Medical Management in Early Psychosis

A Guide for Medical Practitioners

Orygen
The National Centre of Excellence in Youth Mental Health

EPPIC
Early Psychosis Prevention and Intervention Centre

The EPPIC National Support Program of Orygen Youth Health Research Centre has produced this document as part of its work to support the scaling up of the EPPIC model within headspace, the National Youth Mental Health Foundation, in Australia.

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Contents

Introduction

There is significant evidence that intervening early with psychotic disorders has the potential to achieve the best symptomatic and functional outcomes; early intervention with effective treatment is therefore an ethical imperative. Medication and other medical forms of treatment will form a core component of interventions for early psychosis. This is a highly specialised area and must be managed extremely carefully. It is not enough to simply prescribe medication without considering the particular context of early psychosis and the unique issues relevant to this population. Young people can be difficult to engage in treatment, are less likely to adhere to antipsychotic medication and are more vulnerable to its side-effects than the older adult population with established illness. However, getting medical interventions 'right' will have a major impact on the clinical and functional outcomes and lived experience of young people and their families, and have a profound effect on their future.

About this manual

Medical management in early psychosis: a guide for medical practitioners is one of a series of manuals produced as part of the EPPIC National Support Program (ENSP) to support the implementation of the Early Psychosis Prevention and Intervention Centre (EPPIC) Model in early psychosis services. The EPPIC Model is a model of specialised early intervention in psychosis that aims to provide early detection and developmentally appropriate, effective, evidence-based care for young people (aged 12–25 years) at risk of or experiencing a first episode of psychosis. It has been developed from many years experience within the clinical program at Orygen Youth Health and further informed by the National Advisory Council on Mental Health's Early Psychosis Feasibility Study (2011), which sought international consensus from early psychosis experts from around the world. The appropriate medical management of young people with early psychosis is one of the 16 core components that make up the EPPIC Model.

Although the treatment of young people with early psychosis involves a comprehensive range of biopsychosocial interventions, this manual focuses specifically on medical treatments for early psychosis. It is intended as a guide to the medical management of young people with early psychosis, covering the role of doctors in assessing, diagnosing and managing young people and their medical treatment. Clinicians should always follow appropriate clinical guidelines when prescribing and managing medical interventions. Note that the EPPIC Model is informed by the *Australian Clinical Guidelines for Early Psychosis* (2010).[1] However, further minimum standards for medical management and intervention in early psychosis in the EPPIC Model are described in the *EPPIC Model and Service Implementation Guide*.[2]

How to use this manual

This manual is aimed at all medical practitioners – particularly psychiatrists and trainee psychiatrists, but also general practitioners (GPs) – who work with young people with early psychosis. It may also be useful for nurse practitioners, service managers and other mental health professionals working in an early psychosis service to help them understand the requirements, approaches and challenges of medical management in young people with early psychosis.

The manual is divided into six parts: 'Working with young people in early psychosis' details the considerations clinicians need to make when treating young people with early psychosis; 'Assessment: formulation, diagnosis and risk' covers the process of medical assessment and diagnosis of young people with suspected psychosis and presents strategies for managing risk and crisis; 'Medical interventions for early psychosis' focuses on prescribing principles in young people and medical management for young people at each phase of a psychotic episode and recovery; 'Physical health management and monitoring in early psychosis' deals specifically with recommended care for young people on antipsychotic medication; 'Service level considerations' outlines the role of the doctor within an early psychosis

service; and finally, promising advances in psychosis treatment are presented in 'New advances in medical treatment of psychosis'.

Case scenarios and anecdotes from young people who have been treated in the EPPIC service in the Orygen Youth Health Clinical Program are presented throughout to provide real-world context.

Definitions in early psychosis

First episode psychosis and ultra high risk for psychosis

It should be noted that for the purposes of this manual, the term 'early psychosis' encompasses both young people who have experienced a first episode of psychosis and those considered as being at ultra high risk of developing psychosis (UHR; see also page 28). Further information specific to the UHR population can be found in the manual *A stitch in time: interventions for young people at ultra high risk of psychosis*.

Models of early psychosis: the clinical staging and phases models

The 'phases' model of psychosis and the Australian Clinical Guidelines for Early Psychosis clinical staging model are two models of psychosis that although different in focus, are congruent and consistent with each other.

The clinical staging model for early psychosis

The concept of clinical staging has been used in mainstream medicine, such as cancer treatment, for some years now. The idea is that earlier recognition of illness will allow more benign treatments that have fewer side-effects to be used and also produce better outcomes than if treatment is started at a later stage. For people with more severe illness, more invasive or extensive treatment options may be required; these may also cost more and carry greater risks of side-effects.

More recently, the clinical staging model has been applied to first episode psychosis (FEP) whereby staging provides a heuristic model outlining a framework for grading the stage of psychotic illness (Table 1).[1] As a result, appropriately phased and more benign evidence-based treatments (e.g. omega-3 fatty acids or cognitive-behavioural therapy [CBT]) can be provided for people at UHR for psychosis, while medications associated with more adverse effects are reserved for later stages (e.g. clozapine for treatment-resistant psychosis).

The assessment of a young person should identify their stage of psychosis, which can then be used to guide the types of interventions that will be required, taking into account individual needs.

TABLE 1. **THE CLINICAL STAGING MODEL OF PSYCHOSIS**

STAGE	PSYCHOSIS	POTENTIAL TREATMENTS
0	Increased risk/no symptoms	Indicated prevention of FEP, e.g. • Improved mental health literacy • Family education • Drug education
1a	Mild or non-specific symptoms and functional decline	Indicated secondary prevention, e.g. • Formal mental health literacy • Family psychoeducation • CBT • Actively reduce substance use
1b	UHR – sub-threshold	Indicated secondary prevention, e.g. • Psychoeducation • CBT • Substance use work (cessation or harm reduction) • Omega-3 fatty acids • Antidepressants
2	FEP – full-threshold	Early intervention for FEP, e.g. • Psychoeducation • CBT • Substance use work • SGA medication • Vocational rehabilitation
3a	Incomplete remission from first episode of care	Early intervention for FEP As for stage 2, with additional emphasis on medical and psychosocial strategies to achieve remission
3b	Recurrence or relapse stabilised with treatment but still residual symptoms	Early intervention for FEP As for stage 3a, with additional emphasis on relapse prevention
3c	Multiple relapses with clinical deterioration	Early intervention for FEP As for stage 3b, but with emphasis on long-term stabilisation
4	Severe, persistent OR unremitting illness as judged by symptoms, neurocognition and disability criteria	As for stage 3c, but with emphasis on clozapine, other tertiary treatments and social participation despite ongoing disability

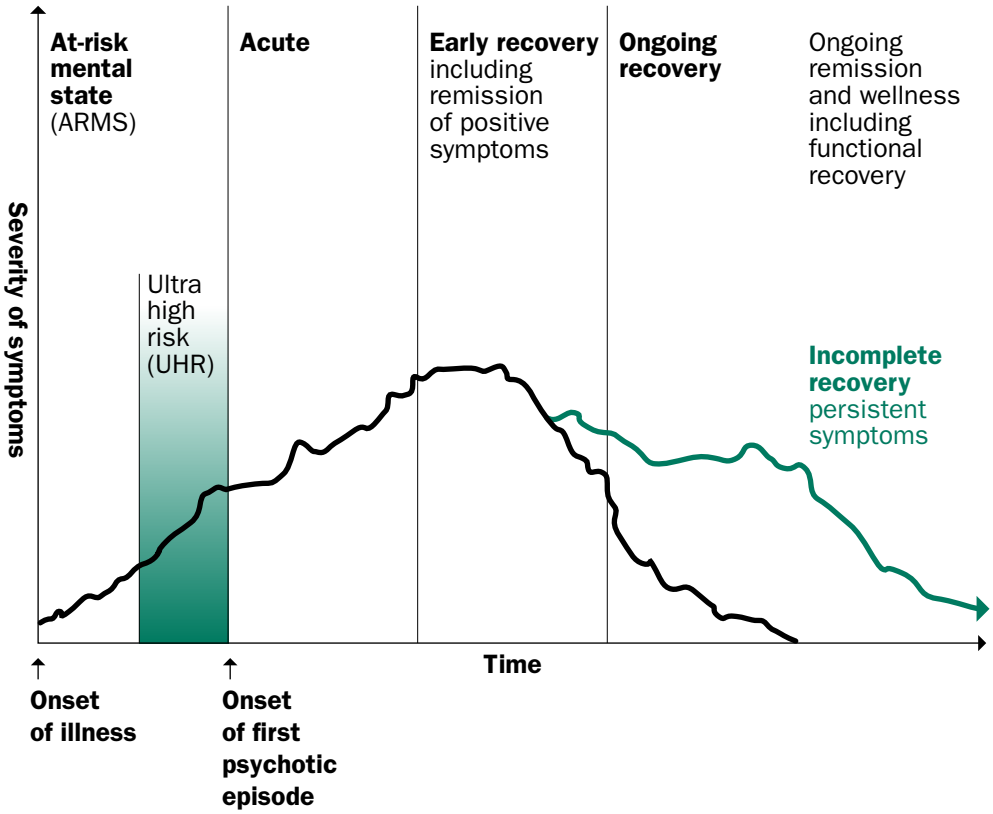
CBT, cognitive-behavioural therapy; FEP, first episode psychosis; SGA, second-generation antipsychotic; UHR, ultra high risk of psychosis.

Adapted from the Australian Clinical Guidelines for Early Psychosis (2010).[1]

The phases model of psychosis and recovery

The phases model describes the course of psychotic illness and recovery as passing through distinct phases. For any individual, the course of their illness as described by the phase-based model may be completely contained within a single stage of the clinical staging model. The phases model is a more qualitative and clinically informative way of describing where an individual is in the course of their illness and treatment. The phases in this model are: at-risk mental state (ARMS, which includes young people at UHR for psychosis), acute, early recovery, late recovery and ongoing or incomplete recovery. Not everyone who is at the UHR phase will transition to a first episode of psychosis, and of those who do, it is expected that some may go on to make a complete or incomplete recovery. The presentation of young people at the different phases has different characteristics and warrants a treatment approach that is mindful of the phase of illness yet tailored to meet individual needs.

FIGURE 1. **THE PHASES MODEL OF PSYCHOSIS**



Working with young people in early psychosis

Working with young people in early psychosis

Introduction

The period of peak onset of early psychosis – adolescence and early adulthood – paradoxically occurs at a time when most young people are experiencing the healthiest phase of their life. In this context, commencing an ongoing medical treatment regimen can be overwhelming for young people, who generally will have had little or no experience of needing to take medication. Adhering to a treatment regimen while dealing with symptoms, side-effects and trying to maintain a semblance of normal adolescent life, requires a lot from a young person. They need to be supported throughout their period of treatment, and the role of providing this support falls to all members of the treating team.

Developmental stage, onset of psychosis and the rationale for early intervention

Late adolescence and early adulthood form a developmental stage that is sometimes associated with considerable turmoil.[3] Specifically, adolescence often involves significant cognitive, neurological, emotional, social, and physical changes (reviewed in Macneil et al. 2009[4]).

Developing any significant health disorder, and a mental health disorder in particular, during early adulthood can be problematic, due to its potential impact on developmental milestones. While adolescence is often defined as a stage in which people increase their independence and autonomy, developing a psychotic disorder clearly has the potential to interrupt and delay this trajectory.[5]

The National Advisory Council on Mental Health's Early Psychosis Feasibility Study Report (2011) also described the potential impact of psychosis. It stated, 'Left unrecognised, untreated, or poorly treated, psychotic illnesses during this critical developmental period not only lead to considerable personal and family distress and increased severity of illness, but also contribute to poor academic performance, premature exit from school and higher education, unemployment, sustained disability and premature death'.[6]

Research has emphasised the importance of early intervention in psychosis, describing a 'critical period' early in the course of psychosis (see Box 1) that is 'particularly malleable to intervention, with major implications for secondary prevention'.[7] A crucial aim of early intervention is to reduce the duration of

untreated psychosis (DUP) in each young person who develops a first psychotic episode. DUP represents the time from onset of continual or intermittent psychotic symptoms until the initiation of treatment. A longer DUP has been associated with worse outcomes in people who experience a first episode of psychosis.[8]

Early psychosis services therefore play an important role in identifying young people developing or at risk of early psychosis and treating it as soon as practicable. International evidence has indicated the effectiveness of specialist early psychosis services to improve symptomatic and functional outcomes,[9-12] lower inpatient admission levels[13] and significantly lower levels of drop-out,[14] at a lower cost than treatment as usual.[15,16]

BOX 1. THE CRITICAL PERIOD HYPOTHESIS

The critical period hypothesis proposes that symptomatic and psychosocial deterioration occurs rapidly in the early years of psychosis and plateaus thereafter.[17] The period of rapid deterioration is seen as a 'critical' period during which the disorder is more responsive to intervention.[18] Therefore, targeted intervention, especially within the first 2–3 and even up to 5 years following a first episode of psychosis, is considered crucial in the prevention of long-term symptomatic and psychosocial disability.[7,18]

Engaging young people in treatment

Engagement is crucial to effective treatment in psychosis, as it is for any other condition where ongoing medication is required. Studies of interventions in young people with early psychosis have shown that improved engagement can lead to better treatment adherence and improved outcomes regarding hostility risk, wellbeing and functioning.[19,20] However, an average of 58% of people fail to make a first outpatient appointment after psychiatric hospitalisation,[19] and approximately 30% of people disengage from services over the long term.[21] Young people in particular appear to be more likely to disengage from services or not attend appointments.[21]

Treatment for psychosis will often involve the initiation of an ongoing medication regimen for the person being treated – using psychotropic medications that can cause substantial side-effects if used inexpertly. For young people experiencing a first episode of psychosis, this can be a particularly difficult and even frightening process. It is unlikely they have had much experience of having to take medicine on a daily, ongoing basis. Furthermore, there is significant stigma attached to antipsychotic medication, and this, along with physical side-effects, can affect a young person's development both socially and biologically. Treatment choice is therefore crucial, and the effect of medication choice on engagement must be considered (see 'Key practice point', over the page).

‘I wanted to try every other kind of thing before actually turning to medication. So I think that [doctors] need to not be forceful with it and just accept that it might take some time, or that [a young person] might never go on medication, and that’s their choice.’

– Young person,
EPPIC, Orygen Youth Health Clinical Program.

KEY PRACTICE POINT: **CONSIDER THE EFFECT OF MEDICATION ON ENGAGEMENT**

A key factor that will positively influence a young person’s engagement with treatment is that the treatment makes them feel better, not worse. For example, when a young person is first referred, it is preferable to use benzodiazepines as first-line treatment for agitation and distress caused by the psychotic episode, followed by antipsychotic medication as needed for psychotic symptoms. Likewise, side-effects of medication need to be managed so that they are not perceived to outweigh any benefits of medication. See also ‘Start low, go slow’ on page 51 and ‘Physical health management and monitoring’ on page 100.

There are a number of other considerations that impact on the willingness or ability of a young person with early psychosis to engage with a mental health service and with medical treatment. These include:

- Young people are often not ‘help-seeking’, and may have been brought to an early psychosis service through the intervention of family, carers, police or hospital emergency departments rather than through their own volition.
- Adolescence is otherwise a time of best health for people, and contact with an early psychosis service may be a young person’s first encounter with a health service since childhood.
- The ‘immortality of youth’ can make the idea of having to attend a health service challenging for young people.
- Mental ill-health still has considerable stigma, especially for young people because they don’t want to be ‘different’ from their peers and may therefore avoid contact with psychiatric services.
- Young people may have misleading ideas about what mental health treatment involves, based on media portrayals of mental ill-health.
- Becoming reliant on a service may represent a loss of independence at a time when most young people are beginning to achieve the developmental goal of individuation and separation from authority figures.

- Factors related to trauma (this can be from previous trauma, trauma caused by the experience of psychotic symptoms and/or trauma caused by admission) can be a deterrent to further engagement and/or treatment.
- Substance use may make a young person unwilling or unable to engage with mental health services.

Efforts therefore need to be made to engage young people and their families from their first point of contact with an early psychosis service. A relaxed, non-judgemental, collaborative and youth-orientated approach will assist with this.

It is important to ensure that young people and their families have access to information about the risks of not receiving treatment, including appropriate medications. Clinicians should highlight to young people identified as UHR of psychosis that rates of transition to a first episode of psychosis are lower for people who seek help and engage with an early intervention service (see page 68).[22]

Involuntary treatment

If a young person is difficult to engage, the service and clinicians should work hard to engage the young person, taking an assertive and flexible approach, working with their family and others. They should not simply discharge the young person because of non-attendance. Sometimes, despite the best efforts of the service and others, it is not possible to engage a young person, and use of legislation to support compulsory assessment and/or treatment under the Mental Health Act should be considered. If this is not felt to be appropriate because the risks are not significant enough, the young person should be carefully monitored by the early psychosis service, in partnership with the young person's primary care provider or GP. They should NOT be discharged back to their GP or another service if psychosis is suspected. If no improvement in engagement occurs and psychosis persists, this is an indication for involuntary treatment initially at least. Many services reserve involuntary treatment for young people who display a high level of risk to self or others; however, untreated psychosis poses severe risks to self and others and is a medical emergency. Individual services are advised to develop a local disengagement policy to be followed and documented.

For more information on engaging young people, see the ENSP manual *Get on board: engaging young people and their families in early psychosis*.

The importance of a collaborative approach to working with young people

The involvement of people in decision-making regarding their own medical treatment, including consideration of their preferences, is becoming increasingly recognised as a core component of practice in all areas of health care.[23] It is therefore not enough to prescribe medication and expect a young person to adhere to whatever regimen is given. They must be consulted and engaged in the decision-making process, and clinicians should strive to build a trusting, honest and egalitarian therapeutic relationship with each young person they treat. This collaboration is essential to working effectively with young people in early psychosis.

The collaborative process should include the young person, their case manager, their family, the medical team, the multidisciplinary team and any other key people, professionals or services that are central to the young person's life.

It should be assumed that a young person's family is involved in discussions of treatment strategies, and this should be the default unless the young person does not want their family to be involved; however, any reluctance for family involvement should be revisited throughout the episode of care. Clinicians should explain to the young person the importance of family involvement, but also make it clear that the amount of information shared with their family can be tailored to the individual (see 'Confidentiality', below).

The aim should always be to have an informed, shared decision-making process regarding the young person's treatment. Shared decision-making is a flexible process that aims to improve the young person's involvement and satisfaction with treatment decisions by promoting the selection of treatment based on the young person's preferences and their needs as well as medical evidence. An example of a tool that could help with shared decision-making is a medications table that compares the doses and side-effects of different antipsychotic medications, as well as how they are thought to work, how long the young person should take them for, and how they should discontinue taking them.

> 'I felt that I was forced to take medication. Like, every time I saw my doctor we'd reassess. And the reassessment was basically them going, "Yep, you should be on medication," and me going, "I don't want to be on medication," and they'd go, "Well let's keep trying until the next assessment". I'd rather they asked me, and had more of a plan, like, "Let's try this for a month and see ..."'
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

A young person's capacity to make decisions about treatment must be assessed and considered when planning interventions. Many factors may influence this capacity, some of which are disorder-related (e.g. poor insight, cognitive difficulties) and therefore temporary. It is therefore essential to reassess capacity regularly and to be aware that this is not an 'all or nothing' concept: a young person's capacity may be limited in making decisions about one aspect of their life, but not all.

Confidentiality

Young people are often apprehensive about how information about them will be shared, particularly information relating to sexual health and drug use. A commonly voiced concern is the degree to which information they have disclosed will be discussed with their parents or guardians. Clinicians need to make sure that it is clear from the outset which information is confidential and the circumstances under which it may be disclosed (e.g. where there is significant danger or concern for the young person's safety or the safety of others). If the young person is reluctant to have their family involved in their treatment, it is especially important to be clear about what information might be shared with their family and how. In cases where confidentiality needs to be broken, this should be discussed with the clinical team first and reasons for the breach recorded in the case notes. For more information on this topic, refer to the ENSP manual *In this together: family work in early psychosis*.

Practical challenges of working with young people

Working with young people presents a number of practical challenges. For example:

- The typical 50-minute consultation may not be enough for a thorough assessment. It may not be possible to get all the required information from the first consultation, and clinicians may instead need to focus on engaging the young person and trying not to 'interrogate' them, and schedule another appointment to finish the assessment.
- Engagement may be an issue. If this is the case, clinicians should try to organise what is essential. The first consultation may only be an assessment of risk and establishing a structure to enhance further assessment.
- Young people are likely to be unfamiliar with the assessment processes, especially if they have not had contact with mental health services before. Clinicians should try to set the scene for them at the beginning of the first consultation; this will include explaining why it is necessary to ask them a lot of questions.
- Appointments may need to be rescheduled at short notice. Clinicians should be flexible about the timing of appointments and be prepared to reschedule if the young person (or their family) arrives late or needs to leave early because it is important that they are seen.

Clinicians should try to manage consultations in a youth-friendly manner, avoiding unnecessary medical jargon. Skills for engaging young people take time to develop, and individual clinicians will have their own particular style that should be honest, empathetic, non-judgmental and yet still assertive.

Flexibility in the service provided is also needed. Clinicians should be able to deal with crises and be prepared to engage with young people in less conventional ways than face-to-face interviews, for example phone interviews. The early psychosis service should not be too focused on outpatient visits and clinics for assessments.

SUMMARY

The importance of early intervention in psychosis

- The onset of a psychotic episode can impact the normal developmental trajectory of young people.
- Early intervention is crucial, to reduce DUP, begin treatment during the 'critical period' and give young people the best chance of recovery.
- Early psychosis services have been shown to improve outcomes and reduce hospitalisation and drop-out rates.

Engaging young people

- Young people who are engaged with services and their treatment have better adherence and outcomes.
- Effort needs to be made to engage young people and their families from the first time they come into contact with an early psychosis service.
- If a young person with suspected psychosis does not engage with an early psychosis service, they should be carefully monitored by the service, in partnership with the young person's primary care provider. They should NOT be discharged back to their GP or another service.
- A collaborative approach is essential. Clinicians should involve young people and their families in decisions about medication and treatment plans, ensuring they are well informed and consulted about treatment options.
- Clinicians should try to manage consultations in a youth-friendly manner, avoid unnecessary medical jargon and be empathetic, honest and non-judgemental.

Assessment, formulation, diagnosis and risk

Assessing young people in early psychosis

Principles of assessment in early psychosis

Assessment, formulation and diagnosis in early psychosis are often complex, challenging and time-consuming. Engaging the young person in treatment can be difficult, distressing and may require the use of the Mental Health Act. The support and information needs of the young person and their family are high, and a considerable amount of time needs to be devoted to explaining the condition, the risks and the treatment options. Therefore, each young person within an early psychosis service must be assigned to a consultant (along with the medical staff under their supervision) from the outset and ideally remain with that consultant throughout their contact with the service (see also 'Service level considerations' on page 112).

The purpose of data-gathering, clinical assessment and appropriate investigations is to build up a picture of why this individual has presented with this disorder at this time. A comprehensive biopsychosocial approach, with contributions from all members of the multidisciplinary team, is important to this formulation. Specific skills the psychiatrist can offer include:

- the ability to exclude medical, or 'organic', presentations of psychosis
- recognition of developmental disorders, learning disabilities or comorbid conditions, including medical conditions, anxiety disorder, substance use or personality disorder.

They can also contribute to the construction of a comprehensive and collaborative risk assessment or management plan. It is important to include the young person's view of the illness and their attitudes to treatments, as this will affect the management plan.

The following sections cover the process of assessment in an early psychosis service and the role of psychiatrists. They include initial assessment, extended assessment and the specific investigations involved. Further detail about conducting early psychosis assessments can be found in the ENSP manual *'Let me understand': assessment in early psychosis*.

Initial assessment

In the EPPIC Model, young people referred to the service are first seen by the intake team to determine whether they are eligible for an initial assessment by the service (e.g. if they meet age or location criteria for entry to the service). If they are not deemed to need assessing for psychosis, a warm referral should be made to another, appropriate service and the young person actively enagaged with the service.

The initial assessment may take up to 6 weeks to complete, though a good picture of the young person's presentation needs to be assembled quickly after referral. All young people deemed eligible for assessment at intake (see Figure 2) should be seen within 24 hours by an early psychosis clinician after referral. If a young person is acutely unwell, or a high level of risk has been identified, they should also be seen by a doctor as soon as possible within 24 hours. A medical review should take place for all others within 48 hours of referral. The young person should then be seen by the team's consultant psychiatrist within 1 week.

In the initial medical review, clinicians should discuss with the young person the possible medical investigations that will be needed to determine if the psychosis has an organic cause. Doctors should organise medical investigations as appropriate as soon as possible after this first meeting (see 'Medical investigations in assessment of early psychosis' on page 24). A written summary describing the outcome of the first psychiatric appointment should be sent out within 2 weeks to the young person's GP; however, important information, such as the young person's risk assessment, should be communicated earlier as appropriate.

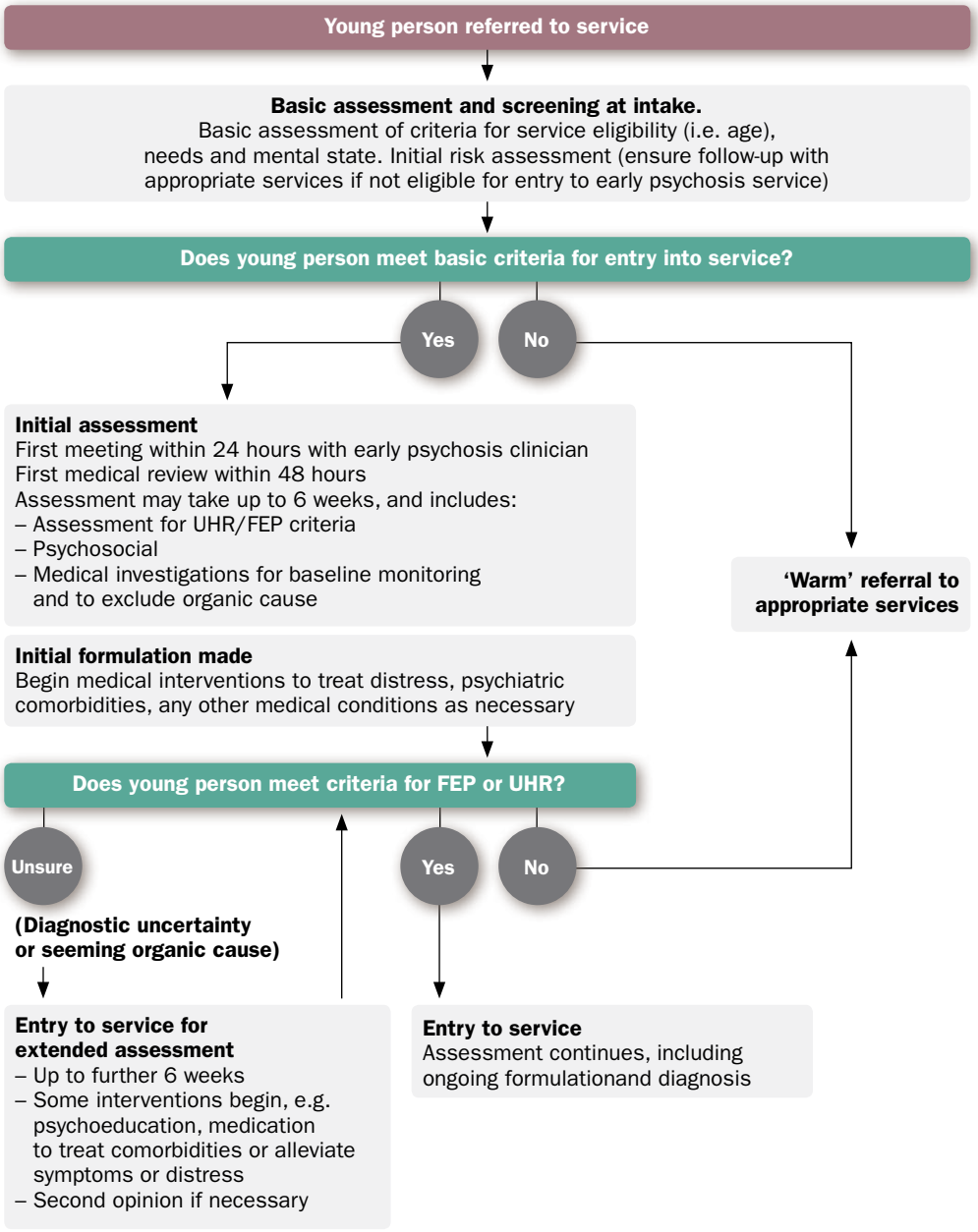
One member of the clinical team should be allocated to carry out the ongoing assessment, depending on availability or whether assessment requires specialised skills in a particular area (e.g. autism spectrum condition). The allocated clinician should liaise with other agencies or key people that are involved (e.g. the young person's family, social services, existing child or adult mental health teams, the young person's GP) to aid formulation and develop a risk management plan (see page 35). The initial assessment should include:

- a thorough history to obtain information relating to symptom onset, duration, type, severity and associated impairment and distress
- collateral history from family or other supports and from GP records is essential, as the young person with FEP may have limited or no insight into their difficulties.
- other important historical information, such as substance use, medical and psychiatric history, social, family and developmental history and forensic and risk history
- assessment of the young person's mental state, focusing on behaviour, mood, psychotic symptoms and insight, to support the historical information and aid diagnosis
- consideration of the young person's physical health issues
- discussion and consideration of medication with the young person, if appropriate
- assessment for medical presentations of psychosis.

The aims of the initial assessment include:

- distinguishing young people who are possibly experiencing FEP or who are UHR for psychosis from those with other non-psychotic conditions or organic psychosis (see Box 2)
- detection of any comorbidities
- biopsychosocial formulation with the multidisciplinary team of the young person's presenting problems
- agreement on a treatment plan made in collaboration with the young person and their family.

FIGURE 2. **ASSESSMENT ALGORITHM FOR EARLY PSYCHOSIS SERVICES**



It is important for clinicians to maintain a low threshold of suspicion for psychosis, as a first presentation before significant illness progression may represent an important opportunity to intervene while the young person retains some insight, allowing greater collaboration in planning treatment and better risk management.

Assessment of risk and formulation of a risk management plan should also be commenced as soon as a young person makes contact with an early psychosis service, due to the elevated risk of suicide and violence in the early stages of early psychosis. The initial risk management plan can be built on and elaborated as a young person's assessment, treatment and recovery progress. Details of how to assess risk in a young person are covered in 'Risk assessment and management' on page 35.

BOX 2. **ORGANIC PSYCHOSIS**

Approximately 3% of people who present with suspected FEP have some degree of organic psychosis; that is, psychosis resulting from medical conditions known to cause psychotic symptoms. Medical conditions that can present with psychosis include systemic lupus erythematosus (SLE), HIV infection, multiple sclerosis, epilepsy, sleep disorders, space-occupying brain lesions, some metabolic conditions and neurological conditions such as anti-NMDA receptor encephalitis. Young people with potential organic causes of psychosis should be seen promptly by relevant specialists and the underlying condition treated. They may still require treatment strategies similar to that provided for either non-affective or affective psychosis and sometimes may still be appropriately followed up within an early psychosis service alongside specialist medical care.

On completion, initial assessments should inform the team decision as to whether the young person meets the criteria for UHR or FEP and is therefore suitable for entry into the early psychosis service. The initial management plan should be communicated with the young person, their family, their GP, the referrer and other key agencies involved. There should be regular documentation in electronic and paper-based patient records to reflect this activity and management plan.

If there is reasonable doubt regarding the diagnosis (e.g. due to comorbidities such as autism spectrum condition or chronic drug intoxication), or if the available information suggests FEP, but the assessment is incomplete because of difficulties with engagement, the young person may be taken on for an extended assessment period of up to a further 6 weeks. This outcome should be communicated with the young person, their family, their GP and the referrer.

The assessment period will also likely involve some initial work to ameliorate presenting problems and reduce risk. This may include psychological intervention, family work, social or vocational work and medication. The assessment period also offers a good opportunity for engagement with the young person and their family. They should all be provided with psychoeducation, and if any members of the family are identified as having specific needs these should be dealt with by an appropriate agency (e.g. family specialist worker, the family member's GP, social services).

Young people who do not meet the criteria for entry into an early psychosis service should be actively engaged in another service (or part of the existing service) that best meets their needs. A copy of the initial assessment and any recommendations that have been made should be provided to the new service provider. It is important that no young person is left without a transfer of care where there are identified problems or needs.

It may become necessary to involve acute services, including hospital emergency departments, external services such as a crisis intervention team (depending on where the person lives) or an inpatient unit at some point during the assessment period. In emergency situations, the police can be involved if an immediate response is required to manage risk. Thereafter, use of mental health legislation to assess for compulsory treatment may be required. In some instances the young person may already be involved with acute services at the point of referral to the early psychosis service, in which case the two services should work jointly for a period before arranging a comprehensive handover.

Psychometric measures for assessment

Specialist psychiatric assessment tools are available to evaluate psychotic symptoms and quantify their severity, including:

- the Positive and Negative Syndrome Scale (PANSS)
- the Brief Psychiatric Rating Scale (BPRS)
- the Scale for Assessment of Negative Symptoms (SANS)
- the Comprehensive Assessment for At-Risk Mental State (CAARMS).

Scales for measuring functioning include the Social and Occupational Functioning Assessment Scale (SOFAS).

Specialist mental health professionals generally use these scales to aid diagnosis and measure the response to treatment. While specialist assessments of cognitive difficulties by a psychologist can be important, such resources may not be widely available.

If psychosis is determined, this should always be confirmed by a consultant psychiatrist with training and expertise in early intervention. Diagnosing a psychotic disorder is a serious undertaking that potentially has life-long implications and risks for the young person. There are also significant medico-legal challenges and it is important that staff are not exposed to undue liability.

Medical investigations for assessment of early psychosis

As approximately 3% of people referred with suspected FEP may in fact have psychosis from an organic cause (see Box 2),[24] it is important to screen for such causes during assessment by physical examination and biological investigations. These investigations will also serve to establish a medical baseline so that the young person can be monitored for physical and biological morbidity related to medication. Non-invasive medical investigations could also be used in the UHR group to exclude organic causes.

A suggested medical assessment is outlined in Box 3. This is not an exhaustive list, but provides an initial work-up for early psychosis; additional tests should be considered based on a young person's history or risk factors. Some tests have a stronger cost–benefit argument than others. Other potential investigations may be indicated, especially when physical or neurological symptoms are evident. Brain imaging by magnetic resonance imaging (MRI) should be carried out, especially if there are any focal neurological signs, history of head injury, cognitive decline or a syndromic presentation (see Table 2).

KEY PRACTICE POINT: **ALL YOUNG PEOPLE WITH FEP SHOULD BE FULLY INVESTIGATED FOR ORGANIC CAUSES**

It is crucial that clinicians organise a full medical investigation – including MRI – for all young people with suspected FEP to rule out an organic cause of psychosis. This first period of contact with an early psychosis service may represent the only opportunity to discover any biological cause. It is quite possible that once someone enters the mental health system they will not be thoroughly investigated again for organic psychosis; if such a condition is missed initially, they may spend years on unnecessary treatment and without proper treatment for their condition.

Readers are referred to Freudenreich et al. (2009) for a detailed review of medical investigations for FEP.[24]

TABLE 2. **ARGUMENTS FOR AND AGAINST THE USE OF MRI IN MEDICAL INVESTIGATIONS FOR FEP**

FOR	AGAINST
MRI can substitute for other screening (e.g. temporal lobe sclerosis of epilepsy; metabolic disorders affecting white matter)*	Low yield (< 8% may require referral)
Medico-legal (e.g. missed brain tumour)	Many incidental findings
Baseline for chronic disorder	Abnormal finding does not establish causality
Negative scan establishes 'functional' nature of psychosis, provides reassurance and helps young person and family to accept diagnosis.	

*Not empirically validated.
MRI, magnetic resonance imaging.
Adapted from Freudenreich et al. (2009)[24]

Physical examination at baseline and ongoing monitoring are important to recognise abnormalities at first presentation, and later as a consequence of medication prescribed. People with mental illness (especially psychosis) are known to have greatly increased physical morbidity. It is important to recognise that individuals with psychotic illnesses have a significantly reduced life expectancy, mainly due to cardiovascular risk factors, and therefore healthy lifestyle must be promoted.[25] Antipsychotic medications may cause additional cardiometabolic side-effects, including diabetes/pre-diabetes and dyslipidaemia (see 'Physical health management and monitoring' on page 100).

BOX 3. RECOMMENDATIONS FOR MEDICAL INVESTIGATIONS IN EARLY PSYCHOSIS

The following are recommended for all young people admitted to an early psychosis service (UHR and FEP).

Physical status

Physical exam

- Neurological examination
- Weight, waist circumference, waist/hip ratio and BMI

Vital signs

- Blood pressure, pulse, temperature

Medical history

Family history, notably of cardiac or lipid abnormalities and diabetes

Smoking history

History of alcohol and other drug use

Physical activity levels

Menstrual history and possibility of pregnancy

ECG (if cardiac risk)

Laboratory tests

Haematology

Electrolytes, including calcium

Renal function (blood, urea, nitrogen; creatinine ratio)

Liver function tests

Erythrocyte sedimentation rate (ESR)

Antinuclear antibodies (ANA)

Fasting glucose

Lipid profile

Prolactin level

Consider hepatitis C if risk factors present

Urine drug screen

BOX 3. **RECOMMENDATIONS FOR MEDICAL INVESTIGATIONS IN EARLY PSYCHOSIS** CONTINUED

The following are recommended only for those young people with suspected FEP.

Laboratory tests

Tests for other treatable disorders

- Thyroid function tests (basal thyroid-stimulating hormone, total and free triiodothyronine/thyroxine)
- Serum copper and ceruloplasmin for Wilson's disease
- Fuorescent treponemal antibody absorbed (FTA-ABS) for neurosyphilis
- Vitamin B12/folate
- HIV

Neuroimaging

MRI (see Table 2)

Other tests

Expand aetiological search if indicated, for example:

- EEG, chest X-ray, lumbar puncture, karyotyping, heavy metal testing

Expand medical monitoring if indicated (e.g. eye exam if risk factors for cataracts)

Adapted from Freudenreich et al. (2009).[24]

Cognitive assessment

Cognitive impairment is a common feature of schizophrenia and often appears before the onset of psychosis.[26,27] It may persist throughout life, regardless of whether there is remission of psychosis, and is correlated with functional outcomes.[26,27] Cognitive impairment in young people may be of particular importance because it interferes with a critical period of time for social, emotional and academic development, potentially impacting on the trajectory of attainment of occupational functioning, social development, academic achievement and independent living.[27]

Although clinicians often prefer to defer cognitive assessments until a degree of clinical stability has been achieved, an assessment of cognitive functioning should be made in all young people at initial presentation at an early psychosis service. Even a short neurocognitive assessment can help treatment options to be appropriately tailored to each person. It can also help focus interventions

(e.g. emotion recognition) and inform diagnosis.

Formulation and diagnosis

Following a comprehensive assessment of a young person presenting with a possible psychotic episode, clinicians should then begin to consider the underlying aetiology of the presentation, using a formulation-based approach. The first step for this is to ascertain the stage of illness, based on following criteria.

Criteria for UHR of psychosis

Pre-psychotic symptoms may last for weeks or months, with the ARMS/UHR period often characterised by non-specific symptoms and behaviours, such as sleep disturbance, mood changes, irritability and social withdrawal. In addition, sub-threshold psychotic-like symptoms (e.g. suspiciousness) and mild perceptual disturbances (e.g. fleeting or low-intensity auditory hallucinations) are usually accompanied by a decline in overall social functioning. Individuals may or may not seek help for their symptoms during this period.

The specific criteria for UHR can be catergorised into three groups (Box 4). To be identified as UHR, a young person must meet the criteria of one of these groups, in addition to being help-seeking and having shown a significant decline in functioning (see Figure 3).

An objective measurement tool, such as the Comprehensive Assessment for At-Risk Mental State (CAARMS), can be useful in identifying these help-seeking young people. For further information on the CAARMS tool and how to use it see the ENSP manual *The CAARMS: assessing young people at ultra high risk of psychosis*. The EPPIC Model includes interventions for help-seeking young people who meet the UHR criteria and should therefore be assessed and receive the most appropriate interventions. See ‘Management during the UHR phase’ on page 68 for further information.

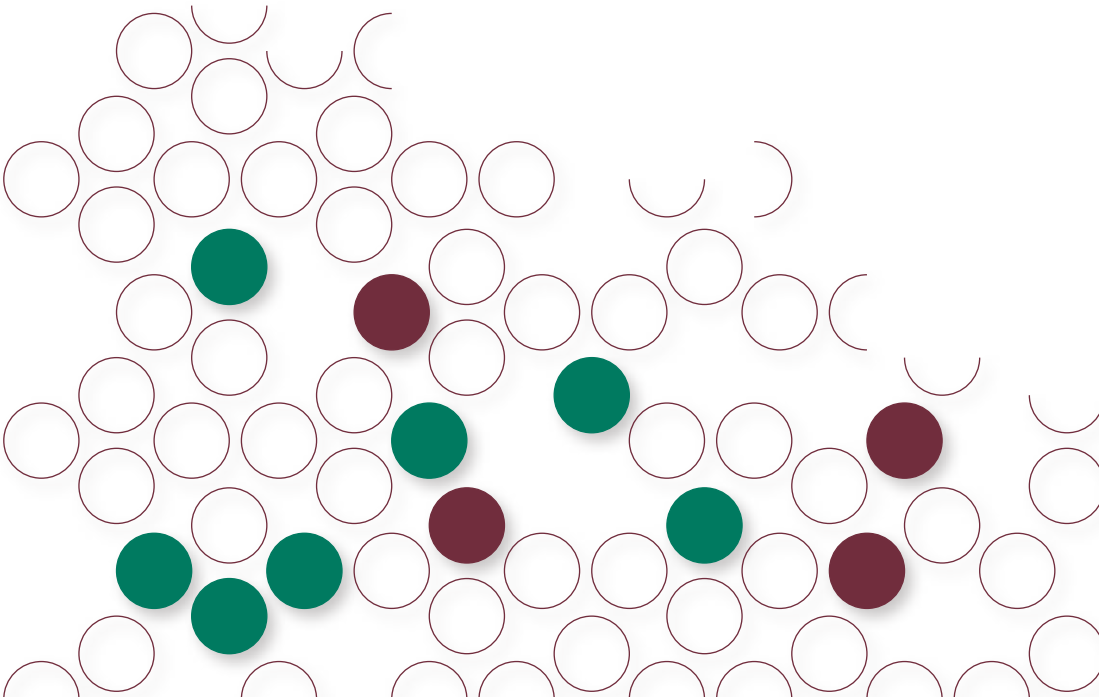
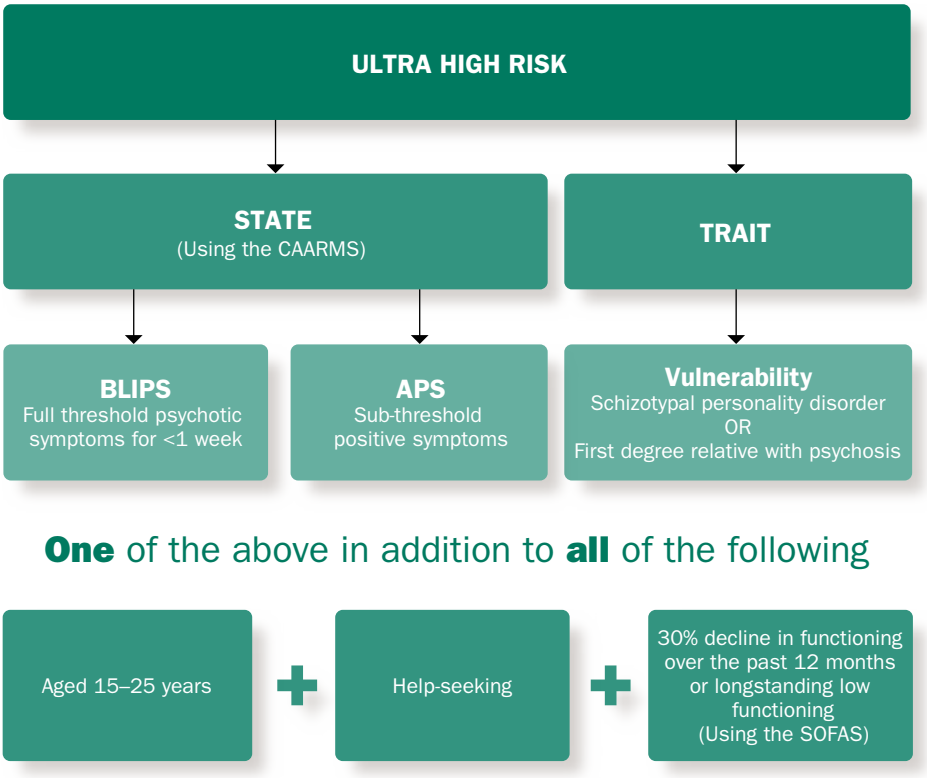


FIGURE 3. **CRITERIA FOR IDENTIFICATION OF A YOUNG PERSON AS UHR FOR PSYCHOSIS**



APS, attenuated psychotic symptoms;
BLIPS, brief limited intermittent psychotic symptoms.

BOX 4. **GROUPS USED TO IDENTIFY YOUNG PEOPLE AT UHR FOR PSYCHOSIS**

Young people must meet the criteria for ONE of these groups PLUS the criteria outlined in Figure 3 to be considered as UHR for psychosis

1. Vulnerability Group

Family history of psychotic disorder in a first degree relative (e.g. mother, father, brother, sister); or

Presence of a schizotypal personality disorder

Must also be associated with a significant decline in functioning or chronic low functioning

2. Attenuated Psychosis Group

Group 2a)

- Attenuated psychotic features at sub-threshold INTENSITY for psychosis
- Overvalued ideas, mild paranoia, perceptual distortions
- Frequency:
  - at least 2 per week of more than 1 hour duration (scores 3–6 on CAARMS); or
  - 3–6 per week of less than 1 hour duration
- Duration: at least 1 week
- Within the last 12 months
- Must also have a significant decline in functioning or chronic low functioning

OR

Group 2b)

- Psychotic symptoms at sub-threshold FREQUENCY for psychosis
- Delusions, hallucinations at higher intensity
- Frequency:
  - 2 per week of more than 1 hour duration (scores 3 on the CAARMS); or
  - 3–6 per week of less than 1 hour duration
- Within the last 12 months
- Must also have a significant decline in functioning or chronic low functioning

3. Brief limited intermittent psychotic symptoms (BLIPS)

- Frank psychotic features
- Resolve spontaneously within 7 days (i.e. WITHOUT antipsychotics)
- Within the last 12 months
- Can be drug-induced but not due to drug intoxication. Only include psychotic symptoms that do not occur exclusively during peak intoxication

CASE SCENARIO **JASMINE**

Jasmine is a 24-year-old woman who has been living with her parents since dropping out of art college 2 years ago. She managed to complete the first 2 years of the 3-year course and was known as a lively, sociable student. During the final year of her course, Jasmine became socially withdrawn and interested in spiritual matters; she was not previously a spiritual person. She was finding it increasingly difficult to focus at college and could not keep up with her assignments. Eventually, following the advice of her tutors, Jasmine agreed to defer her studies, but planned to return the following year.

Since returning to her parents' house, Jasmine has withdrawn to her bedroom. She sleeps excessively and eats regular meals that her mum cooks. Both Jasmine's parents work during the day, which means that Jasmine is alone for most of the day. Jasmine has two brothers and a sister, all older than her, who have left home already. One brother has a confirmed diagnosis of schizophrenia and lives in supported accommodation nearby.

Jasmine's parents become worried that their daughter is depressed or using drugs. Jasmine denies both of these, saying she is simply 'waiting to see what the world has in store' for her. Jasmine acknowledges some difficulty concentrating, but agrees only to take a multivitamin supplement.

At this stage, possible causes of Jasmine's presentation are:

- Depressive episode
- Drug use (e.g. cannabis) with amotivation
- At-risk mental state
- Emerging first episode psychosis

Criteria for FEP

Criteria for a diagnosis of FEP are somewhat arbitrary and vary internationally. Admission to an EPPIC Model service is based on a clinical assessment that determines that a young person has experienced definite full threshold FEP as indicated by the presence of full threshold psychotic symptoms (hallucinations, delusions or formal thought disorder), which are present for longer than 7 days within the previous 2 months.

Note that psychotic symptoms must have been experienced every day for more than 7 consecutive days, or for periods of longer than 1 hour per occasion on 3–6 days in a week in order to meet the psychosis threshold.

Where there is doubt about the veracity or severity of reported psychotic symptoms, the following are also required:

- functional decline or sustained low functioning (30% drop in SOFAS score maintained for 1 month within the last 12 months, or SOFAS score lower than 50 for the last 12 months or more), and/or
- significant distress associated with the psychotic symptoms.

These cases will require assessment or review by a consultant psychiatrist to determine (a) if the young person is accepted into the service, and if so, which stage of illness or (b) whether the young person will be referred out of the service and actively engaged in a more appropriate service. The young person, the family and the new service provider need to be informed that the young person can be reassessed if the clinical situation becomes clearer or changes.

CASE SCENARIO **JASMINE** CONTINUED from page 31

Four weeks later, Jasmine begins to display unusual behaviours, such as adopting strange postures, talking to herself and unplugging all the phones in the house. She is staying awake most of the night and sleeps during the day and has stopped eating, not drinking much either. Jasmine's parents call the family GP, who makes a home visit. Jasmine tells the doctor that she is being 'controlled' – perhaps by government secret agents – and that she can hear them talking to her. She believes the house has been bugged, which is why she unplugged all the phones. Jasmine does not believe she has any mental health problems and becomes agitated when the doctor suggests she needs to see a mental health team and think about getting some help. The visit ends with Jasmine shouting at the GP and telling her to get out of the house, slamming the door after her.

Jasmine needs urgent assessment and treatment given the likelihood of psychotic illness, demonstrated by her self-neglect, agitation, threatening behaviour and description of psychotic symptoms.

As Jasmine's GP, what would be your management plan at this stage?

- Referral to local early psychosis service for specialist crisis intervention and assessment.
- Consider the use of the Mental Health Act if risks are of a level of concern to warrant its use.

Diagnostic uncertainty

The initial diagnosis in FEP is not particularly stable, except for individuals with clear schizophrenia or psychotic mania presentations.[28] For this reason, a certain level of diagnostic uncertainty in early psychosis should be tolerated. In addition, hasty diagnosis can lead to misdiagnosis and incorrect or even harmful treatment, and early labelling (for example with a diagnosis of schizophrenia) can lead to self-stigmatisation or lowered expectations from mental health professionals.

Given that a diagnosis is, however, required so the psychosis can be treated, the term 'first episode of psychosis' is necessary and sufficient for selecting a working diagnosis. This term encompasses a broad range of possible disorders, is less stigmatising and does not directly imply any particular prognostic trajectory. In this way, the clinician can treat the symptoms of the presentation while continuing to assess and encourage the young person and ensure that a message of hope is promoted to the young person and their family from the very beginning.

Not everyone will be comfortable with the concept of diagnostic uncertainty. Other clinicians, the young person, or their family may insist on being given a definitive diagnosis. It is important to understand the young person and their family's need for information during the first stages of their contact with an early psychosis service, and that being given a diagnosis can be an important part of that need. However, it is critical to explain the nature of psychiatric diagnosis and how it is essentially descriptive and a guide only to treatment and prognosis. Some approaches that can help explain diagnostic uncertainty and help people be more comfortable with an uncertain diagnosis include:

- providing an initial diagnosis of 'first episode psychosis' and explaining this may change further on
- providing psychoeducation about why it isn't possible to always give an exact diagnosis
- explaining that you wish to reduce stigma by avoiding early labelling of the young person
- emphasising that it is more important to focus on treating symptoms rather than making a fixed diagnosis.

Once FEP is suspected, ideally a 48-hour period of antipsychotic-free observation should be arranged, unless the risks to the young person are too great or the psychotic symptoms have clearly been present for an extended period of time (see 'Evidence for an antipsychotic-free period of assessment' on page 47).

Differential diagnosis

The steps towards making a diagnosis should include:

1. Rule out organic psychosis.
2. Distinguish affective from non-affective psychosis, especially mania, as this changes the treatment strategy significantly (see page 74).
3. Identify the stage of the psychosis.
4. Identify any comorbidities.

The range of disorders presenting as FEP are as follows:[29]

- schizophrenia spectrum disorder
- affective psychoses (bipolar and unipolar disorders)
- schizoaffective disorder
- delusional disorder
- acute and transient psychotic disorder
- drug-induced psychosis
- organic psychosis
- post-traumatic stress disorder (PTSD)
- obsessive-compulsive disorder (OCD)
- autistic spectrum condition (e.g. Asperger's syndrome).

Substance use and psychosis

A significant number of people with FEP will be using drugs before and at the time of the onset of their illness. It may be that the psychotic symptoms displayed by a young person result from, or overlap with symptoms of, substance use. Where substance use is suspected to be contributing to psychotic symptoms, the distinction needs to be made between acute intoxication and drug-induced psychosis.

Acute intoxication is directly related to the effects of the substance and should resolve once the substance is cleared from the body. Drug-induced psychosis persists longer than intoxication would be expected to, and the effects may last for a number of days; however, a full recovery should occur within 28 days of abstinence. It is important not to underestimate the seriousness or be dismissive of drug-induced psychosis, as a significant number of young people with such presentations go on to develop a primary psychotic disorder, for example, schizophrenia or bipolar disorder.[30] All young people presenting with FEP must be followed up for the 2-year period provided for by the EPPIC Model, including those experiencing drug-induced psychosis.

CASE SCENARIO **SHAUN**

Shaun is a 21-year-old young man who has been using cannabis since he was 14. Over the past two years he has been smoking daily as well as using amphetamines at weekends. He has dropped out of college but still lives in shared student accommodation and enjoys partying with his college friends. Shaun has been taken to hospital with a psychotic presentation on five occasions during the past year, with brief admissions of less than a week on each occasion. His medical records emphasise his drug use and he is therefore formulated as having a drug-induced psychosis.

After being discharged from his fifth hospital admission, Shaun rapidly disengages from community follow up. On his sixth admission, he assaults a member of staff and is transferred to a psychiatric intensive care unit, where he remains in a contained environment. He is carefully assessed and found to be experiencing a primary psychotic disorder, which has been under-treated for the past year because of the assumption, perpetuated by his medical records and previous treating clinicians, that he had drug-induced psychosis. Shaun is commenced on a low-dose oral second-generation antipsychotic and given a range of psychosocial interventions to address his needs, including support to abstain from drugs. Because of these interventions, Shaun is able to make a good recovery.

Risk assessment and management

Overview

Young people with early psychosis may be exposed to risk from a number of sources relating to the illness, their environment or individual factors such as personality traits. Ideally, once identified, these risks would be eliminated; however, this is often not possible. Managing risk is therefore a critical part of treatment. A strong commitment by clinicians and early psychosis services to engaging each young person and to providing the best care possible should inform all risk management – optimal care is the best antidote to risk.

Assessing and identifying risk

For a particular risk to be managed it must first be identified – this is the purpose of risk assessment. A risk assessment should be carried out following a young person's first contact with an early psychosis service, with the initial assessment reviewed following each subsequent contact and after any major events that occur in the young person's life, such as an inpatient admission, instances of self-harming, the young person's becoming homeless or the ending of a relationship. The broad categories of risk that should be considered in an assessment include:

- risk to self, including:
  - risk of self-harm and suicide
  - intentional and non-intentional harm
  - physical and non-physical harm (e.g. risk to reputation, psychological risk due to disinhibition)
- risk to others, including:
  - aggression, violence and homicide
  - threats of harm, verbal and physical aggression
  - general risk to others (e.g. driving while acutely unwell)
- risk from others:
  - victimisation, neglect and vulnerability
  - environmental risks (includes homelessness, substance use, non-violent offending)
- risk of non-adherence and disengagement
  - risk of treatment non-adherence
  - risk of absconding and disengagement
  - risk of delayed recovery/treatment resistance/chronicity.

This list is not exhaustive, and risk assessments need to be creative and well thought-out. They should be personalised to include risks that are specific to each young person. Structured risk assessment tools such as the HCR-20[31] or the SAVRY (for under-18s)[32] are used to assess risk of violence and can inform development of a risk management plan. Such tools should be used to guide structured, professional judgement rather than being used in place of clinical risk assessment.[23]

Elevated risk in early psychosis

Risk to self and others

Suicide, violence and homicide all represent elevated risk for young people with early psychosis and they need to be routinely enquired about and assessed. Often a history of suicide attempts and aggression or violence are cited as the most robust predictors of future risk; however, in the early psychosis population this history may not be present, due to the younger age and earlier stage of illness of people being seen by an early psychosis service.[33,34] In general, risks are higher when psychosis is untreated, during periods of relapse, following hospital admission and during periods of transition in care, such as change in treating team or discharge from hospital.[35,36] Newly referred young people who are difficult to engage should be regarded as high-risk (especially for harm to self) until the clinician or team have gathered enough information to demonstrate otherwise.

Approximately 15% of young people with FEP have already attempted suicide before presentation at a clinic or hospital, and another 5–10% will attempt suicide during the first 18 months of treatment. In the 18 months following the first psychotic episode, up to 15% of young people will continue to have high levels of suicidality.[37]

Risk to others can also be elevated during early psychosis. The first episode is when people are particularly at risk of harming others, with violent crime rates among people with schizophrenia shown to peak in the 4 years prior to their first admission to treatment. There is also evidence that people experiencing a first episode of psychosis have a much higher risk of committing homicide than those who have received treatment.[38]

Vulnerability risk

An often under-recognised risk is that of vulnerability risk, for example risk of being taken advantage of or risk of damage to reputation. This is particularly an issue for young people who experience manic episodes, which may manifest in uncharacteristic sexualised behaviour or public displays of unusual or bizarre behaviour.

Formulating risk

Risk is not a purely static phenomenon. It can relate to dynamic factors, and can change quickly and unpredictably, according to the young person's personal and social situation, mental state and other variables such as illness, intoxication, threats and ambient stress, insight, impulsivity, recent loss and treatment adherence.[39] Static risk factors include personality, past experiences, genetic make-up and congenital or permanent health issues. Dynamic risk factors are open to change, whereas static risk factors cannot be altered, although the individual's perception of them might be. Risk factors are usually individualised, and are best integrated into a documented formulation of risk, so that the risk is easily understood and communicated.[40]

A risk formulation is a description of the potential nature of the risk, patterns, potential victims, underlying motives, triggers and perpetuating and protective factors. Categorical descriptions of risk such as 'low', 'medium' or 'high', may be useful in settings where there is an established understanding of what these categories mean, and where there are established protocols for managing risk in each category, such as observation in an inpatient setting.[40] However, a

formulation-based approach is a more clinically useful way of communicating risk in community settings than a categorical one.[40] Such an approach also allows for more individualised and dynamic risk assessment.[39]

Risk assessment and formulation should involve the multidisciplinary team and collate information from external and historical sources. Ideally the risk assessment and management plan should be a collaborative process that involves the young person, their family and any other relevant supports.[35]

CASE SCENARIO **JUSTIN**

Justin is a 21-year-old university student. In the last week of university before the summer break, Justin has been out partying a lot with friends, smoking cannabis heavily and using other drugs like amphetamines and 'legal highs' (novel psychoactive substances). He has slept only a little as there was so much going on.

When Justin arrives home for the holidays, his parents are struck by his energy and confidence. He is talkative and insists on taking everyone out for lunch at a local restaurant in order to celebrate his certain success and future plans. When the bill arrives, Justin tells the waiter he doesn't need to pay as everything is being 'covered' for him. The waiter calls his manager, and he and Justin begin to argue. Justin tips over a vase and leaves, leaving his father to pay the bill.

Outside, Justin is fuming, saying that he has been 'chosen' and that he should never have to pay for anything again. His parents are unable to interrupt him, and it appears that Justin is engaged in a conversation with someone they can't see or hear. They manage to get Justin into the car and drive him home.

That night Justin does not sleep at all. He paces the house and becomes increasingly irritable and frustrated, muttering to himself. He begins piling all the furniture in his bedroom into a corner to make more floor space, then lays out pieces of paper on which he has drawn various figures, numbers and symbols on. His parents try to calm him, bringing cups of tea and talking to him. Eventually Justin's dad suggests they call a doctor, at which point Justin starts screaming at him and runs out of the house. Justin's parents call the police, explaining they are worried about their son.

A couple of hours later Justin is picked up by the police after trying to climb a building in the city. He is by this stage talking incessantly and difficult to follow. He says he is engaged in government work and should not be stopped. He is friends with several politicians, and says that unless the police release him immediately there will be trouble. He is irritable and sometimes laughs hysterically.

CASE SCENARIO **JUSTIN** CONTINUED from page 37

The options for managing Justin at this stage include:

- keeping him in police custody as a 'place of safety' and calling a mobile community assessment and treatment team to assess and arrange for treatment in hospital or possibly at home
- informing his parents of the situation
- monitoring Justin in his cell and ensuring he doesn't harm himself or deteriorate

The differential diagnoses for Justin are:

- psychotic episode – manic
- drug-induced psychosis
- drug/alcohol intoxication
- organic psychosis

Risks to Justin include:

- vulnerability
- accidental harm – not expressing thoughts of harming himself or others
- absconding
- deterioration
- non-engagement due to lack of insight
- neglect

Responding to risk

Once a risk has been identified, strategies can be put in place to moderate the interaction between the mental health problem and the identified risk.[40] These strategies will form the young person's risk management plan. It is important to recognise that although it is difficult when first seeing a young person to gather all of the necessary information for a comprehensive risk assessment, this should not prevent an initial risk management plan from being formulated, implemented and communicated to all members of the treating team, the young person and their family or supports. The risk assessment of a young person will evolve as the treating team gets to know the individual, their strengths and supports, and as circumstances change over time.[40] The risk management plan will therefore need to evolve as well, day by day, or even hour by hour.

Risk management plans aim to reduce risk by targeting the dynamic and modifiable factors that contribute to increased risk and increasing the support and assistance that is available to young people.[40] Rather than eliminating all risk, this approach allows some room for positive risk-taking (see Box 5). Risk management plans must have a crisis or contingency plan incorporated into them, which should be shared with the young person and their family so they are aware of what action to take in the event of a crisis.[35]

BOX 5. **POSITIVE RISK-TAKING**

'Positive risk-taking' refers to a risk management plan where the treating team (led by the consultant psychiatrist) tolerates a level of potential risk if they believe it may help to promote recovery. For example, the treating team may decide not to arrange hospital admission for a young person with FEP who has ceased taking medication and is showing signs of relapse, instead continuing with a community-based treatment approach involving intensive home-based care. This approach may actually promote engagement and development of a trusting relationship between the young person and the treating team, and therefore lead to better outcomes than what might have been achieved by a hospital admission.

Clearly, such positive risk-taking must be a team decision, with a comprehensive risk assessment underpinning the decision-making. Frequent review is also essential.

Documenting risk

Effective risk management not only relies on good assessment and formulation, but also on clear and consistent documentation that is easily accessible by all clinicians and teams in the service. Good documentation is important to articulate decisions made by the clinical team and should be incorporated into the broader risk management plan. Most services use a risk assessment/management proforma to document development of risk management plans. Such documents can serve as a useful *aide memoire* for the clinician, but they should be individualised and regularly reviewed and updated. A young person's risk assessment and management plan should be available for out-of-hours or emergency staff to access in a crisis situation.

Occasionally a risk factor can change and become unmanageable in the context of the current risk management plan. In these cases the change in risk must be acknowledged, documented and communicated to all key people involved in the management plan and a new strategy developed to manage this risk. It is through creative and collaborative thinking that risk is best managed by a team.

Frequency of review

At times of heightened risk, the frequency and intensity of face-to-face contact with the young person and families need to be reviewed and plans made to mitigate risk. There will likely be a need for a more frequent, more intense level of contact with the young person and family. For example, the young person may require daily or twice-daily home visits for a sustained period until the heightened level of risk subsides. A team and even service-wide approach may be needed to provide this level of care in a community setting. A more detailed look at decision-making regarding risk and home-based care can be found in the ENSP manuals *'Let me understand': assessment in early psychosis* and *There's no place like home: home-based care in early psychosis*.

It is important to note that thorough risk management and reduction allows a service to run smoothly and safely and promote recovery of young people. Risk assessment and management underpin each young person's recovery/care plan and are critical, not only from a safety point of view, but also to protect clinicians practising in what can be a risky environment. Hence good documentation and communication are important and should not be overlooked.

Confidentiality and risk management

Sometimes issues of confidentiality can confuse clinicians. In general, clinicians and teams should always encourage the young person and family to be involved in the risk management plan, and clinicians should never assume that families are aware of the risks to the young person.[35] The question of when to share confidential information, and with whom, can be difficult if the young person is reluctant to share information about risk with others. Clinicians should always inform the young people and families they work with about the service's standard confidentiality agreement and the exclusion criteria for this agreement. Broadly, this can be summarised as, all information held on the individual will remain confidential unless there is felt to be a significant risk to that person or to others, in which case the information would be shared with key agencies on a 'need to know' basis to manage the identified risks.

Decisions about when confidentiality needs to be breached to protect the young person or third parties require careful consideration of the potential risk posed, especially in the cases of risk of suicide or threat of violence to an identified person.[40] In such cases, these decisions must be discussed with the treating consultant, on-call consultant or medical director.

Consent and duty of care

Because early psychosis services work with a 12–25 years age range, clinicians need to have an understanding of capacity to consent in minors (under 16 years usually) and confidentiality issues regarding involving family or other supports in a treatment plan. Ideally all young people under 16 years should have an identified adult carer (usually a parent) who has some involvement in the treatment plan. This is especially important when managing risk and prescribing psychotropic medication or arranging investigations. Occasionally a minor may not allow the team to contact their parent or guardian, sometimes with good reason. In such cases, clinicians should explore other ways of involving a significant adult in the young person's care plan. Extensive clinical experience in the EPPIC program confirms that with negotiation and patience it is rare for a stalemate to be reached on this point.

Child protection issues can sometimes be identified, in which case the clinician must discuss concerns with a senior member of staff and follow the local child protection policy. This is a statutory duty of care and action should not be delayed if there are concerns. More junior clinicians are advised to discuss with a senior colleague before taking immediate action, as this is an area of practice that requires careful and considered yet decisive action.

Where a young person is an adult but appears to be vulnerable to exploitation or abuse by others, there may be a less immediate legal imperative to protect the individual; however, similar procedures or policies should be followed, and it is recommended to involve senior colleagues and the team in making decisions.

Crisis management

Although often seen to be synonymous with a relapse of psychotic symptoms, 'crisis' in fact represents any change in a young person's circumstances that overwhelms their capacity to cope and results in their being brought to the attention of services. For example, a young person might experience a crisis as a result of a relationship breakdown, a change in home life or losing their job. Ideally, good crisis management aims to prevent relapse, by encouraging and enabling a young person to access the early psychosis service before relapse occurs.

Crisis management plans

Some crises may be predictable, either because of their nature (e.g. a relapse) or because they have happened to a particular individual before (e.g. substance use, aggression, self-harming). Predictable crises can have specific crisis contingency plans, which should aim to bring the young person or family out of crisis as swiftly and as safely as possible. These potential crises should be identified and plans agreed on with the young person and family when constructing the care plan. This crisis contingency plan should also be communicated to all others involved in the young person's care, such as other members of the treating team or the young person's GP.

Other crises cannot be predicted, but this does not mean there can be no contingency plan. For example, most crisis plans will advise the individual or family to call an out-of-hours number for advice, involve the crisis team component of the service, or present to a hospital emergency department if there is no agreed contingency plan in place or if a situation cannot be safely contained.

Managing crisis in the community setting

A crisis may be an individual's response to excessive stress, when the demands from life outstrip the resources available, whether internal or external. Stress reduction will therefore contribute to crisis resolution. It is crucial that crisis management involves not just medical intervention, but also psychosocial interventions to address underlying stressors, support the young person emotionally and provide them with practical strategies to manage crises.

Generally, a young person in crisis will require:

- increased frequency and intensity of contact
- increased emotional and practical support
- a service-wide, team-based approach to intervention
- time taken by clinicians to engage with the young person.

Psychosocial interventions for crisis include:

- basic counselling skills
- emotional support
- problem-solving techniques
- focusing on increasing social supports
- psychoeducation and increased support for families, to enable them to support the young person through the crisis.

For those experiencing a crisis because of a deterioration in mental state, medical management may involve:[29,41]

- stress reduction by short-term use of sedative medication to reduce anxiety and promote sleep (e.g. benzodiazepines or 'z medications' [zopiclone, zolpidem]).
- a temporary increase in existing prescribed medication, which can sometimes help to reduce any breakthrough symptoms and increase sedation (e.g. antipsychotic medication)
- an increase in antidepressant medication if the young person's mood is significantly depressed – however, care must be taken to assess suicide risk and manage this appropriately, especially as a lift in mood or an increase in antidepressant medication may increase suicide risk temporarily
- swift increase in sedative, antipsychotic or mood-stabilising medication for young people presenting with elevated mood – this may contain a crisis when combined with an increase in support for the young person.

For those in crisis secondary to external situations, such as homelessness, arguments at home or a relationship breakdown, it may be possible to resolve the crisis successfully through removing the identified stressor (e.g. finding temporary housing for the young person or arranging them to move in with a friend of the family for respite). The approach to solving these kinds of problems should be collaborative, to promote future resilience in the young person, and should involve the multidisciplinary team for their specific expertise. Early psychosis services and clinicians need to be aware of what resources are available out-of-hours for young people experiencing a crisis, such as crisis teams or youth homeless outreach services. Emergency departments may be seen as a temporary place of safety if all else fails.

Hospitalisation as a result of crisis

Some crises are not manageable in a community setting, even with involvement of intensive home-based outreach intervention. In these cases it may be necessary to offer hospital admission as a way of managing risk and expediting recovery. A clear admission plan with identifiable and agreed goals should be constructed at the earliest opportunity, ideally prior to admission, and communicated to the inpatient staff. This can then be used to construct a care plan in hospital, review progress and minimise the risk of hospitalisation becoming a 'holding exercise' rather than a therapeutic intervention. It is important that when young people enrolled with an early psychosis service are admitted to hospital that the community-based team remain involved and continue engaging the young person to facilitate some continuity and prepare for discharge.

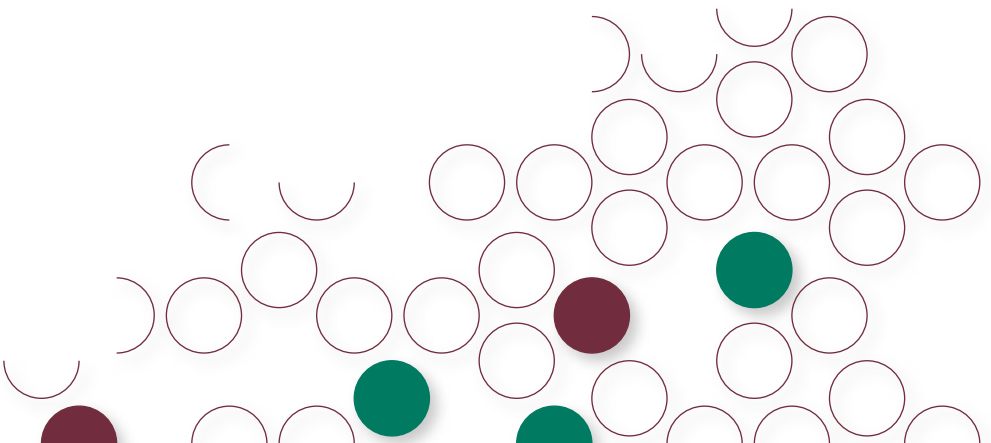
In some situations a collaborative response to crisis is not possible, for example in severely unwell individuals, those with poor insight or who otherwise have significant risks. In such situations consideration of Mental Health Act legislation is required to safely contain risk and promote recovery. This may involve involuntary admission to hospital with appropriate treatment. The use of involuntary treatment after discharge from hospital is a somewhat controversial issue and may or may not have a positive effect on outcomes for young people. It appears that some individuals with severe mental illness and poor insight or treatment adherence can benefit from compulsory community treatment. Clinicians are referred to their local Mental Health Act legislation for further information.

Assessing young people during a crisis

Crisis management from a medical perspective will involve, in addition to the generic assessment, a focus on assessment of mental state, risk, intoxication or withdrawal from substances, drug overdose, self-harm, side-effects of medication, physical health issues and capacity or insight regarding safety planning and consent to treatment. The assessment should also build upon the young person's strengths, what interventions have worked previously and their supports available. It should also consider any major changes, life events or stresses that may need to be managed. An agreed 'guarantee of safety' from the young person should not be taken as such by the treating team: while it may perhaps indicate a degree of willingness to work collaboratively, it is no more than that.

Ideally, the young person will have a crisis plan incorporated into their care plan that clinicians can refer to; however, this may not be the case in the early stages of assessment, and therefore an interim crisis plan should be agreed upon with the young person and their family and communicated to others in the care team (e.g. the young person's GP). If collaborative agreement on the crisis plan cannot be achieved, other means of managing a crisis such as home-based crisis team intervention, hospital admission and use of involuntary or more restrictive treatment will need to be considered.

Once a crisis has been resolved, the treating team, young person and family should review the plan with the aim of learning from the crisis. This way a crisis can be reframed as a 'learning experience' and contribute to promoting recovery. Frequent crises should prompt a multidisciplinary team review of the care plan, which may involve other agencies who are involved in the care of the young person, for example, after-hours support teams, emergency department units, inpatient units, ambulance and in some cases, police.



SUMMARY

Assessment

- Young people referred to an early psychosis service should be seen within 24 hours for assessment by an early psychosis clinician, with a review by a medical practitioner conducted within 48 hours.
- Assessment of young people with suspected FEP should involve a comprehensive biopsychosocial approach, with contributions from all members of the multidisciplinary team.
- Specific tasks for medical practitioners in assessment include exclusion of organic causes of psychosis and diagnosis of developmental disorders and comorbid conditions.
- All young people with suspected FEP should have a comprehensive medical investigation for organic causes of psychosis.

Formulation and diagnosis

- Diagnostic uncertainty is common in early psychosis and should be tolerated to avoid misdiagnosis and stigmatisation caused by hasty diagnosis. Clinicians should treat the young person's symptoms while continuing to assess them and formulate a diagnosis.
- However, it is important to distinguish between affective and non-affective psychosis, especially to recognise mania.
- Drug-induced psychosis should be taken seriously, and not dismissively applied as a diagnosis, as many young people presenting with apparently drug-induced psychosis go on to develop a primary psychotic disorder. Any psychotic disorder, even a single episode, needs to be followed up for a period of at least 12–24 months.

Risk assessment and management

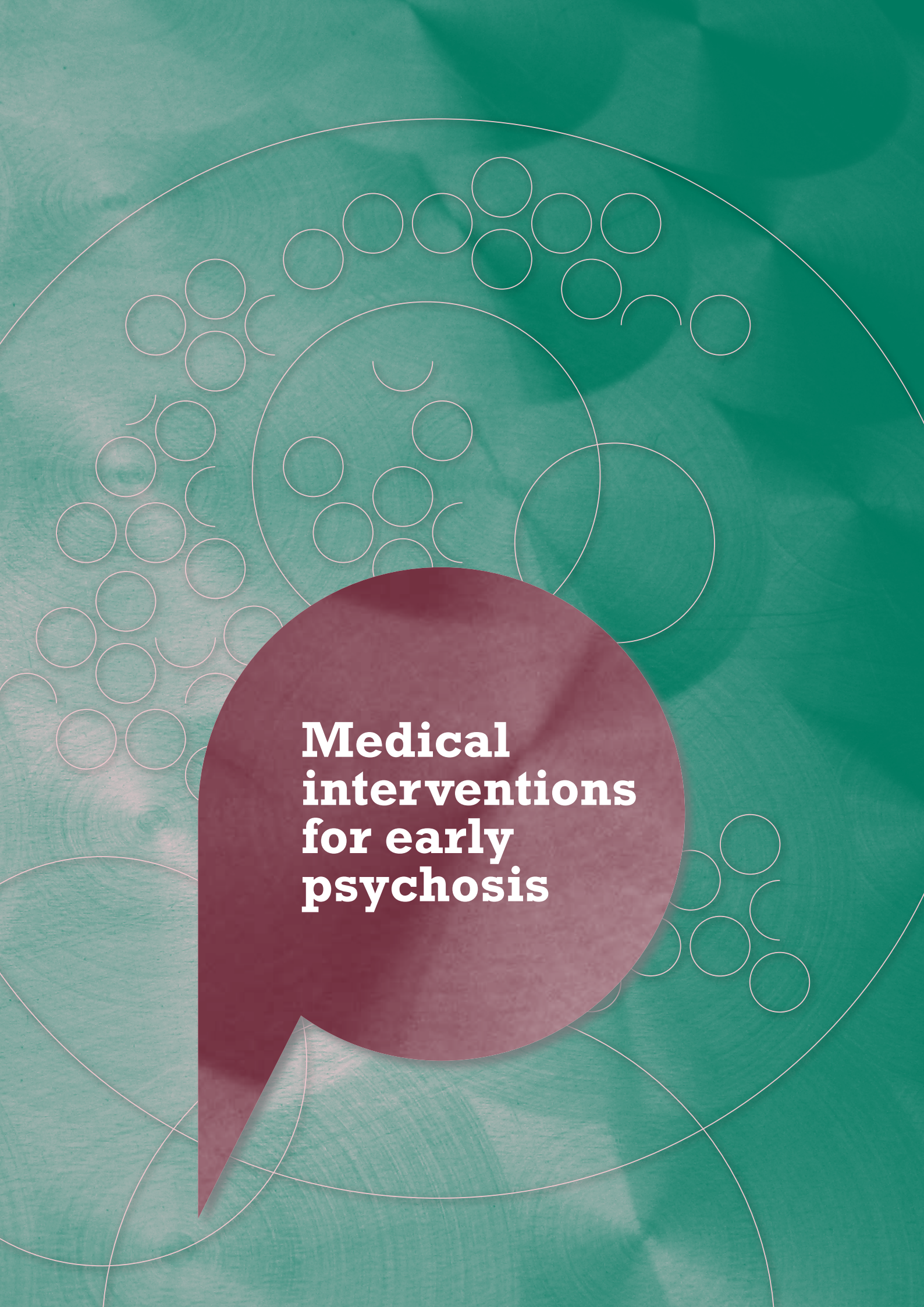
- Young people with early psychosis may be exposed to risk from a number of sources, including the illness, the young person's environment and individual factors such as personality traits.
- Risk can be categorised by risk to self, risk to others, risk from others and risk of non-adherence and disengagement.
- Suicide is a particular source of risk. Approximately 15% of young people with FEP have already attempted suicide before presentation at a clinic or hospital, and another 5–10% will attempt suicide during the first 18 months of treatment.
- Young people are at far greater risk of committing violence or homicide during the first episode of psychosis than they are following treatment.
- Newly referred young people who are difficult to engage should be regarded as high-risk until enough is known to demonstrate otherwise.

SUMMARY CONTINUED

- The risk a young person is exposed to derives from static and dynamic factors. A proper formulation of each young person's risk factors needs to be undertaken and documented.
- Aiming to eliminate all risk is unrealistic; instead, clinicians should aim to manage risk, with a focus on engaging the young person and providing them with the best care possible.
- Risk assessment and development of a young person's management plan should be a collaborative process that involves the young person, their family and any other relevant supports.

Crisis management

- Crises may be predictable or non-predictable, but in both cases a good crisis management plan will help mitigate the impact of a crisis.
- Management of a crisis that is a result of a deterioration in mental state should involve psychosocial interventions as well as medical interventions.
- Management of crises caused by external stressors, such as homelessness or relationship breakdowns, should involve a collaborative approach to help remove the stressor from the young person, or the young person from the stressor.
- If a young person enrolled with an early psychosis service is admitted to hospital, the community-based team should remain involved and continue engaging the young person.
- Once a crisis has been resolved, the treating team, the young person and their family should review the crisis management plan with the aim of learning from the crisis.



Medical interventions for early psychosis

Considerations for medical treatment in early psychosis

This section outlines some general considerations for clinicians managing medical treatment for young people with early psychosis, regarding prescription of pharmacotherapy and associated side-effects and issues with non-adherence to treatment. Prescribing guidelines and principles given are drawn from the *Australian Clinical Guidelines for Early Psychosis 2010* (ACGEP), with reference to more recently published evidence where available. Clinicians may also wish to refer to the British National Institute for Health and Care Excellence's (NICE) guideline for recognition and management of schizophrenia and psychosis in children and young people.[42] Prescribing algorithms for affective and non-affective psychosis, as recommended by the ACGEP, are presented on pages 54 and 55.

Evidence for an antipsychotic-free period of assessment

Where practicable, a 48-hour medication-free observation period is recommended prior to commencing antipsychotic medication to confirm the diagnosis of psychosis and exclude organic causes.[43-45]

Benzodiazepines can be used during this observation period, and beyond, to help to alleviate distress and promote rest and sleep.[44] They may also be used to manage withdrawal from certain substances, including alcohol, cannabis and some other street drugs.

A key principle of early intervention for psychosis is to minimise the duration of untreated psychosis (DUP). This is the time from the onset of frank psychosis to the initiation of treatment (usually with an antipsychotic medication). A longer DUP is generally associated with worse symptomatic and psychosocial outcomes.[8] Initiating treatment as soon as it is practical, and when a diagnosis of sustained psychosis is clear, keeps the DUP to a minimum without compromising safety and diagnostic integrity. Of course a balance is needed, and the antipsychotic-free observation period should therefore not be prolonged once the diagnosis is clear.

If psychotic symptoms persist beyond this observation period, treatment with an oral second-generation antipsychotic should be offered. As antipsychotic medications take at least 2–3 weeks to affect core positive psychotic symptoms, benzodiazepines and psychosocial support are critical strategies to help the young person cope with distress and symptoms related to the psychosis and to avoid unnecessary dose escalation and overtreatment with antipsychotic medication.

Principles of pharmacological treatment in young people with FEP

This section outlines nine principles that should be followed when prescribing antipsychotic medication in the FEP population, as recommended by the ACGEP.[1]

Pharmacotherapy is a first-line treatment for psychotic disorders. There are a number of differences between young people with FEP and people with established schizophrenia that should be considered when prescribing pharmacological treatments for FEP. A summary of the issues particular to this group is presented in Box 6. The safety and efficacy of antipsychotics and mood-stabilising medications have not been systematically evaluated in young people, and extrapolation from adult studies, clinical experience and expert opinion governs their off-label use in this population.[46,47] Little information is available about the long-term effects of antipsychotic medications on the development of the central nervous system.[46]

Atypical, or second-generation, antipsychotics (SGAs) are preferred over typical, or first-generation, antipsychotics (FGAs) for initiation of antipsychotic treatment in young people, due to better tolerability (see Principle 1, below).[1] It is also possible that SGAs may have better effects on cognition, although the evidence is currently equivocal (see Box 7).

BOX 6. PARTICULAR CONSIDERATIONS FOR PHARMACOTHERAPY IN THE FEP GROUP

Young people with FEP are often antipsychotic-naïve.

A young person's first experience of antipsychotic medication (response and side-effects) will influence their engagement and adherence.[49-52]

People with FEP often respond to much lower antipsychotic doses than those with established illness.[50,52]

People with FEP generally show a more rapid improvement in symptoms than people with established schizophrenia.[50,52]

Positive symptoms in people with FEP are generally responsive to treatment in terms of overall response rate and degree of symptom reduction.[53]

People with FEP and young people may be particularly sensitive to antipsychotic-associated extrapyramidal side-effects.[51-54]

People with FEP are more susceptible to antipsychotic-associated weight gain and metabolic side-effects than those with more chronic illness, due to their younger age and often being antipsychotic-naïve.[53,54]

Diagnostic instability in FEP may require ongoing adaptation of pharmacological interventions.[50]

BOX 7. **IMPROVEMENTS IN COGNITION IN FEP: SGAS VERSUS FGAS**

While it has been suggested that SGAs may produce greater improvements in cognition than FGAs due to a different pharmacological action,[26,48] the design of many of the studies supporting the superiority of SGAs has been called into question. This is in part due to the high doses of the FGA comparator used.[26] As even low doses of FGAs increase the risk of extrapyramidal side-effects (EPSEs), the increased use of anticholinergic medications to treat EPSEs may be responsible for impaired motor skills and cognitive speed in the FGA comparison groups.[26]

In the European First Episode Schizophrenia Trial (EUFEST) of first-episode schizophrenia, Davidson et al. (2009) compared cognitive performance after 6 months of treatment with low-dose haloperidol or olanzapine, amisulpride, ziprasidone or quetiapine. They found moderate improvements from baseline cognitive scores, with no differences between the five treatment groups.[26] Worse (lower) cognitive scores at baseline were predictive of greater cognitive improvement after treatment.[26] However, in a recent study in which young people with early-onset psychosis – many of whom were antipsychotic-naïve – were treated with quetiapine or olanzapine for 6 months, there was no significant improvement in any of the cognitive parameters despite clinical improvement in psychosis. No significant differences were observed between the two treatment groups.[27]

Principle 1. Take side-effect profiles into consideration

Young people appear to have a higher risk than adults for antipsychotic-associated weight gain, hyperprolactinaemia, extrapyramidal side-effects (EPSEs) and sedation, and associated metabolic abnormalities.[55] At a time when young people are experiencing psychological and physical maturation, the impact of these side-effects may be different from that in adults.[55]

In a Cochrane review of the efficacy of SGAs in adolescents, Kumar et al. (2013) found that there was no convincing evidence to date that SGAs have superior efficacy in young people to FGAs,[48,56] with the exception of clozapine in treatment-refractory schizophrenia.[56] However, an open randomised clinical trial in 498 people with first-episode schizophrenia has shown higher response and remission rates for SGAs compared with the FGA haloperidol.[57]

Regardless, the tolerability of SGAs appears to be greater in the early psychosis population, with fewer side-effects seen in the short term.[48] While there is little evidence to suggest that one SGA is preferable to another in this context, side-effect profiles of SGAs vary markedly, and these should be taken into consideration when prescribing antipsychotics to young people.[48] For example, SGAs with a known propensity to cause weight gain, such as olanzapine,[48,58,59] should be avoided as first-line pharmacotherapy, while those with the lowest risk of weight gain (e.g. aripiprazole and ziprasidone) should be preferred. See also ‘Side-effects of antipsychotic therapy’ on page 59 and Box 8 on page 60.

The main considerations when selecting an antipsychotic for FEP in young people should be their response to a trial of this medication and the most relevant side-effects for the each person.[48]

> ‘They didn’t give enough warning about the side effects might be.’
>
> ‘I think if I’d had more information, I would have tried another brand with less side-effects maybe. Instead of just taking the first one that was offered to me.’
>
> – Young people,
> EPPIC, Orygen Youth Health Clinical Program.

Principle 2. Prevent and treat psychiatric emergencies

The immediate goals of emergency management of aggression or agitation are to assure the safety of the young person who is experiencing these symptoms and healthcare providers, and to help the young person manage their emotions and distress and control their behaviour, while minimising the psychological and physiological impact on them.[60,61]

Non-coercive psychological and practical attempts at ‘de-escalation’ of an aggressive or agitated person are strongly encouraged as first-line management.[61,62] If such strategies are not successful within a safe timeframe, then medication should be offered with the aim of achieving a state of calm.[63] Oral medication should be offered in the first instance.[64]

Antipsychotics or benzodiazepines are used to quickly alleviate distress.[65] Both FGA and SGA medications appear to be effective, but benzodiazepines and SGAs have better tolerability.[66] Furthermore, the observed efficacy of SGAs may be dose-dependent.[67]

Despite being commonly used in clinical practice, the available data comparing the efficacy of benzodiazepines and antipsychotics in controlling psychosis-induced symptoms of aggression and agitation are limited and of poor quality (for a meta-analysis, see Gillies et al. 2013[65]). Based on this information, benzodiazepines appear to be as effective as antipsychotics alone, but with fewer side-effects such as EPSEs.[65] The combination of a benzodiazepine and an antipsychotic does not convey any advantage over either drug alone.[65]

If it is safe to do so, short-acting intramuscular (IM) benzodiazepines such as midazolam may be used in emergency situations where oral medication is not accepted or suitable. These have been used either alone or in combination with an antipsychotic.[68] The antidote, flumazenil, and resuscitation equipment must be at hand.

IM antipsychotic medication is occasionally necessary,[64,68] and as with general medication principles in this group, the lowest possible dose to treat the symptoms should be used; the use of multiple antipsychotics is discouraged.[64] The young person should have close, regular medical and nursing monitoring for several hours following an IM injection.[64]

A recent meta-analysis[68] concluded that IM SGAs were as efficacious as IM FGAs, and in some studies showed a superior and more rapid response. Furthermore, SGAs were better tolerated with respect to EPSEs.[68] FGAs should therefore now not be used in FEP psychiatric emergencies.

Principle 3. Distinguish between affective and non-affective psychosis

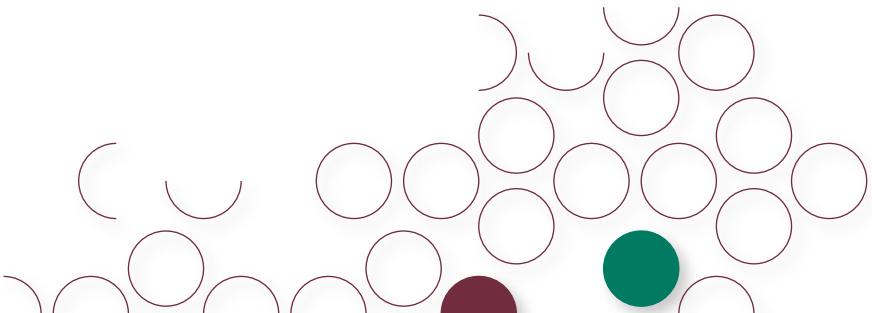
While differentiation between specific diagnostic entities may be difficult at initial presentation, a pragmatic approach to deciding which pharmacotherapy is initiated according to a broad definition of 'affective' or 'non-affective' psychosis is recommended.[52] An early diagnostic distinction between affective and non-affective presentation is important in light of the different treatment recommendations for these subgroups in the acute phase, in particular the utility of adding a mood stabiliser as the cornerstone of treatment for people experiencing an acute manic psychosis.[52]

Principle 4. 'Start low, go slow'

Evidence suggests that there is a biological sensitivity to antipsychotics during the first onset of psychosis. People with FEP respond more rapidly to antipsychotic medication and have a greater response, and generally require lower doses to do so, than people with more established illness.[50] In addition, side-effects of antipsychotics can occur at substantially lower doses in the first-exposure population than in people re-exposed to antipsychotics.[50] Rapid titration may also increase the incidence of side-effects.[69] Accordingly, a 'start low, go slow' prescribing approach is absolutely essential, using the lowest possible dose to control symptoms.[42]

KEY PRACTICE POINT: **USE BENZODIAZEPINES FOR SEDATION**

The principle of 'start low, go slow' cannot be stressed enough. Doses of antipsychotic medication should commence at the lowest effective dose **for the treatment of psychotic symptoms**. Although clinicians often increase doses of antipsychotic medication to produce a sedative effect, there is no reason to do this, and it is recommended that clinicians use benzodiazepines for sedative purposes. Antipsychotic dose escalation should be done slowly in a series of careful 'steps', over many weeks, and only if required.



Principle 5. Avoid antipsychotic polypharmacy

Although relatively common in clinical practice,[43,70] there is little empirical evidence to suggest that combining antipsychotic medications has superior efficacy to monotherapy in the treatment of psychosis.[43,70] Furthermore, combining antipsychotic medications is associated with an increased risk of side-effects, non-adherence and drug interactions.[70] The majority of international guidelines for schizophrenia and psychosis recommend against the use of more than one antipsychotic,[42,43,71] except when changing medications[42,71] or during augmentation with clozapine in treatment-resistant cases.[70] Although there have been no direct randomised controlled trials of antipsychotic polypharmacy in FEP populations, the increased propensity for side-effects in this population would not support this practice.

Principle 6. Monitor adherence

Non-adherence to medication is particularly prevalent in young people,[72] and people with FEP who are non-adherent tend to be younger.[73] Although compliance therapy has been proposed as a way to promote adherence to a range of interventions, there is insufficient evidence to date that it improves adherence with pharmacological treatment.[74]

Other strategies for managing non-adherence have been shown to be effective in people with established schizophrenia, and may also be useful in FEP. These include training for case managers (nurses) in medication management, and person-specific tailoring strategies and programs to compensate for cognitive deficits in people with schizophrenia, such as telephone intervention and cognitive adaptation training.[74] Intervention strategies that span a longer period of time are beneficial, particularly in FEP.[74] Strategies to improve adherence to medication in FEP are discussed further in the section ‘Medication adherence in young people with FEP’ (page 63).

Principle 7. Monitor and manage adverse events and side-effects

Antipsychotic medication may cause side-effects which are distressing or disabling for young people.[52] Well known side-effects of psychotropic drugs are discussed on page 59, in ‘Side-effects of antipsychotic therapy’.

There are consistently strong relationships between people’s assessment of the impact of side-effects and non-adherence.[75] In addition to actively enquiring about side-effects and discussing their concerns, a validated self-rating tool to measure the young person’s perception of the side-effects they are experiencing (e.g. the Liverpool University Neuroleptic Side Effect Rating Scale[76]) may provide additional information on the tolerability of their treatment regimen.

Principle 8. Identify failure to respond, but provide a sufficient period for treatment response and remission

Symptomatic response and remission may be measured in a number of ways, as reviewed in the ACGEP.[1] Further details of predicting response and management of non-response to medications are outlined on page 76.

Principle 9. Treat comorbidities

Psychiatric comorbidities are common in people with FEP, and are often present before the first episode of psychosis occurs.[77] In addition, people with schizophrenia have a higher risk of anxiety or depressive disorders than the general population.[78] As many as 80–90% of people with FEP fulfil the diagnostic criteria for at least one comorbid psychiatric disorder.[52] Major depression, anxiety disorders (including social phobia and post-traumatic stress disorders) and obsessive-compulsive disorder can occur concurrently with FEP.[52]

Depression and anxiety in people with psychosis are often associated with poorer outcomes such as increased hospitalisation rates and subjective assessment of psychosis-related difficulties.[79] Anxiety and depression levels are also related to rates of suicide and self-harm.[54,79,80]

Comorbid substance use, including nicotine and alcohol, is common in people experiencing a first episode of psychosis,[50] and may increase risk factors for relapse even in people who are adherent to their medication. Comorbid substance use is also associated with a worse prognosis in general, including more severe positive symptoms, longer periods of hospitalisation and poorer adherence to medication.[50]

Defining the boundaries of comorbid conditions may be difficult due to the interaction between the symptoms of the primary disorder and those of comorbid conditions.[52,54,78] Periodic reassessment in people with FEP is often required.[52,54] Therapeutic interventions are recommended when the presence of comorbidities impacts on the effective management of the primary psychotic disorder.[52,79] Pharmacological treatment of psychosis also has side-effects that can affect the young person's health or pre-existing medical comorbidities, as discussed on page 100.

FIGURE 4. **PHARMACOLOGICAL TREATMENT FOR FIRST EPISODE NON-AFFECTIVE PSYCHOSIS**

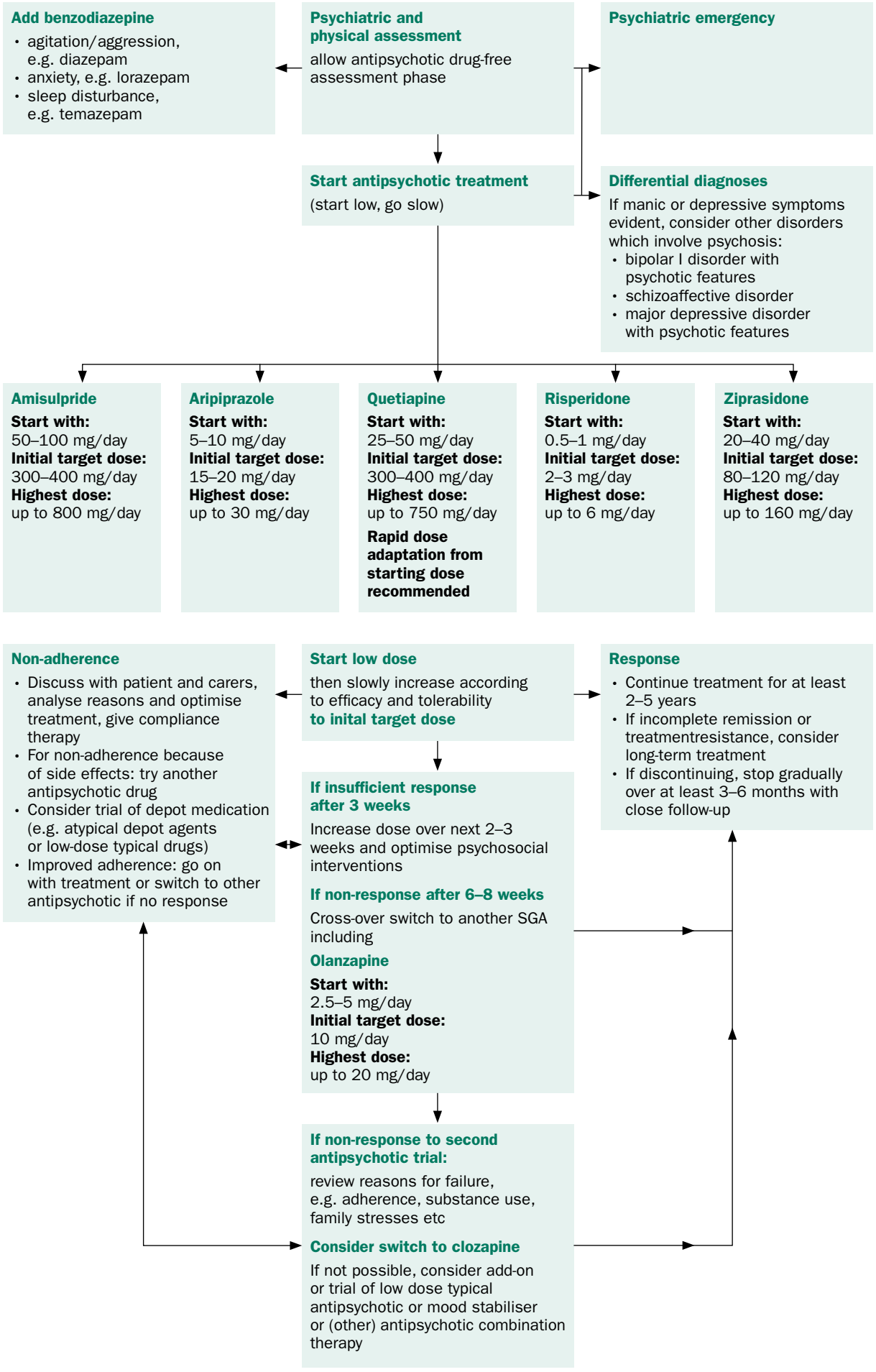
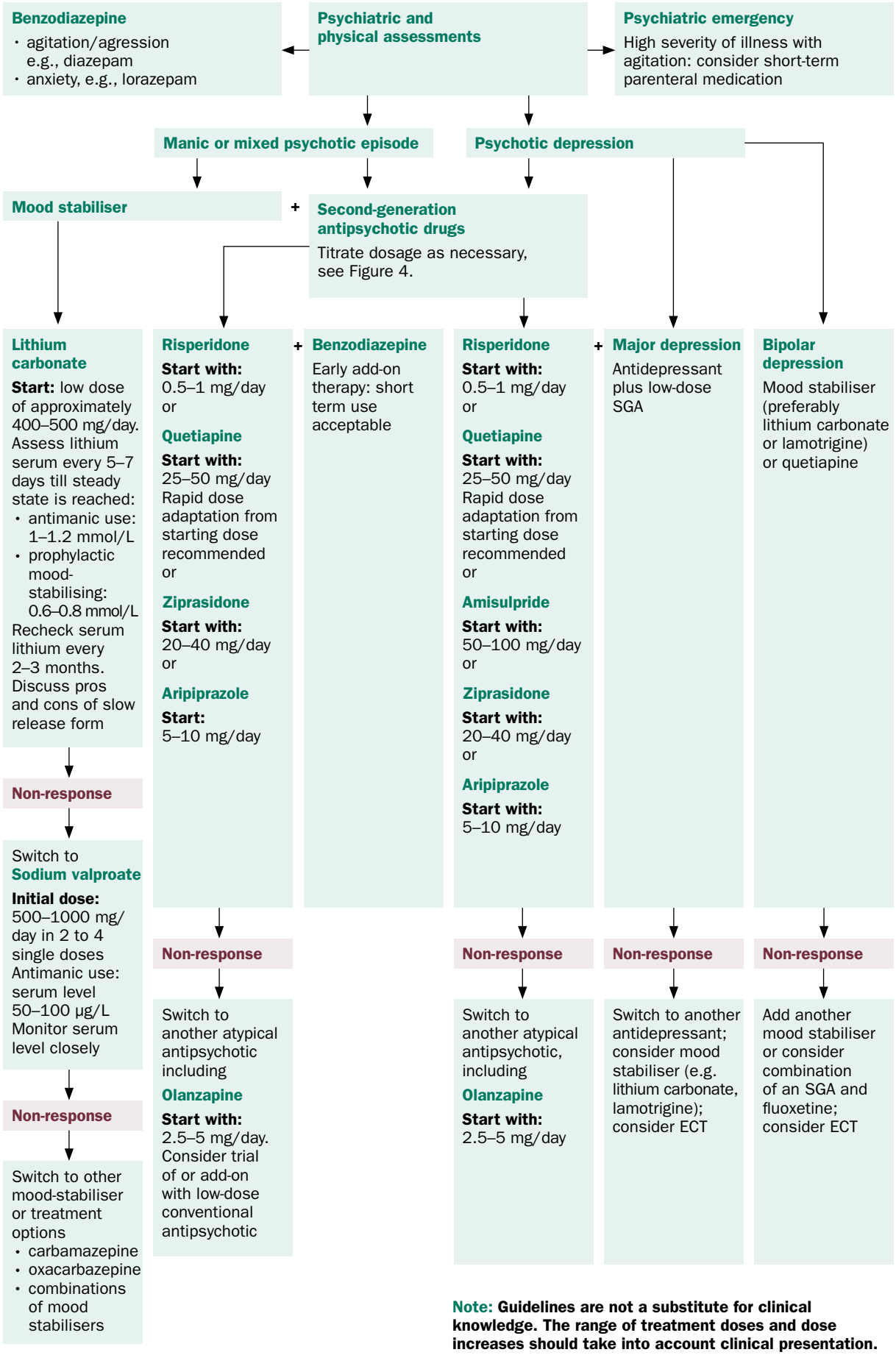


FIGURE 5. **PHARMACOLOGICAL TREATMENT FOR FIRST EPISODE AFFECTIVE PSYCHOSIS**



Note: Guidelines are not a substitute for clinical knowledge. The range of treatment doses and dose increases should take into account clinical presentation.

Quetiapine (quetiapine fumarate) in this algorithm refers to non-extended release formulation.

Prescribing in special populations

Children

There are no dosing recommendations for amisulpride, aripiprazole, olanzapine and ziprasidone in people aged under 18 years, for clozapine in people aged under 16 years or for risperidone in people aged under 15 years.[81-86] Quetiapine is indicated for bipolar disorder in young people from the age of 10 years, and in schizophrenia from the age of 13 years.[87] Amisulpride is contraindicated in pre-pubertal children.[81]

Children and adolescents are thought to be more susceptible than adults to EPSEs caused by FGAs and metabolic abnormalities associated with SGAs, especially weight gain.[46] Obesity in young people appears to carry a greater risk of future adverse cardiovascular outcomes than adult-onset obesity.[47] For this reason, olanzapine, which is associated with the highest risk of weight gain of the SGAs,[59] is not considered a first-line antipsychotic medication in children and adolescents.[46] Increased prolactin levels in this population should also be considered in the light of physical growth and bone mineralisation.[46]

Less information is available on the use of mood stabilisers in children.[47] The mood stabiliser lamotrigine is associated, in both adults and children, with the development of potentially life-threatening rashes, such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis in both adults and children.[88] However, the risk of serious skin rashes is higher in children than in adults.[88] Lamotrigine is used off-label to treat bipolar disorder in children and adolescents aged under 18 years.[88]

Treatment with antidepressants is associated with an increased risk of suicidal thinking and behaviour in children and adolescents with major depressive disorder and other psychiatric disorders.[89] Close observation for any signs of increased risk of suicide should be maintained in children and adolescents with depression.[89]

Women of child-bearing age and during pregnancy

In young women of child-bearing age, special consideration must be given to the risk to the foetus from exposure to psychotropic medication, balanced with the risk to the mother and child from deterioration or relapse of psychosis if treatment is discontinued.[90] This is of particular relevance to women with psychotic disorders, as they have an increased risk of unplanned pregnancy compared with the general population.[91,92]

The risk of foetal malformation is greatest in the first trimester, and it is possible that the pregnancy may not be recognised until after this time.[90] The risks associated with the use of psychotropic medications during pregnancy should therefore be discussed with all young women of child-bearing age and a collaborative plan developed.[90] Sodium valproate is not recommended for use in women of child-bearing potential unless alternative therapeutic options are ineffective or not tolerated.[93] Women of child-bearing age should receive counselling about effective forms of contraception if using psychotropic medications.

Hormonal contraceptives have been shown to increase the clearance of lamotrigine.[88] In women currently taking oral contraceptives who are starting lamotrigine, no adjustments are required to the recommended dose escalation guidelines.[88] However, in women on maintenance doses of lamotrigine who

are starting oral contraceptives, the maintenance dose of lamotrigine will need to be increased by as much as two-fold.[88] Similarly, when discontinuing oral contraceptives that have been used concurrently with lamotrigine, it may be necessary to halve the maintenance dose of lamotrigine.[88]

Mood stabilisers are assigned to Australian pregnancy category D, and should not be used during pregnancy unless there is no other suitable therapeutic option, with the risk to the foetus from exposure balanced against the risks associated with untreated or undertreated major mental illness during pregnancy.[90] In a recent systematic review of mood stabilisers (carbamazepine, sodium valproate, lamotrigine and lithium) during pregnancy, all were associated with increased risk of foetal malformation.[90] These were predominantly structural malformations, most commonly neural tube defects but also including cardiac and craniofacial defects.[90] Sodium valproate was associated with the highest rate of malformations, particularly at doses above 1000 mg/day.[90] Mood stabilisers are also associated with neonatal complications, necessitating careful assessment and monitoring of newborns exposed to these medications.[94]

SGA medications have an Australian pregnancy category C classification, and their use during pregnancy is recommended only if the anticipated benefit outweighs the risk; the administered dose and duration of treatment should be as low and as short as possible. Although there are limited data on their safety, the risk of teratogenicity with SGAs does not appear to be increased over the background rate.[94] Exposure to FGAs and SGAs during the third trimester of pregnancy has been associated with extrapyramidal neurological disturbances and/or withdrawal symptoms in the newborn following delivery.[81-87,94]

Breastfeeding mothers

Antipsychotics and mood stabilisers are excreted in human breast milk and there is limited information on potential long-term effects on the infant.[95] Women should therefore be counselled about the benefits of breastfeeding versus the risk of exposure to the infant.[95] While in many cases the concentrations of drug in human breast milk are low, levels which approach clinical significance have been reported for some drugs.[95] Accordingly, manufacturers of these medications do not recommend their use while breastfeeding.[81-88,93] Clozapine is not recommended due to an association with infant agranulocytosis, decreased suckling, seizures and cardiovascular instability.[96] Ziprasidone may have adrenergic effects.[96] While any antipsychotic should be used with caution, olanzapine and FGAs, such as haloperidol, may carry lower risk.[96] Sodium valproate and carbamazepine appear to be relatively low risk during breastfeeding.[96] Infants exposed to lamotrigine should be monitored for Stevens-Johnson syndrome (see use in children and adolescents).[96] Lithium is associated with risks of neonatal toxicity, and thyroid or renal dysfunctions and is not recommended for use in breastfeeding women.[96]

Young people with diabetes

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in people taking SGAs.[81-87] The relationship between SGA medications and blood glucose abnormalities is not fully understood, and is confounded by an increased background risk of diabetes mellitus in people with schizophrenia.[81-87] People with an existing diagnosis of diabetes mellitus should be closely monitored for worsening of glucose control

when prescribed SGAs.[81-87] Similarly, people with risk factors for the development of diabetes should undergo fasting blood glucose measurement and periodic monitoring during treatment.[81-87] People who develop symptoms of hyperglycaemia during treatment with SGAs should also undergo fasting blood glucose testing.[81-87] See 'Physical health management and monitoring' on page 100 for more information.

Pharmacogenomics and drug efficacy and tolerability

Pharmacogenomics describes the genetic differences between individuals that contribute to variations in the efficacy and side-effects of some medications.[97] Because biological variation is largely due to individual genetic and epigenetic factors, the identification and use of genetic biomarkers is promising as a means of identifying the most appropriate drug for a particular person, given the great heterogeneity in the population in response to psychotropic drugs.[97]

Genetic biomarkers have been identified that may provide an indication of the likely response to antipsychotic medications in schizophrenia.[97] Single nucleotide polymorphisms of synaptic vesicle 2 proteins, which are localised on the surface of the synaptic vesicles of all neurons, have been associated with a response to ziprasidone and risperidone, but not quetiapine or olanzapine.[97]

Genetic variations in the metabolic capacity of enzymes determine the duration and extent of a drug's pharmacological activity, with corresponding effects on efficacy and tolerability.[97]

Pharmacogenetic testing that assesses the functional status of cytochrome P450 (CYP) enzymes can provide information about individual metabolism of antipsychotic, anxiolytic, and antidepressant drugs and enable more accurate estimation of the appropriate dose.[97] For example, incidences of lower-activity variant alleles of the CYP2D6 and CYP2C19 enzymes are higher in East Asian populations compared with Western populations.[98] People with these variant alleles have a lower capacity to metabolise drugs that are substrates of CYP2D6 and CYP2C19, including antipsychotics and antidepressants. Low starting and maintenance doses should be considered for people with these variant alleles.[98]

Genotyping is currently possible for predicting whether someone will metabolise some drugs properly or whether they are likely to experience side-effects. It may be possible to predict antipsychotic-associated weight gain in some people, as variants of the HTR2C and MC4R genes have been found to be strongly associated with this side-effect.[97] Information on genetic variants associated with the development of tardive dyskinesia and clozapine-induced agranulocytosis is also emerging.[97]

Side-effects of antipsychotic therapy

The following presents a summary of side-effects that may be experienced by young people when taking antipsychotics. Suggested strategies to address common side-effects and serious adverse events associated with SGA medication are provided in tables 3 and 4 on page 62.

Physical health

Obesity, metabolic abnormalities and weight gain in young people are strong predictors of adult obesity, metabolic syndrome, hypertension, cardiovascular morbidity, sleep apnoea, osteoarthritis and cancer risk.[58]

As a group, SGAs are associated with a two-fold average increase in weight and body mass index (BMI) compared with FGAs; however, there is considerable variation between individual SGA medications.[56,58] A recent meta-analysis of antipsychotics in adolescents with psychosis found an association between olanzapine, risperidone and clozapine and weight gain, although it did not identify differences between these medications.[48] However, wider reviews of the side-effects of antipsychotics in young people, including those with non-psychotic conditions, reported that olanzapine was associated with the most gain, followed, in descending order, by clozapine, risperidone, quetiapine, aripiprazole and ziprasidone.[58,99] The mean weight change with SGAs in individual short-term studies ranged from –0.2 kg (ziprasidone) to 4.3 kg (olanzapine), and all weight changes other than for ziprasidone were statistically significant compared with placebo in the majority of studies.[58] Olanzapine was consistently found to be associated with weight gain across studies[48,58,59] (see Box 8). The results in young people were generally similar to findings in adults.[58]

There is a lack of studies in young people that directly compare the SGAs that are known to cause less weight gain, such as aripiprazole and ziprasidone, with FGAs.[56] One review found that young people who did not have metabolic syndrome who started treatment with SGAs had three times higher odds of developing metabolic syndrome than those using a FGA.[58] The SGAs that are associated with the largest weight gain also appear to be associated with the greatest changes in blood glucose and lipid levels.[58,99]

BOX 8. **OLANZAPINE AS SECOND-LINE TREATMENT FOR YOUNG PEOPLE WITH FEP: THE EVIDENCE**

For the past 15 years, evidence has been accumulating that the antipsychotic-induced weight gain that occurs with olanzapine use in individuals with serious mental illness is equivalent to that seen with clozapine, and is greater than that observed with other SGAs.[100-102] The evidence is particularly clear, from studies that focused on early psychosis cohorts, that clinically significant weight gain occurs far more frequently with olanzapine than with alternative first-line treatment options for psychosis.[103-105]

Multiple short-term studies in healthy volunteers have found evidence that olanzapine can cause significant metabolic changes within hours or days of commencing treatment. Changes include:

- impaired insulin action on glucose[106]
- elevated fasting plasma leptin and triglycerides[107]
- elevated post-prandial insulin and accompanying insulin resistance[108]
- decreased glucose effectiveness and raised fasting glucose[109]
- increased food intake.[110]

These studies clearly demonstrate the negative metabolic effects of short-term olanzapine administration, either linked to changes in weight and/or appetite, or in some cases to direct effects on key measures of metabolic function independent of changes in body mass or food intake. These studies, in over 90 healthy volunteers, are not confounded by participants experiencing psychotic symptoms, or any underlying genetic risk for metabolic disease that some have suggested may be linked to psychosis.

Applying the Hippocratic principle of *'primum non nocere'*, and given the greater propensity of olanzapine to induce weight gain and other metabolic complications in comparison with other available SGAs, we therefore strongly recommend that **olanzapine use in first episode psychosis is limited to those young people in whom a trial of at least one other SGA has demonstrated inadequate control of psychotic symptoms.**

Prolactin and sexual side-effects

Hyperprolactinaemia is associated with a range of symptoms, including sexual dysfunction and decreased libido, hypogonadism, breast changes (stimulation of glandular growth, galactorrhoea, gynaecomastia) and hirsutism in females.[58] Increases in serum prolactin are more common with FGAs than SGAs,[111] although the effect is variable across the range of available SGAs and is also dose-dependent.[58]

Results from randomised controlled trials in populations aged under 18 years were generally consistent with the findings of studies in adult populations, with the largest (dose-dependent) increase in prolactin levels seen with risperidone.[58] Olanzapine was also associated with increased serum prolactin levels, and there were mixed results for quetiapine and ziprasidone.[58] Aripiprazole was not associated with hyperprolactinaemia in most individuals.[48]

The clinical impact of prolactin elevations varies between medications and side-effects. The side-effects most frequently reported in clinical studies in young people were gynaecomastia (olanzapine, haloperidol > risperidone) and irregular menses (haloperidol > quetiapine > risperidone). Up to a quarter of young people report sexual side-effects and diminished sexual performance, a lower level than that reported in adults, although many studies in this population did not assess this side-effect.[111] Further longitudinal studies are required to explore the persistence of prolactin elevation and the clinical impact of elevated serum prolactin levels in young people.[56,111]

Extrapyramidal side-effects

In general, young people, particularly those who are antipsychotic-naïve, are more susceptible to EPSEs of antipsychotics than adults.[55,112] SGAs are less likely than FGAs to cause acute side-effects such as EPSEs at therapeutic doses, and have thus become the standard antipsychotic treatment for young people.[112] Studies on EPSEs in young people have shown that SGAs are associated with a lower risk of extrapyramidal motor symptoms and akathisia than FGAs.[56]

In adolescents with psychosis, risperidone has been associated with EPSEs at low doses (0.15–0.6 mg), with the risk increased at higher doses (1.5–6 mg).[48] In a broader meta-analysis where the use of antipsychotics was not restricted to psychosis, EPSEs occurred with only low frequency with SGAs, with the exception of ziprasidone.[99]

Cognitive side-effects

Somnolence or drowsiness, as a side-effect of antipsychotics, may also have an impact on young people, particularly those who are undertaking secondary or tertiary education.[112] Sedation appears to occur at greater rates in young people than in adults.[55] Sedation rates vary between agents, ranging from 0–33% for aripiprazole, 42–69% for ziprasidone, 25–80% for quetiapine, 29–89% for risperidone, 44–94% for olanzapine and 46–90% with clozapine.[55] However, sedation is dose-dependent and tolerance develops over time.[55,112]

Despite many studies in adult populations demonstrating improved cognitive function with SGA treatment, further investigation is required into treatment strategies and medications that improve cognitive impairment in young people with FEP.[27] In addition, the possible impact of antipsychotic medications on brain maturation at different ages and according to duration of exposure is still unclear.[113]

TABLE 3. **SUGGESTED STRATEGIES TO MANAGE COMMON SIDE-EFFECTS OF ATYPICAL (SGA) ANTIPSYCHOTIC MEDICATIONS**

SIDE-EFFECT	SUGGESTED INTERVENTIONS
Metabolic syndrome	See 'Physical health management and monitoring' on page 100
Sexual side-effects	Reduce dose if possible while maintaining therapeutic dose Switch to another antipsychotic with lesser sexual side-effect profile Take a sexual history Monitor prolactin levels Rule out other reasons for sexual side-effects Young people are unlikely to report sexual problems or loss of libido, so education and active monitoring of these side-effects is important
Sedation	Promote good sleep patterns Reduce dosage if possible while maintaining therapeutic dose Night-time administration only may help day time drowsiness Slow release preparations (e.g. quetiapine SR) may help decrease rapid sleep onset Switch to another antipsychotic with less somnolent profile
Extrapyramidal side-effects (EPSEs) • **Acute dyskinesias** • **Dystonic reactions** • **Parkinsonism** • **Akinesia** • **Akathisia**	Reduce dosage if possible while maintaining therapeutic dose. Anticholinergic medication (e.g. benztropine) Propanolol Clonazepam/diazepam Switch to another antipsychotic
Anticholinergic effects • **Constipation** • **Dry mouth** • **Blurred vision**	Constipation: • Recommend regular and increased fibre and fluid intake • Consider short term laxative use • Consult GP to rule out other causes Dry mouth: • Chewing lollies or gum may help • Rule out other causes Blurred vision: • Consider reducing dose • Check dose of anticholinergic agent used for EPSEs

TABLE 4. **SUGGESTED STRATEGIES TO MANAGE SERIOUS ADVERSE EVENTS ASSOCIATED WITH ATYPICAL (SGA) ANTIPSYCHOTIC MEDICATIONS**

ADVERSE EVENT	SUGGESTED INTERVENTIONS
Neuroleptic malignant syndrome (NMS)	Stop antipsychotic medication Consider transfer to general medical ward for monitoring of vital signs, rehydration and other supportive measures
Tardive dyskinesia (TD)	Reduce dose if possible while maintaining therapeutic dose Switch to another antipsychotic Pharmacological management
Leukopenia	May need repeat blood tests May need urgent referral to a GP or specialist
QTc prolongation	Monitor ECG Consider cardiology referral Reduce dose if possible while maintaining therapeutic dose Switch to another antipsychotic with less effect on QTc interval.

Medication adherence in young people with FEP

Factors affecting adherence

Non-adherence is common in FEP. One study found that during the first 6 months of treatment, 45% of people with FEP were non-adherent with antipsychotic therapy; although non-adherence was defined as 75% or fewer doses taken, the mean for the non-adherent group was under half of doses taken.[114] In another study in people with FEP, using the same adherence measures, 26% of people were non-adherent at 4 years.[115] There are a multitude of factors that are particularly relevant to young people with FEP that can affect medication adherence, some of which are presented in Box 9 over the page.

BOX 9. **FACTORS THAT AFFECT MEDICATION ADHERENCE IN YOUNG PEOPLE WITH FEP**

The young person's environment, including the level of social support they receive[49]

Family attitude to mental illness medication and the young person's relationship with family members[49]

Sensitivity to medication side-effects[116]

Limited insight or acceptance of the illness, (particularly important in young people with FEP, who have no previous experience of psychotic illness)[49]

A belief that treatment is unnecessary[116]

Substance use[49]

Homelessness or housing instability[49]

Strategies to help with adherence

It is important to address problems with adherence, as a lack of adherence is a major contributor to non-response and relapse. While it may not be possible to achieve complete adherence, young people should be encouraged to take their medication as prescribed the majority of the time.

Young people are more likely to adhere to a medication if it is perceived to be beneficial. It is therefore important to consider how a medication's efficacy and side-effect profile may affect adherence.[49] Features of the psychotic episode may also affect how beneficial a medication is perceived to be by the young person. For example, a prolonged DUP can affect the length of time to remission and the degree of remission, making the antipsychotic prescribed appear less effective.[49]

> 'I think most people probably don't want to take medication at all, and so you can feel like you're doing something because you kind of have to, and then if people aren't supportive about that and really helpful and don't let you know what you're doing properly, then it's not a good situation.'
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

The shared decision-making model (Box 10), in which the young person and their family are involved in treatment decisions, may help to improve adherence, particularly if it is used from an early stage of the care process. With the shared decision-making approach the young person plays an active role in choosing which medications they are prescribed, which is likely to increase concordance (i.e. the degree to which the young person's behaviour agrees with clinical advice). The decision-making process for antipsychotic medication should include psychoeducation about why treatment is necessary and why medications must be continued after the young person's symptoms have responded to treatment. It should also include an open and honest discussion about the possible side-effects of medication. The young person should be informed that switching medications is an option if they experience intolerable side-effects with their initial treatment, as side-effects are a common reason for non-adherence.

BOX 10. **SHARED DECISION-MAKING IN MEDICAL TREATMENTS**

Shared decision-making is well established in general medicine as a way to include people's preferences in decisions about their treatment.[54] In the broader mental health setting, a strong therapeutic alliance and a collaborative communication style is associated with more favourable treatment adherence.[117]

There are few studies of shared decision-making in psychosis, where the individuals' decision-making capacity may be impaired, at least temporarily.[54,118] However, an effective working alliance, with agreement between the clinician and young person regarding the goals of treatment, the tasks to achieve these goals and the development of a personal bond, has been shown to increase medication adherence in FEP.[119] Another study investigating the impact of shared decision-making on young people's satisfaction and medication adherence in FEP is underway.[118]

Therefore, a shared decision-making model that involves participation by the young person in treatment-planning and consideration of their preferences may be a promising method of reducing negative attitudes towards treatment for FEP and improving medication adherence.[52,54,117] The role of the clinician in the shared decision-making process is to inform the young person about their condition and treatment options, so that decisions about therapy can be made together.[54]

A non-judgemental reaction to non-adherence will encourage honesty and ongoing engagement. The young person's reasons for non-adherence should be discussed, as they may suggest a strategy to address this issue. For example, if cognitive difficulties and/or memory impairment have contributed to non-adherence, strategies that help the young person remember to take their medication should be tried, such as involving a family member or significant other in reminding the young person to take their medication as prescribed. A motivational interviewing approach could also be effective.

Side-effects such as weight gain, sedation, cognitive dulling and others are strongly related to non-adherence.[75] Clinicians should try to anticipate and address side-effects to reduce the chance of non-adherence (e.g. clinicians can anticipate weight gain by providing education about diet and exercise as soon as a young person is commenced on an antipsychotic. See also 'How to monitor and manage physical health in young people' on page 103). Persistent endocrine and sexual side-effects may warrant a switch of medication.[1]

Depot medication could be offered as an alternative to oral antipsychotics, rather than as a last resort, as some young people may prefer to receive a monthly injection. These are discussed in more detail in the next section.

Long-acting injectable (depot) medications

Long-acting injectable (LAI), or depot, medications may be considered in FEP if adherence to oral antipsychotic treatment is known or suspected to be a problem.[49] Depot injections may be particularly useful to address covert non-adherence, as the clinician is involved in the administration of the medication.[74,120] Assured administration of medication delivers a reasonably constant dose of antipsychotic and may minimise side-effects and the risk of overdose.[121] Avoiding the peaks and troughs in blood levels of antipsychotic medications that occur with oral formulations may also improve tolerability.[116]

There may be some resistance to a long-acting treatment among people with FEP, as this population has not had personal experience with a relapse; however, long-acting antipsychotics are also not routinely offered to people with FEP.[120]

Early use of LAIs as treatment in FEP

Although traditionally reserved for people with psychosis who are uncooperative, are thought to be poorly adherent to therapy, or have not responded to previous antipsychotic therapy, LAI SGA medication may be of benefit in FEP when the young person has a preference for this type of treatment, or where avoiding covert non-adherence is a clinical priority.[43,116] Despite their perceived reluctance to accept depot injections, young people with FEP may in fact find them effective and acceptable.[120] For example, a young person might prefer depot over oral treatment, as it does not serve as a constant reminder of their illness, or because it is more convenient, particularly for those who forget to take regular medication or have cognitive or social barriers to regular medication adherence.[122] For these young people, the longer half-life of depot injections may mean that missed doses are less problematic.[122]

If the treating team thinks it may be of benefit, depot medication should be presented to a young person as one of many early treatment options. It is important that the young person is also provided with appropriate information about depot medication to ensure a collaborative decision is made. Premature coercive use of LAIs **must** be avoided. It is crucial to ensure that depot use is not linked with a message that this type of treatment will necessarily be long-term or lifelong. Ultimately, the aim should always be to improve chances of a complete recovery.

Medical management at the different phases of psychosis and recovery

Overview

This section focus on the management of medical interventions at each of the phases of psychosis (see Figure 1 on page 10) for young people once they have been admitted to an early psychosis service. It expands on the previous sections to provide recommendations for the aims of treatment at each phase, the interventions that might be required and how to manage them, and the frequency of medical review. Please refer to pages 20–34 for details regarding the process of assessment and diagnosis. Prescribing principles in early psychosis are presented on page 48 of this manual.

Clinical interventions should follow the latest evidence-based clinical guidelines (e.g. the ACGEP), which will guide when assessments are completed, treatment started, medication doses adjusted, response and remission achieved, side-effects monitored, and individual care plans reviewed. Some recommended non-medical interventions are given throughout (see also Box 11); however, clinicians should refer to other manuals in the ENSP series for more detail regarding these interventions.

Note that aside from the recommendations for medical review given below, more frequent reviews may be needed following:

- any change in medication due to responsiveness, side-effects, non-adherence or discontinuation
- a significant change in the young person's mental state (which also highlights the importance of communication within the multidisciplinary team)
- an increase in risk (e.g. of suicide or harm to others).

BOX 11. NON-MEDICAL INTERVENTIONS RECOMMENDED DURING RECOVERY FROM A PSYCHOTIC EPISODE

An overview of the comprehensive service approach and clinical interventions can be found in *EPPIC Model Service and Service Implementation Guide*. More specific detail on some of the following interventions can be found in the full range of ENSP manuals. The following interventions are recommended for every phase of recovery from an episode of psychosis:

- involvement in groups between reviews to provide extra support and peer contact for the young person
- ongoing family work with possible referral to a specialist family worker or therapist for more complex cases
- promotion of social and vocational recovery
- liaison with employers, schools or tertiary institutions to plan young person's return to work or study
- adaptation to illness work
- psychological interventions to address comorbid difficulties such as depression, anxiety, or substance abuse, and to build resilience and coping skills
- relapse prevention work.

Management during the UHR phase

Young people identified as UHR for psychosis (see page 28) have a relatively high transition rate to a psychotic disorder over a 1 to 5-year period.[123] Effective identification of young people who are in this phase, and intervention during this period, may reduce the risk of transition to psychosis, delay its onset or minimise its impact.[123-125] Although the majority of young people identified as UHR for psychosis will not progress to a psychotic disorder and indeed may remit spontaneously,[126] international consensus guidelines recommend specific interventions at this phase of illness.[127] These interventions are qualitatively different to those recommended during later phases of psychosis, and this difference emphasises the need to consider at what point along this potential pathway to psychosis the benefits of a particular intervention outweigh the disadvantages.

Aims of interventions in this phase

The primary aim of interventions in this phase is to delay or prevent the onset of a full-threshold psychotic episode, reduce attenuated psychotic symptoms, reduce comorbid symptoms, such as anxiety or depression, and facilitate a full functional recovery. Intervention during this UHR phase also ensures that, in the event that transition occurs, the individual is already engaged with treatment services; this will facilitate rapid and non-traumatic commencement of treatment of FEP.[125]

Frequency of medical review

In the first few weeks following initial assessment, the young person should be seen at least weekly. Subsequent frequency of medical contact is guided by the severity and complexity of the each young person, but should occur at least every 6 weeks, if not more frequently. More medical contacts are arranged if the young person appears to be close to transitioning to psychosis, in crisis, presenting with acute risks, or if symptoms are worsening.

Interventions

It is unusual for young people who are at UHR of psychosis to require admission to hospital and this generally occurs in the context of significant comorbidity or suicidality. Comorbid depression, with or without anxiety, is common in this group and should be treated, as the symptoms and associated functional disability may be more of a concern for young people than their sub-threshold psychotic symptoms.[125,128] Young people in particular are susceptible to impairment of social development during the period before the onset of psychotic symptoms.[129]

Options to manage this phase include psychological and pharmacological strategies, detailed below (see the ACGEP for a detailed discussion[1]). Young people who seek help for distress and disability associated with their symptoms should be engaged, supported and offered specific treatment for comorbid conditions such as depression, anxiety and substance abuse.[1]

Non-medical interventions in the UHR phase

Non-medical interventions in this phase include interventions to reduce the effect of predisposing, precipitating and perpetuating factors (e.g. family work, group work, addressing substance use and addressing insomnia) and psychological interventions such as cognitive-behavioural therapy (CBT), which has been shown to reduce transition rates to FEP and the likelihood of being prescribed antipsychotic medication.[22] Recommended CBT interventions include those that address:

- stress management
- positive symptoms
- depression/negative symptoms
- basic symptoms
- other comorbidities.

A full description of CBT interventions for young people at ultra high risk of psychosis can be found in *A stitch in time: interventions for young people at ultra high risk of psychosis,* which is part of the ENSP series of clinical manuals.

Medical interventions in the UHR phase

Omega-3 fatty acids

Omega-3 fatty acids have been found to have beneficial effects when taken during the UHR phase. Compared with placebo, omega-3 fatty acids prevented transition to psychotic disorder, with greater improvement in Global Assessment of Functioning (GAF) scores, and a time to onset of 4 weeks.[130,131] Larger trials are in progress to validate these findings.[124] Eicosapentoic acid (EPA) increases glutathione, the principal antioxidant defence of the brain, and its efficacy in recent-onset psychosis, but not chronic schizophrenia, may suggest differential pathophysiological pathways in early onset illness that may be amenable to intervention.[22] Omega-3 fatty

acids have also shown a generalised positive effect on mental health, including major depression, that suggests that they may modulate mood, impulsivity and aggression.[22]

Antidepressants

Antidepressants should be used when clinically indicated (i.e. when CBT is not effective) to treat any significant comorbid depression, OCD or anxiety. There is limited evidence that they may play a role in reducing the risk of transition to psychosis by improving mood and perception of experiences and environmental stressors.[22] Two studies have suggested that antidepressants may reduce the risk of subsequent psychosis to a greater extent than antipsychotics do; however, these were uncontrolled studies and should be interpreted with caution, due to adherence being lower for antipsychotics than for antidepressants and the possibility of differences in baseline symptoms and functioning.[22] Antidepressants alone would be a very unwise choice in those with high-risk indicators for mania or bipolar disorder.

Mood stabilisers

Mood stabilisers should be used to treat any comorbid conditions, such as bipolar disorder, as indicated by clinical guidelines. The finding that mood stabilisers appear to have a neuroprotective role has led to some commentators recommending their use in the UHR/prodromal phase. However, there are no studies to support their use, and given the range of side-effects and complications associated with them (e.g. risk in pregnancy) it would be wise to wait until clear evidence emerges in their favour.

Antipsychotics

The currently available evidence suggests that antipsychotic medications should not be used as first-line therapy for young people in the UHR phase.[132] Although earlier trials have suggested that low-dose antipsychotic medication may be effective, either alone or in conjunction with CBT, in preventing or delaying a transition to psychosis,[1] more recent studies have not demonstrated a pronounced difference between supportive therapy and intervention with either CBT or CBT and antipsychotic medication.[123,132]

Initiation of antipsychotic medication is therefore not generally indicated unless the young person meets the DSM-5/ICD-10 criteria for full-threshold psychotic disorder.[1] In exceptional circumstances, antipsychotic medication may be considered as third-line treatment, for example, where a young person is displaying rapidly worsening symptoms or functional deterioration, when treatment of any depression has proved ineffective and there is a severe risk of suicide, or when there is increasing aggression or hostility that poses a risk to others.[1] SGAs in low doses should be considered in these situations, as a therapeutic trial for a limited period.[1]

Medical management in the acute phase of FEP

Aims of intervention in the acute phase

The treatment priority in the acute phase is to reduce the DUP and effect a full recovery, returning the young person to normal life as quickly as possible. Medical input at this early stage is central to undertaking assessment and investigations, developing a formulation, consideration of diagnosis, risk assessment and construction of an individualised care plan.

About 80% of young people with FEP treated within early psychosis services will be expected to achieve full or partial remission within the first 18 months of treatment.[11,49] About 6% will remain acutely psychotic despite treatment.[133]

Frequency of review

A young person must be offered a medical review within 24 hours of referral to an early psychosis service if they are acutely unwell and at a high risk of harm. All others should receive a medical review within 48 hours of referral. They should then be seen by a consultant within the first week, then at least weekly by a medical practitioner.[1] Other early psychosis clinicians will provide interventions and monitoring in between medical reviews. This requires a considerable, but appropriate, amount of medical resources from the outset as assessment continues, investigations are undertaken and medication is adjusted. Families will need to be closely involved in this process and should have regular access to medical staff for psychoeducation, feedback, support and advice about investigations, diagnoses, treatment, recovery issues, and risks. Families may find family peer support particularly beneficial during this phase. Medical reviews can be reduced gradually as the young person responds to treatment and recovery becomes established.

Interventions

Unlike individuals identified during the UHR phase, for many young people with FEP their first contact with mental health services is through hospital admission, too often under the mental health act.[11] Once discharged from hospital, these young people require assertive outreach follow-up in the community.

Medical interventions for non-affective psychosis

Clinicians should follow the principles of pharmacotherapy outlined on pages 48–53 and the treatment algorithm shown in Figure 4 on page 54. Briefly, management of medical interventions should involve:

- initiation of antipsychotic medication quickly to reduce DUP an achieve remission sooner. Dose recommendations are shown in Box 12. Note that no advantage is conferred by a loading dose, and in fact this only increases the risk of side-effects, disengagement, and potentially long-term dopamine receptor sensitivity
- use of SGA medication over FGAs
- use of a shared decision-making tool to engage the young person in ownership of adherence to medication (some useful tools can be found at www.choiceandmedication.org/hscni/conditions/9/)
- discussion with the young person about metabolic risk from the start of the young person's treatment
- close monitoring for metabolic side-effects
- switching of medication if no clinical response after 2–3 weeks (see page 77).

CASE SCENARIO **JASMINE** CONTINUED from page 32

Following the GP's visit, Jasmine becomes more agitated and aggressive, and a Mental Health Act assessment is arranged. Jasmine is later admitted to the inpatient unit of an early psychosis service for assessment.

The initial management in hospital comprises:

- a period of 48 hours observation, ideally without antipsychotic medication
- gathering of Jasmine's history, a risk assessment and development of risk management plan. Multidisciplinary team to decide on level of observations and leave allowance
- use of benzodiazepines and night sedation to help treat anxiety/agitation/distress and insomnia. Further investigations to be conducted as per protocols
- a physical health check and baseline measurements, including fluid balance chart
- a named nurse to assist with engaging Jasmine
- support offered to both Jasmine and her family by providing psychoeducation and managing the potential trauma associated with hospital admission
- shared decision-making to consider Jasmine's options for medical treatment.

Once Jasmine has been assessed as meeting the threshold criteria for FEP, she is started on 50 mg quetiapine, as she stated during the shared decision-making process that she needed help with insomnia and agitation. Her medication dose is optimised over the following week, and her symptoms begin to settle. Jasmine's insight gradually improves and she is able to take periods of escorted leave from the ward. She begins engaging with the early psychosis service team and can acknowledge that something has not been right with her mental health for some time.

Jasmine has two trials of overnight leave after agreeing to continue treatment and engage with the inpatient unit and early psychosis service. She is eventually discharged back to her parents' house and followed up by the home-based care treating team to ensure she continues her antipsychotic medication. She still experiences some psychotic symptoms, primarily paranoia and auditory hallucinations, but to a lesser extent and associated with less distress.

BOX 12. **DOSING RECOMMENDATIONS FOR INITIATION OF ANTIPSYCHOTIC MEDICATION IN FEP**

- Start at lowest effective dose, with consideration of each young person's risk of side-effects or factors, such as smoking, that may reduce efficacy of medication. The recommended starting daily doses according to the ACGEP are as follows:[1]
  - Risperidone: 0.5–1 mg/day
  - Quetiapine: 25–50 mg/day
  - Amisulpride: 50–100 mg/day
  - Aripiprazole: 5–10 mg/day
- If no significant response is observed within 2–3 weeks, or only partial remission observed by 4–6 weeks, increase medication, by increments of the initial dose
- Increase made every 2–3 weeks, depending on acuity and risk. Enough time should be allowed between increases for responses to emerge.

A slower and less complete response is to be expected in those with longer DUP. People with FEP are particularly susceptible to side-effects and should be monitored closely if progressing to higher doses.

Augmentation medications

If omega-3 fatty acids have a role in prevention of psychosis, it would seem sensible to prescribe them in FEP, even if the research in this population is limited, as they may assist with cognitive deficits.

Lithium augmentation has been recommended by some authors based on the findings of a small number of studies. However, lithium is frequently complicated by very significant and enduring side-effects and it is best avoided unless clearly indicated, particularly in young people and women of childbearing age.

Treating depression after an acute psychotic episode

Post-psychotic depression occurs commonly after acute psychotic symptoms remit, and should be treated. Post-psychotic depressive symptoms appear to be different to those experienced during the acute episode.[134] The latter appear to result from the psychosis itself and tend to remit, along with the psychotic symptoms, following antipsychotic treatment. In contrast, post-psychotic depressive symptoms do not respond to antipsychotic therapy alone and may require additional treatment.[134]

Although to some extent the features of post-psychotic depression (low mood, anxiety, stigma, self-doubt, social withdrawal and hopelessness) are indicators of normal emotional responses to a major life event, they can cause residual cognitive deficits and negative features that can be severely debilitating. Importantly, they can be rather resistant to psychosocial interventions.

Antidepressant medication does appear to have some effect in lifting mood in post-psychotic depression, but unfortunately has little effect on negative features and cognitive deficits. Changing antipsychotic medication may be a better option. If antidepressant medication is considered, SSRIs are the first choice, to be prescribed consistent with clinical recommendations for major depression, and should be continued for at least 6 months. As mood lifts, the focus should turn to engaging the young person in psychosocial interventions that aid functional recovery.

Even though cognitive-oriented therapies would seem a sensible intervention in post-psychotic depression, the evidence is unfortunately limited. Therapy may have its own 'side-effects', and too much emphasis in sessions on asking the young person to revisit their experience of the psychotic episode may actually be detrimental – similar to picking repeatedly at a scab and thereby preventing normal healing. A certain amount of healthy denial and time to process what has happened needs to be allowed. Similarly, parents and other supports need to be mindful of allowing the young person time to recover and try to avoid repeatedly burdening the young person with their own concerns and issues.

Medical interventions for affective psychosis

Acute manic psychosis

Acute manic psychosis should be treated with a combination of mood stabiliser and antipsychotic (see Figure 5 on page 55), as monotherapy is shown to be less effective.[52] However, convincing someone who is acutely manic that they should start medication is a considerable challenge and antipsychotic medication would be often the easier to commence in such cases.

The following are recommended dosing regimens for medication in affective psychosis:

- Antipsychotic dose regimens follow the same as non-affective psychosis.
- If antipsychotics are continued after the acute episode as a prophylactic option instead of mood stabilisers, they should be continued for at least 18 months, but with consideration of lowering the dose.
- Antipsychotics that are used in combination with a mood stabiliser can be gradually withdrawn within several months after the manic episode has remitted.
- Mood stabilisers (not including SGAs) should be commenced from the start and increased to anti-manic doses relatively quickly. If there is a significant chance of pregnancy, mood stabilisers should be avoided.
  - Lithium is the gold standard, and its mood stabilising effect usually begins within the first week as long as blood levels are close to 1.0 mM/L. Sodium valproate should be considered if there is no response to lithium. Other mood stabilisers (e.g. carbamazepine, lamotrigine) have a very limited role in acute manic psychosis.
  - Continue for 18 months after the first episode. This may be much longer in young people with established bipolar (i.e. previous episodes of depression and hypomania) or if there are additional risk factors (e.g. family history, ongoing drug use, stressors).

CASE SCENARIO **JUSTIN** CONTINUED from page 38

A mobile assessment and treatment (MAT) team from a nearby early psychosis service is called to assess Justin. They believe he is presenting as manic, and as he appears unable to consent to voluntary treatment, the team arranges a hospital admission under the Mental Health Act. His parents are called to obtain some collateral history.

Justin has never been treated for mental illness, although he has experienced at least two episodes of depression that lasted for several months, which were not treated because they resolved. Otherwise Justin is fit and well. He does not ordinarily use drugs, although he occasionally smokes cannabis with friends. There is a family history of bipolar affective disorder on his father's side. Prior to returning home for the summer break, Justin had been studying hard to keep his grades up and had been quite stressed.

Justin's risk factors for developing a first episode of psychosis are:

- positive family history of bipolar affective disorder
- substance use
- stress from exams
- lack of sleep

The initial treatment for Justin should include:

- safety/risk management
- ensuring he gets enough sleep
- symptom control
- assessment and appropriate investigations
- placing him in a low stimulus, contained environment
- support for Justin and family
- psychoeducation
- monitoring Justin's sleep, food and fluid intake

CASE SCENARIO **JUSTIN** CONTINUED from page 75

On admission to hospital, Justin is offered diazepam and night sedation orally, which he accepts, sleeping a few hours that night. His initial examination and investigations are normal and do not suggest acute intoxication or an organic presentation. After an initial 48-hour period of observation on the ward, Justin settles slightly after treatment with the medication; however, he remains irritable and agitated, talking to himself about how he is special and should not be prevented from his mission.

The management of Justin's treatment includes:

- commencing him on a mood stabiliser – lithium as first choice – and titrating rapidly, aiming for serum level of 1.0 mM/L
- offering him low-dose oral antipsychotic medication (SGA initially). An initial dose of an IM SGA could be considered, but only if Justin refuses all oral medication. Antipsychotic medication would be expected to be necessary only for the acute phase, as an adjunct to lithium
- encouraging his choice for medication type as much as possible
- continuing diazepam and night sedation if needed
- continuing to assess Justin in the ward environment, including assessing and managing risks
- monitoring Justin's sleep, food and fluid intake

Psychotic depression

Psychotic depression should also be treated with combination therapy (i.e. antipsychotic and antidepressant) during the acute phase.[52] Monotherapy alone is usually ineffective once a depressive episode is complicated by psychotic features.

- The same antipsychotic dose regimen should be used as for non-affective psychosis.
- Antidepressant medication treatment should follow clinical guidelines for depression.
- If there is a history of hypomania or family history of bipolar disorder, mood stabilisers are advisable in the long-term. Caution is advised with ongoing use of antidepressant medication to avoid risking a subsequent manic episode.

Managing response to treatment

Predicting response

It is important to identify non-responders to antipsychotic treatment as early as possible to prevent unnecessary persistence with an ineffective treatment.[135]

In one analysis, 53.3% of adolescents and adults with FEP had responses within 6 weeks of starting treatment with antipsychotics, while other studies have shown that approximately 75% of people with FEP experience remission within the first

6 months.[49,136] A poorer response to medication was associated with less severe symptoms at baseline, a lengthy DUP, poorer premorbid adjustment during adolescence and a family history of psychosis.[136]

An early response, or an improvement (reduction) of ≥ 30% in the Positive and Negative Syndrome Scale (PANSS) total score in the first two weeks, has been shown to be a significant predictor of response and remission in people with FEP after 8 weeks.[137] However, it is not known whether people who are not early-responders would benefit from switching medications.[137] A later study found that a reduction of ≥ 50% in the PANSS total score at 6 weeks was a more accurate predictor of the maintenance of response at 1 year.[138] While individuals could still be accurately assessed as responders with a ≥ 20% improvement in the PANSS total score, the later assessment was 40% more likely to correctly identify non-responders.[138]

The lack of a prompt response to antipsychotic medication is not always an indicator that the medication is ineffective. Although some people respond rapidly, within 1 week of commencing treatment, the time to response can be as long as 10 weeks; the median response time is 3 weeks.[135] Emsley et al. (2006) found that of individuals who had not responded at week 1, 40% had responded by week 4, and a total of 65.3% eventually achieved a clinical response.[135] Gallego et al. (2011)[139] found that the cumulative response rate increased from 39.6% at 8 weeks to 65.2% at 16 weeks, while in a trial of very low-dose risperidone, McGorry et al. (2011) found that 58.7% of participants responded within 4 weeks, increasing to 65% at 8 weeks.[140]

Clinically, an insufficient response after 6–8 weeks is often used as a predictor of future non-response,[51] although some people experiencing FEP will take longer than 8 weeks to respond.[139]

Medical management for incomplete recovery is discussed on page 87.

Switching medication in the acute phase

If no clinical response is observed after 2–3 weeks on the highest dose of the first SGA (see Figure 6) then a switch to a second line SGA is advisable.

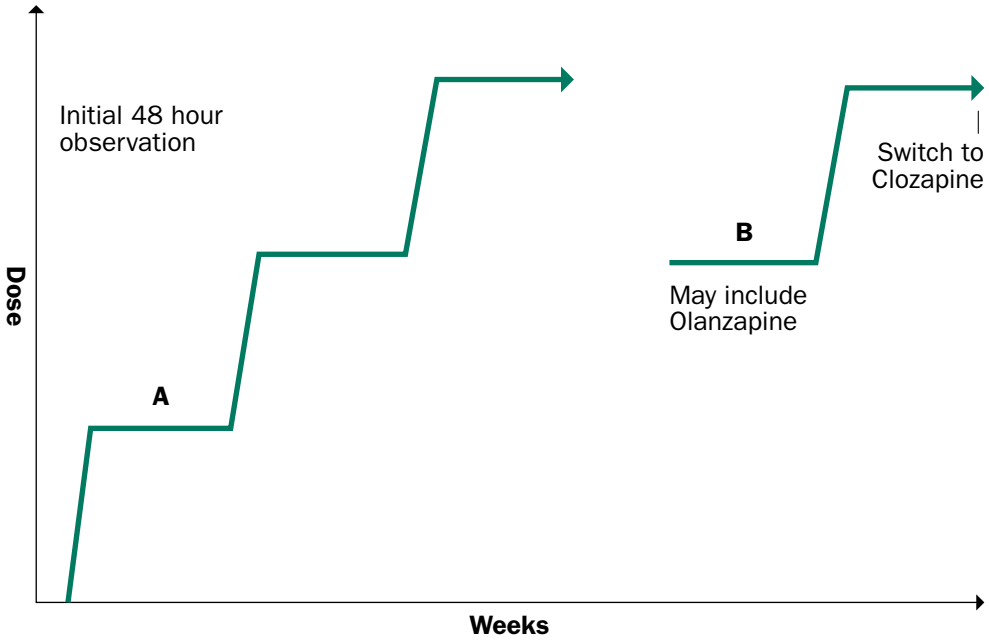
The general principles for switching medications in FEP are that changes should only be made to one drug at a time,[141] avoiding abrupt switching. Overlapping switching strategies, such as cross-titration or a plateau switch over a few weeks, are recommended, particularly when changing between medications with different levels of sedating effects or differing pharmacological actions.[141]

However, early on in the acute phase, there may be little advantage to overlapping switching, as the time the young person has spent so far on medication is short, and doubling up on medication will only increase the risk of side-effects. Clinicians may wish to cross-titrate if they wish to initially preserve the sedating effects of the first SGA or are concerned about EPSE or sedating side-effects of the second SGA.

Recommendations for switching antipsychotic medications after 2–3 weeks of no response are:

- Introduce second SGA at the mid-range dose for 2–3 weeks (at half-dose for first 2 days to minimise side-effects).
- Increase to the top dose if no response.
- If no response to a trial of two SGAs is observed (as in Figure 6), clozapine should be seriously considered.

FIGURE 6. **SWITCHING GUIDELINES FOR FIRST EPISODE NON-AFFECTIVE PSYCHOSIS**



Starting daily doses[1]	
Risperidone	0.5–1 mg/day
Quetiapine	25–50 mg/day
Amisulpride	50–100 mg/day
Aripiprazole	5–10 mg/day
Olanzapine (second line)	2.5–5 mg/day
Top daily doses[1]	
Risperidone	6 mg/day
Quetiapine	750 mg/day
Amisulpride	800 mg/day
Aripiprazole	30 mg/day
Olanzapine (second line)	20 mg/day

CASE SCENARIO **JASMINE** CONTINUED from page 73

After 2 months, Jasmine is still struggling with residual psychotic symptoms and complains of low mood, despite adherence to her medication and abstinence from drug use. She is on the maximum recommended dose of quetiapine.

What would you consider next?

- Reviewing adherence and substance use.
- Switching antipsychotic to another oral SGA – involve Jasmine in the choice.
- Starting Jasmine on an SSRI.
- Adding CBT if she is not already receiving this.
- Monitoring mood/risk – especially hopelessness and suicidality.

Jasmine's quetiapine medication is discontinued and she is switched to aripiprazole; the medication dose is adjusted accordingly. Jasmine also has low mood and feelings of hopelessness (without suicidal thinking) due to her ongoing symptoms and a perceived delay in her progress. She agrees to commence on an SSRI to help improve her mood.

Medical management in the early recovery phase

The early recovery phase is characterised by a reduction in acute psychotic symptoms. A young person's recovery from a first episode of psychosis may be defined in terms of symptom resolution, or remission, improvement in social and vocational functioning, or by a more personalised model of recovery set out by the individual.

Although there is no universal definition of what constitutes 'remission', it refers specifically to a sustained reduction in psychiatric symptoms, as measured by scales such as the Clinical Global Impressions Scale.

'Recovery' differs from the concept of remission in that it may signify that a young person is able to function adequately and has an acceptable quality of life while also experiencing some ongoing symptoms.

Aims of interventions in early recovery

Interventions should focus more on helping the young person to understand the nature and onset of the psychotic episode (using their explanatory model) and develop plans for and commence activities that will support their return to normal function. Ongoing family work, particularly in relation to repeated psychoeducation and involvement in treatment planning, is important.

Frequency of review

Face-to-face review is recommended weekly or even more frequently by the case manager, with medical review weekly. Telephone contact can be helpful in between reviews.

Interventions

Once acute psychotic symptoms have remitted, it is not uncommon for side-effects to 'catch up', especially if excessive doses have been used. Young people may complain of lethargy, tiredness, weight gain, and oversedation. Clinicians must monitor for side-effects and work to prevent or reduce them, as there is a risk they may cause the young person to stop taking their medication. If side-effects do occur, consider changing to a different medication at equivalent doses and switching over gradually by 'overlap and discontinuation' over a 2–4-week period (i.e. introducing one in slowly up to equivalent doses and then withdrawing the other gradually).

The period after a psychotic episode begins to resolve appears to be when a young person is most receptive to psychoeducation about their illness and the possibility of relapse. This is therefore a good time for relapse prevention and medication adherence work. Psychological treatment should be continued, and other non-medical interventions should be included as appropriate (see Box 11).

Maintenance medication and discontinuation of treatment

There is no consensus on the optimal duration of maintenance antipsychotic treatment following the remission of psychotic symptoms.[42] Guidelines for treatment of young people with FEP note that the duration of maintenance therapy in current clinical practice ranges from 1 year to an indefinite period, and recommend that consideration be given to the severity of the initial episode and the response to treatment when deciding how long to continue antipsychotic maintenance.[42,51]

Importantly, much of the focus has been on prevention of relapse, without consideration of other important aspects of recovery, such as functional status.[142]

Varying comparative rates of relapse between maintenance medication and discontinuation have been reported. Zipurksy et al. (2014)[143] found a marked difference in 1-year relapse rates in people with FEP who had been stabilised on medication for a period ranging from 12 to 24 months. The 1-year risk of relapse in people on maintenance medication was estimated to be only 3%, while people who had discontinued medication had a risk of 77%. Robinson et al. (1999)[144] reported that discontinuation of antipsychotic medication increased the risk of a first and second relapse by five times. However, many of the studies investigating relapse did not allow for sufficient psychosocial interventions, which are of utmost importance for the effectiveness of pharmacotherapy.[54]

In a study comparing guided discontinuation and maintenance treatments in adults with FEP after 6 months of positive symptom remission, Wunderink et al. (2007)[145] found that the relapse rate in the discontinuation group was double that of the maintenance group (43% vs 21%). Only 20% of the discontinuation group successfully discontinued treatment, while approximately half of the group was unable to discontinue treatment at all. At this time point, there was no difference between the treatment groups in functional outcome. However, in a follow-up of the

same groups at 7 years, striking differences were observed.[142] The relapse rates in the guided discontinuation group had flattened out at around the 3-year time point, and by 7 years, symptom remission and relapse rates were equivalent in both groups. Functional remission in the guided discontinuation group was more than twice that of the maintenance treatment group (46.2% vs 19.6%). It appeared that despite the short-term drawbacks of dose reduction, in terms of a higher relapse rate, there were marked benefits in the key domains of functional capacity, which were not apparent until long-term evaluation.

Relapse prevention has long been the main goal of treatment. This is not surprising, given that relapses are risky, distressing, and can set back recovery in all domains. The high rate of medication non-adherence/discontinuation in young people with early psychosis is one of the strongest risk factors for relapses in young people with early psychosis.[146] However, given the results of the Wunderink study, modest exacerbations of symptoms, which are more common in the first 3–5 years after diagnosis, may be a price worth paying – in early remitters at least – for better longer-term functional recovery.[147] This is particularly relevant for young people, who tend to give more weight to the recovery of their social functioning, as opposed to symptom recovery alone.[148,149] Furthermore, there is good evidence to suggest that a significant percentage of young people who experience a first psychotic episode can achieve full functional recovery, even in the presence of residual positive symptoms.[150] More research is needed to determine whether dose-reduction strategies combined with proactive psychosocial recovery interventions will lead to improved functional recovery rates in FEP.[147]

See ‘Helping young people transition to discharge’, on page 95, for practical information about managing discontinuation.

KEY PRACTICE POINT: **DISCONTINUING ANTIPSYCHOTIC MEDICATION**

How long a young person should remain on medication once symptoms have remitted has not been established. It is not possible to tell which young people will benefit from discontinuing antipsychotic treatment early and which will not. However many will want to discontinue. It is ultimately best to be guided by the young person’s choice in the matter. The key thing to remember is if a young person decides to discontinue medication, they should be supported and provided with relapse prevention strategies, crisis management plans and constant monitoring. It is vital that they are retained in the early psychosis service.

CASE SCENARIO **JUSTIN** CONTINUED from page 76

Within 2 weeks of being initiated on a combination of lithium and a low-dose oral SGA, Justin begins to improve. His sleep patterns and food and fluid intake return to normal, and his insight improves. Justin is able to have short periods of escorted leave from the ward, and can talk to his primary nurse about his recent experience, acknowledging that something hasn't been quite right for the last few weeks. A diagnosis of first episode psychosis (manic) is made by the inpatient multidisciplinary team. While in hospital, Justin is allocated a case manager and treating doctor from the early psychosis continuing care team to facilitate engagement while he is an inpatient.

Justin is discharged into his parents' care after a 4-week admission and a successful trial of overnight leave. The engagement process with his case manager from the continuing care team has already begun and he is happy to continue seeing her on a regular basis. He agrees to continue medication and understands the importance of looking after himself and avoiding drugs. The MAT team are involved in Justin's transition from hospital to home. They visit him every day for the first week following discharge then hand care over Justin's case manager.

Justin is seen by his case manager and doctor twice a week initially; however, this is reduced to once-weekly after 2 weeks, as he is managing well with support from his family. The case manager also supports Justin to get back into regular activities, including joining the local gym.

Now that Justin has recovered from the acute episode and is being treated in a community setting, his treatment plan should include:

- ongoing monitoring of his mental state, medication adherence and risks
- medication monitoring
- tapering of antipsychotic medication once all psychotic symptoms have abated and remitted fully
- continuing lithium but reducing dose slightly if necessary as the episode resolves, if his serum levels rise above 1.0
- physical health monitoring and promoting good physical health – smoking cessation, drug abstinence, exercise, diet
- social and vocational recovery
- relapse prevention and psychoeducation
- psychological interventions
- family work
- work to ensure he remains engaged with the service – especially once his recovery is underway but not fully resolved. The service should remain in contact over the next 2–5 years for monitoring, even once Justin becomes well.

Medical management in the ongoing recovery phase

The ongoing, or late, recovery phase is characterised by a remission of positive symptoms and the young person's returning to their normal level of functioning (e.g. school, work, friendships, social activities and family life) and continuing to live a meaningful life.

Aims of interventions in this phase

The main aims of interventions in the late recovery phase are to maintain wellness and maintain normal functioning in education, employment or social activities. A smooth transition from the service to the next service provider is also a focus.

Frequency of review

EPPIC Model minimum standards recommend face-to-face review every 2–4 weeks by the case manager with a medical review every 4 weeks at a minimum.[2] Telephone contact may be made in between, which may include liaison with family or those people or services involved in functional recovery. Clinical reviews involving the multidisciplinary team occur on a 3-monthly basis or more frequently if required due to increased risk or problems related to deterioration. Again, non-medical interventions should be continued (Box 11).

Interventions

As discussed on page 80 ('Maintenance medication and discontinuation of treatment') there is no consensus regarding the ideal time for young people to remain on medication following remission. Whatever is decided, the importance of relapse prevention work in this phase cannot be understated. It is important to work with the young person to implement strategies for relapse prevention (see Box 13) – if a young person does experience a relapse, the implementation of a good relapse plan and provision of psychoeducation can help limit the potential damage, so that the relapse does not become a significant set-back in the recovery process.

BOX 13. **STRATEGIES FOR RELAPSE PREVENTION IN EARLY PSYCHOSIS**

The following strategies are critical to ensuring a young person has the best chance of avoiding a major relapse:

- helping the young person to understand why they may have developed psychosis in the first place (including exploring what their predisposing, precipitating and perpetuating factors might be)
- working with the young person and their family to identify possible early warning signs of relapse and construct a relapse plan
- reviewing the 'relapse signature' of a relapse (if young person has already experienced a relapse)
- building resilience in the young person and minimising stressors
- managing substance use
- promoting social and vocational recovery
- working with the young person and family to help create a home environment that promotes recovery.

CASE SCENARIO **JUSTIN** CONTINUED from page 82

Justin makes a good initial recovery over the next few weeks; however, he opts to defer returning to university for a year to feel more confident, as he has noticed he doesn't feel enjoy seeing people as much as he used to. He is also sleeping too much and has trouble motivating himself. His case manager identifies depressed mood as a problem and arranges for him to see his psychiatrist. At the review, Justin reports depressed mood (3/10) with biological features and some suicidal ideation, with no serious intent but some hopelessness. He denies any recent substance use and says he is taking his medication (lithium alone by now) as prescribed.

Depression is a common occurrence following a first episode of psychosis, especially after a manic episode. Treatment of bipolar depression can be difficult and requires a biopsychosocial approach. Risk assessment is also important, as risk of suicide is high in FEP with depression.

The psychiatrist opts to add an SSRI antidepressant to the lithium and specific mood-related work with Justin by his case manager with support from the senior psychologist in the team.

At this stage, the risks of starting the SSRI includes the risk of cycle destabilisation, although this is less likely if Justin's lithium is continued. The psychiatrist advises Justin of this risk, and tells him they will need to monitor his mood. Another medication option to consider would be quetiapine as an adjunct if the SSRI or an SNRI are unsuccessful.

Justin's mood improves over the next 2 months. He enrols in a part time music course, is seeing more of his friends and begins going out at the weekends. Justin continues to see his case manager to learn about staying well. By the following spring he feels well enough to arrange a return to university.

Medical management in a subsequent acute phase (relapse)

As many as 20% of people with psychotic disorders will only experience a single psychotic episode.[151] However, Alvarez-Jimenez et al. (2012) found in a systematic review and meta-analysis examining rates of relapse in people with FEP that the pooled prevalence of positive symptoms was 28% at 1 year follow-up, 43% at 2 years and 54% at 3 years.[146] Whether these rates are lower in young people coming through early psychosis services remains to be seen, but they do emphasise the need for a new approach to intervention in FEP. With each relapse, a young person's chance of recovery becomes lower and the likelihood of persistent symptoms increases.[146]

In the review mentioned above, factors consistently associated with an increased risk of relapse were non-adherence to medication, substance use disorder and poor premorbid adjustment. Critical comments from family or supports were also associated with increased risk.[146] There was no significant association between

the risk of relapse and DUP; however, there was significant heterogeneity across studies. One study found DUP to be a significant predictor of relapse over a 7.5-year follow-up, showing that early treatment (within 2 months of onset of psychotic symptoms) and social support significantly reduced the vulnerability of young people with FEP to subsequent psychotic episodes.[151] In contrast, four other studies showed no significant association between DUP and relapse over follow-up periods ranging from 1 to 3 years.[146]

Aims of interventions in this phase

The aims of intervention at this phase of illness are to minimise the length of the period of relapse and minimise any negative sequelae resulting from a relapse. These include distress associated with psychotic symptoms, loss of function, exposure to stigma-related issues and loss of optimism around recovery.

Frequency of review

Following a relapse, a formal assessment, using a formulation-based approach, of the factors that contributed to the relapse, is essential, as some contributing factors may be avoidable (e.g. cannabis use).

An increase in the frequency of medical reviews to at least weekly is also essential. Home-based care with the support of a mobile assessment and treatment team should be considered. (See the ENSP manual *There's no place like home: home-based care in early psychosis* for more information.)

Interventions

Investigations may need to be repeated and a review made of baseline measures (e.g. neurocognitive deficits, daily living skills, occupational and social functioning) and family stresses and functioning. This should be reviewed with the young person and their family so a new recovery and maintenance plan can be agreed upon and put into action.

Considerations for medical intervention in this phase include:

- Hospital admission may be required if the young person's needs exceed the capacity for home-based care.
- Doses of medication may need to be higher than those given during the first episode to achieve the same effect.
- A longer period on maintenance medication may be required following remission from a relapse.
- There may be higher risk of treatment non-adherence following a relapse. If treatment adherence is suspected to have caused the relapse, and the young person's level of risk is high, then LAI antipsychotic medication should be offered (see page 66). A number of SGAs now come in depot form, including risperidone and palperidone.
- Psychosocial interventions should be revisited, with even greater emphasis on functional recovery and relapse prevention. Suicidality should be monitored closely as this group of young people is at greater risk.[35]

TABLE 5. **CUMULATIVE RELAPSE RATES FOLLOWING RECOVERY FROM A FIRST EPISODE OF SCHIZOPHRENIA**

ORDER OF RELAPSE	YEARS AFTER RECOVERY FROM PREVIOUS EPISODE	RELAPSE RATES (%)
First	1	16.2
	2	53.7
	3	63.1
	4	74.7
	5	81.9
Second	1	19.1
	2	48.7
	3	56.0
	4	56.0
	5	78.0
Third	1	12.5
	2	31.1
	3	72.4
	4	86.2

Adapted from Robinson et al. 1999[144]

Medical management during incomplete recovery

'Incomplete recovery' is a preferred term to define those individuals who, despite receiving or having access to treatment, have not recovered from the onset of a psychotic episode.[152] The term includes those people who are 'treatment resistant' (i.e. are receiving evidence-based treatments, but are not adequately responding to the treatment provided) and those who may be 'resistant to treatment' (i.e. those individuals who have access to treatment, but are partially or fully non-adherent or disengaged). The actual prevalence of incomplete recovery varies depending on the diagnostic group assessed and definitions and criteria for 'recovery' or 'treatment resistance', but ranges between 10–50%.[153] The need for early intervention is paramount, with less prevalence of incomplete recovery shown in those services with an early intervention in psychosis model.[11,133]

In the EPPIC Model, a young person is considered to be experiencing incomplete recovery if they have not recovered by 6 months following treatment for the first psychotic episode. However, **every** young person should be screened for signs of incomplete recovery at 3 months after initiating treatment, and those who show predictors for incomplete recovery at first presentation (see Box 14) should be flagged as being at risk.

BOX 14. **IDENTIFICATION OF YOUNG PEOPLE EXPERIENCING INCOMPLETE RECOVERY**

Predicting incomplete recovery

A number of predictors of incomplete recovery have been identified, which can be used to flag young people at risk of incomplete recovery. These include:

- a longer DUP
- a poor premorbid level of functioning
- poor functioning in the first year pre-treatment
- severe negative symptoms
- ongoing substance use
- high severity of symptoms
- cognitive deficits
- poor insight
- partial or complete medication non-adherence
- poor response in the first 6 to 12 weeks of treatment
- disengagement from the early psychosis service
- male gender.

Screening for incomplete recovery

Screen (at 3 months) for:[152]

- positive and negative symptoms
- cognitive symptoms, including insight
- affective symptoms
- suicidality
- social withdrawal, antisocial behaviour
- social functioning, reduced quality of life, impaired activities of daily living (IADL)

Aims of interventions in this phase

Interventions in this phase should aim to minimise DUP and achieve both symptomatic and functional recovery. Clinicians need to identify any factors that may be contributing to a young person's incomplete recovery and ensure that interventions target them accordingly. A comprehensive, case formulation-based approach is therefore essential.

Frequency of review

The level of face-to-face review with the case manager and doctor will need to be sustained as for the early recovery phase or increased, although this may fluctuate depending on need and treatment plans. For example, if a young person has high acuity or level of risk, or if they are commenced on clozapine, more frequent medical appointments are required. There may be a need for more regular review of care plans and diagnosis than for young people who have made a good recovery.

Interventions

Young people who are experiencing incomplete recovery need to be identified as soon as possible. A systemic, service-wide approach has been shown to be effective in early identification and management of incomplete recovery.[154] This approach should involve a clinical management panel of senior clinicians that is available to all clinicians to advise on interventions to aid recovery.

It is important to remember that 'recovery' refers not only to remission of positive symptoms, but also to remission of negative symptoms and recovery of social and vocational functioning. As shown in Box 14, there are a number of domains that need to be screened to identify incomplete recovery. Interventions for incomplete recovery should accordingly address all these domains of recovery.[152]

A case formulation-based approach is essential to helping clinicians identify factors that are contributing to an incomplete recovery and address those that are modifiable, such as non-adherence or substance use. Medical investigations may be required, including testing plasma levels to check for therapeutic doses or non-adherence.

In this phase, non-medical interventions provided by the early psychosis service may need to be provided more intensively – for example, CBT has been shown in a recent meta-analysis to be effective for managing symptoms of psychosis that have not responded to medical treatment.[155] Other interventions include family behavioural therapy, intensive vocational support and drug and alcohol interventions. A mobile outreach approach may be required, where case managers (with medical support) assertively engage the young person and provideinterventions offsite (e.g. in the young person's home).

Note that the role a young person's family plays in promoting recovery can be significant. A 2010 Cochrane review showed that interventions with families of people with schizophrenia may decrease their frequency of relapse, reduce hospital admissions and encourage adherence to medication, although the authors conclude that further research needs to be done in this area.[156] See the ENSP manual *In this together: family work in early psychosis* for more information about working with families to help promote recovery and prevent relapse in early psychosis.

Use of clozapine for treatment-resistant psychosis

In the FEP population, there is a high response rate to most antipsychotic medications, regardless of which one is used.[157] However, there is a subset of people with FEP who do not respond to first- or second-line antipsychotic treatment. Clozapine should be considered when remission does not occur despite the sequential use (with good adherence) of two antipsychotic medications for a period of 6–8 weeks.[42,71] Clozapine may also be recommended in people with a sustained or prominent suicide risk, either without depression, or when treatment for depression is ineffective.[71]

Clozapine is effective in treatment-refractory psychosis, producing improvements in positive and negative symptoms and having a low risk of EPSEs.[158] Despite these benefits, the use of clozapine is restricted to individuals who are either unresponsive or intolerant of other antipsychotic agents[159] because it may cause potentially serious and life-threatening agranulocytosis.[160]

The majority of cases of agranulocytosis occur within the first 6 months of treatment with clozapine, with the risk being highest during the first 3 months.[160] Haematological monitoring should be carried out within the 10 days prior to initiation of clozapine and repeated weekly for the first 18 weeks of treatment with clozapine, then every 28 days thereafter. More frequent monitoring is required if moderate decreases in the white blood cell (WBC) and/or neutrophil count are detected, and clozapine should be discontinued for people with very low WBC and/or neutrophil counts.[159] Monitoring for haematological adverse events is well established for clozapine, but it has been proposed that metabolic and cardiac adverse events also be assessed, as described by Berk et al.[159] and Ronaldson et al.[161] Clinicians should consult their local guidelines for recommended protocols for cardiac monitoring, as these vary. A consensus monitoring protocol developed in hospitals in Victoria is presented in Box 15.

BOX 15. **SUGGESTED MONITORING OF YOUNG PEOPLE PRIOR TO AND DURING THERAPY WITH CLOZAPINE**

Baseline

Clinical history and examination

Weight, blood pressure, heart rate

ECG

Transthoracic echocardiogram

Troponin and CK-MB level

Lipid profile and blood glucose level

WBC count and differential (repeat in 1 week if in amber range*)

Liver function tests

0–18 weeks

WBC count and differential (weekly if in green range* or twice weekly if in amber range)

Clinical evaluation, ECG, plasma troponin and CK-MB levels days 7 and 14

> 18 weeks

WBC count and differential (every 28 days if in green range or twice weekly if in amber range)

BOX 15. **SUGGESTED MONITORING OF YOUNG PEOPLE PRIOR TO AND DURING THERAPY WITH CLOZAPINE** CONTINUED

6 and 12 months

Lipid profile

Blood glucose level

Liver function tests

Transthoracic echocardiogram

Ongoing

WBC count and differential (monthly)

Blood glucose level (biannually)

Transthoracic echocardiogram (annually)

Lipid profile (annually)

Weight, blood pressure, heart rate, troponin and liver function test (as required)

Additional

Chest x-ray (if cardiac dysfunction suspected)

Inflammatory markers (if myocarditis suspected)

Selenium level (if cardiomyopathy suspected)

*'Green range' = WBC count > 3.5×10^9/L and neutrophil count > 2.0×10^9/L; 'Amber range' = WBC count between 3.0 and 3.5×10^9/L and/or neutrophil count between 1.5 and 2.0×10^9/L; 'Red range' = WBC count <3.0×10^9/L and neutrophil count <1.5×10^9/L.

CK-MB, creatinine kinase MB isozyme; ECG, electrocardiogram; WBC, white blood cell.

Adapted from Berk et al. 2007.[159]

Despite its efficacy in many people with treatment-resistant psychosis, still over 50% of people may not respond adequately to clozapine.[162,163] The appropriate duration of a clozapine trial has not been fully clarified, with recommendations ranging from 3–6 months to as long as a year to identify late-responders.[162,163]

In people who are clozapine-resistant, augmentation with a second antipsychotic medication is common clinical practice; however this should be balanced with the principle of minimising polypharmacy. While some people will benefit from this approach, two recent reviews[163,164] found little consistent research support and the potential for an increased risk of side-effects.[162] It is possible that a small subgroup of clozapine-resistant individuals will respond to augmentation with a second antipsychotic, but a means of identifying early responders has not yet been recognised.[165] Furthermore, antipsychotic polypharmacy is associated with increased risk of mortality, metabolic syndrome, cognitive impairment and nonadherence.[70] In light of the potentially serious risks and modest clinical benefits, augmentation of clozapine with a second antipsychotic should be weighed against the benefits and risks of other interventions for treatment-resistant psychosis.[70] Augmentation with SSRIs is often employed when negative or depressive symptoms are present, or in people with anxiety or obsessive-compulsive symptoms.[163] Some efficacy of antidepressants has been reported, notably fluvoxamine. Fluvoxamine

decreases the metabolism of clozapine, so it is unclear whether the observed clinical improvement is related to increased serum clozapine levels or the activity of fluvoxamine itself.[162,163] Mirtazapine, and to a smaller extent, paroxetine, sertraline and, in one randomised controlled trial, citalopram, produced improvements in negative symptoms, while fluoxetine showed no benefits.[162,163]

Mood stabilisers may be used to prevent seizures in people receiving high-dose clozapine regimens, in addition to people with mood instability.[162,163]

Electroconvulsive therapy (ECT) has been also investigated as an augmentation strategy for clozapine, although the available literature has reporting and methodological concerns, which make it difficult to draw conclusions.[162,163] However, limited clinical studies in young people suggest that ECT may be an option for clozapine-resistant schizophrenia.[167]

CASE SCENARIO **JASMINE** CONTINUED from page 79

Jasmine remains unwell, with ongoing psychotic symptoms and moderate distress, for another 6 weeks, despite taking the maximum dose of aripiprazole. However, she is not displaying risky behaviour or suicidal ideation.

What would be the next option for treatment?

- Consider clozapine – this should be offered at an early stage if there is a history of poor or limited response to treatment despite medication adherence or ongoing substance use. The diagnosis should be reviewed by the treating team prior to commencement.

Jasmine decides to try clozapine and is commenced on clozapine in the inpatient unit. It is administered according to the outlined clozapine clinical protocols, with appropriate investigations, monitoring, psychoeducation and consent provided. Jasmine is discharged from the inpatient unit after a brief stay, and the early psychosis service's home-based care team continues titrating the clozapine dose according to the appropriate clozapine protocols. After several weeks, Jasmine reports an improvement in her psychotic symptoms and a reduction in distress. Her mood improves, and she feels more self-confident and is engaging in more social activities.

Electroconvulsive therapy

ECT may be of use if symptoms persist, but it should be viewed as a treatment of last resort for resolving the acute episode, not least because of the significant stigma attached to this treatment.

Other than use as augmentation for people on clozapine, as described above, ECT may be of benefit to a select group of young people with treatment-resistant FEP.[168] It may be considered as an adjunctive treatment for people with schizophrenia who show a limited response to medication alone, and when a rapid reduction in symptoms and global improvement is desirable.[168] A combination of ECT and risperidone has been shown to be effective in this setting.[168]

People with catatonic schizophrenia have been shown to respond more rapidly to ECT than those with non-catatonic schizophrenia,[168] and to be more likely to respond to ECT than to antipsychotics or lorazepam.[168]

ECT also appears to be safe and effective in young people with FEP. Zhang et al. (2012)[169] found that young people treated with ECT in combination with antipsychotic medication had a significantly reduced length of hospital stay and a higher cumulative response rate over a 7-week period compared with antipsychotic medication alone.

ECT is also commonly used for acutely suicidal and other severely depressed people, although studies investigating the protective effect of ECT against suicide in people with affective schizophrenia had varying results, from positive to negative.[168]

Caution is required with concurrent administration of lithium or anticonvulsant mood stabilisers with ECT. Both safe usage and increased neurological complications, such as confusion, memory loss, disorientation and spontaneous or prolonged seizure activity have been reported.[170] Anticonvulsant mood stabilisers may raise the seizure threshold, interfering with ECT efficacy and increasing the risk of post-ECT confusion. In both cases, consideration should be given to tapering these medications prior to ECT.[170]

More research is needed to clarify whether ECT conveys a long-term decrease in illness severity.[168] Importantly, there were no significant differences in clinical or neuropsychological variables at a 2-year follow-up assessing long-term cognitive effects in adolescents with schizophrenia or schizoaffective disorder undergoing ECT compared with those who did not receive ECT.[171]

Ending treatment: helping young people transition to discharge

The decision to end treatment

It is not uncommon for a young person who has recovered from a psychotic episode to decide they no longer wish to attend an early psychosis service or continue with treatment. This may be because they prefer to 'forget about' the episode and return to 'normal' life. While this is understandable, it is important to remember that part of the success of the early intervention model is due to the length of the period of care offered and this care should not be withdrawn as soon as a young person achieves remission of symptoms. The EPPIC Model allows for 2–5 years of treatment within an early psychosis service; however, this does not necessarily imply 2–5 years of medication. If a young person decides to discontinue treatment within an early psychosis service, the treating team should try to negotiate role for themselves in the young person's life for a period of time, perhaps increasing focus on social and vocational recovery issues rather than directly illness-related ones. If a young person is insistent that they wish to be discharged from the service, it is important to make sure they have a good relapse plan and that this is shared with others, such as their family or GP.

Some young people may decide to end treatment and disengage from an early psychosis service because they have limited insight and do not believe they have been unwell. This may be more worrying, as they will be less likely to seek help should they experience a relapse. If there is significant risk and the young person is or becomes unwell, involuntary treatment should be considered as a last resort. However, it is usually possible through careful negotiation and skilful practice to retain young people in treatment. This is after all one of the key aims of early psychosis services – better access, engagement and retention in treatment. See the ENSP manual *Get on board: engaging young people and their families in early psychosis* for more information.

Most services will have a disengagement policy that should be followed, with all steps that led to the young person's disengaging documented. As always, good communication and record-keeping are important, not only to demonstrate good practice, but also to give other services or out-of-hours teams a young person comes into contact with easy access to the information they need about the young person to manage them safely.

CASE SCENARIO **JUSTIN** CONTINUED from page 85

In a review with his case manager, Justin admits he has stopped all his medication as he has been feeling so well. It is now 10 months since his hospital admission for the manic episode. He also discloses that he has been using cannabis again and has taken amphetamines on a couple of occasions. The case manager does not feel Justin is showing signs of relapse at this point.

Options to manage Justin's treatment at this stage include:

- monitor Justin more closely and frequently, as he has an increased risk of relapse due to discontinuing his medication early and using drugs again
- a focus on relapse prevention work, including providing balanced psychoeducation about the pros and cons of early medication discontinuation and drug use
- negotiate re-commencement of lithium and avoidance of drug use
- positively reinforce the progress he has made, and aim to maintain his engagement
- link Justin with the peer support service so he can hear about others' recovery stories.

Justin decides to recommence lithium and to cease his drug use. He meets with a couple of other young people who have experienced FEP and finds this helpful. Things settle, and Justin successfully returns to university, continuing to see his case manager at the early psychosis service.

Future considerations for Justin's management include:

- his risk of relapse (see 'Medical management in a subsequent acute phase' on page 85)
- when and how he might cease medication
- discharge from the early psychosis service – whether he is discharged into primary care or an adult mental health service will depend on severity, risk, complexity and engagement.

Transition to ongoing care

Following the 2–5-year period of care with an early psychosis service, a young person will transition back to primary health care (a GP at a minimum) or to an adult mental health service, depending on the individual needs of the young person and their family. The decision about where a young person is discharged to should be made with the young person, their family and the multidisciplinary team. It should focus on issues such as the young person's ongoing wellness, illness or disability, their ongoing need for certain medication (e.g. clozapine or LAI medication) and their complexity, level of risk, available supports, stability (internal and external) and ease of engagement.

> ‘I’m happy to stop coming now, but one thing that does concern me is that I’m on clozapine and I don’t know, like, where I’ll find a doctor who will keep an eye on my clozapine, ’cause at the moment I’m doing weekly blood tests and things like that. So I just worry a bit about the management of my medication more than anything after discharge.’
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

Managing a young person’s discharge from a service

The discharge of a young person from an early psychosis service needs to be well prepared for, as it can be stressful and may precipitate a relapse in psychosis, depression or other deteriorations in mental state. Furthermore, ending with the service and transfer of care may bring about feelings of loss for young people[10] and significantly derail engagement with treatment and services. This is important to guard against, as disengagement from services after discharge may undo much of the gains made during treatment within the early psychosis service.[10]

Discharge from psychiatric care has also been shown to be a time of increased suicide risk for people with psychiatric disorders.[35,36] Young people can become attached to their clinical team and case manager, meaning when it comes time for a young person move on from these therapeutic relationships they may feel hopeless, abandoned or overwhelmed. If severe, these feelings may be accompanied by suicidal ideation and intent, especially if the young person is moving on to an adult mental health service and feels they have ‘failed’ to recover.

It is therefore critical that a young person’s risk assessment is reviewed and their risk management plan updated at this time of significant change. Their risk assessment and crisis management plan should be documented by their treating team, with recommendations made for future management, in a discharge summary that is discussed with and provided to their new service provider. Effective communication and advance planning will contribute to a safer discharge or transition to a new service. The destabilising effect of change and transition should not be underestimated from the young person’s point of view, especially as they will likely have formed significant supportive relationships with the key clinicians from the service.

> ‘They said to me, “We’re just going to transfer you back to your psychologist,” or whatever, and that made me really nervous, because I can usually only see my psychologist like twice a month and I was still, like, struggling with some stuff. I felt quite anxious about that.’
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

Discharge and transition are processes that should be proactively managed. It may be useful for services to work alongside any new service providers for a period to allow time for the young person to engage with the new service. A period of ‘step down’ care, where the young person gradually reduces contact with a service prior to discharge, may also be useful. Ideally, the new service will provide support based on the principles of early intervention (youth-friendly, recovery-focused). Indeed, research has shown that a lower intensity level of specialised intervention after the initial 2 years is effective in maintaining the clinical and social gains from early intervention.[9]

Some flexibility around timing of discharge may be necessary so that it does not happen at the same time as other stressful events (e.g. difficult anniversaries, eviction from home, leaving school/university or work). Once again, with careful planning and involvement of the multidisciplinary team, the young person, their family and their GP, discharge can usually be managed without significant problems. Preparation for discharge can also offer an opportunity to talk with the young person and their family about plans, hopes and goals for future treatment.

A handover meeting is essential to ensure important information is communicated to the receiving team or GP and that the young person and their family are clear about who is responsible for their ongoing care following discharge from the early psychosis service. A discharge summary should be provided to the new service provider to enhance continuity of care. This summary contains a history of the presenting problems, case formulation, treatment summary, risks, crisis and relapse plans, current treatment and outcome.

> ‘There’s not going to be some sort of, like, perfect end note. It doesn’t work like that, ’cause your life just goes on anyway.’
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

SUMMARY

Considerations for medical treatment in early psychosis

- Antipsychotic treatment should not be prescribed in young people at UHR for psychosis unless in exceptional circumstances.
- Where possible, an antipsychotic-free observation period should be held before commencing young people on antipsychotic medication.
- There are a number of differences between young people with FEP and people with established schizophrenia that should be considered when prescribing pharmacological treatments for FEP.
- 'Start low, go slow' is a core principle of pharmacological treatment in young people with FEP.
- Strategies to help with adherence to medication include using a shared decision-making approach to the young person's treatment, encouraging discussion of reasons for non-adherence by the young person, psychoeducation, and acknowledgement and effective management of side-effects.
- Due to its metabolic effects, olanzapine should not be used as first-line treatment for FEP.

Medical management at the different phases of psychosis

- The primary aim of interventions in the UHR phase is to delay or prevent a full-blown psychotic episode, reduce prodromal symptoms and facilitate a full functional recovery.
- The treatment priority in the acute phase is to reduce DUP and effect a full recovery.
- Interventions during the early recovery phase should focus on helping the young person understand the nature and onset of the psychotic episode and plan activities to support their returning to normal function.
- There is no consensus on the ideal maintenance period of antipsychotic medication following remission. It appears that although early dose reduction leads to a higher relapse rate in the short term, in the long term, it leads to better outcomes in functional capacity; however, more research is needed in this area. Ultimately, clinicians may do best to be guided by the young person's wishes regarding discontinuing medication.
- Strategies for relapse prevention include psychoeducation, development of an early warning signs and relapse management plan, managing substance use and helping the young person and their family create an emotional environment that promotes recovery.
- Clinicians should screen for indicators of which young people may experience incomplete recovery. Interventions in this phase may include more intensive psychosocial interventions, clozapine and ECT.
- The discharge of a young person from an early psychosis service can be stressful and may precipitate a relapse in psychosis, depression or other deteriorations in mental state. It therefore needs to be well prepared for.

Physical health management and monitoring in early psychosis

Monitoring the physical health of young people on antipsychotics

Overview

The majority of young people experiencing a first episode of psychosis will be prescribed an antipsychotic medication. The significant physical health side-effects that accompany antipsychotic medication, particularly SGA medication, can occur within weeks of beginning treatment, and they need to be acknowledged, understood and taken seriously.

It is essential that those involved in prescribing and managing antipsychotic use in young people take responsibility for screening, monitoring and managing physical health side-effects of these medications. Young people and their families, where possible, also need to be actively involved in this. A major goal of early intervention is to minimise the impact of psychosis and prevent ongoing disability. Addressing and endeavouring to improve – not worsen – the physical heath of a young person should form a major part of this goal.

This section presents the evidence and rationale for monitoring physical health issues in young people, followed by recommended algorithms and strategies for monitoring and screening of this important area.

Evidence and rationale for the need to monitor and manage physical health issues

Why intervene?

The physical health of people experiencing psychosis is considerably worse than the general population, resulting in a reduction in life expectancy of between 13 and 16 years.[25,172] People with schizophrenia have high rates of medical comorbidities, but these are underdiagnosed compared with the general population, resulting in high morbidity and mortality.[80] Some comorbidities, such as a higher prevalence of epilepsy, have no clear pathological mechanism, while others, such as diabetes, obesity and metabolic syndrome, may be related to an unhealthy lifestyle.[80] Indeed, up to 60% of people experiencing psychosis meet the criteria for the metabolic syndrome,[173] defined by the International Diabetes Federation (IDF) as a cluster of risk factors including obesity, hypercholesterolaemia, hypertension and impaired fasting blood glucose.[174] (see Box 16)

BOX 16. **CRITERIA FOR THE METABOLIC SYNDROME**

According to the International Diabetes Federation, a person defined as having the metabolic syndrome must have:[175]

central obesity (defined as waist circumference using ethnicity-specific values or BMI ≥ 30 kg/m^2)*

- males ≥ 94 cm (South Asians and Central Americans ≥ 90 cm)
- females ≥ 80 cm

plus any two of the following:

- raised triglycerides
  - ≥ 1.7 mmol/L
  - or specific treatment for this lipid abnormality
- reduced HDL cholesterol
  - < 1.03 mmol/L in males
  - < 1.29 mmol/L in females
  - or specific treatment for this lipid abnormality
- raised blood pressure
  - systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg
  - or treatment of previously diagnosed hypertension
- raised fasting plasma glucose
  - ≥ 5.6 mmol/L
  - or previously diagnosed type 2 diabetes

*Age 16 years and over. Age 10–15 years, ≥ 90th percentile cut-off.

Rates of overweight and obesity are 2–3 times higher in people with psychosis than in the general population, with hypercholesterolaemia five times more prevalent among people with serious mental illness.[172] The prevalence of hypertension in people with serious mental illness has been reported to be as high as 54%,[176] and smoking rates are 2–3 times higher than in the general population.[172] This poor physical health profile results from a mixture of both modifiable and non-modifiable risk factors. They include side-effects from antipsychotic medications and lifestyle-related factors such as sedentary behaviour and poor dietary habits.[99,102,177]

Weight gain is known to affect 80% of individuals treated with antipsychotic medication, with the rate of weight gain 3–4-fold greater in young people with limited previous antipsychotic exposure.[178] The prevalence of cardiometabolic abnormalities in FEP has been reported to be greater than 40%, with 12.5% of people with FEP in one Australian sample meeting the criteria for metabolic syndrome after a median treatment duration of 8 months.[179]

> 'I really think that it is an area in our care that isn't addressed properly a lot of the time, that actually they're focusing so much on your mind that they're not really giving the attention to your physical wellbeing. You know – they put you on a medication and then six months later you've put on twenty kilos.'
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

All antipsychotic medications and mood stabilisers may lead to weight gain, with SGA medication frequently associated with clinically significant weight gain.[58,102,180,181] Some, especially olanzapine and clozapine, are known to have a greater propensity for significant weight gain and should be avoided as a first-line treatment in FEP (see Table 6).[181,182]

TABLE 6: **COMPARATIVE POTENTIAL OF ANTIPSYCHOTICS TO CAUSE WEIGHT GAIN**[181]

ANTIPSYCHOTIC	POTENTIAL FOR WEIGHT GAIN
Amisulpride	+
Aripiprazole	+
Clozapine	+++
Haloperidol	++
Olanzapine	+++
Paliperidone	++
Quetiapine	++
Risperidone	++
Ziprasidone	+

Evidence-based interventions for managing physical health

Despite increased awareness of the cardiometabolic sequelae of antipsychotic treatment in young people with FEP, and the recent development of screening and monitoring tools, there have been few trials that have demonstrated positive results in young people with FEP who have recently started antipsychotic medications.

Evidence suggests that lifestyle intervention can attenuate weight gain,[183,184] with recent Australian data demonstrating that a 12-week structured lifestyle intervention, including nutritional and physical activity components, prevented weight gain and central obesity in young people with FEP who were receiving antipsychotic medications, compared with standard care.[185] Lifestyle interventions implemented at the time of medication initiation resulted in clinically significant weight gain occurring in only 13% of participants, compared with 75% of the standard care group. Longer-term studies in young people with FEP are lacking; however, lifestyle interventions as well as metformin have been found to reduce weight or attenuate weight gain in people with established psychosis.

How to monitor and manage physical health in young people

Recommendations for physical health screening

As a minimum, physical health screening should incorporate:

- waist circumference
- weight
- BMI (height required)
- blood pressure
- level of physical activity
- smoking (cigarettes per day)
- fasting pathology (lipid profile, glucose, liver function tests, vitamin D).

Routine monitoring of cardiometabolic health in all young people experiencing psychosis is recommended to guide detection, prevention and intervention strategies and reduce future cardiovascular risk.[186] A number of metabolic monitoring algorithms exist, including:

- The New South Wales Health Education and Training Institute's *Positive cardiometabolic health* algorithm (http://www.heti.nsw.gov.au/cmalgorithm)
- Western Australian guidelines for people of any age taking antipsychotics[187]
- Youth-specific guidelines developed by Orygen Youth Health (see Appendix 1)
- Canadian guidelines developed by Pringsheim et al. (2011) for adolescents.[188]

Other physical health monitoring areas that require monitoring by appropriate healthcare professionals include:

- dental reviews
- sexual safety advice
- vision and hearing examinations
- education on alcohol and drug risks.

Don't just screen, intervene: strategies to target physical health issues

Interventions designed to prevent physical health issues arising in young people with FEP should be integrated as part of routine practice in an early psychosis service. A framework for screening, monitoring and providing preventative lifestyle interventions and judicious use of psychotropic medications should be applied in all settings in which young people are receiving care for psychosis. All clinicians should take a role in ensuring this occurs; however, where possible, specialist input from dietitians and exercise physiologists should be included. Psychoeducation is important; however, active, structured lifestyle interventions should be delivered from the onset of psychosis to optimise physical health outcomes.

The following strategies can help with physical health issues faced by young people prescribed antipsychotic medication. Suggested algorithms for monitoring and treating these issues can be found in appendices 1 and 2. Medication doses for treatment of conditions such as high blood pressure should follow appropriate clinical guidelines.

> 'I think they should be talking about these things before it gets too far, rather than, "Oh you've gone from a healthy BMI to medically overweight. Now we're going to fix it."'
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

Reduce tobacco use

Tobacco remains the greatest single risk factor for future cardiovascular morbidity. The prevalence of smoking in young people with FEP has been demonstrated to be as high as 59%, a rate 6 times higher than that observed in young people without psychosis.[189] Furthermore, the initiation of tobacco usage precedes the onset of psychosis by an average of 5.3 years.[189]

Young people with mental illness who smoke often want to and can quit.[190,191] Interventions for smoking that can work for young people experiencing psychosis include:

- brief interventions
- motivational interviewing
- cognitive and behavioural strategies
- tools that show measurable improvement (e.g. FEV_1 tests, CO meters)
- consumer-led smoking plans that identify smoking triggers, withdrawal and ways of coping
- nicotine replacement therapy.

Success rates for smoking cessation are often increased when psychological and behavioural therapies are combined with pharmacotherapy.[191]

Increase physical activity

Insufficient physical activity is a key modifiable risk factor in the development of cardiometabolic abnormalities. Physical activity levels can be assessed via direct measurement using objective monitors such as pedometers, accelerometers and smartphone applications, or more feasibly through simple self-report questionnaires. There is evidence to support the use of the International Physical Activity Questionnaire – Short Form (IPAQ-SF) in people with schizophrenia.[192] The IPAQ-SF consists of four questions, can be self-completed and takes less than five minutes to complete. The Australian Physical Activity Guidelines encourage daily participation in physical activity and recommend that adults accumulate 150 to 300 minutes of moderate intensity physical activity or 75 to 150 minutes of vigorous intensity physical activity, or an equivalent combination of both moderate and vigorous activities, each week. In addition, muscle-strengthening exercises are recommended on at least 2 days per week. Such recommendations should be used as a guide only, as any increase in physical activity participation is likely to be beneficial. In addition, simply reducing sedentary behaviour (including screen time) has been shown to positively impact cardiometabolic health.[193]

All early psychosis clinicians have a role to play in promoting physical exercise to prevent or address metabolic problems. Basic education regarding healthy exercise levels and ways to achieve this are important. Interventions may include supporting access to local gyms, sporting groups (e.g. local netball or football clubs) or providing lifestyle groups within the service as part of the group program. Education and exploration of other basic ways to increase the amount of exercise with the young person may be just as effective. These could include using stairs rather than elevators, walking instead of driving or taking up cycling as a means of transport. Referral to an accredited exercise physiologist or physiotherapist is recommended, where possible, to create individualised interventions.

A useful fact sheet on physical health can be found at www.http://oyh.org.au/oyh-clients/fact-sheets.

Address poor diet

People with psychosis consume more calories and saturated fat, and eat less fruit, vegetables and fibre, compared with the general population.[194] In addition, people with schizophrenia have diets that are lower in milk, potatoes and pulses, and eat more take-away foods than the general population.[195] Assessing a young person's dietary intake provides an opportunity to educate and motivate them about improving their diet, if necessary, and to set dietary goals. Dietary intake can be assessed by a 24-hour recall, a food frequency questionnaire or a food diary, and compared with the Australian Dietary Guidelines.[196] Another useful resource is the *Nutrition standards for consumers of inpatient mental health services in NSW hospitals*, which were developed to provide menus to inpatients that aim to achieve nutritional adequacy for key nutrients and prevent weight gain by moderating intake of foods of low nutritional value.[197]

Interventions to improve diet are important and may involve a variety of approaches, including assessing a young person's will to change, motivational interviewing, nutritional education and setting SMART (specific, measurable, attainable, relevant, time-specific) goals. Education about healthy foods is essential, as is providing young people with strategies for change. An example of a simple dietary strategy is a 'traffic light' system that colour-codes foods so that people can easily recognise which foods are healthier than others. In this system, 'green' refers to foods to eat regularly (fruits and vegetables), 'orange' to foods to eat sometimes (refined grains such as white bread/rice) and 'red' to foods to limit (highly processed takeaway foods and soft drinks). Where young people live at home, it is also important to include parents in education and support, given they may be more likely to prepare meals for the family. Some young people living independently (or at home) may well not have developed healthy shopping habits or cooking skills, so there is a role for group work within the early psychosis service to develop these skills.

The current Australian Dietary Guidelines and additional resources can be found at www.eatforhealth.gov.au.

Rationalise antipsychotic polypharmacy and consider medication switch

As a first step, prescribed antipsychotic dosages should follow recommendations and any polypharmacy rationalised. Where possible, consider switching to a more weight-neutral medication.

Changing antipsychotic medication requires careful clinical judgment to weigh the benefits against the risk of relapse of the psychosis. If clinical judgment and young person's preference support continuing with the same treatment, appropriate further monitoring is required.

Manage high blood pressure

The target blood pressure (BP) is < 130 mmHg systolic, and < 85 mmHg diastolic. Interventions that incorporate lifestyle components (such as structured exercise and dietetic therapy that includes salt reduction) and the prescription of antihypertensive drugs should be considered for young people whose BP is persistently above these targets when lifestyle interventions have been unsuccessful. These interventions should preferably be implemented by a GP or specialist.

Manage elevated blood lipid levels

Lifestyle interventions are the treatment of choice for lipid elevations in young people with psychosis, and also aim to reduce obesity. For young people with persistently elevated total cholesterol or LDL cholesterol despite an adequate trial of intensive lifestyle intervention, consideration should be given to prescribing statins to reduce future cardiovascular risk. Fibrates are recommended for elevated triglycerides if lifestyle interventions and weight loss do not address this adequately. Doses should follow appropriate clinical guidelines.

Manage increased blood glucose

A fasting blood glucose level above 7 mmol/L is indicative of diabetes, and the young person should be referred to appropriate medical treatment by a GP or at a diabetes clinic. Fasting plasma glucose levels of > 5.6 mmol/L, especially if accompanied by central obesity, hypertension or dyslipidaemia, should be actively managed by lifestyle intervention; where this is unsuccessful, metformin treatment should be considered.

Pharmacological strategies to address weight gain and metabolic syndrome

Where lifestyle intervention has been trialled for at least 3 months, and targets for weight, glucose or lipids are not achieved, consideration should be given to the addition of metformin as a specific pharmacological adjunctive strategy. Metformin has been shown to be effective in reducing or attenuating antipsychotic induced weight gain and its sequelae and is safe and effective in young people.[198] Metfomin is used off-label for this purpose and monitoring in young people; dosage recommendations are available in the algorithms presented in the appendices.

Monitor vitamin D

Vitamin D deficiency is seen in a high proportion of people with established psychotic disorders[199] and there is a higher rate of osteoporosis in this population compared with the general population.[200] There is also evidence that those people presenting with a first episode of psychosis are vitamin D deficient at first presentation.[201] It has been hypothesised that this might be a result of:

- long-standing vitamin D deficiency from early in the person's life
- a pre-existing vitamin D deficiency caused by the onset of a prodromal period (increased social isolation and subsequent reduced exposure to sunlight and poorer nutrition)
- a systemic inflammatory response as a result of the onset of psychosis.

Further, there is evidence of antipsychotic use being a factor contributing to increased osteoporosis in those people with chronic psychotic illness, with the likely pathophysiological mechanism being related to the effects of hyperprolactinaemia.[200]

Specific interventions to address vitamin D deficiency include:

- monitoring vitamin D levels twice yearly, including baseline
- promoting outdoor exercise (which may involve addressing underlying mental health problems)
- use of supplemented food sources (e.g. vitamin D-enhanced milk or margarine)
- use of pharmacological supplements – see Appendix 2 for suggested dosage.

Screen for sexual health

Sexually transmitted infections (STIs) are common among young people, with chlamydia being the most prevalent STI among people aged 15–25 years in Australia.[202] The majority of secondary school students (69%) have experienced some form of sexual activity, with 59% of those young people reporting that they have engaged in unsafe sexual behaviour.[203] Young people with emerging mental health issues and those experiencing FEP have an added risk of adverse sexual health outcomes due to comorbid vulnerabilities associated with mental health issues.[204]

Various factors contribute to the increased sexual risk-taking behaviour for young people with mental health problems, including the negative impact of impaired cognition on decision-making and judgment, the development of age-appropriate relationship skills and peer friendships and susceptibility to pressure to have sex and to not practise sex safely.[205] Unemployment can also significantly predict lack of condom use in young people,[204] while substance use is also a predictor for being sexually active and increased sexual risk taking.[202]

The process of opportunistic screening involves ascertaining if a young person is sexually active and following a sexual health algorithm to determine which tests are required based on known risk factors. In NSW, some young people may be able to use the website www.stitest.org.au to screen for STIs. If testing cannot be completed at the mental health service, referral can be made to a youth-friendly sexual health clinic, headspace centre or GP.

Sexual dysfunction as a result of elevated prolactin levels can also affect young people on antipsychotic medication (see also ‘Prolactin and sexual side-effects’ on page 61). Suggested strategies for helping these side-effects include:

- reducing dose if possible, while maintaining therapeutic dose
- switching to another antipsychotic with a lesser sexual side-effect profile
- monitoring prolactin levels
- taking a sexual history
- ruling out other causes of sexual side-effects.

Young people are unlikely to report sexual problems or loss of libido, so education and active monitoring of these side effects is important. ‘Beyond Awkward’ is a booklet published by Orygen Youth Health to help mental health professionals with

conversations with young people about sexuality, gender identity, sexual safety and sexual activity. It is available at http://oyh.org.au/training-resources/free-downloads/beyond-awkward.

Peer support workers

Young people with first-hand experience of psychosis can play an important role as peer support workers in improving physical health care for other young people with early psychosis. These young people can share information about their own experiences and journey, encouraging and supporting participants in the program to look after their own physical health. Peer support workers can get involved in activities such as cooking, sport or other physical activity.

Promoting metabolic monitoring in an early psychosis service

Given that cardiometabolic disturbances and weight gain occur within weeks of the first exposure to antipsychotics,[206] it is vital that monitoring of metabolic health occurs early and regularly in early psychosis services. However, metabolic monitoring of people taking psychotropic medication has been fairly poorly applied historically, with implementation of evidence-based metabolic monitoring strategies not well followed through.[207] Factors that have been shown to contribute to poor monitoring compliance include the perceived potential impact of monitoring on clinicians' rapport with young people, its impact on consultation length, clinicians' confidence in carrying out monitoring and access to necessary equipment.[208,209]

Thompson et al. (2011)[207] developed a method of improving metabolic monitoring that used an implementation science approach based on researched barriers and enablers of metabolic monitoring. This method consisted of:

- development and dissemination of local guidelines
- educational intervention aimed at professionals
- service and structural changes (e.g. forms, monitoring sheets and designated staff members responsible for reminding clinicians of the metabolic monitoring process), and
- provision of metabolic monitoring equipment.

This strategy substantially increased routine metabolic screening and monitoring of young people in an early psychosis service, and emphasises the need for a service-level approach to implementing routine metabolic monitoring of young people.

Metabolic monitoring: who is responsible?

Regular monitoring of weight gain and metabolic indicators in young people who are prescribed antipsychotics can help identify those who require early intervention for weight gain or metabolic disturbance to prevent long-term negative outcomes – but whose responsibility is this?

The short answer is that **everyone** is responsible for metabolic monitoring and supporting clinical interventions to prevent or address metabolic problems. This does not mean that each person involved in the care of a young person needs to take responsibility for every aspect, but that each person needs to be aware of their specific role in the monitoring process.

All clinicians can take an active role in psychoeducation around the physical side-effects of SGAs and the implementation of strategies to mitigate the harmful impact of these side-effects. With basic training, non-medical clinicians can also take a role in collecting and recording certain measurements (e.g. weight, waist circumference) and communicating results to the medical team. However, it is the responsibility of medical staff to ensure these measurements are taken, reviewed and interpreted at the intervals recommended by appropriate clinical guidelines. The responsibility of medical staff continues into developing collaborative management plans to manage and mitigate any ongoing metabolic side-effects, with input from the clinical team, young person and their family.

Although it is most beneficial to keep metabolic monitoring within the treating team, for reasons such as engagement and ensuring metabolic monitoring is completed, other (external) medical specialists may take a role in metabolic monitoring and subsequent interventions. Occasions where this might occur include when a young person is approaching discharge, with care moving on to a GP, or if a specialist opinion is warranted (e.g. through an endocrinologist).

CASE SCENARIO **JASMINE** CONTINUED from page 92

After several weeks on clozapine, Jasmine's symptoms improve. However, her monitoring regimen shows that Jasmine has begun to put on weight. Her doctor and case manager provide specific interventions to help Jasmine manage the weight gain, including dietary advice and an exercise plan. They also arrange regular blood tests, in addition to the clozapine monitoring, to identify any possible onset of diabetes or dyslipidaemia. These interventions help Jasmine's weight to return to normal.

Eventually, Jasmine is able to return to college, move into her own apartment and make a good recovery from FEP. She continues to take clozapine and work with the early psychosis service for another 2 years. Although she decides she no longer needs regular contact with her treating team after this, she remains in contact with them for another 3 years, before transitioning to the local community mental health service.

International physical health in youth working group (iphYs)

The International Physical Health in Youth (iphYs) working group is an international collaboration of concerned youth mental health clinicians and researchers that was formed to address the issue of physical health in young people experiencing an episode of psychosis. One of the key outcomes of this group has been the Healthy Active Lives (HeAL) consensus statement, which sets out a number of goals, principles and 5-year targets for improving physical health in young people. More information can be obtained at www.iphys.org.au.

SUMMARY

Monitoring the physical health of young people on antipsychotic medication

- Rates of overweight and obesity are 2–3 times higher in people with psychosis than in the general population, and up to 60% of people with psychosis meet the criteria for the metabolic syndrome.
- Everyone involved in a young person's care is responsible for screening, monitoring and managing the physical health and metabolic side-effects caused by antipsychotic medication, particularly SGA medication.
- Interventions designed to prevent physical health issues arising in young people with FEP should be part of routine practice in early psychosis services. Active, structured lifestyle interventions should be delivered from the onset of psychosis to optimise physical health outcomes.
- Young people on antipsychotics may experience sexual dysfunction as a result of elevated prolactin levels. As young people are unlikely to report sexual problems or loss of libido, clinicians should be proactive about providing education about and monitoring these side-effects.
- A service-level method for improving metabolic monitoring may include development and dissemination of service guidelines on monitoring, education of clinical staff about the need to monitor, structural changes to enable monitoring and provision of monitoring equipment to staff.

Service-level considerations

Service-level considerations for medical treatments in early psychosis

Structure, leadership and clinical governance

The structure of the clinical team is an important component of a successful early psychosis service. A medical director, who is accountable for both the medical staff and the treatment they provide, should head the service. Each team should include a consultant psychiatrist and registrar, as opposed to a visiting psychiatrist.

Medical staffing of early intervention services generally includes a mix of registrars, trainee psychiatrists and consultants. Configuration of medical staffing and medical case load management depends on factors such as the size of the service and the expected number of referrals based on prevalence figures. Experience from a number of early psychosis services suggests that one full-time consultant and one full-time registrar per 100 FEP cases is a reasonable set up.

Psychiatry registrars usually provide front-line medical services, with consultants reserved for confirming diagnoses, explaining treatment options, providing feedback to family, managing or reviewing more difficult and complex cases, supervising individual care planning meeting, and providing supervision and training, although it is not unusual for consultants to carry a smaller case load also.

Lines of clinical, professional, academic, and administrative accountability need to be clearly demarcated. Where staff work in a variety of roles or across a number of service structures, unclear lines of accountability can become particularly hazardous, for example when a young person experiences a crisis.

Medical staff involved in portfolios related to service development need to be able to respect and work with the youth and family participation arms of the service, which will contribute to the planning, implementation and evaluation of early psychosis services.

Ensuring continuity of care

Continuity of care by doctors in the early psychosis service is an important goal, as it helps the young person engage with the service. Ideally, the service should also provide the possibility of a second opinion or choice of doctor for young people. However, it may not always be feasible to provide a choice of doctors (e.g. due to gender preference) within the resourcing level of the service.

Services should have a system in place that automatically assigns a specific medical staff member and consultant to each young person from the beginning of care. This should remain uninterrupted throughout the young person's contact with the service. This system should run in parallel with the case management system, so that each young person has an allocated case manager and consultant (or medical doctor under the consultant's supervision). Case managers in an early psychosis service have caseloads of approximately 15–20 to allow for intensive psychosocial interventions and assertive follow-up, while medical caseloads will be much greater (e.g. 60–100).

As registrars tend to rotate every 6–12 months as part of their training, their carrying medical caseloads can have drawbacks, as their rotations will disrupt the young person's continuity of care. This disruption can be minimised by ensuring registrars have regular joint medical reviews of young people with the consultant and by including case managers in all medical reviews.

> 'You get to know a doctor, and he or she is managing meds and everything, and then six months later they're off somewhere else and you're just like, "Well that sucks." I am someone who prefers a bit of consistency and stability.'
>
> – Young person,
> EPPIC, Orygen Youth Health Clinical Program

The role of psychiatrists within the multidisciplinary team

It is important that there is a multidisciplinary team approach to care, and that the treating psychiatrists and the rest of the team have similar understandings of the early psychosis model and approach to treatment (e.g. embracing diagnostic uncertainty, prescribing principles, active engagement with young people who seek help and providing psychoeducation).

Each member of the multidisciplinary team has an important role to play in a young person's care and brings their own set of skills and experience to the service. While the doctor does have a role as an 'expert', it is important that they and others are aware of the expertise and experience of other members of the multidisciplinary team and appreciate the skills and professional opinions of their colleagues. The doctor is not the leader of the multidisciplinary team, and neither should they be viewed only as a prescriber of pharmacological treatments. Rather, they are key members of the team who are often able to see the 'bigger picture' with regard to other needs (e.g. formulations, psychological therapies, other treatment approaches). Doctors should also encourage and support self-sufficiency, learning and development of skills and expertise among other team members.

Medical staff, in particular consultant psychiatrists, need to be drivers of the early psychosis service's culture and should model best practice in early psychosis. It is important that medical staff are supported by the service to provide training in early psychosis and the youth mental health model in academic institutions and other clinical psychiatric services (e.g. adult psychiatry, child and adolescent psychiatry, general practice). Doctors working in early psychosis also have a role to play

educating colleagues in the wider medical community, to both increase appropriate referrals and address myths and stigma related to mental illness, and psychosis in particular.

In addition to working within the team, medical staff will interface with other medical practitioners outside the early psychosis service, including GPs, private psychiatrists, paediatricians and other specialists. This interaction will include feedback from referrals, and raising the profile of early intervention as a specific approach.

The role of general practitioners

General practitioners play a key role in the primary health care for young people, and many of the initial referrals to early psychosis services originate from GPs. Early psychosis services that provide education to GPs to support a good understanding of the principles and rationale for early intervention in psychosis, as well as the referral pathways to care, are imperative. However, many, if not most young people entering an early psychosis service will not have a GP that they regularly attend. If this is the case, linking young people with a GP is essential in order to optimise a holistic approach to mental health care.

In Australia and in regions where headspace centres exist, some of these centres provide an ideal platform whereby primary mental health services also provide a tertiary level early psychosis service. This co-location of primary and tertiary level services in one service provides a smoother pathway to care, a unique continuity of care and access to specialist physical health care for young people. In these services, GPs are seen as members of the multidisciplinary team who can provide specialised input into issues such as co-occurring physical health problems (e.g. metabolic syndrome and sexual health).

SUMMARY

Service-level considerations for medical treatment

- It is important that there is a multidisciplinary approach to care, and that the treating psychiatrists and the rest of the team have similar understandings of the early psychosis model and approach to treatment.
- Continuity of care by doctors in the early psychosis service is an important goal, as it helps young people engage with the service. A specific medical staff member and consultant should be assigned to each young person from the beginning of care. This should remain uninterrupted throughout the young person's contact with the service.
- While the doctor does have a role as an 'expert', they should be aware of the expertise and experience of other members of the multidisciplinary team and appreciate the skills and professional opinions of their colleagues.
- Doctors should also encourage and support self-sufficiency, learning and the development of skills and expertise among other team members.

New advances in treatment of psychosis

New advances in treatment of psychosis

Research in the field of psychosis is progressing in a number of directions, with particularly significant growth in the area of UHR and biomarker identification. The following presents a brief, and by no means comprehensive, overview of some of the more promising findings from recent research.

Genetic markers

Genetic epidemiological studies have consistently shown that schizophrenia is highly heritable.[210,211] A number of single nucleotide polymorphisms associated with schizophrenia have been identified, but the odds ratios are very small and only explain a very small proportion of the genetic risk.[211] Approximately half of the genetic risk is attributed to a very large number of alleles, possibly thousands, many of which are common and have only a small effect.[211] Debate on the reason for apparent low effect sizes of the known contributing variants has suggested that either common alleles have low effect sizes, or variants with a greater effect are too rare to have been detected among the available samples. An emerging view is that a spectrum of risk alleles, both common and rare, and with small and large effects, all contribute a small proportion to the total individual risk.[211]

An overlap of risk alleles between schizophrenia and bipolar disorder suggests that the two conditions are not distinct disease entities.[210,211] Submicroscopic deletions and duplications of segments of DNA, or CNVs, have been identified that not only confer a risk of schizophrenia, but also a range of neurodevelopmental conditions including autism, attention-deficit hyperactivity disorder (ADHD), idiopathic generalised epilepsy and mental retardation, suggesting that these conditions may be viewed as phenotypic variations, influenced by environmental risk.[210,211]

Studies with increased sample sizes and increased genetic variation are expected to identify further commonly occurring risk variants.[210] The identification of individual genes or groups of genes can provide both insights into pathophysiology and guidance for pharmaceutical development.[212]

Technological interventions

Internet- and mobile-based technologies provide a means to overcome barriers in accessibility to psychological support, including costs, geographic distance and the social stigma associated with mental health treatment.[213] Internet-based interventions may include psychoeducation, CBT, internet-based therapy and online forums, while mobile phone interventions via SMS that target auditory hallucinations, medication adherence and socialisation have been assessed. These interventions appeared to be a useful and acceptable means of receiving interventions for people with psychosis. How well these technologies are taken up depends on both the attributes of potential users – such as cognitive variables, level of functioning and age – and the characteristics of the interventions, such as content, different features and how they are integrated into care.[213]

A smartphone intervention program that consists of auditory and visual alerts, brief algorithm-driven assessments and prompted or on-demand illness self-management resources and suggested coping strategies has been assessed. Satisfaction with the system and acceptability was high, and the intervention was helpful in the reduction of positive symptoms, depression and general symptoms of psychopathology over the one-month trial.[214]

For more information about using technology to assist with engaging young people with treatment, see the ENSP manual *Get on board: engaging young people and their families in early psychosis*.

Novel agents

Cannabis use is associated with an increased risk of developing psychosis, with the associated cannabinoid being delta-9-tetrahydrocannabinol (THC). However, another cannabis constituent, cannabidiol (CBD), may have antipsychotic properties. Schubart et al. (2014) reviewed the currently available literature of the role of the endocannabinoid system in the development of psychosis, with an overview of animal, human experimental, imaging, epidemiological and clinical studies to date. They found that antipsychotic properties of CBD have been demonstrated in a series of fairly small clinical studies in different patient subcategories.[215] A trial comparing CBD with amisulpride showed that CBD reduced psychotic symptoms to the same degree as amisulpride, but with significantly fewer side-effects; however, a larger randomised controlled trial is required to replicate these findings.[215]

The inflammatory hypothesis of schizophrenia was proposed 40 years ago, and increasing evidence suggests a role of the immune system in the pathogenesis of schizophrenia.[216] If increased inflammation of the brain contributes to the clinical symptoms of schizophrenia, then reduction of the inflammatory status may effect clinical improvement.[216] Most established medications for the treatment of psychosis, including antipsychotics, mood stabilisers and SSRIs, possess some anti-inflammatory effects.[216]

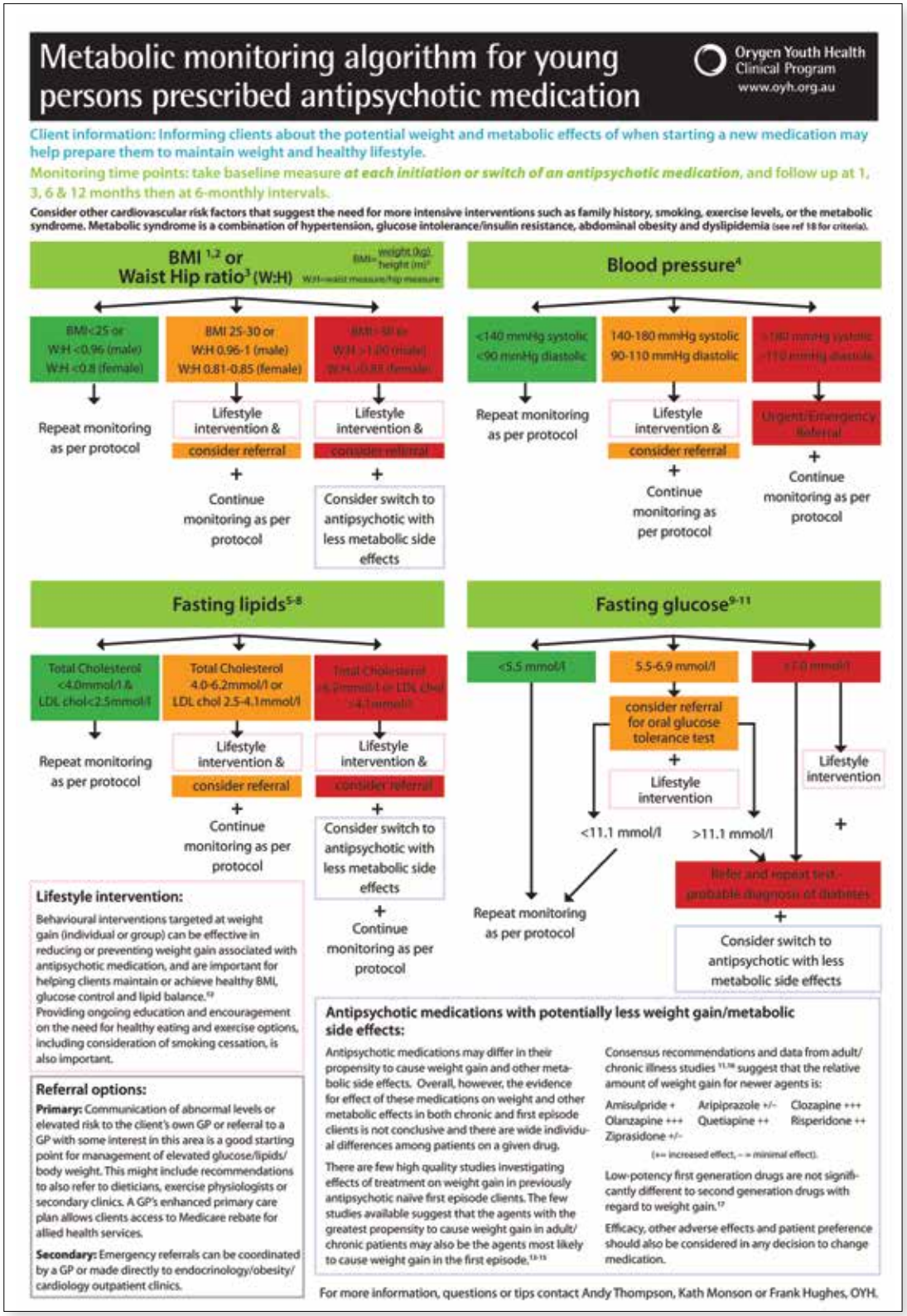
In a recent review, Sommer et al. (2014) provided an update on clinical studies of the efficacy of anti-inflammatory agents on schizophrenic symptoms.[216] The current literature suggests that augmentation with aspirin, oestrogens and N-acetylcysteine are promising, while the addition of celecoxib, minocycline, davunetine or omega-3 fatty acids (EPA or DHA) did not show a beneficial effect. Data are as yet too limited to conclude that the favourable effects of these agents are mediated by their anti-

inflammatory properties, as they also have other mechanisms of action. The effects of other medications with the potential for anti-inflammatory activity, such as glucocorticoids and statins, have not been investigated.

Impairment of cognitive domains such as working memory, attention, visual memory, executive function and social cognition are features of schizophrenia, from the prodromal phase through to chronic schizophrenia.[217] In addition to cognitive remediation therapy, or psychosocial cognitive rehabilitation and enhancement programs, various targets have been proposed for pharmacological augmentation of cognitive function (see the review by Lin et al. 2014[194]). A limited but robust effect of pro-cognitive agents has so far been demonstrated, and further studies with larger sample sizes, particularly ones that include younger people at an earlier stage of illness and with lower baseline impairment, and of longer treatment duration, are required.[194]

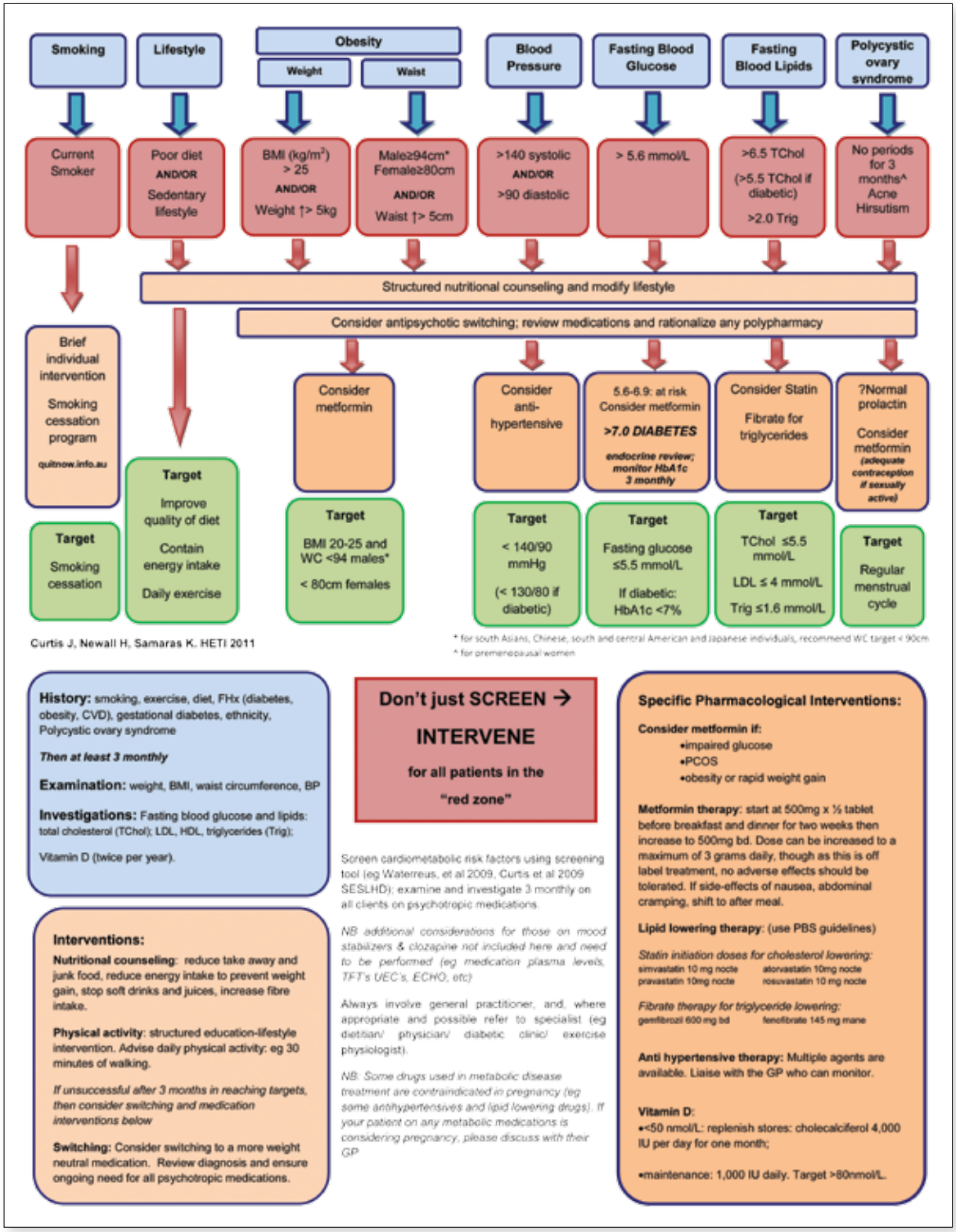
Appendices

Appendix 1. Algorithm for monitoring metabolic side-effects in young people prescribed antipsychotics



Prepared by A. Thompson, K. O'Connor, W. Soong, Y.Yun, M. Willet for the Orygen Youth Health Metabolic Monitoring Project. 2010

Appendix 2. Algorithm for positive cardiometabolic health



References

1. Early Psychosis Guidelines Writing Group. *Australian Clinical Guidelines for Early Psychosis, 2nd edition*. Orygen Youth Health, Melbourne. 2010;
2. Stavely H, Hughes F, Pennel K et al. *EPPIC Model and Service Implementation Guide*. Melbourne: Orygen Youth Health Research Centre, 2014.
3. Harrop C and Trower P. Why does schizophrenia develop at late adolescence? *Clin Psychol Rev* 2001; 21: 241–66.
4. Macneil CA, Hasty M, Conus P et al. *Bipolar disorder in young people: a psychological intervention manual*. NY, USA: Cambridge University Press, 2009.
5. Jackson HJ, Edwards J, Hulbert C et al. Recovery from psychosis: psychological interventions. In McGorry P and Jackson HJ (ed). *The Recognition and Management of Early Psychosis: A Preventive Approach*. Cambridge, 1999.
6. National Advisory Council on Mental Health. *Early Psychosis Feasibilty Study Report*. Melbourne, Australia: 2011.
7. Birchwood M, Todd P and Jackson C. Early intervention in psychosis. The critical period hypothesis. *Br J Psychiatry Suppl* 1998; 172: 53-9.
8. Marshall M, Lewis S, Lockwood A et al. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients. *Arch Gen Psychiatry* 2005; 62: 975–83.
9. Norman RM, Manchanda R, Malla AK et al. Symptom and functional outcomes for a 5 year early intervention program for psychoses. *Schizophr Res* 2011; 129: 111-5.
10. Bertelsen M, Jeppesen P, Petersen L et al. Five-year follow-up of a randomized multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness: the OPUS trial. *Arch Gen Psychiatry* 2008; 65: 762-71.
11. Craig TK, Garety P, Power P et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. *BMJ* 2004; 329: 1067.
12. Tang JY, Wong GH, Hui CL et al. Early intervention for psychosis in Hong Kong–the EASY programme. *Early Interv Psychiatry* 2010; 4: 214-9.
13. Fowler D, Hodgekins J, Howells L et al. Can targeted early intervention improve functional recovery in psychosis? A historical control evaluation of the effectiveness of different models of early intervention service provision in Norfolk 1998–2007. *Early Interv Psychiatr* 2009; 3: 282–88.
14. Baumann PS, Crespi S, Marion-Veyron R et al. Treatment and early intervention in psychosis program (TIPP-Lausanne): Implementation of an early intervention programme for psychosis in Switzerland. *Early Interv Psychiatry* 2013; 7: 322-8.
15. Cocchi A, Mapelli V, Meneghelli A et al. Cost-effectiveness of treating first-episode psychosis: five-year follow-up results from an Italian early intervention programme. *Early Interv Psychiatry* 2011; 5: 203-11.
16. Mihalopoulos C, Harris M, Henry L et al. Is early intervention in psychosis cost-effective over the long term? *Schizophr Bull* 2009; 35: 909-18.
17. Crumlish N, Whitty P, Clarke M et al. Beyond the critical period: longitudinal study of 8-year outcome in first-episode non-affective psychosis. *Br J Psychiatry* 2009; 194: 18-24.
18. McGorry PD. The recognition and optimal management of early psychosis: an evidence-based reform. *World Psychiatry* 2002; 1: 76-83.
19. Kreyenbuhl J, Nossel IR and Dixon LB. Disengagement From Mental Health Treatment Among Individuals With Schizophrenia and Strategies for Facilitating Connections to Care: A Review of the Literature. *Schizophrenia Bulletin* 2009; 35: 696-703.
20. Schley C, Yuen K, Fletcher K et al. Does engagement with an intensive outreach service predict better treatment outcomes in 'high-risk' youth? *Early Interv Psychiatry* 2012; 6: 176–84.
21. O'Brien A, Fahmy R and Singh SP. Disengagement from mental health services. A literature review. *Soc Psychiatry Psychiatr Epidemiol* 2009; 44: 558-68.
22. McGorry PD, Nelson B, Amminger G et al. Intervention in Individuals at Ultra High Risk for Psychosis: A Review and Future Directions. *J Clin Psychiatry* 2009; doi:10.4088/JCP.08r04472:
23. Large MM, Dall B and Nielssen OB. Risk assessment for violence and self-harm in first episode psychosis and the need for early psychosis intervention services. *Aust N Z J Psychiatry* 2014; 48: 94-5.

24. Freudenreich O, Schulz SC and Goff DC. Initial medical work-up of first-episode psychosis: a conceptual review. *Early Interv Psychiatry* 2009; 3: 10-8.

25. Lawrence D, Hancock KJ and Kisely S. The gap in life expectancy from preventable physical illness in psychiatric patients in Western Australia: retrospective analysis of population based registers. *BMJ: British Medical Journal* 2013; 346: f2539.

26. Davidson M, Galderisi S, Weiser M et al. Cognitive effects of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: a randomized, open-label clinical trial (EUFEST). *Am J Psychiatry* 2009; 166: 675-82.

27. Robles O, Zabala A, Bombin I et al. Cognitive efficacy of quetiapine and olanzapine in early-onset first-episode psychosis. *Schizophr Bull* 2011; 37: 405-15.

28. Addington J, Chaves A and Addington D. Diagnostic stability over one year in first-episode psychosis. *Schizophr Res* 2006; 86: 71-5.

29. Byrne P. Managing the acute psychotic episode. *BMJ* 2007; 334: 686–92.

30. Caton CL, Hasin DS, Shrout PE et al. Stability of early-phase primary psychotic disorders with concurrent substance use and substance-induced psychosis. *Br J Psychiatry* 2007; 190: 105-11.

31. Douglas KS, Hart SD, Webster CD et al. HCR-20 *(version 3): assessing risk for violence*. Burnaby, Canada: Mental Health Law and Policy Institute Simon Fraser University, 2013.

32. Borum R, Bartel P and Forth A. *Structured assessment of violence risk in youth (SAVRY)*. Thousand Oaks, CA: Sage Publications, Inc., 2008.

33. Witt K, van Dorn R and Fazel S. Risk Factors for Violence in Psychosis: Systematic Review and Meta-Regression Analysis of 110 Studies. *PloS one* 2013; 8: e55942.

34. Foley SR, Kelly BD, Clarke M et al. Incidence and clinical correlates of aggression and violence at presentation in patients with first episode psychosis. *Schizophr Res* 2005; 72: 161-8.

35. Power PJ and McGowan S. Suicide Risk Management in Early Intervention. 2011

36. Hunt IM, Kapur N, Webb R et al. Suicide in recently discharged psychiatric patients: a case-control study. *Psychol Med* 2009; 39: 443-9.

37. Power PJ, Bell RJ, Mills R et al. Suicide prevention in first episode psychosis: the development of a randomised controlled trial of cognitive therapy for acutely suicidal patients with early psychosis. *Aust N Z J Psychiatry 2003*; 37: 414-20.

38. Nielssen O, Large MM, Ryan C et al. Legal implications of the increased risk of homicide and serious violence in the first episode of psychotic illness. *Crim L J* 2007; 31: 287–94.

39. Meaden A and Hacker D. *Problematic and Risk Behaviours in Psychosis: A Shared Formulation Approach*. Taylor & Francis, 2010.

40. Allnutt SH, Ogloff JR, Adams J et al. Managing aggression and violence: the clinician's role in contemporary mental health care. *Aust N Z J Psychiatry* 2013; 47: 728-36.

41. Fraser R, Berger G and McGorry P. Emerging psychosis in young people – Part 2: key issues for acute management. *Australian Family Physician* 2006; 35: 323–27.

42. National Institute for Health and Clinical Excellence. Psychosis and schizophrenia in children and young people: Recognition and management. *NICE clinical guideline* 155 2013;

43. National Institute for Health and Care Excellence. Psychosis and schizophrenia in adults: treatment and management. *NICE clinical guideline* 178 2014;

44. Spencer E. Management of first-episode psychosis. *Advances in Psychiatric Treatment* 2001; 7: 133-140.

45. Rufino AC, Uchida RR, Vilela JA et al. Stability of the diagnosis of first-episode psychosis made in an emergency setting. *Gen Hosp Psychiatry* 2005; 27: 189-93.

46. Almandil NB and Wong IC. Review on the current use of antipsychotic drugs in children and adolescents. *Arch Dis Child Educ Pract Ed* 2011; 96: 192-6.

47. Correll CU, Sheridan EM and DelBello MP. Antipsychotic and mood stabilizer efficacy and tolerability in pediatric and adult patients with bipolar I mania: a comparative analysis of acute, randomized, placebo-controlled trials. *Bipolar Disord* 2010; 12: 116-41.

48. Kumar A, Datta S, Wright S et al. Atypical antipsychotics for psychosis in adolescents. *Cochrane Database* Syst Rev 2013; 10:

49. Abdel-Baki A, Ouellet-Plamondon C and Malla A. Pharmacotherapy challenges in patients with first-episode psychosis. *J Affect Disord* 2012; 138 Suppl: S3-14.

50. Barnes TR. Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology. *J Psychopharmacol* 2011; 25: 567-620.

51. Lambert M, Conus P, Lambert T et al. Pharmacotherapy of first-episode psychosis. *Expert Opin Pharmocother* 2003; 4:

52. Lambert M. Initial assessment and initial pharmacological treatment in the acute phase. In Jackson HJ and McGorry P (ed). *The Recognition and Management of Early Psychosis: A Preventative Approach*. 2009.

53. Masi G and Liboni F. Management of schizophrenia in children and adolescents: focus on pharmacotherapy. *Drugs* 2011; 71: 179-208.

54. Lambert M and Naber D. *Current schizophrenia*. London, UK.: Springer Healthcare, 2012.

55. Correll CU. Antipsychotic use in children and adolescents: minimizing adverse effects to maximize outcomes. *J Am Acad Child Adolesc Psychiatry* 2008; 47: 9-20.

56. Fraguas D, Correll CU, Merchan-Naranjo J et al. Efficacy and safety of second-generation antipsychotics in children and adolescents with psychotic and bipolar spectrum disorders: comprehensive review of prospective head-to-head and placebo-controlled comparisons. *Eur Neuropsychopharmacol* 2011; 21: 621-45.

57. Boter H, Peuskens J, Libiger J et al. Effectiveness of antipsychotics in first-episode schizophrenia and schizophreniform disorder on response and remission: An open randomized clinical trial (EUFEST). *Schizophr Res* 2009; 115: 97–103.

58. De Hert M, Dobbelaere M, Sheridan EM et al. Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice. *Eur Psychiatry* 2011; 26: 144-58.

59. Almandil NB, Liu Y, Murray ML et al. Weight gain and other metabolic adverse effects associated with atypical antipsychotic treatment of children and adolescents: a systematic review and meta-analysis. *Paediatr Drugs* 2013; 15: 139-50.

60. Humble F and Berk M. Pharmacological management of aggression and violence. *Hum Psychopharmacol* 2003; 18: 423-36.

61. Richmond JS, Berlin JS, Fishkind AB et al. Verbal De-escalation of the Agitated Patient: Consensus Statement of the American Association for Emergency Psychiatry Project BETA De-escalation Workgroup. *West J Emerg Med* 2012; 13: 17-25.

62. Olver J, Love M, Daniel J et al. The impact of a changed environment on arousal levels of patients in a secure extended rehabilitation facility. *Australas Psychiatry* 2009; 17: 207-11.

63. Wilson MP, Pepper D, Currier GW et al. The psychopharmacology of agitation: consensus statement of the american association for emergency psychiatry project Beta psychopharmacology workgroup. *West J Emerg Med* 2012; 13: 26-34.

64. National Institute for Health and Clinical Excellence. Violence: The short-term management of disturbed/violent behaviour in in-patient psychiatric settings and emergency departments. *NICE clinical guideline* 25 2005;

65. Gillies D, Sampson S, Beck A et al. Benzodiazepines for psychosis-induced aggression or agitation. *Cochrane Database Syst Rev* 2013; 4: CD003079.

66. Schleifer JJ. Management of acute agitation in psychosis: an evidence-based approach in the USA. *Advances in Psychiatric Treatment* 2011; 17: 91-100.

67. Walther S, Moggi F, Horn H et al. Rapid tranquilization of severely agitated patients with schizophrenia spectrum disorders: a naturalistic, rater-blinded, randomized, controlled study with oral haloperidol, risperidone, and olanzapine. *J Clin Psychopharmacol* 2014; 34: 124-8.

68. Bosanac P, Hollander Y and Castle D. The comparative efficacy of intramuscular antipsychotics for the management of acute agitation. *Australas Psychiatry* 2013; 21: 554-62.

69. International Early Psychosis Association Writing Group. International clinical practice guidelines for early psychosis. *Br J Psychiatry Suppl* 2005; 48: s120-4.

70. Lochmann van Bennekom MW, Gijsman HJ and Zitman FG. Antipsychotic polypharmacy in psychotic disorders: a critical review of neurobiology, efficacy, tolerability and cost effectiveness. *J Psychopharmacol* 2013; 27: 327-36.

71. Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. *Australian and New Zealand Journal of Psychiatry* 2005; 39: 1-30.

72. Timlin U, Hakko H, Heino R et al. A systematic narrative review of the literature: adherence to pharmacological and nonpharmacological treatments among adolescents with mental disorders. *J Clin Nurs* 2014;

73. Coldham EL, Addington J and Addington D. Medication adherence of individuals with a first episode of psychosis. *Acta Psychiatr Scand* 2002; 106: 286-90.

74. Barkhof E, Meijer CJ, de Sonneville LM et al. Interventions to improve adherence to antipsychotic medication in patients with schizophrenia–a review of the past decade. *Eur Psychiatry* 2012; 27: 9-18.

75. Dibonaventura M, Gabriel S, Dupclay L et al. A patient perspective of the impact of medication side effects on adherence: results of a cross-sectional nationwide survey of patients with schizophrenia. *BMC Psychiatry* 2012; 12: 20.

76. Day JC, Wood G, Dewey M et al. A self-rating scale for measuring neuroleptic side-effects. Validation in a group of schizophrenic patients. *The British Journal of Psychiatry* 1995; 166: 650-653.

77. Strakowski SM, Keck PE, Jr., McElroy SL et al. Chronology of comorbid and principal syndromes in first-episode psychosis. *Compr Psychiatry* 1995; 36: 106-12.

78. Buckley PF, Miller BJ, Lehrer DS et al. Psychiatric comorbidities and schizophrenia. *Schizophr Bull* 2009; 35: 383-402.

79. Hartley S, Barrowclough C and Haddock G. Anxiety and depression in psychosis: a systematic review of associations with positive psychotic symptoms. *Acta Psychiatr Scand* 2013; 128: 327-46.

80. Altamura AC, Serati M, Albano A et al. An epidemiologic and clinical overview of medical and psychopathological comorbidities in major psychoses. *Eur Arch Psychiatry Clin Neurosci* 2011; 261: 489-508.

81. Sanofi-Aventis Australia Pty Ltd. Product information: Solian (Amisulpride) tablets and solution. 2013;

82. Bristol-Myers Squibb Australia Pty Ltd. Product information for Abilify (Aripiprazole) tablets and orally disintegrating tablets. 2013;

83. Eli Lilly Australia Pty Limited. Zyprexa (Olanzapine). 2012;

84. Pfizer Australia Pty Ltd. Product Information: Zeldox (Ziprasidone hydrochloride). 2013;

85. Novartis Pharmaceuticals Australia Pty Ltd. Clozaril (Clozapine). 2014;

86. Janssen-Cilag Pty Ltd. Risperdal, Risperdal Quicklet: Product information. 2013.

87. AstraZeneca Pty Ltd. Seroquel (quetiapine fumarate): Product information. 2013.

88. Aspen Pharmacare Australia Pty Ltd. Product information: Lamictal dispersible/chewable tablets, Lamictal tablets. 2013;

89. Isacsson G and Rich CL. Antidepressant drugs and the risk of suicide in children and adolescents. *Paediatr Drugs* 2014; 16: 115-22.

90. Galbally M, Roberts M and Buist A. Mood stabilizers in pregnancy: a systematic review. *Aust N Z J Psychiatry* 2010; 44: 967-77.

91. Miller LJ and Finnerty M. Sexuality, pregnancy, and childrearing among women with schizophrenia-spectrum disorders. *Psychiatr Serv* 1996; 47: 502-6.

92. Miller LJ. Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophr Bull* 1997; 23: 623-35.

93. Sanofi-Aventis Australia Pty Ltd. Product information: Epilim. 2014.

94. Galbally M, Snellen M, Walker S et al. Management of antipsychotic and mood stabilizer medication in pregnancy: recommendations for antenatal care. *Aust N Z J Psychiatry* 2010; 44: 99-108.

95. Sachs HC. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. *Pediatrics* 2013; 132: e796-809.

96. Genung V. Psychopharmacology column: a review of psychotropic medication lactation risks for infants during breastfeeding. *J Child Adolesc Psychiatr Nurs* 2013; 26: 214-9.

97. Massey BW, Li J and Meltzer HY. Pharmacogenetics in the Treatment of Schizophrenia. 2014; 161-173.

98. Han C and Pae CU. Do we need to consider ethno-cultural variation in the use of atypical antipsychotics for Asian patients with major depressive disorder? *CNS drugs* 2013; 27 Suppl 1: S47-51.

99. Cohen D, Bonnot O, Bodeau N et al. Adverse effects of second-generation antipsychotics in children and adolescents: a Bayesian meta-analysis. *J Clin Psychopharmacol* 2012; 32: 309-16.

100. Allison DB, Mentore JL, Heo M et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry* 1999; 156: 1686-96.

101. Leucht S, Cipriani A, Spineli L et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 2013; 382: 951-62.

102. De Hert M, Detraux J, van Winkel R et al. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nature Reviews Endocrinology* 2012; 8: 114-126.

103. Fleischhacker WW, Siu CO, Boden R et al. Metabolic risk factors in first-episode schizophrenia: baseline prevalence and course analysed from the European First-Episode Schizophrenia Trial. *Int J Neuropsychopharmacol* 2013; 16: 987-95.

104. Patel JK, Buckley PF, Woolson S et al. Metabolic profiles of second-generation antipsychotics in early psychosis: findings from the CAFE study. *Schizophr Res* 2009; 111: 9-16.

105. Pérez-Iglesias R, Martínez-García O, Pardo-Garcia G et al. Course of weight gain and metabolic abnormalities in first treated episode of psychosis: the first year is a critical period for development of cardiovascular risk factors. *The International Journal of Neuropsychopharmacology* 2014; 17: 41-51.

106. Vidarsdottir S, de Leeuw van Weenen JE, Frolich M et al. Effects of olanzapine and haloperidol on the metabolic status of healthy men. *J Clin Endocrinol Metab* 2010; 95: 118-25.

107. Albaugh VL, Singareddy R, Mauger D et al. A double blind, placebo-controlled, randomized crossover study of the acute metabolic effects of olanzapine in healthy volunteers. *PLoS One* 2011; 6: e22662.

108. Teff KL, Rickels MR, Grudziak J et al. Antipsychotic-induced insulin resistance and postprandial hormonal dysregulation independent of weight gain or psychiatric disease. *Diabetes* 2013; 62: 3232-40.

109. Hahn MK, Wolever TM, Arenovich T et al. Acute effects of single-dose olanzapine on metabolic, endocrine, and inflammatory markers in healthy controls. *J Clin Psychopharmacol* 2013; 33: 740-6.

110. Fountaine RJ, Taylor A, Mancuso J et al. Increased food intake and energy expenditure following administration of olanzapine to healthy men. *Obesity (Silver Spring)* 2010; 18: 1646–51.

111. Roke Y, van Harten PN, Boot AM et al. Antipsychotic medication in children and adolescents: a descriptive review of the effects on prolactin level and associated side effects. *J Child Adolesc Psychopharmacol* 2009; 19: 403-14.

112. Ben Amor L. Antipsychotics in pediatric and adolescent patients: a review of comparative safety data. *J Affect Disord* 2012; 138 Suppl: S22-30.

113. Vitiello B, Correll C, van Zwieten-Boot B et al. Antipsychotics in children and adolescents: increasing use, evidence for efficacy and safety concerns. *Eur Neuropsychopharmacol* 2009; 19: 629-35.

114. Rabinovitch M, Bechard-Evans L, Schmitz N et al. Early predictors of nonadherence to antipsychotic therapy in first-episode psychosis. *Can J Psychiatry* 2009; 54: 28-35.

115. Hill M, Crumlish N, Whitty P et al. Nonadherence to medication four years after a first episode of psychosis and associated risk factors. *Psychiatr Serv* 2010; 61: 189-92.

116. Taylor M and Ng KY. Should long-acting (depot) antipsychotics be used in early schizophrenia? A systematic review. *Aust N Z J Psychiatry* 2013; 47: 624-30.

117. Thompson L and McCabe R. The effect of clinician-patient alliance and communication on treatment adherence in mental health care: a systematic review. *BMC Psychiatry* 2012; 12: 87.

118. Ishii M, Okumura Y, Sugiyama N et al. Efficacy of shared decision making on treatment satisfaction for patients with first-admission schizophrenia: study protocol for a randomised controlled trial. *BMC Psychiatry* 2014; 14: 111.

119. Montreuil TC, Cassidy CM, Rabinovitch M et al. Case manager- and patient-rated alliance as a predictor of medication adherence in first-episode psychosis. *J Clin Psychopharmacol* 2012; 32: 465-9.

120. Prikryl R, Prikrylova Kucerova H, Vrzalova M et al. Role of long-acting injectable second-generation antipsychotics in the treatment of first-episode schizophrenia: a clinical perspective. *Schizophr Res Treatment* 2012; 2012: 764769.

121. Heres S, Schmitz FS, Leucht S et al. The attitude of patients towards antipsychotic depot treatment. *Int Clin Psychopharmacol* 2007; 22: 275-82.

122. Lambert TJ. Practical management of schizophrenia: the role of long-acting Antipsychotics. *Int Clin Psychopharmacol* 2013;

123. Yung AR, Phillips LJ, Nelson B et al. Randomized controlled trial of interventions for young people at ultra high risk for psychosis: 6-month analysis. *J Clin Psychiatry* 2011; 72: 430-40.

124. van der Gaag M, Smit F, Bechdolf A et al. Preventing a first episode of psychosis: meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups. *Schizophr Res* 2013; 149: 56-62.

125. Yung A and Nelson B. Young people at ultra high risk for psycosis: research from the PACE clinic. *Revista Brasileira de Psiquiatria* 2011; 33: S143.

126. Preti A and Cella M. Randomized-controlled trials in people at ultra high risk of psychosis: a review of treatment effectiveness. *Schizophr Res* 2010; 123: 30-6.

127. Bertolote J and McGorry P. Early intervention and recovery for young people with early psychosis: consensus statement. *Br J Psychiatry* 2005; 187: S116–19.

128. Fusar-Poli P, Nelson B, Valmaggia L et al. Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophr Bull* 2014; 40: 120-31.

129. Hafner H, Maurer K, Loffler W et al. Modelling the early course schizophrenia. *Schizophr Bull* 2003; 29: 325-40.

130. Amminger G, Chanen A, Ohmann S et al. Omega-3 fatty acid supplementation in adolescents with borderline personality disorder and ultra-high risk criteria for psychosis: a post hoc subgroup analysis of a double-blind, randomized controlled trial. *Can J Psychiatry* 2013; 58: 402–8.

131. Mossaheb N, Schafer MR, Schlogelhofer M et al. Effect of omega-3 fatty acids for indicated prevention of young patients at risk for psychosis: when do they begin to be effective? *Schizophr Res* 2013; 148: 163-7.

132. McGorry PD, Nelson B, Phillips LJ et al. Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: twelve-month outcome. *J Clin Psychiatry* 2013; 74: 349-56.

133. Edwards J, Maude D, McGorry PD et al. Prolonged recovery in first-episode psychosis. *Br J Psychiatry Suppl* 1998; 172: 107-16.

134. Oosthuizen P, Emsley R, Niehaus D et al. The relationships between depression and remission in first-episode psychosis. *World Psychiatry* 2006; 5: 172–76.

135. Emsley R, Rabinowitz J and Medori R. Time course for antipsychotic treatment response in first-episode schizophrenia. *Am J Psychiatry* 2006; 163: 743-5.

136. Crespo-Facorro B, de la Foz VO, Ayesa-Arriola R et al. Prediction of acute clinical response following a first episode of non affective psychosis: results of a cohort of 375 patients from the Spanish PAFIP study. *Prog Neuropsychopharmacol Biol Psychiatry* 2013; 44: 162-7.

137. Schennach-Wolff R, Jager M, Mayr A et al. Predictors of response and remission in the acute treatment of first-episode schizophrenia patients–is it all about early response? *Eur Neuropsychopharmacol* 2011; 21: 370-8.

138. Schennach R, Riesbeck M, Mayr A et al. Should early improvement be re-defined to better predict the maintenance of response in first-episode schizophrenia patients? *Acta Psychiatr Scand* 2013; 127: 474-81.

139. Gallego JA, Robinson DG, Sevy SM et al. Time to treatment response in first-episode schizophrenia: should acute treatment trials last several months? *J Clin Psychiatry* 2011; 72: 1691-6.

140. McGorry PD, Cocks J, Power P et al. Very low-dose risperidone in first-episode psychosis: a safe and effective way to initiate treatment. *Schizophr Res Treatment* 2011; 2011: 631690.

141. Schimmelmann BG, Schmidt SJ, Carbon M et al. Treatment of adolescents with early-onset schizophrenia spectrum disorders: in search of a rational, evidence-informed approach. *Curr Opin Psychiatry* 2013; 26: 219-30.

142. Wunderink L, Nieboer RM, Wiersma D et al. Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation or maintenance treatment strategy: long-term follow-up of a 2-year randomized clinical trial. *JAMA Psychiatry* 2013; 70: 913-20.

143. Zipursky RB, Menezes NM and Streiner DL. Risk of symptom recurrence with medication discontinuation in first-episode psychosis: a systematic review. *Schizophr Res* 2014; 152: 408-14.

144. Robinson D, Woerner MG, Alvir JM et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry* 1999; 56: 241-7.

145. Wunderink L, Nienhuis FJ, Sytema S et al. Guided discontinuation versus maintenance treatment in remitted first-episode psychosis: relapse rates and functional outcome. *J Clin Psychiatry* 2007; 68: 654-61.

146. Alvarez-Jimenez M, Priede A, Hetrick SE et al. Risk factors for relapse following treatment for first episode psychosis: a systematic review and meta-analysis of longitudinal studies. *Schizophr Res* 2012; 139: 116-28.

147. McGorry P, Alvarez-Jimenez M and Killackey E. Antipsychotic medication during the critical period following remission from first-episode psychosis: less is more. *JAMA Psychiatry* 2013; 70: 898-900.

148. Iyer SN, Loohuis H, Pawliuk N et al. Concerns reported by family members of individuals with first-episode psychosis. *Early Interv Psychiatry* 2011; 5: 163-7.

149. Ramsay C, Broussard B, Goulding S et al. Life and treatment goals of individuals hospitalized for first-episode nonaffective psychosis *Psychiatr Res* 2011; 189: 344–48.

150. Alvarez-Jiménez M, Gleeson JF, Henry L et al. Road to full recovery: longitudinal relationship between symptomatic remission and psychosocial recovery in first-episode psychosis over 7.5 years. *Psychological Medicine* 2012; 42: 595–606.

151. Alvarez-Jimenez M, Gleeson JF, Henry LP et al. Prediction of a single psychotic episode: a 7.5-year, prospective study in first-episode psychosis. *Schizophr Res* 2011; 125: 236-46.

152. Pantelis C and Lambert T. Managing patients with "treatment-resistant" schizophrenia. *Med J Aust* 2003; 178: S62–S66.

153. Huber C, Naber D and Lambert M. Incomplete remission and treatment resistance in first-episode psychosis: definition, prevalence and predictors. *Expert Opin Pharmacother* 2008; 9: 2027–38.

154. Edwards J, Maude D, Herrmann-Doig T et al. A service response to prolonged recovery in early psychosis. *Psychiatr Serv* 2002; 53: 1067–69.

155. Burns AM, Erickson DH and Brenner CA. Cognitive-Behavioral Therapy for Medication-Resistant Psychosis: A Meta-Analytic Review. *Psychiatr Serv* 2014;

156. Pharoah F, Mari JJ, Rathbone J et al. Family intervention for schizophrenia. *Cochrane Database of Systematic Reviews* 2010.

157. Remington G, Agid O, Foussias G et al. Clozapine's role in the treatment of first-episode schizophrenia. *Am J Psychiatry* 2013; 170: 146-51.

158. Kane J, Honigfeld G, Singer J et al. Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine. *Arch Gen Psychiatry* 1988; 45: 789-96.

159. Berk M, Fitzsimons J, Lambert T et al. Monitoring the safe use of clozapine: a consensus view from Victoria, Australia. *CNS Drugs* 2007; 21: 117-27.

160. Alvir JM, Lieberman JA, Safferman AZ et al. Clozapine-induced agranulocytosis. Incidence and risk factors in the United States. *N Engl J Med* 1993; 329: 162-7.

161. Ronaldson KJ, Fitzgerald PB, Taylor AJ et al. A new monitoring protocol for clozapine-induced myocarditis based on an analysis of 75 cases and 94 controls. *Aust N Z J Psychiatry* 2011; 45: 458-65.

162. Castle DJK, N. What Can We Do If Clozapine Fails? Pharmacologic Choices and Differential Outcomes. In Buckley P and Gaughran F (ed). *Treatment-Refractory Schizophrenia*. 2014.

163. Porcelli S, Balzarro B and Serretti A. Clozapine resistance: augmentation strategies. *Eur Neuropsychopharmacol* 2012; 22: 165-82.

164. Sommer IE, Begemann MJ, Temmerman A et al. Pharmacological augmentation strategies for schizophrenia patients with insufficient response to clozapine: a quantitative literature review. *Schizophr Bull* 2012; 38: 1003-11.

165. Taylor DM, Smith L, Gee SH et al. Augmentation of clozapine with a second antipsychotic - a meta-analysis. *Acta Psychiatr Scand* 2012; 125: 15-24.

166. Suzuki K, Awata S, Takano T et al. Improvement of psychiatric symptoms after electroconvulsive therapy in young adults with intractable first-episode schizophrenia and schizophreniform disorder. *Tohoku J Exp Med* 2006; 210: 213–20.

167. Kho KH, Blansjaar BA, de Vries S et al. Electroconvulsive therapy for the treatment of clozapine nonresponders suffering from schizophrenia–an open label study. *Eur Arch Psychiatry Clin Neurosci* 2004; 254: 372-9.

168. Pompili M, Lester D, Dominici G et al. Indications for electroconvulsive treatment in schizophrenia: a systematic review. *Schizophr Res* 2013; 146: 1-9.

169. Zhang ZJ, Chen YC, Wang HN et al. Electroconvulsive therapy improves antipsychotic and somnographic responses in adolescents with first-episode psychosis–a case-control study. *Schizophr Res* 2012; 137: 97-103.

170. Loo C, Katalinic N, Mitchell PB et al. Physical treatments for bipolar disorder: a review of electroconvulsive therapy, stereotactic surgery and other brain stimulation techniques. *J Affect Disord* 2011; 132: 1-13.

171. de la Serna E, Flamarique I, Castro-Fornieles J et al. Two-year follow-up of cognitive functions in schizophrenia spectrum disorders of adolescent patients treated with electroconvulsive therapy. *J Child Adolesc Psychopharmacol* 2011; 21: 611-9.

172. National Mental Health Commission. A Contributing Life, the 2012 National Report Card on Mental Health and Suicide Prevention. 2012.

173. Galletly CA, Foley DL, Waterreus A et al. Cardiometabolic risk factors in people with psychotic disorders: The second Australian national survey of psychosis. *Australian and New Zealand Journal of Psychiatry* 2012; 46: 753-761.

174. Alberti K, Eckel R, Grundy S et al. Harmonizing the Metabolic Syndrome A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; 120: 1640-1645.

175. International Diabetes Foundation. *The IDF consensus worldwide definition of the metabolic syndrome*. Brussels: 2006.

176. Morgan V, McGrath J, Jablensky A et al. Psychosis prevalence and physical, metabolic and cognitive co-morbidity: data from the second Australian national survey of psychosis. *Psychological Medicine in press* 2013;

177. Kwan CL, Gelberg HA, Rosen JA et al. Nutritional Counseling for Adults with Severe Mental Illness: Key Lessons Learned. *Journal of the Academy of Nutrition and Dietetics* 2014; 114: 369-374.

178. Alvarez-Jimenez M, Gonzalez-Blanch C, Crespo-Facorro B et al. Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders. *CNS drugs* 2008; 22: 547-562.

179. Curtis J, Henry C, Watkins A et al. Metabolic abnormalities in an early psychosis service: a retrospective, naturalistic cross, sectional study. *Early Intervention in Psychiatry* 2011; 5: 108-114.

180. Correll CU and Carlson HE. Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry* 2006; 45: 771-791.

181. Correll CU, Manu P, Olshanskiy V et al. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA: The Journal of the American Medical Association* 2009; 302: 1765-1773.

182. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004; 27: 596–601.

183. Alvarez-Jiménez M, González-Blanch C, Crespo-Facorro B et al. Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders: a systematic critical reappraisal. *CNS Drugs* 2008; 22: 547-62.

184. Alvarez-Jiménez M, Martínez-García O, Pérez-Iglesias R et al. Prevention of antipsychotic-induced weight gain with early behavioural intervention in first-episode psychosis: 2-year results of a randomized controlled trial. *Schizophr Res* 2010; 116: 16-9.

185. Curtis J, Watkins A, Rosenbaum S et al. Keeping the body in mind for young people with first episode psychosis. *Schizophr Res* 2014; 153: S259–S260.

186. Curtis J, Newall HD and Samaras K. The heart of the matter: cardiometabolic care in youth with psychosis. *Early Intervention in Psychiatry* 2012; 6: 347-353.

187. Waterreus AJ and Laugharne J. Screening for the metabolic syndrome in patients receiving antipsychotic treatment: a proposed algorithm. *Med J Aust* 2009; 190: 185-9.

188. Pringsheim T, Panagiotopoulos C, Davidson J et al. Evidence-based recommendations for monitoring safety of second-generation antipsychotics in children and youth. *Paediatrics and Child Health* 2011; 16: 581.

189. Myles N, Newall HD, Curtis J et al. Tobacco use before, at and after first-episode psychosis: a systematic meta-analysis. *J Clin Psychiatry* 2012; 73: 468-475.

190. Cooper J, Mancuso S, Borland R et al. Tobacco smoking among people living with a psychotic illness: the second Australian Survey of Psychosis. *Aust N Z J Psychiatry* 2012; 46: 851–63.

191. Ragg M and Ahmed T. Smoke and mirrors: a review of the literature on smoking and mental illness. In (ed). *Tackling Tobacco Program Research Series No. 1.* Sydney: Cancer Council NSW, 2008.

192. Faulkner G, Cohn T and Remington G. Validation of a physical activity assessment tool for individuals with schizophrenia. *Schizophrenia Research* 2006; 82: 225-231.

193. Biddle S, Petrolini I and Pearson N. Interventions designed to reduce sedentary behaviours in young people: a review of reviews. *Brit J Sport Med* 2014; 48: 182–86.

194. Dipasquale S, Pariante CM, Dazzan P et al. The dietary pattern of patients with schizophrenia: A systematic review. *Journal of Psychiatric Research* 2012; 47: 197-207.

195. McCreadie RG. Diet, smoking and cardiovascular risk in people with schizophrenia Descriptive study. *The British Journal of Psychiatry* 2003; 183: 534-539.

196. *National Health and Medical Research Council Australian Dietary Guidelines.* Canberra: National Health and Medical Research Council. 2013.

197. Agency for Clinical Innovation. *Nutrition Standards for Consumers of Inpatient Mental Health Services in NSW*. Chatswood: ACI Nutrition Network, 2013.

198. Curtis J, Newall H, Myles N et al. Considering metformin in cardiometabolic protection in psychosis. *Acta Psychiatrica Scandinavica* 2012; 126: 302-303.

199. Belvederi Murri M, Respino M, Masotti M et al. Vitamin D and psychosis: mini meta-analysis. *Schizophr Res* 2013; DOI: 10.1016/j.schres.2013.07.017:

200. Wu H, Den L, Zhao L et al. Osteoporosis associated with antipsychotic treatment in schizophrenia. *Int J Endocrinology* 2013; DOI: 10.1155/2013/167138:

201. Crews M, Lally J, Gardner-Sood P et al. Vitamin D deficiency in first episode psychosis: A case–control study. *Schizophr Res* 2013; DOI: 10.1016/j.schres.2013.08.036:

202. Kang M, Rochford A, Skinner SR et al. Sexual behaviour, sexually transmitted infections and attitudes to chlamydia testing among a unique national sample of young Australians: baseline data from a randomised controlled trial. *BMC Public Health* 2014; 14: 12.

203. Mitchell A, Patrick K, Heywood L et al. 5th National Survey of Australian Secondary Students and Sexual Health 2013. 2014;

204. Brown A, Yung A, Cosgrave E et al. Depressed mood as a risk factor for unprotected sex in young people. *Australasian Psychiatry* 2006; 14: 310-312.

205. Brown A, Lubman DI and Paxton SJ. Reducing sexually-transmitted infection risk in young people with first-episode psychosis. *International Journal of Mental Health Nursing* 2011; 20: 12-20.

206. Foley DL and Morley KI. Systematic review of early cardiometabolic outcomes of the first treated episode of psychosis. *Archives of General Psychiatry* 2011; 68: 609.

207. Thompson A, Hetrick S, Alvarez-Jiménez M et al. Targeted intervention to improve monitoring of antipsychotic-induced weight gain and metabolic disturbance in first episode psychosis. *Aust N Z J Psychiatry* 2011; 45: 740–48.

208. Hetrick S, Ålvarez-Jiménez, Mario, Parker A et al. Promoting physical health in youth mental health services: ensuring routine monitoring of weight and metabolic indices in a first episode psychosis clinic. *Australasian Psychiatry* 2010; 18: 451-455.

209. Haupt D, Rosenblatt L, Kim E et al. Prevalence and predictors of lipid and glucose monitoring in commercially insured patients treated with second-generation antipsychotic agents. *American Journal of Psychiatry* 2009; 166: 345-353.

210. Cardno AG and Owen MJ. Genetic relationships between schizophrenia, bipolar disorder, and schizoaffective disorder. *Schizophr Bull* 2014; 40: 504-15.

211. Doherty JL, O'Donovan MC and Owen MJ. Recent genomic advances in schizophrenia. *Clin Genet* 2012; 81: 103-9.

212. Sanders AR. Genetics of Schizophrenia. In Janicak P et al. (eds) Schizophrenia: *Recent Advances in Diagnosis and Treatment*. New York: 2014.

213. Alvarez-Jimenez M, Alcazar-Corcoles MA, Gonzalez-Blanch C et al. Online, social media and mobile technologies for psychosis treatment: A systematic review on novel user-led interventions. *Schizophr Res* 2014; 156: 96-106.

214. Ben-Zeev D, Brenner CJ, Begale M et al. Feasibility, Acceptability, and Preliminary Efficacy of a Smartphone Intervention for Schizophrenia. *Schizophr Bull* 2014;

215. Schubart CD, Sommer IE, Fusar-Poli P et al. Cannabidiol as a potential treatment for psychosis. *Eur Neuropsychopharmacol* 2014; 24: 51-64.

216. Sommer IE, van Westrhenen R, Begemann MJ et al. Efficacy of anti-inflammatory agents to improve symptoms in patients with schizophrenia: an update. *Schizophr Bull* 2014; 40: 181-91.

217. Lin C, Tsai G and Lane H. Assessing and treating cognitive impairment in schizophrenia: current and future. *Curr Pharm Design* 2014; 20: 00.

NOTES

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