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Gender-specific associations between coronary heart disease and other chronic diseases: cross-sectional evaluation of national survey data from adult residents of Germany

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Abstract

Background Combinations of coronary heart disease (CHD) and other chronic conditions complicate clinical management and increase healthcare costs. The aim of this study was to evaluate gender-specific relationships between CHD and other comorbidities. **Methods** We analyzed data from the German Health Interview and Examination Survey (DEGS1), a national survey of 8152 adults aged 18−79 years. Female and male participants with self-reported CHD were compared for 23 chronic medical conditions. Regression models were applied to determine potential associations between CHD and these 23 conditions. **Results** The prevalence of CHD was 9% (547 participants): 34% (185) were female CHD participants and 66% (362) male. In women, CHD was associated with hypertension (OR = 3.28 (1.81−5.9)), lipid disorders (OR = 2.40 (1.50−3.83)), diabetes mellitus (OR = 2.08 (1.24−3.50)), kidney disease (OR = 2.66 (1.101−6.99)), thyroid disease (OR = 1.81 (1.18−2.79)), gout/high uric acid levels (OR = 2.08 (1.22−3.56)) and osteoporosis (OR = 1.69 (1.01−2.84)). In men, CHD patients were more likely to have hypertension (OR = 2.80 (1.94−4.04)), diabetes mellitus (OR = 1.87 (1.29−2.71)), lipid disorder (OR = 1.82 (1.34−2.47)), and chronic kidney disease (OR = 3.28 (1.81−5.9)). **Conclusion** Our analysis revealed two sets of chronic conditions associated with CHD. The first set occurred in both women and men, and comprised known risk factors: hypertension, lipid disorders, kidney disease, and diabetes mellitus. The second set appeared unique to women: thyroid disease, osteoporosis, and gout/high uric acid. Identification of shared and unique gender-related associations between CHD and other conditions provides potential to tailor screening, preventive, and therapeutic options.

1 Introduction

There is growing awareness of the increased prevalence of chronic health conditions and the impact of these conditions on healthcare utilization.[1] One such chronic condition is coronary heart disease (CHD). CHD represents the single largest cause of death worldwide and its management is complicated by frequent associations with other multiple chronic conditions.[2] Furthermore, CHD exhibits gender differences; although the traditional risk factors do not differ between genders, the risk profiles and chronic diseases associated with CHD do.[3,4] CHD in women usually develops 7 to 10 years later than in men and remains the major cause of death. Estrogen exposure is assumed to account for the delayed CHD development.[3] However, women presenting with CHD often exhibit a wider array of different concomitant chronic diseases.[5,6] In addition, risk levels exhibit gender-related differences. For example, women with diabetes have a significantly greater risk of developing CHD versus diabetic men.[7] Also, mean low-density lipoprotein (LDL) in postmenopausal women is significantly higher than in men.[8] Furthermore, management of CHD presents more challenges and outcomes appear generally worse in women.[5] Such differences may be explained because women receive fewer screening tests and fewer medications for primary and secondary prevention of cardiovascular risk factors and CHD.[9]

The aim of our study was to assess the relationships between CHD and common chronic diseases using data from a national survey of adult residents of Germany. Identification of gender-related similarities and differences in the spec-

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trum of chronic diseases associated with CHD could improve screening approaches and enhance healthcare delivery.

2   Methods

2.1   Data

This study used data from the German Health Interview and Examination Survey for Adults (DEGS1), a national survey carried out by the Robert-Koch Institute.[10] The sample included 8152 adult permanent residents of Germany aged 18−79 years. Of these, 4193 persons were newly enlisted for the DEGS1 survey and 3959 had participated in the National Health Interview and Examination Survey (BGS98). Sampling was performed using a two-stage stratified cluster design. In the first stage, sample points were selected from a list of German communities and in the second stage, men and women were randomly selected from local population registries for each community. Information on health status, medical history, health-related behavior, socio-demographics, and anthropometry were collected from interviews, self-administered questionnaires, physical examinations, and from blood and urine samples. Description of the sampling strategy and the evaluation protocol have been published.[11]

2.2   Study population and study variables

Our study focused on participants with a self-reported history of CHD, with or without a history of myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention. A list of the questions asked and the answer options for each parameter in the survey is provided in supplementary Table S1. We identified 547 cases of self-reported CHD; all above 40 years of age. Consequently, we limited our analyses to people aged 40−79 years (5782 adults (3037 women and 2745 men)). The prevalence of the 23 common chronic conditions assessed in the survey was calculated for both women and men with and without CHD. We used multivariable logistic regression models to determine which of the 23 conditions were associated with CHD in women and men.

2.3   Statistical analysis

Descriptive statistics were used to examine characteristics of the study population. The multivariable logistic regression models used DEGS1 sample weights. These weights were adjusted for sampling and loss to follow-up, as well as deviations between the design-weighted net sample and German population statistics with respect to age, gender, region, nationality, municipality, and education, to represent the German population.[11] In accordance with previous studies, we also adjusted for age, social status, educational level, employment status, smoking status, and body mass index (BMI).[12] Results are presented as odds ratios (OR) with 95% confidence intervals (CI) and *P* values. To examine the robustness of our models, regression analyses were performed with and without sample weights, as well as with and without adjustment (Supplementary data, Table S2.1− S2.8). Analysis was performed using Stata (v.14.1; Stata-Corp, College Station, TX, USA).

3   Results

3.1   Population characteristics

In the DEGS1 survey, participation rate was 42% for first-time participants and 62% for participants who had taken part in the BGS98 survey. Of the 5782 participants, 9% self-reported CHD; 185 women and 362 men (66% *vs.* 34%; *P* < 0.001; Table 1). Social status and employment status were lower in women than men (low social status, 26% *vs.* 19%, low education status, 32% *vs.* 9%; both *P* < 0.001).

3.2   Prevalence of chronic diseases

Table 2 shows the prevalence of the chronic conditions in women and men with and without CHD. In the CHD population, hypertension was the most common chronic disease in both genders, affecting 81% of men and 80% of women. More than one-third of patients with CHD had a BMI ≥ 30 kg/m^2 in both genders. The prevalence of thyroid disease, depression, osteoporosis, anxiety disorders and migraine were higher in women with CHD than in men with CHD (all *P* < 0.001).

3.3   Associations between CHD and other chronic diseases

After controlling for possible confounders in multivariable analyses, CHD was significantly associated with seven of the examined chronic diseases in women and with four in men (Table 3, Model 3). All chronic diseases and their association with CHD in both genders are given in the supplementary data with and without DEGS1 population weights (supplementary Table S2.1−S2.6). In women, CHD showed the strongest association with hypertension (OR = 3.28, 95% CI: 1.81−5.94, *P* < 0.001). In addition, female CHD patients were more likely to have lipid disorders (OR = 2.4; 95% CI: 1.50−3.83, *P* < 0.001), diabetes mellitus (OR = 2.08; 95% CI: 1.24−3.50, *P* = 0.006), chronic kidney disease (OR= 2.66; 95% CI: 1.01−6.99, *P* = 0.047), thyroid disease

Table 1. Main characteristics of the study population (CHD population = 547 participants)

	Female (*n* = 185)	Male (*n* = 362)	*P*-value
CHD			
Within gender of study population	6.1%	13.3%	< 0.001
Within CHD population	33.8%	66.2%	< 0.001
Age groups			
40–49 yrs	9 (4.9%)	16 (4.4%)	
50–59 yrs	14 (7.6%)	46 (12.7%)	0.408
60–69 yrs	74 (40%)	135 (37.3%)	
70–79 yrs	88 (47.6%)	165 (45.6%)	
BMI status			
< 18.5 kg/m^2	1 (0.5%)	0	
18.5–25 kg/m^2	50 (27.5%)	79 (21.9%)	0.61
25 < 30 kg/m^2	68 (37.4%)	164 (45.6%)	
≥ 30 kg/m^2	63 (34.6%)	117 (32.5%)	
Physical activity (> 2.5 h/w)			
No	143 (84.1%)	280 (80.5%)	0.299
Yes	27 (15.9%)	68 (19.5%)	
Smoking status			
Smoker	85 (15.7%)	52 (14.4%)	
Ex-smoker	37 (20.6%)	223 (61.8%)	< 0.001
Never smoker	110 (61.1%)	86 (23.8%)	
Social status*			
Low	47 (26.1%)	67 (18.7%)	
Middle	112 (62.2%)	202 (56.3%)	< 0.001
High	21 (11.6%)	90 (25.1%)	
Educational status#			
Low	57 (31.7%)	33 (9.2%)	
Middle	97 (36.9%)	166 (46.2%)	< 0.001
High	26 (14.4%)	160 (44.6%)	
Employment status			
Never	8 (4.6%)	4 (1.2%)	
Previous	135 (78%)	259 (74.6%)	0.017
Current	30 (17.3%)	84 (24.2%)	

Data are presented as *n* (%) unless other indicated. The prevalence rates are adjusted with weights to reflect the German population. *Social status was defined according to a previously published index by Lampert, *et al*.[51] #Educational status was defined according to the International Standard Classification of Education (ISCED) 1997, low: (ISCED 0, 1 or 2), middle (ISCED 3 or 4), high (ISCED 5 or 6). BMI: body mass index; CHD: coronary heart disease.

(OR = 1.81; 95% CI: 1.18–2.79, *P* = 0.007), gout/high uric acid levels (OR = 2.08; 95% CI: 1.22–3.56, *P* = 0.008) and osteoporosis (OR = 1.69; 95% CI: 1.01–2.84, *P* = 0.047).

In men, the strongest association was between CHD and chronic kidney disease (CKD) (OR = 3.16; 95% CI: 1.49–6.73, *P* = 0.003). Male participants with CHD were also more likely to have hypertension (OR = 2.78; 95% CI: 1.94–4.04, *P* < 0.001), diabetes (OR = 1.87; 95% CI: 1.29–2.71, *P* = 0.001), lipid disorder (OR = 1.82; 95% CI: 1.34–2.43, *P* < 0.001).

Overall, no significant differences were found between analyses with and without DEGS1 weights, supporting the robustness of the identified associations (Table 3 and Table S2.1–S2.6). Adjustment for baseline covariates and for sample weights changed the results only for chronic kidney disease in women with CHD. Without adjustment and sample weighs, CHD was not associated with chronic kidney disease in women.

4 Discussion

In this analysis of national health survey date, we found that about 10% of participants suffered from CHD above 40 years of age. We identified several chronic conditions, all with important healthcare relevance, associated with CHD; some were unspecific to gender, while others appeared unique to women.

In general, traditional risk factors for CHD are considered to be similar in women and men. Nevertheless, there are gender differences in the prevalence of risk factors and chronic diseases. In our study, hypertension was overall the most common chronic disease in both genders, affecting 80% of women and 81% of men. This result is consistent with previous studies showing that hypertension is the most prevalent chronic disease in Germany, nearly equally represented in women and men.[13,14] Other chronic diseases such as thyroid disease, depression, osteoporosis, anxiety disorders, and migraine were significantly more frequent in women than in men.

We found that CHD was significantly associated with four chronic conditions in both genders, after adjustment for potential confounders. Three of these conditions, hypertension, diabetes and lipid disorders are well-known risk factors for CHD, described in detail in previous studies.[15,16] Our study supports prior research, but with added weight because the data were obtained from a national survey. Moreover, we found CHD was particularly associated with hypertension, with an odds ratio of more than threefold in female and more than twofold in male participants.

In addition to these chronic diseases, women and men with CHD seemed to be more likely to also have chronic kidney diseases. The association between CKD and CHD has been the subject of numerous studies; however, most trials assessed patients with CKD and evaluated the likelihood of also having CHD.[17,18] For example, Chonchol, *et al*.[18] demonstrated that patients with CKD had a high

Table 2.   Distribution of chronic diseases in women and men with and without CHD.

	Participants with CHD			Participants without CHD	
	Female (*n* = 185)	Male (*n* = 362)	*P*-value	Female (*n* = 2852)	Male (*n* = 2383)
	%	%		%	%
Hypertension	80.2	81.3	0.789	43.6	46.7
Joint pain in the last 12 months	79.8	67.2	0.003	67.6	58.6
Dyslipidemia	68.9	64.0	0.261	34.6	37.2
Osteoarthritis	51.1	37.8	0.004	33.1	23.9
Obesity (BMI ≥ 30 kg/m^2)	34.6	32.5	0.621	26.8	25.8
Gout or high uric acid	25	31.8	0.109	7.6	17.2
Diabetes mellitus	28	28.5	0.886	7.7	9.7
Thyroid disease	59.7	20.1	< 0.001	42.5	13.0
Stomach ulcers disease	14.8	16.2	0.68	8.1	9.7
Cancer	14	13.5	0.83	10.3	7.9
Depression	25.1	10.5	< 0.001	16.7	8.5
Stroke	9.4	9.5	0.961	2.0	3.2
Hepatitis	12	9.5	0.362	7.8	6.9
Chronic kidney disease	9.2	7.5	0.482	1.7	1.6
Asthma	12.7	6.9	0.026	8.5	6.0
Osteoporosis	28.7	5.9	< 0.001	11.6	3.0
Anxiety disorder	14.6	5.0	< 0.001	7.1	3.0
Migraine	25.7	4.4	< 0.001	18.6	5.0
Rheumatic arthritis	6.8	4.2	0.195	4.0	2.3
Burnout syndrome	5.4	2.8	0.127	5.7	4.2
Chronic inflammatory bowel disease	2.2	1.7	0.658	1.7	1.2
Epilepsy	1.6	1.1	0.609	1.2	1.7
Liver cirrhosis	0	0.8	0.261	0.2	0.8

The prevalence rates are adjusted with weights to reflect the German population. BMI: body mass index; CHD: coronary heart disease.

Table 3.   Association between CHD and chronic diseases in female and male.

Gender	Health condition	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Female	Hypertension	3.45 (2.00–5.93)*	2.83 (1.63–4.92)*	3.28 (1.81–5.94)*
	Lipid disorders	2.42 (1.56–3.76)*	2.15 (1.38–3.35)*	2.40 (1.50–3.83)*
	Diabetes	2.51 (1.54–4.10)*	2.24 (1.36–3.69)*	2.08 (1.24–3.50)*
	Chronic kidney disease	2.43 (0.99–5.95)	2.37 (0.92–6.13)	2.66 (1.01–6.99)*
	High uric acid or gout	2.06 (1.24–3.42)*	2.07 (1.23–3.47)*	2.08 (1.22–3.56)*
	Thyroid disease	1.62 (1.08–2.44)*	1.67 (1.10–2.53)*	1.81 (1.18–2.79)*
	Osteoporosis	2.33 (1.43–3.80)*	1.82 (1.11–2.99)*	1.69 (1.01–2.84)*
Male	Hypertension	3.09 (2.19–4.34)*	2.67 (1.87–3.78)*	2.78 (1.94–4.04)*
	Lipid disorders	1.85 (1.39–2.48)*	1.89 (1.39–2.55)*	1.82 (1.34–2.43)*
	Diabetes	2.22 (1.57–3.13)*	1.85 (1.29–2.65)*	1.87 (1.29–2.71)*
	Chronic kidney disease	3.58 (1.78–7.22)*	3.56 (1.74–7.31)*	3.16 (1.49–6.73)*
	High uric acid or gout	1.05 (0.76–1.46)	1.06 (0.75–1.48)	1.09 (0.77–1.55)
	Thyroid disease	1.40 (0.98–2.00)	1.22 (0.84–1.76)	1.13 (0.77–1.67)
	Osteoporosis	1.82 (0.91–3.65)	1.86 (0.92–3.77)	1.40 (0.65–3.03)

Odds ratio (OR) and 95% confidence interval (CI) obtained from multivariable logistic regression analysis; *Significant association. Model 1: Crude OR; Model 2: OR adjusted for age group, social status, education and employment status, smoking status, and body mass index; Model 3: OR adjusted for age group, social status, education and employment status, smoking status, and body mass index and with sample weights. CHD: coronary heart disease.

prevalence of CHD. The likelihood of CHD increased monotonically as glomerular filtration rate decreased not only is the frequent association between the two diseases important, but also the cumulative risk when both conditions are present in the same person.[19] It is well-known that the population with CHD and CKD has higher mortality regardless of the treatment used for coronary disease.[20] For example, among patients with acute coronary syndrome (ACS) who also have CKD, mortality is increased twofold versus patients with ACS and normal kidney function.[21] As far as we are aware, only one other study, by Sabe, *et al*.,[22] compared patients with and without CHD in regards to kidney function. They reported that patients with CHD were more likely to progress to end-stage renal disease.

The main pathophysiological mechanism involved in the CHD-CKD relationship appears to be endothelial dysfunction, which leads to the progression of atherosclerotic lesions.[23] Nonetheless, other mechanisms including inflammation, systemic arterial hypertension, and vascular calcification play important roles in the development of both chronic conditions.[24–26]

In women, CHD was also significantly associated with thyroid disease, gout or high uric acid levels, and osteoporosis. There is evidence to suggest an association between abnormal thyroid function and CHD.[27,28] For instance, Mayer, *et al*.[28] examined patients after acute myocardial infarction and demonstrated hypothyroidism was more prevalent in patients with clinical CHD. Similar to our study, thyroid dysfunction was more prevalent in female than in male CHD patients (23% *vs*. 7%, respectively). Consequently, thyroid function screening seems warranted, especially in female coronary patients. This is important because CHD, with concomitant thyroid dysfunction, is associated with a more severe clinical condition and with poorer clinical outcomes.[23,29] For example, Friberg, *et al*.[29] reported about 20% of patients experienced a decrease of free triiodo-thyronine (FT3) levels after myocardial infarction. FT3 was the most important predictor of subsequent cardiac events.[23] In another study of patients with CHD, thyroid dysfunction including subclinical hypothyroidism, subclinical hyperthyroidism and low T3 syndrome were associated with higher incidence of major cardiac events.[30] Furthermore, thyroid concentration alterations have been associated with worse prognosis in patients with ischemic left ventricular dysfunction in chronic stable heart failure.[31] Potential mechanisms that link coronary artery disease with thyroid dysfunction are endothelial dysfunction, dyslipidemia, myocardial systolic and diastolic dysfunction, and changes in blood pressure.[32–34] Several studies have demonstrated that thyroid

hormones regulate endothelial nitric oxide production and vascular tone and that patients with hypothyroidism exhibit impaired endothelial function.[35] Also, hypothyroidism is associated with hypercholesteremia and a marked increases in low-density lipoproteins and apolipoprotein B, which promotes atherogenesis.[34] In contrast, hyperthyroidism causes a hyperdynamic circulation with increased blood pressure, cardiac output, and contractility.[33]

CHD was also associated with gout or high uric acid levels in women. Gout and cardiovascular disease frequently coexist in the general population.[36] Our results confirmed this relationship and suggest that female CHD patients are more likely to also have gout than female patients without CHD. This is important because the co-occurrence of both chronic conditions may worsen outcomes. A recent study assessed the long-term association between gout and CHD in men and women.[37] The data suggest gout is associated with worse long-term cardiovascular clinical outcomes and all-cause mortality in patients with CHD. Another study focused on male patients with gout and known CHD. In this Canadian survey, the presence of gout was associated with a 26% increase in the risk of cardiovascular death.[38] Possible mechanisms that may provide a link between gout and CHD are oxidative stress and inflammation.[39] Oxidative stress is generated by xanthine oxidase, an enzyme that catalyzes the formation of uric acid.[40] Allopurinol, a xanthine oxidase inhibitor, has been shown to reduce oxidative stress and mitigate endothelial dysfunction in patients with stable CHD.[41] Furthermore, low-grade inflammation has an important role in the pathogenesis of CHD and gout.[42] Previous work has failed to establish if uric acid plays a definite role in CHD or is simply highly correlated with known risk factors such as hypertension and lipid disorders.[43] However, the association in women, but not in men, gives support to the former interpretation.

In women, CHD was also associated with osteoporosis. Research demonstrates that CHD and osteoporosis often present together. For example, women with osteoporosis showed a 3.9-fold increased risk for cardiovascular events.[44] Another study, by Markovitz, *et al*.,[45] demonstrated that osteoporosis was associated with angiographically-determined CHD in women (OR = 5.6; 95% CI: 2.6–12.0). Both chronic conditions share common risk factors, such as smoking, low physical activity, and elevated BMI.[46] In addition, potential pathophysiological mechanisms that may link osteoporosis and CHD have been suggested. These include low bone mineral density, oestrogen deficiency, inflammatory process, oxidized lipids, vitamin K deficiency, and vitamin D metabolism.[47]

Our results demonstrate that the association between CHD and other chronic diseases differ in women and men. Identifying gender-specific needs is essential to develop new strategies to improve patients' outcomes and manage resource allocation. Future research should aim to clarify if special programs for CHD patients addressing these gender-specific comorbidity associations in advance reduce inpatient care and decrease healthcare costs.

4.1 Limitations

The diagnosis for CHD was obtained by a self-administered questionnaire. Misclassification of CHD cannot be excluded, because, especially in women, CHD is often under-diagnosed due to public and professional under-appreciation of women's coronary risk.[48] Nevertheless, a Norwegian survey found a very high positive predictive value (93%) for CHD.[49] Similarly, our study used self-reported measures of behavioral factors, such as smoking status, and chronic diseases and so their prevalence may be underestimated.[50] Although the survey's overall participation rate (about 50%) was similar to other European national health surveys, we cannot rule out selection bias.[50] Reasons for non-participation were lack of time, health-related issues and language problems.[10] The main limitation of cross-sectional studies is that cause and effect cannot be determined. Therefore, we do not know if CHD was present before the other comorbidities, occurred afterwards, or developed simultaneously. These distinctions will be relevant for screening, but, not in terms of treatment once they are present. Lastly, we cannot rule out the presence of residual confounding.

4.2 Conclusion

Our analysis of national survey data revealed that CHD was associated with two sets of chronic condition, one shared by both genders and the second found only in women. The shared set comprised three well-known risk factors for CHD (hypertension, lipid disorders, and diabetes mellitus) and chronic kidney disease. The second set found in women consisting of thyroid disease, osteoporosis and gout/high uric acid may be of greater interest in terms of both optimizing screening and treatment strategies.

Acknowledgments

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Supplementary Data

Table S1.   DEGS1 survey and list of variables.

Variable	Variable code	Questions and answer categories
Gender	Sex	What is your gender? 1 Male 2 Female
Age	Age10B	When were you born? Day/months/year
BMI	USbmi_st	How much do you weight without clothes? How tall are you without shoes?
Physical activity	KAempf_k2	Do you exercise 2.5 hours per week or more? 1 Yes 2 No
Smoking	RCstat_k	Do you currently smoke-even if it's only occasionally? 1 Yes, daily 2 Yes, occasionally 3 No, not anymore 4 Have never smoked
Social status*	SDses	Socioeconomic status: 1 low 2 medium 3 high
Education status	SDisced97eu	Education level: 0 Pre-primary 1 Primary 2 lower secondary 3 Upper secondary 4 Post-secondary non-tertiary 5 First stage tertiary 6 Second stage of tertiary education Low (ISCED 0,1 or 2) Middle (ISCED 3 or 4) High (ISCED 5 or 6)
Employment status	SDerwtB	Are you currently employed? This means any paid activity or activity associated with income, regardless of the timescale? Note: occasional workers, who are not presently in work, are also regarded as employed. 1 Yes 2 No
Chronic diseases		
CHD	KHkhkmyo	Has a doctor ever told you that you have circulatory disorders in the heart or a narrowing of the coronary arteries? Note: coronary heart disease or angina pectoris is also referred to here. 1 Yes 2 No Or Has a doctor ever diagnosed you with a heart attack? 1 Yes 2 No
Hypertension	KHhyp	Has a doctor ever told you that you have high blood pressure or hypertonia in you? Note: this only means medical diagnoses! 1 Yes 2 No
Joint pain	SZglk12	Have you had joint pain in the last 12 months?
Dyslipidemia	KHlipB	Has a doctor ever detected elevated blood lipids or high cholesterol levels in you? 1 Yes 2 No
Obesity	USadipos	Measured weight
Osteoarthritis	KHdge	Has a doctor ever told you that you have arthrosis or degenerative joint disease? Note: arthrosis = osteoarthritis. 1 Yes 2 No
Thyroid disease	KHsd	Has a doctor ever told you that you have a disease of the thyroid? 1 Yes 2 No
Gout/high uric acid level	KHhs	Has a doctor ever told you that you have a high uric acid level or gout? 1 Yes 2 No
Diabetes mellitus	KHdiab	Has a doctor ever told you that you have a sugar‐related illness or diabetes? 1 Yes 2 No
Depression	PKdepB	Are you currently treated for depression? 1 Yes 2 No
Cancer	KHkarz	Has a doctor ever told you that you have cancer or a malignant tumor? 1 Yes 2 No
Stroke	KHsa	Has a doctor ever told you that you have a stroke? 1 Yes 2 No
Ulcus disease	KHulc	Has a doctor ever told you that you have an ulcer disease? 1 Yes 2 No
Chronic kidney disease	KHni	Has a doctor ever told you that you have chronic kidney disease? 1 Yes 2 No
Asthma	KHab	Has a doctor ever told you that you have asthma? 1 Yes 2 No
Migraine	KHmig	Has a doctor ever told you that you have migraine? 1 Yes 2 No
Burn out syndrome	KHbos	Has a doctor ever told you that you have burn out syndrome? 1 Yes 2 No
Chronic inflammatory bowel disease	KHced	Has a doctor ever told you that you have chronic inflammatory bowel disease? 1 Yes 2 No
Epilepsy	KHelep	Has a doctor ever told you that you have epilepsy? 1 Yes 2 No
Liver cirrhosis	KHlz	Has a doctor ever told you that you have liver cirrhosis? 1 Yes 2 No
Anxiety Disorder	PKangst	Has a doctor ever told you that you have anxiety disorder? 1 Yes 2 No
Osteoporosis	KHos	Has a doctor ever told you that you have osteoporosis\? 1 Yes 2 No
Rheumatic arthritis	KHraC	Has a doctor ever told you that you have rheumatic arthritis? 1 Yes 2 No
Hepatitis	KHhep	Has a doctor ever told you that you have hepatitis? 1 Yes 2 No

*The social status was calculated with a previously published index by Lampert et al. (2013).[51]

Table S2.1. Model 1- Association between CHD and chronic diseases analyzed in women without weights and without adjustment.

Chronic disease	OR	95% CI	p-value
Hypertension	3.45	2.00 to 5.93	0.000
Stroke	1.67	0.74 to 3.78	0.221
Diabetes mellitus	2.51	1.54 to 4.10	0.000
Thyroid disease	1.62	1.08 to 2.44	0.020
Adiposity (BMI ≥ 30)	1.05	0.67 to 1.65	0.832
Dyslipidemia	2.42	1.56 to 3.76	0.000
Chronic kidney disease	2.43	0.99 to 5.95	0.051
Cancer	1.26	0.72 to 2.18	0.420
Gastric ulcer	0.95	0.51 to 1.78	0.879
Chronic inflammatory bowel syndrome	0.94	0.23 to 3.94	0.934
Liver cirrhosis	0.00	0.00	0.999
Osteoarthrosis	1.09	0.70 to 1.70	0.696
Rheumatic arthritis	0.79	0.31 to 2.04	0.632
Osteoporosis	2.33	1.43 to 3.80	0.001
Gout or high uric acid	2.06	1.24 to 3.42	0.005
Migraine	1.19	0.73 to 1.94	0.490
Epilepsy	0.47	0.05 to 4.33	0.507
Depression	0.87	0.49 to 1.56	0.648
Anxiety disorder	1.80	0.88 to 3.68	0.105
Burn out syndrome	0.43	0.14 to 1.37	0.154
Asthma	1.28	0.68 to 2.43	0.447
Joint pain in the last 12 months	0.94	0.55 to 1.59	0.807
Hepatitis	1.02	0.52 to 1.98	0.961

Table S2.2. Model 1- Association between CHD and chronic diseases analyzed in men without weights and without adjustment.

Chronic disease	OR	95% CI	p-value
Hypertension	3.09	2.19 to 4.34	0.0001
Stroke	1.29	0.73 to 2.31	0.380
Diabetes mellitus	2.22	1.57 to 3.13	0.0001
Thyroid disease	1.40	0.98 to 2.00	0.063
Adiposity (BMI ≥ 30)	1.06	0.77 to 1.46	0.709
Dyslipidemia	1.85	1.39 to 2.48	0.0001
Chronic kidney disease	3.58	1.78 to 7.22	0.0001
Cancer	1.32	0.87 to 2.01	0.194
Gastric ulcer	1.13	0.74 to 1.71	0.576
Chronic inflammatory bowel syndrome	0.96	0.26 to 3.53	0.956
Liver cirrhosis	0.77	0.18 to 3.22	0.715
Osteoarthrosis	1.16	0.84 to 1.59	0.375
Rheumatic arthritis	1.36	0.63 to 2.96	0.436
Osteoporosis	1.82	0.91 to 3.65	0.093
Gout or high uric acid	1.05	0.76 to 1.46	0.756
Migraine	0.79	0.382 to 1.64	0.525
Epilepsy	0.65	0.16 to 2.59	0.541
Depression	1.05	0.60 to 1.82	0.873
Anxiety disorder	1.95	0.90 to 4.20	0.089
Burn out syndrome	0.38	0.13 to 1.14	0.083
Asthma	0.91	0.49 to 1.71	0.775
Joint pain in the last 12 months	1.12	0.82 to 1.54	0.475
Hepatitis	1.63	0.98 to 2.59	0.036

Table S2.3. Model 2- Association between CHD and chronic diseases analyzed in women without weights and adjusted for age group, social status, education and employment status, smoking status, and body mass index.

Chronic disease	OR	95% CI	p-value
Hypertension	2.83	1.63 to 4.92	0.0001
Stroke	1.36	0.59 to 3.07	0.466
Diabetes mellitus	2.24	1.36 to 3.69	0.002
Thyroid disease	1.67	1.10 to 2.53	0.016
Adiposity (BMI ≥ 30)	1.05	0.66 to 1.67	0.827
Dyslipidemia	2.15	1.38 to 3.35	0.001
Chronic kidney disease	2.37	0.92 to 6.13	0.074
Cancer	1.13	0.65 to 1.98	0.667
Gastric ulcer	0.86	0.46 to 1.62	0.647
Chronic inflammatory bowel syndrome	1.15	0.27 to 4.78	0.845
Liver cirrhosis	0.00	0.00	0.999
Osteoarthrosis	0.94	0.59 to 1.47	0.779
Rheumatic arthritis	0.82	0.32 to 2.12	0.678
Osteoporosis	1.82	1.11 to 2.99	0.058
Gout or high uric acid	2.07	1.23 to 3.47	0.006
Migraine	1.24	0.75 to 2.05	0.411
Epilepsy	0.66	0.08 to 5.51	0.701
Depression	0.93	0.51 to 1.68	0.801
Anxiety disorder	1.71	0.83 to 3.50	0.145
Burn out syndrome	0.62	0.19 to 2.03	0.426
Asthma	1.20	0.62 to 2.32	0.599
Joint pain in the last 12 months	1.01	0.59 to 1.72	0.974
Hepatitis	0.98	0.49 to 1.98	0.961

Table S2.4. Model 2- Association between CHD and chronic diseases analyzed in men without weights and adjusted for age group, social status, education and employment status, smoking status, and body mass index.

Chronic disease	OR	95% CI	p-value
Hypertension	2.67	1.87 to 3.78	0.000
Stroke	0.91	0.50 to 1.67	0.769
Diabetes mellitus	1.85	1.29 to 2.65	0.001
Thyroid disease	1.22	0.84 to 1.76	0.304
Adiposity (BMI ≥ 30)	1.19	0.85 to 1.67	0.310
Dyslipidemia	1.89	1.39 to 2.55	0.000
Chronic kidney disease	3.56	1.74 to 7.31	0.001
Cancer	0.99	0.64 to 1.54	0.979
Gastric ulcer	0.99	0.64 to 1.54	0.988
Chronic inflammatory bowel syndrome	0.84	0.22 to 3.14	0.791
Liver cirrhosis	0.60	0.13 to 2.73	0.513
Osteoarthrosis	1.05	0.76 to 1.48	0.747
Rheumatic arthritis	1.09	0.49 to 2.44	0.823
Osteoporosis	1.86	0.92 to 3.77	0.085
Gout or high uric acid	1.06	0.75 to 1.48	0.757
Migraine	0.92	0.44 to 1.95	0.835
Epilepsy	0.74	0.19 to 2.91	0.667
Depression	1.18	0.68 to 2.07	0.555
Anxiety disorder	1.86	0.85 to 4.09	0.121
Burn out syndrome	0.53	0.17 to 1.63	0.268
Asthma	0.89	0.47 to 1.70	0.728
Joint pain in the last 12 months	1.18	0.85 to 1.65	0.322
Hepatitis	1.60	0.99 to 2.58	0.053

Table S2.5. Model 3- Association between CHD and chronic diseases analyzed in women with weights and adjusted for age group, social status, education and employment status, smoking status, and body mass index.

Chronic disease	OR	95% CI	p-value
Hypertension	3.28	1.81 to 5.94	0.0001
Stroke	1.46	0.63 to 3.39	0.374
Diabetes mellitus	2.08	1.24 to 3.50	0.006
Thyroid disease	1.81	1.18 to 2.79	0.007
Adiposity (BMI ≥ 30)	1.02	0.63 to 1.64	0.934
Dyslipidemia	2.40	1.50 to 3.83	0.0001
Chronic kidney disease	2.66	1.01 to 6.99	0.047
Cancer	1.01	0.56 to 1.83	0.972
Gastric ulcer	0.694	0.35 to 1.37	0.291
Chronic inflammatory bowel syndrome	1.21	0.27 to 5.38	0.799
Liver cirrhosis	0.000	0.000	0.999
Osteoarthrosis	0.98	0.61 to 1.56	0.923
Rheumatic arthritis	0.89	0.34 to 2.35	0.818
Osteoporosis	1.69	1.01 to 2.84	0.055
Gout or high uric acid	2.08	1.22 to 3.56	0.008
Migraine	1.31	0.08 to 2.21	0.308
Epilepsy	0.64	0.07 to 5.71	0.690
Depression	1.03	0.56 to 1.88	0.926
Anxiety disorder	1.56	0.74 to 3.30	0.243
Burn out syndrome	0.63	0.19 to 2.10	0.449
Asthma	1.32	0.67 to 2.59	0.418
Joint pain in the last 12 months	1.02	0.59 to 1.8	0.945
Hepatitis	1.18	0.59 to 2.40	0.636

Table S2.6. Model 3- Association between CHD and chronic diseases analyzed in men with weights and adjusted for age group, social status, education and employment status, smoking status, and body mass index.

Chronic disease	OR	95% CI	p-value
Hypertension	2.80	1.94 to 4.04	0.0001
Stroke	0.94	0.51 to 1.74	0.837
Diabetes mellitus	1.87	1.29 to 2.71	0.001
Thyroid disease	1.13	0.77 to 1.67	0.527
Adiposity (BMI ≥ 30)	1.10	0.78 to 1.56	0.578
Dyslipidemia	1.82	1.34 to 2.47	0.0001
Chronic kidney disease	3.16	1.49 to 6.73	0.003
Cancer	1.05	0.67 to 1.65	0.822
Gastric ulcer	1.05	0.67 to 1.63	0.840
Chronic inflammatory bowel syndrome	0.89	0.23 to 3.41	0.862
Liver cirrhosis	0.74	0.16 to 3.47	0.698
Osteoarthrosis	0.99	0.71 to 1.41	0.982
Rheumatic arthritis	1.17	0.53 to 2.61	0.695
Osteoporosis	1.40	0.65 to 3.03	0.388
Gout or high uric acid	1.09	0.77 to 1.55	0.608
Migraine	0.95	0.45 to 2.01	0.896
Epilepsy	0.52	0.11 to 2.53	0.418
Depression	1.16	0.66 to 2.06	0.604
Anxiety disorder	1.56	0.662 to 3.68	0.308
Burn out syndrome	0.57	0.19 to 1.75	0.324
Asthma	0.89	0.46 to 1.73	0.733
Joint pain in the last 12 months	1.28	0.91 to 1.80	0.153
Hepatitis	1.52	0.92 to 2.50	0.100