Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Mortality in people with psychotic disorders in Finland: A population-based 13-year follow-up study

Jaakko Keinänen [a,b,*], Outi Mantere [b,c,d], Niina Markkula [a,e], Krista Partti [a,f], Jonna Perälä [a,b], Samuli I. Saarni [a,g], Tommi Härkänen [h], Jaana Suvisaari [a]

[a] National Institute for Health and Welfare, Department of Public Health Solutions, Mental Health Unit, P.O. Box 30, FIN-00271 Helsinki, Finland
[b] Department of Psychiatry, University of Helsinki and Helsinki University Hospital, P.O. Box 590, FIN-00029, HUS, Helsinki, Finland
[c] Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montréal, QC H3A 1A1, Canada
[d] Bipolar Disorders Clinic, Douglas Mental Health University Institute, 6875 LaSalle Boulevard, Montréal, QC H4H 1R3, Canada
[e] Universidad del Desarrollo, Av. Plaza 680, San Carlos de Apoquindo, Las Condes, Santiago, Chile
[f] University of Helsinki, Doctoral Program in Clinical Research, P.O. Box 700, FIN-00029 HUS, Finland
[g] Turku University Hospital and the University of Turku, P.O. Box 52, FIN-20521, Turku, Finland
[h] National Institute for Health and Welfare, Department of Public Health Solutions, Health Monitoring Unit, P.O. Box 30, FIN-00271, Helsinki, Finland

ARTICLE INFO

Article history:
Received 2 January 2017
Received in revised form 21 April 2017
Accepted 30 April 2017
Available online xxxx

Keywords:
Mortality
Psychotic disorders
Somatic disease
Comorbidity

ABSTRACT

Objectives: We conducted a population based study aiming at finding predictors of mortality in psychotic disorders and evaluating the extent to which sociodemographic, lifestyle and health-related factors explain the excess mortality.
Methods: In a nationally representative sample of Finns aged 30–70 years (n = 5642), psychotic disorders were diagnosed using structured interviews and medical records in 2000–2001. Information on mortality and causes of death was obtained of those who died by the end of year 2013. Cox proportional hazards models were used to investigate the mortality risk.
Results: No people with affective psychoses (n = 36) died during the follow-up, thus the analysis was restricted to non-affective psychotic disorders (NAP) (n = 106). Adjusting for age and sex, NAP was statistically significantly associated with all-cause mortality (hazard ratio (HR) 2.99, 95% CI 2.03–4.41) and natural-cause mortality (HR 2.81, 95% CI 1.85–4.28). After adjusting for sociodemographic factors, health status, inflammation and smoking, the HR dropped to 2.11 (95% CI 1.10–4.05) for all-cause and to 1.98 (95% CI 0.94–4.16) for natural-cause mortality. Within the NAP group, antipsychotic use at baseline was associated with reduced HR for natural-cause mortality (HR 0.25, 95% CI 0.07–0.96), and smoking with increased HR (HR 3.54, 95% CI 1.07–11.69).
Conclusions: The elevated mortality risk in people with NAP is only partly explained by socioeconomic factors, lifestyle, cardio-metabolic comorbidities and inflammation. Smoking cessation should be prioritized in treatment of psychotic disorders. More research is needed on the quality of treatment of somatic diseases in people with psychotic disorders.

1. Introduction

Schizophrenia shortens the lifespan of those affected by up to 20–30 years (Olfson et al., 2015; Laursen et al., 2014). The excess mortality is mainly due to diseases and medical conditions, the leading causes being cardiovascular diseases, cancer, respiratory diseases and diabetes (Crump et al., 2013a; Suvisaari et al., 2013; Termorshuizen et al., 2013; Olfson et al., 2015). Studies indicate that during recent decades, the mortality gap between people with serious mental illness and the general population has at best narrowed only by a small amount (Wahlbeck et al., 2011), or has in fact increased (Saha et al., 2007; Olfson et al., 2015; Lumme et al., 2016; Osby et al., 2016).

Several factors predispose people with psychotic disorders to an increased risk of somatic diseases. Antipsychotic medication causes weight gain and increases the risk of metabolic syndrome, type 2 diabetes mellitus (T2DM), and cardiovascular disease (Foley and Morley, 2011). Sedentary lifestyle and poor diet, both common among people with psychotic disorders, further add to the metabolic burden (Dipasquale et al., 2013; Stubbs et al., 2016). Low income (McCallum et al., 2013) and living alone (Koskinen et al., 2007) are associated with excess mortality in the general population, and these factors may

* Corresponding author at: National Institute for Health and Welfare, Department of Public Health Solutions, Mental Health Unit, P.O. Box 30, FIN-00271, Helsinki, Finland.
E-mail addresses: jaakko.keinanen@thl.fi (J. Keinänen), outi.mantere@douglas.mcgill.ca (O. Mantere), niina.markkula@helsinki.fi (N. Markkula), krista.partti@thl.fi (K. Partti), jonna.perala@hus.fi (J. Perälä), samuli.saarni@tyks.fi (S.I. Saarni), tommi.harkanen@thl.fi (T. Härkänen), jaana.suvisaari@thl.fi (J. Suvisaari).

http://dx.doi.org/10.1016/j.schres.2017.04.048
0920-9964/

also contribute to excess mortality in people with psychotic disorders. Low-grade inflammation associated with schizophrenia (Potvin et al., 2008; Dickerson et al., 2013; Miller et al., 2014; Fernandes et al., 2016a) could be a peripheral marker of elevated mortality risk, as it is in the general population (Emerging Risk Factors Collaboration et al., 2010).

In people with psychotic disorders, the mortality from medical conditions is disproportionately high compared to morbidity (Crump et al., 2013a). This applies both to cardiovascular diseases and to cancer (Kisely et al., 2013). Both under-detection (Crump et al., 2013a) and poorer treatment (Kisely et al., 2013) of medical conditions contribute. In this study, we investigated mortality in non-affective psychosis (NAP) during a 13-year follow-up using data from the nationally representative Health 2000 Survey. We aimed to find predictors of mortality in NAP. Specifically, we wanted to see whether excess mortality in psychotic disorders can be explained by previously known sociodemographic and health-related factors. Further, we hypothesized that C-reactive protein (CRP) predicts mortality also in NAP but is not an independent predictor when somatic risk factors are controlled for.

2. Methods

2.1. Study design

The Finnish Health 2000 Survey (BRIF8901) sample consisted of 8028 persons aged 30 years or older. A nationally representative sample was achieved using a two-stage stratified cluster sampling procedure. The data were collected between September 2000 and June 2001. The survey consisted of an interview, a health examination and a shortened version of the Munich version of the Composite International Diagnostic Interview (M-CIDI) (Wittchen et al., 1998). Register information on the whole sample was collected to supplement interview and health examination data (Aromaa and Koskinen, 2004).

In the Psychoses in Finland study, we screened persons from the Health 2000 Survey sample for possible psychotic disorder and interviewed them using the research version of the Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 2002). Persons were invited to participate in the SCID-I interview using the following screening criteria: (1) self-reported psychotic disorder, (2) a diagnosis of possible or definite psychotic disorder based on the physician's health examination, (3) psychotic or manic symptoms in the M-CIDI interview, (4) hospital treatment of any psychotic disorder according to the Hospital Discharge Register, (5) entitled to free outpatient antipsychotic medication, (6) disability pension due to psychotic disorder, and (7) mood-stabilizing medication use without a diagnosis of epilepsy or other neurological disease. Detailed description about sensitivity and specificity of these screens is reported in Perala et al. (2007).

The participation rate to the SCID-I was 63.4%. In addition, we obtained all lifetime hospital and outpatient case records from psychiatric and primary care units for all Health 2000 participants. Using all available information, J.S., J.P., and S.I.S. made the final DSM-IV based diagnoses and assessed whether people had a current psychiatric treatment contact (Perala et al., 2007).

The Health 2000 Survey and the Psychoses in Finland study were approved by the Ethics Committees of the National Public Health Institute (the National Institute for Health and Welfare since 2009) and the Hospital District of Helsinki and Uusimaa. Participants gave a written informed consent after having received a complete description of the study.

2.2. Study population

In the analysis, we excluded (1) persons aged 70 years and older to avoid confounding our analysis with the high mortality of the oldest age groups and (2) persons with substance-induced psychotic disorders or psychotic disorders due to a general medical condition. The original study sample included 6334 persons aged under 70 years, from whom 5642 (89.1%) had participated in the Health 2000 study and were followed up in the current study. Weights were used to correct for non-response, as described in Section 2.5.

In this study, we investigated people with NAP, including schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder and psychotic disorder not otherwise specified. Descriptive data are reported from people with affective psychosis (bipolar I disorder or major depressive disorder with psychotic features) as well, but a predictor analysis was not possible due to no deaths in this group in people aged under 70 years.

2.3. Predictors of mortality

2.3.1. Antipsychotic medication

Participants reported their current medication at baseline and that information was used to code the antipsychotic medication use. Participants had brought their prescriptions or medications to the interview to assist in recording medication use.

2.3.2. Socioeconomic factors

Marital status was coded as married or cohabiting, or unmarried (divorced, never-married or widowed) at baseline. The registers of the Finnish Tax Administration were used to determine family income, adjusted for family size and divided into quintiles.

2.3.3. Lifestyle and health variables

Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Participants were categorized as current smokers or nonsmokers based on their own report at baseline.

2.3.4. Chronic somatic diseases

T2DM was diagnosed according to the WHO 1999 criteria (World Health Organization Expert Committee, 1999). The diagnostic procedure for possible or definite coronary heart disease (CHD) based on health examination, electrocardiogram, and register data as described in Kattainen et al. (2006).

Diagnosis of metabolic syndrome was based on The National Cholesterol Education Program's Adult Treatment Panel III criteria (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001).

The detailed diagnostic process for these conditions and for the laboratory and other measures are described in supplementary methods.

2.3.5. Low-grade inflammation

Low-grade inflammation was analyzed using a categorical variable as measured by the highest quintile of CRP concentration (2.43 mg/L) as a cut-off.

2.4. Information on mortality and causes of death

Information on mortality up to December 31st 2013 and causes of death were obtained from the Cause of Death statistics kept by Statistics Finland. The statistics contain data from death certificates completed either by the treating physician or by the physician who performed the autopsy. The medicolegal autopsy rate in Finland is exceptionally high (Lunetta et al., 2007), and the Cause of Death statistics is considered reliable.

Causes of death were classified into natural causes (ICD-10 A00–R99), including alcohol-related diseases and accidental poisoning by alcohol (F10, G312, G4051, G621, G721, I426, K292, K70, K852, K860, O354, P043, Q860, X45), and unnatural causes, including suicide (X60–X84, Y870) and other unnatural causes (V01–X44, X46–X59, X85–Y86, Y871–Y89).

Please cite this article as: Keinänen, J., et al., Mortality in people with psychotic disorders in Finland: A population-based 13-year follow-up study, Schizophr. Res. (2017), http://dx.doi.org/10.1016/j.schres.2017.04.048