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Emerging psychosis in young people – Part 2

Key issues for acute management

BACKGROUND

To optimise the management of emerging psychotic disorders in young people, close collaboration between the general practitioner and youth friendly specialist mental health services is favourable. Ideally, a multidisciplinary team including individual case management with expertise in early intervention should treat these patients for the initial 2–5 years. However, only a few areas across Australia currently provide this type of specialised service. Most GPs will at some point be faced with the reality of personally managing young patients with emerging psychotic disorders on their own, sometimes with very limited support.

OBJECTIVE

This article summarises key issues for the optimal management of emerging psychotic disorders, with a particular focus on the role of the GP.

DISCUSSION

Once an emerging psychotic disorder is confirmed, the engagement of the young person into therapy is the primary target. Ideally therapy integrates not only the patient, but also their family, carers and friends. General practitioners need to inform patients about the nature of the emerging psychotic illness, manage related comorbidities such as substance abuse, and initiate antipsychotic medication to avoid any unnecessary delay in resolution of symptoms. It is important to monitor the patient on a regular basis even after symptom recovery as up to 80% of cases that cease medication will relapse within 5 years.

General practitioners are often the first point of contact for a distressed family or young person experiencing symptoms of an emerging psychotic illness. Once a psychotic illness has been confirmed, it is essential to formulate and implement an appropriate management plan. Ideally early referral to a specialised early psychosis service (eg. the Early Psychosis Prevention & Intervention Centre (EPPIC) of ORYGEN Youth Health) should be arranged so that appropriate treatment can be initiated. Unfortunately in many areas such services do not exist and alternatives such as adult or child mental health services or private services are unable to respond in a timely fashion. Under these circumstances, GPs may have to initiate management of the young patient themselves, as the evidence base consistently supports early intervention with the aim of reducing the duration of untreated psychosis and minimising social and cognitive incapacity in order to improve overall outcome.¹⁻⁴

Management of the first psychotic episode

An integrated bio-psycho-social treatment approach

Optimal treatment integrates biological, psychological and social interventions at the earliest possible opportunity.⁵ The ideal model for the optimal therapy of a first psychotic episode involves a multidisciplinary approach including the GP, a psychiatrist, psychologist, mental health nurse, occupational therapist, social worker, and most importantly, long term case management with vocational recovery goals. Any of the above clinicians can take on the role of the case manager and it may depend on the individual needs of the patient and the available resources as to who is best suited. The case manager will maintain contact – even after full recovery – to monitor, along with the GP, maintenance treatment and to look out for the early warning signs of relapse.

At the EPPIC program of ORYGEN Youth Health, each patient is allocated a case manager to: coordinate

care, promote development of the individual, minimise psychosocial stressors, and ensure ongoing treatment adherence and engagement with services. This approach is particularly important in the early phase of illness until the patient is able to take on a large proportion of responsibility for the management of his/her illness. Unfortunately such services are not yet available in most areas of Australia. Adult mental health services may not be appropriately resourced or motivated to follow up early psychosis cases after the initial recovery, and frequently discharge patients prematurely during early recovery with limited follow up. General practitioners are then often responsible for the ongoing care of these patients.

Keeping patients engaged – the therapeutic alliance

The engagement of the patient in a long term therapeutic alliance where treatment can be tailored to the patient's individual needs is a prerequisite to achieve optimal outcome.⁴⁻⁶ A common perception is that the mainstay of treatment in first episode psychosis is solely antipsychotic medication. This may be true to some extent, as recent evidence suggests that newer antipsychotic medications protect the brain from damage in patients undergoing a first psychotic episode⁷ and can be beneficial in enhancing cognitive functioning.⁸ However, treatment adherence is very poor – in the region of 60% for patients with psychosis⁹ and relapses are frequent.⁹⁻¹² About 80% of patients who cease antipsychotic medication relapse within 5 years.¹³ The likelihood of remission drops with every relapse.¹⁴ Therefore, the engagement of the patient into a long term therapeutic alliance for several years is recommended (see *Case history Mary*).

Antipsychotic medication – first impressions

The patient's initial experience with using antipsychotic medication is a key factor in determining their long term attitude toward medication.¹⁵⁻¹⁷ The newer atypical antipsychotic medications (eg. olanzapine, quetiapine, risperidone or aripiprazole) provide fewer troublesome experiences such as extrapyramidal side effects (dystonia, tremor), restlessness, or sexual dysfunction compared to conventional

Case history Mary – first episode psychosis

Mary, 24 years of age, has had long standing social problems as well as a substance abuse problem. She has moved around within temporary accommodation settings for the past 8 years since she left home. She has no contact with her family and does not appear to have any close friends. She does not have a job and appears to have no goals in life. Over the past few weeks she has been noticed to be listening intently to 'the silence' or focusing on apparently blank walls. At other times she has mixed excessive quantities of salt into her food in order to 'neutralise the poisons in it'. Her accommodation worker now reports that she has not left her room for 3 days and there are concerns for her wellbeing.

Discussion – Mary is clearly unwell and requires urgent assessment of her mental state and associated risks. From the history it sounds as though she has developed a psychotic illness following a fairly lengthy prodrome or 'at risk mental state'. It will be important to consider where she is assessed and to consider a brief inpatient admission in order to ensure proper support and supervision while treatment is initiated.

antipsychotic medications. The risk of long term side effects such as tardive dyskinesia is also lower. They may also have greater efficacy in the treatment of negative symptoms and better long term outcome, and their subjective tolerability is better;¹⁸ and are therefore less likely to be discontinued prematurely.^{19,20}

Which is the right drug for my patient?

Atypical antipsychotics have demonstrated efficacy in reducing positive (eg. hallucinations and delusions) and negative (eg. social withdrawal) symptoms associated with psychotic illnesses such as schizophrenia²¹⁻²⁴ or bipolar disorder.²⁵ Overall, most atypical antipsychotics have similar efficacy^{26,27} and the choice of agent is more dependant on side effect profile and the patient's preference than on efficacy. In cases where sleep disturbance is a major problem, the prescription of a sedating drug such as quetiapine or olanzapine as a once daily dose at night may be beneficial compared to other less sedating atypical antipsychotic medications. Alternatively, the prescription of an antipsychotic medication with no or minimal weight gain may be preferable in an already overweight patient or for those very conscious of their body image. In young sexually active males, one might avoid medications with high rates of prolactin elevation (eg. amisulpride, risperidone) as a first line treatment to prevent premature discontinuation. To promote treatment adherence, it is important that the prescribing doctor involves the patient in the

decision making process – which atypical antipsychotic is best suited for the needs of the individual patient together with information about the most common side effects, which will be transient in most cases. The doctor needs to monitor emerging side effects closely and adapt the treatment accordingly to further promote adherence.

Start low and go slow (finding the optimal dose)

In general, the dose of antipsychotic medication in drug naïve first episode psychosis patients is usually about half the recommended dose for chronic schizophrenia²⁸ (*Table 1*). However, finding the individual minimal effective dose – this should be the lowest dose of medication providing symptom control – is not an easy task (in particular with the newer antipsychotic agents) and there is a risk of unnecessary dose escalation. To ensure appropriate dose titration, frequent assessment of clinical response and side effects (at least weekly) after treatment initiation is necessary. This will also help to establish a therapeutic alliance.

Antipsychotic medication usually takes 1–2 weeks to show a symptomatic response. If first episode psychosis patients do not show a marked improvement within the initial 2 weeks of treatment, the atypical antipsychotic medication dose should be increased at fortnightly intervals until clear signs of response occur, but only within the limits of side effect emergence (eg. sedation and extrapyramidal

symptoms). We recommend the following steps for dose increases:

- 1 mg for risperidone
- 100 mg for amisulpride
- 5 mg for olanzapine
- 100–200 mg for quetiapine, and
- 5–10 mg for aripiprazole.

For many patients this phase of illness is difficult due to ongoing symptoms. Short term use of benzodiazepines (eg. diazepam 2 mg 3 times per day and diazepam as required) to control tension, agitation or sleep disturbance can help and is recommended.

If the first line treatment does not show satisfactory symptomatic response within 6–8 weeks at an appropriate dose, we recommend switching to another atypical antipsychotic. Again, the choice of second line treatment should be discussed with the patient and the individual preferences of the patient should be taken into account. Cross tapering old and new treatment is the preferred method for switching and involves tapering off the previous antipsychotic agent and any adjunctive treatment (sedatives, anticholinergic medication), while gradually titrating the new atypical antipsychotic agent to the established therapeutic dose. The second line treatment will usually require higher doses than the recommended dose for drug naïve first episode psychosis patients (*Table 1*).

Never change a winning horse

The antipsychotic drug resulting in a symptomatic and functional recovery should be continued for at least a year (or longer) in order to minimise the risk of relapse and should not be changed gratuitously. However, despite encouraging high initial response rates to antipsychotic medication in first episode psychosis,^{29–31} up to 80% of patients will relapse due to high rates of discontinuation,¹³ even after 1 year of persistent remission of symptoms.³² The lifestyle change being expected of the young person with an emerging psychotic disorder represents a major challenge. Similar adjustment difficulties are seen in other potentially chronic illnesses such as juvenile onset diabetes, arthritis and asthma. The key predictors of medication adherence are the relationship with the prescribing clinician, previous experiences with hospital admissions, and insight into having a mental illness and the

need for treatment.¹⁷ In most service areas across Australia, GPs will manage fully recovered first episode psychosis patients. They can make a big difference by engaging these patients in a long term therapeutic alliance, preventing traumatic admissions, and providing them with flexible approaches to manage their pharmacological treatment in a low stigma environment. To keep patients engaged, it may be necessary to negotiate a compromise, and intermittent antipsychotic medication may be preferable to ceasing the medication altogether.^{33,34}

Treating comorbidity

Comorbidity is very common in emerging psychotic disorders and needs to be managed carefully. Depression and anxiety occur in up to 50% of patients with a first episode psychosis^{35,36} and requires an integrated treatment approach. In most cases, depressive symptoms will resolve once the psychosis has been treated effectively.³⁷ If depressive symptoms persist or are the dominant feature of the first psychotic episode, the use of selective serotonin reuptake inhibitors (SSRIs) to treat comorbid depression and anxiety is recommended, however the evidence is weak.³⁵ More recent concerns regarding the use of SSRIs (except fluoxetine) potentially increasing suicide risk in children and adolescents³⁸ has led to caution in prescribing for this age group. The combination of antipsychotic medication with mood stabilisers (eg. lithium and sodium valproate) to treat mood swings may be indicated, in particular in cases where the mood

component is dominant or with a family history of treatment response to lithium. It may be that the mood stabiliser will be the primary long term treatment in some cases³⁶ (see *Case history Natalie*). However, in such complex cases of emerging psychotic disorders, it is advisable to establish a treatment plan in liaison with a specialist service.

The link between drug use and psychosis is now well established³⁹ and substance use disorder should be addressed either by the treating clinician or by specialist services. Use of illicit drugs can make teasing out complex symptomatology and assessing treatment response difficult for clinicians.

Personality factors can also complicate the overall picture, interacting with primary mental illness pathology and affecting clinical management. However, focusing on psychosis as a medical condition may facilitate treatment of these often difficult to engage patients. The GP is well placed to slowly engage such complex patients and initiate treatment and facilitate referral to a specialist mental health service once trust has been established.

Identifying and managing risk

Risk assessment and management in early psychosis represents a critical component of the care plan. In particular, risk of suicide and violence are vital to quantify and manage. Around 10–15% of psychotic patients will eventually commit suicide⁴⁰ and the risk is greatest in the first few years of illness.^{41,42}

Although no individual intervention has

Table 1. Dose recommendations in acutely ill first episode psychosis patients^{48,49}

Suggested lowest effective dose to treat	Neuroleptic naïve FEP patients	Previously neuroleptic treated patients
Risperidone	2 mg/day	2–6 mg/day
Olanzapine	7.5 mg/day	15–30 mg/day
Quetiapine	200–300* mg/day	300–800 mg/day
Amisulpride	200–300*† mg/day	>400† mg/day
Aripiprazole	5–10* mg/day	10–30 mg/day

Maintenance doses may vary on an individual basis
 * Optimal dose has yet to be established for drug naïve first episode psychosis
 † Lower doses to treat negative symptoms only (eg. 100 mg)

Case history Natalie – a manic episode

Natalie, 22 years of age, lives with her partner and works in a busy office. She has been referred to the family doctor by her mother who reports that while Natalie's partner was away for the past few days she has not slept at all and believes that she has to 'save' the business she works for from financial ruin by putting in as many hours as possible and running constant internet searches on their competitors. It is her belief that she is the only person in the company who truly 'understands' the complexities of the stock exchange. In addition to her sleep disturbance and grandiose beliefs she is having difficulty focusing her racing thoughts and has been spending too much money. On further enquiry it becomes apparent that she has been hearing a voice (her 'spirit guide') that has been encouraging her to keep going and take greater risks. She says she has never been better and that any kind of interference in her plans will not be tolerated as 'time is limited'. The only way her mother could get her to attend the surgery was to tell her that she needed antibiotics for her sore throat – a product of her dramatically increased smoking habit.

Discussion – Natalie is experiencing a manic episode with psychotic features. She has no insight and is unlikely to accept treatment. The danger of not treating her condition quickly is that she will either exhaust herself or place herself in increasingly risky situations. She is likely to need inpatient admission with appropriate use of the mental health act.

been shown to prevent suicide there are some strategies that may be of benefit.^{43,44} Psychosocial and psychological interventions including cognitive behavioural therapy (CBT) may reduce suicide risk. Such interventions aim to reduce stress, provide intensive support and decrease critical expressed emotion. Pharmacological management may involve the early use of clozapine in treatment resistant or highly suicidal patients with schizophrenia, lithium maintenance therapy in patients with affective psychosis, or consideration of electroconvulsive therapy (ECT) or the use of antidepressant medication to treat comorbid depression.⁴⁴

Predictors of serious violence tend to be similar to those for violence in the general population and include male gender, unemployment and substance abuse. Individuals diagnosed with psychotic illness can be at higher risk of harming others.^{45–47} Evidence regarding the relationship between specific symptoms and violence is not straightforward. Although it is important to recognise and address possible risk factors for violence in those with emerging psychosis, it is also important not to reinforce the stereotype of the 'violent schizophrenic' and perpetuate stigmatisation within mental illness.

Making your patient an expert (psychoeducation)

Mental illness awareness in patients and

mental health literacy among patients and relatives of those with a first episode psychosis is poor.¹⁷ Providing knowledge about mental illness and treatment for patients and their families constitutes an important part of the management plan. Psychoeducation should be initiated at an early stage, focusing on illness explanation, treatment options and prognosis. This involves the patient, their family, carers and others such as teachers or friends. It is important to convey a message of hope and to promote therapeutic optimism for the patient and their family.

Conclusion

The role of the GP in the management of emerging major mental illnesses is important and generally adopts a shared care model with specialist mental health services. From initial recognition of the psychotic illness through to continuing care and relapse prevention, the GP should be involved in supporting the patient and their family. Regular communication between the mental health service and the GP is desirable in order to avoid confusion and minimise the chance of treatment failure. However, in many areas across Australia, GPs will be faced with the reality that they have to manage patients with emerging psychotic disorders with very limited support. In these instances it may be possible to obtain consultation from a specialist

mental health service.

The management of first episode psychosis involves a journey through care for both the patient and their family. General practitioners play a pivotal role in initial recognition of illness, engagement of the patient, referral for specialist assessment, psychoeducation, regular monitoring of physical and mental health, and evidence based medication management.

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References

- Harrigan SM, McGorry PD, Krstev H. Does treatment delay in first episode psychosis really matter? *Psychol Med* 2003;33:97–110.
- Amminger GP, Edwards J, Brewer WJ, Harrigan S, McGorry PD. Duration of untreated psychosis and cognitive deterioration in first episode schizophrenia. *Schizophr Res* 2002;54:223–30.
- Carbone S, Harrigan S, McGorry PD, Curry C, Elkins K. Duration of untreated psychosis and 12 month outcome in first episode psychosis: the impact of treatment approach. *Acta Psychiatr Scand* 1999;100:96–104.
- McGorry PD. 'A stitch in time'... the scope for preventive strategies in early psychosis. *Eur Arch Psychiatry Clin Neurosci* 1998;248:22–31.
- Wyatt RJ, Damiani LM, Henter ID. First episode schizophrenia. Early intervention and medication discontinuation in the context of course and treatment. *Br J Psychiatry* 1998;172(Suppl):77–83.
- McGorry PD, Killackey EJ. Early intervention in psychosis: a new evidence based paradigm. *Epidemiol Psychiatr Soc* 2002;11:237–47.
- Lieberman JA, Toljefson GD, Charles C, et al. Antipsychotic drug effects on brain morphology in first episode psychosis. *Arch Gen Psychiatry* 2005;62:361–70.
- Buchanan RW, Davis M, Goff D, et al. A summary of the FDA-NIMH-MATRICES workshop on clinical trial design for neurocognitive drugs for schizophrenia. *Schizophr Bull* 2005;31:5–19.
- Cramer J, Rosenheck R. Compliance with medication regimens for mental and physical disorders. *Psychiatric Services* 1998;49:196–201.
- Leucht S, Barnes TR, Kissling W, Engel RR, Correll C, Kane JM. Relapse prevention in schizophrenia with new generation antipsychotics: a systematic review and exploratory meta-analysis of randomised, controlled trials. *Am J Psychiatry* 2003;160:1209–22.
- Lieberman J, Stroup S, Schneider L. Prevention of relapse in schizophrenia. *N Engl J Med* 2002;346:1412–3; author reply 1412–3.
- Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005;353:1209–23.
- 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.
- Lieberman JA, Phillips M, Gu H, et al. Atypical and conventional antipsychotic drugs in treatment naive first episode schizophrenia: a 52 week randomised trial of

- clozapine vs chlorpromazine. *Neuropsychopharmacology* 2003;28:995–1003.
15. Mutsatsa SH, Joyce EM, Hutton SB, et al. Clinical correlates of early medication adherence: West London first episode schizophrenia study. *Acta Psychiatr Scand* 2003;108:439–46.
 16. Castle D, Morgan V, Jablensky A. Antipsychotic use in Australia: the patients' perspective. *Aust N Z J Psychiatry* 2002;36:633–41.
 17. Day JC, Bentall RP, Roberts C, et al. Attitudes toward antipsychotic medication: the impact of clinical variables and relationships with health professionals. *Arch Gen Psychiatry* 2005;62:717–24.
 18. Voruganti L, Cortese L, Oyewumi L, Cernovsky Z, Zirul S, Awad A. Comparative evaluation of conventional and novel antipsychotic drugs with reference to their subjective tolerability, side effect profile and impact on quality of life. *Schizophr Res* 2000;43:135–45.
 19. Hellewell JS, Haddad PM. Differing tolerability profiles among atypical antipsychotics. *Am J Psychiatry* 2001;158:501–2.
 20. Kasper S. First episode schizophrenia: the importance of early intervention and subjective tolerability. *J Clin Psychiatry* 1999;60(Suppl)23:5–9.
 21. Thornley B, Rathbone J, Adams CE, Awad G. Chlorpromazine versus placebo for schizophrenia. *Cochrane Database Syst Rev* 2003(2):CD000284.
 22. Sultana A, McMonagle T. Pimozide for schizophrenia or related psychoses. *Cochrane Database Syst Rev* 2000(2):CD001949.
 23. Joy CB, Adams CE, Lawrie SM. Haloperidol versus placebo for schizophrenia. *Cochrane Database Syst Rev* 2001(2):CD003082.
 24. Hunter RH, Joy CB, Kennedy E, Gilbody SM, Song F. Risperidone versus typical antipsychotic medication for schizophrenia. *Cochrane Database Syst Rev* 2003(2):CD000440.
 25. Vieta E, Goikolea JM. Atypical antipsychotics: newer options for mania and maintenance therapy. *Bipolar Disord* 2005;7(Suppl 4):21–33.
 26. Davis JM, Chen N, Glick ID. A meta-analysis of the efficacy of second generation antipsychotics. *Arch Gen Psychiatry* 2003;60:553–64.
 27. Chakos M, Lieberman J, Hoffman E, Bradford D, Sheitman B. Effectiveness of second generation antipsychotics in patients with treatment resistant schizophrenia: a review and meta-analysis of randomised trials. *Am J Psychiatry* 2001;158:518–26.
 28. McEvoy JP, Hogarty GE, Steingard S. Optimal dose of neuroleptic in acute schizophrenia. A controlled study of the neuroleptic threshold and higher haloperidol dose. *Arch Gen Psychiatry* 1991;48:739–45.
 29. Viguera AC, Baldessarini RJ, Hegarty JD, van Kammen DP, Tohen M. Clinical risk following abrupt and gradual withdrawal of maintenance neuroleptic treatment. *Arch Gen Psychiatry* 1997;54:49–55.
 30. Lieberman JA. Prediction of outcome in first episode schizophrenia. *J Clin Psychiatry* 1993;54(Suppl):13–7.
 31. Carpenter WT, Jr. Maintenance therapy of persons with schizophrenia. *J Clin Psychiatry* 1996;57(Suppl 9):10–8.
 32. Davis JM, Chen N. Choice of maintenance medication for schizophrenia. *J Clin Psychiatry* 2003;64(Suppl 16):24–33.
 33. Boshes RA, Manschreck TC. Review of antipsychotic medication administration: a proposal of intermittent dosing. *Schizophr Bull* 2002;28:203–22.
 34. Gaebel W, Janner M, Frommann N, et al. First vs multiple episode schizophrenia: two-year outcome of intermittent and maintenance medication strategies. *Schizophr Res* 2002;53:145–59.
 35. Whitehead C, Moss S, Cardno A, Lewis G. Antidepressants for people with both schizophrenia and depression. *Cochrane Database Syst Rev* 2002(2):CD002305.
 36. Whitehead C, Moss S, Cardno A, Lewis G. Antidepressants for the treatment of depression in people with schizophrenia: a systematic review. *Psychol Med* 2003;33:589–99.
 36. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. *Aust N Z J Psychiatry* 2005;39:1–30.
 37. Koreen AR, Siris SG, Chakos M, Alvir J, Mayerhoff D, Lieberman J. Depression in first episode schizophrenia. *Am J Psychiatry* 1993;150:1643–8.
 38. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004;363:1341–5.
 39. Arseneault L, Cannon M, Witton J, Murray RM. Causal association between cannabis and psychosis: examination of the evidence. *Br J Psychiatry* 2004;184:110–7.
 40. Westermeyer JF, Harrow M, Marengo JT. Risk for suicide in schizophrenia and other psychotic and non-psychotic disorders. *J Nerv Ment Dis* 1991;179:259–66.
 41. Verdoux H, Liraud F, Gonzales B, Assens F, Abalan F, van Os J. Suicidality and substance misuse in first admitted subjects with psychotic disorder. *Acta Psychiatr Scand* 1999;100:389–95.
 42. Krausz M, Muller-Thomsen T, Haasen C. Suicide among schizophrenic adolescents in the long term course of illness. *Psychopathology* 1995;28:95–103.
 43. 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.
 44. Mann JJ, Apter A, Bertolote J, et al. Suicide prevention strategies: a systematic review. *Jama* 2005;294:2064–74.
 45. Swanson JW, Swartz MS, Elbogen EB. Effectiveness of atypical antipsychotic medications in reducing violent behaviour among persons with schizophrenia in community based treatment. *Schizophr Bull* 2004;30:3–20.
 46. Swanson JW, Holzer CE, 3rd, Ganju VK, Jono RT. Violence and psychiatric disorder in the community: evidence from the Epidemiologic Catchment Area surveys. *Hosp Community Psychiatry* 1990;41:761–70.
 47. Brennan PA, Mednick SA, Hodgins S. Major mental disorders and criminal violence in a Danish birth cohort. *Arch Gen Psychiatry* 2000;57:494–500.
 48. McGorry PD. RANZCP Clinical Practice Guidelines Team for the Treatment of Schizophrenia. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. *Aust N Z J Psychiatry* 2005;39:1–30.
 49. Remington G. Rational pharmacotherapy in early psychosis. *Br J Psychiatry* 2005;(Suppl)48:s77–84.