Early Psychosis

Diagnosis & Management from a GP Perspective

QUALITY IN PRACTICE COMMITTEE

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Evidence-Based Medicine [1]

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

In this document you will see levels of evidence (indicated by roman numerals, e.g. Ia), and grades of recommendation (indicated by alphabetical letter e.g. A).

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials
Ib Evidence obtained from at least one randomised controlled trial
IIa Evidence obtained from at least one well-designed controlled study without randomisation
IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.
III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV Evidence obtained from expert committee reports or opinions and-or clinical experiences of respected authorities

Grades of Recommendations

A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (Evidence levels Ia, Ib).
B Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (Evidence levels IIa, IIb, III).
C Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (Evidence level IV).1

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Whilst every effort has been made by the Quality in Practice Committee to ensure the accuracy of the information and material contained in this document, errors or omissions may occur in the content.

The guidance represents the view of the ICGP which was arrived at after careful consideration of the evidence available. Whilst we accept that some aspects of the recommendations may be difficult to implement initially due to a lack of facilities or insufficient personnel, we strongly believe that these guidelines represent best practice. Where there are difficulties these should be highlighted locally and elsewhere so that measures are taken to ensure implementation

The guide does not however override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of individual patients in consultation with the patient and/or guardian or carer.

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How to use this document

This document is for General Practitioners to enhance the diagnosis, treatment and management of patients with early psychosis in the Primary Care setting[1]. It does not provide guidance or recommendations on the use of the Mental Health Act, for information on the Act please see:

http://www.icgp.ie/go/courses/mental_health/mental_health_act_2001_faq

Introduction

Delays in detection and treatment of psychosis lead to poorer outcomes [2, 3]. Early treatment is more likely to lead to recovery [4-7].

Incidence

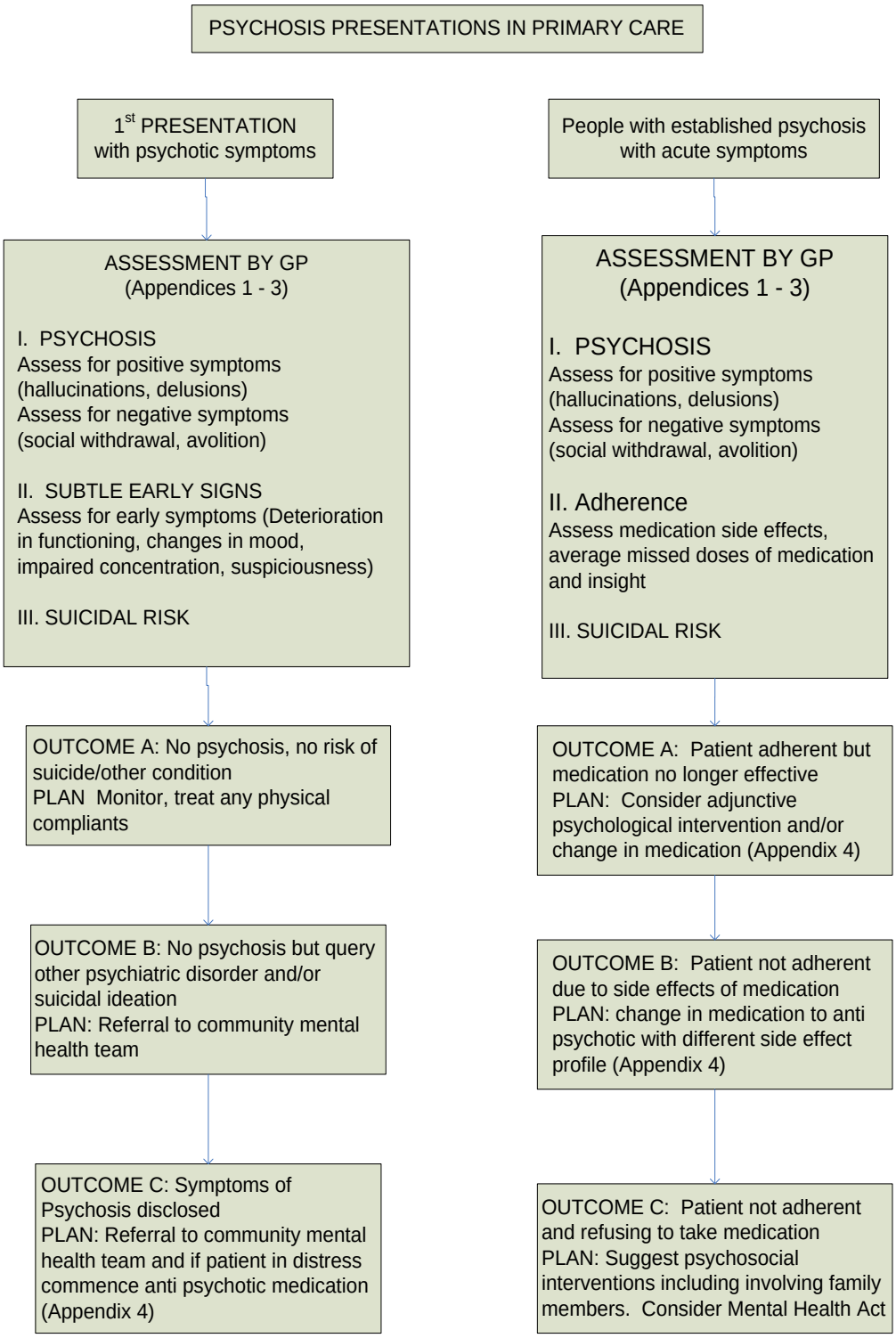
Psychosis is a low incidence high prevalence condition. The incidence is about 30/100,000/annum and the lifetime prevalence of broadly defined psychosis is roughly 2.2% of the population[8]. Onset is typically in late adolescence to mid twenties with females having a later average age at onset by about 5 years[9].

Schizophrenia is the commonest form of psychosis followed by affective disorders with psychotic symptoms, delusional disorder, substance induced psychosis and, less commonly, psychosis attributable to a general medical condition [10].

Although, primary prevention of psychosis is not yet possible, prevention of the secondary disabilities is achievable. General practitioners play a vital role in preventing secondary disabilities through early detection and treatment.

The figure provides a flow chart of assessment and management issues for people presenting either for the first time or for more established cases with acute symptoms.

Management of Psychosis Presentations in Primary Care



Clinical Presentation

Most people who develop psychosis, especially schizophrenia, go through 2 stages:

(i) Early Warning Signs [11-15]

Before developing overt psychosis, most people will display subtle early warning signs (termed the prodrome). These include:

- Deterioration in school/work performance
- Depression
- Social withdrawal
- Diminished self care
- Paranoid ideas
- Fleeting auditory hallucinations (e.g. hearing one's name being called)
- Change in relationships with friends/family (becoming distant, mistrustful)
- Unusual thinking style (becoming more abstract/obtuse in thinking)
- Loss of concentration
- Loss of motivation
- Apathy (without feeling depressed)

Appendix 1 includes questions that can be used to enquire about some of these early signs.

(ii) Overt Psychosis

Psychotic symptoms are divided into positive and negative symptoms.[16]

Positive Symptoms

- Delusions: fixed false beliefs, commonly persecutory or religious.
- Hallucinations: any modality, most commonly auditory.
- Disorganized behaviour: bizarre, agitated/aggressive, ritualistic behavior.
- Thought disorder: reflected in disordered speech.

Negative Symptoms

Symptoms must be an obvious decline from previous level of functioning:

- Avolition/Apathy: inability to persist with goal related activities; school/work.
- Alogia: diminished speech reflecting diminished thinking.
- Anhedonia: loss of enjoyment in activities of interest.
- Asociality: withdrawal from social/sport.
- Flattened affect: impoverished emotional expression.

Appendix 2 includes questions that can be used to elicit psychotic symptoms and appendix 2 can be used to evaluate suicide risk and risk of violence.

Diagnosis[17]

Schizophrenia/Schizophrenia Like Presentations

- Combination of delusions, hallucinations, thought disorder, disorganized behaviour and negative symptoms.
- The above present for a month or less if successfully treated.
- No mood symptoms or the mood symptoms are brief in relation to the total illness.
- Social, occupational or functional decline.
- The illness cannot be explained by a medical condition or substance induced.

Affective Psychosis

- A clear history of mood symptoms (mania or depression) preceding the psychotic symptoms and persisting beyond the psychotic symptoms.
- The psychotic symptoms are mood congruent i.e. grandiose if elated or nihilistic if depressed.

Other Psychotic Presentations

Substance Induced Psychotic Disorder:

- These psychotic disorders have a close temporal relationship with substance use: hallucinations (may be visual) and less negative symptoms. The psychosis must arise during intoxication or withdrawal states in drug induced psychosis.

Delusional Disorder:

- Non-bizarre delusions and no other psychotic symptoms are present.
  The persons behaviour otherwise is not bizarre and their overall functioning otherwise is not impaired.

Psychotic Disorder induced by General Medical Condition:

- Prominent hallucinations or delusions with evidence that the disorder is the direct physiological consequence of the medical condition.

Investigations

(i) Mental State Examination including risk assessment.

(ii) Collateral history from next of kin is important:

- Developmental history.
- Premorbid level of functioning.

- Family history of mental illness.

(iii) Physical Examination/Investigations:

- If neurological signs refer for specialist assessment/MRI.
- Do toxicology screen.

For more detailed information, please see appendix 2 and 3.

Referral

- Refer all suspected first episode psychosis urgently to mental health services. Delays to first effective treatment lead to poorer outcomes.
- People may be reluctant to accept referral in the first instance. It often helps to discuss the referral in terms of what is bothering the patient e.g. insomnia, anxiety and reassure them that the mental health service will be able to help with these symptoms. Where confidentiality allows, discussion with an agreed relative may be of assistance.
- If the person does not accept referral immediately, you should contact the appropriate mental health service and request their advice on the best way to proceed.
- If the person still refuses referral and is distressed you may deem it necessary to initiate pharmacological treatment.
- Inpatient admission under the Mental Health Act may be required.

Management

Pharmacological [18, 19]

In the majority of cases, anti-psychotic treatment will be instigated by a psychiatrist. Occasionally, GPs decide to commence anti-psychotic medication. In the event that you decide to start an anti-psychotic medication: including the patient in deciding which medication to choose improves adherence.[20] Areas for discussion include:

- Any fears they may have about taking medication.
- The rationale (striatal dopamine D2 receptor blockade) for prescribing particularly addressing problems that are worrying them such as sleep disturbance, anxiety.
- The potential side effects (appendix 4) and what they can do to combat them i.e. eat small healthy meals regularly if appetite increases.
- The importance of adherence.
- While the patient may have immediate effects in terms of better sleep etc, warn them that they may need to wait between 3 and 6 weeks before they notice the full benefits of the medication.

Choice of Anti-Psychotic

Second generation anti-psychotics are more commonly used for initial treatment, but are not necessarily more efficacious than first generation anti-psychotics, although some view their side-effect profile as more benign.[21] The National Institute for Clinical Excellence recommend that when starting a patient on anti-psychotic medication, the prescribing clinician discusses the benefits and side-effect profile of each drug with the patient to ensure he/she can make an informed choice (see appendix 4).

- Where possible, start at a low dose, increases can be prescribed at review meetings.[22]
- Consider contraindications with any medication currently prescribed.
- Consider generic forms of medication.
- Prescribe to cover time period to next review or expected appointment with mental health services.
- Monitor the patient weekly until seen by the mental health services.
- People with a first episode psychosis generally should continue anti-psychotics for a minimum of 12-36 months. People with more than one episode require ongoing medication.

People with psychosis tend to:

- have a poor diet, higher rates of smoking, be more sedentary.[23]
- have less checks of blood pressure, cholesterol, urine or weight.[24]
- have less opportunistic advice on smoking, alcohol diet and exercise.

People with schizophrenia:

- have 20% shorter life expectancy than the general population.[24]
- are twice as likely to die from coronary heart disease.[24]
- are twice as likely to have diabetes.[23]
- are four times as likely to die from respiratory disease.[25]

People on anti-psychotics should have regular monitoring of cardiovascular risk factors:

- weight and waist measurement.
- Blood pressure and ECG (ECG to be done at baseline or if dose change).
- Fasting/random blood glucose.
- Fasting lipid profile.

Further details are outlined in appendix 3.
Actions to be taken in the event of ECG abnormalities are detailed in appendix 5.
Appendix 6 provides notes on dealing with special patient presentations e.g. prescribing for older patients, patients with cardiovascular disease.

Psychosocial

Cognitive behavioural therapy and occupational therapy can improve outcomes[26-28] but are not yet widely provided. Family education programmes reduce the risk of relapse by about 20% and reduce distress in families.[29] Advise patients/families/carers to inform themselves and avail of these interventions if available from the local mental health services.

Clinical Audit[33]

Clinical audits that could be carried out using these guidelines are list below. Further audits could be conducted against the recommendations of the NICE guidelines referenced.

Physical Investigations:

Annual audit of adherence to the physical investigation recommendations outlined in Appendix 4; as a whole and separately for cardiovascular risk factors.

Medication:

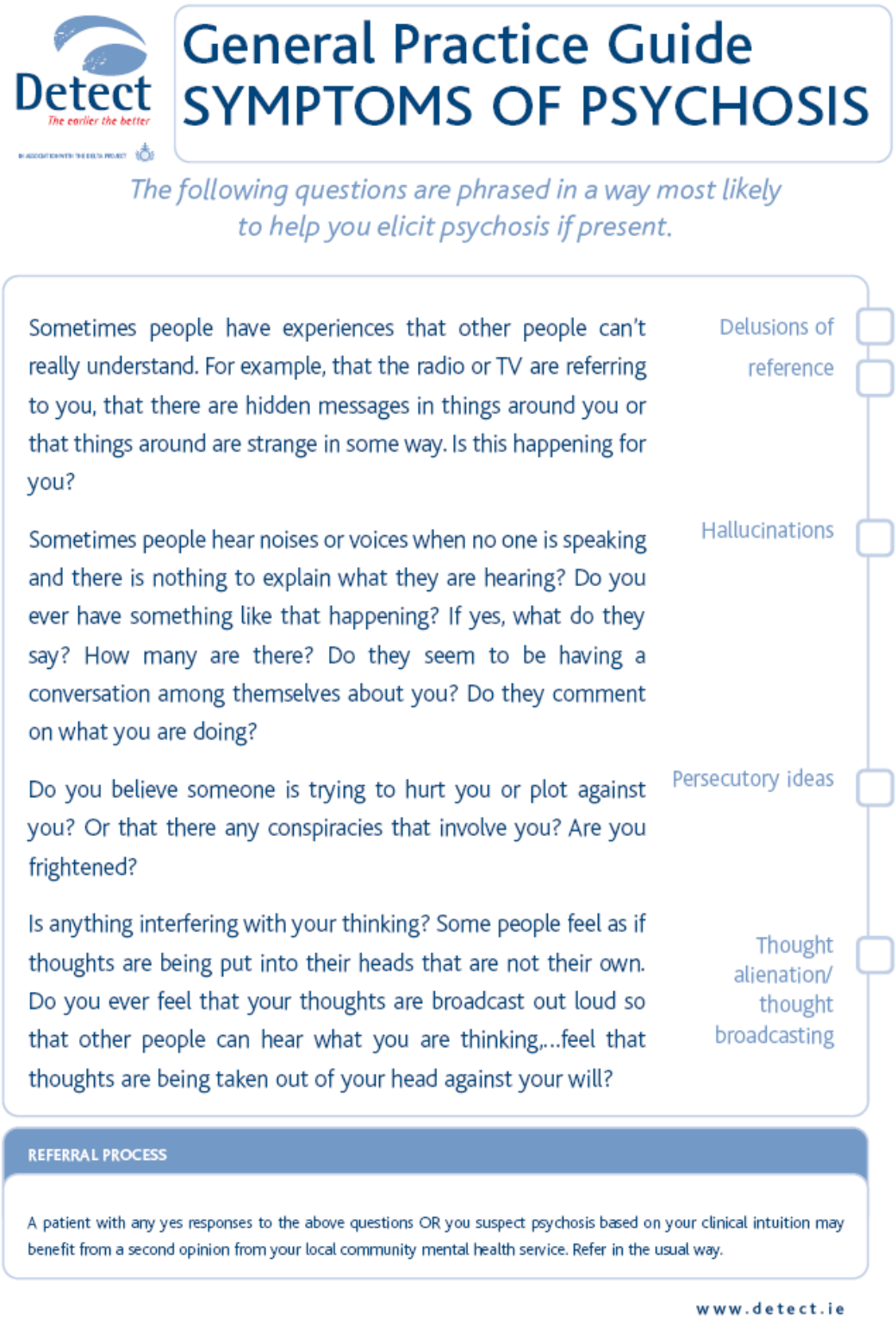
Annual audit of adherence to suggested initial dosages for anti-psychotic medication as outlined in Appendix 5.

Service evaluation:

An audit of number of referrals of people with psychosis to mental health services in the past 24 months.

Appendices

Appendix 1:



Detect
The earlier the better

General Practice Guide
SYMPTOMS OF PSYCHOSIS

The following questions are phrased in a way most likely to help you elicit psychosis if present.

Sometimes people have experiences that other people can't really understand. For example, that the radio or TV are referring to you, that there are hidden messages in things around you or that things around are strange in some way. Is this happening for you?	Delusions of reference
Sometimes people hear noises or voices when no one is speaking and there is nothing to explain what they are hearing? Do you ever have something like that happening? If yes, what do they say? How many are there? Do they seem to be having a conversation among themselves about you? Do they comment on what you are doing?	Hallucinations
Do you believe someone is trying to hurt you or plot against you? Or that there any conspiracies that involve you? Are you frightened?	Persecutory ideas
Is anything interfering with your thinking? Some people feel as if thoughts are being put into their heads that are not their own. Do you ever feel that your thoughts are broadcast out loud so that other people can hear what you are thinking,...feel that thoughts are being taken out of your head against your will?	Thought alienation/ thought broadcasting

REFERRAL PROCESS

A patient with any yes responses to the above questions OR you suspect psychosis based on your clinical intuition may benefit from a second opinion from your local community mental health service. Refer in the usual way.

www.detect.ie

Appendix 1 cont:

Appendix 2: The Mental State Exam and Risk Assessment

Mental State: This involves observations on the following:

- Appearance (e.g. dressed in flamboyant or bizarre clothing, dishevelled).
- Behaviour (e.g. agitated, pacing the room, vigilant, holding unusual postures).
- Affect (e.g. blunted, labile, hostile).
- Rapport.

Questions need to be asked to clarify the following:

- **Mood**: e.g. "How has your mood been recently?" "How have you been feeling in yourself?" Prompts include: sad/down, tearful, irritable, hopeless, low self worth, feelings of unexplained guilt, punishment, inability to feel joy. Ask how they subjectively describe their mood, then make a note of your objective description. Are they congruent?
- **Thoughts**: "Have you been feeling frightened or fearful recently?" "Have you felt like something is going on behind your back?" "Have you been concerned for your safety?" "Have you felt that people are taking special notice of you or trying to hurt/harm you in some way?" "Have you felt that inconsequential things are all linked in some way, or have a new special significance for you?" "Have you felt that your thoughts were not your own, that thoughts are inserted or removed from you mind?"
- **Thought form**: Are the patient's sentences making sense to you? Is the flow of conversation logical, easy to follow? Is the flow speeded up or slowed right down? Is there a loss of rational connection between one thought and the next? If not, there could be formal thought disorder present, a psychotic symptom.
- **Perception**: "Have you heard noises or voices when no-one is around?" Try to normalise this question by explaining that this is not unusual, especially when falling asleep or awakening. "is there more than one voice? How many? Do you hear them inside or outside your head?" "Do they talk to you or about you?" "Do the voices command you to do things?" "Can you resist doing what they tell you?" "Do they ever comment on what you're doing as you're doing it?" Other modalities to be checked – visual, tactile, olfactory and gustatory (very rarely seen in functional illness)
- **Insight**: "What do you think is behind all these difficulties you're having?" "Could it be due to your mind playing tricks on you?" "Could it be due to stress?" "Do you agree specialist opinion is a good idea?" "Would you agree to try some medication in the meantime?"
- **Risk**: "Have you felt things were so tough that you have thought about/planned to end your life?" "What ideas have you considered?" "Have you gone a step further with this idea and done something to try to end your life?" "What has stopped you from carrying out an attempt on your life?" "Have you had any urges or desires to hurt someone else?" "Have you thought how to go about that?" "Have you contact with that person/ what is your relationship to that person?" "What do you think would stop you from hurting him/her?"

In the case of schizophrenia, as well as examining for positive symptoms, negative symptoms and insight it will be important to make clear the following:

- Is this a first episode or a relapse?
- Is there a recent history of drug or alcohol use as a contributing factor relapse?
- Is the individual already prescribed anti-psychotic medication and if so, is he/she adherent?
- Is the individual attending local mental health services regularly?
- Are there particular psychosocial stressors at the moment? Ask specifically about difficulties at home as well as work/school/college.

Appendix 2 cont: Assessing Suicide Risk

All forms of psychosis are associated with a high risk of suicidal behaviour. Up to 40% of people with psychosis harm themselves at some point. The early years of illness are the highest risk period for suicide.

Suicide risk questions and checklist:
The questions below in addition to the suicide risk checklist may be helpful in assessing suicide risk. However no checklist can accurately predict risk. It is not possible to infer an absolute level of risk based on the answers obtained and clinical judgement is critical.

Some questions that could be used in evaluating suicidal risk**:**

1. Have things been so difficult that you've considered ending it all?
2. Is this all too much for you to cope with? Do you feel life is too hard?
3. Do you think you would be better off dead? That others would be better off if you died?
4. Have you been hearing voices telling you to harm or kill yourself?
5. Have you considered ways that it could be done? Which ways in particular?
6. Have you made efforts to organise it? (e.g. buying a rope, testing the strength of a ceiling beam, buying tablets, buying bullets, conducting internet searches on methods of committing suicide).
7. Have you a date, time or place in mind?
8. Is it getting harder to resist the idea of suicide?
9. Do you feel you will do it at some stage?
10. What has stopped you from doing it until now? (e.g. safety nets: children, family, religion)

Individual Risk Profile	**YES**	**NO**
Psychiatric illness present		
Poor social support		
History of Substance abuse		
Sexual/physical abuse history		
Past history of suicide attempt		
Symptom Risk Profile	**YES**	**NO**
Depressive symptoms		
Delusions		
Hallucinations (distressing command hallucinations)		
Hopelessness		
Agitation/akathisia		
Panic attacks		
Anger		
Impulsivity		
Interview Risk Profile	**YES**	**NO**

Current substance abuse		
Current suicidal ideation		
Current suicidal plan		
Current suicidal intent		
Access to lethal means		

Appendix 2 cont: Assessing for Risk of Violence

It is important to note that risk is a dynamic process. There is no gold standard assessment tool for assessing the risk of violence. The checklist below may be used to collate the information necessary to assess risk. As with risk of suicide, it is not possible to infer an absolute level of risk of violence among people with psychosis. Obtain a collateral history from next of kin or family to determine the extent of the individual's aggressive behaviour in order to inform a comprehensive clinical picture.

Individual Risk Profile	**YES**	**NO**
Psychotic illness present		
Alcohol Use		
Drug Use		
Sexual/physical abuse history		
Past history of violence		
Arrests		
Current substance abuse		
Current thoughts of violence		
Current plan		
Current access to weapons		
Access to lethal means		
Current thoughts of violence		
Current plan		
Current access to weapons		
Access to lethal means		
Current substance abuse		
Current thoughts of violence		
Symptom Risk Profile	**YES**	**NO**
Delusions		
Hallucinations (command hallucinations)		
Thoughts/Fantasies/ Daydreams of violence		
Verbal threats of violence		
Physical threats of violence		
Attacks on objects		
Boisterousness		
Irritability/Agitation		
Anger		
Impulsivity		
Intoxicated		

Appendix 3: Investigations for people with psychosis[30]

		Tests	Baseline	3 months	6 months	12 months ł
Substance abuse		Toxicology screen	*			
Medical or neurological cause suspected		Physical assessment, bloodwork as indicated by the suspected condition, CT or MRI, referral to medical services	*			
Metabolic syndrome						
	Body Mass	Height, weight (and hence BMI), abdominal circumference	*	*	*	*
	Blood Sugar	Fasting Glucose	*		*	*
	Hyperlipidaemia	Fasting Cholesterol, LDL, HDL, Triglycerides	*	*		*
Cardiovascular		Physical examination (BP) and vital signs	*	*	*	*
		ECG	*			
Extra pyramidal symptoms and signs		Parkinsonism (bradykinesia, rigidity, tremor) dystonia and dyskinesia, akathesia (inner restlessness)	*		*	
Endocrine and sexual function		Functional enquiry about libido, menses, erectile function; Prolactin where indicated clinically	*		*	*

ł After first year annual monitoring sufficient if medication dose stable, patient is clinically well, and no previous side-effects.

Appendix 4: Pharmacological Management

Side effect profile of common anti-psychotic medication [18, 19, 30]

Side-effect	Risperidone	Olanzapine	Quetiapine	Amisulpiride	Clozapine	Sulpiride	Haloperidol	Chlorpromazine
Extra pyramidal	+	+/-	-	+	-	+	+++	++
Sedation	+	++	++	-	+++	-	+	+++
Weight gain	++	+++	++	+	+++	+	+	++
Anti-cholinergic	+	+	+	-	+++	-	+	++
Raised prolactin	+++	+	-	+++	-	+++	+++	+++
Hypotension	++	+	++	-	+++	-	+	+++

+++ High incidence/severity
++ Moderate incidence/severity
+ Low incidence/severity
- Very low incidence/severity
*Other side-effects not mentioned in this table do occur. Please consult BNF or other prescribing guidelines for side-effects and contra-indications.

Appendix 4 cont: Pharmacotherapy in first episode psychosis[31, 32]

Medication	Starting dose	Titration	First Episode Minimum effective dose/day	Established Cases / Relapse
Risperidone	**1-2mg/day**	**Consider increases depending on response, side effects etc.**	**2 mg**	**4 mg**
Olanzapine	**2.5-5mg/day**	**Consider titrating up to 10mg depending on response, side effects etc.**	**5 mg**	**10 mg**
Quetiapine	**25mg BD**	**Titrate up to 200mg/day over the first 5 days depending on response, side effects etc.**	**200 mg**	**300 mg**
Amisulpride	**100-200mg/ day**	**Titrate up to 400mg/day in divided doses over the first 5 days depending on response, side effects etc.**	**400 mg**	**800 mg**
Sulpiride	**100-200mg/ day**	**Titrate up to 400mg/day in divided doses over the first 5 days depending on response, side effects etc.**	**400 mg**	**800 mg**
Haloperidol	**1.5-3mg/ day**	**Titrate up according to response, side effects etc.**	**1.5-3 mg**	**>4 mg**
Chlorpromazine	**25-50mg/ day**	**Titrate up according to response, side effects etc.**	**150 mg**	**300mg**

*Given the variation in individual response, all doses should be considered as guidance
*If sedation is a potential side-effect (see table above in appendix 5), usually prescribe at night initially

Appendix 5: Action to be taken in the event of elongated QTc interval[30]

ECG Result	Action Required
QTc <440 ms (men) or <470 (women)	No action required unless abnormal T-wave morphology – consider referral to cardiologist if in doubt.
QTc >440 ms (men) or >470ms (women) but <500ms	Consider switching to drug of low effect; re-perform ECG and consider referral to cardiologist.
QTc >500 ms	Stop suspected causative drug(s) and switch to drug of low effect: refer to cardiologist immediately.
Abnormal T-wave morpology	Review treatment. Consider switching to drug of low effect. Refer to cardiologist immediately.

Effect of Antipsychotics on QTc interval[30]

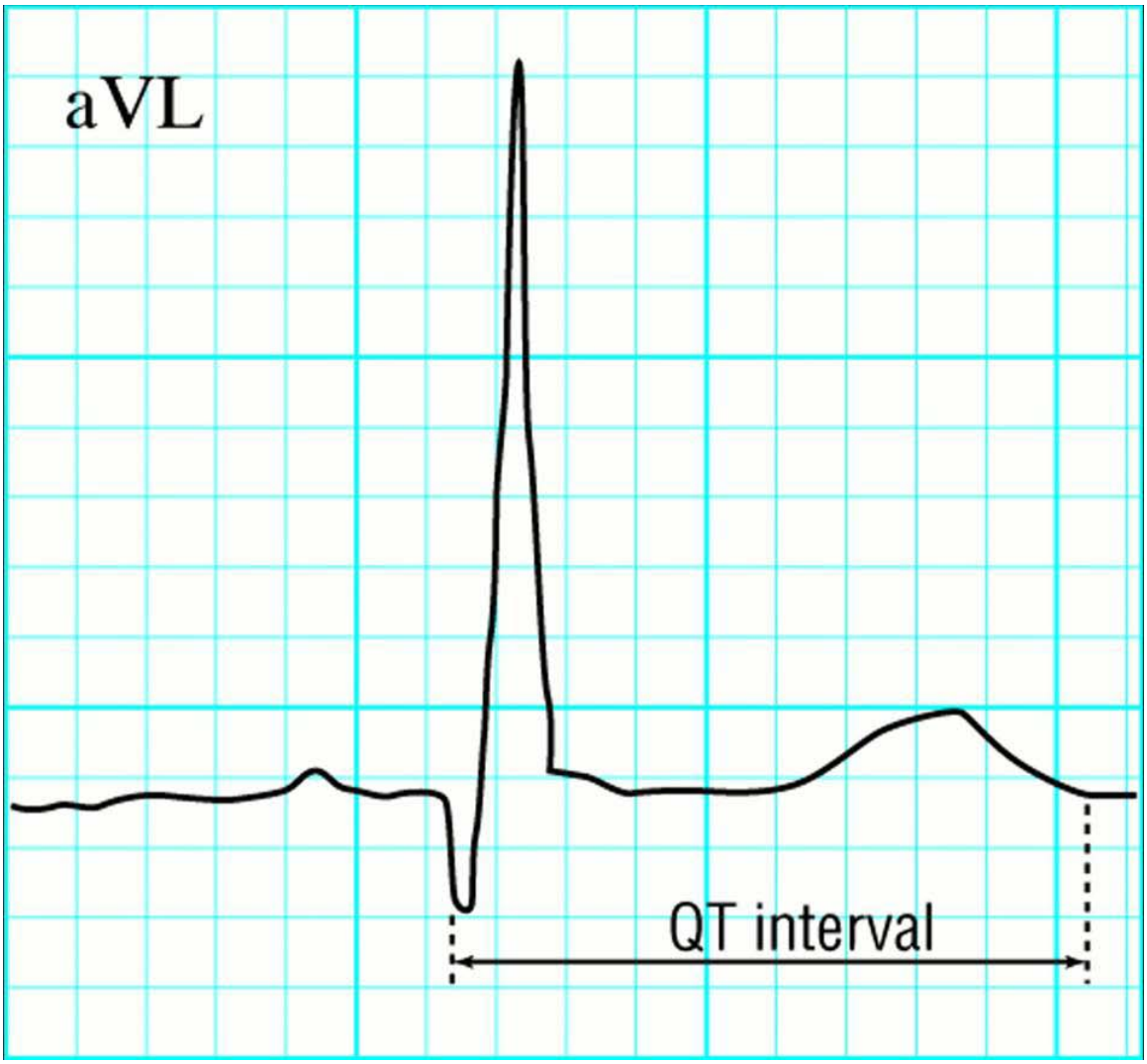
No effect	**Aripiprazole**
Low effect	**Olanzapine** **Risperidone** **Amisulpiride** **Sulpiride** **Clozapine**
Moderate effect	**Quetiapine** **Ziprasidone** **Chlorpromazine**
High effect	**Haloperidol** **Any drug or combination of drugs used in doses exceeding recommended maximum**
Unknown effect	**Zuclopenthixol** **Trifluoperazine**

Appendix 5 cont: Measuring QTc Interval*

The QT interval is a measure of the time from the start of the Q wave until the end of the T wave. On the ECG one small square represents 40 ms (0.04 sec). One large square represents 200ms (0.2 sec). In the example given here (Diagram 1) the QT interval is approximately nine small squares, so the QT interval may be calculated as:
9 X 40ms = 360ms (0.36 sec) The QT interval is dependent on the heart rate (the faster the heart rate, the shorter the QT interval), so the corrected QT interval (QTc) may be calculated to improve the detection of patients at increased risk of arrhythmias due to QTc elongation. The formula for QTc interval is:
$QTc = QT/\sqrt{RR}$, where QTc is the QT interval corrected for heart rate, and RR is the interval between the R waves of two successive QRS complexes.

*Some GPs may wish to refer to their local cardiology department for ECG and interpretation of QTc interval.

Diagram 1 Measurement of the QT Interval



Appendix 6: Notes on Special Patient Characteristics [31]

Note: This is an **incomplete list**. Please always consult a reliable formulary such as the British National Formulary and other prescribing guidelines when prescribing**.**

Characteristic	Notes
Patients at risk of obesity	Many anti-psychotics have a propensity to cause **weight gain**, which may affect adherence and lead to obesity and other problems with general health. Clozapine and olanzapine carry the highest risk of weight gain. **Insulin resistance** may or may not be associated with weight gain. Risk factors include previous history and family history. It is commonest with clozapine and olanzapine. Recommended monitoring as per appendix 3.
Patients with cardiovascular disease	The **cardiotoxic risks** of anti-psychotics include QTc prolongation, arrythmias and sudden death. Second generation anti-psychotics (e.g. olzanapine, risperidone) seem to have less effect on QTc interval than First generation anti-psychotics (e.g. haloperidol) but are not without risk. Examples (from highest risk to lowest) include ziprasidone, risperidone, quetiapine, olanzapine and clozapine.
Pregnancy	Treat only on advice from consultant psychiatrist.
The elderly	The **pharmacokinetics** and **pharmacodynamics** of most drugs are different in the elderly, including changes in gut motility, distribution, metabolism and excretion. These should be taken into account when prescribing, as should possible **interactions** with the non-psychiatric medications many elderly people take.

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