Current care pathway for the management of psychosis

Martin Livingston MD, FRCPsych

The management of psychotic disorders is a community-based collaboration between primary and secondary care. Our Drug review outlines the general care pathway and potential treatment problems, followed by an analysis of the prescription data.

In psychotic illnesses such as schizophrenia, schiz-affective disorder and delusional disorder, perceptions, thought, mood and behaviour are altered. In addition, there may be subtle cognitive impairments. The diagnosis is based on operational criteria, typically using ICD-10 guidelines in the NHS1 (see Table 1). The American Psychiatric Association has published an updated guide, DSM-5,2 which has eliminated schizophrenia sub-types from its lexicon, such as paranoid and catatonic, due to the low reliability in their diagnosis. ICD-11 is due by 2017. It is outside the scope of this paper to discuss psychoses primarily involving mood, that is severe depression and mania.

Other psychotic illnesses include the paranoid psychoses found in dementia, psychoses induced by drug ingestion – whether illicit, over-the-counter or prescribed – and the acute psychosis of a delirium. It is important to recognise how frequently presentations of psychosis relate to substance misuse and it is often very difficult to assess whether the psychosis is entirely due to the ingestion of drugs or whether drug use has precipitated an illness such as schizophrenia. Substance misuse may of course continue, despite the onset of psychosis, resulting in additional treatment problems such as poor response to medication and difficulty adhering to treatments whether drug or psychosocial.

Globally schizophrenia has a point prevalence of approximately 0.45 per cent, a lifetime expectancy rate of 0.7 per cent and is one of the top 15 causes of disability.3 It is likely to be a disorder determined by multiple genes of small effect. The search for a full understanding of the causation of schizophrenia and other psychoses continues. Meantime, increasing knowledge of the course of these illnesses and their outcomes has led to more integrated multidisciplinary approaches to management. Antipsychotic drug treatment is a mainstay of treatment in established cases. Treatment options have been enhanced by the release of a new generation of long-acting injectable preparations (see Table 2). Mental health services, utilising integrated care pathways, work with patients and their carers in a recovery model but unfortunately, if florid schizophrenia has developed, 80 per cent of sufferers will have to contend with long-term impairments and less than 15 per cent will be in work.4
Early intervention

A long duration of untreated psychosis (DUP) is recognised as a poor prognostic factor and services now try to encourage early referral, especially in young people in a first episode before florid illness develops. This has led to the development of early intervention teams consisting of psychiatrists, psychologists, nurses, healthcare assistants and occupational therapists, all of whom link with GP services. There is often a formalised link with primary care not just to share mental health care but also to ensure that patients have good access to treatment for physical health problems. Severe enduring mental illness results in a reduced life span of up to 20 years. Despite a Quality and Outcomes Framework (QOF) requirement for regular monitoring of body mass index (BMI), BP, cholesterol and blood glucose, patients who suffer from a psychotic disorder often fail to attend their GPs. Services aim to manage patients in the community but there is still, at times, a need for inpatient facilities that are non-stigmatising and attuned to the needs of the population to be treated, eg young persons in a first episode.

Prodromal illness

The characteristics of a prodromal phase of psychosis include impaired self-care, difficulties with concentration, memory and communicating as well as an altered mood state, typically depressive. These symptoms are relatively non-specific and diagnosis of a specific psychosis such as schizophrenia is usually not feasible at this stage. Patients should be investigated for substance misuse. Relatives or other close associates are often very helpful in making a diagnosis as they may have recognised a distinct change in the patient’s behaviour and may of course have prompted the referral to secondary care services.

Some early intervention programmes have advocated rapid initiation of antipsychotic medication to prevent the onset of a clearly diagnosable psychosis. But NICE, on reviewing the available studies, concluded that antipsychotic medication was no more effective than psychological interventions or placebo in preventing this transition. Deciding when to intervene in an early stage, and with what, is a decision that requires careful consideration by multidisciplinary teams, patients and their carers. Early intervention teams offer intensive psychological and social approaches to management in addition to drug therapy, where required, typically for periods of around two years before handing over care in those with ongoing mental health problems to the community mental health team.

### General criteria A

At least one of the following must be present most of the time, or at some time during most of the days, during an episode of psychotic illness lasting at least one month:

- thought echo, insertion or withdrawal, or thought broadcasting
- delusions of control, influence or passivity, delusional perception
- hallucinatory voices giving a running commentary on the patient’s behaviour, or discussing the patient between themselves, or other hallucinatory voices coming from some part of the body
- persistent delusions that are culturally inappropriate or involve completely impossible situations

### General criteria B

Or

At least two of the following present most of the time, or at some time during most of the days, during an episode of psychotic illness lasting at least one month:

- persistent hallucinations in any modality occurring daily for at least a month when accompanied by delusions without a clear affective content or when accompanied by persistent over-valued ideas
- neologisms (new word formation) or breaks in the train of thought, resulting in incoherent or irrelevant speech
- catatonic behaviour – excitement, posturing, waxy flexibility, negativism, mutism, stupor
- negative symptoms – marked apathy, paucity of speech, blunting or incongruent emotional response

### Table 1. ICD-10 diagnostic criteria for schizophrenia

<table>
<thead>
<tr>
<th>General criteria A</th>
<th>General criteria B</th>
</tr>
</thead>
<tbody>
<tr>
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### Table 2. Second-generation long-acting antipsychotic injections

<table>
<thead>
<tr>
<th>Long-acting injection</th>
<th>Starting dose</th>
<th>Oral antipsychotic required initially?</th>
<th>Maximum dose</th>
<th>Dose frequency</th>
<th>Injection site</th>
</tr>
</thead>
<tbody>
<tr>
<td>aripiprazole (Abilify Maintena)</td>
<td>400mg</td>
<td>may require initial oral antipsychotic supplements</td>
<td>400mg</td>
<td>monthly</td>
<td>gluteal</td>
</tr>
<tr>
<td>olanzapine (Zypadhera)</td>
<td>210/300mg</td>
<td>no oral antipsychotic supplement required</td>
<td>405mg</td>
<td>2–4 weekly</td>
<td>gluteal</td>
</tr>
<tr>
<td>paliperidone (Xeplion)</td>
<td>150mg day 1 100mg day 8</td>
<td>no oral antipsychotic supplement required</td>
<td>150mg</td>
<td>monthly</td>
<td>first injection deltoid, thereafter either deltoid or gluteal</td>
</tr>
<tr>
<td>risperidone (Risperdal Consta)</td>
<td>25–50mg</td>
<td>may require initial oral antipsychotic supplements</td>
<td>50mg</td>
<td>2 weekly</td>
<td>deltoid or gluteal</td>
</tr>
</tbody>
</table>
**Community mental health teams**

Since the 1970s the balance between hospital and community care has shifted dramatically in the direction of the latter. Community mental health teams (CMHTs) usually offer a similar range of disciplinary input as the early intervention teams. They are succeeding in transforming the lives of people with psychosis, enabling fuller functioning in the community. Once a diagnosis has been established, and treatment in the early intervention team concluded, the CMHT aims to manage the transition from that service and to provide a multidisciplinary-based comprehensive care package. The services of such teams may be further specialised into groupings such as crisis intervention (providing short-term intensive therapeutic input) and assertive outreach (for people who have more complex needs, have severe illnesses, and do not engage well with services).

**Psychosocial treatment programmes and the recovery model**

Many people who suffer from schizophrenia and related psychoses live in urban environments in the UK where there is poor housing and multiple social problems including drug and alcohol addiction. They may be exposed to stigma about their illness and high levels of expressed negative emotion. Psycho-educational programmes try to tackle these issues with patients and their carers and attempt to bolster self-esteem. Additional funding has been made available in England and Wales to provide psychological therapies for patients with severe mental illness.

Increasing awareness of cognitive developmental processes has resulted in the formation of cognitive models of schizophrenia. This knowledge has led to psychologists, or psychologically trained staff from other disciplines such as nursing, attempting to address the vulnerabilities that lead to psychosis. Psychologically-trained staff also help patients and their carers manage the distress associated with the illness, assist them in developing a plan for social and educational recovery and build in relapse prevention strategies.

Patients and their carers may be aware of altered behaviours and feelings that signal the onset of more florid symptoms. Social strategies involve facilitating families and carers to develop supportive approaches to their ill relative. The CMHT will typically advocate more stable lifestyles and give guidance on health issues including diet and avoidance of street drugs. The emphasis is on encouraging the service user to develop and then achieve his or her own recovery goals – the so-called recovery model. Ideally, carers, some of whom quite naturally tend to focus on the burdens, may come to appreciate that caring can be mutually rewarding for carer and the cared person. This is important because as many as 50 per cent of people with schizophrenia have contact with a close relative, of whom two thirds are female. Although there is limited evidence that treatments outlined in the recovery model eradicate symptoms, the key aim is to assist the patient and his/her carers in living with an illness that may have a profound impact on their lives.

**Pharmacotherapy**

For the majority of patients with a frank psychotic illness, antipsychotic drug treatment is essential in the acute phase and is likely to be required indefinitely to prevent recurrence. The choice of an antipsychotic should be based on an individual patient’s needs, for example, whether a high level of sedation is required, weight gain is to be avoided, or adherence enhanced by use of a once-daily regimen, or a rapid-release formulation such as those for olanzapine (Zyprexa Velotab) and risperidone (Risperdal Quicklet) or a long-acting injectable antipsychotic. There are now

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### Table 3. Oral antipsychotic adverse effects

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Switch options</th>
<th>Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute extra-pyramidal symptoms: akathisia, parkinsonian signs/ symptoms, dystonias</td>
<td>amisulpride, aripiprazole, clozapine, quetiapine, lower-dose risperidone, sulpride</td>
<td>most FGAs</td>
</tr>
<tr>
<td>elevated plasma glucose</td>
<td>amisulpride, aripiprazole</td>
<td>clozapine, olanzapine</td>
</tr>
<tr>
<td>elevated prolactin</td>
<td>aripiprazole, clozapine, quetiapine</td>
<td>chlorpromazine, haloperidol, pimozide, trifluoperazine</td>
</tr>
<tr>
<td>lipid derangement</td>
<td>amisulpride, aripiprazole</td>
<td>clozapine, olanzapine</td>
</tr>
<tr>
<td>postural hypotension</td>
<td>amisulpride, aripiprazole, haloperidol, sulpride, trifluoperazine</td>
<td>chlorpromazine</td>
</tr>
<tr>
<td>QT prolongation</td>
<td>aripiprazole</td>
<td>haloperidol, pimozide</td>
</tr>
<tr>
<td>sedation</td>
<td>amisulpride, haloperidol, sulpride, trifluoperazine</td>
<td>chlorpromazine</td>
</tr>
<tr>
<td>sexual dysfunction</td>
<td>aripiprazole, quetiapine</td>
<td>chlorpromazine</td>
</tr>
<tr>
<td>tardive dyskinesia</td>
<td>clozapine, olanzapine, quetiapine</td>
<td>most FGAs</td>
</tr>
<tr>
<td>weight gain</td>
<td>amisulpride, aripiprazole, haloperidol, trifluoperazine</td>
<td>chlorpromazine, olanzapine</td>
</tr>
</tbody>
</table>
First episode of possible psychotic phenomena

Referral
- If young, typically under 35, referral to early intervention service by patient, carer, GP or other agency, eg social work
- If older, referral accepted by CMHT

Assessment
- Extended multidisciplinary assessment involves basic haematology and blood biochemistry and possible neuroimaging if organic cause suspected
- Involvement of patient and carer/relative where appropriate and agreed by patient
- Probable psychosis – accepted for treatment
- Psychosis unlikely – either discharge or referral to other mental health service
- GP informed and invited to participate in care programme
- Physical health assessment, baseline blood testing including lipids and glucose

Care and treatment planning
- psychosis integrated care plan – development of treatment goals by patient and carers, and formulation of an individually designed care and treatment package containing social, educational psychological and medication elements
- Treatment is usually in a community setting but if significant risk to self or others, admission may be required, sometimes compulsorily involving relevant mental health legislation
- Medication may be withheld initially if doubt remains about psychosis while care follow-up is arranged and possibly other non-medication elements of treatment offered

Delivery of care and treatment
- Intensive treatment programme – typically lasting two years if in younger person’s early intervention programme, usually followed by referral to community mental health team
- Continuous reappraisal of treatment goals set by team and patient/carer and treatment options
- Regular physical health checks including blood testing for glucose and lipids

Transition of care from early intervention to CMHT
- Young person accepted by CMHT
- Older person in first or subsequent episodes usually seen initially in community setting by CMHT

Reassessment and setting of relevant care and treatment goals
- Reassessment of patient by CMHT to confirm diagnosis and reappraise need for treatment, especially medication
- Ongoing care and treatment involving patient and carer with admission and input from crisis and intensive care teams as and when required
- Regular physical health checks including blood testing for glucose and lipids
- Medication response re-evaluated. If non-responsiveness to several oral antipsychotic medications is an adherence issue, consider long-acting injections. If adherent, consider initiating clozapine, which requires involvement of clozapine monitoring system

Figure 1. General care pathway for psychosis
Choosing an antipsychotic

Meta-analyses have tended not to support the contention that, as a group, the newer SGAs are superior in antipsychotic efficacy to the first generation antipsychotics (FGAs). There are, however, some differences in the efficacy profiles of the drugs. While clozapine stands out as the only antipsychotic drug indicated for treatment-refractory schizophrenia, amisulpride, in this meta-analysis, did appear to have some efficacy advantages over the rest of the antipsychotic medications studied. Fewest patients discontinued treatment with amisulpride, clozapine caused fewest extra-pyramidal side-effects (EPS), and olanzapine caused most weight gain. Antipsychotics are more effective against positive symptoms, less so in treating negative symptoms and cognitive impairments. These differences present useful treatment options guiding the choice of antipsychotic.

Although higher doses may be required in an acute, floridly psychotic phase, there is little evidence to support supra-BNF dosing. The Royal College of Psychiatrists has issued guidelines outlining the risk of such high-dose regimens and how to monitor them to minimise risk.

Lower doses of medication are often used, at least initially, in early intervention programmes where florid psychotic phenomena have begun to emerge. A useful maxim is ‘start low and go slow’, recognising that this is not always possible when the patient is very disturbed.

The side-effects of antipsychotics include EPS, weight gain, postural hypotension, prolongation of the QT interval, undesired sedation, sexual dysfunction, metabolic abnormalities such as elevated blood glucose and lipids, and increased prolactin secretion (see Table 3). The use of multiple antipsychotics should be avoided and side-effects are best treated by dose reduction or switching. If this is not feasible anticholinergic agents (eg orphenadrine and procyclidine) may counter drug-induced tremor and immobility as well as dystonias. Beta-blockers such as propranolol are useful in treating the restlessness and agitation of akathisia. Due to these side-effects monitoring of weight and BMI, blood pressure, plasma glucose and lipids, prolactin and liver function is recommended on initiation and at least annually. An ECG should be taken at initiation of drug treatment, following switching to a drug such as haloperidol or pimozide (Olap) at higher risk of prolonging the QT interval or if using a high dose regimen.

The only antipsychotic for which superiority in treatment-resistant cases of schizophrenia has been clearly demonstrated is clozapine. This is the case despite its low occupancy of D2 receptor sites. Due to the 3–4 per cent risk of neutropenia, which is potentially fatal, clozapine is reserved for treatment-resistant schizophrenia, non-responsive psychosis in Parkinson’s disorder and other neurological diseases. Treatment resistance is defined as an inadequate response to two or more antipsychotics. The haematological profile of the patient has to be monitored in a prescribed programme. This involves a blood screen weekly for the first 18 weeks, then fortnightly for the rest of the year, monthly thereafter. In addition to being more effective than other antipsychotics, clozapine reduces the risk of suicide. It is important to bear in mind that the rate of suicide in schizophrenia is around 5 per cent. A wide range of neurotransmitters are involved in clozapine’s spectrum of activity – D1, D2, 5HT2, 5HT3 and 5HT4. Although some of these may be implicated in the causation of schizophrenia and other psychoses, knowledge of clozapine’s spectrum of activity has, to date, not led to the development of alternative, safer antipsychotics with clozapine-like efficacy in treatment-resistant schizophrenia.

Conclusions

Treating psychotic disorders is now mainly community based involving a collaboration between primary- and secondary-care services. The general care pathway is outlined in Figure 1 and involves multidisciplinary programmes integrating a wide range of drug treatment options with psychosocial therapies. Patients and their carers are encouraged to establish their own goals for treatment.

References

6. NICE. Psychosis and schizophrenia in adults: treatment and management. CG178. February 2014

Declaration of interests

Dr Livingston has in the past engaged in consultancy and research work with Janssen-Cilag and Lilly in the antipsychotic field. He has not done such work for at least five years.

Dr Martin Livingston is a consultant psychiatrist, Ayrshire and Arran Primary Care Trust and honorary senior clinical lecturer, University of Glasgow
Prescription review

In 2012/13, GPs in England wrote 8.4 million prescriptions for oral antipsychotics at a total cost of £139 million. This compares with 167 000 prescriptions for depot injections costing about £9 million. SGAs dominated prescribing, accounting for 79 per cent of volume and 91 per cent of costs. GPs wrote few prescriptions for clozapine (5000). Of the FGAs, haloperidol and chlorpromazine each account for about 5 per cent of prescriptions.

Most prescribing of SGAs was for quetiapine (33 per cent of volume), olanzapine (29 per cent) and risperidone (22 per cent). Aripiprazole was the most costly in this category, accounting for 45 per cent of spending but only 9 per cent of volume. All formulations of this drug (plain and orodispersible tablets, oral solution) were relatively expensive. The difference in cost between olanzapine and quetiapine was due to the higher rate of generic prescribing for olanzapine (97 per cent), whereas 27 per cent of quetiapine prescribing was for Seroquel XL.

Table 4. Number and cost of prescriptions for the treatment of psychosis, England, 2012/13

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. scrip (000s)</th>
<th>NIC (£000)</th>
<th>NIC per script</th>
</tr>
</thead>
<tbody>
<tr>
<td>amisulpride</td>
<td>388</td>
<td>3 807</td>
<td>9.82</td>
</tr>
<tr>
<td>aripiprazole</td>
<td>622</td>
<td>56 547</td>
<td>90.86</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>389</td>
<td>1 205</td>
<td>3.10</td>
</tr>
<tr>
<td>haloperidol</td>
<td>384</td>
<td>1 377</td>
<td>3.59</td>
</tr>
<tr>
<td>olanzapine</td>
<td>2 090</td>
<td>8 936</td>
<td>4.28</td>
</tr>
<tr>
<td>quetiapine</td>
<td>2 339</td>
<td>47 244</td>
<td>20.20</td>
</tr>
<tr>
<td>risperidone</td>
<td>1 546</td>
<td>6 720</td>
<td>4.35</td>
</tr>
<tr>
<td>sulpiride</td>
<td>166</td>
<td>2 589</td>
<td>15.62</td>
</tr>
</tbody>
</table>

For each section, one of the statements is false – which is it?

1. When considering psychotic illness:
   a. subtle cognitive impairment may be present
   b. in the NHS, diagnosis typically follows the ICD-10 guidelines
   c. the point prevalence of schizophrenia is about 0.45 per cent
   d. one in ten people who develop florid schizophrenia will have to contend with long-term impairments

2. In the management of early psychosis:
   a. early intervention teams aim to manage patients in the community
   b. long duration of untreated psychosis is a poor prognostic factor
   c. there is no role for inpatient services
   d. early intervention teams ensure access to mental and physical health services

3. The CHMT uses non-pharmacological approaches to care built on the following principles:
   a. cognitive strategies have no role for people with schizophrenia
   b. social strategies are useful because many people with psychosis live in poor housing and have multiple social problems
   c. the recovery model encourages service users to develop and achieve their own recovery goals
   d. the aim of using the recovery model is to help people with psychosis live with their disorder, not cure their symptoms

4. When considering drug treatment for schizophrenia, it should be remembered that:
   a. patients should be monitored for at least four hours after an injection of olanzapine embonate
   b. all antipsychotics block D_2 post-synaptic receptors in the mesolimbic area
   c. there is little risk of drug interactions
   d. current evidence suggests that SGAs are not more effective than FGAs

5. With regard to antipsychotic treatment in schizophrenia:
   a. clozapine is the only antipsychotic indicated for treatment-refractory schizophrenia
   b. antipsychotics are more effective against negative than positive symptoms
   c. there is little evidence to support the use of doses greater than those recommended in the BNF
   d. treatment should be initiated at a low dose and increased slowly

6. When managing the adverse effects of antipsychotics:
   a. there is no value in switching to another antipsychotic
   b. an ECG should be carried out when starting treatment
   c. propranolol is useful to treat restlessness and agitation associated with akathisia
   d. metabolic parameters should be monitored on initiation and at least annually

CPD: Management of psychosis

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