



Complete Summary

GUIDELINE TITLE

Schizophrenia.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Schizophrenia. Singapore: Singapore Ministry of Health; 2003 Feb. 40 p. [29 references]

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Schizophrenia

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Psychiatry
Psychology

INTENDED USERS

Allied Health Personnel
Physicians

Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To provide guidance to doctors on the many treatment options available for schizophrenia, based on the best available evidence from the medical literature
- To provide patients with schizophrenia with the best possible care and outcome
- To assist primary health care physicians in clinical decision-making

TARGET POPULATION

Adults with schizophrenia in Singapore

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Assessment

1. Assessment of patient for symptoms of schizophrenia, co-morbid psychiatric illness, co-morbid medical condition, or substance abuse
2. Evaluation of patient's social supports, functioning, and relative risk of self-harm or harm to others

Treatment

1. Pharmacotherapy
 - First-line antipsychotic medications (trifluoperazine, chlorpromazine, thioridazine, haloperidol, sulpiride)
 - Second-line antipsychotic medications (clozapine, risperidone, olanzapine, quetiapine, amisulpride)
 - Depot antipsychotic medications
 - Maintenance and discontinuation of antipsychotics
 - Adjunctive medications, including anticholinergic agents, benzodiazepines, mood stabilizers (e.g., lithium, carbamazepine, valproate), and antidepressants
 - Monitoring of response to medications and adjustments as necessary
2. Electroconvulsive therapy (ECT)
3. Psychosocial interventions
 - Individual and group psychological therapy
 - Psychoeducation/family intervention
 - Social skills training
 - Vocational training
4. Referral to psychiatrist

MAJOR OUTCOMES CONSIDERED

- Effectiveness and safety of medications
- Side effects, adverse effects, and costs of treatment

- Rates of relapse, coping skills, social and vocational functioning, and ability to function independently

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials.

Level Ib: Evidence obtained from at least one randomised controlled trial.

Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation.

Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study.

Level III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies.

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A (evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C (evidence level IV): Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations that follow are those from the guideline's executive summary; detailed recommendations can be found in the original guideline document. Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, Good Practice Points) and level of the evidence (Level I-Level IV) are presented at the end of the Major Recommendations field.

A - Antipsychotic medications are the first-line treatment for psychotic symptoms. (Grade A, Level Ia)

A - Clozapine is not used as a first-line antipsychotic because of the risk of agranulocytosis. Its use is to be considered only after other antipsychotic medications prove inadequate; it can only be prescribed by a registered psychiatrist, and regular blood monitoring is mandatory. (Grade A, Level I a)

A - Most patients respond to a daily antipsychotic dose of 300 to 1,000 chlorpromazine (CPZ) equivalents administered for a minimum of 6 weeks (Dixon, Lehman, & Levine, 1995). Patients with a first episode respond to lower doses than patients with recurrent episodes (McGorry, 1999; Remington, Kapur, & Zipursky, 1998; McEvoy, Hogarty, & Steingard, 1991). (Grade A, Level I a)

GPP - Local Asian patients may respond to a lower daily antipsychotic dose. (GPP)

A - Maintenance dose is generally lower than that used in acute treatment, and the patient should continue with the lowest effective dose of antipsychotic medication. Dosages in excess of 600 CPZ equivalents/day should be avoided unless there are good clinical reasons (e.g., symptom control) for a higher dose (Dixon, Lehman & Levine, 1995). (Grade A, Level I a)

B - Patients who have not responded to recommended antipsychotic medications should be considered for electroconvulsive therapy (ECT). (Grade B, Level III)

C - The prophylactic use of anticholinergic agents should be determined on a case-by-case basis, taking into account risk factors for both extrapyramidal side effects (EPSE) and anticholinergic side effects as well as the propensity of the antipsychotic medication to cause extrapyramidal side effects. (Grade C, Level IV)

B - Patients who experience persistent and clinically significant symptoms of anxiety and those with disruptive, dangerous, or assaultive behaviour should receive a trial of adjunctive benzodiazepines (Johns & Thompson, 1995). (Grade B, Level III)

B - Antidepressants should be considered for persistent depressive symptoms and should be prescribed with an antipsychotic to prevent worsening of psychosis (Black & Andresean, 1999). (Grade B, Level II b)

B - Supportive individual and group psychotherapy in combination with medications can reduce relapses and enhance occupational and vocational functioning (Scott & Dixon, 1995). (Grade B, Level II b)

A - Cognitive Behavioural Therapy is beneficial in reducing the symptoms (especially the positive symptoms) of schizophrenia (Garety, Fowler, & Kuipers, 2000). (Grade A, Level I a)

A - Psychoeducation and family intervention can help reduce relapse rates. (Grade A, Level I b)

A - Social skills training improves social adjustment and coping skills, thereby reducing relapse rates (Benton & Schroeder, 1990; Corrigan, 1991). (Grade A, Level I b)

A - Vocational training is likely to benefit those who a) see competitive employment as a personal goal, b) have a history of prior competitive employment, c) have a minimal history of psychiatric hospitalization, and d) have been assessed to have good work skills (Lehman, 1995). (Grade A, Level I b)

Definitions:

Grades of Recommendations

Grade A (evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

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Grade C (evidence level IV): Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group.

Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials.

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Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation.

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Level III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies.

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

CLINICAL ALGORITHM(S)

An algorithm is provided for pharmacological treatment of schizophrenia in the acute phase.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

- This guideline will provide guidance to doctors on the many treatment options available for schizophrenia and provide patients with the best possible care and outcome.
- Psychosocial interventions can improve the course of schizophrenia when integrated with psychopharmacologic treatment by providing additional benefits for patients in such areas as relapse prevention, improved coping skills, better social and vocational functioning, and ability to function more independently.

Specific Benefits

- Typical antipsychotic medications have been convincingly shown in well over 100 randomised double-blind studies to be more effective than placebo in the treatment of positive symptoms.
- There is evidence that atypical antipsychotics are more or equally effective in controlling all four categories of symptoms in schizophrenia and are better tolerated than typical antipsychotics.
- Controlled trials have shown that clozapine produces significant improvement in at least 30% of patients who show an inadequate response to two typical antipsychotics of different clinical classes.
- Electroconvulsive therapy (ECT) is effective for schizophrenic patients with affective or catatonic symptoms.
- Randomised trials have demonstrated that a combination of family intervention with antipsychotics reduce 1-year relapse rates from a 40 to 53% range to a 2 to 23% range.
- Studies have shown that, when combined with medications, individual and group psychological therapy reduces relapses and enhances occupational and vocational functioning.
- Cognitive Behavioral Therapy (CBT) has been demonstrated to be beneficial in reducing the symptoms (especially positive symptoms) of schizophrenia.
- Studies show that social skills training improves social adjustment and coping skills, thereby reducing relapse rates.

- Controlled studies have shown that vocational interventions can be effective in helping patients find jobs and remain in competitive employment. Characteristics of patients who are more likely to benefit are those who a) see competitive employment as a personal goal, b) have a history of prior competitive employment, c) have a minimal history of psychiatric hospitalization, and d) have been assessed to have good work skills.

POTENTIAL HARMS

Side Effects of Typical Antipsychotics

- Extrapyramidal side effects (e.g., acute dystonia, akathisia, parkinsonism)
- Tardive dyskinesia (involuntary movement disorder) following prolonged use
- Anticholinergic effects (e.g., dry mouth, blurred vision, urinary hesitancy or retention, constipation)
- Anti-adrenergic effects (e.g., postural hypotension, inhibition of ejaculation)
- Sedation
- Lowered seizure threshold
- Cardiovascular effects include electrocardiogram (ECG) changes (e.g., widening of QRS complex, prolonged QT interval), tachycardia, cardiac arrhythmias
- Hyperprolactinaemia (amenorrhoea, galactorrhoea, and breast enlargement in women and impotence and/or gynaecomastia in men)
- Skin and eye effects include allergic and phototoxic skin reactions; long-term use may cause pigmentary changes of skin, and corneal and lens deposits
- Hepatic effects (e.g., minor abnormalities in liver function tests, cholestatic jaundice)
- Neuroleptic malignant syndrome (a rare idiosyncratic and potentially fatal reaction characterized by hyperthermia, muscular rigidity, autonomic instability, alteration in consciousness level, and elevated serum creatinine phosphokinase)
- Others (e.g., weight gain, nausea)

Common Side Effects of Atypical Antipsychotics

Clozapine

- Sedation
- Hypersalivation
- Anticholinergic effects
- Weight gain
- Postural hypotension
- Potentially serious agranulocytosis (about 0.34% per annum)
- Potentially serious lowered seizure threshold in doses beyond 600 mg daily

Olanzapine

- Weight gain
- Sedation
- Dizziness
- Anticholinergic effects (dry mouth, constipation, retention of urine, blurring of vision)

Quetiapine

- Somnolence
- Dizziness
- Postural hypotension
- Anticholinergic effects (dry mouth, constipation, retention of urine, blurring of vision)

Risperidone

- Insomnia
- Anxiety
- Agitation
- Hyperprolactinaemia (amenorrhoea, galactorrhoea, sexual dysfunction)

Amisulpride

- Insomnia
- Anxiety
- Agitation
- Hyperprolactinaemia (amenorrhoea, galactorrhoea, sexual dysfunction)

Cautions for Use of Benzodiazepines

Patients with respiratory difficulties should be treated with caution. All patients should be considered for gradual withdrawal at the earliest opportunity to avoid an unnecessary risk of dependence, and all patients should be observed for the paradoxical effect of disinhibition.

QUALIFYING STATEMENTS

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- These guidelines are not intended to serve as standards of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of the guideline document are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The following clinical audit parameters, based on recommendations in these guidelines, are proposed:

1. Percentage of schizophrenic patients prescribed antipsychotic medication
2. Percentage of schizophrenic patients prescribed clozapine, who are intolerant or unresponsive to other antipsychotic medications
3. Percentage of schizophrenic patients prescribed clozapine, whose full blood count is regularly monitored

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

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Singapore Ministry of Health. Schizophrenia. Singapore: Singapore Ministry of Health; 2003 Feb. 40 p. [29 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Feb

GUIDELINE DEVELOPER(S)

Singapore Ministry of Health - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

Singapore Ministry of Health

GUIDELINE COMMITTEE

Workgroup on Schizophrenia

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on November 28, 2003.

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