

## Clinical Recovery in First-Episode Psychosis

Lex Wunderink<sup>1,2</sup>, Sjoerd Sytema<sup>2</sup>, Fokko J. Nienhuis<sup>2</sup>,  
and Durk Wiersma<sup>2</sup>

<sup>2</sup>University Medical Center Groningen, University Psychiatric  
Center, University of Groningen, The Netherlands

**Introduction:** Generally agreed outcome criteria in psychosis are required to evaluate the effectiveness of new treatment strategies. The aim of this study is to explore clinical recovery in first-episode patients, defined by meeting criteria for both symptomatic and functional remission. **Method:** In a sample of first-episode patients (*N* 125), symptomatic and functional remission during the last 9 months of a 2-year follow-up period were examined, as well as recovery and its predictors. **Results:** Half the patients (52.0%) showed symptomatic remission and a quarter (26.4%) functional remission, while one-fifth (19.2%) met both criteria sets and were considered recovered. Recovery was significantly associated with short duration of untreated psychosis and better baseline functioning. **Conclusion:** Most functionally remitted patients were also symptomatically remitted, while a minority of symptomatically remitted patients were also functionally remitted. Treatment delay may affect chance of recovery.

**Key words:** schizophrenia/remission/social functioning/  
disability/duration of untreated psychosis

### Introduction

From Kraepelin's times, schizophrenia has been primarily considered as a "deficit state," and this view persisted into modern diagnostic systems by including functional deterioration as a diagnostic criterion of schizophrenia.<sup>1,2</sup> However, functional deterioration may be absent in cases previously meeting criteria for schizophrenia and may be present across diagnostic borders, eg, in cases of bipolar disorder. Indeed, modern insights into the pathogenesis of schizophrenia point out that this disorder consists

of subgroups with differential course and outcome.<sup>3–5</sup> Thus, the degree of functional deterioration should be considered a dependent variable of yet largely unknown risk factors instead of being implied in schizophrenia by definition. As a consequence, standardized tools for outcome measurement, including assessment of recovery, are needed in schizophrenia outcome research and to find predictors of prognosis. At present, there are no generally accepted outcome criteria in psychosis.<sup>6</sup> Recently, however, the Remission Working Group proposed standardized criteria for symptomatic remission.<sup>7</sup> A next step would be to define criteria for recovery. According to the Remission Working Group and leaders in the field, recovery in schizophrenia would imply not only being free of psychopathology but also the ability to function in the community, socially, and vocationally.<sup>7–9</sup> Symptomatic remission thus is a prerequisite to recovery but may not be sufficient.<sup>1</sup> On the other hand, some patients may experience functional remission despite their ongoing symptoms.<sup>10–12</sup> The aim of the present study is to examine symptomatic and functional remission as 2 constituents of clinical recovery in a sample of first-episode patients. The present study is a further follow-up of the data collected in the Medication Strategies in First Onset Schizophrenia (MESIFOS) trial.<sup>13</sup> Data on symptomatic remission in this sample were recently published in this journal.<sup>14</sup>

### Conceptualization of Recovery and Symptomatic and Functional Remission

The view of the Remission Working Group that symptomatic remission is a stepping stone toward the more demanding state of recovery, obtainable by many people over time, represents a significant step away from erroneous professional defeatism. However, this concept of recovery falls short of satisfying the demands of patients and their families. Consumers have developed their own experience-based approach to schizophrenia, leading to a quite different concept of recovery. The latter concept of recovery, described by consumer advocates, rehabilitation practitioners, and researchers, refers to a unique and personal process "in which people are able to live, work, learn, and participate fully in their communities" and "to live a fulfilling and productive life despite a disability."<sup>15–17</sup> The American Psychiatric Association

<sup>1</sup>To whom correspondence should be addressed; University Medical Center Groningen, University Psychiatric Center (5.21), University of Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands; tel: +31-50-361-1136, fax: +31-50-361-9722, e-mail: a.wunderink@med.umcg.nl

strongly affirms the application of this concept of recovery to the comprehensive care of chronically and persistently mentally ill adults.<sup>18</sup> As Davidson et al<sup>19</sup> perspicuously state, this second concept of recovery is even applicable to people who do not recover in the clinical sense. These authors coined the term of being “in recovery” for this concept as opposed to “recovery from” schizophrenia. Being “in recovery” then does not reflect a clinical or scientific reality as much as it does a personal experiential one. This concept is about reclaiming autonomy and self-determination without first having to clinically recover from an illness. This article however is restricted to the clinical model of recovery because our data only allow analysis of these aspects. This narrow, clinical definition of recovery is in agreement with the concept of recovery proposed by the Remission Working Group and leading authorities in the field, but it should be noted that this clinical concept does not by any means replace or rule out the consumer perspective on recovery.<sup>7,8</sup>

Another issue is whether recovery should demand not only symptomatic and functional remission but also the absence of medication.<sup>8,20</sup> However, there is overwhelming evidence that continued use of antipsychotics prevents symptomatic relapse and is almost a necessity for sustaining a high level of functioning among persons diagnosed with schizophrenia.<sup>21,22</sup> To account for this fact and to increase the practicability of the recovery concept, continued use of antipsychotics should be allowed.<sup>8</sup> The need for medication thus distinguishes the concept of recovery from cure. This is consistent with the view of the field, and it has also been noted for depression that maintenance medication should not be seen as an obstacle to recovery.<sup>8,23</sup> Although neurocognitive functioning is also an important dimension to be included in operational criteria for recovery, neurocognition was beyond the scope of the parent study. Neurocognitive data therefore were not available.

### *Symptomatic Remission*

Criteria for symptomatic remission were adopted from Andreasen et al.<sup>7</sup> In accordance, the Positive and Negative Syndrome Scale (PANSS) was used to assess the relevant symptoms: P1 (delusions), P2 (conceptual disorganization), P3 (hallucinatory behavior), N1 (blunted affect), N4 (social withdrawal), N6 (lack of spontaneity), G5 (mannerisms/posturing), and G9 (unusual thought content). All relevant item scores have to be 3 (mild) or less on a scale ranging from 1 (not present) to 7 (severe). During a certain observational period (according to Andreasen et al,<sup>7</sup> 6 mo; in this study, 9 mo), patients have to be monitored for symptomatic relapse. Symptomatic relapses are then defined as an exacerbation of symptoms during at least 1 week with at least one relevant PANSS item score above 3 (mild). No symptomatic relapses are allowed during the agreed observational period.

### *Determining Functional Remission: The Assessment of Social Functioning*

According to generally accepted views, functional remission implies proper social functioning in the main domains of every day life: personal care, living, working, and relating to others. However, the assessment of social functioning is quite complicated.<sup>24–26</sup> Many instruments have the drawback of assessing a mixture of instrumental performance of daily life tasks and psychopathology-related behavior instead of measuring the level of functioning in social roles relative to what one may expect based on social position and background. To meet the latter demands, the Groningen Social Disabilities Schedule (GSDS) has been developed in the context of the International Classification of Impairments, Disabilities and Handicaps<sup>27</sup> and the International Classification of Functioning, Disability and Health.<sup>28</sup> The GSDS relies on the sociological framework of social role theory.<sup>29–32</sup> In these World Health Organization (WHO) classifications, a social disability is defined as a deficiency in the ability to perform activities and manifest behavior as would be expected in the context of a well-defined social role. It is important to note that social role functioning has to be measured against normative expectations in a certain cultural context. The reference group consists of people from the same cultural background in a comparable position, and the assessment incorporates expectations of key figures in the individual's inner circle. Social disabilities are assessed by means of a semistructured investigator-based interview measuring social functioning and adjustment over the last 4 weeks in 8 social roles, 7 of which are included in this study (see table 1). The baseline measurement was related to the 1-month period just before the first mental health contact. The parental role was left out because of limited applicability.

A disability is rated by the investigator on a 4-point scale from no (0), minimal (1), obvious (2), and serious (3) disability. The scores on each role have anchor points, describing the nature and severity of the corresponding problems with criteria for (a) the frequency and duration of the functional deficits, (b) the damage inflicted to the individual or to others, and (c) the need for help. A total disability score is calculated by combining 7 role scores, ranging from 0 to 21. The psychometric qualities of the scale have been reported to be good.<sup>30–32</sup> The GSDS also yielded reliable results in cross-national research studies. Factor analysis and item response scaling underlined the validity of a one-dimensional overall role disability scale (Mokken analysis:  $H = 0.48$ ,  $\rho = 0.79$ , and  $\delta = 19.03$ )<sup>29,33</sup>.

An important question is how to define appropriate thresholds in social role functioning scores that correspond to functional remission. Because many people who do not suffer from schizophrenia have persistent social deficits, patients recovering from schizophrenia cannot be expected to have no social impairments at

**Table 1.** Social roles, personal situations, and corresponding role dimensions of the GSDS

Social Role	Personal Situations	Role Dimensions
Self-care		—personal hygiene; physical care —looks and appearance; manners
Housekeeping	Living together	—social activities —economic contribution
	Living alone	—independent living skills —economic independency
Family relationships		—emotional relationship with parents —frequency of contacts with parents
		—emotional quality and frequency of contacts with siblings
partner relationships	Having a partner	—emotional ties
	Being single	—sexual relationship —adequacy of dating activities
Community integration		—interest in social environment —participation in social events, clubs
		—being considerate of others
Relationship with peers		—quality of contacts —frequency and number of contacts
Vocational role	Working, studying	—daily routine —Working performance —contacts with colleagues —goal-directedness of activities
	Housekeeping	—daily routine —performance —goal-directedness of activities
	Unemployed	—goal-directedness of activities
	Retired	—goal-directedness of activities

all. Therefore, minor impairments (in work or in social and intimate relationships) were allowed to be present in functional remission, if not leading to significant impairment to perform in any of the 7 roles. A functionally remitted patient should function adequately in all 7 social roles with none or only a minimal disability in any of them (not allowing a score of 2 or 3 on any GSDS role). Just like symptomatic remission, functional remission should be monitored. Because of the time course of fluctuation of functioning levels, biweekly monitoring is frequent enough to show whether functional remission was sustained during an observational period of, eg, 9 months.

*Operational Criteria for Recovery*

We explore recovery criteria based on 2 dimensions: symptomatic remission and functional remission, which should be sustained during a prolonged period. In this study, the last 9 months of a 24-month follow-up period after first treatment response were chosen as the observational window through which social functioning and symptomatology were monitored to establish the occurrence of recovery status. This 9-month observational window is relatively short compared with most other recovery studies covering periods of 2–5 years and even longer.<sup>34</sup> While these long-term studies are needed to explore sustained recovery, the short observational window in our study enabled close monitoring. This issue is further discussed in the Discussion section of this article. The 9-month observational window was determined by the original MESIFOS design and therefore is rather arbitrarily.

**Methods**

*Patient Sample*

The patients were recruited as part of the MESIFOS study.<sup>13</sup> They were first-episode patients, aged 18–45 years, who had never been treated before, and who consented to be randomized to either maintenance antipsychotics or guided discontinuation strategy if they showed a sufficient response of positive symptoms (maximum of 1 score of 4 on positive subscale of PANSS) and did not relapse during 6 months within the first year of treatment. The operational criteria for first episode were: first episode of uninterrupted positive symptoms, no matter the duration, no symptom remission for 1 month or longer duration, and no antipsychotic treatment for more than 3 months. Fulfillment was determined during a diagnostic interview using items from the Interview for Retrospective Assessment Of Schizophrenia (IRAOS) and confirmed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN).<sup>35,36</sup> Patients were asked to participate as soon as they were able to understand the consequences of participation, usually around the time of the first response of positive symptoms. Recruitment took place from October 2001 through December 2002 in a catchment area of 3.1 million inhabitants in the north, east, and southwest of The Netherlands.<sup>37</sup> After obtaining written informed consent, the patients were diagnosed using the SCAN interview. Only patients with schizophrenia and other nonaffective psychotic disorders were included.

Of 257 treatment-naïve first-episode patients who met the study criteria 149 (58%) gave written informed consent. Two patients committed suicide, and 106 patients refused any participation. There were no differences between participants and nonparticipants regarding gender, age at first contact, marital status, living situation,

and illicit drug use. Of the 149 patients who were willing to participate 18 patients were not included in the medication strategies study: 1 patient committed suicide, 9 patients relapsed within 6 months after response, 8 patients did not respond with adequate positive symptom reduction within 6 months of antipsychotic treatment, 3 patients withdrew informed consent during follow-up, and of another 3 patients PANSS data were missing. This left 125 patients to be included in the present study.<sup>14</sup>

### *Predictors of Recovery*

In order to examine the association of conceivable predictors of outcome with recovery, we recorded gender, duration of untreated psychosis (DUP), time to response (TTR) of positive symptoms, baseline psychopathology (PANSS), social functioning (GSDS), quality of life (WHOQoL-Bref), use of illicit drugs (SCAN interview), and living situation (living alone vs with others). DUP was assessed during the SCAN interview and defined by the time between the first manifestation of any positive psychotic symptom and the start of antipsychotic treatment. TTR was defined by the time from the start of antipsychotic treatment until first treatment response.<sup>37</sup> Quality of life was assessed at baseline with the WHOQoL-Bref, a 26-item self-report questionnaire, comprising satisfaction with health, psychological functioning, social relationships, and environmental opportunities, as experienced over the last 2 weeks. Each item is scored on a 5-point scale, higher scores indicating better quality of life. We will present the total score, ranging from 26 to 130.<sup>38</sup>

### *Follow-up Assessments and Monitoring*

Psychopathology (PANSS) and quality of life (WHOQoL-bref) were assessed 6, 15, and 24 months after response and social role functioning (GSDS) at 15 and 24 months. In addition, the patients were monitored bi-weekly by their clinicians, checking symptom severity levels as well as levels of functional impairment. In case the clinician observed a symptomatic or functional relapse, these were confirmed or refuted by PANSS and GSDS scores rated by members of the research team. Patients were considered to be recovered if at both assessments PANSS criteria for remission according to Andreasen et al<sup>7</sup> were fulfilled and GSDS role functioning scores were  $\leq 1$ , without symptomatic or functional relapse during the observation period.

### *Training and Reliability*

Psychiatrists who were trained by the Groningen WHO Training Center administered the SCAN interview. Training for PANSS and GSDS was provided at investigator meetings, supplemented by written training materials. Training for the PANSS and GSDS included rating

of a videotaped interview, followed by discussion and review of ratings. Regular booster meetings were organized to maintain interrater reliability. Reliability of the GSDS was established by 12 raters all rating the same 11 subjects. We used another 12 subjects, all rated by 11 raters, to establish the reliability of the PANSS. We calculated weighted kappas for each GSDS item. The square weighted kappa scores ranged from 0.55 to 0.88 for each GSDS item, with a mean of 0.67. The 2-way mixed-model intraclass correlation coefficient (ICC) was used to assess the reliability of the PANSS scales. The ICC for the PANSS subscale of positive symptoms was .84 and for the subscale of negative symptoms .83.

### *Statistical Analysis*

Analyses were carried out with the statistical package SPSS (version 14; SPSS Inc, Chicago, IL). The association of symptomatic remission with functional remission was analyzed with a Fisher Exact test. Differences between baseline characteristics of recovered and not-recovered patients were analyzed using Student *t* tests for continuous variables and Pearson chi-square tests for categorical variables. Nonparametric tests (Mann-Whitney *U* tests) were applied for DUP and TTR because of their positively skewed distribution. A linear mixed-models repeated-measures analysis of covariance was used to analyze the relation between recovery and repeated quality-of-life measurements. The dependent variable was WHOQoL-bref total score. Fixed effects were recovery status, time (assessments T0, T6, T15, and T24), and the interaction of recovery status and time. The general covariance matrix (unstructured) was specified for the covariance structure of the residuals of the repeated measurements. The subjects (the observational units in the analysis) were included as a random effect. The type III method to calculate the sums of squares of the fixed effects in the model was applied. To find factors predicting recovery, a binary logistic regression analysis with backward selection was applied with recovery as the dependent variable and the factors significantly associated with recovery in the bivariate analyses as independent variables.

Because of its skewed distribution, DUP was log transformed in this analysis.

### **Results**

Baseline characteristics of the sample are shown in table 2.

The development over time of the PANSS subscale scores, the GSDS total scores, and the WHOQoL-bref total scores in recovered and nonrecovered patients are shown in table 3.

A mixed-models analysis shows that quality of life in recovered patients is slightly but statistically significantly better than in not-recovered patients from the start ( $df = 1$ ,

**Table 2.** Baseline Characteristics of the Sample ( $N = 125$ )

Characteristic	$n$ (%)
Male gender	86 (68.8)
Age at onset of psychosis, y, mean (SD)	25.7 (6.7)
Duration of untreated psychosis, days, mean (SD) [median]	265 (535) [31]
Age at start of treatment, y, mean (SD)	26.4 (6.4)
Time to response, d, mean (SD) [median]	75.9 (52.9) [61.0]
Living alone	46 (36.8)
Married or cohabiting	19 (15.2)
Schizophrenia	57 (45.6)
Other nonaffective psychosis	68 (54.4)
Cannabis dependence/abuse	30 (24.0)

$F = 11.3$ ,  $P < .001$ ) and that there is significant improvement over time in both groups ( $df = 3$ ,  $F = 8.8$ ,  $P < .001$ ) but equally in recovered and not-recovered patients ( $df = 3$ ,  $F = 0.4$ ,  $P = .740$ ). A cross-tabulation of functional remission against symptomatic remission (table 4) shows the contribution of both outcome domains to recovery. Recovery is achieved by 24 patients. There was no relationship between recovery and the arm (maintenance vs discontinuation strategy) in the original trial (Fisher Exact test:  $P = .5$ ). The same applies for symptomatic and functional remission. Of all patients showing functional remission, 72.7% met criteria of recovery, but only 36.9% of all patients with symptomatic remission did. The odds ratios to achieve vs not to achieve recovery were 2.7 for functional remission and 0.6 for symptomatic remission. A Fisher Exact test (2-sided) showed a significant association between symptomatic remission and functional remission ( $P = .008$ ).

Bivariate analyses demonstrated that recovered patients already differed significantly at baseline from nonrecovered patients. The mean DUP in recovered patients was 31.8 days, compared with 320.9 days in non-

recovered patients (Mann-Whitney  $Z$  score of  $-3.407$ ,  $P = .001$ ). Recovered patients had less severe baseline positive ( $t = 2.053$ ,  $P = .042$ ), negative ( $t = 2.177$ ,  $P = .031$ ), and general symptoms ( $t = 2.288$ ,  $P = .024$ ) on the PANSS subscales and less social role performance disability on baseline GSDS total scores ( $t = 3.530$ ,  $P = .001$ ). Recovered patients also were less often initially diagnosed with schizophrenia: only 8.8% of patients with a schizophrenia diagnosis ( $n = 57$ ) recovered compared with 27.9% of patients with other nonaffective psychoses ( $n = 68$ ); (Fisher Exact test, 2-sided,  $P = .011$ ). There was no significant difference between recovered and nonrecovered patients regarding gender, baseline quality of life, TTR, living alone vs with others, or baseline diagnosis of cannabis abuse. To examine the relative contribution to recovery of the factors that were associated with recovery in the bivariate analyses, we tested a logistic regression model with backward selection. Recovery was entered as the dependent variable, and baseline PANSS positive, negative, and general symptom subscale scores; baseline GSDS total score; and DUP (log transformed) were entered as independent variables. Schizophrenia diagnosis was left out because of its interdependency with DUP because a baseline diagnosis of schizophrenia implied a minimum duration of illness before treatment of 6 months. The only significant predictors of recovery that remained were DUP (odds ratio [OR] = 0.531,  $df = 1$ ,  $P = .008$ ) and baseline GSDS total score (OR = 0.858,  $df = 1$ ,  $P = .021$ ).

The mean daily dose of antipsychotics during follow-up did not differ between recovered and not-recovered patients. Most prescribed drugs were risperidone, olanzapine, quetiapine, and clozapine, with a mean duration of prescription per patient of 5.6, 5.3, 1.6, and 0.8 months, respectively. The mean daily dosages were risperidone 2.7 mg, olanzapine 10.4 mg, quetiapine 541 mg, and clozapine 336 mg. Patients were treated according to the guidelines, including psychoeducation, family interventions, and case management.

**Table 3.** Psychopathology, Role Functioning, and Quality-of-Life Measurements Over Time in Recovered (R) and Not-Recovered (NR) Patients

	T0		T6		T15		T24	
	R, Mean (SD)	NR, Mean (SD)	R, Mean (SD)	NR, Mean (SD)	R, Mean (SD)	NR, Mean (SD)	R, Mean (SD)	NR, Mean (SD)
PANSS positive subscale total score	9.2 (2.5)	10.6 (3.0)	8.4 (1.4)	9.4 (2.4)	8.6 (2.1)	10.4 (3.5)	8.7 (1.9)	11.4 (4.3)
PANSS negative subscale total score	11.6 (5.5)	14.1 (5.0)	10.0 (3.6)	13.6 (4.7)	8.4 (2.0)	13.3 (5.1)	8.5 (2.0)	13.7 (5.9)
PANSS general subscale total score	23.2 (6.4)	26.6 (6.5)	21.0 (4.2)	24.2 (6.3)	19.2 (3.4)	24.7 (7.0)	20.6 (4.9)	25.8 (7.0)
GSDS total score	6.3 (3.1)	9.1 (4.7)	NA	NA	1.8 (1.5)	6.7 (3.9)	1.9 (1.7)	6.5 (3.9)
WHOQoL total score	93.6 (11.9)	91.2 (12.4)	93.1 (9.0)	89.2 (10.5)	101.1 (9.5)	94.7 (13.0)	102.0 (10.6)	96.3 (13.3)

Note: T0 = baseline assessment, T6 = assessment after 6 months, T15 = assessment after 15 months, T24 = assessment after 24 months, R = recovered, NR = not-recovered, PANSS = Positive and Negative Syndrome Scale, GSDS = Groningen Social Disability Schedule, WHOQoL (higher scores better QoL) = World Health Organization Quality-of-Life Scale, NA = Not Applicable.

**Table 4.** Cross-tabulation of Symptomatic Remission Against Functional Remission

	Symptomatic Remission, <i>n</i> (%)		Total <i>n</i> (%)
	No	Yes	
Functional remission, <i>N</i> (%)			
No	51 (40.8)	41 (32.8)	92 (73.6)
Yes	9 (7.2)	24 (19.2)	33 (26.4)
Total <i>n</i> (%)	60 (48.0)	65 (52.0)	125 (100.0)

In addition, we divided the nonrecovered group into a group showing neither functional nor symptomatic remission (41%) and a group showing remission in only one of the 2 domains (40%). There were no significant baseline differences between the latter 2 groups.

## Discussion

About 20% of the included sample of first-episode patients met the proposed criteria for recovery at the end of a 2-year follow-up period. Taking into account the 18 patients who consented but were not included because they did not respond, relapsed early, or committed suicide, this percentage would be about 17. This may seem a small proportion of patients, but the proportion of patients meeting recovery criteria may well increase with the duration of follow-up.<sup>39</sup> The proposed criteria of recovery are a combination of the symptomatic remission criteria recently proposed by Andreasen et al<sup>7</sup> and a criteria set relating to social role functioning. The latter set has been based on the GSDS, designed to normatively quantify social role functioning accounting for age, gender, and sociocultural background. This procedure is in accordance with the operational definition of recovery proposed by Liberman et al.<sup>8</sup> The GSDS has the advantage of anchor points for each role and an established reliability and validity. The thresholds in the separate role functioning scores have been chosen such as to allow for minimal impairments in any role. All 7 roles were allowed to have a score of at most 1. This implies that patients who meet these demands are functioning pretty well without apparent impairments.

## Limitations

A substantial number of first-episode patients who were to be included refused to participate. There were however no indications of differences between included and not included patients. Almost all patients who were willing to participate (*n* = 149) were actually included (*n* = 131; 87.9%). These figures are consistent with the results of other studies.<sup>40,41</sup> However, due to the 18 patients not meeting the criteria of the parent

study, the 20% recovery rate of the included sample may overestimate the recovery rate for the entire sample. Another major limitation is the lack of neurocognitive data. Neurocognitive deficits might be present already at baseline and might predict nonrecovery and functional impairment.

## Symptomatic Remission, Functional Remission, and Recovery

About two-thirds of the patients who had a symptomatic remission did not also function properly, while most patients who functioned well were also free from symptoms. Symptomatic remission by definition is a prerequisite to recovery, but it is not sufficient. Moreover, functional improvement does occur in a small minority of patients who are not free from symptomatology. This is consistent with findings in other studies.<sup>10,12</sup> It appeared that subjective quality of life did not differentiate between recovered and nonrecovered patients if taking into account their baseline ratings. This means that patient reported well being may be not a determining or discriminating factor of outcome of recovery in schizophrenia.

## Time Frame of Recovery

The time criterion (in this study, 9 mo) is an arbitrary cut-off. However, a shorter period would be insufficient to implement regained functional capacities in daily life and to permit validation of sustained and stable improvement. A 9-month period seems to be long enough to be meaningful from a clinical perspective and has the advantage of enabling close monitoring, providing a solid base for longer term outcomes research. Indeed, a strong point in the design of our study is the close monitoring of symptomatology and social functioning by clinicians during the observational period of 9 months. Long-term studies (2–5 y) are needed to study sustained recovery over longer periods of time. Studies on longer term recovery propose time frames of 2 years and more.<sup>34</sup> As a consequence, recovery criteria in these studies have been more globally defined and less severe (eg, Global Assessment of Functioning scores of above 60). Because quite a number of patients will move from recovery to a nonrecovered state, and back,<sup>9</sup> longer time frames will exclude more patients who relapse, and less patients will meet a longer term recovery criterion. However, the 20% of recovered patients in our study is rather low compared with most long-term studies that find percentages of 40% and more. This is probably due to the combination and the severity of symptomatic and functional remission criteria in our study.<sup>4,5</sup> In the present study, being recovered would mean to have regained a formerly expected level of day-to-day functioning, while symptoms have been stably mild or absent, and this has been sustained during the 9 months of observation.

### Predictors of Recovery

DUP and baseline social functioning were the only factors that independently predicted recovery after 2 years of follow-up. No recovery occurred in patients with DUP of 6 months and longer. DUP has been shown to predict various outcome parameters by many other studies.<sup>37,42</sup> Though not as strong as DUP, social role functioning before treatment also is an index of better recovery chances. As a corollary of less compromised mental functioning, it may be associated with a better prognosis.

### Diagnostic Inclusion Criteria

The patient sample included in this study consisted of a catchment area based cohort of first-episode patients diagnosed with nonaffective psychosis. The patients were diagnosed at baseline, shortly after coming into treatment. The median DUP in our sample was 31 days, and as a consequence many patients were diagnosed very shortly after their first break of psychosis. The sample thus includes psychoses of limited duration and offers a view into the prognosis of first break psychosis. The present study meets an important requirement for studies into the prognostic features of a group of disorders, such as the schizophrenia-like psychoses: these studies should include first episodes of all nonaffective psychoses and not preselect a sample by its protracted course characteristics, such as implied by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, schizophrenia criteria. Despite this early time of diagnosis, 57 patients (45.6%) were assigned to a diagnosis of schizophrenia, as a consequence of duration of illness of at least 6 months before coming into treatment.

### Further Research

Follow-up is needed to register the patient flow transiting from nonrecovered states into recovery status and back. Patients showing functional remission without symptomatic remission deserve special attention. These patients apparently are on the edge of recovery and may take advantage of targeted approaches for persisting or relapsing symptoms. A number of them may not be bothered by their symptoms, consistent with the finding of psychotic symptomatology in the general population.<sup>43</sup>

The criteria for recovery presented here are meant to serve a heuristic purpose. They are particularly interesting from a clinical point of view and do not acknowledge the consumer perspective on recovery. They will have to show their value in clinical practice with respect to long-term outcomes and stability over time. Our results clearly show that social functioning is an important parameter in schizophrenia outcome research, both as a predictor of future course characteristics and as a more selective index of recovery than symptom remission.

### Funding

ZorgOnderzoekNederland-MW (DO945-01-001); Eli Lilly Nederland; Stichting tot Steun V.C.V.G.Z. (Bennekom); Stichting De Open Ankh (Soesterberg).

### References

1. van Os J, Burns T, Cavallaro R, et al. Standardized remission criteria in schizophrenia. *Acta Psychiatr Scand.* 2006;113:91–95.
2. Kraepelin E. *Dementia Praecox and Paraphrenia*. RB Barclay, trans-ed. Edinburgh, UK: ES Livingston; 1919.
3. Andreasen NC. Standardized remission criteria in schizophrenia. *Acta Psychiatr Scand.* 2006;113:81.
4. Harrison G, Hopper K, Craig T, et al. Recovery from psychotic illness: a 15-and 25-year international follow-up study. *Br J Psychiatry.* 2001;178:506–517.
5. Hopper K, Harrison G, Janca A, Sartorius N. *Recovery From Schizophrenia: An International Perspective. A Report From the WHO Collaborative Project, the International Study of Schizophrenia*. Oxford University Press; 2007.
6. Hegarty JD, Baldessarini RJ, Tohen M, Waternaux C, Oepen G. One hundred years of schizophrenia: a meta-analysis of the outcome literature. *Am J Psychiatry.* 1994;151:1409–1416.
7. Andreasen NC, Carpenter WT, Jr, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry.* 2005;162:441–449.
8. Liberman RP, Kopelowicz A, Ventura J, Gutkind D. Operational criteria and factors related to recovery from schizophrenia. *Int Rev Psychiatry.* 2002;14:256–272.
9. Harrow M, Grossman LS, Jobe TH, Herbener ES. Do patients with schizophrenia ever show periods of recovery? A 15-year multi-follow-up study. *Schizophr Bull.* 2005;31:723–734.
10. Strauss JS, Carpenter WT, Jr. The prediction of outcome in schizophrenia. II. Relationships between predictor and outcome variables: a report from the WHO international pilot study of schizophrenia. *Arch Gen Psychiatry.* 1974;31:37–42.
11. Harding CM, Brooks GW, Ashikaga T, Strauss JS, Breier A. The Vermont longitudinal study of persons with severe mental illness, I: methodology, study sample, and overall status 32 years later. *Am J Psychiatry.* 1987;144:718–726.
12. Harding CM, Brooks GW, Ashikaga T, Strauss JS, Breier A. The Vermont longitudinal study of persons with severe mental illness, II: long-term outcome of subjects who retrospectively met DSM-III criteria for schizophrenia. *Am J Psychiatry.* 1987;144:727–735.
13. Wunderink L, Nienhuis FJ, Sytema S, Slooff CJ, Knegtering R, Wiersma D. Guided discontinuation versus maintenance treatment in remitted first-episode psychosis: relapse rates and functional outcome. *J Clin Psychiatry.* 2007;68:654–661.
14. Wunderink L, Nienhuis FJ, Sytema S, Wiersma D. Predictive validity of proposed remission criteria in first-episode schizophrenic patients responding to antipsychotics. *Schizophr Bull.* 2007;33:792–796.
15. Department of Health and Human Services *Achieving the Promise: Transforming Mental Health Care in America*. Rockville, Md: Substance Abuse and Mental Health Services Administration; 2003.
16. Bellack AS. Scientific and consumer models of recovery in schizophrenia: concordance, contrasts, and implications. *Schizophr Bull.* 2006;32:432–442.

17. Resnick SG, Fontana A, Lehman AF, Rosenheck RA. An empirical conceptualization of the recovery orientation. *Schizophr Res*. 2005;75:119–128.
18. American Psychiatric Association. *Position Statement on the Use of the Concept of Recovery*. Washington, DC: American Psychiatric Association; 2005.
19. Davidson L, Schmutte T, Dinzeo T, Andres-Hyman R. Remission and recovery in schizophrenia: practitioner and patient perspectives. *Schizophr Bull*. 2008;34:5–8.
20. Wyatt RJ, Damiani LM, Henter ID. First-episode schizophrenia. Early intervention and medication discontinuation in the context of course and treatment. *Br J Psychiatry Suppl*. 1998;172:77–83.
21. Gilbert PL, Harris MJ, McAdams LA, Jeste DV. Neuroleptic withdrawal in schizophrenic patients. A review of the literature. *Arch Gen Psychiatry*. 1995;52:173–188.
22. Gitlin M, Nuechterlein K, Subotnik KL, et al. Clinical outcome following neuroleptic discontinuation in patients with remitted recent-onset schizophrenia. *Am J Psychiatry*. 2001;158:1835–1842.
23. Frank E, Prien RF, Jarrett RB, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder. Remission, recovery, relapse, and recurrence. *Arch Gen Psychiatry*. 1991;48:851–855.
24. Link BG, Mesagno FP, Lubner ME, Dohrenwend BP. Problems in measuring role strains and social functioning in relation to psychological symptoms. *J Health Soc Behav*. 1990;31:354–369.
25. Mueser KT, Tarrier N. *Handbook of Social Functioning in Schizophrenia*. Boston, Mass: Allyn and Bacon; 1998.
26. Bellack AS, Green MF, Cook JA, et al. Assessment of community functioning in people with schizophrenia and other severe mental illnesses: a white paper based on an NIMH-sponsored workshop. *Schizophr Bull*. 2007;33:805–822.
27. World Health Organisation. *International Classification of Impairments, Disabilities and Handicaps*. Geneva, Switzerland: World Health Organisation; 1980.
28. World Health Organisation. *International Classification of Functioning, Disability and Health*. Geneva, Switzerland: World Health Organisation; 2001.
29. Kraaijkamp HJM. *Difficult Roles. A study into the Reliability and Validity of the Groningen Social Disabilities Schedule in Psychiatric Patients*. Department of Psychiatry, Groningen University; Groningen, The Netherlands; 1992.
30. Wiersma D, Jong Ad, Ormel J. The Groningen Social Disabilities Schedule: development, relationship with the ICIDH and psychometric properties. *Int J Rehabil Res*. 1988;11:213–224.
31. Wiersma D, de Jong A, Kraaijkamp HJM, Ormel J. *GSDS II, The Groningen Social Disabilities Schedule, Second Version*. Groningen, The Netherlands: Department of Psychiatry, Rijksuniversiteit Groningen; 1990.
32. Wiersma D. Role functioning as a component of quality of life in mental disorders. In: Katschnig H, Freeman H, Sartorius N, eds. *Quality of Life in Mental Disorders*. West Sussex, England. 2nd ed. John Wiley & Sons; 2005. p. 45–56.
33. Schutzwahl M, Jarosz-Nowak J, Briscoe J, Szajowski K, Kallert T. Inter-rater reliability of the Brief Psychiatric Rating Scale and the Groningen Social Disabilities Schedule in a European multi-site randomized controlled trial on the effectiveness of acute psychiatric day hospitals. *Int J Methods Psychiatr Res*. 2003;12:197–207.
34. Liberman RP, Kopelowicz A. Recovery from schizophrenia: a concept in search of research. *Psychiatr Serv*. 2005;56:735–742.
35. Hafner H, Riecher-Rossler A, Hambrecht M, et al. IRAOS: an instrument for the assessment of onset and early course of schizophrenia. *Schizophr Res*. 1992;6:209–223.
36. World Health Organisation. *Schedules for Clinical Assessment in Neuropsychiatry*. 2.1 ed. Geneva, Switzerland: World Health Organisation; 1992.
37. Wunderink A, Nienhuis FJ, Sytema S, Wiersma D. Treatment delay and response rate in first episode psychosis. *Acta Psychiatr Scand*. 2006;113:332–339.
38. O'Carroll RE, Smith K, Couston M, Cossar JA, Hayes PC. A comparison of the WHOQOL-100 and the WHOQOL-BREF in detecting change in quality of life following liver transplantation. *Qual Life Res*. 2000;9:121–124.
39. Liberman RP, Kopelowicz A. Recovery from schizophrenia: a challenge for the 21st century. *Int Rev Psychiatry*. 2002;14:245–255.
40. Loebel AD, Lieberman JA, Alvir JM, Mayerhoff DI, Geisler SH, Szymanski SR. Duration of psychosis and outcome in first-episode schizophrenia. *Am J Psychiatry*. 1992;149:1183–1188.
41. Lieberman J, Jody D, Geisler S, et al. Time course and biologic correlates of treatment response in first-episode schizophrenia. *Arch Gen Psychiatry*. 1993;50:369–376.
42. Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Crounce T. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Arch Gen Psychiatry*. 2005;62:975–983.
43. Hanssen MSS, Bijl RV, Vollebergh W, van Os J. Self-reported psychotic experiences in the general population: a valid screening tool for DSM-III-R psychotic disorders? *Acta Psychiatr Scand*. 2003;107:369–377.