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The prognostic significance of early remission of positive symptoms in first treated psychosis

Ross M.G. Norman [a,b,*,1], Rahul Manchanda [a,b], Deborah Windell [b]

[a] Department of Psychiatry, University of Western Ontario, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario, Canada N6A 5W9
[b] Prevention and Early Intervention Program for Psychoses (PEPP), London Health Sciences Centre, 800 Commissioners Road East, London, Ontario, Canada N6A 5W9

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ABSTRACT

Objectives: We examine the relationship between achieving remission of positive symptoms within 3 months in first episode psychosis and outcomes 5 years later.
Methods: Time to remission of positive symptoms, other early characteristics and 5 year outcomes were assessed in a prospective study of 132 patients being treated for the first time for a psychotic disorder.
Results: Just under 60% of patients showed remission of positive symptoms within 3 months. In comparison to later remitters, they showed lower levels of positive symptoms, greater likelihood of competitive employment and less likelihood of collecting a disability pension at 5 years.
Conclusions: Earlier remission of positive symptoms may have prognostic significance for longer term outcomes.

1. Introduction

One of the most obvious and earliest signs of response to treatment of psychotic disorders is reduction of positive symptoms. Time to remission of positive symptoms has frequently been used as an important indicator of treatment outcome for patients with a psychotic disorder (Lieberman et al., 1993; Ho et al., 2000; Perkins et al., 2004; Malla et al., 2006; Wade et al., 2006).

A recent and detailed examination of positive symptom remission in first episode psychosis (Simonsen et al., 2010), used severity criteria similar to those recommended by the Remission in Schizophrenia Working Group (Andreasen et al., 2005), and reported that 56% of patients showed remission of positive symptoms within 3 months of treatment (which they considered early remission), while by 2 year follow-up 16% of patients had never met criteria for remission of positive symptoms for 1 week. Those patients showing early remission were more likely to be single, have a schizophrenia related diagnosis, and have a shorter duration of untreated psychosis (DUP) and higher levels of negative symptoms.

While early remission of positive symptoms is desirable in itself, there has been little prospective investigation of the role of time to such remission in predicting longer term outcomes. Prospective research on previously untreated patients would be particularly important in addressing this issue. Alvarez-Jimenez, et al. (2011) reported that shorter time to remission of psychosis discriminated first episode patients with a single psychotic episode from those with relapses over a 7.5 year follow-up (Alvarez-Jimenez et al., 2011). In a subsequent paper (Alvarez-Jimenez et al., 2012), they did not find remission of positive symptoms by 8 weeks or 6 months of follow-up to predict functional and social recovery at 7.5 year follow-up, but no duration criteria were applied in the identification of positive symptom remission. Other studies examining the relationship between initial remission and subsequent course have not focused on remission of positive symptoms and/or have not used follow-ups of greater than two years (e.g., Chang et al., 2009; Cassidy et al., 2010a).

In the current study, we report data from a prospective study examining the implications of speed of remission of positive symptoms for symptom and functioning outcomes at 5 years. Our primary purpose is to test the hypothesis that earlier remission of psychotic symptoms is associated with better symptom and functioning outcomes at 5year follow-up. The data also permit further examination of the earlier findings regarding the factors that predict remission of positive symptoms.

* Correspondence to: Department of Psychiatry, University of Western Ontario, A2-643, London Health Sciences Centre-VH, 800 Commissioners Road East, London, Ontario, Canada N6A 5W9. Tel.: +1 519 685 8500x75493; fax: +1 519 667 6657.
E-mail address: rnorman@uwo.ca (R.M.G. Norman).
[1] Department of Epidemiology & Biostatistics, University of Western Ontario, A2-643, London Health Sciences Centre-VH, 800 Commissioners Road East, London, Ontario, Canada N6A 5W9.

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2. Method

2.1. Sample

Participants were recruited from successive admissions to the Prevention and Early Intervention Program for Psychoses (PEPP) in London, Canada. Patients had a psychotic disorder for which they had not previously received treatment. A total of 188 participants provided informed consent as approved by the Western University Ethics Board for Health Sciences Research.

The treatment program in PEPP includes pharmacological and psychosocial intervention for individuals with psychotic disorders (for details see Malla et al., 2003 or www.PEPP.ca). PEPP is primarily intended to treat non-affective psychotic disorders. The treatment program emphasizes continuity of care and an assertive case management model designed to address the needs of a younger population who have not received previous treatment or whose previous treatment did not exceed 30 days. At the end of 2years of treatment, a detailed review of each patient is carried out and he or she usually graduates to a less intensive stepped-down form of care within PEPP.

2.2. Measures and procedures

2.2.1. Early characteristics

Onset and treatment delay were identified using a structured interview (Norman and Malla, 2002), administered to patients and at least one collateral source. Age of onset was the age at which clear symptoms of psychosis emerged. DUP was the period of length of time between onset of psychotic symptoms and initiation of treatment as measured in weeks.

Level of symptoms at time of presentation for treatment were assessed with reference to the month prior to admission using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983), concerning the month prior to admission. Diagnosis is based on the Structured Clinical Interview for DSM-IV (First et al., 1995).

The Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982) was completed using information provided by patients and family. It was completed for developmental periods prior to the onset of symptoms. Parallel to the procedures used by Simonsen et al. (2010), change scores for the social and academic domain were calculated between the last premorbid developmental period and childhood (Simonsen et al., 2010).

Adherence to early treatment was assessed by each patient's primary clinician using a 5-point rating scale ranging from 0-not taking medication to 4-taking medication as prescribed, 75–100% of time. This measure has been found to correlate highly with pill count assessments (Cassidy et al., 2010b). The mean score at 2, 3, 6 and 12 months was used as an index of early adherence.

2.2.2. Outcomes

Course of psychotic symptoms during 5 years was assessed using a relapse-remission chart as part of a modified Life Chart Schedule (Susser et al., 2000). Assessments based on interviews with patients, clinicians and review of case notes, provided a detailed longitudinal assessment of positive symptoms, and allowed charting on a weekly basis of whether the patient had global ratings of less than 3 on items of the SAPS, corresponding to recommended severity criteria for remission of positive symptoms (Andreasen et al., 2005). Consistent with Simonsen et al. (2010) we used two alternate duration criteria for remission of positive symptoms, 1 week and 6 months.

The Global Assessment of Functioning (GAF; American Psychiatric Association, 1994) was completed at the end of the fifth year. In addition, two pragmatic measures of functional outcome were available. These were the number of weeks of full-time competitive employment and weeks on a disability pension during the final 2 years of follow-up. Level of positive and negative symptoms was assessed at the end of the fifth year using the SAPS and SANS.

All assessments were completed by trained and highly experienced research associates. The intra-class correlations between raters on all relevant assessments were at least 0.80.

3. Results

One hundred thirty-two individuals (70.2%) completed the 5year follow-up. Of these, 102 were male and 108 had a diagnosis of a core schizophrenia spectrum disorder (schizophrenia, schizoaffective or schizophreniform disorders). The vast majority (82.6%) were single with just under half (48.5%) not having completed high school at the time of entering treatment. There were no significant differences between those retained and not retained in early characteristics. The mean DUP was 73.7 weeks.

Table 1
Time to initial remission of positive symptoms.

Time	At least 1 week remission [n/(%)]	At least 6 months remission [n/(%)]
Month 1	39 (29.5)	39 (29.5)
Month 2	26 (19.7)	25 (18.9)
Month 3	13 (9.8)	13 (9.8)
Months 4–24	29 (21.2)	30 (22.7)
Years 3–5	12 (9.1)	10 (7.6)
Never remitted	13 (9.8)	15 (11.4)

DUP was positively skewed and a $\log_{10}$ transformation was effective in approximating a normal distribution.

Table 1 provides a classification of the length of time taken to meet criteria for positive symptom remission with duration of at least 1 week or 6 months. Following the precedent of Simonson, et al., those who achieved initial remission within 3 months were considered early remitters, and those who remitted subsequently were later remitters.

Results are very similar to those reported by Simonsen et al. (2010) who found 56.9% of their sample meeting remission criteria of 1 week duration within 3 months and 83.6% having experienced remission by 2 years. Of the 119 patients showing a 1 week remission of positive symptoms, 113 (95%) maintained remission for at least 6 months. Of the 6 patients whose initial remission was less than 6 months, 4 subsequently had a 6 month remission and 2 did not. Length of time to a 6 month remission for all patients is reported in the second column of Table 2. Given the high correspondence between 1 week and 6 month duration criteria (recommended by Andreasen et al. (2005)), we carried out subsequent analyses using 6 months duration.

Table 2 summarizes early characteristics associated with remission status. There was no significant relationship of remission status to sex, marital status, age of onset, initial symptom levels or social premorbid adjustment. Having a core schizophrenia diagnosis was associated with remission status ($\chi^2=8.05$; d.f.$=2$; $p<0.05$), reflecting a lower proportion of early remitters among individuals with a core schizophrenia diagnosis ($Z=2.7$; $p<0.05$). There was also a difference between remission groups in adherence to medication ($F=5.84$; d.f.$=2,113$; $p<0.01$), duration of untreated psychosis ($F=4.97$; d.f.$=2,129$; $p<0.01$), and deterioration of academic premorbid adjustment ($F=6.71$; d.f.$=2,121$; $p<0.01$). When these variables were entered into a logistic regression to predict whether or not an individual was an early remitter, only presence of a schizophrenia spectrum diagnosis was independently associated with remission status.

Table 3 summarizes data on prognostic significance of early remission for symptoms at 5 years. In order to avoid confounding the differences in symptomatology that are intrinsic to non-remission with outcomes, the relevant data do not include patients who had not remitted by the fourth year of follow-up.

Early remitters had significantly lower levels of positive symptoms at 5 years ($t=2.79$; $p<0.01$), higher levels of functioning as assessed by the GAF ($t=2.74$; $p<0.01$), and more weeks of competitive employment ($t=2.12$; $p<0.05$). There was also evidence of a borderline significance of early remitters having lower levels of negative symptoms ($t=1.70$; $p=0.09$) and fewer weeks on a disability pension ($t=1.77$; $p=0.08$).

4. Discussion

Our data concerning the proportion of patients showing remission of positive symptoms within 3 months and those showing later remission or no remission by 2 years, are remarkably similar to those

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