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Cardiovascular risk goes up as your mood goes down: Interaction of depression and socioeconomic status in determination of cardiovascular risk in the CONSTANCES cohort☆

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ABSTRACT

Background: Recent evidence suggests that the association of psychological variables with the risk of coronary heart disease (CHD) might depend upon socioeconomic status (SES). However, it is unclear whether the association between depressive symptoms and CHD risk might differ according to three SES indicators (education, occupational status and household monthly income).
Methods: Among 34,836 working participants of the French CONSTANCES cohort (16,221 men, mean age [SD]: 44.0 [10.4] years) without history of cardiovascular disease, depressive symptoms were assessed with the Center of Epidemiologic Studies Depression scale (CES-D). The Framingham risk equation calibrated to the French population estimated the participant's 10-year risk of CHD. Associations between depressive symptoms and CHD risk were estimated using linear regression models in SES strata.
Results: The estimated 10-year risk of CHD was 16.9% in men and 1.8% in women. In men, the increased CHD risk in those with (versus without) depressive symptoms was more pronounced as occupational status decreased, being 0.65% (−0.57; 1.88), 1.58% (0.50; 2.66) and 3.19% (1.30; 5.07) higher in individuals of high, medium and low occupational status, respectively (p for interaction: 0.01). In contrast, effect modification by education or household income was less evident, despite similar trends. In women, no effect modification was found whatever the SES indicator.
Conclusions: Depressive symptoms and 10-year estimated CHD risk were more tightly linked in individuals of lower SES, at least in men. Occupational status was the SES indicator that displays the most obvious effect modification on this association.

1. Introduction

Several psychosocial factors, including depressive symptoms, have been shown to be associated with increased risk of cardiovascular diseases, as has low socioeconomic status (SES) [1]. Although psychological and social risk factors are often merged under the label of "psychosocial" risk factors, a growing body of evidence suggests that psychological risk factors may interact with social risk factors in the etiology of cardiovascular diseases, especially coronary heart disease (CHD) [2–5]. In other words, SES might modify the effect of psychological variables on CHD. For instance, depressive symptoms may be more

Abbreviations: CES-D, Center of Epidemiologic Studies Depression; CHD, coronary heart disease; CI, confidence interval; HDL, high-density lipoprotein; SES, socioeconomic status; SBP, systolic blood pressure.

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strongly associated with incident cardiac events in persons of low occupational grade than in those of higher grade [5]. While such an interaction has been found in some studies, it is not a universally recognized phenomenon [6]. Further it is not known whether this phenomenon depends on which SES indicator is used in the models.

The most commonly used indicators of SES in epidemiology are: education, income and occupational status. To our knowledge, no study found education to be a moderating factor (i.e. effect modifier) in the association between depressive symptoms and CHD [7,8]. In contrast, the literature suggests that not only depressive symptoms [5], but also psychological distress [3] and work stress [9] are more strongly associated with the risk of CHD in individuals with the lowest occupational status. Finally, income level and perceived stress were found to be synergistic predictors of incident CHD in one study [4]. However, the moderating roles of these three indicators are rarely compared in the same study, apart from one study [6] where none moderated the association between antidepressants use (considered as a proxy of depression) and CHD mortality.

The aim of the present study was to examine the extent to which the association between depressive symptoms and CHD risk might differ according to SES, where SES is measured by various indicators (i.e. education, occupational status and household income). We hypothesized that the association between depressive symptoms and CHD risk would be stronger in individuals of lower SES.

This investigation was conducted among working individuals of the French CONSTANCES cohort, a large prospective population-based cohort. Although it would be preferable to study the depression-CHD relationship with actual incidence rates of CHD among members of the cohort, we are still in the recruitment phase of the CONSTANCES cohort and there are not enough CHD events yet to provide sufficient data for an analysis of CHD incidence. Consequently, we will use as a proxy for the outcome of interest an equation-based estimate of the 10-year CHD incidence based on classic CHD risk factors.

2. Methods

2.1. Participants

The design and main objectives of the CONSTANCES cohort (www.constances.fr) have been previously published [10,11]. The CONSTANCES cohort includes volunteers aged 18–69 years at inception who were randomly selected from French adults who are covered by CNAMTS health insurance (Caisse nationale d'assurance maladie des travailleurs salariés), which is the national health insurance of >85% of the French population. Those who agree (participation rate of 7.3% [12]) have to complete self-administrated questionnaires dealing with lifestyle, health, physical limitations, social and personal characteristics. They are invited to go to one of the twenty-one participating Health Screening Centers throughout France, in order to benefit from an extensive health examination (medical, paraclinic exams, blood tests). Because occupational status is one of the covariates examined, the present analysis was restricted to working participants. Other eligibility criteria of the present study were: having no missing data for selected variables (see below) and being free from history of cardiovascular disease.

All confidentiality, safety and security procedures were approved by the French legal authorities. According to French regulations, the CONSTANCES Cohort project has obtained the authorization of the National Data Protection Authority (Commission Nationale de l'Informatique et des Libertés - CNIL).

2.2. Estimated 10-year CHD risk

An estimation of the risk of CHD over a 10-year period was provided by the Framingham risk function equation calibrated to the French population [13], based on age, sex, age × sex interaction, current smoking status, diabetes mellitus status, systolic blood pressure (SBP) as well as total and high-density lipoprotein (HDL) cholesterol. The estimated 10-year CHD risk was calculated as $1-(0.97832^{\exp(c)})$ where c = 6.53∗(log(age) - mean(log(age))) + 15.04∗(sex - prevalence(sex)) - 3.28∗(sex∗log(age) - mean(sex∗log(age))) + 0.51∗(smoking status - prevalence (smoking status)) + 1.03∗(diabetes status - prevalence(diabetes status)) + 1.87* (log(SBP) - mean(log(SBP))) + 2.02*(log(total cholesterol) - mean(log(total cholesterol))) - 1.21∗(log(HDL cholesterol) - mean(log(HDL cholesterol))), with sex = 1 for men and 0 for women. The output of this equation is an estimate of cumulative 10-year risk expressed as a percentage.

Risk score components were collected from questionnaire and clinical examination. Blood pressure was measured while lying on a bed after a 5-min rest period, using an automated oscillometric sphygmomanometer. Blood pressure was measured once on each arm and a third time (reference measure) on the arm giving the highest SBP value. For this study, only reference measure was considered. Fasting blood samples were taken to measure total and HDL cholesterol as well as glycaemia. Diabetes mellitus status was based on either self-reported type II diabetes during the medical interview or a fasting blood glucose concentration greater than or equal to 7 mmol/L.

Particular attention has been paid to standardizing methods to ensure the successful replication of data collection for all volunteers regardless of when, where and by whom they are performed [14]. Standard Operating Procedures (SOPs, which define the medical device specifications and detail the measurement methods for each type of data) have been developed for each measure (e.g. use of the same sphygmomanometer model across all study sites).

2.3. Depressive symptoms

Depressive symptoms were assessed using the validated self-administered Center of Epidemiologic Studies Depression scale (CES-D) [15,16]. This 20-item questionnaire has been designed for use in community studies. The CES-D scale evaluates the frequency of depressive symptoms during the previous week (e.g., I felt depressed, I felt everything I did was an effort, my sleep was restless). Responses range from 0 (hardly ever) to 3 (most of the time). The CES-D was successively used: either 1) as a binary variable based on the cutoff of ≥ 19 for both men and women, according to the validation of the French version (sensitivity/specificity for the diagnosis of major depression: 0.853/0.859) [17]; or 2) as a continuous variable, taking the interval between the 25th and the 75th percentile (interquartile range) as unit. Indeed the meaning of one-point increase in CES-D might be difficult to figure out whereas one may more intuitively compare a participant in the middle of the upper half of the CES-D score distribution with a participant in the middle of the lower half. Given the satisfactory internal consistency (Cronbach's alpha = 0.89 in the current sample), when < 5 items were missing, the total score was computed based on the mean value of available items multiplied by 20.

2.4. Socioeconomic status

SES was assessed by three self-reported indicators: education, occupational status and household monthly income. Education was categorized into three levels: less than or equal to high school diploma (13 years or less of education), undergraduate degree (14–16 years of education) and postgraduate degree (17 years or more of education). Occupational status was collected according to the French "Occupations and Socio-occupational Categories" [Professions et Categories Socioprofessionnelles (PCS)] classification system [18] then categorized in three broad classes: high (e.g., managers), medium (e.g., clerks or first-line supervisors) and low (e.g., plant and machine operators, cleaners). Household monthly income was categorized into three levels: < 1500 euros, 1500–2800 euros and ≥ 2800 euros.

2.5. Statistical analysis

Statistical analysis was carried out with the Stata software (version 14, Stata Corp., College Station, TX). The three ordinal SES indicators were a priori considered as continuous variables with values 1–3. In order to calculate the estimated 10-year CHD risk, quantitative variables (age, SBP, total and HDL cholesterol) were log-transformed and centered by subtracting their mean, whereas qualitative variables (sex, smoking status and diabetes mellitus status) were centered by subtracting their prevalence. The risk equation was first used in the whole population to obtain an estimated 10-year CHD risk for each participant, individually. Then, since men and women differ as regards both the incidence and the risk factors of CHD [19], as well as regards the incidence of depression [20,21], all analyses have been stratified by sex. The association between depressive symptoms and the estimated 10-year CHD risk was examined with linear regression models computing coefficients (b) and their 95% confidence intervals (CI). To assess possible effect modification, we stratified the depression-CHD risk analyses by each of the three considered indicators of SES, separately, and tested the statistical significance of these interactions. Such interactions were examined by introducing simultaneously depressive symptoms, one of the three SES indicators and their interaction term in the model such as: estimated 10-year CHD risk = b0 + b1∗depressive symptoms + b2∗SES indicator + b3∗depressive symptoms∗SES indicator.

3. Results

A total of 35,205 working participants who were enrolled from February 2013 to December 2015 were without missing data. Supplemental Fig. S1 shows the flowchart for the study population selection and participants with and without missing data are compared in Supplemental Table S1. Participants with missing data were older, more likely to be women, current smokers and diabetic as well as to have a lower socioeconomic status, a higher systolic blood pressure, a lower total cholesterol, a higher CES-D score and a higher estimated risk of CHD. In addition, 369 individuals with a personal history of cardiovascular disease were excluded and 34,836 participants were included in this analysis. Their mean age (SD) was 44.0 (10.4) years