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The incidence of schizophrenia and schizophrenia spectrum disorders in Denmark in the period 2000–2012. A register-based study

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ABSTRACT

Introduction: We aimed to examine changes over time in the incidence of broad and narrow schizophrenia spectrum disorders in Denmark from 2000 to 2012.

Methods: Patients were classified as incident schizophrenia if registered with a first time in- or outpatient contact with relevant diagnostic codes in the Danish Psychiatric Central Register between 2000 and 2012. Their history of contacts was traced back to 1969. Broad schizophrenia included schizophrenia, schizotypal disorder, persistent delusional disorder, acute and transient psychotic disorders, schizoaffective disorders, and other nonorganic and unspecified psychotic disorders, (ICD 10 codes F20–F29). Narrow schizophrenia was defined with the ICD 10 codes F20.0–F20.9. Incidence rates (IR) and incidence rate ratios (IRR) were calculated using Poisson regression.

Results: The IRR for broad schizophrenia increased by 1.43 (CI 95% 1.34–1.52) for females and 1.26 (CI 95% 1.20–1.33) for males. IRR for narrow schizophrenia increased by 1.36 (CI 95% 1.24–1.48) for females and 1.20 (CI 95% 1.11–1.29) for males. There was a significantly increased incidence in patients up to 32 years of age. This was mainly explained by a significant 2–3 fold increase in outpatient incidence. We found a significant decrease in IRR for patients with broad and narrow schizophrenia aged 33 or older for both in- and outpatients.

Conclusion: The increased incidence of schizophrenia could partly be explained by better implementation of the diagnostic criteria for schizophrenia in child and adolescent psychiatry and improved access to early intervention services, but a true increase in incidence of schizophrenia cannot be excluded. The decrease of incidence in the older age group could indicate that the national Danish early intervention strategy was successful.

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1. Introduction

Schizophrenia spectrum disorders often lead to dysfunctional self-care, impaired social and occupational functioning, reduced quality of life and extensive expenses in mental health services (Mueser and McGurk, 2004). Intervention in early phases of schizophrenia has proven to be beneficial for both patients (Marshall and Rathbone, 2011; Nordentoft et al., 2014) and relatives (Jeppesen et al., 2005). Therefore, in the planning of mental health care services, estimates of incidence and prevalence of schizophrenia spectrum disorders are crucial in order to offer timely high quality treatment for this vulnerable group of patients and their relatives.

Moreover, studies of variations in incidence of schizophrenia in different time periods and geographical and cultural settings are highly

important in order to explore the etiology and to identify possibilities for prevention and treatment. Age and sex specific incidence rates in different time periods and different geographical settings are fundamental epidemiological tools. Following the WHO Pilot Study of Schizophrenia (Jablensky et al., 1992), the incidence of schizophrenia was believed to show rather modest variations across different countries worldwide, but a comprehensive review has demonstrated a substantial variation in incidence of schizophrenia (McGrath et al., 2004). Moreover, analyses of sex-specific incidence rates have consistently reported higher rates in males than in females (McGrath et al., 2004; Pedersen et al., 2014; Thorup et al., 2007; van der Werf et al., 2014).

There is conflicting evidence concerning time changes in the incidence of schizophrenia and first episode psychosis in schizophrenia spectrum disorder (McGrath et al., 2004; Boydell et al., 2003; Kirkbride et al., 2006; Suvisaari et al., 1999; Okkels et al., 2013). Therefore large studies with high external validity on this issue are very relevant. Many studies are outdated since both the diagnostic criteria and treatment have changed, and only few studies had access to information about outpatient contacts, which is why most studies were based only

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on admissions. Moreover, many studies did not have access to historical data to ensure that only true incident cases were included.

We wanted to investigate whether the incidence of schizophrenia had increased over the last decade. Our aim was to examine calendar changes in the incidence of broad and narrow schizophrenia spectrum disorders from 2000 to 2012.

2. Methods

2.1. Registers

The study was prospectively designed using nationwide, population-based data from two registries; The Danish Psychiatric Central Register (Mors et al., 2011) and The Civil Registration System (Pedersen et al., 2006).

The Civil Registration System contains a personal identification number given to every citizen in Denmark. The identification number is used in all national registers and ensures accurate linkage of information between registers (Pedersen et al., 2006).

The Danish Psychiatric Central Research Register was established as an electronic register in April 1969, containing data on all admissions to Danish psychiatric inpatient facilities from 1969. In 1995 outpatient contacts were included in the Danish Psychiatric Central Research Register (Mors et al., 2011).

2.2. Observation period

We chose the period 2000 to 2012 in order to evaluate the most recent time change in incidence rate and in addition to avoid the first years after the diagnostic criteria changed in 1994 from ICD 8 to ICD 10. We expected clinicians to have become familiar with the diagnostic criteria in ICD 10 before 2000, and we wanted to examine a time period in which information about outpatient contacts was available throughout the entire period. The years 2000–2002 were chosen as reference in the analyses of time trends.

2.3. Population

All individuals born in Denmark from 1955 and onwards were included. The incidence of schizophrenia was examined in the period 1 January 2000–31 December 2012, the oldest patients thus being 57 years old. A recent meta-analysis found a high diagnostic stability associated with narrow schizophrenia spectrum (ICD 10 code F20.X), while the other diagnoses included in broad schizophrenia spectrum (ICD 10 codes F21–29) were associated with lower levels of diagnostic stability and most of the diagnostic changes were to schizophrenia (Fusar-Poli et al., 2016). Narrow schizophrenia is associated with worse prognosis than the rest of the schizophrenia spectrum (Austin et al., 2013). In order to investigate whether increase in incidence could be due to detection of higher numbers of less severe cases, we examined the incidence rate (IR) and incidence rate ratios (IRR) in two groups:

- 1) Broad spectrum schizophrenia, including schizophrenia, schizotypal disorder, delusional disorders, transient psychotic disorder, schizoaffective disorder and psychosis not otherwise specified (ICD 10 codes F20–F29). Patients diagnosed in ICD 8 with '295.xx', '298.29', '298.39', '298.89', '298.99', '299.05', '299.09', '301.09', '301.29', '295.xx', '297.xx' or with F2x.xx in ICD 10 before year 2000 were excluded.
- 2) Narrow schizophrenia including only schizophrenia (ICD 10 codes F20.0–F20.9). Patients diagnosed in ICD 8 with 295.xx', or with F20.xx in ICD 10 before year 2000 were excluded.

In order to prevent the misclassification of prevalent cases as incident cases, the persons diagnosed with the same diagnostic codes in ICD 10 and the corresponding ICD 8 codes before 2000 were excluded.

To ensure that all patients were included, the lower limit of the youngest age group is five years; knowing the diagnosis of both broad and narrow spectrum schizophrenia is very rare before adolescence (Okkels et al., 2013).

All analyses were performed for males and females separately. IR and IRR were assessed both separately for in- and outpatients and combined. The incident cases were furthermore distributed in the age groups: 5–18 years, 19–24 years, 25–32 years, 33–57 years and the average incidence was examined for the years 2000–2002, 2003–2004, 2005–2006, 2007–2008, 2009–2010, and 2011–2012.

2.4. Statistical analyses

Data were analyzed using the log-linear Poisson regression, with the logarithm to the person years as an offset variable, in the SAS GENMOD version 9.3 procedures. All 95% confidence intervals were calculated by Wald's estimates.

2.5. Ethics

No ethical research committee approval was needed, as data were obtained from registers for statistical purposes only. The study was conducted with permission for the study "Causes and consequences of psychiatric disorders" from the Danish Data Protection Agency.

3. Results

A total of 23,479 persons (13,341 men and 10,138 women) were diagnosed with first episode psychosis in the schizophrenia spectrum during the observation period. Out of these, 13,993 were outpatients with no previous inpatient contact with psychiatry before the registered outpatient contact in this study. Age specific incidence rates are shown in Fig. 1 for males and females separately together with male: female ratio. The highest incidence was found among males aged 19–24 years peaking with an IR of 211 per 100,000 person years for broad spectrum schizophrenia in 2011–2012. The incidence rates for broad schizophrenia were approximately twice as high as for narrow schizophrenia for both genders. In 2011–2012, IR for broad schizophrenia for men was 75 per 100,000 person years compared to an IR of 40 for narrow schizophrenia (data not shown). For women, the IRs for 2011–2012 were 63 (broad schizophrenia) compared to 31 (narrow schizophrenia) per 100,000 person years (data not shown).

Men had higher incidence than women in all years and in all age groups except for the youngest group (up to 18 years old, see Fig. 1c). In most age groups, male: female ratio was fairly stable, but among the up to 18-year-olds, the schizophrenia incidence among girls increased more than among boys, and at the end of the period, the incidence rate for girls exceeds that of boys.

When comparing the years 2000–2002 to the years 2011–2012, the IRR for broad schizophrenia increased by 1.43 (CI 95% 1.34–1.52) for females and 1.26 (CI 95% 1.20–1.33) for males. IRR for narrow schizophrenia increased by 1.36 (CI 95% 1.24–1.48) for females and 1.20 (CI 95% 1.11–1.29) for males.

For both definitions of schizophrenia, the IRR significantly increased in the younger age groups (5–18 years, 19–24 years, and 25–32 years) and significantly decreased among those aged 33 years and older (Fig. 2 and Fig. 3). The increase was mainly explained by changes in incidence of first contacts as outpatients, but the same tendency was found for inpatients. The increase was highest for women, especially the youngest outpatient women (IRR (2000–2002 compared to 2011–2012): broad schizophrenia 3.06 (CI 95% 2.60–3.61) and narrow schizophrenia 3.29 (CI 95% 2.50–4.33)).

Looking at the broad schizophrenia spectrum, IRR (2000–2002 compared to 2011–2012) increased significantly in the age groups 5–18 years, 19–24 years and 25–32 years, respectively 2.28 (CI 95% 2.01–2.59), 1.84 (CI 95% 1.62–2.09), 1.21 (CI 95% 1.04–1.40) for females

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