

# Predicting Real-world Functional Milestones in Schizophrenia

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**Abstract.** Schizophrenia is a severe disorder that often causes impairments in major areas of functioning, and most patients do not achieve expected real-world functional milestones. The aim of this study was to identify which variables of demography, illness activity, and functional capacity predict patients' ability to attain real-world functional milestones. Participants were 235 outpatients, 149 men and 86 women, diagnosed with schizophrenia spectrum disorder. Our results showed that younger patients managed to achieve a higher level of functioning in educational level, marital status, and social contacts. Patients' functional capacity was primarily associated with educational level and housing situation. We also found that women needed less support regarding housing and obtained a higher level of marital status as compared with men. Our findings demonstrate the importance of considering current symptoms, especially negative symptoms, and remission stability over time, together with age, duration of illness, gender, educational level, and current functional capacity, when predicting patients' future real-world functioning. We also conclude that there is an advantage in exploring symptoms divided into positive, negative, and general domains considering their probable impact on functional achievements.

**Keywords:** Schizophrenia; Functional capacity; Real-world functional milestones; Predictive factors.

## 1. Introduction

Schizophrenia is a severe and complex mental disorder that often has disabling consequences for the patients. It involves impairment in one or more major areas of functioning, and most patients do not achieve desired and expected real-world functional milestones (Cardenas et al., 2013 and Harvey, 2013). Educational level, independence in housing, current work situation, marital status, and quantity and quality of social contacts are examples of real-world functional milestones that objectively describe patients' functional achievements. There is, however, no consensus about what constitutes functioning (Gupta et al., 2012). For example, real-world functioning could be described as patients' achieved functional milestones (Harvey, 2013), as observer-rated reports of patient's behavior and skills (Schneider and Struening, 1983), or as functional capacity (Patterson et al., 2001).

The use of real-world functioning variables as measures of function could be problematic as they are not sensitive to manifest changes (Mantovani et al., 2015). Moreover, environmental factors may influence these indicators (Harvey et al., 2009, Helldin et al., 2012 and Priebe, 2007). In order to avoid that the assessments of patients' function are affected by environmental factors – such as the prevailing culture, the welfare system, and the labor market – the use of performance-based assessment instruments measuring functional capacity has increased in recent years (Mantovani et al., 2015 and Moore et al., 2007). One of these performance-based instruments is the University of California, San Diego (UCSD) Performance-Based Skills Assessment (UPSA; Green et al., 2011 and McKibbin et al., 2004). Functional capacity can be assessed at a clinic, in a set environment, where patients perform everyday tasks through role-playing (Bowie et al., 2008, McKibbin et al., 2004 and Patterson et al., 2001).

The discrepancy between a person's potential to perform (functional capacity) and what he or she actually does perform (real-world functional milestones) still remains to be investigated. Previous studies have found real-world functioning to be predicted by functional capacity (Bowie et al., 2008

and Ho et al., 2013), negative symptoms, and cognitive deficits (Bowie et al., 2008). Real-world functioning and functional capacity correlate moderately (Leifker et al., 2011) and explain 17% of each other's variance (Menendez-Miranda et al., 2015). Functional capacity also seems to mediate the relationship between neuropsychological functioning and real-world functioning (Bowie et al., 2008; Ho et al., 2013 and Mantovani et al., 2015). Measures of cognitive performance account for 25–50% of the variance in real-world functioning (Fett et al., 2011 and Harvey et al., 1998), whereas gender, ethnicity, and age have traditionally been the most important demographic factors for predicting real-world functioning (Gould et al., 2012). It is clinically important to explore if other factors exist and, if so, to understand how they influence real-world functioning (Harvey and Strassnig, 2012). Harvey (2013) has suggested that real-world functioning, as measured by separate scales for social, vocational, and residential functioning, should be preferred over combined global functioning scores.

Taking this complex background into account, the aim of this study is to identify which variables of demography and illness activity, together with functional capacity, predict patients' ability to achieve real-world functional milestones. Further, we investigate how these predictors contribute to explain the five functional milestones Educational level, Current work situation, Housing situation, Marital status, and Social contacts.

## 2. Methods

### 2.1. Procedure

Data collection took place within the ongoing project Clinical Long-term Investigation of Psychosis in Sweden (CLIPS), which investigates psychiatric outpatients. Patients partaking in the project were rated annually on several domains, including demographic and functional variables (e.g., age, gender, social function, work capacity, and ability to live independently) and clinical variables (e.g., psychiatric symptoms and remission status). The assessments of demographic and illness activity variables were administered by a case manager with in-depth knowledge of the patient and highly skilled in assessment methodology, and an occupational therapist measured patients' functional capacity. Exclusion criteria for participation in the CLIPS project were comorbidities such as mental retardation and autism. For this study, a total of 259 patients were assessed, and 24 patients were excluded: 17 because of missing data for demographic and illness activity variables from the same assessment session, and seven because they had not been assessed for all functional capacity items.

### 2.2. Participants

In this study, 235 patients participated, 86 women and 149 men, with a mean age of 49.9 years ( $SD=11.4$ , between 24 and 74 years of age). The mean age of the women was 51.5 years ( $SD=12.3$ ) and the mean age of the men was 48.98 years ( $SD=10.8$ ). An independent *t* test ( $p=0.12$ ) showed no significant difference between men and women regarding age. Mean age at illness onset was 26.02 years ( $SD=10.4$ ): 27.68 years ( $SD=11.4$ ) for the women and 25.02 years ( $SD=9.7$ ) for the men, with no significant difference ( $p=0.08$ ). Among the study participants, 157 patients were diagnosed with schizophrenia, 49 patients with schizoaffective disorder, and 29 patients with delusional disorder. At the time of assessment, 117 of the 235 participants were in remission. The mean of the Global Assessment of Functioning Scale (GAF), rated by the case manager, was 45 points, with a variation between 30 and 70 points ( $SD=7.8$ ).

### 2.3. Measures

#### 2.3.1. Demographic variables

The demographic variables were gender, age, age at illness onset, and illness duration.

#### 2.3.2. Illness activity variables

The variables investigated to measure illness activity were current symptoms and remission status stability during the past three years. Patient symptoms were examined using the Positive and Negative Syndrome Scale (PANSS) by Kay et al. (1987). The PANSS is an interview and observation-based instrument with 30 items divided into three domains: positive symptoms (P 1–7), negative symptoms (N 1–7), and general symptoms (A 1–16). Each item is rated on a seven-point scale where low scores indicate low levels of symptom severity and high scores indicate high levels

of symptom severity (Kay et al., 1987). Patients were assessed using a Swedish version of the Structured Clinical Interview – Positive and Negative Syndrome Scale (Lindström et al., 1994). Patients in remission can be identified by examining eight selected items from the PANSS (Andreasen et al., 2005; Lasser et al., 2007).

All patients were regularly followed up by their case manager between assessments over three years. To be in stable remission, the patient had to be in remission at all times measured and with no relapses in between.

#### 2.3.3. Functional capacity

Functional capacity was assessed using the University of California, San Diego (UCSD) Performance-Based Skills Assessment – Brief (UPSA-B; Mausbach et al., 2007), a performance-based observational instrument assessing patients' ability to cope with everyday tasks. The instrument assesses functional capacity in two domains: finance (counting money and paying bills) and communication (e.g., making an emergency call, rescheduling a medical appointment). There are a total of 19 items in the UPSA-B and, by using a standardized calculation of the scores, the total score ranges from 0 to 100 (Mausbach et al., 2007). A study of the Swedish version of the UPSA-B found that this version of the instrument has good psychometric properties regarding both validity and reliability (Olsson et al., 2012).

#### 2.3.4. Functional milestones

Three items from the Strauss-Carpenter scale (Strauss and Carpenter, 1972) were used to assess real-world functional milestones. The chosen items, with three response alternatives, were Current work situation (sickness benefit/unemployed, part time job, or full-time job), Housing situation (supported housing, living with parents, or independent housing), and Social contacts (seldom contact with others, contact with others once a week, or contact with others more than once a week). The original Strauss-Carpenter scale was modified by Lindström et al., 1995 and Helldin et al., 2007 included items for Educational level (primary, secondary, or higher education) and Marital status (single, separated, or married/cohabiting). Information was collected via medical records as well as from interviews with patients, relatives, and medical staff.

#### 2.4. Analyses

The demographic, illness activity, and functional capacity variables and their covariance with functional milestones were examined separately. In the descriptive part of the results, the mean (M), standard deviation (SD), and in some cases percentages are reported. Correlations between continuous variables were determined using Spearman's rho. The Chi-Square test ( $\chi^2$ ) and the Kruskal-Wallis test (H) with multiple comparison tests were used to analyze differences in demographic and clinical variables between independent categories of functional milestones. Ordinal logistic regression analyses were done with the five functional milestones (Educational level, Current work situation, Housing situation, Marital status, and Social contacts) as dependent variables, and the demography, illness activity, and functional capacity variables – which in the previous step showed significant results (correlations or significant group differences) for each of the functional milestones – as predictor variables. As none of the predictors were significantly associated with Current work situation, this functional milestone was excluded from further analyses. The results are presented as odds ratios and 95% confidence intervals.

### 3. Results

Descriptions of patients' demographic, illness activity, functional capacity, and real-world functional milestones data are presented in Table 1. The distribution of data differs between the categories of the functional milestones: educational level has an even distribution compared with Current work situation where 88.5% of the patients are in the same category (sickness benefit/unemployed).

Demographic, illness activity, and functional capacity variables (predictors) were tested for differences between categories of each functional milestone (criterion variables; see Table 2). None of the predictors were significantly associated with Current work situation, so this functional milestone was excluded from further analyses. Most independent variables showed significant group

differences for the functional milestones Housing situation, Marital status, and Social contacts. Differences were most common between the lowest (Group 1) and highest (Group 3) levels of functioning. Age correlated with all the functional milestones except for Current work situation. Due to correlations between age, age at illness onset, and years of illness duration ( $r_s=0.615$  and  $0.425$ ,  $p<0.01$ ), only the patients' age was selected as a predictor in the following regression analyses in order to avoid multicollinearity.

Ordinal logistic regression analyses were conducted to examine the impact of the demographic, illness activity, and functional capacity variables on variance in each of the presented real-world functional milestone variables. The functional milestones (except for Current work situation) were used as dependent variables, and the demographic (except for age at illness onset and illness duration), illness activity, and functional capacity variables that in the first step of the analyses showed a significant result were used as predictors (Table 3).

Educational level was associated with functional capacity and age. An increase in functional capacity (expressed in higher UPSA-B scores) was associated with an increase in the odds of higher level of education, with an odds ratio of 1.036 (95% CI, 1.019–1.054), Wald  $\chi^2(1)=17.635$ ,  $p<0.000$ . A closer examination of UPSA-B mean scores showed that they were lower ( $M=58.41$ ) for patients whose highest educational level was primary school compared with those who had completed secondary school ( $M=75.03$ ) or higher education ( $M=81.56$ ). Patients with primary school as highest educational level were older (mean age 54.50 years) compared with patients who had completed secondary school ( $M=46.22$  years) or higher education ( $M=47.14$  years). The ordinal logistic regression model explained 24.4% of the variance.

Housing situation was associated with gender (OR=0.099), PANSS general symptoms (OR=0.889), and functional capacity (OR=1.033). A closer examination revealed that male patients (12% compared with 6% of the female patients), patients with more severe general symptoms ( $M=35.48$ ), and patients with lower functional capacity ( $M=49.35$ ) lived in supported housing to a higher degree. There were also gender differences in patients who lived together with their parents (9% of the men compared with 1% of the women) and in those who lived independently (79% of the men compared with 93% of the women). Patients who lived in independent housing had a mean score of 70.56 for functional capacity and 28.06 for PANSS general symptoms. The ordinal logistic regression model explained 27.3% of the variance.

The odds ratio for male patients to achieve a higher level in the functional milestone Marital status was 0.246 (95% CI, 0.146–0.479) times that of female patients—a statistically significant effect, Wald  $\chi^2(1)=19.286$ ,  $p<0.001$ . Male patients were more often single (75% compared with 41% for women), and 59% of the women were or had been married/cohabiting compared with just 25% of the men. Marital status was also associated with age (OR=0.966) and PANSS positive symptoms (OR=0.915). A closer examination showed that patients who were single had a lower mean age (47.39 years) and more severe positive symptoms ( $M=13.32$ ) compared with those who were married (mean age 51.95 years, positive symptoms mean score 9.41) and those who were separated (mean age 55.66 years, positive symptoms mean score 12.76). The ordinal logistic regression model explained 24.4% of the variance.

Frequency of social contacts was associated with age (OR=0.942) and PANSS negative symptoms (OR=0.883). A closer examination showed that patients who had more contact with others and met friends and/or families more than once a week had a lower mean age (48.09 years) and less severe negative symptoms ( $M=13.77$ ) compared with those who met friends and/or families once a week (mean age 52.42 years, negative symptoms mean score 17.18) and those who only had short and temporary contacts with others (mean age 54.45 years, negative symptoms mean score 22.10). The ordinal logistic regression model explained 25.8% of the variance.

#### 4. Discussion

This study, which has a large sample across a wide span of ages and years of illness, shows that patients' age, functional capacity, and gender correlate with several functional milestones: younger patients have a higher functional capacity, and women more often attain higher real-world functional

milestones. Our findings also show that there are advantages of dividing symptoms into positive, negative, and general domains as these different symptom domains are associated with different functional milestones.

As expected, there are strong associations between age, illness duration, and attainment of functional milestones. The findings of Barnes and Pant (2005) show that functional impairment in patients with schizophrenia and other psychotic disorders primarily occurs within 5–10 years after illness onset. In the current study, the mean illness duration is close to 24 years, which means that, based on the above reasoning, a majority of the patients' functional impairment can be considered stable. However, the age at illness onset does not have an impact on the functional milestones, except for Marital status. Prevalence of schizophrenia does not differ between men and women, but there may be differences in the course of illness even though no previous consensus has been established (Siegel et al., 2006). Some studies show that women with schizophrenia have a better prognosis than men. This could be explained by later onset of illness among women, which in turn leads to higher premorbid functioning, lower rates of negative symptoms, and better social functioning (Goldstein and Walder, 2006 and Häfner et al., 1998). The mean age for illness onset was 26.02 years in the present study, whereas age of illness onset is generally between 15 and 35 years—in late adolescence or early twenties for men and later twenties or thirties for women (Thomsen, 1996). The later illness onset among women might also explain why they reached a higher level than men in marital status in our study. Furthermore, fewer women lived in supported housing or together with their parents. And 79% of the men and 93% of the women lived independently.

Functional capacity mainly correlates with educational level and the ability to live independently in the community. These findings are well in line with previous results (Gould et al., 2012, Mausbach et al., 2007 and Mausbach et al., 2008; McIntosh et al., 2011). The functional capacity did not significantly predict patients' current work situation, as in a previous study (Mausbach et al., 2011). In our study, only fourteen patients (6%) worked or studied full time, which could be compared with 12% found in a study by Lindström et al. (2007). Hence, unemployment or early retirement are well-recognized outcomes of schizophrenia (Svedberg et al., 2001), and unemployment rates vary across countries and time. The study of Kooyman et al. (2007) shows that 11.5% of a British sample were employed or in sheltered employment, while corresponding rates were 12.9% of a French sample and 22% of a United States sample. Previous findings also show that environmental factors, such as the labor market, may impede the achievement and use of functional skills (Harvey et al., 2009, Helldin et al., 2012 and Priebe, 2007).

Social skills are often linked to a person's ability to keep a job (Shannon et al., 2006). Our analyses of group differences show that patients who remained in remission continuously during the past three years had a higher ability for social contacts, which is in line with previous findings (Helldin et al., 2007). Furthermore, these results emphasize the importance of continuing the pursuit of good symptom control – especially for negative symptoms – and remission stability in order to increase the chances of maintaining high functioning. Previous studies have reported that negative symptoms correlate with real-world functioning (Ventura et al., 2009), but our results show that negative symptoms only predict the functional milestone Social contacts. Furthermore, the present study shows that dividing symptoms into positive, negative, and general domains could be useful for exploring real-life outcomes.

This study has some limitations. Because it is a naturalistic study design, it is difficult to know how representative this specific sample is for the patient population in general. A previous study from the CLIPS project reported that 670 patients fulfilled the inclusion criteria and were invited to join the project (Helldin et al., 2008), and about 35% of these possible participants for the project were included in the present study. Using retrospective data, such as age at illness onset and illness duration, requires extra caution due to, for example, patients' difficulties to recall past events. To reduce such bias, these retrospective data were collected from, and compared with, different sources such as medical records, patients, relatives, and medical staff. Another possible problem, for which we used non-parametric statistics, is the skew distribution among categories that were found in some variables. One strength of this study is that the patients' age as well as illness duration spans across a

much wider range than is usual in this type of study. Our results thus provide a more representative picture, which will help create better conditions for daily clinical work.

There is a growing interest in developing remission criteria for functioning similar to those that exist for symptoms (Lançon et al., 2012 and Spellmann et al., 2012). Variables from several domains are probably required in order to clarify patients' ability to cope with everyday activities. Our results demonstrate that patients' current symptoms – especially negative symptoms – and remission stability over time, together with their age, duration of illness, gender, educational level, and current functional capacity, should be taken into consideration as variables in future studies describing real-world functioning.

## Ethical approval

The study was approved by the Ethical Research Committee at the University of Gothenburg, Sweden (Approval number: Ö537-99, 507-04, 438-10, 423-14), and the investigation was carried out in accordance with the latest version of the Declaration of Helsinki.

## Conflict of interest

No authors declare any conflict of interest.

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