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Mortality associated with depression as compared with other severe mental disorders: A 20-year follow-up study of the GAZEL cohort.

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ABSTRACT

Individuals with severe mental disorders (SMD) have an increased risk of mortality from somatic diseases. This study examined whether this risk is different in persons with depressive disorders compared to those with other SMD (i.e. schizophrenia and bipolar disorder). In 1989, 20,625 employees of the French national gas and electricity company (15,011 men and 5614 women, aged 35–50) agreed to participate in the GAZEL cohort study. Three diagnosis groups were created based on sick leave spells from 1978 onwards: 1) no SMD, 2) depressive disorders and 3) other SMD. Dates and causes of death were available from January 1, 1990 to December 31, 2010. The association of diagnosis groups with mortality was estimated with hazard ratios (HR) and 95% confidence intervals (CI) computed using Cox regression. During a mean follow-up of 19.8 years, 1544 participants died, including 1343 from a natural cause, of which 258 died from cardiovascular diseases. After adjustment for age, gender, occupational status, alcohol consumption, smoking and body-mass index, participants with a history of sickness absence for SMD had a greater risk of natural mortality (HR: 1.24, CI: 1.08–1.43), cardiovascular mortality (HR: 1.49, CI: 1.08–2.05) and non-cardiovascular natural mortality (HR: 1.19, CI: 1.02–1.39). Compared to depressive disorders, other SMD were associated with an increased risk of natural mortality (HR: 1.94, CI: 1.17–3.22) and cardiovascular mortality (HR: 3.58, CI: 1.53–8.39). Job security and systematic medical follow-up may fall short of preventing premature death among workers with sickness absence due to SMD.

1. Introduction

Compared to the general population, individuals with severe mental disorders (SMD) have a two to three-fold higher mortality rate and a lower life expectancy of at least 10 years (Dembling et al., 1999; Hannerz et al., 2001; Colton and Manderscheid, 2006; Chang et al., 2011). Contrary to lay beliefs, suicide accounts for only a small part of this increased premature mortality. Indeed, accumulating evidence suggests that patients with depressive disorders and other SMD (i.e. schizophrenia, schizoaffective disorder and bipolar disorder) have an increased risk of mortality from somatic diseases, henceforth referred to as natural mortality. Regarding schizophrenia, a meta-analysis of 37 studies conducted in 25 countries found a median standardized mortality ratio of 2.41 for natural mortality (Saha et al., 2007) with a trend for an increase between the 1970s and the mid-1990s. Although cardiovascular mortality might account for most of this increased risk among patients with schizophrenia, schizoaffective disorder and bipolar disorder (Osborn et al., 2007; Roshanaei-Moghaddam and Katon, 2009), several studies found an increased risk of death from other causes such as respiratory diseases and cancer (Hansen et al., 2001; Joukamaa et al., 2001; Tran et al., 2009). Regarding depressive disorders, both clinical and subclinical depression have been associated with an increased risk of all-cause mortality (Cuijpers and Smit, 2002). As for other SMD, this increased risk may mostly result from increased cardiovascular mortality (Nicholson et al., 2006). However, depressive disorders may also relate to increased

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cancer mortality (Lemogne et al., 2012; Pinquart and Duberstein, 2010). Nonetheless, it remains unclear whether depressive disorders are associated with increased mortality to the same extent than other SMD.

Although this issue has implication for both clinical practice and health policy, it has been little explored yet. First, many studies considered either depressive disorders or other SMD only, or merged these diagnoses into a single category (Colton and Manderscheid, 2006; Osborn et al., 2007; Ferrie et al., 2009). Second, although many studies that examined these disorders separately found a smaller excess risk for natural mortality associated with depression than other SMD (Joukamaa et al., 2001; Kilbourne et al., 2009; Laursen et al., 2007 but see also Lawrence et al., 2003), only one study had sufficient statistical power to directly compare these two categories (Laursen et al., 2007). Third, most of these studies, including the later, adjusted their analyses for age and gender only (Hannerz et al., 2001; Hansen et al., 2001; Joukamaa et al., 2001; Colton and Manderscheid, 2006; Laursen et al., 2007, 2009). Fourth, many studies were based on convenience samples of individuals selected through psychiatric hospital discharge registries (Hannerz et al., 2001; Hansen et al., 2001) or mental healthcare provider databases (Lawrence et al., 2003; Colton and Manderscheid, 2006; Kilbourne et al., 2009; Chang et al., 2011). The internal and external validity of these studies is thus threatened by selection biases with an increased likelihood of confounding factors such as disease severity, comorbid somatic condition, poor medical adherence or social isolation (Cuijpers and Smit, 2002; Saha et al., 2007; Roshanaei-Moghaddam and Katon, 2009). Fifth, many studies did not examine specific causes of death, thus failing to separate natural mortality from violent deaths (Chang et al., 2011; Chwastiak et al., 2010; Ferrie et al., 2009; Hannerz et al., 2001).

In addition, only one large cohort study examined natural mortality among people with SMD in France. It only included patients with schizophrenia and showed an excess mortality rate from cancer comparatively to the general population (Tran et al., 2009). Most data about natural mortality in people with SMD have been generated by studies conducted in the US, the UK and Scandinavian countries (Cuijpers and Smit, 2002; Saha et al., 2007; Roshanaei-Moghaddam and Katon, 2009; Pinquart and Duberstein, 2010), where the distribution of health characteristics as well as associated risk factors, the organization of the healthcare system or the prescription of psychotropic medications differ from those observed in France. Finally, to the best of our knowledge, this issue was never addressed in a working population.

The present study took advantage of the large French GAZEL cohort to examine associations between depressive disorders, other SMD and natural mortality, adjusting for age, gender, occupational grade, alcohol consumption, smoking and body-mass index. In this working population, patients with SMD were identified through sickness absence spells. Preliminary findings from the GAZEL cohort suggest that sickness absence for any mental disorder is associated with all-cause mortality (Ferrie et al., 2009) and suicide (Melchior et al., 2010) but these studies did not examine depression and other SMD separately. Here we aimed to compare the risk of natural mortality associated with depressive disorders vs. no SMD, other SMD vs. no SMD and other SMD vs. depressive disorders.

2. Materials and methods

2.1. Participants

Details of the GAZEL cohort study are available elsewhere (Goldberg et al., 2007). The target population consisted of 44,992 employees of the French national gas and electricity company "Electricité de France-Gaz de France" (EDF-GDF): 31,411 men aged 40–50 and 13,511 women aged 35–50. The study protocol was approved by the French authority for data confidentiality ("Commission Nationale Informatique et Liberté") and by the Ethics Evaluation Committee of the "Institut National de la Santé et de la Recherche Médicale" (INSERM) (IRB0000388, FWA00005831). In 1989, 20,625 employees (45.8%) (15,011 men and 5614 women) agreed to participate in the GAZEL cohort study. Since 1989, participants have been followed by means of an annual mailed questionnaire, as well as through administrative databases. After 20 years of follow-up, the number of subjects lost to follow-up was exceptionally low (i.e. 0.5%) (Zins et al., 2009).

2.2. Sickness absence for mental disorder

All episodes of sickness absence available from 1978 onwards were extracted from the database of the EDF-GDF medical department. These data include the medical cause of absence verified by a company physician and coded using the abridged version of the International Classification of Diseases (ICD), 9th and 10th Revisions. For the present study, three groups were created: 1) "no major mental disorder" group included participants without psychiatric-related sickness absence, 2) "depressive disorder" group included participants who had received a diagnosis of dysthymic disorder (ICD-9: 300.4), depressive episode or recurrent depressive disorder (ICD-10: F32–F33) or mixed anxiety and depressive disorder (ICD-10: F41.2) and 3) "other severe mental disorder" group included participants who had received a diagnosis of psychosis (ICD-9: 290–299), schizophrenia or delusional disorder (ICD-10: F20–F29), manic episode or bipolar disorder (ICD-10: F30–F31).

2.3. Covariates

Age, gender, and occupational grade (blue-collar workers or clerks, first-line supervisors or sales representatives, management or training) were obtained from the employer's human resources files at baseline. Alcohol consumption, smoking, height and weight were self-reported. Alcohol consumption, as drinks per week, was categorized as none, occasional (1–13 for men, 1–6 for women), moderate (14–27 for men, 7–20 for women) or heavy drinkers ($\geq$28 for men, $\geq$21 for women). Smoking was categorized in 5 classes: never-smokers, ex-smokers and current smokers of fewer than 20 pack-years, and ex-smokers and current smokers of more than 20 pack-years. Body-mass index (BMI) was calculated and categorized as $<$18.5, 18.5–24.9, 25–29.9 or $\geq$30 kg/m^2.

2.4. Mortality data

Living status and the date of death were annually obtained for all participants directly from EDF-GDF as it pays out retirement benefits. Causes of death were available from baseline (i.e. January 1, 1990) to December 31, 2010 and were coded by the French National Cause-of-Death Registry using the International classification of diseases, 9th and 10th Revisions. We considered six categories of mortality outcome: all-cause mortality, suicide (ICD-9: E95; ICD-10: X60–X84), accidents and other external causes of death (ICD-9: E80–E94 and E96–E99; ICD-10: V00–X58 and X92–Y99), natural mortality (i.e. all-cause mortality excluding suicides and accidents), which was further divided into cardiovascular mortality (ICD-9: 389–460; ICD-10: I00–I99) and non-cardiovascular natural mortality.