefit for strength (low certainty) (Gallardo-Gomez et al., 2023). Despite the current low certainty evidence, the Panel considers that improving physical health parameters associated with premature mortality to be of high clinical importance (Firth et al., 2019); hence, a strong recommendation is made.			
We suggest that people with schizophrenia may be offered peer-led interventions to improve cardiorespiratory fitness.	18	Coles et al. (2022)	Weak

(Continued)

Table 10. (Continued)

Recommendation	Evidence table (Appendix)	Main references	Strength of recommendation
Judgement: Peer-led interventions may have a small clinically meaningful effect on improving cardiorespiratory fitness (Coles et al., 2022). While the certainty of the current evidence base is very low, given the likely low harms associated with the intervention and possible easier access for people with schizophrenia, the Panel makes a weak recommendation.			
We suggest that people with schizophrenia may be offered cognitive behaviour therapy for insomnia for sleep disturbance.	18	Wilkinson et al. (2025)	Weak
Judgement: The current certainty of evidence is low for cognitive behaviour therapy for insomnia (CBTi) to improve sleep for people with schizophrenia, and no meta-analysis was conducted in the most recent review but included studies showed moderate to large benefits (Wilkinson et al., 2025). However, CBTi has been found to be acceptable with good adherence (note three out of five included studies modified the therapy to withdraw sleep restriction due to potential risk of this technique on psychotic symptoms) and sleep problem is often a major issue for people with schizophrenia. Therefore, the Panel makes a weak recommendation.			
We recommend that people with schizophrenia should be offered oral health education to improve oral health indices (plaque reduction).	18	Macnamara et al. (2021)	Strong
Judgement: Current evidence is based on one review with very low certainty (Macnamara et al., 2021). While the evidence base is very limited for the outcomes of plaque reduction and debris index (e.g. only three studies on plaque reduction), there is substantial evidence that people with schizophrenia experience poor oral health outcomes (Mishu et al., 2024; Wey et al., 2016). Given the very minimal risks associated with oral health education, the Panel considers that a strong recommendation is warranted.			
We recommend that people with schizophrenia should be offered behavioural interventions (face-to-face, tailored), and pharmacotherapy to assist with smoking abstinence, including varenicline, bupropion and nicotine replacement therapy.	19	Siskind et al. (2020) and Spanakis et al. (2022)	Strong
Judgement: Behavioural interventions showed a small benefit for smoking abstinence (Spanakis et al., 2022), and while all three pharmacotherapies have moderate certainty evidence for smoking abstinence across short durations (less than 12 weeks) (Siskind et al., 2020). The Panel believes that the harms associated with smoking are so high that most individuals who smoke should be offered both behavioural and pharmacological interventions to assist with smoking abstinence. The harms associated with both intervention types are relatively low. It is worth noting that while nausea has been found to be associated with varenicline use, neuropsychiatric outcomes were no greater than placebo for varenicline or any of the pharmacotherapies (Siskind et al., 2020).			
Footnotes: • Certainty of evidence (high, moderate, low or very low) was assessed using the GRADE approach with consideration of risk of bias, precision, directness, consistency, publication bias, dose-response relationships and large effect sizes. The best available evidence was used to rate the certainty of the evidence, with additional resources, such as other clinical practice guidelines and large cohort studies, considered in the evidence-to-decision process. Where GRADE assessments had been conducted by a Cochrane group, these were accepted. CINeMA assessments from network meta-analysis informed certainty of evidence judgements. • Definitions of the estimate/magnitude of effect are described in Supplemental Appendix Table 20. The Panel considered a small effect size to be a minimal clinically meaningful benefit for most outcomes. • The evidence-to-decision framework considered the certainty of the evidence, the balance of benefits and harms, and the values and preferences of people with schizophrenia. Other considerations for some recommendations included feasibility, resource requirements and acceptability. • Values and preferences of people with schizophrenia and their supporters were incorporated through the panel judgement of the balance of benefit, harm and burdens of therapy. The Panel included an expert by experience, and input was also sought from a consumer consultation group.			

Table 11. Overall summary of recommendations.**Pharmacological and physical interventions**

We recommend (strength of recommendation – strong):

- that people with schizophrenia should be given oral second-generation antipsychotic medications with a favourable cardiometabolic side effect (including hyperprolactinemia) profile as the first-line treatment (i.e. aripiprazole, brexpiprazole, cariprazine, lurasidone).
- that people with schizophrenia in the maintenance stages of the illness should be offered long-acting injectable antipsychotic medications as a treatment option.
- that people with treatment-resistant schizophrenia should be offered clozapine.
- that people with schizophrenia should be offered:
 - lifestyle and non-pharmacological interventions at all stages of treatment to mitigate the cardiometabolic side effects of antipsychotic treatment.
 - adjunctive metformin for the management of antipsychotic-induced weight gain. Early utilisation of metformin should be prioritised for people receiving any antipsychotic medication, and co-commencement of metformin on initiation of olanzapine or clozapine is recommended for weight gain prevention.

We suggest (strength of recommendation – weak):

- that people with schizophrenia in the early stages of the illness may be offered long-acting injectable antipsychotic medications.
- that people with treatment-resistant schizophrenia may be offered electroconvulsive therapy.
- that medications used to treat people with schizophrenia may be rationalised when cardiometabolic side effects occur through switching to a more metabolically neutral antipsychotic agent.
- that people with schizophrenia may be offered:
 - the use of a glucagon-like peptide-1 receptor agonist to manage antipsychotic-induced weight gain.
 - adjunctive low-dose propranolol or low-dose mirtazapine for the treatment of akathisia experienced during treatment with antipsychotics, particularly after attempts to rationalise the offending antipsychotic medication have been made.
 - vesicular monoamine transporter 2 inhibitors, valbenazine or deutetrabenazine, if available, followed by Vitamin E supplementation for the treatment of tardive dyskinesia symptoms after attempts to rationalise the offending antipsychotic agent.
 - adjunctive aripiprazole if antipsychotic-induced hyperprolactinaemia persists and is clinically significant after attempts at antipsychotic rationalisation have been made.

Psychological and psychosocial interventions

We recommend (strength of recommendation – strong):

- that people with schizophrenia should be offered:
 - psychoeducation.
 - cognitive behavioural therapy for psychosis.
 - cognitive remediation therapy, particularly those who have cognitive deficits/difficulties or poor functioning.
 - meta-cognitive therapy, particularly those who have persisting positive and negative symptoms of psychosis.

We suggest (strength of recommendation – weak):

- that people with schizophrenia may be offered relapse prevention interventions.

Family, whānau and carers

We recommend (strength of recommendation – strong):

- that the decision to include family/whānau/carers should be negotiated collaboratively and with transparency between providers, people with schizophrenia and family/whānau/carers, and always with the consent of the person with schizophrenia, where possible.
- that family/whānau/carers be offered general information about the nature, potential causes, psychosocial needs, and support and management of mental health difficulties related to a schizophrenia diagnosis.

We suggest (strength of recommendation – weak):

- that family/whānau/carers may be offered family-based interventions.
- that psychoeducation be delivered individually to family/whānau/carers to assist them to better understand and support a person with personal recovery and management of their schizophrenia, and for family peer support. Psychoeducation should also be offered in group contexts with other family/whānau/carers.

(Continued)

Table 11. (Continued)

Treatment of comorbid psychiatric conditions

We recommend (strength of recommendation – strong):

- that people with schizophrenia and comorbid depression should be offered an antidepressant medication.

We suggest (strength of recommendation – weak):

- that people with schizophrenia with comorbid substance use may be offered psychosocial interventions for substance use.
- that people with schizophrenia and comorbid anxiety may be offered cognitive behaviour therapy.
- that people with schizophrenia and comorbid post-traumatic stress disorder may be offered trauma-based psychotherapy.

Physical health and lifestyle interventions

We recommend (strength of recommendation – strong):

- that people with schizophrenia should be offered:
 - physical activity programmes to improve psychiatric symptoms of schizophrenia, including positive symptoms, negative symptoms and global cognition.
 - physical activity to improve global functioning and quality of life.
 - multimodal lifestyle interventions for the management of antipsychotic-induced weight gain from the outset of prescription and throughout all stages of illness.
 - physical activity programmes to improve their physical health, including cardiorespiratory fitness and strength.
 - oral health education to improve oral health indices (plaque reduction).
 - behavioural interventions (face-to-face, tailored), and pharmacotherapy to assist with smoking abstinence, including varenicline, bupropion and nicotine replacement therapy.

We suggest (strength of recommendation – weak):

- that people with schizophrenia may be offered:
 - peer-led interventions to improve cardiorespiratory fitness.
 - cognitive behaviour therapy for insomnia for sleep disturbance.

meta-analysis suggested that paliperidone (3-monthly) and aripiprazole may have greater efficacy for reducing relapse than placebo compared to others (Ostuzzi et al., 2021). Nevertheless, in head-to-head comparisons of LAIs, there was no difference in efficacy apart from haloperidol being inferior compared to aripiprazole, fluphenazine and paliperidone, and only aripiprazole showed superior acceptability compared to other LAIs (Ostuzzi et al., 2021). Moreover, a network meta-analysis using individual participant data from Swedish and Finnish national registries, as well as aggregate data from RCTs, also demonstrated that LAIs were more effective in the real world (i.e. national registry data) compared to the efficacy found in RCTs (Efthimiou et al., 2024). Furthermore, LAI antipsychotics are associated with a lower risk of all-cause and non-suicidal mortality in people with schizophrenia compared to oral antipsychotics (Aymerich et al., 2025). Combined, we recommend choosing the second antipsychotic medication from the remaining agents from the first-line treatment options (aripiprazole, brexpiprazole, cariprazine, or lurasidone) with additional consideration for agents with different receptor profiles such as amisulpride and risperidone (McCutcheon et al., 2023), as well as LAI formulation for aripiprazole and paliperidone. Similar to the initiation process, the choice of the second agent should be guided by the adverse effect profile and individual preference. In addition, we encourage prescribers to consider changing to a medication with a different pharmacodynamic profile (e.g.

if you have already tried a dopamine partial agonist like aripiprazole, brexpiprazole or cariprazine, then try a dopamine antagonist like lurasidone, amisulpride, risperidone or paliperidone LAI) (McCutcheon et al., 2025).

Negative symptoms are common, disabling, and often show limited response to currently available antipsychotic medications (Correll and Schooler, 2020). It is therefore important to consider and address potential secondary causes, including suboptimally treated positive symptoms, depressive symptoms, substance use, untreated medical conditions and side effects of antipsychotic treatment (e.g. extrapyramidal symptoms). Certain medications, such as cariprazine, aripiprazole and low-dose amisulpride, may offer greater efficacy for negative symptoms and antidepressant augmentation may be helpful for some (McCutcheon et al., 2025). Similarly, cognitive symptoms associated with schizophrenia are frequently insufficiently addressed by antipsychotic medications. Furthermore, increased anticholinergic burden from some antipsychotic medications may worsen cognitive functioning. In such cases, dose reduction to minimise anticholinergic burden should be considered (McCutcheon et al., 2025). Non-pharmacological interventions targeting these domains are discussed in the coming sections.

Treatment-resistant schizophrenia

Treatment-resistant schizophrenia is defined as an inadequate response and persisting moderate to severe functional

Table 12. First-episode psychosis workup.

Medical history (not limited to but should include)	Past/current medical diagnoses, family history, development (motor and cognitive), neurological symptoms (gait, seizure-like episodes, abnormal movements, sensory change, migraine), systemically unwell/recent illness (rapid weight change, cough/flu-like illness, palpitations, fever, headache)
Physical examination (not limited to but should include)	Vitals (including postural blood pressure and heart rate), neurology, cardiovascular, the eye examinations Weight, BMI
Baseline investigations	Full blood count, electrolytes, renal function, liver function, prolactin, HbA1c, lipids TFT (if clinically indicated) Urine drug screen ECG Consider pregnancy test Consider MRI brain
Child or history of significant developmental delay or intellectual impairment	Neuropsychology assessment, MRI Consider karyotyping and genetic screening, metabolic testing
Older adult or significant history of cognitive decline	Cognitive assessment, MRI Consider referral to neurology or the geriatric team Consider CSF
Atypical psychosis (catatonia, rapid onset, fluctuating/episodic, cognitive deficits, neurological symptoms/signs, early or excessive EPSE, systematically unwell)	Serum neuronal antibodies (anti-NMDAR, anti-VGKC, anti-GAD antibodies) EEG MRI Consider CSF (plus CSF neuronal antibodies)
At risk sexual behaviour, intravenous drug use, evidence of liver disease, abnormal LFTs	Hepatitis B and C, HIV and syphilis serology.
Occupational exposure (construction/manufacturing/mining/farming)	Consider heavy metal testing

BMI = body mass index; CSF = cerebrospinal fluid; ECG = electrocardiogram; EEG = electroencephalogram; EPSE = extrapyramidal side effects; GAD = glutamic acid decarboxylase; HIV = human immunodeficiency virus; MRI = magnetic resonance imaging; NMDAR = N-methyl-D-aspartate receptor; TFT = thyroid function test; VGKC = voltage-gated potassium channel.

impairment following the use of two different antipsychotic medications, each taken with adequate dose, duration and confirmed adherence (Howes et al., 2017; Kane et al., 1988). The proportion of treatment resistance among people with schizophrenia is estimated to be around 30% (Howes et al., 2017; Kane et al., 2019; Siskind et al., 2022a). For those meeting the threshold for treatment-resistant schizophrenia, clozapine should be considered under the care of tertiary mental health services (Dong et al., 2024; Kane et al., 2019; Samara et al., 2025a). A Cochrane review (Sinclair et al., 2019) found that the addition of electroconvulsive therapy (ECT) may increase clinical response compared to standard care alone (various antipsychotics used as the standard care across different studies, including clozapine), at least in the short term (8–12 weeks). The benefit was not clear when ECT was directly compared to clozapine. It is also estimated that only around 40% of people with treatment-resistant schizophrenia would respond to clozapine (Siskind et al., 2017). Currently, there is limited evidence for treatment options for those who do not respond to clozapine. Some

expert consensus statements (Wagner et al., 2019, 2020) recommend strategies such as augmentation with another antipsychotic medication (e.g. amisulpride and aripiprazole) or ECT for persistent positive symptoms, and combination with certain antidepressants (e.g. fluoxetine, duloxetine, citalopram) for negative symptoms. A recent cohort study found that clozapine combined with sertraline, duloxetine and escitalopram were associated with reduced risk of relapse (Taipale et al., 2025). For suicidality, augmentation with antidepressants or mood stabilisers, or ECT has been suggested, as well as augmentation with a mood-stabiliser or antipsychotic medication for aggression (Siskind et al., 2018; Wagner et al., 2019, 2020). A meta-analysis of antipsychotic augmentation strategies for clozapine among Swedish and Finnish nationwide cohorts demonstrated that only clozapine and medium-dose aripiprazole (9 to <16.5 mg/day) was associated with decreased hospitalisation rates for both psychosis and somatic causes compared to clozapine monotherapy. In contrast, high-dose augmentation with all other examined antipsychotics (olanzapine,

Table 13. Antipsychotic medication algorithm.

First line Recommend starting low and going slow for those with first-episode psychosis	Choose from: aripiprazole (initially oral rather than LAI formulation), brexpiprazole, cariprazine, or lurasidone
Second line - there is no response at all to the initial agent after 2 weeks at dose within target range with confirmed adequate adherence, or - there is a suboptimal response to the maximum recommended dose of the initial agent after 2–4 weeks with confirmed adequate adherence, or - The individual is not able to tolerate the adverse effects of the initial agent (at any dose)	Choose from the remaining agents from the first-line treatment options (aripiprazole, brexpiprazole, cariprazine, or lurasidone) with additional consideration for amisulpride and risperidone as well as LAI formulation for aripiprazole and paliperidone Consider changing to a medication with a different pharmacodynamic profile (e.g. if you have already tried a dopamine partial agonist like aripiprazole, brexpiprazole or cariprazine, then try a dopamine antagonist like lurasidone, amisulpride, risperidone or paliperidone)
Treatment resistant Inadequate response to two different antipsychotic medications, each taken with adequate dose, duration and confirmed adherence	Clozapine
Not fully responsive to clozapine	Consider: augmentation with another antipsychotic medication (e.g. amisulpride and aripiprazole), electroconvulsive therapy, or, combination with certain antidepressants (e.g. fluoxetine, sertraline, citalopram, escitalopram and duloxetine)

LAI=long-acting injectable.

quetiapine or risperidone) was associated with increased hospitalisation rates for psychosis (Tiihonen et al., 2025). Furthermore, suprathreshold doses of antipsychotic medications do not appear to improve response rates (Samara et al., 2018a). The evidence for the effectiveness of antipsychotic polypharmacy is mixed, despite the frequency of its use in clinical practice. Although one systematic review found that antipsychotic polypharmacy was effective in individuals with more severe symptoms (Lochmann van Bennekom et al., 2024), another review found that those with antipsychotic polypharmacy had greater illness severity and poorer outcomes than those treated with antipsychotic monotherapy, and antipsychotic polypharmacy was associated with higher side effect burden, including all-cause mortality (Højlund et al., 2024). Thus, we recommend avoiding suprathreshold doses or polypharmacy in general, unless clinically deemed necessary. In cases of polypharmacy or suprathreshold doses, we suggest close monitoring of both the effectiveness and tolerance assertively. The additional agent should be withdrawn, or the dose should be reduced to the therapeutic dose, if no benefits are seen within 3 months. The summary of the recommended pharmacology algorithm is presented in Table 13.

Tolerability and adverse effect consideration

Side effects are common among people treated with antipsychotic medication, having been reported in over 75% of those treated (Iversen et al., 2018). It is also worth noting that some side effect burdens do not necessarily show a

dose-response pattern. For instance, while most second-generation antipsychotic medications show an initial dose-related weight increase that reaches a plateau at a higher dose, some (e.g. aripiprazole, olanzapine and paliperidone) do not show such a plateau. Other agents, such as quetiapine and ziprasidone, on the other hand, exhibited bell-shaped curves, where the risk of weight gain appears to decrease at higher doses (Wu et al., 2022). Similarly, the discontinuation rates have diverse response patterns. Some antipsychotic medications (including amisulpride, cariprazine, olanzapine and quetiapine) show U-shaped curves, where increases in dosage lead to raised discontinuation rates, while others (including aripiprazole, asenapine, brexpiprazole, clozapine, paliperidone and risperidone) reach plateaus in discontinuation rates with increasing doses (Tian et al., 2025). A few antipsychotic medications, such as haloperidol, lurasidone and ziprasidone, do not reach a plateau within the examined doses (Tian et al., 2025). Combined, these findings underscore the importance of closely monitoring potential adverse effects and making dose adjustments accordingly, as the consequences of side effects are numerous, including negative impacts on physical health, quality of life, adherence and an increased risk of relapse (Pillinger et al., 2020).

While not based on evidence derived from RCTs (Tosh et al., 2014), due to the rapidity of metabolic disturbance, particularly in youth and the antipsychotic naïve (Curtis et al., 2024), numerous international and national expert consensus guidelines call for routine metabolic screening every 6–12 months integrated into multidisciplinary care at

baseline and regular intervals from the outset of psychotropic medication (Hasan et al., 2017; Lambert et al., 2017; McCutcheon et al., 2025). GRADE evidence-based recommendations were formulated to guide the management of the following antipsychotic side effects where meta-analytic evidence was available: weight gain, dysglycaemia, dyslipidaemia, akathisia, tardive dyskinesia and hyperprolactinaemia. For antipsychotic-induced cardiometabolic disturbances, non-pharmacological strategies such as exercise and dietary interventions (detailed further in Section 6) and medication rationalisation steps should be offered for all individuals. Adjunctive metformin has the most evidence for both the prevention and treatment of antipsychotic-induced weight gain (Agarwal et al., 2022; Taylor et al., 2017; Wang et al., 2021; Yu et al., 2024; Zheng et al., 2015) and is generally well tolerated. Early utilisation of metformin is encouraged, and co-commencement of metformin with high-risk metabolic agents such as clozapine and olanzapine is recommended in alignment with other international guidelines (Carolan et al., 2025; McCutcheon et al., 2025). In addition, where available and accessible, glucagon-like peptide-1 receptor agonists (GLP-1RAs) may be considered in light of the emerging evidence of their efficacy in reducing antipsychotic-induced weight gain (Bak et al., 2024; Siskind et al., 2019, 2025; Khaity et al., 2023). Given its distressing nature, akathisia is typically managed through antipsychotic rationalisation in the first instance through attempts to reduce the medication dose and switch to an alternative antipsychotic medication (Furukawa et al., 2024; Gerolymos et al., 2024). When rationalisation attempts are insufficient to treat akathisia, adjunctive propranolol and mirtazapine have some evidence of being beneficial in symptom reduction, although the certainty of evidence is low (Furukawa et al., 2024; Gerolymos et al., 2024). The antipsychotic rationalisation is likewise the first step for the management of tardive dyskinesia. Beyond this, vesicular monoamine transporter 2 inhibitors (VMAT-2I), such as valbenazine and deutetabenazine, have demonstrated evidence of benefits for tardive dyskinesia symptoms (Solmi et al., 2025). However, these compounds are not currently government subsidised in Australia and Aotearoa New Zealand and are not routinely accessible. Otherwise, vitamin E supplementation has low-certainty evidence to reduce further deterioration of tardive dyskinesia symptomatic burden (Bergman et al., 2017; Solmi et al., 2025).

After attempts at medication rationalisation, adjunctive aripiprazole can also be considered in the treatment of antipsychotic-induced hyperprolactinaemia (Lu et al., 2022; Zhang et al., 2021). The decision to treat antipsychotic-induced hyperprolactinaemia should consider symptom burden (e.g. gynaecomastia and sexual dysfunction), as well as risks associated with untreated hyperprolactinaemia (e.g. increased risk of breast cancer and osteoporosis) (Grigg et al., 2017; Solmi et al., 2023a, 2024; Taipale et al., 2021). The main side effects of antipsychotic medications

and possible management options with empirical evidence base have been summarised in Table 14. The physical health monitoring schedule, adopted from the recent Lancet Psychiatry Physical Health Commission (Halstead et al., 2025), is presented in Table 15.

Duration of antipsychotic medication treatment

The risk of relapse in clinically stable people with schizophrenia is increased when undergoing dose reductions to subtherapeutic doses or complete discontinuation of antipsychotic agents (Højlund et al., 2021; Ostuzzi et al., 2022). Even among individuals with first-episode psychosis who have been clinically stable for 6 months to 2 years, antipsychotic medication discontinuation is associated with an increased risk of relapse (Kishi et al., 2019). However, it is important to acknowledge that many people, especially those with first-episode psychosis who have achieved remission, express their desire to discontinue antipsychotic medication. While the current evidence base (Højlund et al., 2021; Kishi et al., 2019; Ostuzzi et al., 2022) suggests that the risk of relapse and related complications is minimised if individuals continue antipsychotic medication within the recommended therapeutic range, the decision may be reached to trial medication discontinuation through a shared decision-making process after discussion with the person with schizophrenia and preferably with their family, whānau and carers. Although empirical evidence remains limited, we suggest that discontinuation of antipsychotic medication be approached through gradual dose reductions over a period of at least 3–6 months, accompanied by close monitoring for early signs and symptoms of relapse. Ideally, individuals should continue to receive support and monitoring for an additional 6–12 months following discontinuation, if not longer. It is essential that individuals, along with their family, whānau and carers, are well informed about potential indicators of relapse and have access to a clear and rapid pathway back to mental health services should the need arise. Further consideration should also be given to distress caused by residual symptoms and whether adjunctive psychological and psychosocial interventions may aid functional improvement in addition to symptom reduction (Cella et al., 2023).

Section 3: psychological and psychosocial interventions

Currently, there is no definitive pharmacotherapy for the negative, neurocognitive and social cognitive symptom domains of schizophrenia. As such, alongside pharmacological interventions, psychological and psychosocial interventions are a critical part of care for people with schizophrenia, especially in the maintenance phase of the illness. Psychological and psychosocial interventions can be categorised into those that should be offered and

Table 14. Management options for antipsychotic side effects.

Side effects	Possible management options
Cardiometabolic side effects (weight gain, hyperglycaemia, dyslipidaemia, hyperprolactinaemia, when secondary to antipsychotic treatment)	Lifestyle and non-pharmacological interventions should be utilised in the first instance to mitigate cardiometabolic side effects of antipsychotic treatment Rationalisation of metabolically adverse antipsychotics should be trialled where clinically appropriate. Switching to a more metabolically neutral antipsychotic, such as aripiprazole, is recommended Adjunctive metformin should be considered for the management of antipsychotic-induced weight gain. Metformin has also demonstrated benefit for the reduction of total cholesterol and fasting blood glucose. Early utilisation of metformin should be prioritised for individuals receiving olanzapine or clozapine GLP-IRAs demonstrate efficacy at weight reduction in cases of antipsychotic-weight gain and should be considered when available and clinically appropriate. Hyperprolactinaemia: Consider switching to a prolactin-lowering antipsychotic (e.g. aripiprazole), in cases of symptomatic hyperprolactinaemia. Adjunctive aripiprazole should be considered in cases of symptomatic hyperprolactinaemia if switching is not feasible due to risks of worsening mental state
Neuromotor and extrapyramidal side effects	In the event of extrapyramidal side effects, antipsychotic(s) should be rationalised with dose reduction and/or switching to a more favourable agent if clinically appropriate in the first instance Akathisia: Low-dose propranolol or low-dose mirtazapine should be considered in the treatment of akathisia in addition to antipsychotic rationalisation Dystonia: Emergency medical approach should be taken and acute anticholinergic treatment should be utilised Parkinsonism: Rationalisation of the antipsychotic is the mainstay of treatment. Anticholinergics should be avoided; if utilised, they should be used sparingly and in a time-limited fashion with regular reviews Tardive dyskinesia: VMAT-2I inhibitors (valbenazine or deutetrabenazine), where available, should be offered for treatment of tardive dyskinesia when symptoms are refractory after antipsychotic rationalisation has been trialled. Vitamin E may assist in mitigating further deterioration of tardive dyskinesia symptoms

GLP-IRA=glucagon-like-peptide-I receptor agonist; VMAT-2=vesicular monoamine transporter.

Table 15. Physical health monitoring schedule.

At baseline: • Vital signs (including postural blood pressure and heart rate) • Weight and BMI • Full blood count, electrolytes, renal function, liver function, prolactin, HbA1c, lipids • TFT (if clinically indicated) • Screen for modifiable lifestyle risk factors (e.g. substance use, physical inactivity, poor diet) • Urine drug screen • ECG • Consider pregnancy test
After medication commencement: At any time: • Monitor for new onset of physical symptoms Short-term: • Within the first 4 weeks: check weight and BMI • After reaching therapeutic dose: repeat ECG and check prolactin (if prescribed prolactin-raising agent) • At 3 months: check other cardiometabolic parameters. Long-term (after the first 3 months): • Monitor cardiometabolic parameters 6-monthly or annually thereafter • Monitor prolactin annually (if prescribed relevant prolactin-raising agents) and consider the need for bone mineral density investigations if prolonged untreated hyperprolactinaemia • Monitor other parameters annually or as required, with reference to types of medications prescribed, standardised monitoring and side effects of concern • Monitor modifiable lifestyle risk factors

Source: Adopted from Halstead et al. (2025).

BMI=body mass index; ECG=electrocardiogram; TFT=thyroid function test.

provided to all individuals with schizophrenia, or those that should be offered and provided to people with specific needs. For example, relapse prevention interventions (including education for recognising early signs and symptoms of relapse, a system of symptom monitoring and a crisis plan) and psychoeducation should be provided to all individuals with schizophrenia as in addition to the need for individuals to know their condition, treatment and recovery, there is evidence that psychoeducation can reduce relapse (Bighelli et al., 2021). Cognitive behavioural therapy for psychosis (CBTp) is another psychological intervention that should be offered and provided to all individuals with schizophrenia, as there is evidence for a small effect in improving positive and negative symptoms and also overall psychiatric symptoms (Jauhar et al., 2014). There is also evidence that CBTp may improve long-term global mental state (Jones et al., 2018) and may reduce relapse (Bighelli et al., 2021). Furthermore, as relapse in schizophrenia can have a devastating impact on recovery for people with schizophrenia and their families, whānau and caregivers, we also recommend that relapse prevention interventions should be routinely offered to people living with schizophrenia (Bighelli et al., 2021).

For the therapies that should be offered and provided to those with specific needs, the choice of interventions should be guided by the symptom profile. Some of these therapies may also focus on functional outcome and self-management of the impact of residual symptoms as distinct from symptom remission. Neurocognitive impairment is common in people with schizophrenia, and cognitive remediation therapy should be offered to people with schizophrenia who present with cognitive deficits and associated poor functioning. While the overall effect of cognitive remediation therapy is very small to moderate for symptom domains such as positive and negative symptoms, the effect size is greater for global cognition and functioning (Vita et al., 2021, 2024a). Cognitive impairments can impact people with schizophrenia across different phases of illness, and pharmacotherapy has little established role in addressing them (Green et al., 2019). Deficits in social cognition are also common in people living with schizophrenia and social cognitive training has been developed to address these challenges. Although a meta-analysis found that social cognitive training was not effective for positive and negative symptoms, social functioning or cognition (Yeo et al., 2022), there is evidence that it may improve theory of mind (D'Arma et al., 2021) as well as emotion perception and social perception emotional recognition (Nijman et al., 2020). These symptom domains can limit social functioning even when neurocognitive symptoms have been addressed (Fett et al., 2011). For individuals who have persistent positive and negative symptoms, meta-cognitive therapy should be offered as it has a small to moderate impact in reducing the intensity of delusions, overall positive symptoms and negative symptoms, while improving

insight and social cognition (Melville et al., 2024). There is also evidence that mindfulness-based interventions may have at least a small effect size on positive and negative symptoms as well as functional outcomes (Meinhart et al., 2025).

Overall, we recommend psychological and psychosocial interventions for people with schizophrenia from the onset of the illness. The type of intervention depends on several factors, including the phase of illness, personal preference and readiness, symptom profile and associated impact on function, as well as the availability of local resources. However, interventions such as psychoeducation, CBTp and relapse prevention should be available for all. Furthermore, cognitive remediation therapy, including social cognitive training, and metacognitive therapy interventions should be available for people with schizophrenia who have ongoing difficulties with specific symptom domains. It is worth emphasising that there is evidence showing enhanced effect when psychosocial interventions are delivered within a rehabilitation model of care (Vita et al., 2021; Wykes et al., 2011). Consideration needs to be given to the potential combined effects of these interventions and the settings in which they are delivered.

Section 4: family, whānau and carers

For the current Guidelines, we have utilised the term 'family, whānau and carers' to encapsulate those who provide unpaid care, support and assistance to a person with a diagnosed mental health condition or experiencing psychological distress. The terms 'family' and 'whānau' in particular are used broadly and inclusively within this document, encompassing kin and other informal supporters, such as friends. Living with schizophrenia takes courage and perseverance for the person and their family, whānau and carers. There can be significant challenges that have profound impacts on multiple aspects of life and relationships for the person and their family, whānau and carers, whether they are a parent, child, sibling, partner, other relative or close friend. 'Carer' is a label that family or friends of the person may or may not acknowledge or recognise, depending on circumstances and the relationship with the person. In Australia, family members who identify as primary mental health carers, on average, spend 40 hours per week providing care (Maybery et al., 2021), and the cost of informal support provided by family carers has been estimated to be approximately AU\$8.4 billion (Diminic et al., 2021).

Family, whānau and carers are more than providers of support tasks, sources of information about the person, or conduits to assist mental health service priorities, including medication adherence, symptom management, and treatment (Cameron et al., 2023). Their priority is the person's whole health and wellbeing. Family, whānau and carers seek collaboration with mental health services because they strive for health professionals to understand and view the

person with a diagnosis of schizophrenia as an individual first (Forcheron et al., 2023; Huang et al., 2021). A Cochrane review of family-based interventions for family, whānau and carers of people with schizophrenia found that they may reduce the relapse of illness and carer burden but did not have a significant impact on hospital readmission (Chien et al., 2024). A systematic review of 24 studies (Iswanti et al., 2023) found support for a professionally engaged relationship between individuals with schizophrenia, families and mental health professionals to optimise care provision. When the illness called schizophrenia becomes part of their lives, many things they hope and expect for their futures change, and everyone must learn how to make sense of their changed lives. It can often be challenging to strike the right balance between involving family, whānau and carers while not overburdening them, as well as navigating systemic complexities and confidentiality issues as part of respecting the person's privacy and autonomy (Jankovic et al., 2011; Landeweert et al., 2017; Vasava et al., 2023). Confidentiality, in particular, is challenging to navigate at times with subtle variations in different jurisdictions and services. Inconsistencies in family involvement often appear to stem from organisational culture, societal attitudes, providers' neglect of family expertise and providers' uncertainty regarding confidentiality policies and the absence of practice guidelines. In some situations, this may mean providing information and alleviating anxiety and tension for family, whānau and carers where the person with schizophrenia does not wish to have them involved or wishes to keep their mental health information confidential (i.e. a means of providing family, whānau and carers with support without breaching confidentiality in relation to the person) (Landeweert et al., 2017; Tham and Solomon, 2024). Psychoeducation and support, from the very onset of the illness, are therefore crucial not only for the person living with schizophrenia but also for their family, whānau and carers (Cameron et al., 2023; Iswanti et al., 2023). Developing strategies and supports within a 'triangle of care' that actively includes the person, their family, whānau and carer, and mental health professionals in the shared decision-making process can ensure that everyone is on the same page about what is helpful, needed and respectful to maximise the person's autonomy, dignity, choice and agency (Cameron et al., 2023; Outram et al., 2015; Schuster et al., 2020).

Section 5: psychiatric comorbidities

Substance misuse and substance-induced psychosis

Comorbid substance use is common in people with schizophrenia, with an estimated one-third diagnosed with a lifetime substance use disorder (Toftdahl et al., 2016). In addition to precipitating psychosis, substance misuse can often develop for the first time after the diagnosis of

schizophrenia (Lappin, 2019; Petersen et al., 2019). Indeed, people with schizophrenia have a more than threefold risk for developing substance misuse, with nicotine, cannabis, alcohol and stimulants the most implicated (Petersen et al., 2019). Given this, we urge clinicians to conduct regular enquiries regarding substance use, including type/s, pattern, effects on relationships and functioning, harms associated with use, and assess readiness for change.

Trauma

People with schizophrenia report higher rates of trauma and post-traumatic stress disorder (PTSD) than the general population, and people who have experienced trauma are more likely to develop psychotic symptoms (Bailey et al., 2018; Carr et al., 2018; De Bont et al., 2015; Trotta et al., 2015; Turner et al., 2019). Importantly, the experience of psychosis itself can give rise to trauma experiences, with the prevalence estimates of psychosis-related PTSD ranging from 14% to 47% (Berry et al., 2013; Buswell et al., 2021). Such trauma may arise both from distressing symptoms, such as derogatory auditory hallucinations and persecutory delusions, and from associated treatment, including restrictive/coercive practices and involuntary hospitalisation (Lu et al., 2017). While trauma-informed care is widely accepted as integral to reducing distress and supporting recovery, much work remains to be done to ensure its comprehensive implementation (Lommen and Restifo, 2009; Read et al., 2005).

Anxiety and depression

Anxiety and depressive symptoms are very common among people with schizophrenia; over 30% have a comorbid major depressive disorder (Etchecopar-Etchart et al., 2021), and nearly 40% have comorbid anxiety disorders, most commonly social phobia followed by PTSD and obsessive-compulsive disorder (OCD) (Achim et al., 2011; Braga et al., 2013). Of note, the rate of OCD increases with a longer duration of schizophrenia (Swets et al., 2014), and some antipsychotic medications may increase the risk of *de novo* OCD or symptoms (Burk et al., 2023). In clinical practice, these symptoms are often mistaken for symptoms of schizophrenia, such as negative symptoms or persecutory delusions. As such, it is crucial to take a thorough history of anxiety and depressive symptoms (including assessing for neurovegetative symptoms in detail and environmental contexts in which anxiety arises) to ensure that treatable symptoms are not missed due to diagnostic overshadowing.

Treatment for psychiatric comorbidities

There is a limited body of evidence related to treatment options specific to people with schizophrenia with a comorbid psychiatric condition. While several reviews have

demonstrated possible benefits of antipsychotic medication (Krause et al., 2019), LAI treatment (Coles et al., 2021), repetitive transcranial magnetic stimulation (Johnstone et al., 2022) and psychological therapies (Bennett et al., 2017) in reducing substance use, and naltrexone in reducing alcohol use (Rosenstand et al., 2024), all were limited by the methodological limitations of the individual studies included. Some observational studies have shown potential beneficial effects of clozapine on reducing substance misuse; however, this finding is not yet sufficiently robust to recommend the use of clozapine for managing comorbid substance use (Rafizadeh et al., 2023). A systematic review (Siddiqui et al., 2024) found that psychosocial interventions did not show a significant benefit in reducing substance use for people with schizophrenia. Overall, despite being a common and important clinical issue, there remains very limited evidence to guide us in managing people with schizophrenia and comorbid substance use or, even more strikingly, those with substance-related psychosis (Fiorentini et al., 2021).

There is emerging evidence that psychological interventions targeting trauma among people with schizophrenia are well tolerated and acceptable (Reid et al., 2024). To date, however, the evidence is inconclusive regarding whether trauma-focussed psychological therapies are effective in reducing PTSD and/or psychotic symptoms (Brand et al., 2018; Reid et al., 2024; Sin et al., 2017) with RCT-level evidence of benefit for eye movement desensitisation and reprocessing (EMDR) and prolonged exposure (PE) (De Bont et al., 2016; Van den Berg et al., 2018). A small number of studies have explored the efficacy of psychological therapies targeting anxiety symptoms among people with schizophrenia (Grover et al., 2019). Although one review concluded that there are benefits of CBT in reducing anxiety (and depressive) symptoms in people with schizophrenia (Opoka and Lincoln, 2017), a Cochrane review found no evidence of benefits with CBT for anxiety symptoms for people with schizophrenia compared to the standard care (Jones et al., 2018). Furthermore, an umbrella review found little evidence to support CBT for depressive or anxiety symptoms in people with schizophrenia (Berendsen et al., 2024). For the treatment of depression in schizophrenia, two meta-analyses showed that antidepressants may be efficacious, especially for those with more severe depressive symptoms, but the current evidence base was found to be limited (Gregory et al., 2017; Helfer et al., 2016). Neither review found a preference for any class or individual antidepressant medication.

Overall, despite high prevalences of comorbid psychiatric conditions among people with schizophrenia, there remains very limited evidence base to make strong recommendations at the moment. Therefore, we suggest: (1) conducting a thorough assessment of comorbid psychiatric symptoms and conditions in people with schizophrenia and (2) providing pharmacological and/or psychosocial

interventions for comorbid conditions as indicated for the specific condition, acknowledging that there is an urgent need to build evidence base specifically for people with schizophrenia with a comorbid psychiatric condition.

Section 6: physical health and lifestyle interventions

Physical health

Preventive healthcare access is often inequitable: people with schizophrenia have lower rates of cancer screening (Solmi et al., 2020), immunisation/vaccination (Raffard et al., 2022), sexual health checks and blood-borne virus screening (Brown et al., 2025) compared to the general population. Oral health is frequently neglected (Mishu et al., 2024; Wey et al., 2016), despite significantly elevated rates of dental caries, tooth loss, periodontal disease and oral cancers (Kisely et al., 2015; Yang et al., 2018). Close collaboration and effective communication between mental health providers and primary care services are essential for addressing health inequities, particularly in coordinating preventive health checks and routine physical healthcare (Morden et al., 2009; Planner et al., 2014; Firth et al., 2019). This collaboration should extend to other allied health, oral health and specialist medical practitioners to ensure holistic recovery-oriented care that also prioritises shared decision-making with individuals, their family, whānau and carers (Halstead et al., 2024b).

Lifestyle interventions

Among lifestyle strategies, physical activity has shown the most consistent benefits for mental health, particularly in reducing negative symptoms (Kim et al., 2023; Maurus et al., 2024), which typically show limited response to pharmacological treatment (Correll and Schooler, 2020). There is moderate certainty evidence supporting the positive effects of physical activity on cognition, global functioning and quality of life (Rissmayer et al., 2024; Korman et al., 2023; Shimada et al., 2022), reinforcing its role as an important adjunctive treatment. Although a range of physical activities (including aerobic, resistance, mind-body) were included in the reviews examined, the majority of evidence is derived from aerobic studies, with greater improvements observed at moderate or greater intensity exercise (Korman et al., 2023; Rissmayer et al., 2024), and when supervised by exercise professionals (Rissmayer et al., 2024; Shimada et al., 2022). There is some evidence that yoga may benefit negative symptoms (Yin et al., 2024); however, the findings are inconsistent (Maurus et al., 2024), with most studies having been conducted outside of Australia and Aotearoa New Zealand, limiting the generalisability of the findings. Although currently based on a small amount of very low certainty evidence, peer-facilitated physical health interventions

show future promise (Coles et al., 2022) and should be investigated further. Access to appropriate physical activity facilities and opportunities is vital, and interventions should incorporate strategies to promote autonomous motivation (Arnautovska et al., 2022; Vancampfort et al., 2025). Physical activity alone has not been found to impact weight loss consistently (Gallardo-Gomez et al., 2023; Maurus et al., 2024), despite often being one of the most commonly stated goals of people with schizophrenia (Firth et al., 2016). Multimodal lifestyle interventions (combinations of nutrition counselling, weight management programmes, physical activity, health education, motivational interviewing and CBT) have had the most significant effects on reducing weight and improving other cardiometabolic parameters (Fernández-Abascal et al., 2021). Although weight loss has been typically modest, we make a strong recommendation that lifestyle interventions should be integrated into usual psychiatric care from the earliest stages of illness and antipsychotic prescription, with prevention of weight gain an important target (Curtis et al., 2016). Factors associated with successful lifestyle interventions include; targeting multiple lifestyle components in one intervention, tailoring the intervention to the individual and their illness, delivery by qualified professionals (e.g. exercise physiologists, physiotherapists and dieticians), embedding lifestyle interventions into usual care and facilitating social networks to support engagement (Curtis et al., 2024; Lederman et al., 2017; Lee et al., 2022; Maurus et al., 2024; Teasdale et al., 2025; Vancampfort et al., 2025).

Smoking

People with schizophrenia continue to have disproportionately high rates of smoking despite declining rates in the general population (Cook et al., 2014). Although quit rates are lower than in the general population, multiple pharmacotherapies (varenicline, bupropion and nicotine replacement therapy) are more effective than placebo, with varenicline demonstrating the strongest evidence (Siskind et al., 2020). Furthermore, moderate certainty evidence supports tailored, behavioural interventions to support smoking cessation in people with schizophrenia (Spanakis et al., 2022).

Sleep

People with schizophrenia experience significant disturbance to both sleep continuity and architecture (Chan et al., 2017), with insomnia, nightmares and daytime hypersomnia commonly experienced (Chiu et al., 2018; Waite et al., 2020). A systematic review (Wilkinson et al., 2025) found that cognitive behavioural therapy for insomnia (CBT-i) was effective and associated with minimal harms; however, sleep restriction was excluded from the majority of studies to reduce the risk of exacerbating psychotic symptoms. Obstructive sleep apnoea (OSA) is highly prevalent among

people with schizophrenia (Myles et al., 2016). Although there is no current RCT evidence, a large case-control study found continuous positive airway pressure (CPAP) therapy to be feasible and effective in people with schizophrenia (Giles et al., 2022). Given the potential for cognitive and cardiovascular health (McEvoy et al., 2016), those at risk of OSA should be proactively screened and supported to access OSA management.

Oral health

Currently, there is only very low certainty evidence for oral education interventions for people with schizophrenia (Macnamara et al., 2021). However, possible strategies for improving oral health may include: facilitating early oral screening; referring to affordable dental clinics; managing psychotropic-induced dry mouth (Kisely et al., 2015); and integrating oral concerns into psychiatric healthcare (Skallefold et al., 2023).

Section 7: special populations

Māori and Aboriginal and Torres Strait Islander peoples

While there is a limited body of research knowledge, especially in Australia, regarding the rates of schizophrenia among Indigenous peoples, it is generally reported that there is a higher prevalence of schizophrenia and related psychoses both in Aboriginal and Torres Strait Islander peoples (Black et al., 2015; Heffernan et al., 2012; Jewell and Mitchell, 2023; Ogilvie et al., 2021) and Māori populations (Kake et al., 2008; Tapsell et al., 2018). Māori and Aboriginal and Torres Strait Islander peoples also experience elevated rates of coercive care (Beaglehole et al., 2024; Kisely et al., 2020), higher social disadvantage (Badcock et al., 2018) and multimorbidity (Carman et al., 2022; Monk et al., 2024). It is important to recognise the possible roles of colonisation, social disadvantage and racism as factors in these mental health inequities.

In terms of effective clinical service models, although there are several important guiding principles such as those outlined in the Closing the Gap and the Gayaa Dhuwi (Proud Spirit) Declaration, the implementation in clinical practice has not been consistent (Grattan et al., 2025; Gupta et al., 2020). Nevertheless, it is essential to foster the development of a workforce that reflects the community it serves and ensures cultural safety in all clinical settings and research (Lacey et al., 2022). To this end, we advocate for universal cultural safety in mental health systems. While each individual determines cultural safety, the outcome of culturally safe health systems is to ensure that people with schizophrenia feel comfortable and secure accessing care. This is particularly important for Aboriginal and Torres Strait Islander peoples in Australia and Māori in Aotearoa New Zealand.

People in rural and regional areas

Rural communities have a significant unmet need for mental health care (Plana-Ripoll et al., 2021). These areas have fewer psychiatrists per population than urban regions, and distances from hospitals are greater (Amos et al., 2023; Darmawan et al., 2023). While there has been an increasing utilisation of telepsychiatry in Australia in recent years (Woon et al., 2024), general practitioners will often be the primary medical contact for people with schizophrenia rather than psychiatrists or mental health professionals in rural communities. To ensure the wellbeing of people with schizophrenia in rural areas, we need to continue to not only deliver service wherever possible, but also have an increased emphasis on upskilling general practitioners and providing support and supervision using appropriate technologies (Amos et al., 2022; Coleman et al., 2022).

Discussion

In the current Guidelines, we have utilised the GRADE approach to formulate recommendations related to different aspects of care provision for people with schizophrenia. At the individual level, we hope that these Guidelines are helpful for clinicians working with people with schizophrenia to provide the most optimal care in conjunction with an individualised, collaborative formulation. At the systematic level, we hope that the Guidelines provide a blueprint to aid clinical directors and policymakers in considering the breadth of workforce structures identified in the evidence presented, as well as the workforce and work environment required to care for people with schizophrenia.

Guideline utilisation and applicability

In considering potential barriers and enablers to implement the recommendations, the importance of systemic support cannot be overemphasised. It is essential, for example, that the quality of the therapists who provide psychological and psychosocial interventions, as well as lifestyle interventions, is adequately maintained through regular training and supervision. Given the strong interactions between mental health and physical health conditions, the link between mental health services and other medical services, including primary health care, should be further strengthened. In treating physical health comorbidities of people with schizophrenia, addressing and reducing organisational silos is critical. While there are examples of successful initiatives at a local level (e.g. Siskind et al., 2022b), there needs to be further efforts at the national and binational levels to improve service delivery. Silos in care may occur at various points, including within mental health services (e.g. from inpatient care to community care and vice versa), when interfacing with other medical services such as primary health care providers, and through non-health organisations, including

non-governmental organisations. It is also important to acknowledge that most people with schizophrenia will not stay in the public mental health system indefinitely. Many people with schizophrenia are managed in the primary health sector with or without additional input from non-health organisations. People with schizophrenia and their family, whānau and carers must be supported in navigating often complex systems to ensure coordinated care at different stages of the illness.

In the current Guidelines, we have presented algorithms to assist with antipsychotic medication choices and side effects monitoring for people with schizophrenia. In addition to publishing these Guidelines and their associated professional presentations, we plan to produce accompanying commentaries and companion documents to disseminate the recommendations widely. Nevertheless, these Guidelines can only be implemented effectively when they are utilised within an adequately resourced workforce with access to multidisciplinary health workers, including a lived experience workforce. High-level principles and models of care mentioned in these Guidelines (e.g. trauma-informed care, the Closing the Gap) can only be meaningfully implemented in real life if there is a stable and thriving mental health workforce and work environment. Related to this, we need to continue to evaluate and consider alternative ways to provide optimal care for people with schizophrenia. For instance, although the current evidence base is limited, peer-led interventions (Coles et al., 2022) and digital technologies (Sawyer et al., 2023) hold promise as complementary delivery modes for lifestyle interventions, particularly in areas where resources for qualified professionals are scarce.

Limitations

Although we tried to be as objective as possible by using the GRADE approach to evaluate the certainty of the existing empirical evidence relevant to clinical practice, the recommendations were based on subjective judgement based on the risks and benefits of each intervention by the Panel (Andrews et al., 2013; Guyatt et al., 2008). To mitigate the inherent biases associated with this process, we established a Panel consisting of psychiatrists with diverse areas of expertise who have worked in multiple settings, a trainee member, a representative with lived experience and a statistics expert. We also sought additional processes, such as consultations with a consumer consultation group and input from external reviewers, to reduce the risk of potential biases and groupthink when making the recommendations. Nevertheless, the values we hold would not be the same as the values of all the people with schizophrenia and those who care for them. These recommendations should be taken as guidelines only to help with the formulation and delivery of care that is most appropriate and optimal for the particular individual in the particular setting. Moreover, as

these Guidelines were GRADE guidelines commissioned by the ANZJP, unlike the Clinical Practice Guidelines previously produced by the RANZCP, we have been limited to areas where there is empirical evidence. As such, we are unable to include expert opinion to cover areas where there is a lack of empirical evidence, limiting the breadth of these Guidelines. Previous RANZCP Clinical Practice Guidelines for schizophrenia (Galletly et al., 2016) should be considered for areas where we could not assess the certainty of empirical evidence.

Another limitation of these Guidelines was that most of the studies included in the reviews were not conducted in Australia or Aotearoa New Zealand. While some findings may be relevant even if based on studies in different settings (e.g. the efficacy of antipsychotic medications; Huhn et al., 2019), most topics examined in the current Guidelines would benefit from more relevant studies to determine their relevance in local settings. In particular, there was very little examination of the effectiveness of models of care for Indigenous peoples in either Australia or Aotearoa New Zealand, or those in rural areas. Given the uniqueness and disproportionate vulnerabilities facing these populations, further research is needed to advance the field. Related to this, we have limited exploration of issues relevant to other special subpopulations of people with schizophrenia in the current Guidelines. These include, but are not limited to, people from culturally and linguistically diverse groups (including refugee and migrant populations), people who are homeless, people who are incarcerated, women and people who identify as members of the lesbian, gay, bisexual, transgender and queer/questioning communities. As these sub-populations often have higher rates of mental health difficulties and unique sets of vulnerabilities and treatment needs, there is an ongoing need to improve the scientific evidence base specific to these cohorts. We plan to examine some of these issues in the upcoming accompanying commentaries.

Another topic with surprisingly little empirical evidence base was that of psychiatric comorbidities faced by people with schizophrenia. Given that comorbidities are common in psychiatry and their impact can be profound (Plana-Ripoll et al., 2020), furthering the understanding of the relationship between schizophrenia and comorbid psychiatric conditions would have significant clinical implications and enable the development of treatments tailored to address this complex comorbidity in people with schizophrenia. In particular, there is currently very little empirical research to guide us on the management of people with schizophrenia who have such comorbid conditions as neurodevelopmental disorders and substance use disorders. This is despite the fact that both attention deficit hyperactivity disorder (Cheng et al., 2025) and autism spectrum disorders (Zheng et al., 2018) are more prevalent among people with schizophrenia than the general population, and

substance-induced psychosis is a very common clinical problem (Fiorentini et al., 2021).

Future directions

While we have attempted to capture what we considered to be the core aspects of care for people with schizophrenia, there remain many unanswered questions and much need for ongoing evaluation and research. Currently, many of our recommendations have been made with low to moderate levels of certainty, and some clinical questions require urgent investigation (e.g. what to do after clozapine therapy fails, and how best to manage comorbid psychiatric conditions, including substance misuse). We urgently need further research at both the basic science level examining the efficacy of different interventions, and the service/public health level evaluating the effectiveness of treatment implementation. For example, although we have made strong recommendations for a range of psychological and psychosocial interventions, implementing these in practice, particularly in rural and remote areas, remains a significant challenge. Novel and innovative models of care are needed to ensure that such interventions are delivered with sufficient quality and accessibility to those who need them most. Furthermore, to meet the GRADE guideline commission, we were unable to cover many important topics. They may include, but are not limited to, topics such as the use of the mental health legislation, pharmacological options for acute behaviour disturbances, medication adherence, substance-induced psychosis, care provision for other vulnerable subgroups, digital interventions, risk assessment and emerging interventions for people with schizophrenia and optimal service component structures. We hope to explore these topics in accompanying commentaries.

Conclusion

In conclusion, we echo the authors of the previous RANZCP clinical practice guidelines (Galletly et al., 2016) in acknowledging the extraordinary courage and perseverance shown by many people with schizophrenia and their families, whānau and carers. We hope that the current Guidelines provide useful recommendations based on the existing evidence base in important aspects of care for people with schizophrenia in Australia and Aotearoa New Zealand, both at the individual and systemic levels.

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Data availability statement

Not applicable.

Supplemental material

Supplemental material for this article is available online.

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