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Course and predictors of symptomatic remission in late-life schizophrenia: A 5-year follow-up study in a Dutch psychiatric catchment area

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ABSTRACT

Background: The number of older schizophrenia patients is growing, the majority being treated in outpatient settings. Reported symptomatic remission rates in younger cohorts vary largely. Further insight into course trajectories and putative predictors of remission in older persons with schizophrenia is needed.
Methods: 5-year follow-up course trajectories of symptomatic remission were examined in a catchment area-based group of 77 older Dutch patients (mean age 66.0 years) with schizophrenia or schizoaffective disorder. A modified version of the 'Remission in Schizophrenia Working Group' criteria was used to determine remission status. In individuals who did not fulfil remission criteria at baseline ($n = 56$), predictors of conversion to remission status at 5-year follow-up were analysed using multivariable regression analyses.
Results: A substantial increase in remission rate at 5-year follow-up (27.3% at baseline (T1), 49.4% at follow-up (T2)) was found. Of all participants, 23.4% was in remission at both assessments and 46.8% was in non-remission at both assessments. 26.0% of the participants converted from non-remission at T1 to remission at T2, while 3.9% fell back from remission at T1 to non-remission at T2. Two significant baseline predictors of conversion to remission at follow-up were found: lower score on the PANSS positive symptom subscale, and having a partner.
Conclusion: Symptomatic remission was as an attainable goal for almost half of all older patients with schizophrenia or schizoaffective disorder at 5-year follow-up. With a lower PANSS positive symptom subscale score, and having a partner emerging as the only predictors of conversion to remission, there remains a need to search for modifiable predictors.

1. Introduction

The consensus definition on remission criteria for schizophrenia, as proposed by Andreasen and colleagues in 2005, has facilitated the search for determinants of the symptomatic outcome of schizophrenia (Andreasen et al., 2005). This definition requires the absence or low intensity of eight core symptoms of schizophrenia (severity criterion) over a period of six months (time criterion). Employing this consensus definition, symptomatic remission rates have varied largely in cross-sectional studies among younger schizophrenia patients, ranging between 17 and 88% (Emsley et al., 2011). Likewise, the percentage of patients remaining in remission during multi-year follow-up varied markedly in younger cohorts (16 to 90%) (Emsley et al., 2011). However, due to differences in methods, lengths of follow-up and assessment frequencies during follow-up, findings are hard to compare across studies (Alaqeel and Margolese, 2012).

Symptomatic remission is considered as a second best to the broader and more demanding concept of recovery that includes satisfying social functioning and quality of life (Emsley et al., 2011). Although some studies have demonstrated correlations between symptomatic remission and measures of social functioning and quality of life (Bobes et al., 2009; Helldin et al., 2006; Lasser et al., 2007; Wunderink et al., 2009), with an important role for disease and treatment related factors (Wunderink et al., 2013), a more conclusive picture of the relation between remission and other indicators of recovery has yet to emerge (Emsley et al., 2011; Schennach-Wolff et al., 2009).

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Older patients are the fastest growing segment of the total population of schizophrenia patients (Palmer et al., 1999), with a distinct clinical profile (Jeste et al., 2003; Meesters et al., 2011). Although various long-term trajectories of schizophrenia in older populations have been reported, it is clear that in a substantial number of persons with schizophrenia symptoms persist into old age, causing long-term impairments (Harrison et al., 2001; Jeste et al., 2003; Jobe and Harrow, 2005; Tandon et al., 2009). Studies on symptomatic remission and predictors of its course in older populations are limited. Two cross-sectional North American studies on convenience samples of older community-dwelling patients with early onset schizophrenia found very similar remission rates of 49% (mean age 61 years) (Bankole et al., 2008) and 47% (mean age 56 years) (Leung et al., 2008). A North American study found a rate of 8% using much stricter criteria to evaluate the rate of sustained remission in outpatients with schizophrenia (mean age 57 years) (Auslander and Jeste, 2004). While Bankole and colleagues (Bankole et al., 2008) identified four predictors of remission (fewer network contacts, greater proportion of intimates, fewer traumatic lifetime events and higher cognitive functioning), Leung and colleagues (Leung et al., 2008) did not find any variables to be associated with remission. In the only available study that used a catchment area design, we reported a more modest remission rate of 29.4% in an older Dutch population (mean age 68.0 years) (Meesters et al., 2011). Our cross-sectional study included both community-living and institutionalized patients, with no restrictions on the age at onset of the disorder. A diagnosis of schizoaffective disorder (versus schizophrenia), satisfactory adherence to psychiatric services, a larger social network and better social functioning predicted symptomatic remission (Meesters et al., 2011).

The only longitudinal study on symptomatic remission in late-life schizophrenia relates to the New York City cohort study cited above (Bankole et al., 2008). This study reported a nonsignificant decline in the percentage attaining remission over time (49% at baseline, 40% at follow-up) (Cohen and Iqbal, 2014). Higher community integration, a greater number of entitlements, fewer psychotropic medications and a lower frequency of psychiatric services at baseline predicted remission at follow-up, while baseline remission predicted more social contacts at follow-up (Cohen and Iqbal, 2014). The study was limited by the number of patients that could be traced (104 of the original 250 individuals), and by a wide variation in follow-up time (mean 54 months, range 12–116 months).

To expand knowledge on the longitudinal course of symptomatic remission in older schizophrenia patients, we evaluated the 5-year course in our catchment area based cohort of older Dutch schizophrenia patients (Meesters et al., 2011). As it has been suggested that in late-life schizophrenia functioning may improve with time (Jeste et al., 2011, 2003), we hypothesized that at 5-year follow-up symptomatic remission would be more prevalent than at baseline. Next, to identify variables predicting conversion from a non-remitted status at baseline to a remitted status at follow-up, we evaluated a range of predictors in the subsample of persons who were not in remission at baseline. We evaluated the same putative predicting variables as in our previous cross-sectional study (Meesters et al., 2011), in which variables were selected based upon what at that time had been published on predictors of remission in younger schizophrenia populations (Bobes et al., 2009; Bodén et al., 2009; De Hert et al., 2007; Helldin et al., 2007; Novick et al., 2009; Wunderink et al., 2007). We hypothesized that in line with our previous cross-sectional findings, a diagnosis of schizoaffective disorder, greater adherence to psychiatric services, and higher scores on measures of social functioning would predict symptomatic remission at 5-year follow-up.

2. Methods

2.1. Participants

The study was conducted in the psychiatric catchment area of the southern district of Amsterdam, the Netherlands. For a detailed description of the design and methods of the original cross-sectional study, we refer to our earlier publication (Meesters et al., 2011). In short, all patients in contact with mental health care services, aged 60 years and over, and with a diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV-TR (American Psychiatric Association, 2000) assessed by the MINI-Plus (Sheehan et al., 1998), were screened for study eligibility during the period between March 2006 and September 2008 (baseline, T1). Of a total of 177 eligible patients, 109 persons (62%) who were able and willing to provide written informed consent participated in the cross-sectional study.

For the present study, at 5-year follow-up (follow-up period ranging from 4 years and 9 months up to 5 years and 3 months) (T2) 77 of the original 109 patients (70.6%) were included. 32 patients were excluded, because of emigration ($n = 1$), poor physical health ($n = 2$), severe cognitive impairment ($n = 6$), refusal of consent at the second assessment ($n = 4$), while 19 patients had died. Attrition was non-differential with respect to gender, diagnosis, remission status at first assessment, Mini Mental State Examination (MMSE)-score, and education, but persons lost to follow-up were older (72.6 vs. 66.0 years, Student's t-test 4.7; $p < 0.001$). 59 of the 77 patients (76.6%) were diagnosed with schizophrenia and 18 patients (23.4%) with schizoaffective disorder. At baseline (T1), mean age was 66.0 years, with 30% male and a mean age of onset of 31 years. 54 of the 77 patients (70%) resided (alone or with others) in the community, 18 (23%) lived in a psychiatric residential care facility, 1 (1%) in a general residential care facility, while 4 (5%) patients were hospitalized. The study was approved by the Medical Ethics Committee of the VU University Medical Center, Amsterdam.

2.2. Symptomatic remission

Symptomatology was determined using the Positive and Negative Syndrome Scale (PANSS (Kay et al., 1987)). All PANSS assessments, both at baseline and at follow-up, were performed by the last author (PDM) who was also the attending psychiatrist of the majority of the patients in this study. Following the remission criteria as proposed by the Remission in Schizophrenia Working Group (Andreasen et al., 2005), remission was defined as a score of 3 (mild) or less, on eight PANSS items (severity criterion). In addition, according to these criteria remission must be stable for at least 6 months (time criterion). Due to our study design, the time criterion was modified, requiring remitted persons to have had no psychiatric hospitalization in the six months previous to T2.

2.3. Predictor variables

Various putative predictors of course were assessed at baseline, including socio-demographics (age, gender, marital and parental status and education), clinical data (diagnosis, age at onset, total PANSS score and positive and negative symptom subscale scores, duration of illness, substance abuse, depressive symptoms, global cognitive state, physical comorbidity, limitations in activities of daily living, use of antipsychotic medication (first- or second-generation antipsychotics) and adherence to medication prescription, intensity of and adherence to psychiatric services), and social characteristics (residence, social network size, social participation, social functioning and quality of life).

The presence of an actual partner was documented at T1. Education was scored as the highest educational level that was completed with a degree, and was categorized into low (up to completed primary school), high (at least completed secondary school at a level permitting entry to academic training) and middle (between low and high). Age of onset was determined as the youngest age at which - in retrospect - DSM-IV-TR criteria for the disorder were fulfilled (procedure described in detail in (Meesters et al., 2012)). Current substance abuse was assessed with the MINI-plus (Sheehan et al., 1998). Self-reported depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale (CES-D (Radloff, 1977)). Global cognitive state was

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evaluated using the Mini-Mental State Examination (MMSE (Folstein et al., 1975)). To evaluate medical comorbidity, participants were asked if they used medication and/or were seeing a doctor for seven chronic disorders (obstructive lung disease, cardiac disease, hypertension, stroke, diabetes, arthritis and cancer). The total number of chronic disorders was computed. Self-reported limitations in daily living activities were evaluated through the Groningen Activity Restriction Scale (GARS (Kempen et al., 1996)). Use of antipsychotic medication was registered at T1, with adherence to medication being evaluated by the patients' principal health worker. The intensity of psychiatric services was measured by the number of face-to-face contacts of patients with mental health staff during the past year, classified as low (less than one contact per month), high (one or more contacts per week), or intermediate. Adherence to psychiatric services (compliance with appointments and attitude towards staff advice) was scored by the patients' principal health worker. Regarding their social network size, patients were asked to estimate the number of persons, outside their household, with whom they had regular and meaningful contact. Self-report of involvement in ten social activities was measured through the Social Participation Scale (Depla et al., 2003), with scores ranging from 0 (no activities) to 20 (regular participation in all activities). The Social and Occupational Functioning Assessment Scale (SOFAS; American Psychiatric Association, 2000) was scored by the interviewer, to assess the level of social functioning in the previous week. SOFAS scores range from 1 to 100, with scores of 61 and higher indicating little or no social impairments. Quality of life was evaluated using the Manchester Short Assessment of Quality of Life (MANSA (Priebe et al., 1999)), which rates patient satisfaction with various aspects of life. The MANSA score ranges from 1 (very dissatisfied) to 7 (very satisfied). The internal reliability scores (Cronbach's alpha) of the scales, including the PANSS, MANSA, and CES-D, were all 0.8 or higher reflecting good internal reliability, except for the PANSS positive symptom subscale score (Cronbach's alpha 0.55).

2.4. Statistical analyses

First, for all participants course trajectories were examined using descriptive statistics, presenting remission and non-remission rates at 5-year follow-up. Next, in the subgroup of participants who were non-remitted at baseline the distribution of characteristics across remitters and non-remitters at 5-year follow-up was analysed using Students *t*-tests for continuous variables and chi-square tests (Fisher's exact if ≤5 observations per cell) for categorical variables. The Mann-Whitney test was used as a non-parametric test. Next, the association between characteristics that differed across groups according to remission status in bivariate analyses (significance level $p < 0.05$), was examined using logistic regression analyses with outcome defined as remission (model 1) (no remission served as reference). These putative predictors were entered one by one in separate analyses to determine unadjusted odds ratios. All predictors that were significantly ($p < 0.05$) associated with remission in model 1 were considered as putative confounders, and, hence, entered in a final, multivariable logistic regression model (model 2). Additionally, multicollinearity was tested using variance inflation factor (VIF). In case of multicollinearity (VIF > 0.3) predictor variables were left out of the analyses. Only total PANSS score was significantly correlated with positive and negative symptom subscale scores, and left out of the multivariable analysis, since subscores were more informative than the total PANSS score. In regression analysis we did not adjust for age and gender since power issues forced us to be restrictive with the number of variables entered in the regression analysis given the sample of 55 subjects.

3. Results

We found a substantial increase in the rate of remission at 5-year follow-up (27.3% at baseline, 49.4% at follow-up). Of the 77 participants, 18 (23.4%) met overall remission criteria at both T1 and T2 and were not hospitalized between both assessments, while 36 (46.8%) remained in a non-remitted status over the 5-year follow-up period. Twenty (26.0%) patients converted from non-remission to remission, while 3 (3.9%) patients converted from remission to non-remission (Fig. 1). Table 1 presents the characteristics at the T1 assessment of the subgroup of 56 participants who were not remitted at T1. Bivariate analyses showed that participants who had converted to remission at follow-up ($n = 20$), at baseline were more often diagnosed with schizoaffective disorder ($p = 0.004$), had lower baseline total PANSS scores ($p < 0.001$) and lower positive ($p = 0.001$) and negative ($p = 0.005$) PANSS symptom subscale scores, had more often a partner ($p = 0.031$), and had a larger social network size ($p = 0.023$) (Table 1).

Next, we examined the association between these variables and remission at 5-year follow-up, using logistic regression analysis. Table 2 presents the unadjusted and adjusted Odd's ratios. In multivariable analysis (adjusting for diagnosis, PANSS positive and negative symptom subscale scores, marital status and social network size), only the PANSS positive symptom subscale score (OR 0.75; 95% CI 0.58–0.96) and having a partner (OR 8.48; 95% CI 1.10–65.5) predicted conversion to remission at 5-year follow-up (Table 2). At trend level, a diagnosis of schizoaffective disorder (versus schizophrenia; OR 11.5; 95% CI 0.97–135.5; $p = 0.053$), and PANSS negative symptom subscale score (OR 0.86; 95% CI 0.74–1.01; *p*-value of 0.067) were associated with conversion to remission at follow-up.

4. Discussion

In this catchment area-based study of older patients with schizophrenia or schizoaffective disorder, we demonstrated a considerable increase in the rate of symptomatic remission at 5-year follow-up. While at baseline less than a third of all participants fulfilled remission criteria (27.3%), at follow-up the remission rate increased to nearly half of the study population (49.4%). Our remission rate at follow-up is in line with two cross-sectional reports on remission in convenience samples of older schizophrenia patients: 49% (Bankole et al., 2008), and 47% (Leung et al., 2008). Nearly a quarter (23.4%) of our cohort was in remission both at baseline and at follow-up, and was not hospitalized between both assessments, suggesting persistent remission over the 5-year period. This rate aligns with the broadly accepted presupposition in younger cohorts that a quarter of patients exhibit enduring symptomatic remission (Tandon et al., 2009). In addition to the 23.4% of patients in stable remission nearly half (46.8%) of our cohort showed stable non-remission, implying that all in all 70% of patients persisted in their remission state over time.

Our findings differ appreciably from the above cited NYC longitudinal study in older persons with schizophrenia, that demonstrated a decrease of remission rates (49% at baseline, 40% at mean follow-up of 54 months) (Cohen and Iqbal, 2014). In the NYC study 25% of all participants converted from remission to non-remission, in contrast to only 3.9% in our study. The NYC study found 25% stable remission, 35% stable non-remission and therefore 60% stability over time (Cohen and Iqbal,

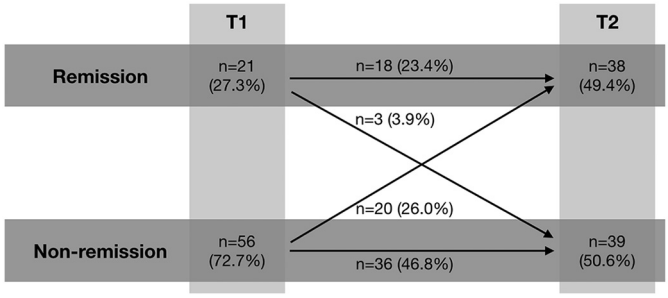

Fig. 1. Transitions in remission status from baseline (T1) to 5-year follow-up (T2).

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Table 1
Characteristics of the subsample of non-remitters at baseline ($N = 56$).

Characteristics	Total $n = 56$	Remitters at T2 $n = 20$	Non-remitters at T2 $n = 36$	Test t; X^2	df	p-value
Demographic data						
Age mean (SD)	66.4 (5.5)	66.0 (6.0)	66.6 (5.3)	$t = 0.39$	54	0.70
Gender: male (%)	17 (30.4)	7 (35.0)	10 (27.7)	$X^2 = 0.32$	1	0.57
Marital status:						
Having a partner (%)	11 (19.6)	7 (35.0)	4 (11.1)	$X^2 = 4.65$	1	**0.03**
Parental status:						
Has children (%)	27 (48.2)	9 (45.0)	18 (50.0)	$X^2 = 0.13$	1	0.72
Education[a]:				$X^2 = 2.90$	2	0.24
Low (%)	14 (25.5)	5 (25.0)	9 (25.0)			
Middle (%)	26 (47.3)	7 (35.0)	19 (52.7)			
High (%)	15 (27.3)	8 (40.0)	7 (19.4)			
Clinical data						
Diagnosis:				$X^2 = 8.26$	1	**0.004**
Schizophrenia (%)	47 (83.9)	13 (65.0)	34 (94.4)			
Schizoaffective disorder (%)	9 (16.1)	7 (35.0)	2 (5.6)			
Age of onset:				$X^2 = 0.47$	2	0.79
Early (<40 years)	39 (69.6)	15 (75.0)	24 (66.7)			
Late (40–60 years)	13 (23.2)	4 (20.0)	9 (25.0)			
Very late (>60 years)	4 (7.1)	1 (5.0)	3 (8.3)			
PANSS total score Mean (SD)	64.1 (12.6)	55.7 (8.6)	68.8 (12.2)	$t = 4.24$	54	**<0.001**
PANSS positive symptom subscale score mean (SD)	16.2 (4.5)	13.5 (4.4)	17.6 (3.9)	$t = 3.67$	54	**0.001**
PANNS negative symptom subscale score mean (SD)	17.3 (6.4)	14.2 (5.3)	19.0 (6.3)	$t = 2.90$	54	**0.005**
Duration of illness: mean years (SD)	36.3 (12.9)	35.1 (12.7)	36.9 (13.2)	$t = 0.51$	54	0.61
Chronic physical disorders mean (SD)	0.80 (1.1)	0.85 (1.0)	0.78 (1.2)	$t = -0.23$	54	0.82
Current substance/alcohol abuse (%)	5 (8.9)	2 (10.0)	3 (8.3)	Fisher's exact		1.00
CES-D score (SD)	15.9 (11.4)	17.8 (11.6)	14.9 (11.3)	$t = 0.93$	54	0.36
MMSE score (SD)	26.8 (3.4)	27.5 (2.9)	26.3 (3.6)	$t = -1.23$	54	0.22
GARS score (SD)	25.9 (9.1)	26.5 (9.0)	25.6 (9.3)	$t = -0.33$	54	0.75
Psychiatric services						
Only FGA (%)	15 (26.8)	7 (35.0)	8 (22.2)	$X^2 = 1.07$	1	0.30
Only SGA (%)	30 (53.6)	8 (40.0)	22 (61.1)	$X^2 = 2.30$	1	0.13
Combination FGA and SGA (%)	2 (3.6)	1 (5.0)	1 (2.8)	Fisher's exact		1.00
No antipsychotics (%)	9 (16.1)	4 (20.0)	5 (13.9)	Fisher's exact		0.71
Adequate compliance with medication[b] (%)	37 (66.1)	13 (65.0)	24 (66.7)	$X^2 = 0.09$	1	0.76
Intensity of service:				$X^2 = 3.44$	2	0.18
Low (%)	12 (21.4)	4 (20.0)	8 (22.2)			
Intermediate (%)	28 (50.0)	13 (65.0)	15 (41.7)			
High (%)	16 (28.6)	3 (15.0)	13 (36.1)			
Adherence to service:				$X^2 = 3.31$	2	0.19
Good (%)	20 (35.7)	7 (35.0)	13 (36.1)			
Fair (%)	31 (55.4)	13 (41.9)	18 (50.0)			
Unsatisfactory (%)	5 (8.9)	0 (0.0)	5 (13.9)			
Social characteristics						
Residence:				$X^2 = 2.64$	2	0.27
Independent (%)	37 (66.1)	15 (75.0)	22 (61.1)			
Dependent (%)	15 (26.8)	5 (25.0)	10 (27.8)			
Social network size:				$X^2 = 7.51$	2	**0.02**
0–1 person (%)	21 (37.5)	3 (15.0)	18 (50.0)			
2–5 persons (%)	18 (32.1)	10 (50.0)	8 (22.2)			
≥6 persons (%)	17 (30.4)	7 (35.0)	10 (27.7)			
Social participation scale						
Score[a] (SD)	9.0 (4.5)	10.0 (4.1)	8.5 (4.7)	$t = -1.14$	53	0.26
SOFAS score (SD)	49.0 (11.8)	50.9 (11.3)	47.9 (12.2)	$t = -0.91$	54	0.37
Quality of life						
MANSA score (SD)	4.8 (1.0)	5.0 (1.0)	4.7 (1.0)	$t = -1.03$	54	0.31

Statistical findings are presented in bold; p-values <0.05. DF = degrees of freedom; SD = standard deviation; CES-D = Centre for Epidemiological Studies Depression Scale; MMSE = Mini Mental State Examination; GARS = Groningen Activity Restriction Scale; FGA = first generation antipsychotics; SGA = second generation antipsychotics; SOFAS = Social and Occupational Functioning Assessment Scale; MANSA = Manchester Short Assessment of Quality of Life.

[a] Data for $n = 55$.

[b] Data for $n = 47$.

2014). Of note, the percentage living independently at baseline in our study sample (70.1%) was substantially higher than in the NYC cohort (34%), with independent residence predicting remission at trend level ($p = 0.06$) in the NYC study. The increase in persons attaining remission in our study is in accordance with the notion that aging has attenuating effects on psychotic symptoms (Jeste et al., 2011, 2003). Next, while our study essentially had a non-interventional design, we cannot exclude that the population under study took advantage of heightened awareness and a more active attitude among treating staff. Furthermore, one can speculate that specific characteristics of the Dutch mental health system, such as comprehensive and well-staffed services that may deliver outreaching care if needed (Meesters et al., 2011), have contributed to advance remission and prevent relapse.

Next, in the subsample of non-remitted participants at baseline ($n = 56$) we examined putative predictors of conversion to remission at 5-year follow-up. In multivariable analyses adjusting for possible confounders, a lower PANSS positive symptom subscale score and having a partner at baseline emerged as the only significant predictors of

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Table 2
logistic regression analysis, examining the association between putative predictors and remission at follow-up.

Variables	Model 1 Unadjusted odds ratio (95% CI)	Wald	df	p-value	Model 2 Adjusted[a] Odds Ratio (95% CI)	Wald	df	p-value
Diagnosis schizoaffective vs. schizophrenia	9.15 (1.68–49.9)	6.54	1	**0.011**	11.5 (0.97–135.5)	3.75	1	0.053
PANSS positive symptom subscale score	0.78 (0.67–0.92)	9.22	1	**0.002**	0.75 (0.58–0.96)	5.18	1	**0.023**
PANSS negative symptom subscale score	0.87 (0.78–0.97)	6.84	1	**0.009**	0.86 (0.74–1.01)	3.35	1	0.067
Marital status: having a partner	4.31 (1.08–17.2)	4.26	1	**0.039**	8.48 (1.10–65.5)	4.20	1	**0.040**
Social network size								
0–1 person	Reference	6.68			Reference	4.14		
2–5 persons	7.50 (1.62–34.8)	6.61	1	**0.010**	5.06 (0.55–46.4)	2.05	1	0.152
≥6 persons	4.20 (0.88–19.9)	3.26	1	0.071	0.60 (0.06–5.72)	0.20	1	0.657

[a] Analyses adjusted for diagnosis, PANSS positive subscale score, PANSS negative subscale score, marital status and social network size. In bold *p*-values <0.05.

conversion to remission at follow-up. Bankole and colleagues (Bankole et al., 2008) found a greater proportion of intimates among network members to be associated with remission. Considering possible mechanisms underlying these associations one could speculate that having a partner may be beneficial, among others, for social connectedness in general, adherence to treatment and early detection of symptomatic deterioration. The finding of the PANSS positive symptom subscale score to be significantly associated with conversion to remission, is in line with the finding of lower symptom severity predicting remission status at follow-up in studies concerning younger populations (Helldin et al., 2007; Lang et al., 2013; Möller et al., 2011; Penttilä et al., 2014; Tandon et al., 2009). In line with our cross-sectional study (Meesters et al., 2011) we documented at trend level an association between schizoaffective disorder and conversion to remission at follow-up, with schizoaffective patients reaching remission almost three times more often than patients with schizophrenia (77.8% compared to 27.6% respectively; OR 8.57; 95% CI = 1.11–66.4).

Although social network size was significantly associated with remission in bivariate analyses, this significance was lost in multivariate analysis. Cohen and colleagues demonstrated that greater community integration was associated with remission at follow-up (Cohen and Iqbal, 2014). While social withdrawal was formerly seen as a key feature of schizophrenia, social connectivity is nowadays considered as protecting against relapse and deterioration (Tandon et al., 2010, 2009), although this relationship may be bidirectional. Next, the NYC longitudinal study found fewer psychotropic medications and fewer psychiatric services to be predictive of remission, whereas in the current study medication and compliance with medication, nor intensity of and adherence to services predicted conversion to remission at follow-up. Also, female gender was not associated with conversion to remission at follow-up, whereas an advantage of female patients in the long-term course of schizophrenia has been suggested (Aleman et al., 2003; Tandon et al., 2009). Next, cognitive functioning was not related to conversion to remission at follow-up, which is in contrast with findings in younger patients of cognitive impairment to be associated with a poorer long-term course of schizophrenia (Tandon et al., 2009), and preliminary findings of positive outcome in schizophrenia in case of superior working memory function (Palmer et al., 2018).

This study is the first longitudinal study of older schizophrenia patients employing a catchment area-based design, in which both community-living and institutionalized patients were included, regardless of age at onset of the disorder. All patients were traced at follow-up, of which 71% participated in the second assessment. In addition, a wide array of putative predictors of course was examined. However, the findings should also be considered in the context of the following limitations. The most important limitation of this study, and also of most previous longitudinal reports, is the lack of information about the interval between the first and second assessment, although hospitalization because of deterioration of symptoms was taken as a proxy of non-remission in the six months previous to assessment. It could well be that movement between remission and non-remission happens more frequently than reported. Hence, a more pleiomorphic long-term course, with frequent relapses and instability of remission remains undetected in this type of study design. Although in the present study drop-out over time was relatively low (13 participants living at T2 did not participate), the baseline cross-sectional study did suffer from non-consent with 109 out of eligible 172 patients (62%) participating. Overall, remission may well have been less prevalent among non-consenting patients (Meesters et al., 2011). Next, the sample size was relatively small, and drawn from a specific catchment area, thereby limiting the generalizability to other populations. The probability of detecting a true effect taken the current sample size ($n = 56$), i.e. the power to detect a significant effect, is maximal 0.60 in the case of logistic regression with a single predictor, and does not exceed the 0.50 level in case of multiple predictors. Furthermore, there is a possibility of type I errors as we did not correct for multiple comparisons in our univariate analyses. Finally, one should remain aware that a sizeable proportion of older individuals diagnosed with schizophrenia or schizoaffective disorder are not served by mental health services, either because of early recovery or of non-cooperation (Harrow et al., 2005; Jobe and Harrow, 2005).

To conclude, our study suggests the possibility of a positive symptomatic course in late-life schizophrenia, with a quarter of patients newly attaining symptomatic remission over a 5-year period. However, with lower intensity of positive psychotic symptoms, and having a partner emerging as the only longitudinal predictors of remission, there remains a clear need to search for modifiable predictors of symptomatic remission.

Conflict of interest

All authors declare that they have no conflicts of interest.

Contributors

Paul David Meesters collected the data. Sjors Lange managed the literature searches and analyses, undertook the statistical analysis, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Role of the funding source

The funding source did not have any influence on the study design.

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