Journal of Affective Disorders 161 (2014) 47–54

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review

Is excess mortality higher in depressed men than in depressed women? A meta-analytic comparison

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ARTICLE INFO

Article history:
Received 21 January 2014
Received in revised form
3 March 2014
Accepted 3 March 2014
Available online 15 March 2014

Keywords:
Depression
Mortality
Gender difference
Meta-analysis
Prospective studies

ABSTRACT

Background: It is not well-established whether excess mortality associated with depression is higher in men than in women.
Methods: We conducted a meta-analysis of prospective studies in which depression was measured at baseline, where mortality rates were reported at follow-up, and in which separate mortality rates for men and women were reported. We conducted systematic searches in bibliographical databases and calculated relative risks of excess mortality in men and women.
Results: Thirteen studies were included. Among the people with depression, excess mortality in men was higher than in women (RR=1.97; 1.63–2.37). Compared with non-depressed participants, excess mortality was increased in depressed women (RR=1.55; 95% CI: 1.32–1.82), but not as much as in men (RR=2.04; 95% CI: 1.76–2.37), and the difference between excess mortality in men was significantly higher than in women ($p < 0.05$).
Conclusions: Excess mortality related to depression is higher in men than in women. Although the exact mechanisms for this difference are not clear, it may point at differential or more intensified pathways leading from depression to increased mortality in depressed men compared to women.

Contents

Abbreviations: BDI, Beck depression inventory; CES-D, Center for epidemiological studies – depression scale; DIS, Diagnostic interview schedule; DRS, Depression rating scale; FU, Follow-up; GDS, Geriatric depression scale; GMS/AGECAT, Geriatric mental state/automated geriatric examination for computer assisted taxonomy; MDD, Major depressive disorder; mind, Minor depression; MINI, Mini international neuropsychiatry interview; PHQ, Patient health questionnaire; PSE, Present state examination; SDS, Selfrating depression scale

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http://dx.doi.org/10.1016/j.jad.2014.03.003
0165-0327/

1. Introduction

Several hundreds of studies have now shown that depressive disorders are associated with excess mortality (Cuijpers et al., 2013). The mortality risk has been found to be independent of disease status (Cuijpers et al., 2013), and has been observed in all kinds of patients and healthy populations including community samples (Cuijpers and Smit, 2002; Saz and Dewey, 2001; Wulsin et al., 1999), heart disease patients (Barth et al., 2004; Nicholson et al., 2006; Sørensen et al., 2005; Van Melle et al., 2004), cancer patients (Chida et al., 2008; Pinquart and Duberstein, 2010), stroke patients (Pan et al., 2011), and diabetes patients (Bruce et al., 2005; Lin et al., 2009). The exact causes for the increased mortality rates in depressed people are not yet known, but may be related to an increased risk for suicide in depressed patients (Botswick and Pankratz, 2000), by hazardous health behaviors, such as physical inactivity (Whooley et al., 2008), increased smoking rates (Dierker et al., 2002), more alcohol consumption (Holahan et al., 2003) and unhealthy eating patterns (Luppino et al., 2009; Penninx et al., 1999), and by biological dysregulation including hyperactivity of the hypothalamic pituitary adrenal axis, neuro-immune dysregulations, and sympathoadrenergic dysregulation (Cesari et al., 2003; Pariante, 2003; Cuijpers and Schoevers, 2004; Penninx et al., 2013). The causal direction of the most of these mechanisms is unclear, however. Depressive disorders may lead to hazardous health behaviors or biological dysregulation, these behaviors and dysregulation may lead to depression, or both may be explained by a third, underlying factor.

It is not yet clear whether excess mortality in depression is higher among men than among women. Some studies have found evidence for such a differential association pointing at higher excess mortality in men than in women (Kopp et al., 2011; Takeida et al., 1997; Ahto et al., 2007), but others have not confirmed this (Faller et al., 2007; Yaffe et al., 2003). Whether or not there is a differential mortality rate in men and women is important because it may point at different causal pathways between men and women with depression. It may also point at more intensified pathways in men or women, which is found for example in suicide where mortality rates in men are higher than in women.

We decided to conduct a meta-analysis of prospective studies in which depression was measured at baseline, mortality rates were reported at follow-up, and in which separate mortality rates for men and women were reported.

2. Method

2.1. Selection and inclusion of studies

Studies were traced by means of several methods. First, we conducted comprehensive literature searches (up to April 2013) in three bibliographical databases (Pubmed, Psycinfo and Embase). In these searches we combined words indicating depression (such as major depression, mood disorder, depression, depressive), mortality (death, survival), and prospective design (incidence, follow up studies, longitudinal studies, prospective studies). Both text and key words were used. We also checked the references of included studies, as well as the references of earlier meta-analyses examining the association between depression and mortality (Cuijpers et al., 2013). We retrieved the full-text papers of studies that possibly met inclusion criteria. Full-text papers were examined by two independent raters for possible inclusion. Disagreements were solved by discussion.

In a separate paper we have reported the results of all 293 prospective studies that examined the relative risk (RR) of dying during follow-up in depressed versus non-depressed people (Cuijpers et al., 2013), indicating that depressed people have a significantly increased mortality rate compared to non-depressed people (RR = 1.64; 95% CI: 1.56–1.76). In the current study, we only included studies (–) with a prospective design (–) in which depression was examined at baseline, (–) all-cause mortality was reported at follow-up, and (–) mortality rates were reported separately for men and women. Depression had to be assessed with a standardized depression measure, which could be either a diagnostic interview or a self-report questionnaire. We included studies in any target group (community, patient and any other sample) as well as case-control studies. Studies were excluded when insufficient data were presented to calculate mortality rates at follow-up in the depressed and non-depressed group. We also excluded studies in which the instrument for assessing depression was not standardized (e.g., use of antidepressants, non-standardized interviews, one question), studies based on trials examining the effects of an intervention, and studies in children and adolescents.

2.2. Data extraction and quality assessment

We rated the number of deaths in the groups of men and women with depression, and in the non-depressed control group. For the subgroup (moderator) analyses we rated several characteristics of the included studies: target population (community sample, patient sample, or other sample); and definition of depression (scoring above a cut-off on a self-report measure versus fulfilling diagnostic criteria for a depressive disorder); and follow-up period (< 3 years; 3–5 years; > 5 years).

There is a risk that studies only report differential outcomes for men and women when this difference is significant. In order to examine this we tested for the presence of publication bias (see below), but we also rated the studies on whether the gender difference was the focus of the study. We assumed that when the gender difference was explicitly part of the research question, there would be a risk that this was reported because the authors found the difference to be significant, and that this may not have been published when the difference would not have been significant. When a study reported the gender difference in the title, described this difference explicitly in the Introduction section of the paper, or described it as part of the research question, we considered this study at high risk for publication bias. Other studies were not considered at increased risk for publication bias..

In order to assess the validity of the studies we used a quality rating scale that was based on the instrument developed by Hayden et al., (2006). We adapted the specific items for use with the studies in this field, but retained five of the six basic areas of potential bias that are assessed with this instrument: study