Schizophrenia Practice Guidelines – An International Survey and Comparison

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Abstract

Background  Schizophrenia guidelines have been developed throughout the world. However, guidelines differ considerably in methodology and content.

Aims  To systematically compare national schizophrenia guidelines from different countries.

Method  An international survey was conducted on guideline development and a methodological comparison was carried out by means of a validated guideline appraisal instrument (AGREE).

Results  The methodological quality of many schizophrenia guidelines was at best moderate. Few guidelines included key stakeholders. Whereas pharmacotherapy recommendations were quite similar, there were strong variations in the type of psychosocial interventions recommended.

Conclusion  Guidelines’ methodological quality has a strong influence on its applicability. However, the lack of financial means to develop and implement guidelines is perceived as a main problem. Independent international organisations may contribute to define a core set of non-biased schizophrenia treatment recommendations. In countries with a shortage of resources, this could be a basis for adaptation to different cultural and economic backgrounds in collaboration with stakeholders.

Declaration of interest  This work was financed by the German Society of Psychiatry, Psychotherapy and Nervous Diseases DGPPN and the German Research Network on Schizophrenia within a guideline programme (S.W.). W.G. is one of the editors of the German schizophrenia guideline from 1998; J.M. is the Chairman of the US Steering Committee on Practice Guidelines.

Keywords

schizophrenia, guidelines, mental health services, international agencies
Mental health disorders pose an increasing burden on societies all over the world (Murray & Lopez, 1996). At the same time, treatment variations within and between countries are prevalent. In the case of schizophrenia, this holds true particularly for the prescription of psychotropic drugs in non-Western societies (Patel & Andrade, 2003; Apiquian et al, 2004), but also for the availability of psychosocial treatments. In different regions of the world, practice guidelines have been developed to improve schizophrenia care. There is no doubt that these practice guidelines have to be based on, or have to adequately consider, scientific evidence with regard to key treatment recommendations (McIntyre, 2002). The World Health Organisation (WHO) has developed Diagnostic and Management Guidelines for Mental Disorders in Primary Care (WHO, 1996) using a consensus approach. These guidelines have also been field-tested (Goldberg et al 1995) and served as a primer for the organisation of mental health systems in some countries. Nevertheless it remains unresolved how a core set of universally valid secondary and tertiary psychiatric care recommendations can be defined which can easily be used to develop national or regional mental health guidelines without disregarding local health systems or cultures.

The aim of the present study was (a) to collect available schizophrenia guidelines from different countries of the world; (b) to evaluate them according to predefined criteria; (c) to compare them with respect to key recommendations; (d) to get expert opinions about the possible impact on psychiatric care in the different countries; and (e) to collect information about possible support on establishing guideline development, implementation and evaluations made in other countries.

**METHOD**

**Guideline identification and assessment**

This guideline comparison project was commissioned by the WHO Regional Office for Europe (W.R.) and the World Psychiatric Association (WPA, N.S.; WPA, Section of Quality
Assurance in Psychiatry, J.M; WPA, Section of Schizophrenia, W.G.). To identify relevant guidelines, 122 member organisations of the World Psychiatric Association from 104 nations and other organisations concerned with guideline development in different countries were contacted by mail and asked to send original documents of national or local practice guidelines in the area of schizophrenia. In addition, the US-American National Guideline Clearinghouse (NGC), the Guidelines International Network (G-I-N), the Centres for Reviews and Dissemination (CRD) of the University of York, the German Guideline Clearinghouse of the German Board of Physicians, and the MEDLINE database (1966–February 2004) were screened for schizophrenia guidelines. Furthermore, scientific psychiatric journals were scanned. Written guideline documents were included that met the following criteria: The disorder was schizophrenia, with or without inclusion of schizoaffective disorder, psychiatric care of the acute and/or chronic phase was considered, the guideline had a national or regional scope, and the authors and the development process were described. Guidelines addressing one particular aspect of schizophrenia treatment and those developed primarily for international use by expert groups from different countries were not included.

To measure the scientific quality of practice guidelines, we selected a recently published instrument developed by an international group of guideline experts, the “Appraisal Guideline Research and Evaluation Europe” (AGREE) rating scale (AGREE collaboration, 2003). The AGREE instrument assesses both the quality of reporting, and the quality of the guideline development process. It provides an appraisal of the predicted validity of a guideline, which is the likelihood that it will achieve its intended outcome. The AGREE instrument consists of 23 key items grouped into six domains with a 4-point Likert scale to score each item: The six domains are: (1) scope and purpose (3 items), (2) stakeholder involvement (4 items), (3) rigour of development (7 items), (4) clarity and presentation (4 items), (5) applicability (3 items), and (6) editorial independence (2 items). Each domain is intended to capture a separate dimension of guideline quality. The total score and the domain scores are calculated
by summing up the scores of the individual items within a domain or the whole six domains, and by standardising the total as a percentage of the maximum possible score. The interrater reliability (intraclass correlations, ICC) for each AGREE domain lies between 0.39 (clarity and presentation) and 0.83 (rigour of development) with two reviewers and between 0.57 – 0.91 with four reviewers (AGREE collaboration, 2003). Two reviewers used this instrument independently, and in the case of disagreement, the average scores were computed. For guidelines written in languages other than English, German, French, Spanish or Italian, we asked assistant doctors with adequate foreign-language skills to extract the relevant information. Therefore, the assessments could not be made blind to the origin of the guidelines. All reviewers received a standard instruction how to use the AGREE instrument.

**Content analysis of guidelines and international guideline survey**

In addition to the AGREE assessment, guidelines were compared with respect to key recommendations, including the following: (1) Pharmacological first-line therapy in acute psychosis (non first-episode) and in treatment-resistant schizophrenia; (2) antipsychotic dosage for acute and maintenance treatment; (3) recommended duration of antipsychotic treatment after first and multiple episodes; (4) management of side effects with first generation antipsychotics; (5) antipsychotic polypharmacy; (6) recommendations for therapy of depressive symptoms; and recommendations for (7) psychoeducation, (8) cognitive behaviour therapy, (9) employment promotion and (10) community treatment.

A survey questionnaire was developed and sent to the WPA member organisations together with the request to send guideline documents. The questionnaire covered questions of guideline use, development and implementation in the respective countries, barriers for guideline development and implementation, and a question about the potential benefit of WHO or WPA help in producing or adopting guidelines for national use.
RESULTS

Identification of guidelines

A total of 27 guidelines from 22 different countries could be identified, published between February 1994 and February 2004 (Fig 1). Two guidelines (Thailand and Japan) could not be evaluated due to language problems, and one guideline (Sweden) could not be retrieved. Therefore, 24 guidelines were evaluated with regard to methodological quality (AGREE guideline appraisal instrument) and content.


13 of 24 guidelines were developed by national psychiatric associations or national boards of physicians, five were developed by health ministries or statutory institutions, and six were developed by independent groups of experts.
**Methodological quality of guidelines**

The methodological quality of the majority of guidelines was moderate (Table I). The National Institute for Clinical Excellence (NICE) guideline (GB1) had the highest methodological quality according to AGREE and the highest scores in five out of six domains, followed by the second edition of the US-American American Psychiatric Association (APA) guideline and the Australian Royal Australian and New Zealand Royal College of Psychiatrists (RANZCP) guideline. However, these three guidelines were completely different. NICE guideline’s strength was in the rigour of development and applicability, and recommendations were evidence-based with a clear description how evidence was synthesised. There were explicit links between recommendations and supporting evidence, but the reader cannot find usable textbook-like background information quickly. On the contrary, the APA guideline’s strength was in the clarity of presentation of different options and the available background information. The RANZCP guideline was methodologically strong in most domains, rather concise and had a special focus on prodromal symptoms and first episode care.

Most guidelines (19/24) did not include key stakeholders like patients or relatives. A systematic literature search with specific inclusion criteria was performed for only 7/24 guidelines. 10/24 guidelines stated how the evidence was synthesised, however, for only 9/24 guidelines there was an explicit link between the recommendations and the supporting evidence. In 18/24 guidelines the majority of the recommendations concerned medication therapy. The average numbers of recommendations were 9 for general management, 26 for medication management, 5 for psychological therapy, and 11 for social therapy or the organisation of mental health services. In only 10/24 guidelines the resources of the respective health system or local systems of care were explicitly taken into account in formulating the recommendations. Only 3/24 guidelines considered health-economic effects of the treatment options or other cost issues (AUS, FIN, GB1), and 5/24 guidelines referred to particular
cultural, ethnic or socioeconomic issues either in diagnostic assessment or treatment planning (AUS, DK, GB1, SGP, USA1). Most guidelines had a text format, and 12/24 included also algorithms. In 15/24 guidelines recommendations were operationalised to some degree, however, in 9/24 guidelines it was hard to identify key recommendations.

Only a minority (4/24) had patient versions of the guideline (AUS, GB1, SGP, ZA). In 8/24 guidelines editorial independence was explicitly stated (AUS, FIN, N, GB1, GB2, SGP, USA1, USA2). 3/24 guidelines disclosed pharmaceutical sponsoring for guideline development, however, in at least four more cases the organisation responsible for guideline development received pharmaceutical sponsoring and grants. Only 6/24 guidelines were reviewed externally by reviewers not involved in guideline development.

**Content analysis of guidelines**

We identified some fields with significant agreement among guideline recommendations. However, in other areas, guidelines differed considerably (Table 2). 9/24 guidelines recommended second generation antipsychotics (SGA) as first-line therapy in multi-episode psychosis, 13/24 recommended first generation antipsychotics (FGA) or SGA, and one recommended only FGA. Most guidelines recommended FGA dosages between 300 and 1000 mg chlorpromazine equivalents (CPZ) for acute care, however, there were two newer guidelines (AUS, N) recommending doses between 200 and 400 mg CPZ. All available guidelines dealing with medication issues recommended clozapine for treatment-resistant schizophrenia with comparable optimal dosages. Whereas most guidelines recommended antipsychotic maintenance treatment to be continued for at least one year after a first psychotic episode and for at least five years after multiple episodes (with the exception of CAN2 and GB1), the recommended dosages for FGA maintenance treatment varied between 150 and 900 CPZ. In the case of side effects with FGA, switching to SGA was more often
recommended than dose reduction. All guidelines recommended pharmacological antidepressive therapy as first-line treatment of depressive symptoms.

We found large variations in the type and frequency of psychosocial interventions recommended. A majority of guidelines (14/24) recommended some kind of family support or family involvement, and half of them (12/24) had recommendations for psychoeducational interventions and vocational rehabilitation. However, recommendations concerning psychosocial interventions were generally not detailed. Only six guidelines (AUS, DK, FIN, GB1, N, USA1) gave background information and detailed recommendations for specific mental health community treatment.

Survey about guideline development and implementation in different countries

21 of the 122 requested WPA member organisations (17.2%) responded to the questionnaire: five Asian countries – Azerbaijan, China, Israel, Russia, and Turkey - ; one American country – USA - ;13 European countries – Czech Republic, Denmark, Finland, Germany, Great Britain, Latvia, Lithuania, Norway, Netherlands, Poland, Slovenia, Sweden, and Spain -; and two African countries - Kenya and Uganda. All responses came from presidents or scientific secretaries of national psychiatric associations.

For 16 of the 21 countries, national schizophrenia guidelines used in the country were available. Most respondents were positive about guideline development, only one country representative in Asia rejected guidelines due to concerns regarding legal exploitation. In four of five Asian countries, in the two African countries as well as in all of the five Eastern European countries, foreign guidelines (primarily American Psychiatric Association, GB-Royal College of Psychiatrists, and Northern European guidelines) or WHO primary care guidelines had been translated or adopted for national use. In 7/9 countries with national health systems, the Health Ministry supports, coordinates or regulates guideline development also in the field of schizophrenia. In all statutory health insurance systems, but also in some
national health systems, national psychiatric associations are the only institutions concerned with schizophrenia guideline development. For the majority of countries (11/21) respondents declared that no efforts had been made to implement or evaluate guidelines. In these countries, guidelines had only been disseminated. In most countries (13/21) national guideline development with local adaptation was considered as most important, but international help and comparison are also welcomed (18 out of 21). With one exception, all countries (20/21) would appreciate WPA and/or WHO help in the following fields: Definition of standards, access to guidelines, exchange between guideline developers, advice in adaptation and expertise.

The main obstacles for guideline development and use as perceived by the countries’ representatives were: lack or shortage of available financial and human resources to develop guidelines (7/21); the need for regular updates (6/21); the academic approach restricting its application (4/21); the lack of considering cultural issues (4/21); the lack of financial means to implement treatment recommendations (4/21); the complexity of treatment options (3/21); low adherence rates and lack of physicians’ interest (3/21); changing diagnostic criteria, therapeutic possibilities (3/21); pharmaceutical company power (2/21); the lack of guideline evaluation results (2/21); and the fear of legal obligation (2/21).

DISCUSSION

Methodological quality of guidelines

Our results show that besides their generally moderate rigour of development, many national schizophrenia guidelines were difficult to apply and had a low legitimisation base, as most development processes did not include key stakeholders other than psychiatric experts. Only a minority had additional patient versions, few guidelines were reviewed externally, and the majority of guidelines did not consider available national or local psychiatric care systems or cultural or socioeconomic issues.
We could show a remarkable superiority of the National Institute for Clinical Excellence’ (NICE) schizophrenia guideline with respect to methodological quality. One explanation might be that this guideline was developed as part of a national policy within an established guideline programme adequately resourced by the health authorities.

It is still not yet clear what guideline quality actually means, and how it can be assessed in an optimal way. With AGREE we used a validated guideline assessment instrument. However, scores relied on how well documented the guideline development process was (Hayward et al, 1995). It is obvious that the quality of a guideline is not only indicated by its explicit scientific evidence base. Factors that are likely to influence implementation are also their applicability in terms of specificity, affordability and acceptance of recommendations. This was reflected by our survey results which point to a considerable gap between desire and reality in guideline development and dissemination in many countries. On the one hand, most countries do not have sufficient resources to review the evidence base systematically on their own in order to improve the guideline’s methodological quality. On the other hand, simply taking over the scientific evidence from US-American, European or Australian guidelines would neither improve the resulting recommendations’ validity nor their acceptance. Search criteria, outcome measures, the set of interventions selected and populations included in experimental studies are subject to ethnic and cultural biases and to value judgements. Furthermore health-economic trade-off decisions may vary according to the resources available in different countries. For example, in countries with marked health inequalities it may be advisable to use both socio-economic and medical evidence for guideline development (Aldrich et al, 2003). In low or middle income countries, it might be more easily achievable to focus on stakeholder involvement, adequate wording and inclusion of local care systems and culture, instead of systematically reviewing the great number of experimental studies available in the literature. The dilemma of culture bias in efficacy studies yet remains unresolved.
Comparison of recommendations

Most guidelines gave more detailed recommendations in the field of medication treatment than in the field of psychosocial therapy. Antipsychotic medication choice was a major concern with the exception of two documents dealing primarily with psychosocial issues (Nordentoft et al., 2001; Scottish Intercollegiate Guidelines Network, 1998). Whereas in some fields recommendations were quite similar among guidelines (clozapine in case of treatment resistance, antidepressant use, and duration of long-term antipsychotic treatment), others differed widely (management of side effects, dose recommendations, and antipsychotic polypharmacy). In the last decade an increasing amount of studies have compared second generation antipsychotics (SGA) to first generation antipsychotics (FGA). There have been activities all over the world, which promote their use despite higher short-term costs (Sartorius et al., 2003). Our results show that SGA have found their way into most schizophrenia guidelines, both as first line therapy as well as treatment option in the case of side effects with FGA. However, while health economic data showing lower total costs of treatment with SGA through a reduction of inpatient treatment despite higher short term medication costs (Hamilton et al., 1999), stems from developed countries, it is far from clear if this holds true also for less developed countries. In countries with extreme shortage of resources, substituting SGA for FGA may cut investments in psychosocial treatments if the total amount of money provided by governments for the treatment of mental disorders does not increase.

In contrast to psychotropic medication, recommendations for psychosocial treatment of schizophrenia were very general and unspecific in many cases. With the exception of one US-American guideline (Lehman et al., 2004) those guidelines with detailed recommendations on psychosocial treatments came from countries with national health systems. That non-drug treatments were considered to a lower degree may be due to the medical perspective of the
Guideline developers, the main target group being psychiatrists whose focus is often dug
treatment, or due to pharmaceutical company support for guideline development.

Guideline content analysis suggested that in many occasions some few reference
guidelines may have been used as primers for others. Among those putative reference
guidelines are the PORT recommendations (Lehman et al, 1998) and the APA guideline
(APA, 1997).

**Problems of worldwide schizophrenia guideline surveys**

The methods we used to identify relevant schizophrenia guidelines do not guarantee that a representative sample had been included. Most guidelines were developed in Europe, USA or Australia. Many requested country representatives did not reply to our survey thus preventing unpublished guidelines from this countries being included. In particular, we could find few guidelines from less developed countries. No Latin American country was included. This limits the generalisability of our survey results comparable to culture biases in treatment efficacy studies as most experimental studies have been carried out in the rich countries of Europe or North America. Future guideline surveys might use other sources to identify relevant documents particularly in less affluent countries such as other national or regional psychiatric organizations or national guideline experts in addition to WPA representatives, medical databases and registered national guideline programmes.

Similarly, the responses of psychiatric associations may not be representative of the whole situation in the different countries. The answers remain as opinions, however, of organisations authorised to represent a group of physicians.

This comparison did not assess whether guidelines used the available evidence adequately in formulating key recommendations. Neither by an evaluation of the methodological quality nor by a comparison of guideline statements in certain areas is a judgement possible about the extent guidelines’ recommendations improved psychiatric care in a particular region.
The originality of this study lies in the systematic comparison of nationally used schizophrenia guidelines including those regarded as relevant by key representatives of the countries’ psychiatric community. Most available most guideline comparisons in the field of mental health have used published or easily accessible guidelines restricting the results more strongly to the Western European or US-American region (Milner et al, 2002).

**Implications: Future directions for guideline development in different countries**

Developing evidence-based mental health guidelines all over the world brings about several challenges. Systematic literature reviews are expensive and time-consuming. Furthermore if conflicting interpretation of the results of different reviews result, decision rules must be established, professional, methodological and consensus judgements must be carried out and a variety of meetings must be organised. The availability of meta-analyses or systematic reviews may lessen the need to assess the evidence base for each newly developed guideline. However, a major challenge will be the development of ethical clinical standards as well as evidence-based guidelines that are both affordable and acceptable in different countries (Rutz, 2003). Besides setting up national mental health programmes, the improvement of national disorder-specific mental health guidelines could be of considerable importance in changing mental health treatment and professional performance. As schizophrenia shows a highly variable course in different countries possibly due to cultural influences (Jablensky et al, 1992), cross-cultural differences have to be reflected also in schizophrenia guidelines. If there is a shortage of time or resources to develop guidelines in some countries, an internationally acceptable and value-free core set of recommendations could be developed as a basis for national or local guideline elaboration. This could be facilitated by independent and international organisations such as the WHO and the WPA. These core recommendations could then be used for adaptation to different cultural, economic and other backgrounds in collaboration with stakeholders of the respective countries and regions. This approach could
lead to a reduction of pharmaceutical company sponsorship for national guideline
development programs particularly in the less affluent countries provided that WHO/WPA
recommendations are truly independent. In addition to this, guideline dissemination and
implementation strategies needs to be developed within the respective countries. Despite the
importance of guideline implementation programmes there is an imperfect evidence base to
support specific tools (Grimshaw et al, 2004).

Clinical Implications

• The methodological quality of most schizophrenia practice guidelines is at best moderate
• Recommendations for pharmacotherapy were quite similar among guidelines, however,
those for psychosocial treatment were very general and unspecific in many cases
• An independent international group may develop a core set of schizophrenia treatment
recommendations which could be used for adaptation to different cultural, economic and
other backgrounds in collaboration with stakeholders of different countries

Limitations

• Reviewed guidelines may not be representative of the situation in different countries
• The influence of guidelines on clinical practice could not be assessed
• The WPA respondents to the guideline survey may not have given comprehensive
information about guideline issues in the respective countries
REFERENCES


World Health Organization (1996) *Diagnostic and Management Guidelines for Mental Disorders in Primary Care: ICD-10 Chapter V Primary Care Version*. Goettingen: Hogrefe & Huber.

Figure I  Guideline identification and guideline survey response
## Table I  Methodological quality of practice guidelines

<table>
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<th>Practice guideline developer (year)</th>
<th>AGREE domain²</th>
<th>Total AGREE score</th>
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**Average score**  
50  23  34  52  18  51  37

1. Numbers are given as percentage of maximum available scores  
2. AGREE indicates Appraisal Guideline Research and Evaluation Europe  
3. AUS (Australia), Royal Australian and New Zealand College of Psychiatrists (RANZCP); A (Austria), Austrian Society of Psychiatry and Psychotherapy; CAN1 (Canada), The Canadian Psychiatric Association; CAN2 (Canada), College of Physicians of Quebec; CZ (Czech Republic), Czech Psychiatric Association; DK (Denmark), Danish Psychiatric Association; E (Spain), Spanish Society of Psychiatry; FIN (Finland), The Finish Medical Society DUODECIM; D (Germany), German Society for Psychiatry, Psychotherapy and Nervous Disease DGPPN; GB1 (Great Britain), National Institute for Clinical Excellence NICE; GB2 (Scotland), Scottish Intercollegiate Guidelines Network SIGN; LV (Latvia), Latvian Psychiatric Society; LT (Lithuania), Chief Psychiatrist of Lithuanian Ministry of Health; NL (Netherlands), Psychiatric Association of the Netherlands; N (Norway), Norwegian Psychiatric Association and Health Ministry; SGP (Singapore), Ministry of Health of Singapore; SLO (Slovenia), Slovenian Republic Psychiatric Collegium; USA1, American Psychiatric Association APA; USA2, Patient Outcomes Research Team PORT; USA3, The Expert consensus panel; USA4, The Texas Medication Algorithm Project TMAP project group; USA5, The Mount Sinai conference on the pharmacotherapy of schizophrenia; ZA (South Africa), Mental Health Information Centre South Africa