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1 **Association of depressive symptoms and socioeconomic status in determination of blood**  
2 **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.

70 **Conclusion:** Gender differences were observed for considering depressive symptoms  
71 according to SES factors for BP variation and hypertension. In women, educational level was  
72 the SES factor which has the main modifying effect on this association.

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74

75 **Keywords:** depressive symptoms, blood pressure, hypertension, CES-D, socioeconomic  
76 status

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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).**

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

116

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

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

143

144

## 145 **METHODS**

### 146 **The CONSTANCES cohort**

147 This ancillary study is a cross-sectional analysis using data from the CONSTANCES study.  
148 The general aim of CONSTANCES is to establish a large population-based cohort to  
149 contribute to the development of epidemiologic research ([www.constances.fr](http://www.constances.fr)). Details about  
150 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**

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

174

### 175 **Study population**

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

181

### 182 **Hypertension and blood pressure**

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

185 arm at 2 min interval after 5 min of rest and using an automated oscillometric  
186 sphygmomanometer. The arm giving the highest SBP was considered the reference arm and a  
187 third BP measure was taken after 1 min of rest, the average of these two measurements was  
188 considered. Prevalent HTN was defined by a SBP at least 140 mmHg and/or a DBP at least  
189 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  
198 with taking the interval between the 25<sup>th</sup> and the 75<sup>th</sup> percentile as unit, the meaning of one-  
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**

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

210 Occupational status was collected according to the French “Occupations and Socio-  
211 occupational Categories” [Professions et Catégories Socioprofessionnelles (PCS)]  
212 classification system (INSEE, 2003) then categorized in three broad classes: high (e.g.,  
213 managers), moderate (e.g., clerks or first-line supervisors) and low (e.g., plant and machine  
214 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. Anti-  
221 hypertensive and antidepressant medications were determined based on the Anatomical  
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/m<sup>2</sup>) 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  $\chi^2$  test was performed for categorical variables. SES factors were



252 considered as ordinal variables. Statistical analyses were stratified on gender since  
253 hypertension differs between men and women (Vallée et al., 2020), as well as depression  
254 (Van de Velde et al., 2010).

255 Associations between depressive symptoms and blood pressure levels were examined with  
256 gender linear regression models computing coefficients (b) and their 95% confidence  
257 intervals. Association between depressive symptoms and hypertension were examined with  
258 gender logistic regression models computing odds ratio (OR) and their 95% confidence  
259 intervals. Gender models were adjusted for age, antihypertensive and antidepressant  
260 medications, BMI, DASH score, alcohol consumption, diabetes, dyslipidemia, physical  
261 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

272 A total of 66,478 volunteers without missing or not categorized data were included in the  
273 study, their characteristics are described in **Table 1**. The mean average CES-D score was 10.6  
274 (8.7) for overall population, with a difference of 9 points between the 25<sup>th</sup> and 75<sup>th</sup>  
275 percentiles, mean CES-D score was 11.8 (9.3) for women and 9.2 (7.8) for men. 6.7% of the  
276 overall population had an antidepressant medication (8.7% for women, 4.4% for men). 28.6%  
277 of the overall population was hypertensive (20.9% for women, 37.4% for men).

278

279 The linear regression coefficient for the association between CES-D score and SBP was  
280 negative and significant in both women  $b=-0.64$  95%CI [-1.08; -0.21] and men  $b=-1.12$   
281 95%CI [-1.55; -0.70]. SBP was decreased of 0.64 mmHg in women and of 1.12 mmHg in  
282 men between the 25<sup>th</sup> and the 75<sup>th</sup> percentiles of CES-D score (**Table 2**).

283 The linear regression coefficient for the association between CES-D score and DBP was  
284 significant neither in women  $b=-0.21$  95%CI [-0.49; 0.07] nor in men  $b=-0.29$  95%CI [-0.61;  
285 0.03] (**Table 2**).

286 The association between CES-D score and hypertension was significant for men, OR=0.86  
287 [0.80; 0.93],  $p<0.001$  but not for women, OR=1.03 [0.96; 1.10],  $p=0.219$  (**Table 2**).

288 Supplementary file presented the regression coefficient and OR for all covariates of  
289 adjustment (**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

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

304 Among women, the interactions between CES-D score and educational levels were significant  
305 for both SBP ( $p=0.028$ ) and DBP ( $p=0.036$ ) (**Figure 2**). When women were categorized by  
306 income level or occupational status, the interactions were not significant for both SBP and  
307 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 25<sup>th</sup>  
311 and the 75<sup>th</sup> percentiles of CES-D score was -1.09 mmHg 95%CI [-1.76; -0.42] for high  
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

319 between CES-D score and hypertension when women were categorized by SES factors  
320 **(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)**.

332  
333

#### 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  $0.70; 0.07]$ ).

340 When excluding antidepressant medications ( $N=4,460$ ) from the analyses, CES-D score  
341 remained significantly associated with SBP among women ( $b=-0.62$   $95\%CI [-1.05; -0.19]$ )  
342 and among men ( $b=-1.20$   $95\%CI [-1.63; -0.77]$ ) but not for DBP analyses among women ( $b=-$   
343  $0.63$   $95\%CI [-1.27; 0.01]$ ) and among men ( $b=-0.41$   $95\%CI [-0.85; 0.03]$ ).

344 When excluding participants who received antihypertensive and/or antidepressant drugs  
345 ( $N=10,891$ ) 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  
384 assumes a common underlying factor that independently enhances the risk for depression, as  
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).

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

444

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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458

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697 **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).

702

703 **Table 1:** Characteristics of the study population

704

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

706 Regression coefficients present the decrease or increase in BP (systolic and diastolic blood  
707 pressure) in participants between the 25<sup>th</sup> and the 75<sup>th</sup> percentile of CES-D.

708 Odds ratio (OR) present the association between hypertension and the different covariates,  
709 and in participants between the 25<sup>th</sup> and the 75<sup>th</sup> percentile of CES-D.

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

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713

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

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

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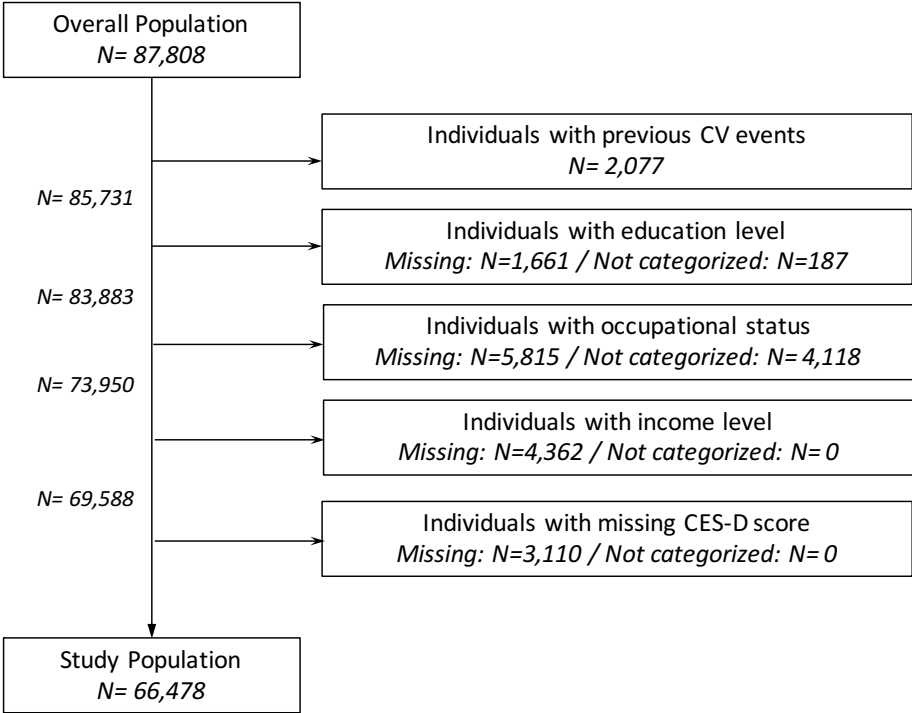
733

734

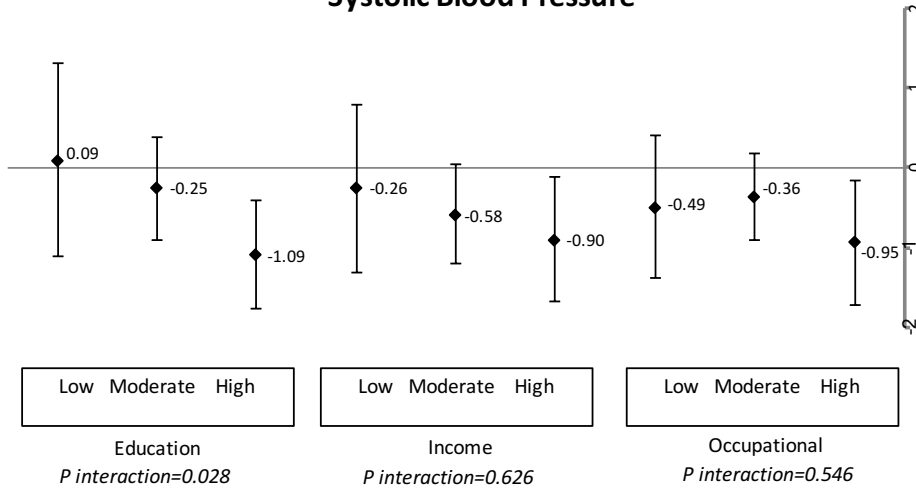
735

736

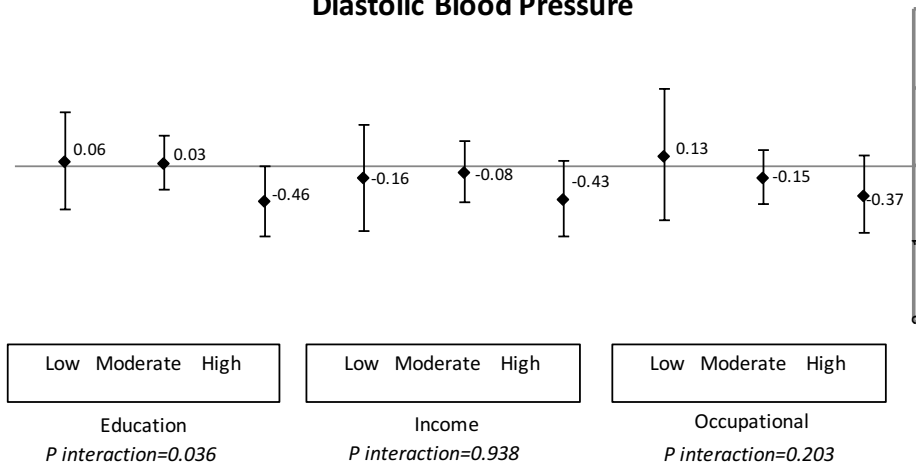
737



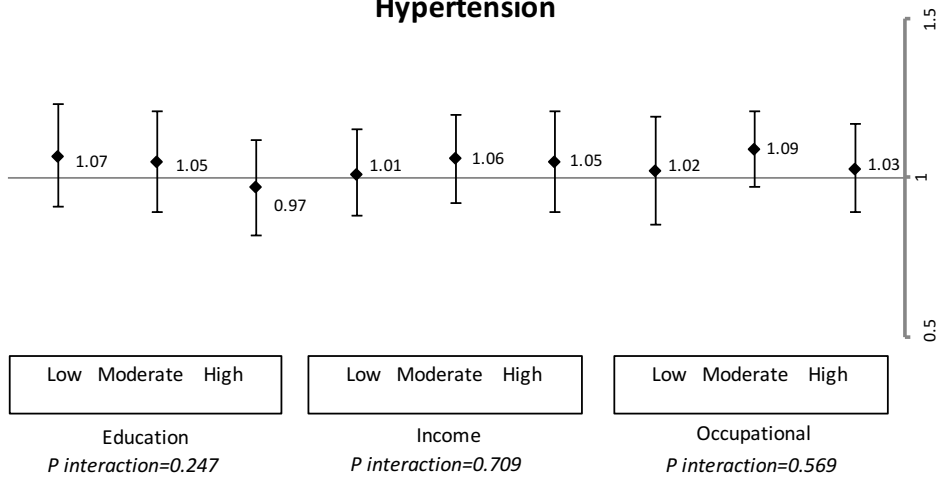
### Systolic Blood Pressure



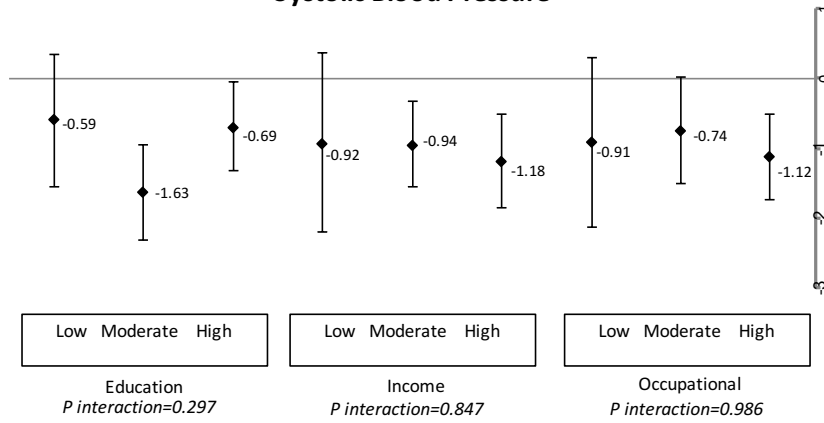
### Diastolic Blood Pressure



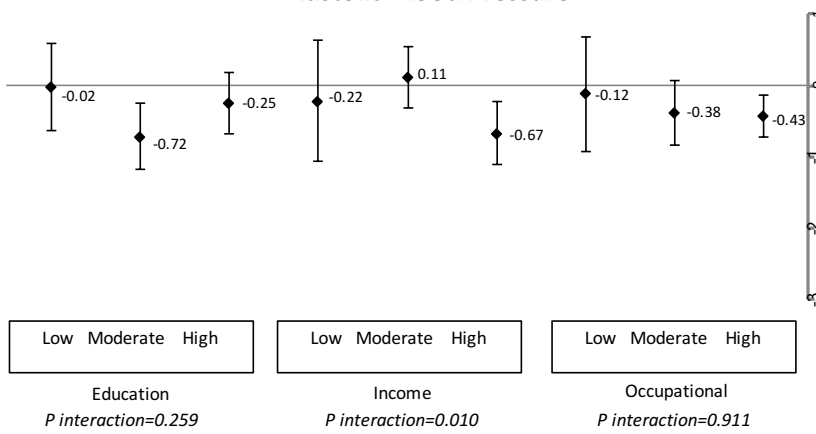
### Hypertension



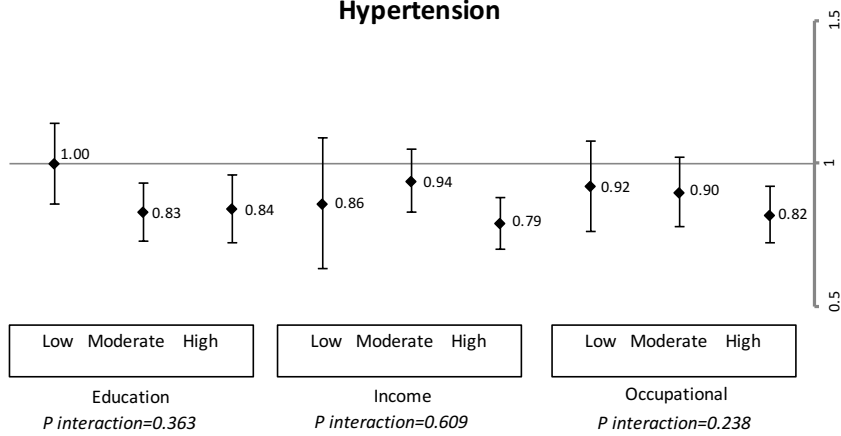
### Systolic Blood Pressure



### Diastolic Blood Pressure



### Hypertension



**Table 1: Characteristics of the study population**

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

\*Depressive symptoms were defined as CES-D $\geq$ 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 25<sup>th</sup> and the 75<sup>th</sup> percentile of CES-D.

Odds ratio (OR) present the association between hypertension and the different covariates, and in participants between the 25<sup>th</sup> and the 75<sup>th</sup> 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 Blood Pressure					
Parameters	B 95% CI	P value	Parameters	B 95% CI	P value
<b>Age</b>	0.42 (0.40; 0.44)	<0.001	<b>Age</b>	0.47 (0.45; 0.49)	<0.001
<b>CES-D score</b>	-0.64 (-1.08; -0.21)	0.004	<b>CES-D score</b>	-1.12 (-1.55; -0.70)	<0.001
<b>Income</b>		<0.001	<b>Income</b>		<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
<b>Occupational status</b>		0.006	<b>Occupational status</b>		0.002
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
<b>Education</b>		<0.001	<b>Education</b>		<0.001
Low	Ref.		Low	Ref.	
Moderate	-0.54 (-0.99; -0.08)	0.020	Moderate	-0.45 (-0.89; -0.01)	0.050
High	-1.31 (-1.86; -0.38)	<0.001	High	-1.19 (-1.75; -0.63)	<0.0001
Diastolic Blood Pressure					
Parameters	B 95% CI	P value	Parameters	B 95% CI	P value
<b>Age</b>	0.13 (0.12; 0.15)	<0.001	<b>Age</b>	0.19 (0.18; 0.20)	<0.001
<b>CES-D score</b>	-0.21 (-0.49; 0.07)	0.135	<b>CES-D score</b>	-0.29 (-0.61; 0.03)	0.082
<b>Income</b>		0.229	<b>Income</b>		0.705
Low	Ref.		Low	Ref.	
Moderate	-0.26 (-0.55; 0.04)	0.089	Moderate	0.09 (-0.42; 0.23)	0.584
High	-0.21 (-0.58; -0.16)	0.265	High	0.01 (-0.39; 0.40)	0.982
<b>Occupational status</b>		0.166	<b>Occupational status</b>		0.137
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
<b>Education</b>		<0.001	<b>Education</b>		<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
Hypertension					
Parameters	OR 95% CI	P value	Parameters	OR 95% CI	P value
<b>Age</b>	1.08 [1.07 – 1.09]	<0.001	<b>Age</b>	1.06 [1.05 - 1.07]	<0.001
<b>CES-D score</b>	1.03 [0.96 – 1.10]	0.219	<b>CES-D score</b>	0.86 [0.80 – 0.93]	<0.001
<b>Income</b>			<b>Income</b>		
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
<b>Occupational status</b>			<b>Occupational status</b>		
Low	Ref.		Low	Ref.	
Moderate	0.91 [0.77 – 1.08]	0.285	Moderate	0.99 [0.91 – 1.08]	0.889

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