

Clinical Overview Article

Standardized remission criteria in schizophrenia

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Objective: Recent work has focussed on schizophrenia as a ‘deficit’ state but little attention has been paid to defining illness plasticity in terms of symptomatic remission.

Method: A qualitative review of a recently proposed concept of remission [N.C. Andreasen, W.T. Carpenter Jr, J.M. Kane, R.A. Lasser, S.R. Marder, D.R. Weinberger (2005) *Am J Psychiatry* 162: 441] is presented.

Results: The proposed definition of remission is conceptually viable, and can be easily implemented in clinical trials and clinical practice. Its increasing acceptance may reset expectations of treatment to a higher level, improve documentation of clinical status and facilitate dialogue on treatment expectations. The availability of validated outcome measures based on remission will enhance the conduct and reporting of clinical investigations, and could facilitate the design and interpretation of new studies on cognition and functional outcomes. While useful as a concept, it is important to consider that remission is distinct from recovery.

Conclusion: The introduction of standardized remission criteria may offer significant opportunities for clinical practice, health services research and clinical trials.

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Clinical Recommendations

- That patients with a diagnosis of schizophrenia have the potential to achieve remission is a challenging but important concept. The definition of remission is conceptually viable, and can be easily implemented in clinical trials and clinical practice.
- Remission criteria challenge to re-evaluate our expectations for patients, to set more ambitious goals for long-term outcomes, and to communicate these to our patients. In doing so, while remaining within reasonable limits, we may help patients and their families to think more positively about their illness, and to regard schizophrenia as a manageable disorder.
- Acceptance and application of the criteria has the potential to improve documentation of clinical status in medical records, by providing an objective measure of illness course and treatment effect that is applicable to routine clinical care.

Additional comments

- Remission is not the same as recovery, which is a higher hurdle and long-term goal.
- Remission criteria can be applied only to patients who have previously been diagnosed using recognized criteria.
- Although the criteria are not set unreasonably high, not all patients may achieve this degree of improvement.
- Application of the criteria does not imply or depend on any preconceptions about the causal mechanisms underlying the illness, or those that may have brought about remission (i.e. remission can be spontaneous or can be achieved as a result of treatment).

Introduction

A 2002 review article in the prestigious journal *Science* (1) stated that ‘once the symptoms of schizophrenia occur (usually in young adulthood) they persist for the entire lifetime of the patient and are almost totally disabling’. This statement flies in the face of evidence, collected over a century of research, that there is a high level of heterogeneity in the course and outcome of schizophrenia and that symptomatic remission is common (2). However, even though the DSM criteria for schizophrenia have remained essentially similar over the last decade, a degree of therapeutic pessimism in the context of an informal redefinition of schizophrenia as a permanent ‘deficit’ brain disorder is noticeable. While there is certainly evidence that a proportion of patients with a diagnosis of schizophrenia have poor outcome, and it is possible to apply criteria of ‘deficit’ to these, it could be argued that patients and clinicians are also in need of criteria for remission that, if patients do not fulfil them, represent something that patients and clinicians can work towards.

Two working groups, one US and one European, have recently considered the question of symptomatic remission in schizophrenia, culminating in a recent publication by the US working group, in which a consensus definition of remission in schizophrenia was proposed and, based on this definition, specific operational criteria for assessment of remission in patients with a diagnosis of schizophrenia were developed (3). The timely introduction of remission criteria for schizophrenia will help clinicians, patients and relatives refocus on positively formulated, achievable and objective treatment outcomes and facilitate the assessment of the true heterogeneity of psychotic disorders. The proposed symptomatic remission criteria consist of two elements: a symptom-based criterion covering the core symptoms of schizophrenia (low scores on eight diagnostically relevant symptoms in the Positive and Negative Syndrome Scale (PANSS):

1. Delusions; 2. Unusual thought content; 3. Hallucinatory behaviour; 4. Conceptual disorganization; 5. Mannerisms/posturing; 6. Blunted affect; 7. Passive/apathetic social withdrawal; 8. Lack of spontaneity and flow of conversation), coupled with a time criterion (duration of 6 months). The symptom-based criterion can also be assessed using the Brief Psychiatric Rating Scale (BPRS) and Scale for Negative Symptoms/Scale for Positive Symptoms (SANS/SAPS).

Aims of the study

The aims of the study were to i) analyse the remission criteria, with a particular focus on the possible advantages and uses of symptomatic remission criteria in schizophrenia, ii) provide strategies for clinical validation, and iii) discuss how remission ought to be distinguished from recovery.

Material and methods

In order to address the aims of the study, a comparison with the literature on the concept of remission in disorders other than schizophrenia was conducted and reported. A literature search was also conducted to identify early attempts at validation of the remission criteria.

Results

Standardized remission criteria in psychiatric disorders

Analysed in the context of the literature on remission in non-psychotic disorders, the development of criteria for remission of schizophrenia appears to be a welcome and timely development. In major depression, the concept of remission was first contemplated more than 20 years ago (4), and remission is now regarded as a realistic treatment goal for not only patients with depression, but also patients with anxiety disorders, regardless of the fact that such illnesses often run a waxing and waning

Table 1. Proposed remission criteria and relationship to diagnostic criteria

Diagnostic criteria		Remission criteria
DSM-IV (at least 2 are present)	ICD-10	PANSS items (score 3 or less on all items)
Delusions	Delusions Thought echo, insertion or withdrawal; thought broadcasting	P1. Delusions G9. Unusual thought content
Hallucinations	Hallucinations	P3. Hallucinatory behaviour
Disorganized speech	Breaks in train of thought; incoherence or irrelevant speech	P2. Conceptual disorganization
Grossly disorganized or catatonic behaviour	Catatonic behaviour	G5. Mannerisms/posturing
Negative symptoms	Negative symptoms (apathy, paucity of speech, blunting or incongruity of affect) Loss of interest; aimlessness; idleness; self-absorbed attitude; social withdrawal	N1. Blunted affect N4. Passive/apathetic social withdrawal N6. Lack of spontaneity and flow of conversation

course when followed over longer periods of time (5–7). The suggestion that symptomatic remission is an achievable objective for a significant proportion of patients with a diagnosis of schizophrenia is a challenging but not unreasonable concept, given the ongoing improvements in our understanding of the condition and its course, and the ongoing search for better treatments. As clinicians, we are challenged to re-evaluate our expectations for patients, to set more ambitious goals for long-term outcomes, and to communicate these to our patients. In doing so, while remaining within reasonable limits, we will help patients and their families to think more positively about their illness, and to regard schizophrenia as a manageable disease.

Analysis of consensus criteria for remission

The criteria proposed by the US working group focus on the three dimensions of psychopathology that have been identified within schizophrenia (negative symptoms, disorganization and psychoticism). These three dimensions correspond to five separate symptom domains in the DSM-IV and ICD-10 diagnostic criteria (Table 1). Likewise, the five symptom domains of DSM-IV and ICD-10 are represented by eight items of the PANSS scale (8), as shown in Table 1. As the PANSS scale provides ratings that are not only based on symptom severity, but also on functional impairment, the US and European groups considered that a score of mild or less (PANSS score of three or less) simultaneously on all eight items was representative of a level of impairment consistent with symptomatic remission of the illness. It was proposed that for a patient to be regarded as being in remission, the symptom severity criteria should be achieved for a minimum period of 6 months.

Another issue relates to the PANSS items selected, and the reason to include some and not all PANSS items in the criteria. Clearly, the eight

items used to define remission are the most diagnostically specific for schizophrenia of all those in the PANSS scale. Other items (e.g. depression, anxiety, guilt) relate to symptoms that are not diagnostic for schizophrenia. So, as is the case for the remission criteria for depression, limiting the criteria to these core diagnostic symptoms provides for both specificity and sensitivity. Use of the criteria in clinical trials will allow further validation and elucidation of the most meaningful predictors (i.e. which PANSS items are most sensitive in detecting a state of remission). This may lead to refinements of the current criteria.

Other factors, such as cognitive deficits, psychosocial functioning, and suicidality might also be encompassed by a definition of remission, but the current criteria focus on remission of core symptoms of the illness. It is reasonable that symptom domains that are not diagnostically relevant or characteristic for the disorder should not be included. Importantly, functional outcomes are also highly influenced by other factors, such as healthcare provision and cultural issues, which show great geographic and socioeconomic variability. Moreover, given the lack of universally recognized assessment instruments, and the multiple influences on both cognition and psychosocial functioning, these aspects of the disorder are currently beyond the scope of any employable and practical definition.

Another valid reason to base the criteria on the severity of core psychopathology is that decisions around admission to (and discharge from) hospital are most often based on the severity of these symptoms. While symptoms of excitement also have an influence on hospital admission, it is rare for patients with a diagnosis of schizophrenia who are no longer acutely psychotic to be excited. Moreover, as excitement is not a diagnostic symptom, it would be unreasonable to add it to the remission criteria.

The time criterion of 6 months is to some extent an arbitrary cut-off. However, a shorter cut-off period would be insufficient to permit validation of sustained and stable improvement. A 6-month period is long enough to be meaningful from a clinical perspective, and provides a useful framework for assessment and research on long-term outcomes. Being 'in remission' would therefore mean that symptoms had been at a low level and stable, both of which are necessary for improvements in day-to-day functioning.

Remission is not recovery

The proposed criteria clearly encompass symptomatic remission only, and moreover do not require symptoms to be completely absent. This is in line with the remission criteria currently applied to other chronic illnesses with relapsing and remitting courses, such as multiple sclerosis, where remission is associated with some residual symptomatology (9), and also with the remission criteria developed for use in other chronic psychiatric conditions. The severity thresholds proposed are such that symptoms will not interfere significantly with day-to-day functioning, although it must be acknowledged that being in symptomatic remission does not necessarily mean that the patient is functioning well, because other components of the illness (such as enduring affective or cognitive symptoms) may lead to functional impairments. This definition of symptomatic remission is clinically meaningful, appears achievable for a significant proportion of patients in routine clinical practice, and is applicable across the course of the illness (i.e. to those with a recent onset, as well as more chronically ill patients). Remission is a necessary (but not sufficient) step towards recovery, which is a higher hurdle and longer-term goal. We anticipate that possible future operational definitions of recovery, in the sense of moving forward and rebuilding one's life, will incorporate improvements in other areas, such as empowerment, quality of life and psychosocial functioning.

Validation strategies

The first applications of remission criteria suggest that around two-thirds of patients who are considered clinically 'stable' in fact do not meet criteria for remission. Of these, around 30% do move into remission over the course of 1 year with adequate treatment (10). These data suggest that application of remission criteria is extremely useful, as clinically 'stable' patients in fact show significant plasticity in terms of moving to better clinical outcomes

when exposed to adequate treatment, and this appears to be adequately captured by application of remission criteria. Another longitudinal study examined the validity of the remission criteria in terms of whether changes in remission status would be associated with parameters of needs, satisfaction, social functioning and quality of life, and found that change over time in the symptomatic remission criterion was associated with substantial changes in unmet needs, GAF scores, satisfaction with services and, to a lesser extent, quality of life (11). While more studies are needed, these first analyses suggest that the remission concept may have sufficient plasticity and validity for use in clinical practice, health services research and clinical trials.

Discussion

It is essential to point out that the remission criteria can be applied only to patients who have previously been diagnosed using recognized criteria. Furthermore, although the criteria are not set unreasonably high, not all patients may achieve this degree of improvement. While fulfilling the remission criteria does not mean that the diagnosis is no longer applicable, use of the time criterion should ensure that reductions in symptoms are robust and sustained. Application of the criteria does not imply or depend on any preconceptions about the causal mechanisms underlying the illness, or those that may have brought about remission (i.e. remission can be spontaneous or can be achieved as a result of treatment).

That patients with a diagnosis of schizophrenia have the potential to achieve remission is a challenging but important concept. The definition of remission is conceptually viable, and can be easily implemented in clinical trials and clinical practice. We anticipate that its increasing acceptance will reset our expectations of treatment to a higher level, allowing us to set achievable and realistic treatment goals, and to better articulate our expectations for patients. Acceptance and application of the criteria has the potential to improve documentation of clinical status in medical records, by providing an objective measure of illness course and treatment effect that is applicable to routine clinical care. Improving the longitudinal documentation of clinical status should facilitate dialogue on treatment expectations among physicians, patients and carers, healthcare administrators, and policy makers.

The availability of improved, consolidated outcome measures based on remission will enhance the conduct and reporting of clinical investigations,

and could facilitate the design and interpretation of new studies of the impact of psychopathology and other factors such as cognitive deficits on functional outcomes. We anticipate that as the remission concept becomes more recognized among the clinical and research community, so the criteria will be applied in clinical trials, which will thus provide objective validation.

The availability of clinically meaningful outcome measures will also help to promote research studies on longer-term outcomes. This is in line with the recommendations of authorities such as the National Institute for Clinical Excellence in the UK, given their preference for studies with longer-term outcomes that are clinically meaningful for patients (12, 13).

Declaration of interest

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