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ORIGINAL ARTICLE

Unfavourable life-course social gradient of coronary heart disease within Spain: a low-incidence welfare-state country

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Abstract
Objective Social position has yet to be established as a risk factor of coronary heart disease (CHD). Our aim was to investigate an individual life-course social position gradient link with CHD incidence in the EPIC-Spain cohort.
Methods 41,066 participants, mostly 30–65 years old, and free of cardiovascular disease at baseline (1992–1996) were followed up for a mean of 10.4 years. A combined score of paternal occupation in childhood and own adult education was used to assess individual life-course risk accumulation. Hazard ratios of CHD were estimated using Cox models, stratifying by centre, and age, and adjusting for cardiovascular risk factors.
Results 583 participants (80 % men) developed a definite CHD event. Paternal occupational class IV was associated with CHD in all models in men. The educational gradient remained significant after adjusting for diet and physical activity ($p = 0.01$). All adjusted risk of incident CHD rose by 23 % (95 % CI 6–42 %) per category increase of life-course social position score in men. No significant associations were found in women.
Conclusions Individual life-course social position gradient was adversely related to incident CHD in Spanish men.

Keywords Coronary heart disease · Life-course social position · Cohort study · Cardiovascular risk factors · Spain

Introduction

Poor social and economic circumstances affect health throughout life (Wilkinson and Marmot 2010). Disease in

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adulthood is often a result of the cumulative effect of pathological conditions or risk factors over a long period of time, some of which take place during infancy and childhood. According to the cumulative life-course hypothesis, social factors in early and later life may give rise to disease risk in adulthood (Davey-Smith et al. 1998; Ben-Shlomo and Kuh 2002). Most prospective evidence suggests that socio-economic circumstances during both childhood and adulthood contribute to adult coronary heart disease (CHD) mortality (Galobardes et al. 2006). Furthermore, a literature review of prospective studies showed not only higher levels of cardiovascular disease risk factors among disfavoured socio-economic groups, but also that childhood and adulthood socio-economic circumstances were important determinants for developing or dying from a cardiovascular disease (Galobardes et al. 2004, 2008). Cohort studies focusing on incident CHD have been mainly performed in Western countries with high coronary mortality rates (WHO 2010a), such as the USA, UK, and Scandinavia (Loucks et al. 2009; Pollitt et al. 2005; Singh-Manoux et al. 2004). Welfare regimes and wealthy social democracies show the most consistent salutary effects on population health outcomes (Muntaner et al. 2011), but socio-economic differences in health may still persist even in these settings. A recent meta-analysis evidenced a significant increase in the risk of acute myocardial infarction amongst the lowest socio-economic position categories, which was less consistent in low- or middle-income countries (Manrique-Garcia et al. 2011). However, only a limited number of prospective studies (Salomaa et al. 2000; Diez Roux et al. 2001; Rosvall et al. 2006; Rosenlund et al. 2009; Andersen et al. 2005) in that meta-analysis addressed the key issue of whether a gradient existed across the whole range of social positions rather than between a disfavoured minority or stratum and favoured groups (Manrique-Garcia et al. 2011). Very few prospective data on social determinants of CHD risk exist in affluent countries with low CHD, except for Japan, where no associations between education and incident coronary heart disease were found (Honjo et al. 2010), and France, where life-course adult occupational trajectory was found to be a predictor of cardiovascular mortality, regardless of childhood socio-economic circumstances (Melchior et al. 2006). In Spain, the country rates of CHD incidence and mortality have historically been among the lowest, after Japan and France (Marrugat et al. 2004; WHO 2010a).

In this context, our objective was to assess if there is an individual life-course social position gradient in the incidence of CHD risk in adult women and men within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort in Spain.

Methods

Sample characteristics

The EPIC research project is a large prospective study involving population from ten European countries. Details of the methodology employed in the EPIC study have been published previously (Riboli and Kaaks 1997; Riboli et al. 2002). The present analysis studied 41,438 Spanish participants (62 % women), recruited among healthy volunteers, including blood donors, civil servants, and the general population. The cohort covers a diverse range of socio-occupational levels and territorial idiosyncrasies of five Spanish provinces from the north/Atlantic Ocean (Asturias, Guipúzcoa, Navarra) and south/Mediterranean Sea (Murcia and Granada) environments, mostly aged 30–65 years at recruitment in 1992–1996 and who were followed up until December 2004 (mean follow-up = 10.4 years). At recruitment, all participants gave their informed consent, and the Ethical Review Board of Bellvitge Hospital (Barcelona) approved the project.

Assessment of life-course social position

Data on education and paternal occupation were gathered by trained personnel during a personal interview. Participants were asked about the age at which they had finished their studies and their highest educational qualification attained, and grouped into: no formal education, primary school, technical training, secondary school, and university degree or higher. The childhood social position based on father's occupation when the participant had been 10 years was also registered, coded into the national version (CNO-94) of the International Standard Classification of Occupations (ISCO88), and further assigned to an employment category for standard epidemiological analysis and presentation (Álvarez-Dardet et al. 1995). Occupational grouping was: I (managers, administrators and professionals, higher-grade); II (others managers administrators, and professionals, and technicians); III (self-employed and staff services sector and supervisors workers); IV (semiskilled/skilled manual workers) and V (unskilled manual workers). Less than 6 % of the cohort ($n = 2{,}332$) had missing data on the exposure variables. A hierarchical combination score of childhood and adult social position was then computed in order to assess the individual life-course risk accumulation, as the points sum for own adult education (university = 0 points, secondary = 1 point, technical = 2 points, primary = 3 points, non-primary = 4 points) plus childhood paternal occupational category (I = 0 points, II = 1 point, III = 2 points, IV = 3 points, V = 4 points). A higher score denoted a lower social position. The score was categorised into upper (0–2 points), middle (3–5 points) and lower (6–8 points) classes.

Lifestyle, Mediterranean diet, clinical information and anthropometric measurements

Extensive baseline data were also collected on several risk or protective factors and potential confounders. Habitual dietary intake was assessed with a validated dietary history method (EPIC Group of Spain 1997a, b) which inquired about the foods consumed during a typical week of the previous year. Total energy intake (in kcal/day), alcohol consumption (in g/day) and nutrient intake were estimated with the use of specific food composition tables. A Mediterranean diet score, computed as described by Buckland et al. (2009), was introduced in the models as a means of controlling for the main effect of diet on CHD risk. The non-dietary questionnaire recorded data on cigarette smoking (age at start, age at quitting, and intensity). Smoking status was defined as: never smoker; former smoker for 10 years or more; former smoker for less than 10 years; current smoker of up to 10 cigarettes/day; current smoker of 11–20 cigarettes/day; current smoker of more than 20 cigarettes/day; or unknown. Age at starting cigarette consumption in ever smokers was also accounted for in the analyses. Moreover, the non-dietary questionnaire documented self-reported prevalence of diabetes (yes/no/unknown), hypertension (yes/no/unknown), and hyperlipidaemia (yes/no/unknown). Women were asked about ever use of oral contraceptives or hormonal replacement therapy, as well as menopausal status. The Cambridge Physical Activity Index was used as an overall measure of physical activity level (inactive, moderately inactive, moderately active, and active) (Wareham et al. 2003). Height (in cm), weight (in kg), and waist circumference (in cm) were measured in all participants following standard procedures. Body mass index was computed as weight divided by square height and grouped into standard normal categories (normal weight, <25 kg/m^2; overweight, 25–30 kg/m^2; and obese, $\geq$ 30 kg/m^2). Drug use during the past 7 days was recorded and coded according to the WHO Anatomical Therapeutic Chemical classification. Consumption of antithrombotic or antihaemorrhagic (codes B01, B02), or cardiovascular drugs (codes C01–C10) and salicylic acid derivatives (code N02BA) was controlled for in the analyses.

Ascertainment and validation of coronary heart disease endpoints

Fatal and non-fatal CHD events were identified from self-reported questionnaire data at recruitment and at 3-year follow-up in all centres, as well as by record linkage with three sources of information covering the 1992–2004 period: (a) hospital discharge databases; (b) population-based myocardial infarction registries (Navarra, Guipúzcoa, and Murcia); and, for fatal events, (c) regional and national mortality registries in all centres (Larrañaga et al. 2009). The linkage between mortality and hospital discharges was made by reviewing the following International Classification of Disease (ICD) codes for CHD (codes ICD-9: 410–414; ICD-10: I20–I25). A validation process was carried out to confirm and classify the coronary events identified. Patient hospital medical and coroner autopsy reports of potential cases were reviewed by a team of trained nurses and physicians. The coronary heart events were classified on the basis of symptoms, enzymes, electrocardiograms and biomarker findings, and autopsy results according to the MONICA criteria (WHO 2010b) and the American Heart Association scientific statement of 2003 (Luepker et al. 2003). CHD events were defined as definite (fatal or non-fatal myocardial infarction or unstable angina requiring revascularisation procedures), or possible (fatal or non-fatal myocardial infarction in those cases which did not meet all diagnostic criteria, and fatal CHD with insufficient information). The event was considered an incident if there was no indication of a definite CHD in the patient's records before recruitment. Otherwise, CHD cases were considered as prevalent and excluded from analyses ($n = 193$). Events that did not meet all diagnostic criteria and fatal CHD events with insufficient information were censored at the time of the cardiovascular event and considered as non-cases ($n = 100$). After exclusion of prevalent cases ($n = 193$) and participants with extreme energy intake ($n = 167$), or missing values on the exposure ($n = 2{,}271$) or follow-up data ($n = 12$), a total of 583 definite incident CHD cases (80 % men) were available for analysis: 448 acute myocardial infarctions and 135 heart anginas treated with coronary revascularisation surgery.

Statistical analyses

Summary statistics are presented as mean and standard deviations for continuous data, and absolute and relative frequencies for categorical variables. Separate results for women and men are shown stratified by own education and father's occupation. Educational and occupational indicators gradients were obtained for descriptive baseline data by means of linear regression slopes and their statistical significance. Hazard ratios (HR) and 95 % confidence intervals (95 % CI) of incident CHD risk by levels of social indicators were calculated using Cox proportional hazards regression. All models were stratified by centre and age at recruitment (in 5-year categories). Age was the underlying time variable, with entry time defined as age at recruitment, and exit time as age at the date of the CHD diagnosis, emigration, death, or end of follow-up, whichever occurred first.

Models were fitted separately for women and men. Final models were controlled for height, weight, waist circumference, Mediterranean diet score (per unit increase), total energy intake, alcohol consumption, physical activity index, smoking status, start of cigarette smoking before age of 20, and self-reported diabetes, hypertension, hyperlipidaemia and cardiovascular drug use. Models for women were additionally adjusted for ever use of contraceptive pills, hormonal replacement therapy, and menopausal status. The highest level of the social indicators was selected as the reference category. The proportionality assumption was tested on the basis of Schoenfeld residuals, and no major violations were detected.

All statistical analyses were performed with STATA (version 10, StatCorp LP, College Station, TX). The level of statistical significance was set at 5 %.

Results

Table 1 shows the distribution of CHD cases according to categories of social indicators. The incidence of CHD in the whole cohort was higher among men and women with childhood paternal occupational classes IV as well as among men with primary education completed, but, on the contrary, among the most educated women.

Sample baseline characteristics for women and men are presented in Tables 2 and 3, respectively, according to childhood paternal occupation and own educational attainment, together with significant values (beta coefficients) for social gradient. In women, both childhood and adult indicators were inversely associated to BMI; while in men only adult own education was. Gradients towards lower height and larger waist circumference were found by decreasing social categories, in both sexes. Men of lower social position during childhood were more physically active, whereas women of lower childhood or adult social position were more inactive. The life-course score of social

Table 1 Distribution of coronary heart disease cases (CHD) by childhood paternal occupation, own adult education and life-course social position. The EPIC-Spain Cohort, 1992–1996 to 2004

	N (men/women)	Men			Women		
		Person-years	Cases	CHD rate (95 % CI)[a]	Person-years	Cases	CHD rate (95 % CI)[a]
Childhood paternal occupation[b]							
I	421/594	4,438	7	153.8 (38.1–269.4)	6,231	1	21.4 (0–63.2)
II	1,589/2,693	16,638	35	240.6 (130.8–350.5)	28,084	17	59.3 (29.1–89.5)
III	5,073/7,840	52,588	153	275.3 (223.7–326.9)	81,471	32	46.5 (30.3–62.8)
IV	2,372/3,510	24,634	103	379.2 (303.1–455.3)	36,735	19	67.8 (36.4–99.3)
V	5,306/9,307	54,425	169	273.8 (232.1–315.4)	96,029	47	57.7 (40.8–74.7)
Unemployed	40/50	422	0	–	505	0	–
Own adult education							
University	2,267/2,420	23,943	44	241.2 (159.5–323.0)	25,260	11	70.3 (24.2–116.5)
Secondary	1,226/1,410	12,737	30	267.4 (167.3–367.6)	14,698	6	52.2 (0–107.3)
Technical	1,955/1,388	20,447	50	243.7 (167.6–319.7)	14,417	2	32.8 (0–88.7)
Primary	5,710/10,022	59,332	205	307.5 (264.1–350.8)	105,697	33	41.4 (26.1–56.6)
No primary	3,643/8,754	36,687	138	292.9 (240.4–345.4)	88,982	64	57.7 (43.3–72.1)
Life-course social position							
Upper	1,936/2,254	20,461	42	258.2 (168.1–348.3)	23,609	11	70.7 (25.2–116.3)
Middle	5,582/7,641	58,154	147	246.8 (205.3–288.4)	79,868	26	41.1 (24.1–58.2)
Lower	7,243/14,049	74,108	278	312.4 (275.5–349.4)	145,073	79	58.2 (45.2–71.2)
All	14,801/23,994	153,146	467	283.7 (254.1–313.2)	249,055	116	54.4 (44.2–64.6)

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[a] CHD rates per 100,000 person-years and for the 30–64 years age-band standardised to the European Standard population using the direct method

[b] Occupational class: I (professionals, administrators and managers, higher-grade), II (other professionals, administrators and managers, and technicians), III (self-employed, services sector and supervisors workers), IV (semiskilled and skilled manual workers) and V (unskilled manual workers)

Table 2 Baseline characteristics of the 23,994 women participants according to childhood paternal occupation and own adult education. The EPIC-Spain Cohort, 1992–1996 to 2004

	Childhood paternal occupation[a]							Own adult education					
	All (n = 23,994)	I (n = 594)	II (n = 2,693)	III (n = 7,840)	IV (n = 3,510)	V (n = 9,307)	p value for gradient	University (n = 2,415)	Secondary (n = 1,409)	Technical (n = 1,386)	Primary (n = 9,993)	Non-primary (n = 8,741)	p value for gradient
Mean (SD)													
Age at enrolment (years)	47 (8)	46 (8)	48 (8)	49 (8)	46 (8)	47 (8)	NS	43 (7)	43 (7)	43 (6)	46 (7)	51 (7)	NS
BMI (kg/m^2)	28 (5)	26 (4)	27 (5)	28 (5)	28 (5)	29 (5)	**	25 (4)	26 (4)	26 (4)	28 (4)	30 (5)	*
Height (cm)	157 (6)	159 (6)	158 (6)	157 (6)	157 (6)	156 (6)	*	159 (6)	159 (6)	159 (5)	157 (6)	155 (6)	*
Weight (kg)	69 (11)	66 (11)	67 (11)	69 (11)	68 (11)	70 (12)	**	63 (10)	65 (10)	65 (10)	69 (11)	72 (11)	*
Waist circumference (cm)	87 (11)	83 (11)	85 (11)	87 (11)	86 (11)	88 (11)	*	80 (9)	81 (10)	82 (10)	86 (11)	91 (11)	*
Hip circumference (cm)	106 (9)	103 (9)	104 (9)	105 (9)	105 (9)	106 (10)	*	101 (8)	102 (9)	102 (9)	105 (9)	108 (10)	*
Energy intake (kcal/day)	1,958 (575)	1,989 (587)	1,975 (593)	1,970 (569)	1,917 (565)	1,958 (578)	**	1,992 (571)	1,956 (571)	1,997 (565)	1,987 (583)	1,910 (567)	NS
Mediterranean diet score	8 (3)	8 (3)	8 (3)	8 (3)	8 (3)	8 (3)	NS	8 (3)	8 (3)	8 (3)	8 (3)	9 (3)	NS
Alcohol consumption (g/day)	5 (10)	7 (12)	6 (10)	5 (10)	5 (11)	4 (9)	NS	6 (10)	6 (11)	7 (12)	5 (10)	4 (8)	NS
Percentage													
Cambridge physical activity index													
Inactive	48	37	42	46	47	52	***	32	42	37	47	56	*
Moderately inactive	35	36	37	37	35	34	NS	41	36	39	36	33	NS
Moderately active	12	18	15	13	13	11	**	19	16	17	13	9	*
Active	4	9	6	4	4	4	NS	8	6	7	5	3	*
Smoking status													
Non-smoker	70	45	62	71	66	75	NS	42	41	50	70	86	*
Former smoker ≥10 years	7	12	11	8	8	6	**	17	15	13	7	3	**
Former smoker <10 years	3	6	4	3	3	2	*	7	7	5	3	1	***
Current smoker (1–10 cig/day)	9	17	10	9	10	9	NS	15	16	14	10	6	*
Current smoker (11–20 cig/day)	8	16	10	7	10	7	NS	14	16	14	9	4	*
Current smoker >20 cig/day	2	5	2	2	3	1	MS	4	5	3	2	1	*
Started cigarette smoking before age 20 years[b]	58	62	62	55	60	56	NS	65	70	67	56	40	NS
Diabetic	4	2	3	4	3	5	*	2	1	2	3	7	NS
Hypertensive	18	11	15	18	18	20	*	8	9	9	16	27	*
Hyperlipidaemic	16	17	16	16	15	16	NS	13	11	12	14	20	NS
Use of oral contraceptives	43	54	48	41	48	42	NS	59	60	60	44	33	*
Use of hormonal replacement therapy	9	11	11	10	9	9	NS	8	6	7	9	11	NS
Postmenopausic	35	30	37	37	29	35	NS	19	18	16	29	52	NS
Use of cardiovascular drugs													
Antithrombotic/antihaemorrhagic	0	0	0	0	0	1	NS	0	0	0	0	1	NS

Table 2 continued

	Childhood paternal occupation[a]							Own adult education					
	All (n = 23,994)	I (n = 594)	II (n = 2,693)	III (n = 7,840)	IV (n = 3,510)	V (n = 9,307)	p value for gradient	University (n = 2,415)	Secondary (n = 1,409)	Technical (n = 1,386)	Primary (n = 9,993)	Non-primary (n = 8,741)	p value for gradient
Cardiovascular	11	10	10	11	9	12	NS	6	5	5	9	17	NS
Aspirin	4	5	4	4	4	4	NS	4	4	4	4	4	NS

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*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$ statistical significance for social gradient by beta coefficient of exposure variables

[a] Occupational class: I (professionals, administrators and managers, higher-grade), II (other professionals, administrators and managers, and technicians), III (self-employed, services sector and supervisors workers), IV (semiskilled and skilled manual workers) and V (unskilled manual workers)

[b] Only smokers

position was inversely associated with obesity, waist circumference, diabetes, and hypertension, in both sexes (Fig. 1). Furthermore, lower social position was associated with hyperlipidaemia in women and to lower Mediterranean diet score in men. Finally, current cigarette smoking was more frequent in men of low social position but, conversely, in women of high-social position. Furthermore, women and men showed an opposite and significant social gradient in current cigarette smoking and physical inactivity, revealing more unhealthy habits in upper class women.

Table 4 presents the hazard ratios (HR) of CHD by categories of social position. Results showed that paternal occupation during childhood and own educational level in men were individually associated with CHD in centre- and age-adjusted models (p for gradient for own education = 0.01 and p for gradient for occupation = 0.02). However, only the effect of education was independently associated with CHD (p for gradient = 0.03) after mutually adjusting for paternal occupation and own education. The educational gradient in CHD incidence in men remained significant after controlling for dietary and physical activity habits (p for gradient = 0.01), but not when cardiovascular risk factors or anthropometric variables were taken into account. No overall social position gradient was found with regard to the occupational class of the father in any model. However, the possibility of childhood effects should not be disregarded, given the higher CHD risk in group IV of paternal occupation across all models (HR = 2.31, 95 % CI 1.06–5.02, in the final model). Models showed no significant associations for women.

The life-course social position score was highly correlated with own adult education and the father's occupation, across age and sex groups (average Spearman's correlation coefficient (ρ) was 0.80 and 0.76, respectively), but not in-between components ($\rho = 0.26$).

Table 5 analyses the influence of life-course social position and risk of coronary events. Results are supportive of the existence of a social gradient in CHD occurrence in men. Risk estimates of CHD rose by up to 23 % (95 % CI 6–42 %) per category increase (i.e., with decreasing social position), after controlling for potential confounders. On the contrary, the social indicators studied were not predictive of coronary risk in women.

Discussion

A life-course individual social position gradient was inversely related to incident CHD in Spanish men; however, no such association was found in women. Although literature on life-course social position and CHD is very scarce in low-incidence countries, our results are in

Table 3 Baseline characteristics of the 14,801 men participants according to childhood paternal occupation and own adult education. The EPIC-Spain Cohort, 1992–1996 to 2004

	Childhood paternal occupation[a]							Own adult education					
	All ($n = 14,801$)	I ($n = 412$)	II ($n = 1,589$)	III ($n = 5,073$)	IV ($n = 2,372$)	V ($n = 5,306$)	p value for gradient	University ($n = 2,264$)	Secondary ($n = 1,220$)	Technical ($n = 1,951$)	Primary ($n = 5,695$)	Non-primary ($n = 3,631$)	p value for gradient
Mean (SD)													
Age at enrolment (years)	50 (7)	50 (7)	50 (7)	50 (7)	49 (7)	50 (7)	NS	48 (6)	48 (7)	48 (6)	50 (6)	54 (6)	NS
BMI (kg/m^2)	28 (3)	28 (4)	28 (4)	28 (3)	28 (3)	29 (4)	NS	27 (3)	28 (3)	28 (3)	29 (3)	29 (4)	**
Height (cm)	169 (6)	171 (6)	170 (6)	169 (6)	170 (6)	168 (6)	**	171 (6)	171 (6)	170 (6)	169 (6)	167 (6)	**
Weight (kg)	81 (11)	83 (11)	82 (11)	81 (10)	81 (11)	81 (11)	*	80 (11)	82 (11)	81 (10)	82 (11)	82 (11)	NS
Waist circumference (cm)	99 (9)	99 (9)	100 (9)	99 (9)	99 (9)	100 (9)	*	97 (9)	98 (9)	98 (8)	100 (9)	102 (9)	*
Hip circumference (cm)	105 (7)	106 (7)	105 (7)	105 (6)	105 (7)	105 (7)	***	104 (6)	105 (7)	104 (6)	105 (7)	106 (7)	NS
Energy intake (kcal/day)	2,696 (707)	2,586 (637)	2,652 (705)	2,727 (719)	2,633 (699)	2,720 (702)	*	2,507 (625)	2,624 (692)	2,719 (675)	2,769 (717)	2,712 (736)	NS
Mediterranean diet score	9 (3)	9 (3)	9 (3)	9 (3)	9 (3)	9 (3)	NS	9 (3)	9 (3)	9 (3)	9 (3)	9 (3)	***
Alcohol consumption (g/day)	33 (34)	32 (34)	30 (31)	32 (33)	33 (35)	34 (34)	NS	24 (26)	30 (31)	34 (33)	35 (35)	35 (35)	*
Percentage													
Cambridge physical activity index													
Inactive	21	26	25	21	22	20	*	30	28	17	18	22	NS
Moderately inactive	30	33	34	31	29	28	*	34	35	27	30	28	NS
Moderately active	27	24	24	29	26	27	NS	20	20	29	29	29	NS
Active	22	16	17	19	24	25	**	15	16	27	24	21	NS
Cigarette smoking status													
Non-smoker	29	22	27	32	27	29	NS	30	23	28	30	31	NS
Former smoker ≥10 years	27	31	29	27	27	26	*	30	28	28	25	26	*
Former smoker <10 years	7	8	8	7	7	7	NS	8	9	8	7	7	NS
Current smoker (1–10 cig/day)	11	14	12	11	11	11	NS	11	12	12	12	10	NS
Current smoker (11–20 cig/day)	13	15	12	11	15	13	NS	11	15	12	14	12	NS
Current smoker >20 cig/day	7	6	8	7	7	6	NS	8	10	7	6	6	NS
Started cigarette smoking before age 20 years[b]	70	71	71	69	71	71	NS	69	72	70	70	71	NS
Diabetic	5	5	6	5	5	6	NS	4	3	4	6	8	*
Hypertensive	21	17	21	20	20	22	NS	16	19	17	21	27	NS
Hyperlipidaemic	26	26	24	26	28	25	NS	24	27	26	27	26	NS
Use of cardiovascular drugs													
Antithrombotic/antihaemorrhagic	1	0	1	1	1	1	NS	0	1	0	0	1	NS

Table 3 continued

	Childhood paternal occupation[a]							Own adult education					
	All ($n = 14{,}801$)	I ($n = 412$)	II ($n = 1{,}589$)	III ($n = 5{,}073$)	IV ($n = 2{,}372$)	V ($n = 5{,}306$)	p value for gradient	University ($n = 2{,}264$)	Secondary ($n = 1{,}220$)	Technical ($n = 1{,}951$)	Primary ($n = 5{,}695$)	Non-primary ($n = 3{,}631$)	p value for gradient
Cardiovascular	10	10	11	10	9	10	NS	9	9	5	9	13	NS
Aspirin	4	7	3	4	3	3	NS	4	4	4	3	3	NS

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*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$ statistical significance for social gradient by beta coefficient of exposure variables

[a] Occupational class: I (professionals, administrators and managers, higher-grade), II (other professionals, administrators and managers, and technicians), III (self-employed, services sector and supervisors workers), IV (semiskilled and skilled manual workers) and V (unskilled manual workers)

[b] Only smokers

agreement with prospective evidence from other cohort studies in diverse international settings (Galobardes et al. 2006; Loucks et al. 2009; Pollitt et al. 2005; Singh-Manoux et al. 2004). Results from the French GAZEL cohort showed an increased risk of premature cardiovascular death in adult men associated with lower parent and own occupational trajectory, while accounting for tobacco smoking, alcohol consumption, BMI, and intake of fruits and vegetables in adjusted models (Melchior et al. 2006). Singh-Manoux et al. (2004) found that socio-economic circumstances prospectively predicted CHD risk in men and women from the Whitehall II study, using a trichotomous categorisation of socio-economic trajectories: childhood socio-economic status during childhood, education and employment grade (Singh-Manoux et al. 2004). In the US, Loucks et al. (2009) also reported a significant association for cumulative life-course socio-economic position (father's education, and own education and occupation), combining men and women and adjusting for BMI, systolic blood pressure, total-HDL cholesterol ratio, fasting glucose, and hypertensive medication use.

Strengths of the present study include the large sample size, the prospective design, and the validation of all CHD cases, thus reducing the potential of misclassification bias. Besides, a wide set of variables of the behavioural pathway for cardiovascular outcomes were available for analysis, such as the Mediterranean diet score—shown to be predictive of CHD incidence (Buckland et al. 2009)—a validated physical activity index (Wareham et al. 2003), anthropometric data and information on alcohol intake, in addition to classical cardiovascular risk factors (smoking, hypertension, hyperlipidaemia, diabetes), and, in women, reproductive status and hormonal drug therapy. Thus, several models of relationship between social indicators and CHD could be evaluated and which accounted for different types of confounders, giving insight into the social underlying pathways of CHD.

On the other hand, the study also has some limitations, among which the use of national educational and occupational classifications (instead of international standards) should be considered. Nevertheless, most international classifications of education in Western countries rely on the ISCO (Harrison and Rose 2010) and are, therefore, closely related. Furthermore, the Spanish National Classification of Occupations (CNO-94) is a hierarchical classification with high correspondence to the ISCO-88 (COM), the European Union variant of the International Standard Classification of Occupations, which enhances the comparability of our results. Additionally, the occupational grouping of the Spanish epidemiological association, derived from the British Registrar General's Social Class Classification (Álvarez-Dardet et al. 1995; Harrison and Rose 2010), is similar to most Western

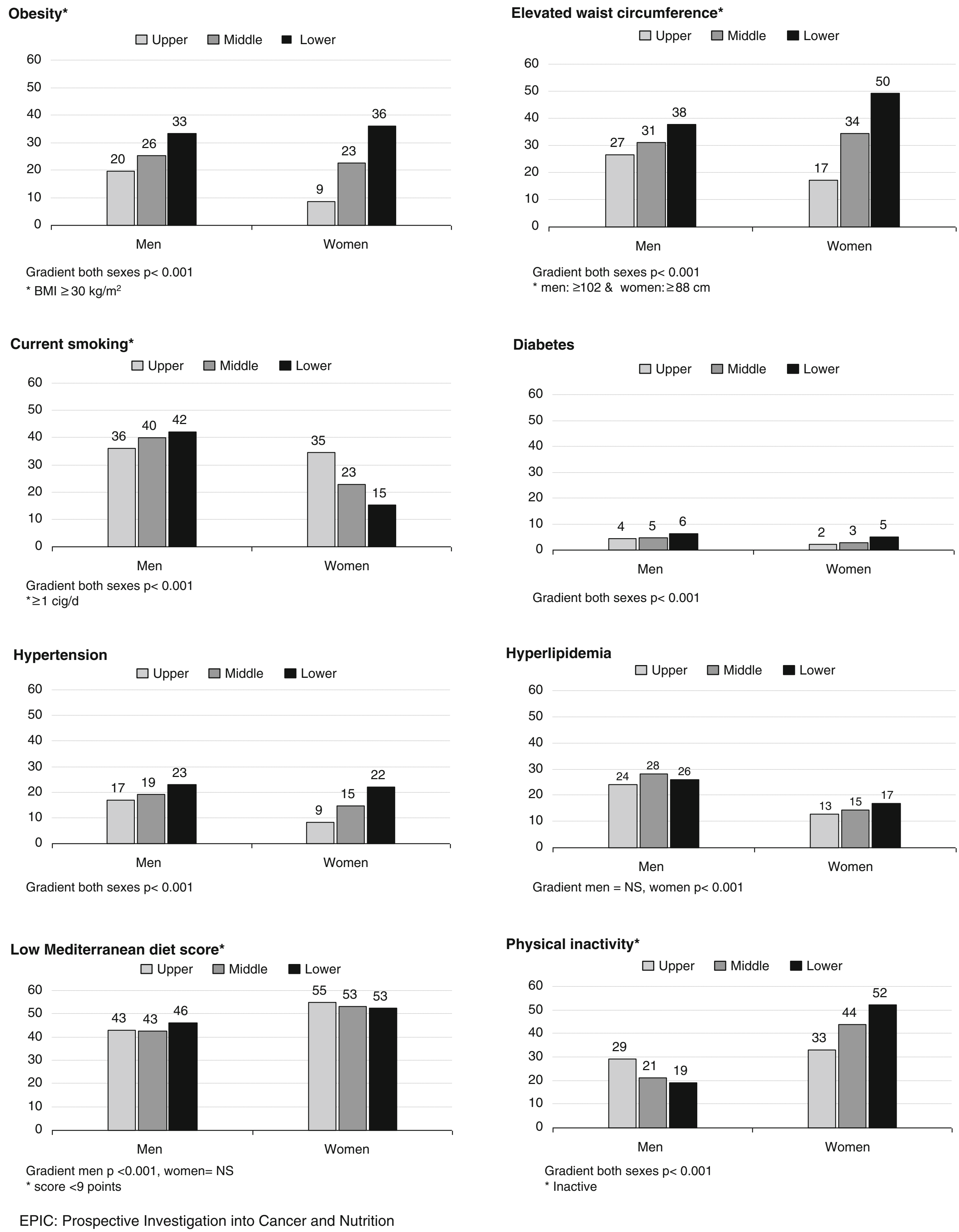

Fig. 1 Percentage of participants with selected coronary heart disease risk factors by life-course social position and sex. The EPIC-Spain cohort, 1992–1996 to 2004

Table 4 Hazard ratios (HR) and 95 % confidence intervals (CI) of coronary heart disease (CHD) in men and women by childhood paternal occupation and own adult education. The EPIC-Spain Cohort, 1992–1996 to 2004

	N	Person-years	CHD	Simple[b]		Education and paternal occupation[c]		Anthropometry[d]		Diet and physical activity[e]		Classical risk factors, drugs (and hormonal status in women)[f]		Final[g]	
				HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI
Men															
Childhood paternal occupation[a]															
I	421	4,438	7	1		1		1		1		1		1	
II	1,589	16,638	35	1.30	(0.58 2.94)	1.26	(0.56 2.83)	1.23	(0.54 2.77)	1.26	(0.56 2.85)	1.30	(0.57 2.94)	1.28	(0.56 2.89)
III	5,073	52,588	153	1.74	(0.82 3.72)	1.58	(0.73 3.39)	1.52	(0.71 3.27)	1.60	(0.74 3.44)	1.67	(0.78 3.60)	1.63	(0.76 3.52)
IV	2,372	24,634	103	2.62	(1.22 5.65)	2.39	(1.10 5.18)	2.30	(1.06 4.99)	2.38	(1.10 5.16)	2.40	(1.11 5.22)	2.31	(1.06 5.02)
V	5,306	54,425	169	1.87	(0.88 4.00)	1.65	(0.77 3.56)	1.54	(0.72 3.33)	1.69	(0.78 3.64)	1.71	(0.79 3.70)	1.64	(0.76 3.53)
p value for gradient					0.02		NS		NS		NS		NS		NS
Own adult education															
University	2,267	23,943	44	1		1		1		1		1		1	
Secondary	1,226	12,737	30	1.20	(0.75 1.91)	1.16	(0.73 1.85)	1.12	(0.70 1.79)	1.20	(0.75 1.91)	1.02	(0.64 1.64)	1.03	(0.64 1.64)
Technical	1,955	20,447	50	1.16	(0.77 1.75)	1.05	(0.69 1.59)	0.98	(0.64 1.48)	1.17	(0.77 1.77)	1.00	(0.66 1.53)	1.01	(0.66 1.55)
Primary	5,710	59,332	205	1.54	(1.11 2.15)	1.42	(1.01 1.98)	1.24	(0.88 1.75)	1.54	(1.10 2.17)	1.35	(0.96 1.90)	1.31	(0.92 1.85)
Non-primary	3,643	36,687	138	1.46	(1.03 2.07)	1.36	(0.95 1.95)	1.15	(0.80 1.66)	1.48	(1.03 2.13)	1.32	(0.92 1.90)	1.25	(0.86 1.81)
p value for gradient					0.01		0.03		NS		0.01		NS		NS
Women															
Childhood paternal occupation[a]															
I + II	3,287	34,315	18	1		1		1		1		1		1	
III	7,840	81,471	32	0.78	(0.43 1.39)	0.81	(0.45 1.48)	0.79	(0.44 1.44)	0.79	(0.44 1.44)	0.77	(0.43 1.40)	0.75	(0.41 1.37)
IV	3,510	36,735	19	1.15	(0.60 2.22)	1.27	(0.65 2.47)	1.20	(0.61 2.34)	1.22	(0.62 2.38)	1.21	(0.62 2.38)	1.13	(0.57 2.24)
V	9,307	96,029	47	1.02	(0.59 1.76)	1.09	(0.61 1.96)	1.02	(0.57 1.84)	1.05	(0.59 1.90)	0.97	(0.54 1.76)	0.93	(0.51 1.68)
p value for gradient					NS		NS		NS		NS		NS		NS
Own adult education															
University	2,420	25,260	11	1		1		1		1		1		1	
Secondary	1,410	14,698	6	1.05	(0.38 2.85)	1.04	(0.38 2.84)	1.05	(0.38 2.86)	1.01	(0.37 2.76)	1.07	(0.39 2.94)	1.05	(0.38 2.89)
Technical	1,388	14,417	2	0.44	(0.10 1.98)	0.41	(0.09 1.87)	0.40	(0.09 1.83)	0.40	(0.09 1.83)	0.40	(0.09 1.85)	0.41	(0.09 1.87)
Primary	10,022	105,697	33	0.60	(0.30 1.20)	0.57	(0.28 1.16)	0.51	(0.25 1.05)	0.55	(0.27 1.13)	0.56	(0.27 1.17)	0.53	(0.25 1.10)
Non-primary	8,754	88,982	64	0.79	(0.41 1.53)	0.75	(0.38 1.50)	0.63	(0.31 1.28)	0.72	(0.36 1.45)	0.70	(0.34 1.42)	0.63	(0.30 1.31)
p value for gradient					NS		NS		NS		NS		NS		NS

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[a] Occupational class: I (professionals, administrators and managers, higher-grade), II (other professionals, administrators and managers, and technicians), III (self-employed, services sector and supervisors workers), IV (semiskilled and skilled manual workers) and V (unskilled manual workers)

[b] Univariate proportional hazards Cox model stratified by centre and age (in 5-year categories)

[c] Multivariate proportional hazards Cox model mutually adjusted by paternal occupation and own education levels, stratified on centre and age (in 5-year categories)

[d] Model 2 additionally adjusted by height (cm), weight (kg), and waist circumference (cm)

[e] Model 2 additionally adjusted by energy intake (kcal/day), alcohol consumption (g/day), Mediterranean diet score and Cambridge physical activity index

[f] Model 2 additionally adjusted by smoking status, age at starting smoking, diabetes, hypertension, hyperlipidemia, and cardiovascular drugs use, plus ever use of oral contraceptives, hormonal replacement therapy, and postmenopausal status in women

[g] Model including all above-mentioned variables

Table 5 Hazard ratios (HR) and 95 % confidence intervals (CI) of coronary heart disease (CHD) by life-course social position score in men and woman. The EPIC-Spain Cohort, 1992–1996 to 2004

Life-course social position	*n*	Person-years	CHD	HR_1	95 % CI	HR_2	95 % CI
Men							
Upper (0–2 points)	1,936	20,461	42	1		1	
Middle (3–5 points)	5,582	58,154	147	1.09	(0.77–1.54)	1.04	(0.73–1.49)
Lower (6–8 points)	7,243	74,108	278	1.47	(1.06–2.04)	1.37	(0.98–1.93)
p value for gradient					0.001		0.007
Continuous (per category increase)	14,761	152,724	467	1.27	(1.10–1.46)	1.23	(1.06–1.42)
Women							
Upper (0–2 points)	2,254	23,609	11	1			
Middle (3–5 points)	7,641	79,868	26	0.61	(0.30–1.23)	0.56	(0.27–1.17)
Lower (6–8 points)	14,049	145,073	79	0.77	(0.41–1.47)	0.62	(0.31–1.24)
p value for gradient					NS		NS
Continuous (per category increase)	23,944	248,550	116	1.01	(0.75–1.36)	0.90	(0.65–1.23)

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[a] Univariate proportional hazards Cox models stratified by centre and age (in 5-years categories)

[b] Multivariate proportional hazards Cox models stratified on centre and age (in 5-years categories), additionally adjusted by height (cm), weight (kg), waist circumference (cm), Mediterranean diet score, energy (kcal/day) and alcohol intake (g/day), Cambridge physical activity index, smoking status, age at starting smoking, diabetes, hypertension, hyperlipidaemia, and cardiovascular, oral contraceptives (women), hormonal replacement therapy (women) drugs use, and postmenopausal status (women)

countries official socio-economic classifications, thus further supporting the external validity of the reported associations. Another limitation concerns the self-reported nature of data on diabetes, hypertension and hyperlipidaemia (hypercholesterolaemia or elevated blood lipids). In previous studies on Spanish populations, self-reports showed good validity for diabetes and moderate validity for hypertension, but low validity for hyperlipidaemia (Huerta et al. 2009; Tormo et al. 2000). Nevertheless, there is evidence suggesting that validity of self-reported hyperlipidaemia could be higher if the question specifically refers to hypercholesterolaemia, as in the present study (Baena-Díez et al. 2009). Our results are also consistent with previous evidence showing an increased CHD risk in relation to smoking, hypertension and hyperlipidaemia in men, and to smoking and chronic disease in women. The lack of individual psychological self-perception of mental health might be regarded as a limitation, since poor self-perceived health, but not minor psychiatric disorders, has been associated with cumulative exposition to unfavourable socio-economic circumstances over the life-course (Singh-Manoux et al. 2004). However, symptoms of depression and anxiety did not appear to mediate the relationship between educational attainment and incident CHD in a general population representative of the US (Thurston et al. 2006). Finally, as in most longitudinal studies, data on potential confounders were only available at baseline, so it was therefore not possible to control for differential exposures to CHD-related factors at different times through life.

Our model is consistent with the hypothesis that social disadvantages accumulate over life-course to increase disease risk (Pollitt et al. 2005). The possibility of childhood effects should not be disregarded, since results show that there was an independent increased risk of CHD for group IV of paternal occupation, across all the blocks of variables considered [the education–occupation model, HR = 2.39 (95 % CI 1.10–5.18) and for the final model it was 2.31 (95 % CI 1.06–5.02)]. Furthermore, our results also suggest an inverse association in men between height (in cm) and CHD incidence risk (HR = 0.96, 95 % CI 0.95–0.98; data not shown). Unfortunately, further generational effects on the social trajectory of participants, beyond those related to the social position of the father could not be discarded due to the cohort design of the study.

The lack of association of social indicators with CHD risk in women could be attributed to the limited number of coronary cases. However, null results were consistent in all models regardless of the level of adjustment, in contrast to the effects described for men. The lack of social gradient for these indicators may also suggest a better social characterisation of women on the basis of own or partner occupation (Arber and Lahelma 1993; Krieger et al. 2001). Furthermore, there is no evidence for a differential recall bias by sex, and the indicators used proved valid for assessing the social gradient of CHD in men. More likely, the larger proportion of smokers (and inactive physical activity) among socially advantaged women contributed to counterbalance the lower CHD risk expected according to their social position, thus resulting in a null net social gradient of CHD in women.

Summing up, in a developed country with low incidence of CHD such as Spain, adverse life-course cumulative social gradient was associated with the risk of suffering a first coronary event in men. This association was not accounted for by the major known factors of CHD. Results support that graded social position should be taken into consideration as a target CHD risk factor by worldwide health heart associations (Arber and Lahelma 1993; Lloyd-Jones et al. 2010; Manderbacka and Elovainio 2010). Further investigation is warranted to assess the consistency of these social gradient life-course results in other settings and to gain a deeper understanding of the pathways underlying the social effects on CHD. It should be recalled that reducing the gap in health inequalities in the near future by means of public political action is a public health goal of the WHO (2010c).

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