



## Mortality, morbidity and medical resources utilization of patients with schizophrenia: A case-control community-based study

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### ABSTRACT

Patients with schizophrenia have higher level of mortality and physical comorbidity compared to control population. However the association to primary-, secondary- and tertiary-medical resources utilization is not clear. We used a retrospective community-based cohort of patients with schizophrenia ( $n=1389$ ; age 37.53 years, 64.3% males) and, age-, gender-, and socioeconomic status-matched controls ( $n=4095$ ; age 37.34 years; 64.3% males) who were followed-up for nine years. Mortality rate of patients was almost twice as high as that of matched controls (7% versus 3.8%). Diagnoses of ischemic heart disease and hypertension were more prevalent among controls than patients (8.2% versus 5%, and 21.6% versus 15.8%, respectively). Tertiary medical resources utilization was higher among patients with schizophrenia than control population (mean hospital admissions per year: 0.2 versus 0.12, emergency department visits: 0.48 versus 0.36). Patients that died were more likely to have cardiovascular disease, to be admitted to general hospital and to spend more days in hospital than patients that did not die. There is a discrepancy between lower rates of cardiovascular disease diagnoses but higher rates of mortality and tertiary medical resources utilization among patients with schizophrenia when compared to control population. This may stem from an under-diagnosis and, eventually, under-treatment of these patients.

### 1. Introduction

Schizophrenia is one of the most severe mental health disorders, and has been described as a “life-shortening disease” (Lambert et al., 2003). Several meta-analyses have demonstrated that approximately 15 years of life are lost among people with schizophrenia (Wahlbeck et al., 2011; De Hert et al., 2009; Hjorthoj et al., 2017). The rapid pace of scientific discoveries and advances achieved over the past few decades have revolutionized treatment and increased longevity of the general population. The mortality gap between members of the general population and schizophrenia patients, however, not only has remain stable during the past few decades, but, if anything, appears to be widening (Nielsen et al., 2013).

It now transpires that although suicide and substance abuse may lead to death, the majority (over 70%) of the early deaths among people with schizophrenia are attributed to physical health conditions (Correll et al., 2017; Lawrence et al., 2013). It is concerning to note that people with schizophrenia are at increased risk of various physical health conditions (Langan et al., 2013; De Hert et al., 2011; Stubbs et al., 2016b; Moore et al., 2015; Vancampfort et al., 2013; Stubbs et al., 2016b). Of greatest concern are the high levels of cardiovascular, metabolic and respiratory diseases among people with schizophrenia (Vancampfort et al., 2016; Vancampfort et al., 2015; Correll et al., 2017). The reasons for the poor health outcomes in patients with schizophrenia are multifactorial and include side-effects of psychotropic medication (Stubbs et al., 2016b; Vancampfort et al., 2015),

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genetic predisposition (Dieset et al., 2016), poor lifestyle habits (Teasdale et al., 2017; Stubbs et al., 2016a; Stubbs et al., 2016c) and disparities in healthcare provision (Docherty et al., 2016; Firth et al., 2016). Disparities in the equity of medical service provision to patients with schizophrenia may be attributed to diagnostic over-shadowing (Crawford et al., 2014; Moore et al., 2015) and negative attitudes of clinicians (Vahia et al., 2008; Mitchell et al., 2012). Understanding how access to medical care among people with schizophrenia may be related to mortality offers a valuable insight into this potentially modifiable risk factor in attempt to address the scandal of premature mortality (Thornicroft, 2011).

The medical care of patients with schizophrenia is often fragmented and frequently involves multiple secondary and tertiary medical specialists who, at times, treat the patient without inclusion or participation of the primary care team, making it challenging to develop coordinated care (Oud et al., 2010). This is despite the fact that patients with schizophrenia are more likely to die younger due to physical health conditions. While imparities in medical healthcare contribute to the situation, little is actually known about how physical care across services is related to mortality in this neglected population. Given this, we sought to explore the level of primary-, secondary- and tertiary-medical resources utilization by patients with schizophrenia versus matched controls and to assess the association with physical health morbidity and mortality.

## 2. Methods

We conducted a retrospective, longitudinal, case-control study using electronic medical records of the largest health care provider in Israel (Clalit Health Services) in a regional catchment area (about 500,000 inhabitants) encompassing primary-, secondary- and tertiary-medical care services. The health system in Israel (Rosen et al., 2015) is designed such that patients have a strong incentive to access primary care and obtain prescription medications within the Clalit Health Services system because primary care visits are free of charge to members and medications included in the benefit package are subject to highly reduced co-payments (approximately four to seven US Dollars per month for most medications). Disadvantaged sub-populations are entitled to additional discounts. The study was approved by the Community Studies ethic committee of Clalit Health Services and the Institutional Review Board.

### 2.1. Population

All individuals with a recorded diagnosis of schizophrenia in the primary care case records (coded according to ICD-10: F.20 criteria) from 1.1.2005 to 31.12.2013 were included. Diagnosis was based on this primary care registry and further validated by data from mental health admissions or outpatient engagements of those patients. The control population was randomly selected from the same community cohort, on a basis of 1:3, and was matched for gender, year of birth and socioeconomic status. Patients and controls were retrospectively followed-up for nine years (1.1.2005 – 31.12.2013) until death or end of follow-up period.

### 2.2. Study protocol

Demographic data included gender, year of birth, death and date of death (derived from the Ministry of Interior data), marital status, smoking status and socioeconomic status (categorized into low, moderate and high) based on ecological data of the geographical location of the primary care clinic. Clinical data on patients and controls was retrieved from case records of general practitioners, medical specialist consultants, general medical hospitals and emergency departments. We included the following medical diagnoses: ischemic heart disease, diabetes mellitus, hypertension, hyperlipidemia, obesity and congestive

heart failure. Those diagnoses are coded (ICD-10) by general practitioners but are further validated by registries from hospital admissions and drug prescriptions. We also retrieved indices of medical resource utilization of primary care (general practitioner practice visits per year), secondary care (medical specialist consultation visits per year) and tertiary care (number of hospitalizations, length of hospitalization and emergency department visits per year). We also used Charlson's Comorbidity Index (CCI) as a summation measure of comorbid burden.

### 2.3. Statistical analysis

We used SPSS version 20 (Chicago, IL) for analyses. We compared variables between cases and controls using univariate student's *t*-test, Mann-Whitney test or  $\chi^2$  as appropriate. For mortality, we employed a Kaplan-Meier survival analysis. We then performed a multivariate survival analysis for predictors of mortality by using a Cox regression model. We considered  $p < 0.05$  as a significant result.

## 3. Results

A total of 1389 patients diagnosed with schizophrenia and 4095 matched controls were included in the study. Population baseline characteristics are shown in Table 1. It is of note (Table 1), that smoking status was higher among patients with schizophrenia than among matched-controls (44.5% versus 38.7%,  $p < 0.05$ ) and more patients with schizophrenia were single (79.6% versus 45.7%,  $p < 0.05$ ).

### 3.1. Mortality

Out of 1389 patients, 97 individuals have died during follow-up period, while out of 4095 controls, 153 individuals have died during the same period of time. Patients with schizophrenia had a significantly higher mortality rate than matched-controls (7% versus 3.7%,  $\chi^2 = 25.13$ ,  $p < 0.0001$ ). Using a Cox hazard model, patients with schizophrenia had a hazard ratio of 1.89 (95% confidence interval (CI): 1.46 – 2.44) for death. Patients also died at a higher rate during follow-up, as shown in a Kaplan-Meier analysis: mean survival time for patients with schizophrenia was 8.6 years (95% CI: 8.53 – 8.86), while control mean survival time was 8.9 years (95% CI: 8.83 – 8.93), log-rank Mantel-Cox = 27,  $p < 0.0001$ ). When adjusted for Charlson's Comorbidity Index (CCI) as a composite index of physical morbidity, in a multivariate model, patients with schizophrenia had a hazard ratio of 1.4 (95% CI: 0.99 – 1.96) for death in relation to matched-controls (age, gender and

**Table 1**  
Study sample description of patients with schizophrenia and age-, gender- and socioeconomic status-matched controls.

Variable	Control (n = 4095)		Patients with schizophrenia (n = 1389)	
	n	%	n	%
Gender				
Male	2632	64.3	893	64.3
Female	1463	35.7	496	35.7
Immigrants <sup>a</sup>	1626	39.7	339	24.4
Socioeconomic Status				
Low	1217	29.7	438	31.5
Moderate	1844	45.1	650	46.8
High	1032	25.2	301	21.7
Single <sup>a</sup>	1871	45.7	1105	79.6
Age at study entry				
Mean	37.34		37.53	
Standard deviation	13.15		13.22	
Median	36.6		36.7	
Smoker <sup>a</sup>	1585	38.7	618	44.5

<sup>a</sup>  $p < 0.05$  for comparison between groups,  $\chi^2$  test for categorical variables.

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