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Research report

A comorbid anxiety disorder does not result in an excess risk of death among patients with a depressive disorder

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ABSTRACT

Background: Several studies have demonstrated increased mortality associated with depression and with anxiety. Mortality due to comorbidity of two mental disorders may be even more increased. Therefore, we investigated the mortality among patients with depression, with anxiety and with both diagnoses.
Methods: By linking the longitudinal Psychiatric Case Register Middle-Netherlands, which contains all patients of psychiatric services in the Utrecht region, to the death register of Statistics Netherlands, hazard ratio's of death were estimated overall and for different categories of death causes separately.
Results: We found an increased risk of death among patients with an anxiety disorder (N = 6919): HR = 1.45 (95%CI: 1.25–1.69), and among patients with a depression (N = 14,778): HR = 1.83, (95%CI: 1.72–1.95), compared to controls (N = 103,824). The hazard ratios among both disorders combined (N = 4260) were similar to those with only a depression: HR = 1.91, (95% CI: 1.64–2.23). Among patients with a depression, mortality across all important disease-related categories of death causes (neoplasms, cardiovascular, respiratory, and other diseases) and due to suicide was increased, without an excess mortality in case of comorbid anxiety.
Limitations: The presented data are restricted to broad categories of patients in specialist services. No data on behavioral or intermediate factors were available.
Conclusions: Although anxiety is associated with an increased risk of death, the presence of anxiety as comorbid disorder does not give an additional increase in the risk of death among patients with a depressive disorder. The increased mortality among patients with depression is not restricted to suicide and cardiovascular diseases, but associated with a broad range of death causes.

1. Introduction

Depressive and anxiety disorders are among the most common mental disorders in the Western world. In the USA, the 12-months prevalence of these disorders was estimated as high as 10% and 18%, the lifetime-cumulative prevalence was estimated as high as 21% and 29%, respectively (Kessler et al., 2005a, 2005b). Figures in other Western and non-Western countries, although somewhat lower, also demonstrate that the lifetime prevalence of these disorders is high (Kessler et al., 2007) (de Graaf et al., 2011).

Depressive disorders have an unfavorable impact on health related quality of life and morbidity, and are also associated with increased mortality, due to cardiovascular diseases and other death causes (Chang et al., 2009; Murphy et al., 2008;

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Mykletun et al., 2009; Rapp et al., 2008) (Batterham et al., 2010; Herrmann et al., 2000; Holwerda et al., 2007; Wulsin et al., 1999) (Mykletun et al., 2007).

Studies on the association between anxiety and mortality are less unequivocal, with results indicating an absent (Batterham et al., 2010; Holwerda et al., 2007), favorable (Harris and Barraclough, 1998; Herrmann et al., 2000; Lee et al., 2006; Mykletun et al., 2007), unfavorable (Denollet et al., 2009; Dewey and Chen, 2004; Harris and Barraclough, 1998), or even an U shape relationship (Mykletun et al., 2009). In addition, only few studies investigated whether the co-occurrence of a depressive and an anxiety disorder results in an excess death risk, as compared to that of the individual diagnoses. The importance of this issue is highlighted by the fact that both disorders frequently co-occur, and possibly even share a common underlying pathophysiology (Dewey and Chen, 2004; Hettema, 2008; Lamers et al., 2011; Middeldorp et al., 2005; Pollack, 2005; Tyrer, 2001).

Previous studies on the mortality in patients with depression report unfavorable (Goodwin et al., 2001; Johnson et al., 1990; Spijker et al., 2010), favorable or absent associations (Holwerda et al., 2007; Mykletun et al., 2009) with comorbid anxiety. These diverging results may be explained by differences in inclusion of psychiatric disorders, patient- and diagnosis characteristics and causes of death (Batterham et al., 2010; Holwerda et al., 2007; Mykletun et al., 2007).

In the present study, we assessed the mortality risk among patients with a documented diagnosis of depression or anxiety disorder, and analyzed the excess mortality risk in case of the presence of both diagnoses.

2. Methods

2.1. Databases

We performed a dynamic cohort study using two databases. The first database is the Psychiatric Case Register Middle Netherlands (PCR-MN). The PCR-MN registers all diagnoses of in- and outpatient of psychiatric services and related healthcare consumption in the province of Utrecht, the Netherlands. It was founded in 1999 and covers an urbanized region with roughly 780,000 inhabitants. The second database is the causes of death register of Statistics Netherlands (Centraal Bureau voor de Statistiek, CBS). The CBS is responsible for collecting and processing all individual and population health care data in the Netherlands to be used in practice, by policymakers and for scientific research (CBS, 2011). Physicians in the Netherlands are obliged to report the cause of death to the civil registry of the town where the person died. This is forwarded to the CBS, where the death report is ICD-10 coded (WHO, Version 2007) and entered into the database.

2.2. Data extraction

The data of all patients with either a registered diagnosis of an anxiety disorder, a depressive disorder, or both diagnoses in the period January, 1999 until January, 2008 were extracted from the PCR-MN database. By linking the PCR-MN database to the register of the CBS we were able to identify the causes of death of all psychiatric diagnosed persons in the PCR-MN region. The linking of databases was performed by the CBS by using the date of birth, a part of the postal code and sex. Dutch privacy law allows the use of personal (healthcare) data on behalf of scientific research if these data cannot be traced to a unique person by the researchers. To ensure anonymity, postal code and day of birth were removed by the CBS from the analysis files.

2.3. Participants

Four groups of patients/persons were compared. The first group consisted of all inhabitants diagnosed with a depressive mood disorder (Dep), which was defined as a DSM-IV (1994) diagnosis registered in the PCR-MN database between January, 1999 and January, 2008 with codes 296.2x (Major depressive disorder, single episode), 296.3x (Major depressive disorder, recurrent), 311 (Depressive disorder, NOS), or 300.4 (Dysthymic disorder). The second group consisted of all inhabitants with an anxiety disorder (Anx), which was defined as a DSM-IV diagnosis of codes 300.21/300.01 (Panic disorders), 300.02 (Generalized anxiety disorder), 300.22/300.23/300.29 (Phobias), 300.30 (Obsessive Compulsive disorder), 309.81/308.30 (Stress disorders) or 293.89 (Anxiety disorder due to medical condition), 300.00 (Anxiety disorder NOS) registered during that same period. The third group consisted of inhabitants who were diagnosed with both a depression and an anxiety disorder (using the previously mentioned codes) during that same period (Anx + Dep). Other comorbid conditions were no reason for exclusion. The fourth, reference, group consisted of a random sample from the population register of the CBS of inhabitants from the PCR-MN region without a registered psychiatric disorder, restricted to the age range 15–90 years at January, 1999, which covers the age range found in the PCR-MN. The sample size of this reference group was four times the size of the first three groups together. The four groups were mutually exclusive.

2.4. Study period

The follow-up started at the date of diagnosis for Anx and Dep, and in January, 1999 for the reference group. For Anx + Dep the follow-up started at the time of diagnosis of the second disorder. For every cohort member the follow-up ended at December 31, 2009, or at the date of death if this came earlier.

2.5. Outcome

The main outcome of interest of the study was all-cause mortality. Secondary outcomes were the four most common disease-related causes of death in the Netherlands, being cancer, cardiovascular disease, respiratory disease and the remaining causes of disease-related death (RIVM, 2010), and the non-disease related causes of death, subdivided in suicide vs. non-suicide.

2.6. Statistical analysis

Data-management, record linking, description of the study cohort and standardization of mortality rates for age and gender were performed using SPSS, version 14.0. The Cox regression analyses were performed using STATA, version