

Association of depressive symptoms and socioeconomic status in determination of blood pressure levels and hypertension: The CONSTANCES population based study

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1 2	Association of depressive symptoms and socioeconomic status in determination of blood pressure levels and hypertension: the CONSTANCES population based study
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49 ABSTRACT

- 50 **Background:** Inconsistent association between depression and hypertension has been 51 highlighted. The association of depression with blood pressure (BP) might depend upon 52 socioeconomic status (SES), but evidence remains weak.
- 53 **Objectives:** This study aimed to examine how the associations between depressive symptoms
- 54 and BP levels and hypertension and then, according to SES variables (education, income,
- 55 occupational status).
- 56 Methods: Among 66,478 volunteers of the French CONSTANCES cohort (31,093 men;
- 57 mean age (standard deviation): 47.8 (12.9) years), depressive symptoms were assessed with
- 58 the Center of Epidemiologic Studies Depression scale (CES-D). Overall associations between
- 59 depressive symptoms and BP and hypertension were estimated using regressions and by
- 60 stratifying on SES.
- 61 Results: SES were associated with BP in both genders. CES-D score was negatively 62 associated with systolic BP (SBP) in women (b=-0.62 95%CI [-1.03; -0.21] and in men (b=-63 1.03 95%CI [-1.45; -0.61]) but not with diastolic BP (DBP) in both genders. In women, the 64 decrease in SBP and DBP was more pronounced as educational level increases (p for 65 interaction: 0.012 and 0.013, respectively). In men, few interactions were observed between 66 CES-D score and SES factors for BP levels. The association between CES-D score and 67 hypertension was significant for men, OR=0.86, 95%CI [0.80; 0.93] but not for women, 68 OR=1.03, 95%CI [0.96; 1.10]. No interactions were observed between CES-D score and SES 69 for hypertension.
- Conclusion: Gender differences were observed for considering depressive symptoms
 according to SES factors for BP variation and hypertension. In women, educational level was
 the SES factor which has the main modifying effect on this association.
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- 75 Keywords: depressive symptoms, blood pressure, hypertension, CES-D, socioeconomic
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83 INTRODUCTION

84 Hypertension is a major risk factor for cardiovascular diseases (Stokes et al., 1989) and could 85 be more prevalent in persons with psychopathology (Carroll et al., 2001; Matthews et al., 86 2004). The World Mental Health Survey estimates that depression affects 350 million people 87 worldwide (World Health Organization, 2012). Depression became the second global disease 88 burden after ischemic heart disease since 2020. Recent large population studies have shown 89 that psychiatric disorders were associated with hypertension (Sandström et al., 2016) and 90 some studies have suggested that blood pressure (BP) may explain a part of the well-known 91 association between psychopathology and cardiovascular diseases (CVD) (Scuteri, 2008). 92 Nevertheless, some studies which have investigated the association between depression 93 symptoms and BP have reported positive (Cuffee et al., 2014; Jackson et al., 2016; Maatouk 94 et al., 2016), negative (Hildrum et al., 2011; Park et al., 2018; Wiernik et al., 2018) or 95 nonexistent associations (Grimsrud et al., 2009; Yan et al., 2003). The meta-analysis of Meng 96 et al. has shown that depression is associated with increased risk of hypertension incidence 97 suggesting that it is an independent risk factor of hypertension (Meng et al., 2012). However, 98 studies have observed a significant and negative association between levels of depressive 99 symptoms and BP among large populations (Hildrum et al., 2011; Licht et al., 2009) and 100 among elderly people (Liu et al., 2020). Globally, transversal studies have suggested that 101 depression was negatively associated with blood pressure whereas longitudinal studies have 102 shown a positive association (Nabi et al., 2011).

103 The literature has accumulated some evaluating effects of psychosocial factors with 104 depression (Michal et al., 2013). Depressive symptoms varied considerably according to the 105 role of contextual factors, including economic, environmental and demographic factors 106 (Kessler et al., 2009). Socioeconomic status (SES) has come into focus as crucial determinant 107 of depressive symptoms (Dinardo et al., 2014), showing that low SES-individuals presented 108 higher odds of being depressed (V et al., 2007).

In parallel, many psychological factors, including depression, have been associated with increased risk of CVD, as has low SES (Havranek et al., 2015). Currently, the notion of social risk factors has been suggested to interact with psychological risk factors as etiology of CVD (Lemogne et al., 2017; Wiernik et al., 2018). Different levels of SES indicators (e.g., education, occupational status, income) could modify the effects of psychological factors in incidence of CVD. Psychosocial changes have brought transformations in social organizations.

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The relationship between depressive symptoms and blood pressure has been investigated in many epidemiological studies (Jani et al., 2016; Kim et al., 2010). In parallel, hypertension was mainly associated with SES factors (Cherfan et al., 2019; Leng et al., 2015). Nevertheless, at our knowledge, no study has focused on the interactions between depressive symptoms, hypertension and SES. We hypothesized that depressive symptoms may have different associations with BP and hypertension according to the different levels of SES factors.

124 Main part of the studies investigating these associations are not representative of general 125 population or country, and standardized measurements or definitions for SES and depression 126 were lacking (Freeman et al., 2016). The CONSTANCES cohort is a large prospective 127 population based cohort designed as a research infrastructure and as a large random sample of 128 the French adult population (Goldberg et al., 2017). The main strengths of the 129 CONSTANCES cohort is that it provides standardized measurements for blood pressure, and 130 standardized definitions of a broad scope of health conditions and determinants, occupational 131 factors and outcomes, including participants living and working in either urban or rural 132 neighborhoods and diversified in terms of jobs of socioeconomic status. In the 133 CONSTANCES cohort, depressive symptoms were evaluated with de CES-D score, which 134 was a self-report scale designed to measure depressive symptomatology in the general 135 population. Validity was established by pat terms of correlations with other self-report 136 measures, by correlations with clinical ratings of depression, and by relationships with other 137 variables which support its construct validity (Radloff, 1977; Wiernik et al., 2018).

Thus, the purpose of our study was to investigate, stratified by gender, the association between depressive symptoms, estimated by the CES-D score, with blood pressure levels and hypertension. Then, we investigated the extent to which the association between depressive symptoms, estimated by the CES-D score, and BP levels and hypertension might differ according to SES variables based on the CONSTANCES population.

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144

145 **METHODS**

146 The CONSTANCES cohort

This ancillary study is a cross-sectional analysis using data from the CONSTANCES study. The general aim of CONSTANCES is to establish a large population-based cohort to contribute to the development of epidemiologic research (www.constances.fr). Details about the study design and methods have been extensively discussed (Zins et al., 2015). 151 CONSTANCES is an ongoing prospective cohort that started in 2012. Adults aged 18–69 at 152 inception were randomly selected from the National Health Insurance Fund (CNAMTS: 153 *Caisse Nationale d'Assurance Maladie des Travailleurs Salariés*) that covers salaried 154 workers, professionally active or retired and their dependents (more than 85% of the French 155 population) following a sampling scheme stratified on age, sex, socioeconomic status and 156 region of France to ensure a representative sample of the CNAMTS.

157

158 Data collection

159 At enrollment, volunteer participants completed self-administered questionnaires where 160 social, demographic, health information including personal and family history of diseases and 161 events, and lifestyle behavior characteristics were gathered. In addition, they presented to the 162 nearest of the 22-selected health-screening centers (HSCs) located throughout France, to 163 benefit from a comprehensive health examination whereby medical, clinic exams, 164 anthropometric measurements and biologic tests were performed. Furthermore, participants 165 were linked through national social and health administrative databases, through which 166 detailed information concerning health events and medical acts (medication, hospitalization) 167 were noted.

168

169 **Ethical considerations**

All the participants included in the CONSTANCES cohort have signed an informed consent
form. This research follows the tenets of the Declaration of Helsinki and was approved by the
National Data Protection Authority (No. 910486) and the Institutional Review Board of the
National Institute for Medical Research and the local Committee for Persons Protection.

174

175 **Study population**

Between February 2012 and January 2018, a total of 87,808 volunteers were recruited and linked to the French health insurance administrative database. Of them, we excluded 21,330 for missing data and not categorized variables and excluding participants with previous CV events. CV events were commonly recognize as cause of depression (Hare et al., 2014). We therefore analyzed data from 66,478 volunteers (**Figure 1**).

181

182 Hypertension and blood pressure

BP measurements were taken during the clinical examination at the HSC based on
standardized operational procedures (Ruiz et al., 2016). SBP and DBP were measured in each

arm at 2 min interval after 5 min of rest and using an automated oscillometric sphygmomanometer. The arm giving the highest SBP was considered the reference arm and a third BP measure was taken after 1 min of rest, the average of these two measurements was considered. Prevalent HTN was defined by a SBP at least 140 mmHg and/or a DBP at least 90mmHg or by individuals taking antihypertensive medications (Williams et al., 2018).

190

191 **Depressive symptoms**

192 Depressive symptoms were assessed using the validated self-administered Center of 193 Epidemiologic Studies Depression scale (CES-D) (Fuhrer and Rouillon, 1989; Radloff, 1977). 194 This 20-item questionnaire has been designed for use in community studies. The CES-D score 195 evaluates the frequency of depressive symptoms during the previous week (e.g., I felt 196 depressed, I felt everything I did was an effort, my sleep was restless). Responses range from 197 0 (hardly ever) to 3 (most of the time). The CES-D score was used as a continuous variable with taking the interval between the 25th and the 75th percentile as unit, the meaning of one-198 199 point increase in CES-D could be hard to figure out while one could more intuitively compare 200 an individual in the middle of the upper half of the CES-D score distribution with an 201 individual in the middle of the lower half.

202

203 Socioeconomic factors

Educational level was collected according to the International Standard Classification of Education (Schneider, 2013) and was then classified into three levels: Low (High school diploma or less for 13 years of education), moderate (undergraduate degree for 14–16 years of education) and high (postgraduate degree for >17 years of education). Household monthly income was categorized into: low (less than 2100 Euros per month); moderate (2100–4199); and high (at least 4200).

Occupational status was collected according to the French "Occupations and Sociooccupational Categories" [Professions et Categories Socioprofessionnelles (PCS)]
classification system (INSEE, 2003) then categorized in three broad classes: high (e.g.,
managers), moderate (e.g., clerks or first-line supervisors) and low (e.g., plant and machine
operators, cleaners).

215

216 **Drugs treatments**

217 Reimbursement of anti-hypertensive and antidepressant treatments were obtained by 218 matching the individual data of the subjects included in the study with the data from the 219 SNDS (Système national des données de santé). The names of the treatments and the 220 reimbursement date in the year preceding the health examination were collected. Antihypertensive and antidepressant medications were determined based on the Anatomical 221 222 Therapeutic Chemical (ATC) code assigned to respondents' medications. Codes indicative of 223 anti-hypertensive medications were: beta blockers (ATC codes C07, excluding C07AA07, 224 C07AA12 and C07AG02); agents acting on the renin- angiotensin system (ATC codes C09); 225 thiazide diuretics (ATC codes C03, excluding C03BA08 and C03CA01); calcium channel 226 antagonists (ATC codes C08); and miscellaneous anti-hypertensive medication (ATC codes 227 C02, excluding C02KX01). Codes indicative of antidepressant medications were ATC codes 228 N06A.

229

230 Covariates

231 Age, gender, couple status (couple life or single which included widowed or 232 separated/divorced), alcohol consumption, dietary intake, physical activity, and smoking 233 status (never, former, current smokers) were collected with a self-reported questionnaire. 234 Body mass index (BMI, kg/m²) was measured at the examination. Alcohol consumption was 235 defined in g/day of alcohol consumption. Dietary assessment was done through a validated 236 52- items food frequency questionnaire from which a DASH score was constructed based on 237 food groups described by Fung et al. (Cherfan et al., 2019; Fung et al., 2008). Physical activity 238 (PA) was assessed through three questions that considered the frequency of transferring, 239 leisure time activity and sports. A score of 0-6 was calculated and physical activity level was 240 classified as low (0-2), moderate(3-4) and high (5-6) (Merle et al., 2018). Diabetes mellitus 241 status was based on either self-reported type II diabetes, receiving anti-diabetic medication or 242 a fasting blood glucose concentration greater than or equal to 7mmol/l. Dyslipidemia was 243 defined as having hypercholesterolemia and/or hypertriglyceridemia; either recorded by the 244 health care practitioner at the HSC or by a fasting plasma total-cholesterol or triglycerides 245 level of at least 6.61mmol/l or more than 1.7mmol/l, respectively.

246

247 Statistical analysis

248 Characteristics of the study population were described as the means with standard deviation 249 (SD) for continuous variables. Categorical variables were described as numbers and 250 proportions. Comparisons between groups were performed using Student's test for continuous 251 variables. Pearson's χ^2 test was performed for categorical variables. SES factors were considered as ordinal variables. Statistical analyses were stratified on gender since
hypertension differs between men and women (Vallée et al., 2020), as well as depression
(Van de Velde et al., 2010).

Associations between depressive symptoms and blood pressure levels were examined with gender linear regression models computing coefficients (b) and their 95% confidence intervals. Association between depressive symptoms and hypertension were examined with gender logistic regression models computing odds ratio (OR) and their 95% confidence intervals. Gender models were adjusted for age, antihypertensive and antidepressant medications, BMI, DASH score, alcohol consumption, diabetes, dyslipidemia, physical activity, tobacco habits and couple status.

262 First, we performed regression models including CES-D score with all covariates in same 263 models to determine their significant impact on blood pressure and hypertension. Second, to 264 assess possible effect modification, we stratified the CES-D score and blood pressure levels 265 and hypertension analyses by each of the three SES variables, separately, and tested the 266 statistical significance of these associations. Interactions were examined by including 267 simultaneously CES-D score and one of the three SES factors and their interaction term. 268 Statistics were performed using SAS software (version 9.4; SAS Institute, Carry, NC). A p 269 value <0.05 was considered statistically significant.

270

271 **RESULTS**

A total of 66,478 volunteers without missing or not categorized data were included in the study, their characteristics are described in **Table 1**. The mean average CES-D score was 10.6 (8.7) for overall population, with a difference of 9 points between the 25th and 75th percentiles, mean CES-D score was 11.8 (9.3) for women and 9.2 (7.8) for men. 6.7% of the overall population had an antidepressant medication (8.7% for women, 4.4% for men). 28.6% of the overall population was hypertensive (20.9% for women, 37.4% for men).

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The linear regression coefficient for the association between CES-D score and SBP was negative and significant in both women b=-0.64 95%CI [-1.08; -0.21] and men b=-1.1295%CI [-1.55: -0.70]. SBP was decreased of 0.64 mmHg in women and of 1.12 mmHg in men between the 25th and the 75th percentiles of CES-D score (**Table 2**).

The linear regression coefficient for the association between CES-D score and DBP was significant neither in women b=-0.21 95%CI [-0.49; 0.07] nor in men b=-0.29 95%CI [-0.61: 0.03] (**Table 2**).

- The association between CES-D score and hypertension was significant for men, OR=0.86
 [0.80; 0.93], p<0.001 but not for women, OR=1.03 [0.96; 1.10], p=0.219 (Table 2).
- Supplementary file presented the regression coefficient and OR for all covariates ofadjustment (Supplementary file 1).
- 290 When considering CES-D score as continuous variable, after adjustment on covariates, the 291 linear regression coefficient for the association between CES-D score and SBP was negative 292 and significant in both women b=-0.04 95%CI [-0.06; -0.02], p<0.001 and men, b=-0.07 293 95%CI [-0.09; -0.05], p<0.001, but not for DBP (in women, b=-0.01 [-0.03; 0.01], p=0.401 294 and in men, b=-0.001 [-0.01; 0.01], p=0.937). In multivariate logistic regression, a significant 295 association was observed between CES-D score, as continuous variable, and hypertension 296 prevalence among men (OR=0.98 [0.97; 0.99], p<0.001), but not among women (OR=1.01 297 [0.99; 1.02], p=0.569).
- 298

Figure 2 and Figure 3 present the regression coefficients and OR and their 95%CI for the different interactions between CES-D score and SES factors for BP and hypertension according to gender. The regression coefficients correspond to the mean difference in mmHg between participants in the middle of the upper half and thus in the middle of the lower half of the CES-D score distribution.

Among women, the interactions between CES-D score and educational levels were significant for both SBP (p=0.028) and DBP (p=0.036) (**Figure 2**). When women were categorized by income level or occupational status, the interactions were not significant for both SBP and DBP.

308 The association between CES-D score and SBP, which was not significant among participants 309 with low educational level, became progressively more negative with increase educational 310 level, being significant for high educational level. The mean SBP difference between the 25th and the 75th percentiles of CES-D score was -1.09 mmHg 95%CI [-1.76; -0.42] for high 311 312 educational level (Figure 2). Likewise, the associations between CES-D score and DBP were 313 not significant among women participants with low and moderate educational level but 314 became significant for high educational level. The mean DBP difference was -0.46 mmHg 315 95%CI [-0.90; -0.02] for high educational level. Moreover, when the three factors of SES and 316 their interactions with CES-D score were simultaneously included in the women model, only 317 the interaction between CES-D score and educational level remained significant (p=0.045 for 318 SBP and p=0.022 for DBP). No significant associations and interactions were observed

between CES-D score and hypertension when women were categorized by SES factors(Figure 2).

321 Among men, none of the three analyses yielded significant interactions between SES factors 322 and SBP. Only the interaction between income level and CES-D score was significant for 323 DBP in men (p=0.010) (Figure 3). When introducing the three SES factors and their 324 interactions with CES-D score simultaneously in the SBP model in men, none of the three 325 were significant. When the three SES factors and their interactions were including 326 simultaneously in DBP men model with CES-D score, only income level interaction was 327 significant (p=0.010). No significant difference was observed among low and moderate 328 income for DBP whereas high income level showed a significant difference b=-0.67 mmHg 329 95%CI [-1.11; -0.23]. No interactions were significantly observed among men between SES 330 factors and hypertension although high income level presented the highest significant 331 association, with OR=0.79, 95%CI [0.70; 0.88] (Figure 3).

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334 Sensitivity analyses

335 When excluding from the analyses participants who received antihypertensive drugs

336 (N=7,298), CES-D score remained significantly associated with SBP among women (b=-0.62

337 95%CI [-1.07; -0.18] and among men (b=-1.23 95%CI [-1.67; -0.80] but not for DBP

- 338 analyses among women (b=-0.18 95%CI [-0.47; 0.10]) and among men (b=-0.53 95%CI [-
- **339 0.70**; **0.07**]).
- When excluding antidepressant medications (N=4,460) from the analyses, CES-D score remained significantly associated with SBP among women (b=-0.62 95%CI [-1.05; -0.19]) and among men (b=-1.20 95%CI [-1.63; -0.77]) but not for DBP analyses among women (b=-
- $0.63\ 95\%$ CI [-1.27; 0.01]) and among men (b=-0.41\ 95\%CI [-0.85; 0.03]).
- When excluding participants who received antihypertensive and/or antidepressant drugs (N=10,891) from the models, CES-D score remained significantly associated with SBP
- 346 among women (b=-0.63 95%CI [-1.07; -0.17] and among men (b=-1.31 95%CI [-1.76; -0.87]
- 347 but not for DBP among women (b=-0.20 95%CI [-0.49; 0.10]) and among men (b=-0.45 348 95%CI [-0.97; 0.07]).
- 349 When excluding participants who received antidepressant drugs (N=4,460) from hypertension
- 350 prevalence models, CES-D remained significantly associated with hypertension among men
- 351 (OR=0.85 [0.79; 0.91], but not for women (OR=1.06 [0.97; 1.15]).
- 352

353

354 **DISCUSSION**

355 Our study investigated the association between CES-D score and BP levels and hypertension 356 and then, how these associations could differ between participants according to their SES 357 levels. Our main finding is that SBP was inversely associated with CES-D score in both 358 genders. But, only men presented a negative association between CES-D score and 359 hypertension prevalence, whereas women presented no significant association. For SBP, 360 women, a significant interaction was observed between CES-D score and educational level 361 whereas in men there was no significant interaction between SES factors and CES-D score. 362 For DBP, women presented a significant interaction between CES-D score and educational 363 level whereas men presented a significant interaction between CES-D score and income level. 364 The association between CES-D score and SES factors was stronger in women with high 365 educational level for SBP and DBP and for DBP of men with high income level. No 366 interactions between CES-D score and SES factors for hypertension prevalence were 367 observed in both men and women.

368

369 Studies examining the association between depression and blood pressure and hypertension 370 yielded inconsistent results (Trudel-Fitzgerald et al., 2015) although many found a negative 371 association (Hildrum et al., 2011; Lenoir et al., 2008; Licht et al., 2009; Park et al., 2018; 372 Shah et al., 2013; Wiernik et al., 2018), so that depression was associated with lower BP in 373 cross-sectional studies. Longitudinal studies have suggested that depression may be a risk 374 factor of incident hypertension (Meng et al., 2012). Nevertheless, a follow-up conducted on 375 over 20 years in the Nord-Trondelag Health Study (HUNT) showed that low BP was 376 associated with increased prevalence of depression (Hildrum et al., 2011).

377 Several possible mechanisms for low BP in depressive symptoms have been hypothesized. 378 First, chronic low BP itself could be a cause of depressive symptoms, as fatigue and cognitive 379 impairment (Licht et al., 2009). This possibility has been shown in recent longitudinal studies, 380 although with inconsistent results, that low BP at baseline could be considered as a predictive 381 factor for depressive symptoms at follow-up but not the other way around (Paterniti et al., 382 2000), whereas other studies have found the opposite association (Hildrum et al., 2008). 383 Another explanation for the observed association does not assume causality but instead assumes a common underlying factor that independently enhances the risk for depression, as 384 385 well as the factor to conserve a low BP level. The central monoamine system could be a 386 possible cause of this factor (Head, 1992; Stahl, 2000). For instance, depression is 387 characterized by the alteration of neuropeptide Y levels, a major modulator of the 388 norepinephrine signaling. Dysregulation in neuropeptide Y could decrease the sympathetic 389 activity and BP (Karl and Herzog, 2007; Michalkiewicz et al., 2003). More studies are 390 required to unravel these underlying mechanisms implicated in the low BP of subjects with 391 depression.

392

393 In our study, we have included participants with antihypertensive and antidepressant drugs. 394 Previous studies suggested that depression could be a side effect of some antihypertensive 395 agents (Prisant et al., 1991). Hypertension awareness may also induce depressive symptoms. 396 Moreover, antidepressant drugs may increase BP (Razavi Ratki et al., 2016). Regulation of 397 the circulatory system and the autonomic vascular tone by serotonin and nitric-oxide may 398 explain this mechanism. Nevertheless, sensitive analyses were performed in our study by 399 excluding antihypertensive and antidepressant drugs and showed similar associations in our 400 overall population and groups excluding these drugs.

401

402 Our results suggest that men had a somewhat stronger association between CES-D score and 403 SBP than women. This result could be explained by many mechanisms. The prevalence of 404 depression and hypertension differ between genders. Women had higher prevalence of 405 depression and lower prevalence of hypertension than men. In the present study, SES 406 interactions were observed in women but not in men. The association between depression and 407 SES may result from several pathways that may differ to some extent between women and 408 men. For instance, alcohol use, which is a risk factor of elevated BP, may mediate this 409 association to a greater extent in men than women (Chazelle et al., 2011). Regarding, the 410 association between hypertension and SES seems to be based mainly on dietary habits and 411 especially salt intake. Individuals risk factors of hypertension could be influenced by 412 individual behaviors depending on SES status (Psaltopoulou et al., 2017). Salt consumption 413 has been considered as one of the main cause of hypertension (Gibbs et al., 2000), and its use 414 differed between gender (Vallée et al., 2019). The importance of salt consumption was mainly 415 observed among SES underprivileged groups who usually consume snacks of fast type of 416 food full of salt (Psaltopoulou et al., 2017). Moreover, psychosocial processes could be 417 additional pathways by which SES affects blood pressure. (Pickering, 1999) However, these 418 links remained unclear in literacy (Grotto et al., 2008). Epidemiologic studies have shown 419 that poor SES groups had more health problem than others (Davari et al., 2019). Another 420 study has shown that lowest education category was associated with a greater risk of 421 hypertension (Hoang et al., 2007). Moreover, the lack of knowledge of hypertension as well 422 as its predictive factors among less educated layers could result to an unawareness of 423 hypertension prevention and a misunderstanding in detrimental health dietary lifestyle 424 (Fenech et al., 2020; Grotto et al., 2008). Difference in health behaviors between men and 425 women can also affect SES status (Ryu et al., 2020). Health status varies by gender and the 426 different aspects of SES have varying degrees of impact on health status between gender. 427 Education and income levels are mainly associated with obesity, diabetes and hypertension 428 and could explain the gender differences (Zhang et al., 2017).

429

430 Strengths and Limitations

431 The main strength of our study is the design of CONSTANCES, which ensure sufficient 432 power; we adopted a population-based approach using a large nationwide randomly selected 433 sample of participants. In addition, we used standardized protocols to collect anthropometric 434 data including BP measurements; this ensures replication of data collection for all volunteers 435 regardless of when, where and by whom they are performed and adds validity to our results 436 (Ruiz et al., 2016). Furthermore, data were collected through different reliable methods, using 437 national databases and validated questionnaires. Moreover, the CONSTANCES cohort 438 randomly recruited its participants, this population may be representative of the general 439 population (Rothman et al., 2013).

However, some our study presents some limitations. socio-economic data were collected by
self-reporting. Medical history and comorbidities have been collected by self-reporting and
physician assertion during medical examination in health centers. The cross-sectional design
of the study may represent a limitation since reverse causation cannot be excluded.

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- 445

446 **CONCLUSION**

447 Our study highlighted that increased CES-D score was associated with lower SBP in both 448 genders but only with low rate of hypertension in men. Moreover, our current results show 449 that in women, CES-D score was associated with lowered BP among high educational level. 450 Men present few interaction between CES-D score and SES factors. Thus, our results support 451 an importance of considering depressive symptoms according to SES factors for blood 452 pressure variation among women. Nevertheless, gender differences should be mainly explored 453 in longitudinal cohorts to warrant the association between SES factors and depressive 454 symptoms with hypertension.

- 455
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- 457 **Conflict of interests**: none

458

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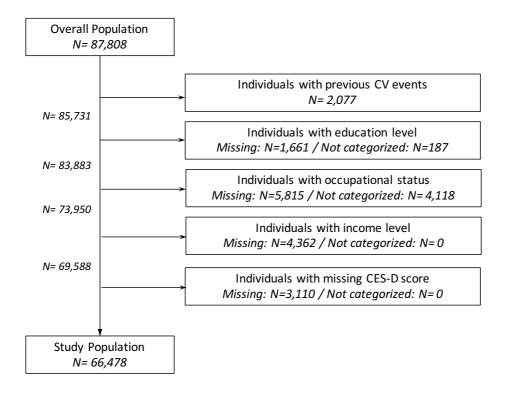
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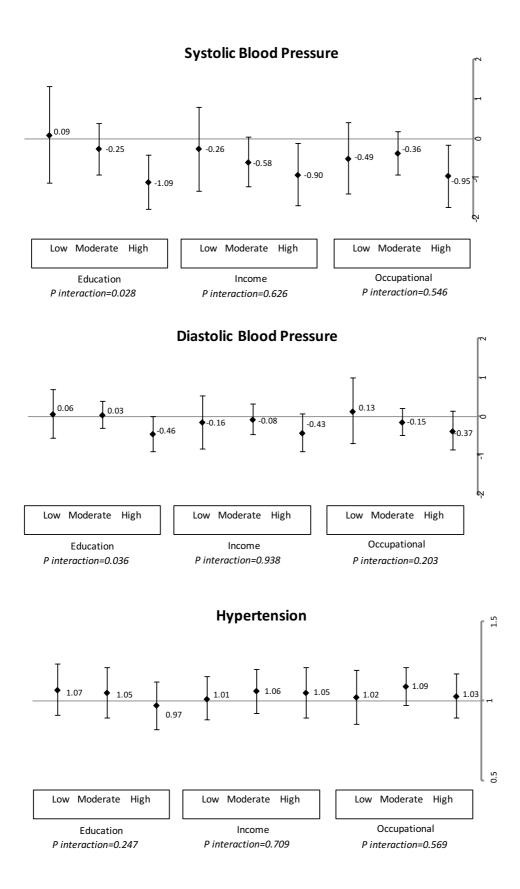
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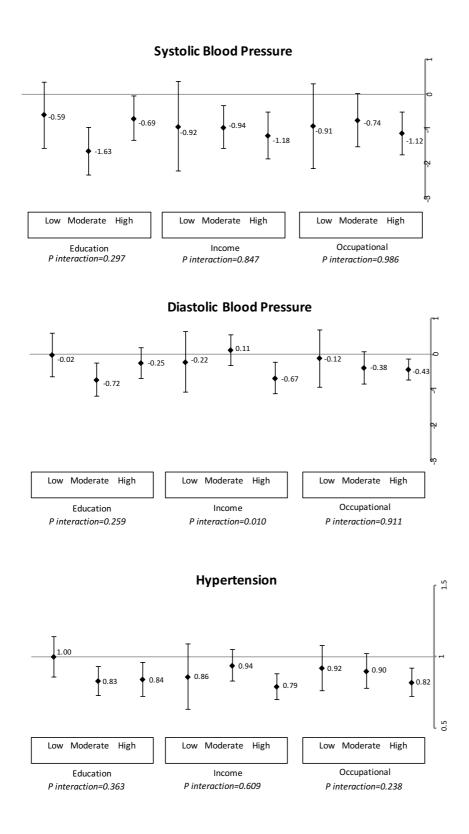
- **Figure 1:** Flow chart
- 698 Not categorized data refer to participants whose responses were not missing but could not be
- 699 included in the ordered classification of each SES variable (e.g. "other diploma", "craftsman"
- 700 or "farmer" and "don't know the answer", for educational level, occupation status and income
- 701 level).
- **Table 1:** Characteristics of the study population
- 705 Table 2: Regression models for SBP, DBP and hypertension according to genders
- Regression coefficients present the decrease or increase in BP (systolic and diastolic blood
 pressure) in participants between the 25th and the 75th percentile of CES-D.
- 708 Odds ratio (OR) present the association between hypertension and the different covariates, 709 and in participants between the 25^{th} and the 75^{th} percentile of CES-D.
- Models were adjusted for antihypertensive, antidepressant drugs, BMI, DASH score, Alcohol
 consumption, Diabetes, Dyslipidemia, Physical activity, Tobacco habits and couple status.

Figure 2: Regression coefficients and 95% confidence interval for the association between
CES-D score interquartile and Blood Pressure and Odds ratio (OR) with 5% CI for the
association between CES-D score interquartile and hypertension prevalence according to SES
factors among women.

Figure 3: Regression coefficients and 95% confidence interval for the association between
CES-D score interquartile and Blood Pressure and Odds ratio (OR) with 5% CI for the
association between CES-D score interquartile and hypertension prevalence according to SES
factors among men.







	Overall	Women	Men	P value
	population	vv onnen	wien	i vulue
	N=66,478	N=35,385	N=31,093	
Age	47.2 (12.8)	46.7 (12.8)	47.8 (12.8)	<0.001
SBP	129 (16)	124 (16)	135 (15)	<0.001
DBP	77 (10)	75 (9)	79 (10)	<0.001
Hypertension	19,013 (28.6)	7,386 (20.9)	11,627 (37.4)	<0.001
CES-D score	10.6 (8.7)	11.8 (9.3)	9.2 (7.8)	<0.001
Depressive	12,492 (18.8)	8,331 (23.5)	4,161 (13.4)	<0.001
symptoms*				
Education level				<0.001
Low	14,548 (21.9)	6,674 (18.9)	7,874 (25.3)	
Moderate	28,058 (42.2)	16,506 (46.7)	11,552 (37.2)	
High	23,872 (35.9)	12,205 (34.5)	11,667 (37.5)	
Income level				<0.001
Low	13,680 (20.6)	8,128 (23.0)	5,552 (17.9)	
Moderate	32,328 (48.6)	17,341 (49.0)	14,987 (48.2)	
High	20,470 (30.8)	9,916 (28.0)	10,554 (33.9)	
Occupational				<0.001
status	(144, (0, 0))	1 0 2 5 (2 5)	4 000 (15 0)	
Low	6,144 (9.2)	1,235 (3.5)	4,909 (15.8)	
Moderate	37,599 (56.6)	24,767 (70.0)	12,832 (41.3)	
High	22,735 (34.2)	9,383 (26.5)	13,352 (42.9)	.0.001
Antihypertensive	7,298 (11.0)	3,537 (10.0)	3,761 (12.1)	<0.001
drugs	4 4(0 ((7)	2 002 (0 7)	1 277 (4 4)	<0.001
Antidepressant	4,460 (6.7)	3,083 (8.7)	1,377 (4.4)	<0.001
drugs	49,731 (74.8)	25,346 (71.3)	24,385 (78.4)	<0.001
Couple Diabetes	2211 (3.3)	800 (2.3)	1,411 (4.5)	<0.001
	19, 318 (29.1)		10,871 (35.0)	<0.001
Dyslipidemia Physical activity	19, 518 (29.1)	8,447 (23.9)	10,871 (33.0)	<0.001
High	33,690 (50.7)	18,123 (51.2)	15,567 (50.1)	NU.UU 1
Moderate	26,444 (39.8)	14,106 (39.9)	12,338 (39.7)	
Low	6344 (9.5)	3,156 (8.9)	3,188 (10.2)	
Tobacco	0011 (0.0)	5,150 (0.7)	5,100 (10.2)	<0.001
Current	12,102 (18.2)	6,206 (17.5)	5,896 (19.0)	
Past	22,022 (33.1)	10,640 (30.1)	11,382 (36.6)	
Never	32,354 (48.7)	19,539 (52.4)	13,815 (44.4)	
BMI (kg/m2)	24.8 (4.3)	24.3 (4.6)	25.5 (3.8)	<0.001
_				<0.001
Alcohol (g/day)	1.2(1.5)	0.8(1.0)	1.6 (1.8)	
DASH score	26 (4)	27 (4)	25 (4)	<0.001

Table 1: Characteristics of the study population

*Depressive symptoms were defined as CES-D≥19 and/or antidepressant drugs use SBP: systolic blood pressure

DBP: diastolic blood pressure

CES-D score: Center of Epidemiologic Studies Depression score

Table 2: Regression models for SBP, DBP and hypertension according to genders

Regression coefficients present the decrease or increase in BP (systolic and diastolic blood pressure) in participants between the 25th and the 75th percentile of CES-D. Odds ratio (OR) present the association between hypertension and the different covariates, and in participants between the 25th and the 75th percentile of CES-D.

Models were adjusted for antihypertensive, antidepressant drugs, BMI, DASH score, Alcohol consumption, Diabetes, Dyslipidemia, Physical activity, Tobacco habits and couple status.

	WOMEN			MEN	
		Systolic Blo	od Pressure		
Parameters	B 95%CI	P value	Parameters	B 95% CI	P value
Age	0.42 (0.40; 0.44)	<0.001	Age	0.47 (0.45; 0.49)	<0.001
CES-D score	-0.64 (-1.08; -0.21)	0.004	CES-D score	-1.12 (-1.55; -0.70)	<0.001
Income		<0.001	Income		<0.001
Low	Ref.		Low	Ref.	
Moderate	-1.30 (-1.76; -0.84)	<0.001	Moderate	-0.90 (-1.40; -0.40)	0.004
High	-2.18 (-2.76; -1.59)	<0.001	High	-2.04 (-2.65; -1.43)	<0.001
Occupational		0.006	Occupational		0.002
status			status		
Low	Ref.		Low	Ref.	
Moderate	-0.62 (-1.51; 0.27)	0.175	Moderate	-0.04 (-0.53; 0.46)	0.878
High	-1.24 (-2.22; -0.26)	0.013	High	-0.79 (-1.41; -0.18)	0.011
Education	Def	<0.001	Education	Dof	<0.001
Low Moderate	Ref. -0.54 (-0.99; -0.08)	0.020	Low Moderate	Ref. -0.45 (-0.89; -0.01)	0.050
High	-0.34 (-0.99, -0.08) -1.31 (-1.86; -0.38)	<0.020	High	-0.43 (-0.89, -0.01) -1.19 (-1.75; -0.63)	<0.0001
Ingn	-1.51 (-1.00, -0.50)		ood Pressure	-1.17 (-1.75, -0.05)	NO.0001
			1		
Parameters	B 95% CI	P value	Parameters	B 95% CI	P value
Age	0.13 (0.12; 0.15)	< 0.001	Age	0.19 (0.18; 0.20)	< 0.001
CES-D score	-0.21 (-0.49; 0.07)	0.135	CES-D score	-0.29 (-0.61; 0.03)	0.082
Income	Dí	0.229	Income	D	0.705
Low	Ref.	0.020	Low Moderate	Ref.	0.594
Moderate High	-0.26 (-0.55; 0.04) -0.21 (-0.58; -0.16)	0.089 0.265	High	0.09 (-0.42; 0.23) 0.01 (-0.39, 0.40)	0.584 0.982
Occupational	-0.21 (-0.36, -0.10)	0.205	Occupational	0.01 (-0.39, 0.40)	0.982
status		0.100	status		0.157
Low	Ref.		Low	Ref.	
Moderate	-0.32 (-0.84; 0.20)	0.235	Moderate	-0.29 (-0.63; 0.03)	0.079
High	-0.59 (-1.17; -0.01)	0.049	High	-0.13 (-0.54; -0.27)	0.528
Education		<0.001	Education		<0.001
Low	Ref.		Low	Ref.	
Moderate	0.06 (-0.23; 0.35)	0.689	Moderate	-0.56 (-0.86; -0.26)	0.002
High	-0.19 (-0.54; 0.16)	0.301	High	-1.06 (-1.43; -0.69)	<0.001
			tension		
Parameters	OR 95%CI	P value	Parameters	OR 95% CI	P value
Age	1.08 [1.07 – 1.09]	<0.001	Age	1.06 [1.05 - 1.07]	<0.001
CES-D score	1.03 [0.96 – 1.10]	0.219	CES-D score	0.86 [0.80 – 0.93]	<0.001
Income			Income		
Low	Ref.		Low	Ref.	
Moderate	0.90 [0.81 – 0.99]	0.037	Moderate	0.89 [0.81 – 0.97]	0.011
High	0.84 [0.75 – 0.96]	0.008	High	0.77 [0.69 – 0.87]	<0.001
Occupational			Occupational		
status Low	Ref.		status Low	Ref.	
<i>Moderate</i>	0.91 [0.77 – 1.08]	0.285	Moderate	0.99 [0.91 – 1.08]	0.889
mouerale	0.71[0.77 - 1.00]	0.205	mouerate	0.77 [0.71 - 1.00]	0.009

High	0.80 [0.66 – 0.96]	0.019	High	0.91 [0.82 - 1.01]	0.089
Education			Education		
Low	Ref.		Low	Ref.	
Moderate	0.89 [0.82 - 0.97]	0.006	Moderate	0.97 [0.90 – 1.05]	0.474
High	0.86 [0.77 - 0.96]	0.005	High	0.87 [0.79 – 0.96]	0.005