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Letter to the Editor

The Clinical Relevance of Percentage Improvements on the PANSS Score

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Sir

Stefan Leucht and co-workers have, in two recent reports in the Journal (Leucht and Engel, 2006; Leucht *et al*, 2006), contributed significantly to the understanding of the clinical relevance of scores on the two rating scales most widely used to evaluate treatment outcomes in schizophrenia patients. They have found that total score changes on the Brief Psychiatric Rating Scale (BPRS) and the Positive and Negative Symptom Scale (PANSS) correlate well with global judgments quantified by the Clinical Global Impression scale (CGI). In the discussion sections of their papers, they underscore the fact that these findings have implications with regard to planning and interpreting clinical trials.

In the following we would like to take those discussions a step further, especially regarding relative improvements on rating scales. Percentage changes on the BPRS and the PANSS are increasingly used as primary outcome variables in studies evaluating treatment effects in schizophrenia. This is also endorsed by regulators (EMEA, 1998). The example given in the following was chosen to extend the discussion put forward by Leucht and co-workers and to raise awareness of the potential fallacies of using such outcome criteria.

A patient with an acute exacerbation of schizophrenia is admitted to the hospital in a psychotic, highly agitated state. Accordingly, the patient's score is very high on the following PANSS items: tension, excitement, anxiety as well as some other unspecific symptoms. After a few days of treatment, the patient calms down, establishes a good relationship with the treatment team, and cooperates, while the core symptoms of schizophrenia remain unchanged. When he is rated again, most of the unspecific behavioral symptoms have improved considerably despite the fact that there has been no change in his psychotic symptoms. This disease course is commonly encountered in acute intake treatment facilities. When calculating PANSS scores (see Table 1, for numbers) one finds that despite the fact that symptoms considered pathognomonic for schizophrenia have not changed in severity, the total PANSS score has decreased by 20%. If this patient were in a clinical trial using percentage change as an outcome criterion, he would be considered a responder, even though none of the disease specific psychopathological symptoms have changed. As antipsychotic drugs are given to reduce psychotic symptoms, such a patient would be falsely classified as an antipsychotic responder.

The field badly needs outcome criteria that leave less room for misinterpretation. Relative improvement, if used at all, must be related to core symptoms of the disorder in order to be potentially indicative for true treatment response. Using 'core positive symptoms' (hallucinatory behavior, delusions, bizarre thinking, etc.) as is sometimes

Table 1 20% Improvement in PANSS Total Score

	Baseline	End of study
PANSS item		
PP4 (excitement)	6	2
PG1 (somatic concern)	5	2
PG2 (anxiety)	6	3
PG4 (tension)	6	2
PG6 (depression)	5	3
PG11 (poor attention)	7	3
All others	65	65
PANSS subscales		
Positive symptoms	28	24 (−14%)
Negative symptoms	22	22 (±0%)
General symptoms	50	34 (−32%)
PANSS total score	100	80 (−20%)

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done in clinical trials, or the newly proposed symptomatic remission criteria (Andreasen *et al*, 2005; Van Os *et al*, 2006) may also be feasible options. Alternatively, new rating scales that are more specifically geared towards measuring effects on treatment targets could be designed. This should not only foster objective drug development but also help close the gap between results from psychopharmacological studies and everyday clinical practice.

REFERENCES

Andreasen NC, Carpenter Jr WT, Kane JM, Lasser RA, Marder SR, Weinberger DR (2005). Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry* **162**: 441–449.

EMEA (1998). http://www.emea.europa.eu/pdfs/human/ewp/055995en.pdf.

Leucht S, Engel RR (2006). The relative sensitivity of the Clinical Global Impressions Scale and the Brief Psychiatric Rating Scale in antipsychotic drug trials. *Neuropsychopharmacology* **31**: 406–412.

Leucht S, Kane JM, Etschel E, Kissling W, Hamann J, Engel RR (2006). Linking the PANSS, BRPS, and CGI: clinical implications. *Neuropsychopharmacology* **31**: 2318–2325.

Van Os J, Burns T, Cavallaro R, Leucht S, Peuskens J, Helldin L *et al* (2006). Standardized remission criteria in schizophrenia. *Acta Psychiatr Scand* **113**: 91–95.