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# Disability multilevel modelling in first episodes of psychosis at 3-year follow-up

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#### ABSTRACT

The description of longitudinal bio-psycho-social profiles in FEP samples may be useful for the prediction of disability trajectories. This study aimed to describe the differences between disability status of FEP patients at baseline and their change over time, analysing how variables associated to the psychological status, and the environment of the patient can affect his or her disability trajectory, once the influence of health condition and socio-demographic variables has been controlled for. Using data from a 3-year follow-up study on early psychosis (PAFIP), a multilevel structure in which the longitudinal measurements (within level) were nested within the individuals (between level), was modeled. The contribution of the different time-varying and time-invariant variables to the patients' disability outcomes was tested through eight nested models. Consecutive models, that successively added health related, socio-demographic, psychological and environmental variables to the unconditional model were estimated, by means of deviance and fit statistics.

The present work revealed the importance of psychological and environmental factors in the explanation of disability changes in the context of FEP.

We may conclude that longitudinal assessments of time-varying predictors – living situation (b = -0.10, p < 0.05), economic support (b = 0.11, p < 0.01) and insight (b = -0.08, p < 0.05) – explain a relevant amount of disability variation over time, independently from symptoms' severity, duration of untreated psychosis, age, gender and years of education. Additionally, the level of premorbid adjustment (b = 0.05, p < 0.001) was associated to differences in disability outcomes among FEP patients.

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#### 1. Introduction

Psychosocial difficulties frequently constitute a disabling disadvantage that adds up to the intrinsic burden of schizophrenia spectrum disorder symptoms (Switaj et al., 2012). The dimension of a patient's perceived disability should be considered when analysing functional restoration (Harvey and Bellack, 2009). Wiersma et al. (2000) found that the remission of symptoms during the first two years in a sample of patients with first episode of schizophrenia from six European cohorts did not play a very important role in explaining the variation of disability scores. Notwithstanding, few studies have considered disability as a relevant outcome variable using longitudinal designs in the context of FEP (Cornblatt et al., 2012; Hodgekins et al., 2015).

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http://dx.doi.org/10.1016/j.schres.2016.12.014 0920-9964/© 2016 Elsevier B.V. All rights reserved. Changes over time in relevant factors such as psychosocial abilities (DeSisto et al., 1995), stressful life events, social and family support networks, patient reactions to illness, and self-attitudes (Wing, 1988) and antipsychotic medication (Robinson et al., 1999), may have an impact on the disability evolution of first episode of psychosis (FEP) patients. In fact, past research addressing risk factors for disability has found that variables measured at baseline do not contribute significantly to variance in the functioning outcome (Gonzalez-Blanch et al., 2015).

As Ayesa-Arriola et al. (2013) have hypothesized, the low predictive capacity of baseline cognitive and health-related factors on follow-up functioning outcomes might be explained by chronicity and other disorder traits. Baseline measures of gender (Jablensky et al., 1992), cognitive functions (Allott et al., 2011), negative symptoms (Milev et al., 2005), premorbid adjustment (Jeppesen et al., 2008) or years of education (Ayesa-Arriola et al., 2013) have shown an association with FEP patients' disability status, yet with a high percentage of disability variance remaining unexplained in the long term.

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Along these lines, a recent study illustrated how the disorder profiles in a FEP sample could be studied based on measures collected 6 months after the onset of symptoms, and that the association between baseline indicators and degree of outcome disability was influenced by follow-up duration (Schubert et al., 2015).

All the above-mentioned evidence from past studies seems to indicate that investigations of disability changes taking successive followup assessments and time-varying risk factors measurements into account could result in useful tools for explaining disability variation and its time-varying predictors. A methodological approach able to capture these two facets of within-patient vs. between-patient change as part of a trajectory of change over time, and that simultaneously addresses between-patient time-invariant variability, is Multilevel Analysis (Snijders and Boskers, 1999) applied to repeated measures, which has scarcely been explored (Hayes, 2006).

With this method, all participants' data can be analysed despite attrition, and different modalities of variables may be included. Therefore, it offers an advantageous alternative to traditional techniques (Gadelrab et al., 2010). In the present work, the aim was to examine the longitudinal effect that a range of time-varying factors have on the change in disability outcomes over time in patients with FEP. We postulate that changes in psychological and environmental factors will play an important role in the variation in disability at the 3-year assessment in addition to health status-related variables.

#### 2. Methods

#### 2.1. Design

The present research is based on data from a 3-year follow-up FEP longitudinal intervention study (PAFIP) conducted at the Marques de Valdecilla University Hospital in Santander (Cantabria, Spain) (Crespo-Facorro et al., 2006). More details about the PAFIP project have been provided by Pelayo-Teran et al. (2008).

#### 2.2. Sample

The present study analysed the data from all patients who were recruited (i.e., they had their baseline evaluation) in the PAFIP study between 16 February 2001 and 23 July 2012 (N = 449). They were followed up during a period of three years.

The patients enrolled in the study met the following inclusion criteria: a) age between 15 and 60 years; b) living in the catchment area; c) going through a first episode of psychosis; d) with no previous antipsychotic drugs treatment history or, else, adequate antipsychotic medication and or treated for only six weeks or less; e) a diagnosis of schizophrenia (35.6%), schizophreniform disorder (31.4%), brief psychotic disorder (23.2%), schizoaffective disorder (0.2%), or delusional disorder (0.9%) according to DSM-IV criteria diagnosed by means of the Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 1996) by an experienced psychiatrist (BC-F) 6 months after the baseline interview.

From the four hundred and forty nine subjects enrolled in the study, 42.3% were women (n = 190) and 57.7% men (n = 259). Only patients providing data for all the study variables during follow-up, and those who were assessed from the beginning of the study to the 1-year and 3-year follow-up were finally analysed.

A pharmacological medication protocol was applied during the first 6 weeks after baseline, and dose and type of medication was changed during the follow-up according to the patient clinical status.

No significant differences in treatment – aripiprazole (23.6%), risperidone (20.5%), olanzapine (12.7%), quetiapine (15.6%), ziprasidone (14.7%), or haloperidol (12.7%), assigned depending on randomly created groups – were found among diagnosis subsamples with regard to treatment – mean chlorpromazine equivalent dose (Gardner et al., 2010), or concomitant medications. This observational study was part of the Phase IV Study of the Effectiveness of Aripiprazole, Quetiapine and Ziprasidone in the Treatment of First Episode of Non-affective Psychosis Individuals Included in the First Episode Psychosis Clinical Program (PAFIP II), a project approved by the Ethics Committee of Marqués de Valdecilla University Hospital, Santander, Spain. The project has been registered with the number NCT 02305823 at www.clinicaltrials.gov and has been conducted according to international standards for ethics in research, in agreement with the Charter of Fundamental Rights of the EU (Art. 3), and the Helsinki Declaration in its latest version. In the present study, an informed consent form was signed by all patients and their families, and patients did not receive any money for their participation.

#### 2.3. Variables relevant to the analysis

#### 2.3.1. Dependent variable

Disability outcomes were measured by the Spanish version of the Disability Assessment Schedule (DAS) (Maná et al., 1998) on every assessment. This tool was specifically designed for psychiatric populations and assesses the functioning status during the previous 30 days. An overall judgement of total disability, ranging from 0 to 5, with a greater score designating a greater degree of disability, was used. This outcome was dichotomized: scores equal to zero indicated absence of disability, while scores higher than zero indicated presence of disability.

#### 2.3.2. Independent variables

*Health status-related variables:* 

- Duration of untreated illness (DUI) refers to the time between disorder onset and the first dispensation of drug treatment.
- The Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) were included in the study protocol. The Brief Psychiatric Rating Scale (BPRS) was applied to identify other psychiatric symptoms (Overall and Gorham, 1962) at each assessment time point. The disorder's evolution and the patient's response to medication were evaluated with the Clinical Global Impressions (CGI) Scale (Guy, 1976).

#### Socio-demographic variables:

• Gender, age and number of years of education were collected at baseline.

#### Psychological factors:

- Premorbid Adjustment Scale (Cannon-Spoor et al., 1982) was applied once, to assess the degree of achievement of developmental goals over the course of childhood and adolescence.
- Insight was assessed at 6 months, 1 year and 3 years using the first item (conscience of illness) on the Scale of Unawareness of Mental Disorder (SUMD) (Amador et al., 1994) and dichotomized (with/ without any conscience of disorder).
- The assessment of premorbid IQ was performed by means of the vocabulary subtest on the Wechsler Adult Intelligence Scale-III (Wechsler, 1999) at baseline, and at 1- and 3-year follow-ups.

#### Environmental factors:

- The existence of economic support (with/without), substance use (use of drugs/no use of drugs) and the patient's living situation (with family of origin/independent) and any history of academic support (yes/no), were registered at each time point assessment.
- Time variable was addressed according to the three specific assessment points in the study: baseline, 1 year and 3 years. Because of the specificity of the notion of insight and its development throughout the course of the disorder, this particular indicator was assessed at

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