



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: [www.elsevier.com/locate/schres](http://www.elsevier.com/locate/schres)

## Determinants of duration of untreated psychosis among first-episode psychosis patients in Denmark: A nationwide register-based study

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### ARTICLE INFO

#### Article history:

Received 20 January 2017

Received in revised form 24 May 2017

Accepted 24 May 2017

Available online xxx

#### Keywords:

Duration of untreated psychosis

Register study

Early intervention in psychosis

### ABSTRACT

**Background:** Information on determinants of duration of untreated psychosis (DUP) is still needed to inform campaigns targeting people with first episode psychosis (FEP). This nation-wide study analysed the association between demographic factors (age, sex, ethnicity, marital status, and geographic area), premorbid and illness-related factors (global functional level, substance misuse, and contact to police), healthcare factors (referral source and first FEP contact) and DUP.

**Method:** The study population of 1266 patients aged 15–25 years diagnosed with FEP (ICD10 F20.0–F20.99) was drawn from the Danish National Indicator Project during 2009–2011. The study population was combined with data from national administrative registers. A multinomial regression model was estimated to analyse the impact of demographic, premorbid and illness-related, and healthcare factors on DUP.

**Results:** One third of the population had a DUP below 6 months. DUP longer than 12 months was associated with older age at onset, being female, having cannabis misuse, and living in peripheral municipalities. Being charged by the criminal authorities during one year before FEP was associated with a DUP over 6 months.

**Conclusion:** DUP is related to a number of demographic, premorbid and healthcare factors. These findings suggest that future information campaigns should focus on increasing the awareness of early signs of psychosis not only among mental health professionals but also other professionals in contact with adolescents such as the police. It may also be useful to consider how to target information campaigns towards persons living in peripheral areas.

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### 1. Introduction

A long duration of untreated psychosis (DUP) is associated with poor prognosis (Marshall et al., 2005; Perkins et al., 2005) and causes distress to patients and their families (Clarke et al., 2007). Research has demonstrated that early detection teams in combination with targeted public campaigns can reduce DUP (Lloyd-Evans et al., 2011; Malla et al., 2002; McGorry, 2007; Melle et al., 2004). It is important to increase knowledge on the factors that determine DUP and patients' pathways to care in order to better tailor future interventions and information campaigns (Anderson et al., 2010; Hegelstad et al., 2012).

Relatively few empirical studies so far have identified determinants of DUP, and the complexity of these determinants is not fully understood (Melle et al., 2004). Hence it is still unclear what determines a long DUP. There is consensus that an insidious mode of onset predicts a long DUP (Broussard et al., 2013; Morgan et al., 2006), while it is not clear, how other factors e.g. age and gender are associated with DUP (Cascio et al., 2012). The determinants have been classified in the

following categories; demographic factors (e.g. gender), premorbid and onset-related factors (e.g. mode of onset), illness-related factors (e.g. social and global functioning), family-level factors (e.g. parents' attitudes), societal factors (coping capacity of social network), and health service/system level factors (e.g. referral source) (Compton and Broussard, 2011).

In Denmark, early intervention services (EIS) have been developed and implemented during the years since 2000, and have been the standard treatment for first episode psychosis patients (FEP) in all Danish regions since 2013 (Nordentoft et al., 2015). The first Danish early detection team (called TOP-team) was developed in 2012 in Region Zealand as part of the project to investigate whether implementation of an early detection team in combination with public campaigns could facilitate access to mental health services for FEP patients between 15 and 25 years. Using data from this nation-wide register study, our first aim was to document DUP in Denmark before Region Zealand implemented the first Danish early detection team. The second aim was to test the hypotheses that a long DUP is associated with demographic characteristics (age, gender, migration, marital status and geographic area), premorbid and illness-related factors (global functional level, substance abuse and contact to police), and health-service factors (referral source and first psychiatric contact with FEP).

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## 2. Material and methods

### 2.1. Setting and sample

The study includes Danish patients (aged between 15 and 25 years) diagnosed with FEP (ICD10 F20.0–F20.99) between 2009 and 2011. We drew the study population from the Danish National Indicator Project (DNIP), which is a national multidisciplinary quality improvement database that has existed since 2003. DNIP contains quantitative measures of quality of care of all Danish patients diagnosed with schizophrenia (ICD10 F20.0–F20.99) (Pedersen et al., 2012). All data has been collected during routine clinical practice. In Denmark, it is mandatory for all psychiatric hospital units and relevant clinical departments to report data on all patients with schizophrenia to the registry (Jørgensen et al., 2015). The coverage of the DNIP during the study period has been estimated to include records for over 86% of all inpatients and outpatients with schizophrenia in the Danish health care system (NIP, 2011).

DUP is reported in DNIP as a categorical variable (DUP < 6 months; DUP ≥ 6 months and < 12 months; and DUP ≥ 12 months). In Denmark, DUP is defined as the interval from onset of psychotic symptoms to initiation of appropriate treatment (Malla et al., 2002), which in most cases is initiation of antipsychotic medication and standard treatment in early intervention services. Determination of DUP is based on a clinical judgement by clinicians during routine clinical practice and reported to DNIP by a designated key person in each clinical unit.

We extracted individual data on all patients from DNIP on DUP, Global Assessment of Function (GAF-F), age, sex, substance misuse, and municipality of residence at the time of FEP and combined each individual's contacts with public services from national administrative registers by the use of a unique personal identify number. We obtained data on immigrant and civil status at baseline from the Danish Civil Registration System. Contacts to mental health services (inpatient, outpatient, and emergency services) were drawn from the Danish Psychiatric Register (Mors et al., 2011; Munk-Jørgensen and Ostergaard, 2011), which referral source that led to the contact where the patient was diagnosed with FEP. Finally, we extracted data on criminal charges during the year prior to FEP from the Criminal Statistics Register.

### 2.2. Data analysis

A total of 1347 patients in the age group 15 to 25 years were diagnosed with FEP in DNIP between 2009 and 2011. After having coupled data from DNIP with data from Danish Psychiatric Central Register, we found that 83 of patients registered in DNIP had been diagnosed with schizophrenia (F20–F20.99) before 2009. We also observed that for some patients there was a time lag in the registration of the diagnosis of FEP in DNIP compared to Psychiatric Research Register. In these cases, we corrected the index date according to the date in Psychiatric Research Register. We excluded all patients with FEP before 2009, and the study population for this analysis was 1266 patients.

Age was divided into a categorical variable: age below 20 years; age between 21 and 23 years; and age older than 23. Immigration status was converted into a dummy variable: Danish versus others (immigrant or descendant). We divided criminal charges into the following three categories: i) charges against penal code (sexual offences, crimes of violence, and offences against property), ii) charges against traffic laws (drunken driving, vehicle defect offences, and other road traffic acts), and iii) special laws (euphoric substances acts, firearms acts, and other special laws). To analyse the impact of geographic area on DUP, we used the rural area classification system based on population density, distance or accessibility to urban centers and socio-economic indicators to divide the municipalities into the following four classes: i) peripheral, ii) rural, iii) intermediate, and iv) urban municipalities (Thuesen, 2010).

We divided type of referral source to FEP into three dummy variables: i) general practitioner vs. all others, ii) emergency wards vs. all others, and iii) other hospital services vs. all others. We also defined first psychiatric contact where the patient was diagnosed with FEP into a variable named *first FEP contact*: inpatients vs. outpatient contact.

For our analyses, we used DUP divided in the three categories (shorter than 6 months, between 6 and 12 months, and longer than 12 months) as dependent variable. We analysed the association between DUP and background variables first by univariate analysis and secondly by testing statistically significant variables in multiple regression analysis. We used multinomial regression analysis that estimates models for ordinal or nominal dependent variables. The final model was estimated by backwards elimination procedures. Since we wanted to analyse predictors of a longer DUP, we chose DUP below 6 months as reference category. The model was tested for interactions and we conducted VIF-test to test for multicollinearity. We used the *mlogtest* procedure in STATA to test the assumptions of the multinomial model (Long and Freese, 2014). Since DUP was missing in nearly 17% of the cases we also tested if characteristics differed in individuals where DUP was missing. All statistics was performed using STATA 14.0 via remote access at Statistics Denmark. We used a level of significance at 0.05.

## 3. Results

### 3.1. Duration of untreated psychosis

The descriptive statistics is displayed in Table 1. Two hundred and twelve patients (32.7%) had a DUP below 6 months, and among 223 (17.7%) of patients DUP was longer than 6 months and shorter than 12 months. 414 (32.8%) had a DUP longer than 12 months. In 212 cases (16.8%), information on DUP was missing in DNIP. We found no differences in characteristics between individuals where DUP was registered in DNIP at baseline and where DUP was missing.

### 3.2. Associations between DUP and patient characteristics

The univariate analyses found that higher age, lower GAF-F score, and having cannabis misuse was associated with a DUP longer than 12 months (Table 2). Furthermore, patients with longer DUP (between 6 and 12 months) were more likely to have been charged by the police during the year before FEP. Patients with a DUP longer than 12 months were less likely to be referred from emergency services to EIS than patients with shorter DUP. Furthermore, patients with DUP over 12 months were more likely to be diagnosed with FEP in contact with outpatient services than during hospital admission.

The final multinomial regression model estimated by backwards selection procedures included the variables gender, age, cannabis misuse, having been charged by the police, peripheral area, first FEP contact. Controlling for other variables in the analysis, the multinomial logistic regression analysis showed that males were less likely than females to have a DUP over 12 months (RRR = 0.72; 95% CI: 0.53; 0.97,  $p < 0.03$ ) (Table 3). The oldest age group (23–25 years) (RRR = 1.25; 95% CI: 1.06; 1.48,  $p < 0.007$ ) and patients with cannabis misuse (RRR = 1.53; 95% CI: 1.09; 2.13,  $p < 0.013$ ) were more likely to have a DUP over 12 months. Furthermore patients living in peripheral areas of Denmark were more likely to have a DUP over 12 months (RRR = 1.69; 95% CI: 1.04; 2.75  $p < 0.033$ ). The analysis also showed that patients who had been charged by criminal authorities during the year prior to FEP were more likely to have a DUP between 6 and 12 months (RRR = 2.29; 95% CI: 1.42; 3.69,  $p < 0.001$ ). We also found that patients who were diagnosed with FEP in hospital services rather than outpatient services were less likely to have a DUP over 12 months (RRR = 0.58; 95% CI: 0.43; 0.77,  $p < 0.000$ ).

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