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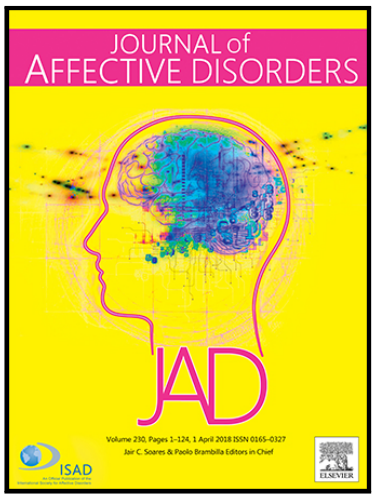

Gender analysis of the frequency and course of depressive disorders and relationship with personality traits in general population: a prospective cohort study

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Gender analysis of the frequency and course of depressive disorders and relationship with personality traits in general population: a prospective cohort study

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Highlights

- Gender gap affects prevalence, incidence and recurrence-persistence rates of depressive disorders in general population.
- The relationship between personality traits and the frequency and course of depressive disorders is different among men and women.
- Neuroticism and conscientiousness are important for subthreshold depressive symptomatology in men and for major depressive episode in women.

Background: We aimed to determine the prevalence and course of subthreshold depressive symptomatology (sDS) and probable major depressive episode (MDE) and to examine their association with personality traits among men and women. **Methods:** A community-based sample aged 35 years or older was examined in two waves (median follow-up of 6.9 years). The Patient Health Questionnaire-9 (PHQ-9) was used to assess sDS and MDE. The 10-item version of the Big Five Inventory was used to assess personality traits. Prevalence was assessed at baseline (n=5,557) and incidence and persistence-recurrence rates were computed at follow up (n=3,102). Logistic regression models were adjusted to explore the association of personality traits with prevalence and course of depressive disorders. **Results:** The prevalence of sDS and MDE was 14.04% (95% CI = 17.04-19.08) and 8.54 (95% CI=7.82-9.31), the incidence was 14.30 per 1,000 person-years (95% CI=12.49-16.31) and 4.34 per 1,000 person-years (95% CI=3.46-5.36), and the persistence-recurrence was 35.04 per 1,000 person-years (95% CI=29.00-41.96) and 28.8 per 1,000 person-years (95% CI=20.49-38.14). The gender gap was higher for MDE. Personality traits were differentially associated with the prevalence and course of depressive disorders between men and women. **Limitations:** Because this study used questionnaires to assess depressive disorders and personality traits, information bias could not be ruled out. **Conclusions:** The gender gap was higher for the prevalence and course of the probable MDE. There were more personality traits related with

the course of the sDS and they had a major role in the course of the probable MDE in women.

Keywords: Epidemiology; Population; Depression; Personality; Sex differences

1. Introduction

Depressive disorders are among the most frequent mental health diseases which are associated with disability, increased multimorbidity and high healthcare costs (Ferrari et al., 2013). According to the Global Burden of Disease study, the number of new cases of depression worldwide has increased from 172 million in 1990 to 258 million in 2017, representing an increase of 50% (Liu et al., 2020). Depressive disorders are clinical syndromes characterized by emotional, perceptual, cognitive, behavioural and somatic signs and symptoms that adversely affect the normal functioning (Park and Kim, 2018). These syndromes are classified into several disorders using the Diagnostic and Statistical Manual of Mental Disorders 5th edition (American Psychiatric Association, 2016) or the International Classification of Diseases 10th edition (World Health Organization, 2004) according to the number and severity of symptoms (from mild to severe), the duration (from months to years), the previous history (unique, persistent or recurrent episode), and the suspected aetiology (social, psychological and biological factors).

Even though the diagnostic criteria are suitable for the clinical practice, there are controversies regarding the categorical or dimensional features of the depressive disorders (Andrews et al., 2007; Fried and Nesse, 2015; Wakefield and Schmitz, 2013). Depressive disorders exist on dimensions of greater or lesser severity, persistence or recurrence over time, and subthreshold depressive symptomatology (sDS) could be a stage or phase of illness along a dimensional longitudinal continuum of symptomatic severity of a specific depressive

disorder. For example, current evidence suggest that there is a continuum of genetic liability for subthreshold and major depression (Corfield et al., 2017), and a similar impairment of the resting-state functional connectivity of the cognitive control network has been described for both conditions (Hwang et al., 2015). Likewise, people with sDS have an increased risk of major depressive episode (MDE) (Lee et al., 2019) and worse health outcomes, including disability, worse quality of life and increased health services use (Rodríguez et al., 2012). However, it is still in discussion whether the subthreshold depressive symptomatology could be an independent diagnostic entity from the major depressive episode, at least for advanced age groups (Biella et al., 2019).

Community-based epidemiological studies of depressive disorders have used various approaches to identify valid cases, including structured diagnostic interview techniques to check specific clinical diagnostic criteria or the cutoff scores on validated questionnaires based on the number and severity of symptoms. Depending on the case-definition method, the frequency estimates of prevalence, incidence or persistence may vary. For instance, it has been found that the prevalence of the MDE declines with age (Collaborators, 2018), but the prevalence of sDS increases with advancing age (Meeks et al., 2011). Regardless of the case-definition approach, either categorical or dimensional, the epidemiological evidence shows substantial gender differences in depressive disorders across the full lifespan between men and women (Kuehner, 2017). Findings from diverse sociocultural settings have quantified a gender gap showing that women are about twice as likely as men to develop depressive disorders during their lifetime, starting from the late adolescence and maintained up to advanced ages (Bromet et al., 2011; Kessler and Bromet, 2013; Lin et al., 2021; Van de Velde et al., 2010). The reasons for this gender gap comprises biological vulnerability (genetic factors including gene-environment interactions, hormones and physiological stress response), psychological susceptibility (personality traits and coping styles), and

environmental determinants at micro level (early adversity, interpersonal violence, life events) and macro level (societal structural gender inequities) (Kuehner, 2017).

Personality traits are characterized by enduring patterns of thoughts, feelings and behaviors, which are formed through childhood and increase in consistency throughout the lifespan (Corr and Matthews, 2009) . One of the most common conceptualization of personality is the Five-Factor Model, describing agreeableness, conscientiousness, extraversion, neuroticism and openness to experience as the fundamental traits that characterize the personality (McCrae and Costa, 2003). Several systematic reviews, meta-analyses and cross-cultural studies have described moderately-sized differences between men and women regarding the personality traits distribution (Hyde, 2014). The association between personality characteristics and depressive disorders has been extensively explored and a variety of models have been proposed. These models include common causes of personality characteristics and depressive disorders (common cause model), personality as a precursor of depressive disorders (precursor model), personality and depressive disorders forming a continuous spectrum (continuum model), personality as a vulnerability factor (predisposition model), personality a cause of pathoplastic effects on depression (pathoplasticity model), depression as a modifier of personality traits concurrently (concomitant model) or over the long-term (scar model) (Klein et al., 2011). An important meta-analysis including ten community-based cohort studies with 117,899 participants concluded that extraversion, neuroticism, and conscientiousness were are associated with depressive symptoms, which, in turn, appeared to be associated with a future temporary or persistent personality change (Hakulinen et al., 2015). However, this study did not find differences between women and men regarding the baseline cross-sectional associations between personality traits and depressive symptoms.

According to the predisposition model, the greater level of neuroticism documented in women, that leads to a tendency for experiencing negative emotional states and a higher sensitivity to stress, has been suggested as a potential mechanism for the increased vulnerability to depression (Yoon et al., 2013). It has been proposed that the differential association of these personality traits between men and women is mediated by perceived stress (Kim et al., 2016). However, there is little evidence regarding gender differences of the other personality traits and the prevalence, incidence and persistence or recurrence of depressive disorders among adults in the general population.

Since data from large prospective population-based studies on the course of depressive disorders are limited, we aimed 1) to report estimates of sDS and probable MDE prevalence and course, 2) to quantify the gender gap between age groups, and 3) to explore the association of personality traits with the prevalence and course of depressive disorders between men and women. Considering previous findings, we hypothesized, that 1) sDS prevalence and incidence would be greater than estimates for probable MDE; 2) persistence-recurrence rates would be higher for probable MDE; 3) women would have higher estimates than men for all age groups; and 4) the association between personality traits and depressive disorders frequency and course would be strongest for women and more intense for the sDS.

2. Methods

2.1 Study design, population and sample

This is a cohort study that used data from the fourth and fifth waves of the Regicor Study, a prospective and population-based study about cardiovascular risk factors (http://www.regicor.org). The Regicor Study includes three population-based samples of inhabitants of the province of Girona (Catalonia, Spain) recruited in 1995, 2000 and 2005. Additional details of sampling procedures can be found elsewhere (Grau et al., 2007). In our

analyses, we used the data from participants belonging to the three Regicor cohorts who were examined in wave 4 during the period between September 1st 2008 and January 28th 2013, and reexamined in wave 5 between May 5th 2017 and October 14th 2019. The median time between wave 4 and wave 5 examinations was 6.9 years (interquartile range=2.29). The Figure 1 reports the study participation flow-chart for both waves.

2.2 Data collection and instruments

In both waves the study team performed the data collection in the Primary Care consultation offices of the towns of the study participants. They received the participants after being informed by postal mail and having received a telephone call to schedule a visit. The examination was standardized and all the participants were examined following the same order. The clinical interview included sociodemographic information and the completion of health questionnaires. Gender was self-reported by the study participants. Civil status was recorded as married or other situation. Education level was recorded according to the years of education of the participants: up to 8 years of education (Low level), between 8 and 12 years (Average level) and more than 12 years (High level). Physical function status was measured according to the question "*Which of the following statements describes your ability to make physical efforts*?", and rated on a 3-point scale (1=no limitation to make efforts; 2= moderate limitation to make efforts, and 3= important limitation to make efforts). The number of self-referred cardiovascular risk factors was registered (hypertension, diabetes, and dyslipidemia). Body mass index was calculated as weight divided by squared height. Weight and height were measured using a precision scale of easy calibration, with participants in underwear and barefoot.

We used the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001) to assess depressive symptomatology in both waves. The PHQ-9 is a common questionnaire used as depression screening tool in primary care and other medical settings with a cutoff ≥10, which

has a sensitivity and specificity of 0.88 and 0.85, respectively, to detect a probable MDE (Levis et al., 2019). The PHQ-9 includes nine questions to quantify the frequency (during the previous two weeks) of nine symptoms derived from diagnostic criteria for a major depressive episode of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (American Psychiatric Association, 2000). The PHQ-9 score can range between 0 and 27, with higher scores indicating higher severity. PHQ-9 scores between 5 and 9 are defined as mild depressive symptoms that require watchful waiting and were used to categorize sDS. Depression history was assessed after administering the PHQ-9 questionnaire according to the following question included in the Mini-Neuropsychiatric (Sheehan et al., 1998): "*During your lifetime, did you have other episodes of two weeks or more when you felt depressed or uninterested in most things, and had most of the problems we just talked about?*" . Personality traits were assessed with the 10-item version of the Big Five Inventory (BFI-10) (Rammstedt and John, 2007), which measures agreeableness, conscientiousness, extraversion, neuroticism and openness to experience. This brief questionnaire, that has demonstrate appropriate reliability and validity indicators, includes two items for each trait and uses a 5-point Likert scale (1= strongly disagree to 5=strongly agree). The score for each personality trait ranges between 2 and 10 points, and higher scores indicate higher levels of the trait. All the clinical examinations and questionnaires were performed and administered by trained nurses. The study protocol was approved by the Ethics Committee of the IDIAP Jordi Gol, and all the study participants signed an informed consent.

2.3 Statistical analysis

A descriptive analysis of the study variables was carried out using absolute and relative frequencies for qualitative variables, and central tendency and dispersion measures for quantitative variables.

Two-week point prevalence of depressive disorders (sDS and probable MDE) was computed for wave 4 and incidence and persistence-recurrence density rates of depressive symptomatology were calculated for wave 5. The person-years method of estimating incidence density rates was used (Breslow N, 1994). Person-years were defined as the time in years for which subjects were at risk of developing the disease during the study period. The number of person-years at risk was determined as the sum of the years of follow-up for between wave 4 and wave 5.Ninety-five percent confidence intervals (95% CIs) for prevalence, incidence and persistence-recurrence rates were calculated assuming a Poisson distribution for the number of cases within each age interval. We computed the prevalence ratio (PR) and the incidence and persistence-recurrence rate ratios (IRR and PRR) as the ratios of having prevalent, incident and persistent-recurrent depressive disorder respectively for women to the same rates for men.

Bivariate analyses were performed using t-tests to check for differences in the personality trait scores according depression outcomes (prevalence, incidence and persistence-recurrence) for both women and men. Three sex-stratified multivariate logistic regression models were adjusted to quantify the association between personality traits and the prevalence, the incidence and the persistence-recurrence of depressive disorders. We used the score of the PHQ-9 as the dependent variable (depressive episode vs. no-depression defined by the cutoff) and the personality traits scores as the independent variables. Age, educational level, civil status, the physical function limitation level, the number of cardiovascular risk factors, and the history of depression were included as covariates. Multicollinearity was assessed using the variance inflation factor (VIF) of the independent variables and the covariates. In addition, possible interactions for the prevalence, incidence and the persistence-recurrence of depressive disorders between gender and personality traits were examined by the inclusion of cross-product terms of gender with each personality trait.

Results are expressed as absolute numbers and percentages, mean or median, standard deviation or interquartile range, odd ratios or incidence ratios, and 95% CIs. Statistical test were considered to be significant with a 2-tailed *p* value <0.05. Processing and analysis of the data were performed using the statistical software STATA version 12.

3. Results

3.1 Sample description

Valid cases for this study consisted of 5,557 individuals at baseline (98.42% of the participants in the original Regicor Study wave 4 samples). The mean age was 61.65 years (SD=11.89; range=34 - 94), 53.91% were women, 77.41% were living with partner, and the educational level was high for 19.91%, average for 28.06% and low for 52.04%. Depression history was reported by 36.75%. Regarding physical function, 68.47% did not report difficulties to make efforts, 26.09% referred moderate limitations, and 5.44% severe limitations. Prevalence of hypertension, diabetes, and dyslipidemia was 53.10%, 14.58%, and 39.50% respectively while 31.58% did not have any of those cardiovascular risk factors. Regarding the personality traits assessed with the BFI-10, the mean score for agreeableness was 5.29 (SD=1.70), for conscientiousness was 6.14 (SD=1.67), for extraversion was 4.96 (SD=2.06), for neuroticism was 3.80 (SD=2.22) and for openness to experience was 5.00 (SD=1.94). Table 1 shows the participant's characteristics in wave 4 stratified by gender.

Participants in wave 5 included 3,102 individuals, which represented 71.22% of the valid candidates. The reasons for missing follow-up were the absence of interest to participate (40.20%), unable to contact (31.41%), deceased (18.47%), and being hospitalized or having a severe disease (9.92%). Study attrition analysis showed that non-participants were characterized for being older (65.47 years vs. 58.62 years; $p<0.001$), with a higher proportion of non-living with partner (26.38% vs. 19.61%; $p<0.001$), low education level

(60.38% vs. 45.48%; p<0.001), and higher frequency of moderate or severe difficulties to make efforts (41.34% vs. 23.85%; p <0.001). History of depression was similar between non-participants and participants in wave 5 (36.33% vs. 37.07%; p=0.585), but the prevalence of sDS and probable MDE in wave 4 was higher for non-participants in wave 5 (21.59% vs. 18.31%; p=0.004 and 10.02% vs. 7.38%; p <0.001). Non-participants in both waves scored slightly lower in the extraversion trait of personality (4.42±1.92 vs. 4.95±2.01; p =0.017), and there were no differences on the other four personality traits among both groups.

3.2 Frequency and course of depressive disorders

The prevalence of sDS and probable MDE was 18.04% (95% CI=17.04 – 19.08) and 8.54% (95% CI=7.82 – 9.31) respectively. Women had an increased risk for the sDS (PR=2.03; 95%CI=1.75 – 2.35) and probable MDE (PR=3.56; 95% CI=2.83 – 4.52). Table 2 reports the prevalence rates stratified by gender and age groups. The incidence rate of sDS was 14.30 cases per 1,000 person-years (95% CI=12.49 – 16.31) and for probable MDE was 4.34 person-years (95% CI=3.46 – 5.36). Women had an increased risk for both sDS (IRR=1.74; 95% CI=1.32 – 2.31) and probable MDE (IRR=3.42; 95% CI=2.00 – 6.11). Table 3 reports the incidence rates stratified by gender and age groups. Regarding the persistence-recurrence, the density rate for sDS was 35.04 cases per 1,000 person-years (95% CI=29.00 – 41.96) and for probable MDE was 28.8 cases per 1,000 person-years (95% CI=20.49 – 38.14). The persistence-recurrence of sDS and the probable MDE was higher for women (PRR=2.10; 95% CI=1.33- 3.44 and PRR=3.66; 95% CI=1.16 – 18.51). Table 4 reports the persistence-recurrence rates stratified by gender and age groups.

3.3 Personality determinants of depressive symptomatology frequency and course

The bivariate analyses of the personality traits score according to the three examined depression outcomes (prevalence, incidence and persistence-recurrence) showed differences in men and women both in the sDS and the probable MDE (Supplemental tables 1 and 2).

None of the adjusted multivariate logistic regression models were suggestive to be affected by collinearity and all VIF values were below 1.35. Table 5 shows the results of the adjusted models for the prevalence, incidence and persistence-recurrence of sDS and probable MDE stratified by gender. Neuroticism was the personality trait that was significantly associated with all the frequency estimates of sDS in both men and women. Conscientiousness was related with prevalence and incidence only in men, and was significantly associated with persistence-recurrence of sDS only in women. Openness increased the risk of prevalent sDS in women and the risk of persistence-recurrence in men. Higher extraversion was a protective factor for incident sDS in men. Regarding the probable MDE, neuroticism was related to the prevalence for both men and women and having an elevated conscientiousness was a protective factor. An increased neuroticism was related to the incidence and persistence-recurrence in women and agreeableness appeared to be related with a reduction of the persistence-recurrence only in men. There were significant interactions between gender and conscientiousness for the incidence of sDS (OR=1.40; 95% CI=1.18 – 1.65) and neuroticism for the incidence (1.21; 95% CI=1.08 – 1.53) and persistence-recurrence of probable MDE (OR=1.42; 95% CI=1.17 – 2.09) (Supplemental table 1).

4. Discussion

We aimed to assess the frequency and course of sDS and probable MDE by age groups among men and women, and to explore its association with personality traits from a population-based perspective. As we expected, sDS prevalence and incidence rates were higher than those for a probable MDE, however we did not find differences regarding the persistence-recurrence rate. Women had a higher prevalence for both depressive disorders in all age groups, and incidence rates were also higher for women up to 74 years old. The

gender gap was more important for the prevalence and incidence of the probable MDE than for the sDS, but we found a similar gender gap regarding the persistence-recurrence of both conditions. Likewise, we identified a differential association between the personality traits and the frequency and course of depressive disorders among men and women.

For sDS our overall prevalence of 18.04% was within the high boundary of the range reported by a systematic review of 17 community-based studies of older adults (4.0% to 22.9%) (Meeks et al., 2011), and did not vary among age groups in men but did increased with age in women. There was a gender gap of 10.95% and the differences increased with age, ranging from 1.78 times higher in women younger than 55 years compared with men to 2.53 times for those aged 75 years and above. Similarly, a population-based study of participants aged 70 to 74 years old in Italy identified a gender gap of the sDS of 12.64%, being 3.09 times higher in women (Vaccaro et al., 2017). Data from the United Kingdom sample of the second edition of the European Health Interview Survey, that used the PHQ-8 to determine the prevalence of mild depressive symptoms, reported a global difference of 3.60% between men and women aged 16 years and over, being higher for the age ranges between 16 to 29 years (6.70%) and 60 to 74 years (4.20%) (Arias de la Torre et al., 2021). Our results showed that the prevalence of probable MDE slightly increased with age for men and was similar for all age groups in women. Although the overall prevalence difference between men and women was 8.68%, the gender gap tended to decrease in those aged 75 years and over (6.72%). These results are in consonance with those reported by the European Health Interview Survey for the Spanish population (Arias-De La Torre et al., 2018), even though the gender gap was higher in our study, probably due to differences in the age of the populations. It should be noted that the gender gap was found larger for the probable MDE, being 3.56 times higher than the sDS ratio (2.03 times higher). This result is similar to a comparable population-based study with elder population aged 60 years or older from Korea,

which reported that the sDS was 1.6 times more prevalent in women than in men, and the prevalence for the MDE was 2.2 times higher in women (Oh et al., 2020).

Our incidence estimate of 14.30 episodes of sDS per 1000 person years was slightly lower than those presented by other studies (21.7 per 1000 person-years in Korea (Oh et al., 2020) and 19.3 per 1000 person-years in The Netherlands (Luijendijk et al., 2008)). The incidence density rate was higher for women up to the 65 to 74 year group, and similar between men and women for the group aged 75 years and over. For the probable MDE, the incidence rate was higher in women for the group under 55 years and for the 65 to 74 years group. The lack of differences found in the incidence rates in both conditions between men and women aged 75 years and over is consistent with previous research suggesting that the influence of other variables such as psychosocial factors and physical health status reduces the gender gap in advanced ages (Büchtemann et al., 2012; Sutin et al., 2013). Again, the gender gap was more important for the incidence of probable MDE, being 3.42 times higher in women than in men while sDS was only 1.74 times higher in women. These findings are in disagreement with results from Korea in older individuals aged 60 years and over, which indicated that the gender gap for incidence estimates was two times higher in women for sDS than for the probable MDE (Oh et al., 2020). A possible explanation for this difference may be the variability in the follow-up periods between studies.

The persistence-recurrence of sDS and probable MDE among age groups should be interpreted cautiously because of the low precision due to a limited sample size that compromised our rates estimation. Our density rates were higher than those previously reported for depressive symptoms (19.3 per 1000 person-years) and depressive syndromes (11.6 per 1000 person-years) in a community-dwelling Dutch cohort aged 56 years and over (Luijendijk et al., 2008). However, the gap between men and women was statistically significant for both conditions. Previous research have reported that 40.5% of older adults

participating in the Longitudinal Aging Study Amsterdam remained with sDS after 6 years of follow-up and the gender gap was 1.22 higher between in women (Jeuring et al., 2016).

The gender analysis of the association between the personality traits and the frequency and course of the sDS and the probable MDE revealed interesting differential results. First of all, as hypothesized, we found a greater number of associations between personality traits and sDS than those found with the probable MDE. Second, personality traits showed a slightly stronger association with sDS frequency and course in men. Third, personality traits were strongly associated to the probable MDE course in women. Higher neuroticism was related with the prevalence, incidence and persistence-recurrence of sDS similarly in women and men. This result could be interpreted as a consequence of the use of maladaptive emotion regulation strategies when coping with stress of individuals with higher neuroticism that lead to the emergence and/or persistence-recurrence of depressive symptoms in both ~~in~~ men and women (Muris et al., 2005). Neuroticism was associated with the probable MDE prevalence in both genders, while the effect of neuroticism in the incidence and persistence-recurrence of the probable MDE was only present in women. Our results, supported by the interactions found between gender and neuroticism, point to a neuroticism-related vulnerability for the incidence or persistence-recurrence of a depressive episode only in women. This finding is consistent with previous research that has demonstrated that the relation between neuroticism and the risk of major depression is due to the effect of genetic factors that predispose to both neuroticism and major depression (Fanous et al., 2007; Kendler et al., 1993). In this sense, it has been described an association of neuroticism with resting-state regional cerebral blood-flow activity in the hippocampus and midbrain in women but not in men, and neuroticism predicted incident depressive symptomatology through greater activity of these regions implicated in emotional processing and regulation, suggesting one neural mechanism between neuroticism and depression only in women (Sutin

et al., 2010). Likewise, high conscientiousness had a differential effect among men and women. In men, a low score on this personality trait was associated with the prevalence and incidence of sDS and the prevalence of probable MDE. In women, low values of this trait were associated with the prevalence and incidence of probable MDE and the persistence-recurrence of sDS. Previous research has identified that high conscientiousness is associated with more effective coping strategies that prevent from negative life events and stressful experiences and reduce the risk of depression (Weiss et al., 2009). The interaction found between gender and conscientiousness for the incidence of sDS suggest a greater protective effect of this personality trait in men. Furthermore, the relationship with persistence-recurrence is in agreement with previous findings that have identified higher levels of conscientiousness associated with help-seeking in persons with a diagnosis of major depression (Schomerus et al., 2013) . In addition, we found a differential pattern of association regarding the remaining personality traits between men and women. Specifically, openness was associated with increased odds of prevalent sDS in women and of persistence-recurrence in men, and agreeableness and extraversion were related with a reduced risk of the incidence of sDS and the persistence-recurrence of probable MDE respectively only in men. Previous research has reported contradictory results regarding the association of these personality traits with depressive disorders. Openness is a personality trait related with a tendency to be open to exploring new situations and may foster an approach orientation to novel stressors that may increase the risk to develop depressive symptoms as a reaction to negative events (Khoo and Simms, 2018; Wolfenstein and Trull, 1997). Low extraversion and agreeableness have been associated with the onset and course of depressive disorders in clinical samples, but community-based studies have reported mixed results (Kendler et al., 2006; Rosellini and Brown, 2011).

Our results are supported by a number of strengths, including a large population-based sample size and a long-term prospective follow-up of 6.9 years on average. However, there should be interpreted keeping in mind several potentially important methodological limitations and because differences in methods and populations between studies make comparisons of results difficult to interpret. First, although the participation rate at follow-up reached 70%, the attrition analysis revealed a higher proportion of individuals with depressive symptoms at baseline that did not participate at follow-up. In this sense, the generalization of our results is restricted, and persistence-recurrence rates obtained in this study may be underestimated. Second, we used a self-report depression questionnaire for which valid cut-off points for probable MDE have been established (Costantini et al., 2021). However, we could not rule out an information bias regarding the categorical definition of the MDE. Third, depression in most patients often has a long-term course with relapsing-remitting episodes and the risk of recurrence and persistence of depressive symptoms is greater after a first episode and increases with following episodes. Although we could adjust the analyses for lifetime depression history, we were not able to distinguish between persistent and recurrent episodes due to a recall bias risk nor brief depressive episodes because the assessments were performed in two single points during a 4- to 10- year interval. Fourth, because detailed treatment data with antidepressive drugs during the follow-up were lacking, we could not adjust for this important covariate. Fifth, since this was a large community-based longitudinal study, the measure of the personality traits was based in a brief questionnaire which reduced the reliability of the measurement. Sixth, we were able to adjust for multiple potential confounders such as sociodemographic and health-related factors, however, residual confusion could not be ruled out because relevant variables such as perceived stress were not measured.

In summary, the results of this study suggest an elevated prevalence and incidence of sDS in the general population, a major gender gap regarding the probable MDE, and similar rates of persistence-recurrence among both depressive disorders. Moreover, our findings corroborate the robust cross-sectional and longitudinal relationship of personality traits such as neuroticism and conscientiousness with depressive disorders in women, and suggest a significant role of the personality traits regarding the prevalence and course of sDS in men. Further studies are needed to investigate mediating pathways differences between personality traits and depressive disorders that could help to design public health programs focused on the prevention or treatment of depressive disorders considering a gender-specific approach.

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CRediT authorship contribution statement

Domènec Serrano-Sarbosa: Writing original draft, review and editing

Ruth Martí-Lluch: Writing, review and editing, Project administration

Mérida Cárdenas: Conceptualization, Writing, review and editing,

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Declaration of Competing Interest

None of the authors have any financial interest, patents, company holdings, or stock to disclose related to this project.

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Table 1. Characteristics of the study sample at baseline stratified by gender (n=5,557)

	Men	**Women**
Age group, n (%)		
<=54	832 (32.49)	1,002 (33.44)
55 to 64	724 (28.27)	852 (28.44)
65 to 74	533 (21.59)	668 (22.30)
75+	452 (17.65)	474 (15.82)
Education level, n (%)		
High	559 (22.06)	535 (18.06)
Average	701 (27.66)	841 (28.39)
Low	1,274 (50.28)	1,586 (53.54)
Marital status, n (%)		
Living with partner	2,196 (86.25)	2,080 (69.85)
Other	350 (13.75)	898 (30.15)
Self-reported depression history, n (%)	577 (24.19)	1,333 (47.40)
Physical function, n (%)		
No limitation	1,923 (75.09)	1,862 (62.32)
Moderate limitation	536 (20.93)	921 (30.82)
Important limitations	102 (3.98)	205 (6,86)
Number of CVRF, median (IQR)	1.00 (0 – 3)	1.00 (0 – 3)
BMI, mean (SD)**	27.77 (3.96)	27.09 (5.03)
Extraversion, mean (SD)**	4.76 (2.06)	5.12 (2.04)
Agreeableness, mean (SD)	5.29 (1.70)	5.30 (1.69)
Conscientiousness, mean (SD)*	6.08 (1.67)	6.20 (1.68)
Neuroticism, mean (SD)**	3.37 (2.14)	4.17 (2.22)
Openness, mean (SD)*	4.91 (1.90)	5.08 (1.97)

CVRF: cardiovascular risk factors; IQR: interquartile range; SD: standard deviation; BMI: body mass index
* p <0.05; ** p <0.001

Table 2. Prevalence (%) and 95% CI for sDS and probable MDE stratified by gender and prevalence ratio

sDS			
Age groups	**Men**	**Women**	**Prevalence ratio**
<=54	14.81 (12.41 – 17.46)	23.69 (20-91 – 26.64)	**1.78 (1.38 – 2.31)**
55 to 64	14.10 (11.61 – 16.89)	21.59 (18.68 – 24.73)	**1.67 (1.26 – 2.23)**
65 to 74	12.52 (9.83 – 15.62)	27.57 (23.97 – 31.38)	**2.65 (1.92 – 3.69)**
75 +	14.72 (11.49 – 18.43)	30.46 (26.07 – 35.12)	**2.53 (1.78 – 3.62)**
Total	14.09 (12.74 – 15.53)	25.04 (23.38 – 26.74)	**2.03 (1.75 – 2.35)**
Probable MDE			
<=54	4.21 (2.94 – 5.80)	12.38 (10.39 – 14.57)	**3.21 (2.16 – 4.88)**
55 to 64	3.04 (1.91 – 4.56)	13.03 (10.84 – 15.47)	**4.77 (2.96 – 8.01)**
65 to 74	3.25 (1.94 – 5.09)	12.57 (10.15 – 15.33)	**4.27 (2.50 – 7.65)**
75 +	5.31 (3.43 – 7.79)	12.03 (9.23 – 15-29)	**2.43 (1.45 – 4.18)**
Total	3.87 (3.15 – 4.68)	12.55 (11.38 – 13.78)	**3.56 (2.83 – 4.52)**

$p \leq 0.05$ shown in bold

Table 3. Incidence (cases per 1,000 person-years) and 95% CI for sDS and probable MDE stratified by gender and incidence rate ratio

sDS			
Age groups	**Men**	**Women**	**Incidence rate ratio**
<=54	10.11 (5.53 – 16.09)	22.60 (15.36 – 32.09)	**2.23 (1.15 – 4.54)**
55 to 64	7.27 (4.31 – 11.50)	16.28 (11.46 – 22.44)	**2.23 (1.24 – 4.17)**
65 to 74	6.34 (3.69 – 10.16)	16.36 (11.74 – 22.20)	**2.57 (1.43 – 4.84)**
75 +	23.21 (16.25 – 32.13)	21.14 (14.27 – 30.20)	0.91 (0.54 – 1.52)
Total	10.51 (8.39 – 12.99)	18.36 (15.44 – 21.68)	**1.74 (1.32 – 2.31)**
Probable MDE			
<=54	0.60 (<0.1 – 3.37)	7.02 (3.74 – 12.01)	**5.60 (1.74 –9.30)**
55 to 64	2.43 (0.97 – 5.00)	5.28 (3.02 – 8.58)	2.17 (0.84 – 16.24)
65 to 74	1.60 (0.52 – 3.74)	6.64 (4.16 – 10.06)	**4.13 (1.52 – 13.99)**
75 +	2.88 (0.93 – 6.72)	7.92 (4.53 – 12.87)	2.74 (0.96 – 9.59)
Total	1.91 (1.13 – 3.03)	6.56 (5.08 – 8.33)	**3.42 (2.00 – 6.11)**

$p \leq 0.05$ shown in bold

Table 4. Persistence-recurrence (cases per 1,000 person-years) and 95% CI for sDS and probable MDE stratified by gender and persistence-recurrence rate ratio

sDS			
Age groups	**Men**	**Women**	**Persistence-recurrence rate ratio**
<=54	23.0 (8.43 – 50.22)	35.6 (19.57 – 60.01)	1.55 (0.56 – 4.92)
55 to 64	14.0 (4.54 – 32.68)	44.8 (30.06 – 64.47)	**3.20 (1.22 -10.60)**
65 to 74	20.0 (8.63 – 39.4)	48.0 (32.86 – 67.82)	**2.40 (1.08 – 6.04)**
75 +	31.8 (10.34 – 74.32)	39.0 (23.53 – 61.05)	1.22 (0.44 – 4.19)
Total	20.41 (13.07 – 30.37)	42.88 (34.65 – 52.48)	**2.10 (1.33 – 3.44)**
Probable MDE			
<=54	9.58 (2.43 – 53.57)	51.48 (24.71 – 94.79)	5.37 (0.76 – 23.06)
55 to 64	8.06 (0.20 – 44.93)	28.71 (14.33 – 51.38)	3.57 (0.51 – 15.73)
65 to 74	16.12 (0.40 – 89.86)	39.20 (22.41 – 63.68)	2.43 (0.37 – 10.13)
75 +	0.00 (0.00 – 102.4) *	14.58 (30.17 – 42.76)	--
Total	9.16 (1.89 – 26.78)	33.58 (23.99 – 45.73)	**3.66 (1.16 -18.51)**

(*) one-sided, 97.5% confidence interval; $p \leq 0.05$ shown in bold

Table 5. Multivariate logistic regression results (adjusted odds ratios*) of the association between personality traits and the prevalence and course of sDS and probable MDE

Prevalence	**sDS**		**Probable MDE**	
	Men	**Women**	**Men**	**Women**
Extraversion	0.99 (0.91 – 1.09)	1,01 (0.93 – 1.07)	1.02 (0.88 – 1.19)	0.99 (0.90 – 1.08)
Agreeableness	1.04 (0.94 – 1.16)	0.98 (0.91 – 1.06)	1.09 (0.90 – 1.32)	1.03 (0.92 – (1.14)
Conscientiousness	**0.88 (0.79 – 0.98)**	0.97 (0.89 – 1.05)	**0.80 (0.67 – 0.96)**	**0.86 (0.78 – 0.95)**
Neuroticism	**1.16 (1.06 – 1.26)**	**1.09 (1.02 – 1.16)**	**1.19 (1.02 – 1.39)**	**1.20 (1.10 – 1.30)**
Openness	1.03 (0.93 – 1.13)	**1.07 (1.01 -1.15)**	1.02 (0.86 – 1.21)	0.98 (0.89 – 1.08)
Incidence				
Extraversion	**0.88 (0.77 – 0.98)**	0.90 (0.82 – 1.01)	0.86 (0.62 – 1.28)	0.92 (0.77 – 1.09)
Agreeableness	0.95 (0.82 – 1.11)	1.01 (0.90 – 1.13)	1.24 (0.79 – 1.09)	1.24 (0.79 – 1.65)
Conscientiousness	**0.70 (0.61 – 0.81)**	0.96 (0.85 – 1.08)	0.73 (0.51 – 1.05)	**0.76 (0.63 – 0.92)**
Neuroticism	**1.28 (1.14 – 1.44)**	**1.18 (1.07 – 1.29)**	1.19 (0.85 – 1.66)	**1.34 (1.13 – 1.59)**
Openness	1.02 (0.89 – 1.17)	0.99 (0.89 – 1.10)	1.08 (0.75 – 1.54)	1.08 (0.90 -1.31)
Persistence-recurrence				
Extraversion	0.99 (0.78 – 1.27)	0.98 (0.78 – 1.27)	0.70 (0.34 – 1.42)	0.99 (0.78 – 1.25)
Agreeableness	1.08 (0.75 – 1.57)	1.06 (0.89 – 1.25)	**0.57 (0.36 – 0.84)**	1.06 (0.82 – 1.37)
Conscientiousness	0.88 (0.62 – 1.23)	**0.84 (0.72 – 0.98)**	1.23 (0.65 – 1.82)	0.81 (0.64 – 1.03)
Neuroticism	**1.49 (1.10 – 1.98)**	**1.28 (1.11 – 1.48)**	0.72 (0.44 – 1.18)	**1.35 (1.05 – 1.74)**
Openness	**1.41 (1.02 – 1.97)**	1.03 (0.88 – 1.20)	0.80 (0.75 – 1.23)	0.96 (0.85 – 1.33)

(*) adjusted for age, education level, marital status, depression history, physical function, number of cardiovascular risk factors and body mass index; $p \leq 0.05$ shown in bold

Figure 1 Inclusion and follow-up of the participants