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ORIGINAL ARTICLE

The association of depressive symptoms and ischemic heart disease in older adults is not moderated by gender, marital status or education

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Abstract
Objectives To investigate whether the association of depression and ischemic heart disease (IHD) is moderated by gender, marital status or education.
Methods Data from the 1998 Medicare Health Outcome Survey (HOS) with a 2 year follow-up were re-analyzed. 63,965 older adults who had not reported IHD at baseline were included. Logistic regression analysis modelled the effects of depression, somatic risk factors, and demographic variables on IHD after 2 years.
Results Two year reported incidence of IHD was 6.2%. Depression was associated with a 1.53-fold risk of developing IHD after controlling for somatic risk factors and demographic variables. Male gender, lower than high-school education, and being married were associated with IHD. Neither of these variables yielded significant interactions with depression, nor did any of the higher-order interaction terms.
Conclusions The association of depression and IHD seems independent from pivotal demographic variables. Possibly the impact of psychosocial factors in this sample of older people is weak compared to medical conditions and age. Also the possibility exists that a common factor such as a shared genetic vulnerability contributes to both depressive symptoms and IHD.

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Keywords Depression · Coronary heart disease · Gender · Marital status · Education · Epidemiology

Introduction

Depressive symptoms are associated with ischemic heart disease (IHD) in a bidirectional relationship. Heart disease and depression are commonly comorbid (Herrmann-Lingen and Buss 2006), and there is strong evidence that depression is a risk factor for the development and progression of IHD independent of other somatic risk factors (Barth et al. 2004; Frasure-Smith and Lespérance 2006; Nabi et al. 2010; Rugulies 2002; Van der Kooy et al. 2007; Wulsin and Singal 2003). Depression is estimated to almost double the risk of subsequent IHD. Several mechanisms that may explain the effects of depression have been hypothesized. Depression is associated with several behavioural and social risk factors such as smoking, sedentary lifestyle, decreased treatment adherence, and low social support. Also, biological mechanisms, particularly autonomic, endocrine and immune alterations (inflammation), are involved in the link between depression and IHD (for an excellent overview see Huffman et al. 2010). There are a large number of studies supporting these behavioural and physiological pathways (Carney et al. 2009; Lett et al. 2004; Skala et al. 2006; Stewart et al. 2009; Vaccarino et al. 2007). Beyond that, the possibility of a common genetic vulnerability contributing to both, depressive symptoms and IHD, has been pondered in recent years (McCaffery et al. 2006).

Here we pursued the question of whether the association of depressive symptoms and IHD is moderated in any way by education, marital status or gender. These factors in themselves are also associated with health in a variety of ways. There is a consistent social gradient in morbidity and

mortality that is particularly evident for ischemic heart disease (Thurston et al. 2005). This gradient persists beyond retirement age and even increases with age (Marmot and Shipley 1996). Socio-economic differences in health are generally supposed to be weaker for women than for men, but there is also evidence that low education, for instance, is associated with greater risks for women (Thurston et al. 2005). Marriage, after all, benefits people's health, but the protective effects on average are stronger for men than for women (Kiecolt-Glaser and Newton 2001).

It is assumed that education, here taken as a proxy for socio-economic status, or social support by a spouse should alter the strength of the association between depressive symptoms and IHD either by influencing behavioural pathways (e.g. healthier lifestyle, medical adherence), or else buffering the physiological impact of depression. We also hypothesized that these effects would be different in women and men (Meisinger et al. 2009; Sbarra 2009) expecting, for instance, that marriage would yield higher protective effects in men with depressive symptoms than in women. In short, we were exploring pivotal variables that presumably would moderate the impact of depression on subsequent IHD, and we looked for interactions between these variables and depression as to the development of IHD in particular.

Methods

Study design and setting

We re-analysed public use file data from the Medicare Health Outcome Survey (HOS). HOS was a longitudinal cohort survey administered to Medicare beneficiaries who have been continuously enrolled in various managed care plans for at least 6 months. The survey includes random samples of 1,000 beneficiaries from each of >250 managed care plans in the US. The HOS collects health status information from individuals at one time point and again 2 years later. The main elements of the HOS measure are the Medical Outcomes Study 36-item short-form health survey (SF-36), questions on chronic conditions, and basic demographic information (Health Services Advisory Group 2005). The present survey was administered to the cohort at baseline in 1998. We used the Medicare Health Outcomes Survey (HOS) Cohort I Analytic Public Use File (C1APUF.TXT) as the basis for our analysis.

Participants

The baseline cohort included a random sample of 279,135 beneficiaries from 287 managed care market areas or reporting units. Persons were eligible if they were seniors (age 65 or older) or disabled (less than age 65), and were enrolled in a managed care organisation for a 6 month period. Persons were included into analysis if they provided sufficient data to calculate SF-36 Physical Component Summary (PCS) score and/or Mental Component Summary (MCS) score. Sixty-two percent ($n = 172{,}314$) of the sampled beneficiaries provided a sufficient amount of the baseline survey. The Cohort I Analytic Public Use File includes all beneficiaries for whom data were available from the baseline and who were continuously enrolled in their original managed care organisation at follow-up. It comprises 134,076 beneficiaries (Health Services Advisory Group 2005). This reduction is due to a number of managed care organisations that discontinued services to beneficiaries between 1998 and 2000 (Health Services Advisory Group 2005).

From the Cohort I Analytic Public Use File we selected only community dwelling whites over 65 years (=88% of the total sample), and we excluded proxy responses. Of the remaining group 63,965 subjects (81.3%) had not reported any indications of IHD at baseline and were included in the present analysis. The selection process and resulting numbers are displayed in a flow chart (Fig. 1).

Variables

IHD was assessed by two questions: "Has a doctor ever told you that you had angina pectoris or coronary artery disease?"; "Has a doctor ever told you that you had a myocardial infarction or heart attack?" If any of these items were answered positively (yes) the existence of IHD was assumed. The same set of questions was used to assess possible IHD at follow-up.

Depression was assessed by three items: "In the past year, have you had 2 weeks or more during which you felt sad, blue or depressed; or when you lost interest or pleasure in things that you usually cared about or enjoyed?"; "In the past year, have you felt depressed or sad much of the time?"; "Have you ever had 2 years or more in your life when you felt depressed or sad most days, even if you felt ok sometimes?". Positive responses (yes) to any of these items were taken as an indication of depressive symptoms or episodes in the past.

Gender, marital status ("What is your current marital status?" married/non-married), and education ("What is the highest grade or level of school that you have completed?" less than high school education/high school education/greater than high school education were assessed at baseline. We controlled for diabetes mellitus ("Has a doctor ever told you that you had diabetes, high blood sugar, or sugar in the urine?"), hypertension ("Has a doctor

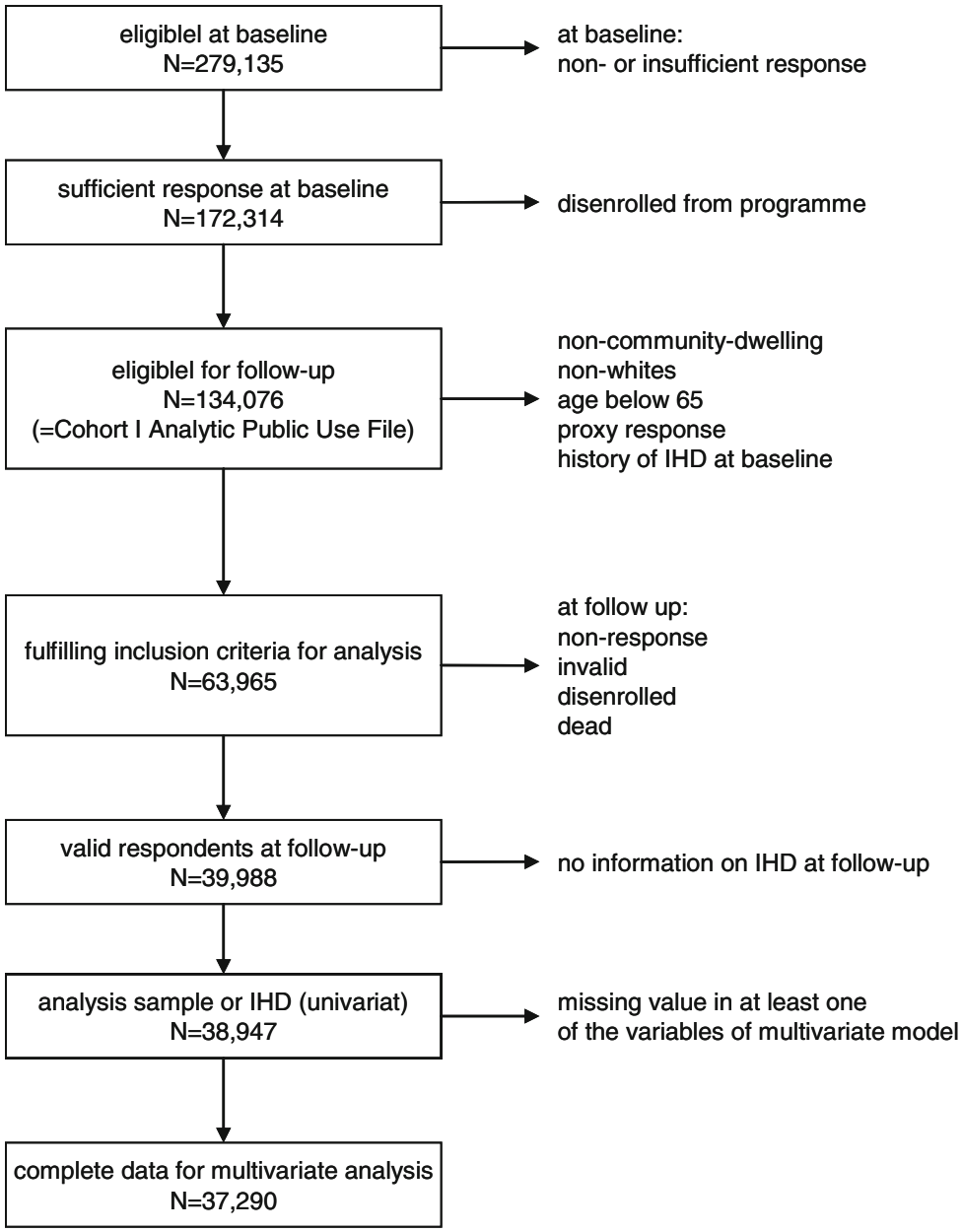

Fig. 1 Selection process of final analyses (flow chart); Medicare Health Outcome Survey, USA, 1998–2000

ever told you that you had hypertension or high blood pressure?"), and smoking ("every day" or "some days").

Statistical methods

We performed a logistic regression analysis using occurrence of incident IHD at follow-up as the criterion variable. We calculated both a main effects model as well as models including 1-, 2- and 3-way interaction terms between depression, gender, education and marital status. Because of the large sample included in the analysis, p values $<.01$ were regarded as significant, and 99% confidence intervals (CI) were calculated accordingly. The original public use file was converted into a SPSS data file. All computations were done using SPSS for Windows (16.0.2).

Results

Information on IHD at follow-up was available for 97.4% of the beneficiaries with valid responses at follow-up (38,947/39,988; Table 1). Of these, 2,424 beneficiaries newly developed IHD, i.e. the reported incidence of IHD during the 2 year period was 6.2%. The characteristics of the total sample and beneficiaries who developed IHD or not over the 2 years of follow up are shown in Table 1.

Table 1 Characteristics of the sample fulfilling inclusion criteria for analysis at baseline and follow-up; at follow-up contrasting beneficiaries who developed ischemic heart disease over 2 years or not (number and valid percent; due to missing values in single variables numbers in last two columns do not necessarily sum up to *N* at follow-up); Medicare Health Outcome Survey, USA, 1998–2000

	Baseline	Follow-up	
Complete *N*	63,965	39,988	
With information on ischemic heart disease at follow-up:		38,947	
		IHD at follow-up $N = 2{,}424$	Free of IHD at follow-up $N = 36{,}523$
Gender			
Male	26,011 (40.7%)	1,205 (49.8%)	14,451 (39.6%)
Female	37,831 (59.1%)	1,216 (50.2%)	21,997 (60.4%)
Age			
65–74	40,755 (63.7%)	1,405 (58.0%)	23,847 (65.3%)
75+	23,210 (36.3%)	1,019 (42.0%)	12,676 (34.7%)
Marital status			
Married	39,477 (61.9%)	1,596 (66.1%)	22,844 (62.7%)
Non-married	24,335 (38.1%)	818 (33.9%)	13,606 (37.3%)
Depression			
2 weeks or more feeling sad …	10,302 (16.2%)	495 (20.5%)	5,246 (14.4%)
Depressed much of the time …	5,675 (8.9%)	284 (11.8%)	2,813 (7.7%)
2 years or more depressed …	6,285 (9.9%)	277 (11.5%)	3,258 (9.0%)
At least one of the above …	13,707 (21.6%)	641 (26.6%)	7,064 (19.5%)
Education			
Less than high school	14,723 (23.3%)	644 (26.9%)	7,832 (21.7%)
High school	23,674 (37.0%)	885 (37.0%)	13,811 (38.2%)
Greater than high school	24,745 (38.7%)	863 (36.1%)	14,468 (40.1%)
Smoking status			
Ever smoked	7,916 (12.4%)	331 (13.7%)	4,156 (11.4%)
Never	55,988 (87.6%)	2,086 (86.3%	32,342 (88.6%)
Diabetes mellitus			
Ever had*	7,601 (12.0%)	460 (19.1%)	3,951 (10.9%)
Never	55,969 (88.0%)	1,951 (80.9%)	32,365 (89.1%)
Hypertension			
Ever had*	29,788 (46.8%)	1,402 (58.0%)	16,554 (45.5%)
Never	33,918 (53.2%)	1,015 (42.0%)	19,818 (54.5%)

* "Has your doctor ever told you that you had…"

Depression was associated with a 1.63-fold risk (99% CI: 1.43–1.85) of developing IHD after controlling for sex and age. Additionally adjusting for hypertension, diabetes, and smoking history resulted in an odds-ratio (OR) =1.53 (99% CI: 1.34–1.74). Male gender, lower than high-school education and being married (most pronounced in men ≥75 years of age) were positively associated with IHD. However, neither of the latter variables showed significant interactions with depression, nor did any higher order interactions yield statistical significance (Table 2).

Since the 3-way-interaction with an OR of 2.86 comes close to statistical significance, we illustrated the interrelations of gender, SES and marital status with regard to IHD (Fig. 1). No clear picture emerges, but it seems that married men with low SES are particularly at risk if they show depressive symptoms (Fig. 2).

Discussion

The associations between demographic and somatic risk factors (gender, age, smoking, hypertension, and diabetes mellitus) and IHD are within the expected range (Yusuf et al. 2004) except for marital status, which, surprisingly, yields a positive association with IHD, especially in older men. One possible explanation for this is that relatively

Table 2 Results of logistic regression modelling; regression coefficients *b* and their standard errors, odds ratios (OR) and 99% confidence intervals (CI) ($N = 37{,}290$); Medicare Health Outcome Survey, USA, 1998–2000

Variable	Regression coefficient *b*	Standard error of *b*	OR	99% CI
Main effects model				
Depression (0/1)	.425	.050	1.53	(1.34; 1.74)
Age (0 = 65–74/1 = ≥75)	.331	.045	1.39	(1.24; 1.56)
Gender (0 = f/1 = m)	.384	.048	1.47	(1.30; 1.66)
Education (0/1)*	.207	.050	1.23	(1.08; 1.40)
Marital status (0 = single/1 = ∞)	.128	.049	1.14	(1.002; 1.29)
Ever smoked (0/1)	.194	.047	1.21	(1.08; 1.37)
Diabetes mellitus (0/1)	.519	.057	1.68	(1.45; 1.94)
Hypertension (0/1)	.449	.044	1.57	(1.40; 1.76)
Additional separate interaction models				
+1-way interactions				
Depression × gender	.042	.104	1.04	(0.80; 1.36)
Depression × education	.072	.107	1.08	(0.82; 1.42)
Depression × marital status	.152	.106	1.16	(0.89; 1.53)
+2-way interactions				
Depression × gender × education	−.160	.190	0.85	(0.52; 1.39)
Depression × gender × marital status	.018	.186	1.02	(0.63; 1.65)
Depression × education × marital status	.134	.187	1.14	(0.71; 1.85)
+3-way interaction				
Depression × gender × education × marital status	1.050	.414	2.86	(0.99; 8.29)

The association of depressive symptoms

* Dichotomized as lower than high school education versus equal to or higher

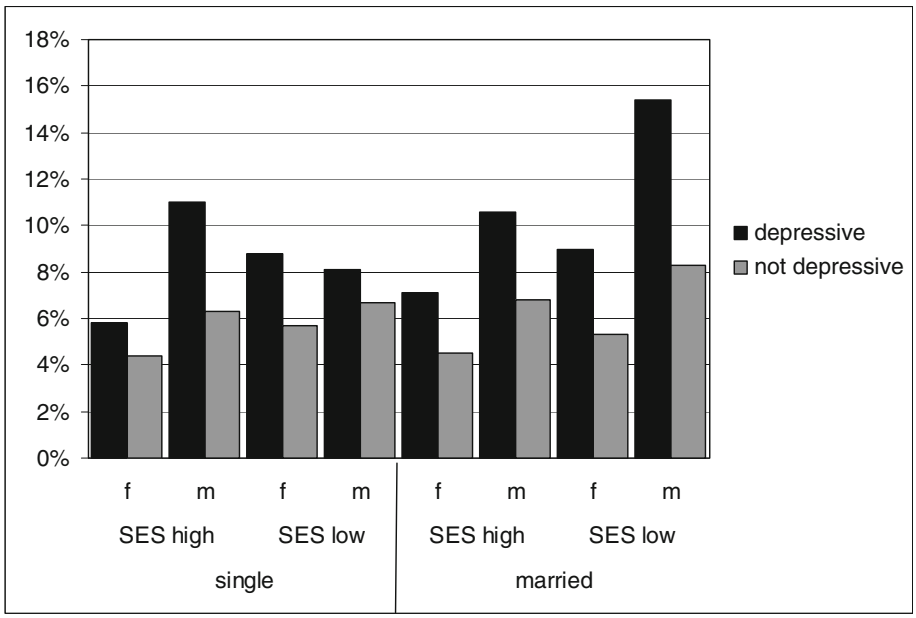

Fig. 2 Three-way-interactions of gender, education (socio-economic status; SES) and marital status with regard to ischemic heart disease morbidity (%); Medicare Health Outcome survey USA, 1998–2000

unhealthy men tend to remain in marriage longer or else remarry early (Lillard and Panis 1996), thus spuriously suggesting marriage being a risk factor. The impact of depression on subsequent coronary disease is consistent with other research (Barth et al. 2004; Nabi et al. 2010; Rugulies 2002). The risk of developing IHD within the following 2 years is about 50 percent higher in adults with depressive symptoms. This association is only weakened

marginally when controlling for somatic and behavioural risk factors such as smoking.

Contrary to what we hypothesized, we did not find any indication that gender, marital status, or education either alone or in combination moderate the association of depression and subsequent IHD in this sample of older adults. None of the interaction terms yielded statistical significance. That means the impact of depression was comparably strong in women and men, in well or less well educated persons, and in married people and singles alike. Also any possible combination of these variables (e.g. gender and marital status) yielded no statistically significant effects. These findings are all the more important since the sample is sufficiently powered to detect even small effects.

Other research has yielded similar results. Rosengren et al. (2004) found that the strength of the relationship between depression and the development of IHD was consistent across cultures, ethnicities, and also in women and men. Comparable results as to sex were presented by Frasure-Smith et al. (1999); Ariyo et al. (2000); Parashar et al. (2009). Surtees et al. (2008) found that the association between depression and IHD mortality was independent of age, sex, social class, and major behavioural or somatic risk factors. In a study of middle-aged women Horsten et al. (2000) found that the impact of depressive symptoms on the prognosis of IHD was independent of social support. With regard to marital status, Panagiotakos et al. (2008) found no interaction with depression on the short-term prognosis of acute coronary syndrome patients.

However, other studies have found higher cardiac mortality risks only in (elderly) women (Mendes de Leon et al. 1998) or else only in men (Marzari et al. 2005). Frasure-Smith et al. (2000), re-analysing data from previous trials, yielded a significant interaction between depression and social support, but only very high levels of social support appeared to buffer the impact of depression on cardiac mortality.

The paucity of persuasive findings on moderating effects of gender, SES and marital status on the association of depression and IHD seems striking. Our results also suggest that the association of depression and IHD is independent of pivotal demographic variables for the most part. One possible explanation for this finding is that the impact of factors that could buffer or amplify health hazards in this sample of older people might be weak as compared to medical conditions and old age as risk factors. However, other studies comprising younger samples have yielded similar results (Frasure-Smith et al. 1999; Surtees et al. 2008; Horsten et al. 2000).

Also, the possibility exists that the observed relationship between depression and subsequent development of IHD may not be predominantly causal, but rather results from a common factor such as a shared genetic vulnerability contributing to both depressive symptoms and IHD. Recently, this hypothesis has been investigated in a number of studies. In an exhaustive review of the existing evidence, McCaffery et al. (2006) presented literature supporting the hypothesis that common genetic mechanisms, in part, underlie depression and IHC (genetic pleiotropy), and they highlighted a number of promising candidate genes. Further research is needed to better understand the pathways linking depression and CHD.

Strength and limitations of this study

A decisive strength of our study is the large sample included and the prospective nature of the underlying data as well. Because of this the results presented here seem robust. Also, to our knowledge this is the only study so far that investigated the influence of three major moderating variables simultaneously. But our approach has several limitations, too. Depressive symptoms were assessed by three items only. This may be an acceptable screener for depressive symptoms (Orth-Gomér et al. 2005) but it is far from providing a diagnosis. However, Meyer et al. (2007) have presented results from the same data base on the association between depression and low back pain that are in favour of the validity of the items used here. Heart disease, diabetes and hypertension were assessed by interview questions and not by medical records, so the chance of recall bias exists. Also, important risk factors (e.g. sedentary lifestyle) are missing in our analysis since HOS does not include these variables. Finally, due to the nature of the underlying survey data, our results are limited to older adults. Further research is needed to reappraise our findings in a sample of younger persons.

Conflict of interest The authors declare that they have no competing interests.

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