CHRONIC DISEASE MANAGEMENT PROGRAMME FOR SCHIZOPHRENIA

(REPRINTED FROM CHRONIC DISEASE MANAGEMENT PROGRAMME – HANDBOOK FOR HEALTHCARE PROFESSIONALS, 2009 EDITION)

1 INTRODUCTION

1.1 Schizophrenia is a major psychiatric disorder with a chronic and often disabling clinical course. It has an estimated lifetime prevalence of seven per thousand of the adult population worldwide. This disorder is characterised by a multiplicity of symptoms affecting the most fundamental human attributes: cognition, emotion and perception. The early age of onset, impairments in intellectual and psychosocial aspects of the individual's life as well as associated stigma, often bring to its victims and families significant emotional and financial distress.

2 SYMPTOMATOLOGY AND PRESENTATION

2.1 Each patient with the disorder will have a unique combination of symptoms and experiences and may present at various phases of their illness. Some might experience a prodromal phase where frank psychotic symptoms had not yet occurred. The prodromal phase is frequently characterised by non-specific symptoms such as depressed mood, anxiety, sleep disturbances, attenuated psychotic symptoms, social withdrawal and deterioration in academic or occupational functioning.

2.2 There are 4 main categories of symptoms in Schizophrenia: positive, negative, disorganized and cognitive symptoms. Various combinations of these symptoms may occur.

2.3 Positive symptoms are those that appear to reflect an excess or distortion of normal functions. Characteristic positive symptoms are delusions and hallucinations. Delusions are fixed, false and firmly held beliefs that are out of the socio-cultural and religious context of the affected individual. Usually, the patient would misinterpret sounds and actions of others as relating to themselves. They may also report unusual experiences or fear that their actions are being monitored and their lives might be in danger. Hallucinations are perceptions in the absence of a stimulus, in a conscious and awake person. Often hallucinations in Schizophrenia occur in the auditory modality and patients would complain of voices talking to them. They may also be noted to mumble, talk, laugh or gesticulate to themselves. Hallucinations could also occur in other sensory modalities such as vision, smell, touch and taste. If these are the predominant hallucinations, care must be exercised to exclude an organic cause for the psychosis.

2.4 Negative symptoms are those that appear to reflect a diminution or loss of normal functions. These often persist in the lives of people with Schizophrenia, even after resolution of positive symptoms, and are difficult to evaluate because they are not grossly abnormal as positive symptoms and may be caused by other factors such as antipsychotic medications. Typical negative symptoms are alogia (limited speech with consequent difficulty in maintaining a conversation), anhedonia (lack of pleasure or interest in life), avolition (lack of initiation, drive and energy), asociality (social withdrawal) and affect flattening (difficulty in expressing emotions). Patients seldom complain about negative symptoms, but their caregivers would report about their "laziness".

2.5 Disorganised symptoms include disturbances in thinking, speech and behaviour. They may talk irrelevantly, answer off the point or manifest bizarre behaviours. Cognitive symptoms include impairments in attention, concentration, memory and executive functioning. Cognitive symptoms have a significant impact on their social, occupational and academic functioning.

2.6 Schizophrenia is associated with significant psychiatric co-morbidities such as depression, anxiety disorders, post-traumatic stress disorders and substance use disorders. These co-morbidities could affect the clinical outcome and delay improvement. Occasionally, the patient with Schizophrenia may first present with features of depression or anxiety rather than complain of hearing voices. Therefore, the clinician should screen for the presence of these disorders during the clinical interviews.

2.7 In the assessment of the patient, it is important to obtain corroborative history from family, friends or caregivers. This is especially so in patients who are not forthcoming during the clinical interviews or downplay their symptoms. During the interview, it is also important to assess the social support system and the patient's self-care, as it will influence subsequent management plans.

2.8 Other important aspects of the interview include risk assessment and physical health. In the risk assessment, clinicians are specifically examining the patient for risk of harm to self and others. Patients suffering from Schizophrenia have an increased risk of suicide. A suicide risk assessment is provided at Annex 2C for reference. As a result of neglect and poor hygiene, they may become malnourished or suffer the physical consequences of it.

3 DIAGNOSIS AND DIFFERENTIALS

3.1 In the diagnosis of Schizophrenia, there are 2 widely used criteria internationally. The International Classification of Diseases (ICD) endorsed by the World Health Organisation, and the Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association.

3.2 Diagnostic guidelines for DSM-IV-TR

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

i) Delusions
ii) Hallucinations
iii) Disorganized speech (e.g., frequent derailment or incoherence)
iv) Grossly disorganized or catatonic behaviour
v) Negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

B. Social/occupational dysfunction: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. Duration: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective and Mood Disorder exclusion: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active- phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. Substance/general medical condition exclusion: The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. Relationship to a Pervasive Developmental Disorder: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

3.3 Diagnostic Guidelines for ICD-10

3.3.1 The normal requirement for a diagnosis of Schizophrenia is that a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any one of the groups listed as (a) to (d) below, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of 1 month or more. Conditions meeting such symptomatic requirements but of duration less than 1 month (whether treated or not) should be diagnosed in the first instance as acute Schizophrenia-like psychotic disorder and are classified as Schizophrenia if the symptoms persist for longer periods.

3.3.2 Although no strictly pathognomonic symptoms can be identified, for practical purposes it is useful to divide the above symptoms into groups that have special importance for the diagnosis and often occur together, such as:

a) thought echo, thought insertion or withdrawal, and thought broadcasting;
b) delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;
c) hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;
d) persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world);
e) persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end;
f) breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms;
g) catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor;
h) "negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication;
i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

3.4 In making a diagnosis of Schizophrenia, it is important to exclude certain differentials. Differential diagnoses can be categorised into functional psychiatric disorders and organic brain disorders.

3.5 Possible psychiatric differential diagnoses include schizoaffective disorder, bipolar disorder and delusional disorder. Some examples of organic brain disorders that may present with psychotic symptoms include delirium, drug- induced states in either intoxication or withdrawal phases, alcoholic hallucinosis, and intracranial pathologies such as meningo-encephalitis, epilepsy and brain tumours.

3.6 Therefore, in the evaluation of the patient, the following steps would be pertinent:

a) A complete history and mental state assessment;
b) A thorough physical examination to exclude some of the differential diagnoses;
c) Laboratory tests such as full blood count, renal and liver panel, thyroid function tests and other relevant investigations may be useful in the initial evaluation;
d) Neuroimaging such as CT or MRI scan of the brain may be necessary if neurological signs are present or intracranial causes are suspected.

4 TREATMENT

4.1 In the holistic management of patients with Schizophrenia, it is essential to consider bio-psycho-social aspects of care. Often, it is useful to enlist the assistance of a multidisciplinary team that includes a case manager, social worker, psychologist and occupational therapist in the assessment and planning of care in the early phase of illness, or when psychosocial aspects of care becomes predominant.

Biological interventions

4.2 Antipsychotic medications

4.2.1 Antipsychotic medications should be used as the first-line treatment for psychotic symptoms. Antipsychotic medications are divided into typical and atypical based on their propensity to cause extrapyramidal side effects (EPSE). Typical antipsychotics have been convincingly shown in numerous trials to be more effective than placebo in the treatment of positive symptoms, but have a greater propensity to cause EPSE. Atypical antipsychotics are equally efficacious in controlling psychotic symptoms, have a lower propensity to cause EPSE, but are generally more costly. Antipsychotic medications may come in various formulations such as tablets, capsules, oro-dispersible, liquid and injections. (refer to Table A.1 for a list of common antipsychotics and their dosage range)

4.2.2 In general, polypharmacy is avoided and antipsychotic medications are started at low doses and titrated upwards in accordance with clinical response and tolerability. It may take up to 2 weeks of antipsychotic medication at therapeutic dosage before clinical response begins. The patient may experience a few outcomes after initiation of medication; (a) adequate response and tolerable side effects, (b) adequate response but intolerable side effects, (c) inadequate response but tolerable side effects, (d) inadequate response and intolerable side effects and (e) refusal to adhere to medication (refer to Figure 1) for treatment algorithm).

FIGURE 1. TREATMENT ALGORITHM FOR SCHIZOPHRENIA

Sequential steps to take	Action
1	Diagnosis of schizophrenia
2	First line e.g. – FGA – Haloperidol, Trifluoperazine; SGA – Resperidone – adequate trial (4-6 weeks) If adequate response -- continue
3	If inadequate response -- Second line – SGA – Olanzapine, Aripiprazole, Quetiapine, Ziprasidone If adequate response without intolerable side effects – continue
4	If inadequate response – Third line – Clozapine If adequate response with intolerable side effects – continue
5	If inadequate response – Augment Clozapine with ECT, Lithium

4.2.3 In patients with adequate response but intolerable EPSE, anticholinergic medications such as benzhexol and benztropine may be prescribed. Usage of anticholinergic medications should be reviewed regularly and balanced against side effects such as dry mouth, constipation, confusion and cognitive impairment. If side effects are preventing upward titration of antipsychotic dosage, a switch in antipsychotic medication may be preferred.

4.2.4 In situations where patients prefer, or adherence to oral medications is doubtful, depot antipsychotic medications can be started. Currently, there are 3 main types of depot typical antipsychotic medications; fluphenazine, flupenthixol and zuclopenthixol and 1 available depot atypical medication, risperidone. In practice, a test dose of depot medication of much lower dose is given first and the patient monitored for up to a week; before a further top up dose of the depot medication is given. Oral antipsychotic medications will be tapered down gradually once the dose of depot antipsychotic medication is stabilised.

4.2.5 Clozapine is indicated for patients with treatment resistant Schizophrenia, defined as inadequate response to 2 trials of antipsychotics for 6 weeks at therapeutic dosages. Clozapine is reserved as third-line because of the need for regular haematological monitoring once started to prevent agranulocytosis. Therefore, patients on clozapine should be reviewed by psychiatrists.

4.3 Adjunct medications

4.3.1 Antidepressants such as selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants (TCA) are prescribed to manage co-morbid psychiatric illnesses such as Depression and anxiety disorders. Mood stabilisers such as sodium valproate and lithium are sometimes used as adjunctive treatments when patients have prominent mood features or are treatment resistant. Short- term benzodiazepines may be useful in management of agitation or disruptive behaviours. However, there should be due consideration of potential drug- drug interactions before prescribing multiple psychotropic medications.

4.4 Electroconvulsive therapy

4.4.1 Electroconvulsive therapy (ECT) is effective in catatonic patients, and is sometimes used in treatment resistant Schizophrenia.

Psychosocial interventions

4.5 Combination of pharmacotherapy and psychosocial interventions has synergistic effects and can improve the course of Schizophrenia. Interventions include basic psychoeducation and counselling that most healthcare professionals can provide, to more complex and specialised interventions such as individual, group or family psychotherapy and vocational rehabilitation.

4.6 Psychoeducation includes educating the patients and their caregivers about the illness, its course, prognosis, as well as treatment. Side effects of medications, costs and treatment options should be discussed where appropriate.

Follow up

4.7 This is one of the most important aspects of care in Schizophrenia. During the follow up appointments, the clinician has to evaluate various aspects of the management. Broadly, they may be categorised as symptoms, medications and physical health (refer to Table A.3).

4.8 Efficacy of treatment should be assessed at each review. This includes changes in symptoms and behaviours, either improvement or deterioration. Early signs of relapse should be sought and can be managed as an outpatient by adjustment of medications. Patients have their own unique relapse signature. The patient or caregiver might be able to describe early warning signs such as increasing intensity or frequency of hallucinations, mood changes or sleep disturbances. During this segment, clinicians should also evaluate for co-morbid psychiatric disorders such as depression.

4.9 Under the category of medications, adherence and side effects should be evaluated. Adherence can be evaluated by asking the patient or caregiver directly, or by asking them to bring their existing stock of medications to check for surpluses. Checking for treatment adherence is necessary as patients frequently reduce or stop their medications on their own for various reasons ranging from a lack of insight into the illness, to complacency once they feel improved. Medication side effects are common reasons why patients do not adhere to their prescription. Therefore, it is important to enquire and examine for the presence of side effects such as EPSE, excessive sedation, sexual dysfunction, and amenorrhoea in females (refer to table A.2).

4.10 Patients with Schizophrenia are at risk of metabolic syndrome and have higher mortality rates from cardiovascular diseases. Antipsychotic medications have been associated with hypertriglyceridemia, hypercholesterolemia, hyperglycemia and weight gain. Patients should also be encouraged to lead a healthy and active lifestyle to modify their cardiovascular risk profile. If necessary, lipid-lowering or oral hypoglycaemic agents should be prescribed to manage these disorders as laid out in the Ministry of Health's clinical practice guidelines.

5 WHEN TO REFER

5.1 Patients with the following indications should be referred to a psychiatrist for further assessment;

a) Initial assessment, diagnosis and initiation of treatment, when in doubt
b) Risk of violence to self or others
c) Unexpected changes in symptomatology
d) Drug-related complications
e) Treatment resistance
f) Switching to clozapine
g) Forensic or medico-legal issues

5.2 Special groups: pregnancy, paediatric or geriatric age group

5.3 If urgent, the patient can be referred to any hospital's emergency department for evaluation. The Institute of Mental Health also has a 24-hour Emergency Room that provides psychiatric consultations.

6 CLINICAL INDICATORS

6.1 Participating medical institutions must monitor the quality of care that patients receive and submit the following clinical indicators via electronic channels to MOH:

a) Clinical Global Impression (CGI) Scale
b) Consultation for CDMP Mental Health
c) Blood test for fasting lipid (only for patients on atypical antipsychotic medication)
d) Blood test for fasting glucose (only for patients on atypical antipsychotic medication)

6.2 The Clinical Global Impression (CGI) Scale is a simple, easy to administer 2-item scale (each item has 7 points) scale to indicate the severity and improvement of the mental condition. It is chosen as it can be applied to reflect severity and improvement in other mental conditions. The scoring details are further described in Annex 4-A.

6.3 As patient compliance to follow-up is an important aspect of care for patients suffering from mental illness, the Consultation for CDMP Mental Health (at least twice per year) is a key care compliance indicator for the Programme.

6.4 For Schizophrenia patients who are prescribed atypical antipsychotic medications, a blood test for fasting lipid and fasting glucose should be performed at least once yearly to alert doctors to possible development of metabolic syndrome, a known complication of treatment with atypical antipsychotics.

6.5 Table A2 summarises the clinical indicators required for monitoring patients with Schizophrenia. The tests for the indicated monitoring parameters should be carried out upon commencement of pharmacotherapy, and thereafter at the recommended frequencies are shown in Table A3.

7 RESOURCES

- DSM IV-TR Diagnostic criteria for Schizophrenia http://www.psychiatryonline.com/content.aspx?aID=8939#8939
- International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Version for 2007 (ICD 10) http://apps.who.int/classifications/apps/icd/icd10online/

TABLE A.1. INITIAL DOSING AND CLINICAL TITRATION OF COMMONLY USED ANTIPSYCHOTIC MEDICATION IN SCHIZOPHRENIA

Antipsychotic	Usual Dosage Range (mg)	Common Side Effects	Remarks
1st Line Anti-psychotic Medication			
Typical Anti-psychotic Medication (FGA)*			
Haloperidol	5-20	1. Extrapyramidal side effects e.g. dystonia, akathisia, parkinsonism	Monitor for EPSE
Chlorpromazine	50-400	2. Tardive dyskinesia	
Trifluoperazine	10-20	3. Hyperprolactinemia (amenorrhoea, galactorrhoea and breast	
Sulpiride	400-800	enlargement in females, and impotence and gynaecomastia in males)	
		4. Antiadrenergic side effects e.g. postural hypotension, delayed ejaculation	
		5. Photosensitivity in chlorpromazine users	
Atypical Anti-psychotic Medication (SGA)*			
Risperidone	2-6	Rhinorrhoea, blocked nose and at higher dosages (more than 6 mg/day) the side effect profile is similar to typical antipsychotic medications with increased EPSE and hyperprolactinemia	Increased EPSE without improved efficacy above 6mg/day
Depot Injections			
Fluphenazine	12.5-75mg/2-6wk		Typical
Flupenthixol	20-40mg/2-4wk		Typical
Zuclopenthixol	200-400mg/2-4wk		Typical
Risperidone	25-37.5mg/2wk		Long-acting Atypical (Consta) injection
2nd Line Anti-psychotic Medication			
Amisulpride	50-800		
Olanzapine	10-25	Sedation, weight gain, postural hypotension and anticholinergic side effects	
Quetiapine	300-850	Sedation, postural hypotension, anticholinergic side effects	Safety and benefit of high doses (>800mg/day not yet established
Aripiprazole	10-30	Headaches, insomnia and anxiety	72-hr half-life; no evidence of improved efficacy > 20 mg/day
Paliperidone	3-12		
3rd Line Anti-psychotics – Only for treatment resistant Schizophrenia			
Clozapine[1]	200-500	Sedation, weight gain, hypersalivation, postural hypotension	Need to regularly monitor full blood counts

Footnotes
[1]To be prescribed only by psychiatrist in treatment resistant Schizophrenia.
** FGA = First generation antipsychotic medication*
** SGA = Second generation antipsychotic medication*
Uncommon side effects of antipsychotic medications – Neuroleptic malignant syndrome; Lowered seizure threshold; Transaminitis

TABLE A.2: CLINICAL INDICATORS FOR MONITORING SCHIZOPHRENIA PATIENTS

Clinical Indicator		Recommended Frequency	Remarks
1	Clinical Global Impression (CGI) Scale: a. Severity b. Improvement	At least once yearly	Provider-administered
2	Consultation for CDMP Mental Health	At least twice per year	Provider-administered
3	Blood test for fasting glucose	At least once yearly	Provider-administered; Only for patients on atypical anti-psychotics
4	Blood test for fasting lipid	At least once yearly	Provider-administered; Only for patients on atypical anti-psychotics

TABLE A.3. MONITORING PROTOCOL FOR PATIENTS ON ATYPICAL ANTI-PSYCHOTICS FOR METABOLIC SYNDROME

Monitoring Parameters	Initial Period After initial 12-24 weeks of treatment	Long-Term Quarterly	Every Year
Weight (BMI)		X	X
Blood Pressure	X		X
Fasting Plasma Glucose	X		X
Fasting Lipid Profile	X		X

ASSESSMENT OF SUICIDE RISK (Annex 2-C)

Assessment of suicide risk is critical. The patient may already have attempted suicide or performed an act of self-harm; it is important to ask. Suicidality is a psychiatric emergency that warrants immediate admission.

Presence of the following features indicates a risk of suicide:

- Demographic factors – the classic profile for a successful attempt is an elderly single male
- Other demographic factors include divorce, widowed, unemployed with no religion
- Poor or no social support
- Presence of a psychiatric condition: especially depression and Schizophrenia
- Comorbid substance abuse and dependence
- Personality traits: impulsive, poor coping with stress, borderline and anti-social personality disorders
- Presence of a painful debilitating condition
- Previous suicide attempts
- Family history of suicide
- Premeditation – e.g. timing and location of the attempt; collection of necessary materials; rehearsal of the act
- Last acts – e.g. writing goodbye letters; distributing personal belongings
- Effort to avoid detection – e.g. attempting suicide while alone in a locked room; choosing a time when the family is away or asleep
- Choosing a method that they perceive as lethal
- Regret that they are still alive
- Absence of specific plans and goals for the future; having nothing to live for

How to inquire about suicidal ideation

It can be very daunting to assess for suicidal ideation for the uninitiated. Rest assured that asking for suicidal ideations will not result in this happening. In fact, you are likely to miss it if you don't enquire. Here is a suggested flow for this line of questioning which is less challenging to ask:

1. "Do you sometimes have a feeling that life isn't worth living, or do you think about death much?"
2. "Do you sometimes think that if you died tomorrow from an accident or illness, that it just wouldn't matter?" ***(Passive ideation)***
3. "Have you had thoughts of killing yourself?" ***(Active ideation)***

CLINICAL GLOBAL IMPRESSION (CGI) SCALE (Annex 4-A)

Considering your total clinical experience with this particular population, how would you rate this patient's mental condition at this time?

1) Severity of Illness

1 = Normal (not at all mentally ill)
2 = Borderline mentally ill
4 = Moderately mentally ill
5 = Markedly mentally ill
6 = Severely mentally ill
7 = Extremely mentally ill

2) Global Improvement

0 = Not assessed
1 = Very much improved
2 = Much improved
3 = Minimally improved
4 = No change
5 = Minimally worse
6 = Much worse
7 = Very much worse