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Research paper

Age- and gender-specific mortality risk profiles for depressive outpatients with major chronic medical diseases

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ABSTRACT

Background: As leading causes of death, chronic medical diseases, particularly common cardiovascular diseases, are associated with depression. The combination of depression and chronic medical disease in turn is linked with poorer health and premature death. Despite numerous studies on mortality in people with depression and chronic medical disease, the effects of age and gender were not consistently considered. To appropriately estimate mortality in the clinical setting, we aimed to analyse age- and gender-specific mortality profiles in outpatients with depression and chronic medical disease by considering depression severity.

Methods: We examined data from $N=327{,}018$ outpatients with depression aged 18 years and older (mean = 60 years), which we obtained from German electronic health-insurance claims data covering the years 2007–2010. We considered major chronic medical disease groups: cardiovascular diseases, diabetes, diseases of the respiratory system and cancer. To analyse both adjusted mortality risk and rates over one year in a comprehensive manner, we calculated General Estimation Equation (GEE) Poisson models for binary data.

Results: The mortality risk increased with age and was higher for males. Especially patients below 60 years of age with cancer or diabetes had an increased mortality risk, but not patients with cardiovascular disease. Mortality was comparably increased in patients with severe depression, diabetes or respiratory disease.

Limitations: We did not have data from a control group without depression.

Conclusions: Notably, not cardiovascular diseases but cancer and, to a lesser extent, diabetes, both in younger patients, respiratory diseases and severity of depression require particular attention in outpatient care to reduce mortality.

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1. Introduction

Worldwide, chronic medical diseases, particular cardiovascular diseases, are the leading causes of death, even for people below 70 years of age (WHO, 2014). Chronic diseases are defined as ongoing, generally incurable, requiring continued medical attention and affecting a person's daily life (AARP, 2009). Accordingly, the World Health Organization (WHO) formulated targets to reduce these premature deaths, for instance by strengthening primary care, by appropriate training of the health care providers and by implementing interventions to decrease risk factors (WHO, 2014). Surprisingly, the role of mental disorders has received too little notice until recently. In particular, the 1-year prevalence of depression is three to seven times higher in those who suffer from chronic medical disease than in those who do not (Moussavi et al., 2007). This comorbidity dramatically worsens the health of those affected (Moussavi et al., 2007) and is associated with a decreased life-time expectancy (Chang et al., 2010; Katon, 2011; Moussavi et al., 2007). Both maladaptive health risk behaviours and psychobiological factors associated with depression may explain depression's negative effect on the outcomes of chronic diseases, even if the direction of the relationship is probably bidirectional (Katon, 2011). According to previous evidence, the severity of depression is of minor relevance for excess mortality, indicating that even subthreshold depression could have an impact on health (Cuijpers and Smith, 2002).

Despite large evidence on mortality in people with depression

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and chronic medical disease in retrospective (Gasse et al., 2014; Lynch et al., 2014; Schoepf et al., 2014) or prospective population-based samples (Atlantis et al., 2012; Everson-Rose et al., 2004; Frasure-Smith et al., 1993; Kimbro et al., 2014; Lichtman et al., 2014; Lin et al., 2009; Meijer et al., 2013; Mykletun et al., 2007; Panagioti et al., 2014; Surtees et al., 2008; van Melle et al., 2004), there are several limitations. In particular, there is a lack of information on the age- and gender-specific mortality risk and mortality rate in outpatients with depression and major chronic medical disease. Age is a particularly relevant factor as it (a) increases general mortality and (b) promotes the development of chronic medical diseases (WHO, 2005). The results on gender and mortality in people with depression are mixed (Sevick et al., 2000), despite a higher prevalence of depression in women than in men (WFMH, 2012). Even if the majority of previous studies controlled for age and/or gender (Everson-Rose et al., 2004; Gasse et al., 2014; Lin et al., 2009; Lynch et al., 2014; Meijer et al., 2013; Mykletun et al., 2007; Panagioti et al., 2014; Pinquart and Duberstein, 2010; Surtees et al., 2008), they largely did not report the age- and gender-specific mortality risk. Moreover, only few studies on mortality in people with depression considered interaction effects of chronic medical disease with age and gender (Gasse et al., 2014) or different age groups (Everson-Rose et al., 2004; Gasse et al., 2014; Kimbro et al., 2014). There is a lack of studies considering non-linear age: even if the majority of chronic medical diseases tend to rise exponentially with age (Harris, 2013), this relationship was not consistently reported (AARP, 2009; Coryell et al., 1999; Gasse et al., 2014; Surtees et al., 2008). Furthermore, although previous studies accounted for medical comorbidity and, to different extents, further covariates, only few studies examined the mortality risk of several major medical chronic diseases in depression (Everson-Rose et al., 2004; Mykletun et al., 2007; Schoepf et al., 2014). Finally, in spite of its significance for primary care, mortality data on outpatients with depression and chronic medical disease are still scarce (Lin et al., 2009).

Primary physicians serve as “gate-keepers”, and therefore are usually the first to identify and manage a variety of health problems before referring patients to specialists. Accordingly, they have a particular responsibility in recognising, diagnosing and treating depression and chronic medical disease (Barnett et al., 2012; Smith et al., 2014). To lower mortality, these practitioners need to be aware of mortality profiles of their patients in order to ensure appropriate interventions on time (e.g. actively assessing mental health in patients presenting a chronic medical disease, coordinated management approaches) (Smith et al., 2014). For this purpose it is not only important to know about the *mortality risk* as the increased likelihood of dying of a specific group compared to another, but also to have information about the *mortality rate* or individual risk to die, expressed by the number of deaths in a particular population, scaled to the size of the population, per unit of time.

To appropriately estimate mortality in the clinical setting, our objective was to investigate the age- and gender-specific all-cause mortality risk and rate of outpatients with depression related to four major chronic medical disease groups: cardiovascular diseases, diabetes, chronic respiratory diseases and cancer. We also considered non-linear effects of age and severity of depression.

2. Methods

2.1. Data description

This study is a retrospective analysis using electronic health-insurance claims data from a statutory health-insurance company [Allgemeine Ortskrankenkasse Plus (AOK Plus)], located in the new Federal States of Germany. The AOK Plus covers about three million insured persons, the majority of whom live in Saxony and Thuringia. AOK-databases used comprised a selected sample on the basis of specific criteria: (a) having a diagnosis of depression [a depressive episode (F32, ICD-10) or a recurrent depressive disorder (F33, ICD-10)] in an outpatient setting between January 1, 2007 and September 30, 2010; (b) having health insurance coverage of at least one day; (c) being at least 18 years old; (d) living in Saxony or Thuringia.

2.2. Sample selection

In this study, we selected relevant information from outpatient and health insurance databases. The health insurance databases included treatment coverage and basic socio-demographic information on patients with a diagnosis of depression. The outpatient databases included all patients who had at least one depression diagnosis between the first quarter of 2007 and the third quarter of 2010 and received treatment for certain ICD-10-diagnoses, mostly from a primary physician, and to a minor extent from another private practitioner (specialist) or from a psychotherapist, psychiatrist or psychiatric outpatient service (Büchtemann et al., 2012). To construct a homogenous sample in terms of age and observation time, we selected a subsample among all patients: (a) The first quarter, with a diagnosis of depression between 2007 and 2009, was the index quarter. We chose this approach because we assumed that patients with depression who were under treatment would get the respective diagnosis early on in the course of treatment. In addition, this approach allowed us to include as many outpatients as possible. Due to the uncertain validity of ICD-10 diagnoses in our health-insurance claims dataset, we preferred this approach compared to a more sophisticated selection procedure. If the same patient was receiving more than one depression diagnosis within an index quarter, we chose the most severe one and a recurrent depressive disorder compared to a depressive episode. If we had clear information on the degree of severity, we preferred this information compared to other or unspecified depression. The diagnosis “other Depression” was weighted higher than "unspecified depression". Other Depression indicates "atypical depression" being characterised by atypical features such as increased appetite and sleep (compared to a lack of appetite and sleep). Atypical depression is the most common form of depression seen in outpatient clinics in psychiatry (Singh and Williams, 2006). Unspecified depression is a preliminary diagnostic category that might be diagnosed if the exact categorisation is not yet clear. Finally, we used the patients' age in the index quarter as relevant age in the observation period. (b) In this index quarter, we recorded whether at least one chronic medical disease was present or not. (c) The maximum observation time per patient was one year. This sample selection process finally resulted in 327,018 patients.

2.3. Predictor variables

We included the basic socio-demographic variables age and gender. In the statistical model, age was centred at the mean of 60 years and divided by 10 to facilitate the interpretation of model estimates. We also considered the severity of depression [mild/remitted = 0 (F32.0, F33.0, F33.4), moderate/other/unspecified = 1 (F32.1, F33.1, F32.8, F32.9, F33.8, F33.9), severe, with or without psychotic features = 2 (F32.2, F32.3, F33.2, F33.3)]. We examined four major chronic disease groups mentioned by the WHO as leading causes of death (WHO, 2014): Cardiovascular diseases, diabetes, chronic respiratory diseases and cancer (see Appendix A).

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