



## Early non-adherence to medication and other risk factors for rehospitalization in schizophrenia and schizoaffective disorder

Robert Bodén<sup>a,b,\*</sup>, Lena Brandt<sup>a</sup>, Helle Kieler<sup>a</sup>, Morten Andersen<sup>a</sup>, Johan Reutfors<sup>a</sup>

<sup>a</sup> Centre for Pharmacoepidemiology (CPE), Department of Medicine, Karolinska Institutet, Solna, Sweden

<sup>b</sup> Department of Neuroscience, Psychiatry, Uppsala University, Sweden

### ARTICLE INFO

#### Article history:

Received 14 June 2011

Received in revised form 12 August 2011

Accepted 29 August 2011

Available online 5 October 2011

#### Keywords:

Schizophrenia

Antipsychotics

Epidemiology

Outcome studies

Adherence

Hospitalization

### ABSTRACT

Non-adherence to antipsychotic medication and hospitalization in psychotic disorders are common and costly problems. Our aim was to identify risk factors for rehospitalization of patients with recent onset schizophrenia or schizoaffective disorder in a population-based cohort study. All patients with a first hospitalization for schizophrenia or schizoaffective disorder between 2006 and 2007 were included ( $n=861$ ). Patients were identified through and data retrieved from national Swedish health and population registers. We investigated how socio-demographic variables, duration of first hospitalization and prescription fills of antipsychotics were associated with rehospitalization in Cox regression models. A higher risk for rehospitalization within 28 days was observed in patients with a first hospitalization that was shorter than two weeks compared with patients who were hospitalized for more than four weeks: hazard ratio (HR) 2.30, 95% confidence interval (CI) 1.42 to 3.74. Further, patients who did not fill a prescription of antipsychotics within the first week after discharge had a higher risk of early rehospitalization than patients who were given antipsychotics (HR 1.75, 95% CI 1.13 to 2.72). More than 12 years of education was associated with a lower risk of early rehospitalization (HR 0.44, 95% CI 0.26 to 0.77). Sex, age, being born in Sweden, urban area residence and prescription fills of antipsychotics prior to first admission did not significantly affect the risk of early rehospitalization. In conclusion, we identified two potentially modifiable risk factors for rehospitalization: short duration of initial hospitalization and early non-adherence to medication.

© 2011 Elsevier B.V. All rights reserved.

### 1. Introduction

Non-adherence to antipsychotic medication regimens and hospitalization are common and costly in the treatment of schizophrenia (Marcus and Olfson, 2008; Tiihonen et al., 2011). Potential consequences of poor adherence to antipsychotic medication include relapse, suicide attempts, violent acts, crime victimization and arrests (Ascher-Svanum et al., 2006; Novick et al., 2010). Several studies have suggested an increased risk of rehospitalization because of gaps in prescription fills of antipsychotics, i.e. not refilling a prescription in time before exhausting one's supply of medication (Weiden et al., 2004; Law et al., 2008). Other risk factors associated with rehospitalization in schizophrenia in Medicaid studies are comorbid substance abuse and use of anticholinergic drugs in patients with schizophrenia (Lang et al., 2010). However, much of the previous knowledge and understanding of non-adherence as a risk factor for rehospitalization is derived from studies with highly selected

populations of multi-episode patients (Weiden et al., 2004; Law et al., 2008; Lang et al., 2010).

Studies of patients in the early phase of schizophrenia are concordant with the above-mentioned multi-episode studies in their observation that even brief periods of non-adherence are associated with a higher risk of relapse (Subotnik et al., 2011). Furthermore, a first-episode psychosis study has shown that a high number of help-seeking contacts to health professionals, police or others (e.g. religious institutions, relatives) before first admission and persistent psychotic symptoms at discharge predict readmission (Cougard et al., 2006). A limitation of most of these first-episode studies is that they were based on small, selected clinical samples with substantial loss to follow-up. A recent Finnish nationwide study assessed risks of rehospitalization in association with antipsychotic medication dispensed to the patients after discharge. In brief, the study reported that only a minority of the patients with a first admission for schizophrenia adhered to their treatment (Tiihonen et al., 2011). However, effects of early non-adherence or socio-demographic factors were not evaluated in the Tiihonen et al. (2011) study. It has also been observed that the majority of patients with first-episode schizophrenia are rehospitalized within a few years (Eaton et al., 1992; Tiihonen et al., 2011) but factors associated with the initial inpatient treatment and subsequent outcome are not well described in the literature

\* Corresponding author at: Department of Neuroscience, Psychiatry, Uppsala University Hospital, Ing 15 3tr, SE-751 85 Uppsala, Sweden. Fax: +46 18515810.

E-mail address: [robert.boden@neuro.uu.se](mailto:robert.boden@neuro.uu.se) (R. Bodén).

(Durbin et al., 2007). Thus, a more elaborate characterization of the risk factors for repeated hospitalizations in clinically generalizable populations is needed.

The present study aimed to investigate risk factors related to rehospitalization, with special attention given to early non-adherence to antipsychotic pharmacotherapy. We hypothesized that non-adherence early after discharge would be associated with a higher risk of rehospitalization.

## 2. Methods

### 2.1. Registers

This population-based cohort was identified using Swedish nationwide registers. Each Swedish citizen has a unique personal identification number that allows linkage of information from these various sources.

The National Patient Register, which is maintained by the National Board of Health and Welfare, contains information on diagnoses from all specialized inpatient and outpatient care in Sweden (excluding primary care facilities), including involuntarily treated and forensic psychiatric patients. The Swedish Prescribed Drug Register, also maintained by the National Board of Health and Welfare, comprises information on all prescription fills in Sweden, including the Anatomical Therapeutic Chemical code (ATC) of the dispensed substances, amount, formulation and date of prescribing and dispensing (Wettermark et al., 2007). However, it does not cover drugs administered at hospitals. The population registers kept by Statistics Sweden include a detailed range of socio-demographic data.

From the National Patient Register, data on number and length of hospitalizations with psychiatric diagnoses (ICD-10 codes F10–F99) were included from 1997 to 2007. Furthermore, earlier schizophrenia and schizoaffective diagnoses (ICD-8 and ICD-9 code 295) recorded between 1969 and 1996 were used to select patients with a first ever diagnosis. Swedish clinical ICD diagnoses of schizophrenia and schizoaffective disorder have been shown to have good validity and high concordance with diagnoses from the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R or DSM-IV) (Dalman et al., 2002; Vares et al., 2006). From the Swedish Prescribed Drug Register, data on all dispenses of antipsychotics (ATC code N05A) were included from the beginning of July 2005 to the end of December 2007. From the population registers, we included data from 2006 to 2007 on country of birth, residential area and the highest attained level of education. The study was approved by the local ethical committee in Stockholm (No: 2009/415-31/4).

### 2.2. Participants

All patients with a first ever discharge diagnosis of schizophrenia or schizoaffective disorder (ICD-10 codes F20 and F25) in 2006 and 2007 and younger than 45 years of age were included. Patients with at least four weeks of hospitalization with another psychiatric diagnosis six months or more before their first hospitalization for schizophrenia or schizoaffective disorder were not included.

### 2.3. Risk factors and outcome

The following factors were included as potential risk factors of rehospitalization: sex, age, being born in Sweden, residence in a metropolitan area, educational level at the time of the first diagnosis of schizophrenia or schizoaffective disorder, years from first other non-affective psychosis diagnosis (such as acute and transient psychosis, delusional disorder or psychosis not otherwise specified) before being diagnosed with schizophrenia or schizoaffective disorder, dispensed antipsychotics before first hospitalization, duration of first hospitalization and early post-discharge non-adherence to antipsychotics (ATC code

N05A). Maintenance treatment with antipsychotics is recommended in schizophrenia and schizoaffective disorder (Buchanan et al., 2009; NICE\_CG82, 2009). Thus, we defined early non-adherence as not having filled a prescription of antipsychotic medication within the first week after discharge from the index hospitalization.

Outcome was defined as time to first rehospitalization. The maximum observation time was two years (from 1 January 2006 to 31 December 2007). Because non-adherence was measured in the first week after discharge, patients could not be at risk of rehospitalization during the first week. Consequently, we excluded patients who were readmitted within the first seven days ( $n = 43$ ). The period of rehospitalization was stratified into two categories (7–28 and  $\geq 29$  days).

### 2.4. Statistical methods

Patients were followed up until first rehospitalization or date of death. The analyses were performed in three steps. First, the effects of the investigated risk factors for rehospitalization were plotted as Kaplan–Meier curves and inspected for proportional hazard over the observed period. Second, the risk factors were investigated one at a time in univariate Cox regression models. Third, we assessed the influence of the duration of hospitalization and filling a prescription within the first week after discharge according to previous use of antipsychotics. In further analyses we investigated the risk of rehospitalization in three periods (7–28, 29–180 and  $\geq 181$  days).

## 3. Results

In total, 861 patients were included in the study. The mean age was 32 years (standard deviation [SD] 8 years) and the median duration from first outpatient schizophrenia or schizoaffective diagnosis was one year (interquartile range [IQR]: 0–5 years). The patients were followed for a median time of 164 days (IQR: 53–355 days). Of the 861 patients included in the study, 382 (42.3%) were rehospitalized and 5 died during the observation period.

Descriptive data and hazard ratios (HRs) of the investigated socio-demographic and treatment-related background factors for rehospitalization are summarized in Table 1. Having achieved an education of more than 12 years was associated with a decreased risk of early rehospitalization. Patients with a first hospitalization shorter than two weeks and patients not filling a prescription of antipsychotics within the first week after discharge had higher risks of rehospitalization. None of the other assessed variables in Table 1 were associated with early rehospitalization.

The Kaplan–Meier curve in Fig. 1 depicts a proportional higher hazard of rehospitalization in patients with an index hospitalization of 14 days or shorter than in patients with a longer initial stay. Moreover, the difference was more pronounced in the antipsychotic naïve group than in patients previously using antipsychotics. Fig. 2 illustrates similarly the proportionally higher hazard for readmission in patients with early non-adherence to antipsychotics than patients who filled prescriptions of antipsychotic medication.

Table 2 summarizes the HRs of rehospitalization stratified by duration of index hospitalization and previous use of antipsychotics. Patients with a hospitalization shorter than two weeks had a more than doubled risk of early rehospitalization (days 7–28) than patients hospitalized for more than four weeks regardless of previous use of antipsychotics. Patients with an index hospitalization of 15–28-days duration did not have a higher risk of rehospitalization than those initially hospitalized for more than four weeks. A similar risk increase was observed in the antipsychotic naïve patients for rehospitalization within 29–180 days but not after 180 days. The antipsychotic naïve patients who did not fill a prescription of antipsychotics within the first week after discharge had double the risk for early rehospitalization (days 7–28) than patients who filled a prescription. From 29 days after discharge, no increased risks could be observed. Patients with

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات