



Consensus five factor PANSS for evaluation of clinical remission: effects on functioning and cognitive performances

Federica Pinna ^a, Marta Bosia ^{b,c}, Roberto Cavallaro ^{b,*},
Bernardo Carpinello ^a, for the Cagliari Recovery Group Study

^a Department of Public Health. Clinical and Molecular Medicine-Section of Psychiatry, University of Cagliari, Via Liguria 13, 09127 Cagliari, Italy

^b Department of Clinical Neurosciences, IRCCS San Raffaele Scientific Institute, Via Stamira d'Ancona 20, 20127, Milan, Italy

^c Institute for Advanced Study, IUSS, Center for Neurolinguistics and TheoreticalSyntax (NeTS), Piazza della Vittoria 15, 27100 Pavia, Italy

ARTICLE INFO

Article history:

Received 1 August 2014

Received in revised form 23 October 2014

Accepted 3 November 2014

Keywords:

Schizophrenia

Remission

PANSS factors

Cognition

Functioning

ABSTRACT

Criteria developed by the Remission in Schizophrenia Working Group (RSWG), based upon 8 core symptoms of PANSS, are generally used for evaluation of Remission. However, some concerns have arisen as regard to the ability of the RSWG criteria to detect truly remitted cases. This study aims to compare the severity criteria of remission defined by the RSWG (RSWG-cr) with more restrictive criteria, based upon the use of PANSS factor model.

Methods: 112 chronic psychotic outpatients were examined. Symptomatic remission according to RSWGcr was compared with remission according to criteria based on the 20-items of PANSS considered in the consensus five factor model (PANSS-FCTcr), in relation to functional and neurocognitive outcomes.

Results: Data from the study demonstrated the superiority of PANSS-FCTcr in identifying patients with higher functional and cognitive outcomes.

Conclusion: PANSS-FCTcr seems to be suitable for use in both common clinical practice and research setting, being associated with improved identification of truly remitted patients.

© 2014 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

1. Introduction

Symptom remission represents the principal target for psychopharmacological interventions (Bottlender et al., 2013; Nasrallah and Lasser, 2006) and it is considered the main component underlying clinical recovery (Emsley et al., 2011), together with improved functioning (Brissos et al., 2011; Lysaker et al., 2010). A series of different criteria has been used to evaluate remission (Cassidy et al., 2010). Currently the Remission in Schizophrenia Working Group criteria (RSWGcr) (Andreasen et al., 2005) may be considered the most widespread method to evaluate remission. RSWGcr have been proved to be conceptually viable and easy to use in both clinical trials and clinical practice. According to RSWGcr, clinical remission is fundamentally based on a symptom severity criterion. Using the Positive and Negative Syndrome Scale (PANSS), remission is evaluated on the basis of eight items of the scale, chosen as being the most diagnostic-specific for schizophrenia, thus excluding symptom domains not diagnostically relevant for the disorder. Although evaluation of remission includes a six-month duration, the symptom severity criterion alone was used in large amount of studies (AlAqueel and Margolese, 2012). As PANSS scale provides ratings investigating not only symptom severity *per se* but also functional impairment, a score of "mild" or better (i.e. 3 points or less) at

all eight "core" symptoms was considered sufficiently representative of a level of impairment consistent with symptomatic remission of the disorder (Van Os et al., 2006a). A number of studies demonstrated the validity of these remission criteria using two different approaches, namely comparison of different definitions of symptomatic remission and association of remission criteria with various outcome dimensions, mainly overall symptomatic status and functional outcome (Lambert et al., 2010). However, several recent studies seem to highlight the potential limitations of severity criteria, as currently conceived, in predicting functioning and other important outcome variables (Karow et al., 2012; Oorshot et al., 2012; Pinna et al., 2013a). Moreover, the use of more stringent criteria of remission, based upon all items of PANSS, was recently reported to be associated with improved identification of truly remitted patients, thus suggesting that the entire scale should be preferred, at least for research purposes (Pinna et al., 2013b). As well-known, the items of PANSS are divided in three subscales (the Positive, the Negative and the General psychopathology scale), but several factor analyses showed that five-factor models better characterize PANSS data. Different model versions may be found in literature, recently merged in a "consensus" five-factor model of the PANSS, based upon 20 items, categorized into Positive, Negative, Disorganized/Concrete, Excited and Depressed factors (Wallwork et al., 2012). Starting from these premises, we hypothesized that using the 20 items of PANSS included in this "consensus" five factor model could lead to results in identifying cases of remission better than those obtained using the eight items indicated in RSWG criteria.

* Corresponding author at: Department of Clinical Neurosciences, IRCCS San Raffaele Scientific Institute, Via Stamira d'Ancona 20, 20127, Milan, Italy. Tel.: +39 0226433218; fax: +39 0226433265.

E-mail address: cavallaro.roberto@hsr.it (R. Cavallaro).

2. Methods

2.1. Sample

The present study is a part of an ongoing study on recovery (Carpiniello et al., 2012; Pinna et al., 2013a,b) which included all outpatients with a diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV-TR, attending a University Community Mental Health Centre (CMHC) in the year 2010, who agreed to participate in the study. Subjects with other comorbid psychiatric and/or somatic disorders were included in the study, except those with comorbid mental retardation or organic brain diseases. All patients received standard care as generally occurs in CMHCs in Italy (clinical monitoring at least on a monthly basis; pharmacological treatment; home care when required, psychosocial and rehabilitation interventions tailored to patient's needs). The study was approved by the institutional Ethical Committee of Local Health Unit of Cagliari (Italy) and was conducted according to national laws. The protocol followed the principles of the Declaration of Helsinki.

2.2. Ratings

Residents in psychiatry performed evaluations using a set of standardized methods, after adequate training in use of all instruments adopted. Personal and social data, and clinical history were collected through a structured interview purposely developed for the study. After providing informed consent, patients were interviewed by means of the Italian versions of SCID-I and SCID-II (First et al., 2000, 2003); inter-rater reliability, assessed using Cohen's K before the study, was higher than 0.80. Symptom severity was evaluated using the Italian version (Panzeri et al., 1995) of PANSS (Positive and Negative Syndrome Scale) (Kay et al., 1987). As previously, interviews were conducted by trained residents in psychiatry, using the Italian version (Kay et al., 1999) of SCI-PANSS (Structured Clinical Interview for the positive and negative scale) (Kay et al., 1992); ratings were based on criteria indicated in the PANSS Manual (Kay et al., 2006); inter-rater reliability of PANSS evaluations in terms of ICC (Intraclass correlation coefficient) for the PANSS total score ranged from 0.65 to 0.95. Wherever possible, PANSS assessment included a standard section of queries addressed to treating clinicians and to caregivers. RSWG criteria (Andreasen et al., 2005), based on ratings at 8 focal symptoms in positive, negative and general psychopathology subscales of PANSS (P1, P2, P3, N1, N4, N6, G5, G9) were applied for clinical remission; patients were judged to be in clinical remission according to a severity criterion (scores obtained at each of these items had to be ≤ 3 points, indicating mild severity of symptoms). Due to the cross-sectional nature of the study, clinical remission was evaluated taking into account the severity criterion alone, excluding the duration criterion (remission maintained for six-months). Moreover, a more restrictive severity criterion for remission was adopted, defined by obtaining scores ≤ 3 at each of the 20 items included in the "consensus" factorial analysis of PANSS by Wallwork et al. (2012), namely items P1, P3, P5 and G9 (Positive Factor), N1, N2, N3, N4, N6 and G7 (Negative Factor), P2, N5 and G11 (Disorganized/concrete Factor), P4, P7, G8 and G14 (Excited factor) and G2, G3 and G6 (Depressed factor). Overall clinical status was also evaluated by the Clinical Global Impression-Schizophrenia scale (CGI-SCH) (Haro et al., 2003). Cognitive functioning was evaluated by means of the Brief Assessment of Cognition in Schizophrenia scale (BACS), (Keefe et al., 2004); gender/age/education adjusted scores and thus equivalent scores were obtained (Anselmetti et al., 2008). Mini Mental State Examination test (MMSE) (Folstein et al., 1975) was also administered, calculating an age/education adjusted score (Measso et al., 1993). Functioning was evaluated by PSP (Personal and Social Performance Scale) (Morosini et al., 2000), which assesses social functioning of patients in 4 main areas: socially useful activities, personal and social relationships, self-care and disturbing/aggressive behaviors.

A non-standardized interview was conducted with the patient, caregivers (when available) and the treating physician, with the aim of assessing functioning by means of PSP. A comprehensive overall score ranging from 1 (maximum dysfunction) to 100 (maximum functioning) was attributed, based on scores obtained at each single area. A total score exceeding 70 indicates a condition of "functional remission", with scores being related to overall good functioning.

2.3. Statistical analysis

Categorical data were analyzed using Pearson's χ^2 Test or Fisher's exact test; continuous variables were assessed by means of Student's "t" test for independent samples. The magnitude of differences in mean scores obtained at different rating scales used in the study was calculated by means of Cohen's "d". To evaluate differences in remission rates observed according to the two proposed criteria, McNemar Test for matched pairs of subjects was used. ROC analysis, with Sensitivity, Specificity and Predictive Value Analysis of the ability of different definitions of Remission to predict good outcomes was calculated. Data analyses were performed using SPSS 19.0. Level of significance was set at a p value ≤ 0.05 for two-tailed hypothesis.

3. Results

3.1. Clinical remission

To evaluate differences in the remission rates observed according to the different proposed criteria, McNemar Test for matched pairs of subjects was used. As expected, the proportion of remitted patients was significantly higher using RSWGcr (50%), compared to PANSS-FCTcr (26.8%) ($p < .0001$).

Differences in sociodemographic, clinical, cognitive and functional measures observed between remitted and non-remitting patients, according to the different criteria adopted, are reported in Tables 1–4.

Regarding sociodemographic variables, we found a significant difference in both education and occupation status between remitted and non-remitting patients, according to both RSWGcr (respectively $p = .05$ and $p < .0001$) and PANSS-FCTcr ($p = .0004$, $p = .004$). Irrespective of the criteria adopted, we observed a higher education level and a greater rate of employment among remitted patients, compared to non-remitting.

Non-remitting patients also showed a more severe course and a longer duration of illness, compared to patients in remission, for both RSWGcr (respectively $p = .008$ and $p = .002$) and PANSS-FCT criteria ($p = .0003$, $p = .005$).

Concerning psychopathology, we found significantly lower scores in all CGI-S and PANSS measures among remitted patients, compared to non-remitting, irrespective of the criteria adopted to define remission (see Table 2 for details).

Student's "t" test on neuropsychological evaluations showed several significant differences between remitted and non-remitting patients. A significantly higher score in MMSE and BACS Digit Sequencing task was observed among remitted patients, according to both RSWGcr (respectively $p = .011$ and $p = .005$) and PANSS-FCT criteria ($p = .04$, $p = .006$). On the other hand, only the PANSS-FCT criterion was able to discriminate between remitted and non-remitting patients for BACS Symbol Coding and Tower of London (respectively $p = .0006$ and $p = .005$).

Regarding functioning, we reported significant differences between remitted and non-remitting patients according to both RSWGcr and PANSS-FCT criteria. Patients who achieved remission showed better performances, compared to non-remitting patients, in PSP Total score and all subscales (see Table 4 for details).

3.2. Prediction of functional and cognitive outcome

We performed diagnostic test evaluations to investigate whether the criteria proposed for clinical remission would reflect differences in functional outcome and cognitive status.

Table 1

Sociodemographic characteristics of remitted and non-remitted patients according to different criteria.

Items	Criteria of remission	Remitted	Non-remitted	Statistics (df)
Education (years) (Means ± SD)	RSWG* PANSS FCT***	11.55 (4.16) 12.93 (4.21)	10.13 (3.43) 10.07 (3.45)	t(110) = 1.981, p = .05 t(110) = 3.655 p < .0004
Occupation (unemployed) N (%)	RSWG* PANSS FCT***	36 (64.3%) 17 (56.7%)	47 (83.9%) 66 (80.5%)	Chisq(1) = 9.775 p < .0001 Chisq(1) = 8.402 p = .004
Course of illness (continuous + episodic with residual symptoms) N (%)	RSWG* PANSS FCT***	39 (69.6%) 19 (65.5%)	50 (89.3%) 70 (89.7%)	Chisq(1) = 9.560, p = .008 Chisq(1) = 8.87 p = .003
Duration of illness (months) (Means ± SD)	RSWG* PANSS FCT***	163.68 (100.01) 147.13 (106.6)	227.48 (112.58) 213.30 (107.48)	t(110) = -3.171, p = .002 t(110) = -2.89, p < .005

Concerning functioning, patients were considered as remitted/non remitted based on PSP total score, with a cut-off of 70. As regard to cognitive performances, we obtained equivalent scores for each subtest of BACS, based on normative data from an Italian sample (Anselmetti et al., 2008) and then used the mean as a measure of general cognitive ability, setting a cut-off of 1. RSWGcr and PANSS FCTcr were compared on their ability to identify patients with better outcomes, using sensitivity, specificity and predictive value analysis. Youden's index and the Area Under the Receiver Operating Characteristic Curve (AUROC) were also calculated to quantify performances of the diagnostic criteria. Results are shown in detail in Table 5.

Positive predictive values (PPV) were low for both RSWGcr and PANSS FCTcr: the highest was 50% for PANSS FCTcr in predicting functional remission. However, this was expected, given that both good functional and cognitive outcomes occur at lower rates than achieving remission criteria. Regarding AUROC and Youden's J, the best values, indicating a moderately accurate test, were observed for PANSS FCT criteria on functional prediction (AUROC = .74, Youden's J = .48).

4. Discussion

The use of standardized remission criteria in schizophrenia has been considered a significant progress in improving documentation of clinical status in medical records. It provides an objective measure of illness course and treatment effect that is applicable to routine clinical care (Van Os et al., 2006b). The RSWG criteria (Andreasen et al., 2005) proved to be a valid and easy-to-use method to evaluate remission, even in common clinical practice. However, a number of studies compared RSWG criteria with others (Lambert et al., 2010) or with a modified version of the same criteria (Beintinger et al., 2008;

Van Os et al., 2006b), pointing out critical differences. A very recent study of our group reported that the use of more stringent severity criteria of remission, based upon all items of PANSS, was associated with improved identification of truly remitted patients, thus suggesting that the entire scale should be preferred, at least for research purposes (Pinna et al., 2013b). However, an evaluation based upon the use of the entire PANSS could be time consuming not only in routine practice, but even for research purposes, so that an intermediate solution could be to use a shortened version of PANSS. For this purpose, we based upon factorial analyses, which generally generate a lower number of items compared to the original scale, assembling them in four or more factors or symptom-dimensions. Considering that a five-factor model seems to better capture PANSS structure in schizophrenia and that there are several factor analytic studies, we decided to adopt the "consensus" five-factor model of PANSS recently developed and validated by Wallwork et al. (2012). This model considers 20 items, grouped in five symptom dimensions (positive, negative, disorganized/concrete, excited, depressed). Adopting this shortened version of PANSS, a new remission criterion, based upon a score ≤3 at each one of these 20 symptoms (PANSS FCT), was developed and compared to RSWG criteria. In our sample 50% of subjects were in clinical remission according to RSWG-cr (Andreasen et al., 2005), a proportion that decreased significantly and was halved when adopting PANSS-FCTcr. Clinical status evaluated by PANSS and CGI was significantly better among remitted patients, independent of the remission criteria adopted. However, the impact of remission on neurocognitive and functional performances varied according to the criterion used. Although some significant differences between remitters and non-remitters were detected in mean scores of many BACS subtests and MMSE score, also using RSWG-cr, such differences were greater and more widespread when using

Table 2

Mean scores ± sd at clinical scales of remitted and non-remitted patients according to different criteria.

Items	Criteria of remission	Remitted	Non-remitted	Statistics/Cohen's d
CGI-S Positive symptoms	RSWG* PANSS FCT***	1.60 (0.95) 1.43 (0.81)	2.95 (1.42) 2.6 (1.42)	t(110) = -5.853, p < .0001/1.17 t(110) = -4.21, p < .0001/0.85
CGI-S Negative symptoms	RSWG* PANSS FCT***	1.78 (0.91) 1.57 (0.68)	3.36 (1.27) 2.95 (1.36)	t(110) = -7.478, p < .0001/1.43 t(110) = -5.33, p < .0001/1.02
CGI-S Depressive symptoms	RSWG* PANSS FCT***	1.71 (0.85) 1.47 (0.78)	2.36 (1.31) 2.25 (1.2)	t(110) = -3.076, p = .003/0.58 t(110) = -3.31, p < .001/0.68
CGI-S Cognitive symptoms	RSWG* PANSS FCT***	1.84 (1.03) 1.6 (0.93)	3.18 (1.20) 2.85 (1.27)	t(110) = -6.298, p < .0001/1.19 t(110) = -4.94, p < .0001/0.95
CGI-S Overall severity	RSWG* PANSS FCT***	2.45 (0.95) 2.2 (0.92)	3.82 (0.76) 3.5 (0.95)	t(110) = -8.309, p < .0001/1.59 t(110) = -6.42, p < .0001/1.18
PANSS Positive scale	RSWG* PANSS FCT***	8.96 (2.09) 8.5 (1.83)	14.39 (4.35) 12.84 (4.44)	t(110) = -8.417, p < .0001/1.59 t(110) = -5.19, p < .0001/0.99
PANSS Negative scale	RSWG* PANSS FCT***	10.57 (3.65) 9.37 (2.94)	18.70 (5.85) 16.56 (6.17)	t(110) = -8.803, p < .0001/1.66 t(110) = -6.12, p < .0001/1.13
PANSS General psychopathology	RSWG* PANSS FCT***	21.98 (4.87) 19.97 (3.40)	32.68 (7.48) 30.02 (7.88)	t(110) = -8.964, p < .0001/1.69 t(110) = -6.75, p < .0001/1.21
PANSS Total scale	RSWG* PANSS FCT***	41.52 (7.92) 37.83 (6.18)	65.77 (13.87) 59.43 (15.38)	t(110) = -11.354, p < .0001/1.69 t(110) = -7.45, p < .0001/1.3

Table 3

Mean score \pm sd at Neuropsychological Tests in remitted and non-remitting patients according to different criteria.

Items	Criteria of Remission	Remitted	Non-remitting	Statistics (df)/Cohen's d
MMSE Total score	RSWG*	26.80 (2.71)	25.02 (4.42)	t(110) = 2.576, p = .011/0.485
	PANSS FCT***	27.13 (2.64)	25.46 (4.02)	t(110) = 2.11, p < .04/0.443
BACS List learning	RSWG*	5.84 (2.28)	4.97 (3.29)	t(99) = 1.55, p = .125/0.312
	PANSS FCT***	6.06 (2.03)	5.15 (3.08)	t(99) = 1.45, p = .15/0.356
BACS Digit sequencing task	RSWG*	14.75 (6.06)	11.26 (6.19)	t(99) = 2.86, p = .005/0.571
	PANSS FCT***	15.57 (6.16)	11.75 (6.16)	t(99) = 2.79, p = .006/0.601
BACS Verbal Fluency/category instances	RSWG*	9.89 (4.98)	8.10 (4.96)	t(99) = 1.801, p = .075/0.360
BACS Verbal Fluency Controlled Oral Words ass. test	PANSS FCT***	9.80 (4.07)	7.83 (4.72)	t(99) = 1.95, p = .053/0.427
BACS Symbol coding	RSWG*	15.05 (3.89)	14.50 (5.49)	t(99) = 0.569, p = .571/0.117
BACS Tower of London	PANSS FCT***	15.75 (5.93)	13.64 (6.26)	t(99) = 1.530, p = .13/0.346
	RSWG*	32.60 (13.64)	28.60 (12.29)	t(99) = 1.549, p = .125/0.309
	PANSS FCT***	34.82 (13.06)	24.55 (12.92)	t(99) = 3.57, p = .0006/0.750
	RSWG*	11.38 (5.98)	9.5 (6.53)	t(99) = 1.445, p = 0.152/0.301
	PANSS FCT***	12.96 (5.66)	9.00 (6.34)	t(99) = 2.88, p = .005/0.621

PANSS-FCT criteria. In particular, only the PANSS-FCT criterion was able to discriminate patients on BACS "Symbol Coding" and "Tower of London". These subtests represent, respectively, a global index of speed of processing and a measure of executive functions in the sub-component of planning, which are considered core domains specifically impaired in schizophrenia. These results thus indicate a better neurocognitive functioning among patients judged as being in clinical remission according to the more selective criteria adopted in this study. To confirm validity of the PANSS-FCTcr with respect to RSWGcr, we compared them with respect to their impact on functioning. A substantial increase in rates of functional remission was observed, ranging from approx. 32% in patients clinically remitted according to RSWGcr, to 50% among patients remitted according to PANSS-FCTcr. Thus, the ability to identify well-functioning patients was much better than using RSWG criteria. Confirmation of this was obtained by evaluating the proportion of patients in clinical remission who were devoid of significant impairment at each single dimension of PSP. With regard to "socially useful activities", this proportion increased from approx. 46% using RSGWcr to 80% using PANSS-FCT criteria. The rates of patients devoid of impairment in "social relationships" were 32%, and 83%,

respectively. Furthermore, 64% of patients viewed as remitted according to RSWGcr were unemployed, as were 57% of the individuals remitted according to PANSS-FCTcr. Again, PANSS-FCT criteria showed better performances in discriminating remitted patients as far as functioning is concerned, with respect to RSWG criteria. Therefore, the use of PANSS-FCT criteria, which are more restrictive for evaluating remission with respect to [Andreasen's et al. \(2005\)](#) criteria, is associated with a better assessment of how patients function in everyday life and identifies patients with a better neurocognitive functioning. Such finding may explain, at least in part, the improved vocational functioning of these patients ([McGurk, 2000](#)). We performed a series of specific analyses in order to better investigate whether the remission criteria proposed would reflect differences in outcome. Comparing RSWGcr and PANSS-FCT criteria as regard to their ability to identify patients with better functional and cognitive outcomes, the assessment of sensitivity, specificity, predictive value, and ROC analysis showed that PANSS-FCT criteria are characterized by the somewhat best performances.

Results from this study should be read considering several limitations such as: the limited sample size; the fact that we considered solely chronic outpatients who referred to the centre over a specific

Table 4

Results at PSP scale in remitted and non-remitting patients according to different criteria.

Items	Criteria of Remission	Remitted	Non-remitting	Statistics (df)/Cohen's d
PSP: Activities (Means \pm SD)	RSWG*	1.88 (1.27)	3.20 (1.21)	t(110) = -5.642, p < .0001/-1.06
	PANSS FCT***	1.3 (1.15)	2.99 (1.20)	t(110) = -6.660, p < .0001/-1.2
PSP: Social rel (Means \pm SD)	RSWG*	2.02 (1.15)	2.86 (1.15)	t(110) = -5.642, p < .0001/-0.73
	PANSS FCT***	1.7 (1.15)	2.71 (1.14)	t(110) = -4.14, p < .0001/-0.83
PSP: Self care (Means \pm SD)	RSWG*	0.34 (0.69)	0.80 (1.16)	t(110) = -2.559, p < .012/-0.48
	PANSS FCT***	0.27 (0.58)	0.68 (1.08)	t(110) = -2.01, p = .05/-0.42
PSP: Aggressive and disturbing behavior (Means \pm SD)	RSWG*	0.14 (0.44)	0.50 (0.81)	t(110) = -2.896, p < .005/-0.55
	PANSS FCT***	0.07 (0.25)	0.41 (0.75)	t(110) = -2.47, p = .01/0.51
PSP Total Score (Means \pm SD)	RSWG*	62.27 (13.65)	50.38 (14.79)	t(110) = 4.419, p < .0001/0.83
	PANSS FCT***	67.80 (11.91)	52.12 (14.38)	t(110) = 5.33, p < .0001/1.02
PSP Total Pts with a score \geq 70 (N, %)	RSWG*	18 (32.1)	5 (8.9)	$\chi^2(1) = 7.879$ p = .005
	PANSS FCT***	15 (50.0)	8 (9.8)	$\chi^2(1) = 21.800$ p < .0001
PSP: Activities Pts with score < 3 (N, %)	RSWG*	26 (46.4)	5 (8.9%)	$\chi^2(1) = 17.841$, p < .0001
	PANSS FCT***	24 (80)	23 (28)	$\chi^2(1) = 24.34$ p < .0001
PSP: Social rel Pts with score < 3 (N, %)	RSWG*	18 (32.2)	7 (12.5)	$\chi^2(1) = 5.149$ p = .023
	PANSS FCT***	25 (83.33)	33 (40.24)	$\chi^2(1) = 16.33$ p < .0001
PSP: Self care Pts with score < 3 (N, %)	RSWG*	51 (91.1)	46 (82.1)	$\chi^2(1) = 1.650$ p = .199
	PANSS FCT***	30 (100)	74 (90.24)	$\chi^2(1) = 3.15$ p = .07
PSP: Aggressive and disturbing behavior Pts with score < 3 (N, %)	RSWG*	54 (96.4)	49 (87.5)	$\chi^2(1) = 1.650$ p = .165
	PANSS FCT***	30 (100)	80 (97.56)	$\chi^2(1) = 0.75$ p = .39

* RSWG = Schizophrenia Working Group Severity Criterion.

** PANSS FCT = PANSS five-factor model.

Table 5

Sensitivity, specificity and predictive value analysis of the ability of the 2 definitions of remission to predict good functional and cognitive outcomes.

	Remission criteria	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUROC	Youden's J
PSP	RSWG	78	57	32	91	0.68	0.36
	PANSS FCT	65	83	50	90	0.74	0.48
BACS	RSWG	59	53	27	81	0.56	0.12
	PANSS FCT	41	76	34	81	0.58	0.16

time period; the fact that we included patients affected by both schizophrenia and schizoaffective disorders with a consequent sample heterogeneity, considered one of the main flaws of remission studies (Lambert et al., 2010), and that we didn't take into account some important variables (i.e. pre-morbid IQ and premorbid functioning) which may be significantly involved in evaluating predictive factors for functioning and cognitive status. Moreover, in evaluating remission we adopted the criterion of severity alone, without duration. Using the severity criterion alone is indeed a crucial change with respect to the original RSWG criteria, with impact on identification of remitted patients, thus we cannot draw any firm conclusions as to the validity of complete remission criteria. Remission studies generally demonstrate how use of the severity criterion alone is associated with higher remission rates (Lambert et al., 2010), compared to use of both severity and duration criteria. However, as pointed out also in a critical review (AlAqueel and Margolese, 2012), the majority of studies used RSWG criteria only, neglecting duration, as this choice is often more feasible for studies design. Moreover, even among studies including longitudinal criteria, there is no consensus on the frequency and duration of follow-up. Without questioning the importance of longitudinal criteria, these evidences suggest that there is a need to define further specifiers and proxy measures of remission that may be more viable in both research and clinical settings, leading to prompt and proper patient-tailored interventions. In this view, it is of the greatest interest to define more stringent remission criteria with higher predictive value, with respect to maintenance over time. We can suppose that the proportional lowering of rates found in this study as the severity remission criteria became more stringent should be confirmed, even if the time component is adopted in evaluating remission. We are planning to test this hypothesis in a follow-up study.

Even in the light of these limitations, in our opinion the evidences of this study would seem to be of interest. The fact that the 20-item PANSS derived by the consensus five-factor model is associated with a better identification of truly remitted patients, at least considering their personal, social and cognitive functioning as markers of remission, seems to us of practical importance. It could allow a somewhat more rapid way to evaluate clinical remission in both routine practice and research contexts, taking into account that in our experience the time commitments involved in assessing remission according to RSWG criterion is approx 5–10 min, and approx. 20 using PANSS-FCT. Considering that “rather than a substitute for the 30 items of PANSS, development of a concise outcome measure for remission would create a benchmark for treatment and maintenance goals in clinical research and general practice” (Opler et al., 2007), we think that the new and more concise way to evaluate remission by means of a shortened but very reliable version of the PANSS could be a significant option for clinicians (Bottlender et al., 2013; Brissos et al., 2011; Cassidy et al., 2010; Emsley et al., 2011).

Role of Funding Source

The authors declare that this study had no sponsor.

Contributors

FP participated in the design and coordination of the study, and helped to draft the manuscript, MB participated in the statistical

analysis and helped to draft the manuscript, RC participated in the study design and the drafting of the manuscript, BC conceived the study, participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

All the authors declare that they have no conflicts of interest.

Acknowledgements

The authors thank the components of the Cagliari Recovery Study Group for their contribution to data collection: Davide Aru, Chiara Bandecchi, Elena Corda, Luca Deriu, Enrica Diana, Francesca Fatteri, Alice Ghiani, Alice Lai, Serena Lai, Lorena Lai, Tiziana Lepori, Raffaella Maccioni, Paola Milia, Valeria Perra, Sonia Pintore, Silvia Pirarba, Elisabetta Piras, Sara Piras, Laura Puddu, Rachele Pisu Randaccio, Lucia Sanna, Elisabetta Sarritzu, Manuela Taberlet, Cristina Tocco, Enrico Zaccheddu, and Anne Farmer for language editing of the English version of the paper.

References

- AlAqueel, B., Margolese, H.C., 2012. Remission in schizophrenia: critical and systematical review. *Harv. Rev. Psychiatry* 20, 281–297.
- Andreasen, N.C., Carpenter Jr., W.T., Kane, J.M., Lasser, R.A., Marder, S.R., Weinberger, D.R., 2005. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am. J. Psychiatry* 162, 441–449.
- Anselmetti, S., Poletti, P., Ermoli, E., Bechi, M., Cappa, S., Venneri, A., Smeraldi, E., Cavallaro, R., 2008. The Brief Assessment of Cognition in Schizophrenia. Normative data for the Italian population. *Neurol. Sci.* 29, 85–92.
- Beintinger, R., Lin, J., Kissling, W., Leucht, S., 2008. Comparative remission frequencies of schizophrenic patients using various remission criteria. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 32, 1643–1651.
- Bottlender, R., Strauss, Moller, H.J., 2013. Association between psychopathology and problems of psychosocial functioning in the long term outcome of patients diagnosed with schizophrenic, schizoaffective and affective disorders. *Eur. Arch. Psychiatry Clin. Neurosci.* 263, 85–92.
- Brissos, S., Videira Dias, V., Balanzà-Martinez, V., Carita, A.I., Figueira, M.L., 2011. Symptomatic remission in schizophrenia patients: relationship with social functioning, quality of life, and neurocognitive performance. *Schizophr. Res.* 129, 133–136.
- Carpinello, B., Pinna, F., Tusconi, M., Zaccheddu, E., Fatteri, F., 2012. Gender differences in remission and recovery of schizophrenic and schizoaffective patients: preliminary results of prospective cohort study. *Schizophr. Res. Treat* 2012, 576369.
- Cassidy, C.M., Norman, R., Manchanda, R., Schmitz, N., Malla, A., 2010. Testing definitions of symptom remission. *Schizophr. Bull.* 36, 1001–1008.
- Emsley, R., Chiliza, B., Asmal, L., Lelhoenya, K., 2011. The concepts of remission and recovery in schizophrenia. *Curr. Opin. Psychiatry* 24, 114–121.
- First, M.B., Spitzer, R.L., Williams, J.B.W., Gibbon, M., 2000. Structured Clinical Interview for DSM IV Axis I Disorders (SCID-I) Versione Italiana a cura di Mazzi, F., Morosini, P., De Girolamo, G., Lusetti, M., Guaraldi, P. Organizzazioni Speciali, Firenze.
- First, M.B., Gibbon, M., Spitzer, R.L., Williams, J.B.W., Benjamin, L., 2003. Structured Clinical Interview for DSM IV Axis II Personality Disorders – Versione Italiana a cura di Mazzi, F., Morosini, P., De Girolamo, G., Lusetti, M., Guaraldi, P. Organizzazioni Speciali, Firenze.
- Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. “Mini Mental State”. A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12, 189–198.
- Haro, J.M., Kamath, S.A., Ochoa, S., Novick, D., Rele, K., Fargas, A., Rodríguez, M.J., Rele, R., Orta, J., Kharbeng, A., Araya, S., Gervin, M., Alonso, J., Mavreas, V., Lavrentzou, E., Liontos, N., Gregor, K., Jones, P.B., 2003. The Clinical Global Impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. *Acta Psychiatr. Scand.* 416, 16–23 (Suppl.).
- Karow, A., Moritz, S., Lambert, M., Schottel, D., Naber, D., EGOFORIS initiative, 2012. Remitted but still impaired? Symptomatic versus functional remission in patients with schizophrenia. *Eur. Psychiatry* 27, 401–405.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261–276.
- Kay, S.R., Opler, R.A., Fiszbein, A., 1992. The Structured Clinical Interview for Positive and Negative Syndromes of Schizophrenia. Multi-Health Systems, New York.
- Kay, S.R., Opler, R.A., Fiszbein, A., 1999. The Structured Clinical Interview for Positive and Negative Syndromes of Schizophrenia. Versione Italiana a cura di Migone, P. Università di Parma, Parma.
- Kay, S.R., Opler, R.A., Fiszbein, A., Ramirez, P.M., 2006. Positive and Negative Syndrome Scale (PANSS) Technical Manual. Multi-Health System, New York.
- Keefe, R.S., Goldberg, T.E., Harvey, P.D., Gold, J.M., Poe, M.P., Coughnour, L., 2004. The Brief Assessment of Cognition in Schizophrenia: reliability, sensitivity and comparison with a standardized neurocognitive battery. *Schizophr. Res.* 68, 283–297.
- Lambert, M., Karow, A., Leucht, S., Schimmelmann, B.G., Naber, D., 2010. Remission in Schizophrenia: validity, frequency, predictors and patients' perspectives 5 years later. *Dialogues Clin. Neurosci.* 12, 393–407.

- Lysaker, P.A., Roe, D., Buck, K.D., 2010. Recovery and wellness amidst schizophrenia: definitions, evidence, and the implications for clinical practice. *J. Am. Psych. Nurs. Ass.* 16, 36–42.
- McGurk, S.R., 2000. Neurocognition as a determinant of employment status in Schizophrenia. *J. Psychiatr. Pract.* 6, 190–196.
- Measso, G., Cavarzeran, F., Zappalà, G., Lebowitz, B.D., Crook, T.H., Pirozzolo, F.S., Amaducci, L., Massari, D., Grigoletto, F., 1993. The Mini Mental State Examination. Normative study of an Italian random sample. *Dev. Neuropsychol.* 9, 77–85.
- Morosini, P.L., Maglano, L., Brambilla, L., Ugolini, S., Pioli, R., 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr. Scand.* 101, 323–329.
- Nasrallah, H.A., Lasser, R., 2006. Improving patients' outcomes in schizophrenia: achieving remission. *J. Psychopharmacol.* 20 (6 Suppl.), 57–61.
- Oorschot, M., Lataster, T., Thewissen, V., Lardinois, M., van Os, J., Delespaul, P.A., Myint-Germeyns, L., 2012. Symptomatic remission in psychosis and real-life functioning. *Br. J. Psychiatry* 201, 215–220.
- Opier, M.G.A., Yang, L.H., Caleo, S., Alberti, P., 2007. Statistical validation of the criteria for symptom remission in schizophrenia: preliminary findings. *BMC Psychiatry* 7, 35.
- Pancheri, P., Brugnoli, R., Carilli, L., Delle Chiaie, R., Marconi, P.L., Petrucci, R.M., 1995. Valutazione dimensionale della sintomatologia schizofrenica. Validazione della versione italiana della Scala per la valutazione dei Sintomi Positivi e Negativi (PANSS). *G. Ital. Psicopat.* 1, 60–75.
- Pinna, F., Deriu, L., Lepori, T., Maccioni, R., Milia, P., Sarritzu, E., Tusconi, M., Carpiniello, B., Cagliari Recovery Study Group, 2013a. Is it true remission? A study of remitted patients affected by schizophrenia and schizoaffective disorders. *Psychiatry Res.* 210 (3), 739–744.
- Pinna, F., Tusconi, M., Bosia, M., Cavallaro, R., Carpiniello, B., Cagliari Recovery Group Study, 2013b. Criteria for symptom remission revisited: a study of patients affected by schizophrenia and schizoaffective disorders. *BMC Psychiatry* 13, 235.
- Van Os, J., Burns, T., Cavallaro, E., Leucht, S., Peuskens, J., Helldin, L., Bernardo, M., Arango, C., Fleischhacker, W., Lachaux, B., Kane, J.M., 2006a. Standardized remission criteria in schizophrenia. *Acta Psychiatr. Scand.* 113, 91–95.
- Van Os, J., Drukker, M., à Campo, J., Meijer, J., Back, M., Delespaul, P., 2006b. Validation of remission criteria for schizophrenia. *Am. J. Psychiatry* 163, 2000–2002.
- Wallwork, R.S., Fortgang, R., Hashimoto, R., Weingerger, D.R., Dickinson, B., 2012. Searching for a consensus five-factor model of the Positive and Negative Scale for schizophrenia. *Schizophr. Res.* 137, 246–250.