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## Research paper

## Gender differences in depression and pain: A two year follow-up study of the Survey of Health, Ageing and Retirement in Europe

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## ABSTRACT

**Background:** The longitudinal association of depression and pain according to gender was investigated using a population-based sample from 13 European countries.

**Methods:** The study population was taken from waves 4–5 of the Survey of Health, Ageing and Retirement in Europe. The sample consisted of 22,280 participants  $\geq 50$  years, who were interviewed at baseline, and after two years. Regression models for each gender were used to assess the variables associated with depression and pain incidence and persistence.

**Results:** Prevalences of depression, pain, and depression–pain co-occurrence, were higher in women than in men (depression: 34.5% vs. 20.3%; OR=2.1; 95% CI=1.9–2.2; pain: 60.2% vs. 53.5%; OR=1.3; 95% CI=1.2–1.4; co-occurrence 25.3% vs. 14.0%; OR=2.3; 95% CI=2.2–2.6). Treated baseline pain in women (OR=1.6; 95% CI=1.3–2.0), and treated/untreated pain in men (untreated OR=1.3; 95% CI=1.1–1.7; treated OR=2.0; 95% CI=1.5–2.7), were associated with incident depression. Untreated baseline depression was associated with incident pain (women OR=1.3; 95% CI=1.1–1.7; men OR=1.8; 95% CI=1.3–2.6), and with persistent pain only in women (OR=1.3; 95% CI=1.1–1.6).

**Limitations:** We lack information on pain severity, and the consumption of analgesics was used as a proxy. We lack information on antidepressants and anxiolytics consumption separately. Participants were interviewed twice in two years, and pain/depression at both interviews were considered persistent although they may have relapsed and recurred.

**Conclusions:** Treated baseline pain is a risk factor for incident depression in both genders; untreated baseline pain is a risk factor only in men. Treating depression at baseline may protect from developing pain in both genders, and in women, it may also protect from pain persistence.

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## 1. Introduction

Depression is highly prevalent in women, with a lifetime prevalence of major depression disorder affecting twice as many women as men (Kessler et al., 2005). Pain is also more common in women, who report more intense and frequent pain, and less response to analgesics than men (Wranker et al., 2015; Shega et al., 2014; Kano et al., 2013). To date, extensive literature describes the co-occurrence of depression and pain (Denkinger et al., 2014; Han and Pae, 2015; Pae et al., 2009; Vietri et al., 2015), which is also more common in women than in men (Haley et al., 1985; Geerlings et al., 2002).

A causal relationship has not been clearly established between depression and pain, although their association is well known (Denkinger et al., 2014; Han and Pae, 2015; Pae et al., 2009; Vietri et al., 2015). To date, several studies in the areas of genetics, epigenetics, cellular biology, structural and functional imaging techniques, neurotransmitter and neuroendocrine disorders have been published (Han and Pae, 2015; Swiergiel et al., 2015), and all of them confirm the existence of a depression–pain link. Moreover, some publications suggest the existence of common coacting factors which would explain the depression and pain apparent clinical relationship and their neurophysiological overlap (Chopra and Arora, 2014). However, the biological mechanisms leading this association remain unknown. Other theories rely on the fear-avoidance model, which would explain that initial pain may persist and develop a chronic pain syndrome through several processes such as hypervigilance, negative affectivity, muscular reactivity and anxiety, among others (Vlaeyen and Linton, 2000).

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Moreover, the reason underlying the increased prevalences in women has not been unveiled either, although several hypotheses have been developed (Kano et al., 2013; Meana, 1998; Jensen et al., 1994; Silverstein and Angst, 2015; Silverstein et al., 2013). For example, in a study using healthy volunteers, it was seen that during the experience of pain women activate brain areas associated with the affective/motivation components of pain, while men displayed increased activity in the supplementary motor area, so it was suggested that women may attribute more emotional importance to pain than men (Kano et al., 2013). Other authors state that women may see depression as a socially acceptable reaction to pain, while men may not (Meana, 1998). Other reports indicate that it is due to the fact that women catastrophize more than men as a reaction to pain, which may lead to depression (Jensen et al., 1994). It has also been suggested that the increased prevalence of depression in women is due to a specific phenotype of depression: the somatic depression – which includes aches and headaches – (Silverstein et al., 2013; Silverstein and Angst, 2015), and that this would be a reactive depressive disorder different from the ‘pure’ endogenous melancholic depression (Silverstein and Angst, 2015).

However, although reports regarding the causal direction of the association of depression and pain yield diverse results, several variables have been identified to intervene in the pain–depression association, such as age, anxiety, physical impairment, or education level, among others (Geerlings et al., 2002; Haley et al., 1985; Iliffe et al., 2009; Jacobi et al., 2004; Markkula et al., 2015; Vietri et al., 2015; Wright et al., 2010; Kessler et al., 2015). To date, several studies have been conducted taking into account these variables (Kessler et al., 2015; Jacobi et al., 2004; Markkula et al., 2015; Denking et al., 2014; Iliffe et al., 2009; Haley et al., 1985; Vietri et al., 2015; Wright et al., 2010; Gerrits et al., 2015). Nevertheless, although gender has also been highlighted as one of the main confounders in the relationship between depression and pain (Geerlings et al., 2002; Meana, 1998; Kessler et al., 2005; Haley et al., 1985), there is a lack of studies focusing on the differences between men and women regarding the variables playing a role in the association between depression and pain (Haley et al., 1985; Geerlings et al., 2002).

Our aim was to describe the variables associated with incident and persistent depression and pain in men and in women separately, by using a longitudinal design in a population-based sample from 13 different European countries (Börsch-Supan et al., 2013a, 2013b; Malter and Börsch-Supan, 2013, 2015).

## 2. Material and methods

### 2.1. Data source and study sample

Data from the waves 4 and 5 of the Survey of Health, Ageing and Retirement in Europe (SHARE, release 1.1.1 from March 28th 2013, release 1.0.0 from March 31st 2015) (Börsch-Supan et al., 2013a, 2013b; Malter and Börsch-Supan, 2013, 2015) were used in the current study. SHARE is a European cross-national and longitudinal research project collecting data among people aged 50 years and over and their partners, regardless of their age. Data collection of waves 4 and 5 was performed in 2011, and 2013, respectively. Waves 4 and 5 were conducted by 13 of the 20 countries participating in SHARE: Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Switzerland, Belgium, Czech Republic, Slovenia, and Estonia. Wave 4 of SHARE and the continuation of the project in wave 5 have been reviewed and approved by the Ethics Council of the Max-Planck-Society for the Advancement of Science. The Ethics Council of the Max-Planck-Society for the Advancement of Science carefully reviewed the

materials of the SHARE project and attested that the overall research project and its procedures, the measures to assure confidentiality and data privacy, and the information given to the participants agree with international ethical standards. The sample consisted of 38,212 respondents in wave 4 and 5, and for this study we selected the participants who provided an answer to the each of the 12 items of the depression scale used in this study in both waves (N=22,280).

The SHARE study consists of an interview with an average duration of 90 minutes, conducted at the respondent's household by trained interviewers. Questions cover a wide range of topics, including health and health related variables, economic variables, and social support variables. Data are freely available to the research community ([www.share-project.org](http://www.share-project.org)).

### 2.2. Measures

#### 2.2.1. Sociodemographic information

Gender, birth year, education, marital status and employment were recorded for each participant. Education was collected using the International Standard Classification of Education-97 (ISCED-97) codes by the UNESCO, and we further clustered the codes in three groups: (i) low education group, which included participants with no education or ISCED-97 codes 1 and 2; these are illiterate participants or those with primary and lower secondary education. (ii) Medium education group, which included participants with ISCED-97 codes 3 and 4, corresponding to secondary and post-secondary non-tertiary education. (iii) High education group, which included participants with ISCED-97 codes 5 and 6, corresponding to first and second stages of tertiary education.

Marital status was coded in 4 groups: married/registered partnership/living together, separated/divorced, single, and widower.

In turn, employment was also clustered in 4 groups: permanently sick or disabled, retired, employed/self employed/home-maker, and unemployed.

#### 2.2.2. Health-related measures

The number of self-reported comorbidities was recorded, and further classified into four clusters: none, 1, 2 or 3, and 4 or more comorbidities. The body mass index (BMI) was calculated from the height and weight reported by the participants. The participants were then classified according to the WHO BMI International Classification: normal (18.50–24.99 Kg/m<sup>2</sup>), underweight (< 18.50 Kg/m<sup>2</sup>), overweight (≥ 25.00 Kg/m<sup>2</sup>) and obese (≥ 30.00 Kg/m<sup>2</sup>).

Basic activities of daily living performance (bADL) was measured as an index considering five tasks: dressing, bathing or showering, eating and cutting up food, walking across the room, and getting in or out of bed. This index ranged from 0 to 5 points, and the higher the index the more difficulties the respondent had with bADL.

Anxiety at baseline was measured using five items from the Beck Anxiety Inventory (BAI), which has been seen to distinguish symptoms of anxiety from depression (Beck et al., 1988; Brenes et al., 2005). The five items were: fear of the worst happening, nervous, hands trembling, fear of dying, and feeling faint. There were four possible responses, ranging from “never” (1 point) to “most of the time” (4 points). An index was obtained by summing all the answers, with a final score ranging from 5 to 20 points. Other authors previously reported that these 5 items contribute, in a one latent factor solution, to one common factor: anxiety, and that the internal consistency of this index was good: Cronbach's  $\alpha=0.81$  (Morin et al., 1999).

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