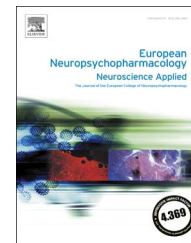




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# Risk of hospitalization for psychiatric disorders among siblings and parents of probands with psychotic or affective disorders: A population-based study

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Received 9 September 2016; received in revised form 19 October 2017; accepted 6 December 2017

## KEYWORDS

Psychotic disorders;  
Affective disorders;  
Familial risk;  
Siblings;  
Hospitalization

## Abstract

Relatives of people diagnosed with psychotic and affective disorders have a higher risk of developing psychiatric disorders compared to the general population. This study examined the risk of hospitalization for psychiatric disorders among siblings and parents of patients affected with major psychiatric disorders. In this large population-based case-control study, 17,895 siblings and parents of 7671 hospitalized subjects with a diagnosis of narrowly defined schizophrenia (SZ), broadly defined SZ, schizoaffective disorder (SAD), bipolar disorder (BD) or unipolar depression (UD) were identified from the Israeli Psychiatric Hospitalization Registry and compared to 71,580 age and gender-matched controls from the Israeli Population Registry. Results indicated that siblings of people diagnosed with broadly defined SZ had a significantly higher risk of hospitalization for broadly (OR=11.06, 95% CI=7.93-15.41) and narrowly defined SZ (OR=10.59, 95% CI=6.8-16.33), SAD (OR=9.69, 95% CI=4.76-19.73), BD (OR=7.46, 95% CI=21.8-25.52), UD (OR=2.84, 95% CI=1.01-8.00), and other psychiatric disorders (OR=1.85, 95% CI=1.16-2.93), compared to controls. Siblings of patients with BD had a significantly higher risk of hospitalization for broadly defined SZ (OR=2.92, 95% CI=1.11-7.71) and for other psychiatric disorders (OR=6.67, 95% CI=2.17-20.50), compared to controls. Parents of probands with SZ were at significantly increased risk for all disorders examined, except for

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<https://doi.org/10.1016/j.euroneuro.2017.12.011>

0924-977X/© 2017 Published by Elsevier B.V.

UD and other psychiatric disorders, which was not significant in parents of probands with BD. This large, population-based study provides evidence for common genetic risk across different psychiatric disorders.

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## 1. Introduction

Studies on the familial occurrence of schizophrenia (SZ) indicate a higher rate of psychosis in first-degree relatives of individuals with SZ compared to the general population (Baron et al., 1985; Dean et al., 2010; Gottesman et al., 2010; Laursen et al., 2005; Li et al., 2009; Lichtenstein et al., 2009; Mortensen et al., 2003; Mortensen et al., 1999), as well as a higher rate of psychotic spectrum disorders such as paranoid and schizotypal personality disorders or schizoaffective disorder (SAD) (Baron et al., 1985; Tsuang et al., 2001). Furthermore, there is evidence implying that this relationship may be non-specific, i.e., that first-degree relatives of probands with SZ may have a higher risk for psychiatric disorders in general (Baron et al., 1985; Dean et al., 2010; DeVylder and Lukens, 2013; Gottesman et al., 2010; Laursen et al., 2005; Li et al., 2009; Lichtenstein et al., 2009; Mortensen et al., 2010; Rasic et al., 2013; Tsuang et al., 2001). This also appears to be true in relation to the relatives of probands with other mental disorders, as studies have shown that first-degree relatives of subjects with various mental disorders are at an increased risk of a wider range of disorders than just the concordant disorder (Byrne et al., 2002; Cardno and Owen, 2014; Dean et al., 2010; Laursen et al., 2005; Lichtenstein et al., 2009; Rasic et al., 2013; Sorensen et al., 2009; Sullivan et al., 2012).

This large population-based study aims to assess the risk of psychiatric hospitalizations among siblings and parents of probands with psychotic or affective disorders.

## 2. Experimental procedures

The study analyzed a population-based dataset to examine the risk of hospitalization for broadly defined SZ, narrowly defined SZ, SAD, bipolar disorder (BD), unipolar depression (UD), and other psychiatric disorders among siblings and parents of probands with psychotic and mood disorders, compared to matched healthy controls.

### 2.1. Israeli Psychiatric Hospitalization Case Registry

The Israeli Psychiatric Hospitalization Case Registry is a complete, nationwide, computerized list of all persons admitted to psychiatric hospitals, day hospitals or to psychiatric units in general hospitals. It was started in 1948 and includes the International Statistical Classification of Diseases and Related Health Problems 10<sup>th</sup> Revision (ICD-10) admission and discharge diagnosis for each hospitalization assigned by a board certified psychiatrist at the facility.

Diagnoses were grouped according to broadly defined SZ (ICD10, F20-F29, excluding F25), narrowly defined SZ (F20.0-F20.9), SAD (F25), BD (F30-F31, F32.3.31, F33.3.31, F34.0, F38.0.00), UD (F30-F39 excluding BD), and other psychiatric disorders (dissociative disorder: F44; pervasive developmental disorder: F84; anxiety disorders: F40-F41; adjustment disorders: F43.2; PTSD: F43.1; eating disorders: F50; personality disorders: F60-F62; mental retardation: F70-79).

### 2.2. Israeli Population Registry

The Israeli Population Registry records all births, deaths, marriages and divorces in the country. It was created upon the establishment of the State in 1948.

The population registry includes family ties between parents, offsprings and siblings for all citizens born after 1970, hence the current manuscript studied patients born after 1970.

Registry diagnoses of schizophrenia (ICD-10 F20.0- F20.9) have a sensitivity of 0.89 (Weiser et al., 2005), and the Psychiatric Hospitalization Case Registry captures 93.1% of all schizophrenia patients in the community (Weiser et al., 2012).

### 2.3. Identification of probands, families and controls

After receiving approval from the local IRB, in June 2004 the managers of the Psychiatric Hospitalization Case Registry compiled a list of probands, defined as all people in the country born after 1970, who were consecutively admitted to any psychiatric ward, and who received a last discharge diagnosis of broadly defined SZ (F20.0-F29.9, without F25,  $n=3968$ ), narrowly defined SZ (F20.0-F20.9,  $n=1960$ ), SAD (F25,  $n=681$ ), BD (F30-F31, F32.3.31, F33.3.31, F34.0, F38.0.00,  $n=572$ ), or

UD (F30-F39 without BD,  $n=490$ ). This file was linked to the Israeli Population Registry, where for each proband, all siblings and parents were identified (17,895). For sibling and parents, four random controls matched for age and gender were selected from the population registry resulting in 71,580 controls who were not related to the probands or to each other. The merged file with probands, siblings, parents and matched controls was then returned to the Psychiatric Hospitalization Case Registry, and data on all psychiatric hospitalizations, with admission and discharge diagnoses were added for all subjects. In order to ensure confidentiality, identifiers were removed from the file before the data were analyzed. One sibling was randomly selected for each proband in order to perform the analysis.

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