

## CLINICAL PRACTICE GUIDELINES

### Treatment of Schizophrenia

## I. Introduction

Clinical practice guidelines (CPGs) have been defined as “systematically developed statements of recommendation for patient management to assist practitioner and patient decisions about appropriate health care for specific situations” (1).

The aim of these guidelines is to improve the assessment and treatment of patients with schizophrenia at all stages of the illness. These guidelines are written primarily for physicians; however they may be of value to other clinicians involved in the treatment of patients (aged 16 years or over) who have schizophrenia. The guidelines may also be useful as a guide to provider organizations developing services, to senior students in allied health disciplines, and to those accrediting services.

The guidelines specify 4 main topics, each of which a physician must consider when seeing a patient: assessment, pharmacotherapy, psychosocial interventions, and delivery of services. Within each of the first 3 topics, 3 phases of the illness are distinguished:

- the “acute” phase, wherein signs and symptoms worsen, usually bringing the patient to medical attention
- the “stabilization” phase, wherein the illness is subsiding after an acute episode
- the “stable” or chronic phase, wherein acute symptoms may have subsided but functioning is often persistently impaired

The guidelines highlight for particular attention the treatment possibilities for 2 groups of patients: 1) those in the demographic majority, who have been ill for many years and may have a poor level of functioning and poor quality of life and who deserve a review that takes new information into

account; and 2) first-episode patients, in whom the chance to improve long-term outcome may be greatest. The guidelines also address special issues such as the prodromal phase, substance use or abuse, coexisting medical illnesses, pregnancy, coexisting depression, and aging patients.

### Rationale

Schizophrenia is a serious but treatable mental illness with significant morbidity and mortality, affecting approximately 0.6% of the general population at some point in their lives (2). Illness onset is most common in young adults, relapses of acute episodes can occur throughout the lifespan, and functioning is often significantly affected. The direct health care and non-health care costs in Canada were estimated to be \$1.12 billion in 1996 (3). Patients with schizophrenia are at significantly increased risk for suicide, violence, substance use or abuse, homelessness, unemployment, medical illnesses, and victimization. Life expectancy for persons with schizophrenia is also significantly reduced (4).

The guidelines assert that symptoms and functioning are improved and the risks for suicide and social dysfunction reduced when patients with schizophrenia are given continuous treatment, long-term care from qualified service providers, and access to appropriate housing and services. New treatments and service delivery options reinforce this therapeutic optimism. Guidelines based on this new information should enable physicians to help patients achieve an improved level of functioning while minimizing the potentially harmful effects of the illness or the treatments. The guidelines describe practical clinical assessment and management strategies tailored to the individual. Further, the guidelines emphasize the

**Table 1 Criteria for rating quality of published evidence in individual articles reviewed**

Ratings	Criteria
I	Evidence from at least one properly randomized controlled trial (RCT)
II-1	Evidence from well-designed controlled trials without randomization (pretest–posttest control group design)
II-2	Evidence from well-designed cohort or case–control analytic studies, preferably from more than one centre or research group
II-3	Evidence from repeated measures studies with no control group (one group pretest–posttest design)
III	Evidence from hypothesis-generating or exploratory studies (modelling, path-analytic or factor-analytic studies) or studies involving subanalyses
IV	Evidence from descriptive, observational, or qualitative studies (case reports, correlational studies, or secondary analyses); opinions of respected authorities, based on clinical experience; reports of expert committees
V-1	Evidence from a metaanalysis, with all studies included in the metaanalysis classified as RCTs
V-2	Evidence from “formal” review (reviews with detailed description of search strategies, such as Cochrane reviews)
V-3	Evidence from “informal” reviews that summarize others’ research, or publication that does not provide review details

benefits of combining physical or medical treatments with behavioural or lifestyle interventions. They reflect a biopsychosocial approach that includes both types of intervention as important aspects of a full treatment plan. The guidelines focus on interventions that are most likely to lead to the greatest benefit and least disruption for the individual patient and his or her caregivers. The medications mentioned include only those available in Canada at the time of writing. The guidelines do not address forensic issues such as criminal responsibility and provincial mental health acts that pertain in a general way to all mental disorders.

### Guideline Development Process

The development of these guidelines was sponsored by the Canadian Psychiatric Association (CPA). The Association has a Special Committee on Clinical Practice Guidelines that oversees the development of clinical practice guidelines. The Committee has written guidelines for CPG development that specify the process and standards that must be followed. The Committee reviews all CPGs before they are given final approval by the CPA Board. The Committee establishes working groups that produce the guidelines. The CPA raises and administers funds for guideline development. There is no contact between the funders and the working group that develops the guidelines. The working group circulates the guidelines to a wide range of stakeholders for review and comment before sending a final version to the Committee. A draft of

these guidelines was also circulated to industry for review and comment regarding errors of fact. All sponsorship is acknowledged when the guidelines are published, and any conflicts of interests of the individual working group members are indicated in the usual *Canadian Journal of Psychiatry* format.

For these guidelines, 2 evidence-based literature reviews were conducted, and their results were combined. One was related to specific treatments, and one was related to models of service delivery. These are described below in more detail. Recommendations were rated on levels of evidence according to an algorithm, also listed below. We also reviewed other schizophrenia clinical practice guidelines, using the AGREE instrument (5), which is designed to provide a framework for assessing the quality of CPGs. This framework and the results of a needs assessment survey were used to develop the outline of the current guidelines.

A systematic needs assessment was conducted with the target audience of psychiatrists. Two processes were used: a focus group at the annual CPA meeting and an on-line survey based on the AGREE framework. The on-line survey was sent to a random sample of 50% of the CPA members, and the response rate was 12%. Ninety percent of respondents were aware of the 1998 CPGs (6). The most frequently referenced section of this guideline was the section on management of refractory symptoms. The top 3 most frequent suggestions were to provide up-to-date information, clear recommendations, and a comprehensive biopsychosocial approach. Finally, the draft

**Table 2 Evidence level summary for rating evidence**

Evidence level	Description
A	Strong research-based evidence, for example, for interventions, consistent evidence from well-designed randomized controlled trials (RCTs); or a metaanalysis, with all the studies included in the statistical pooling classified as RCTs; or consistent evidence from well-designed cohort and case studies (categories I, V-1, II-2 from Table 1); for evidence relating to prevalence, consistent findings from appropriately designed studies
B	Moderate research-based evidence, for example, from well-designed controlled trials without randomization, cohort studies, case-control analytic studies, comparative studies with historical control, and repeated-measures studies with no control group; this rating is also used when there are well-designed RCTs favouring effectiveness, but the evidence from such trials is not consistent (II-1, II-2, II-3)
C	Weak or reasonable evidence from descriptive, observational, or qualitative studies (case reports, correlational studies, or secondary analyses); formal reviews; expert opinions or consensus in the field; hypothesis-generating or exploratory studies, such as modelling, path-analytic or factor-analytic studies, or subanalyses (III, IV, V-2)
D	No evidence of benefit or harm of treatment

guidelines were sent to a national advisory group for review and comment.

#### *Literature Search*

The search strategy covered publications issued between January 1992 and April 2004. In Medline, PubMed, Psycinfo, and CINAHL the following key words were used:

- conventional antipsychotic medications and tranquilizing agents, neuroleptic drugs, effective drug therapy, tranquilizing agents, adjunctive treatments, clozapine and efficacy and side effect profile, ECT, individual psychotherapy, group psychotherapy, family interventions, vocational rehabilitation, psychosocial skills, schizophrenia and social skills training, assertive community treatment, training in community living, family psychoeducation, behavioural family therapy, behavioural family management, cognitive therapy, cognitive-behavioural therapy, token economy
- schizophrenia treatment and group therapy, group homes, psychiatric department hospitals, day care, ambulatory care, outpatients
- cost-utility or cost-benefit analysis, cost effectiveness, health resources, quality of life, case management, outcome assessment, process assessment, patient satisfaction, performance monitoring, performance measures, performance indicators, access to treatment or health services, accessibility, quality indicators, quality measures, health care costs or cost of treatment, mental health delivery system, mental health services, models of care, community care, community mental health services,

hospital care, patient retention or physician-patient relations, patient engagement

In the Cochrane database and Cochrane DARE (Database of Abstracts of Reviews of Effectiveness) the search terms used were Cochrane Schizophrenia Group, as well as the key words schizophrenia and treatment.

#### *Screening Process*

Several steps were taken in the review process. First as mentioned, we conducted computerized searches of relevant literature. These searches were limited to English-language publications with study subjects aged 18 to 65 years. Second, we undertook a preliminary screening of the title and abstract for each reference to determine eligibility for inclusion in the database. Third, the appropriate references were imported into a Reference Manager, Version 10 database (7) specific to the CPG systematic review. As a result of these searches and the initial review of abstracts, 7707 references were imported into the database. A detailed assessment of each abstract and (or) article resulted in the removal of 5009 references. Reasons for exclusion were that the reference was an inappropriate publication type (that is, dissertation or letter) and the subject matter was irrelevant to the CPG update. During the CPG writing, members of the working group identified additional references. Some were papers of historical interest, whereas others were papers published before the dates encompassed in the evidence-based review. We ranked these in the same way as the references in the evidence-based

review and added them to the database. The final database contains 2864 references, with quality ratings assigned.

*Quality-Rating Process*

Each reference was given a quality rating by the research coordinator or research assistant, based on the guidelines provided in Table 1. Interrater reliability was established at the start, with at least 85% agreement on a random selection of 40 references. Each case of disagreement was reviewed with the working group chair, and consensus was reached. These guidelines were originally adapted from the Canadian Task Force Methodology ([www.ctfphc.org/methods.htm](http://www.ctfphc.org/methods.htm)), with further development based on study design detail obtained in *Foundations of Clinical Research: Applications to Practice* (8). Raters blinded to the author name and journal

gave clinical trials a second ranking system according to the Jadad Scale (see Appendix 1).

The final CPG recommendations were also ranked according to the strength of evidence supporting them. These rankings were determined by a consensus process involving the members of the Clinical Practice Guideline Working Group. Table 2 outlines the system for ranking the recommendations.

All the citations will be posted on-line with the CPGs. The score for each article will also be included. Rather than cite all possible references in the GPG, we cited references to be illustrative rather than comprehensive. Several systematic reviews are cited, particularly those that summarize the current balance of opinions.