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Research report

# Increased risk of hypertension in patients with bipolar disorder and patients with anxiety compared to background population and patients with schizophrenia $\stackrel{\leftrightarrow}{\sim}$

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#### Abstract

*Background:* The relationship between depression and bipolar disorders and cardio-vascular diseases has been studied previously although the direction of the correlation is investigated less often. The present study examines the prevalence of hypertension among Danish psychiatric patients admitted with a diagnosis of bipolar affective disorder (BP) and controls.

*Methods:* Demographic, medical and psychiatric data on 25,339 BP patients and 113,698 controls were extracted from The Danish Psychiatric Central Research Register, The Danish National Patient Registry — for somatic patients, The Danish Civil Registration System, and The Danish Causes of Death Registry. Similar information about patients with schizophrenia and anxiety was collected for comparison. *Results:* Hypertension was overrepresented in BP: IRR=1.27, 95% confidence interval (1.16 to 1.39). This association was also found in anxiety patients: IRR=1.96 (1.73 to 2.22), but not among patients with schizophrenia: IRR=0.93 (0.77 to 1.14). *Limitations:* The study uses nationwide data based on administrative health service registers. The data therefore are historical and heterogeneous samples.

*Conclusions:* A significant increase in levels of hypertension in BP patients was observed which may explain some of the increased cardio-vascular morbidity/mortality in BP patients.

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# 1. Introduction

It is only in the last quarter century that investigators have studied the relationship between depression, manic-

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depression, bipolar affective disorders and cardio-vascular morbidity and mortality (Weeke and Waeth, 1986; Weeke et al., 1987; Aromaa et al., 1994; Barefoot and Scroll, 1996; Takemura et al., 1998). Although some studies report hypertension as a possible cause for increased cardio-vascular morbidity in depressive patients (Davidson et al., 2000; Jones-Webb et al., 1996; Simonsick et al., 1995; Carney et al., 2002), most of these studies do not include patients with manic episodes.

Aromaa et al. (1994) reported an association between hypertension and depression in patients below 64 years

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of age. Davidson et al. (2000) also reported an association between hypertension and depression especially in patients aged 18–30 years. Possible causes attributed for this observation include genetic disposition, dysregulation of the adrenergic system in depression, or the behavioural changes that follow depression (e.g. reduced physical activity). Yet two studies did not find any association between hypertension and depression (Jones-Webb et al., 1996; Simonsick et al., 1995). Jones-Webb et al. (1996) looked for an association in 18–30 years old patients but felt that this may be found in a population of older patients.

## 2. Purpose

We embarked on a study of hypertension in bipolar patients. In order to establish whether a possible positive association between bipolar affective disorder (BP) and hypertension should be explained by the affective disorders per se or by mental illness in general, we decided to examine the prevalence of hypertension in two other groups of psychiatric disorders: schizophrenia and anxiety.

#### 3. Materials and methods

## 3.1. Design

The present study is a nationwide register study covering the period from January 1, 1977 to December 31, 2001. The study includes data from four registers: The Danish Psychiatric Central Research Register (DPCR), The Danish National Patient Registry — for somatic patients (NPR), The Danish Civil Registration System (CRS), and The Danish Causes of Death Registry (CDR).

#### 3.2. Method

The cohort of probands was extracted from the DPCR, a nationwide psychiatric patient register (Munk-Jørgensen and Mortensen, 1997). This register contains all psychiatric admissions to inpatient facilities in Denmark since April 1969 and as of January 1, 1995 also all psychiatric out-patient treatments. There are no private psychiatric hospitals in Denmark. Treatment is free of charge as the National Health Service is funded by the state.

The cohort of psychiatric patients was linked to the NPR, a register containing information about all physically ill patients since 1977 (out-patients as of 1995). The cohort was also linked to the CDR, a register containing information about all deaths in Denmark including the date, place, manner and cause of death. The subjects were identified by a ten-digit personal identification number by

which all Danish citizens are registered in the CRS. These numbers contain information on date of birth and gender only and the confidentiality is maintained.

The present register study covers almost 25 years and includes a mixture of diagnoses classified in ICD-8 and ICD-10. Because of the similarities between ICD-8 and ICD-9 the latter was never implemented in Denmark where the shift from ICD-8 to ICD-10 took place in January 1, 1994.

The cohort consists of patients who received one of the following diagnoses between January 1, 1977 and December 31, 1998: Manic-depression (ICD-8: 296), manic episode (ICD-10: F30), bipolar affective disorder (ICD-10: F31) (including out-patient treatment since January 1, 1995).

Patients diagnosed with either anxiety disorders (ICD-8: 300.09, ICD-10: F41), schizophrenia (ICD-8: 295, ICD-10: F20), or organic mental disorders (ICD-8: 290–294, ICD-10: F00) prior to a bipolar disorder diagnosis (BD) were excluded from the analyses, as were patients diagnosed with hypertension (ICD-8: 400–401, ICD-10: 110) who had received this diagnosis before receiving their first psychiatric diagnosis.

For each patient thus identified, up to six controls matched by gender and age (day of birth  $\pm/-1$  month) were identified in the CRS. These controls are characterized by being alive at the time of their probands' initial psychiatric diagnosis and by not being registered in the PCR. Controls that according to the NPR were diagnosed with hypertension prior to their probands' initial psychiatric diagnosis were excluded.

Controls who had died at the time their matched probands received the index-diagnosis were excluded to avoid bias due to difference in life expectancy. In order to establish whether a positive association between mental illness and hypertension was related to the affective disorders or could be explained as a result of general mental illness, similar calculations were made for the two other diagnostic groups: other anxiety disorders (ICD-8: 300.09, ICD-10: F41) and schizophrenia (ICD-8: 295, ICD-10: F20).

As some patients may have had the mental illness before being diagnosed, the period at risk was extended by two years prior to the first psychiatric diagnosis.

#### 3.3. Sample

As there were no registrations in some of the subgroups of the affective spectrum, the diagnoses 296 (ICD-8), F30 and F31 (ICD-10) were considered as one group.

In order to avoid secondary hypertension (ICD-8: 402, 403, and 404, ICD-10: I 15) confounding the potential association between hypertension and the psychiatric diagnosis, we also excluded patients with some of the most

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